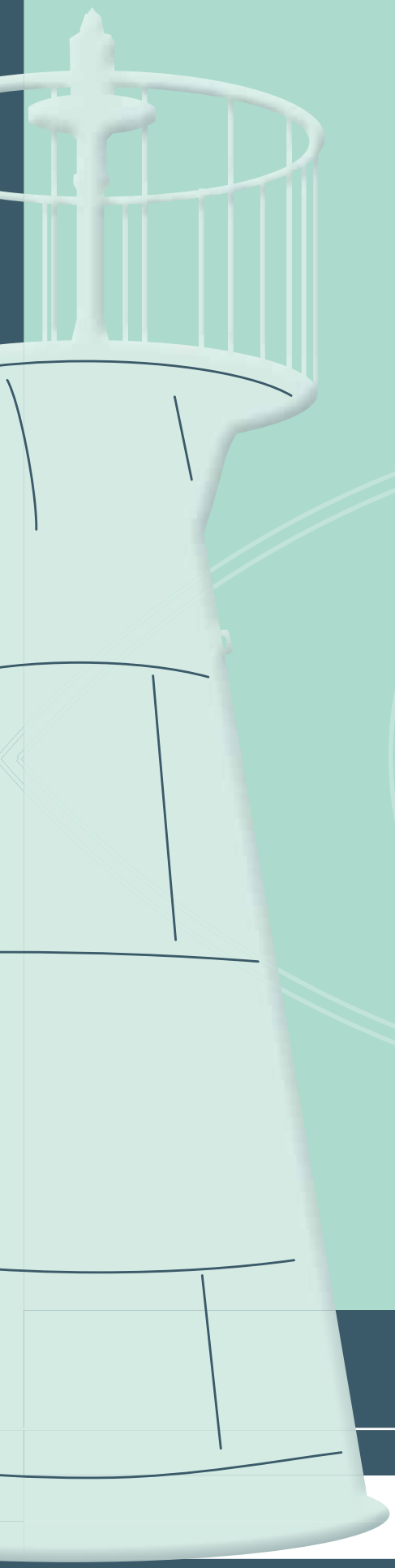
European Association for Vision and Eye Research

EVER 2008

ABSTRACTS



October 1-4, 2008
Portoroz, Slovenia

www.ever.be

EVER travel grants

The following 11 members have received a travel grant from the EVER Sections:

- Anatomy/Cell Biology: **Pavlina TSOKA, Heraklion, Crete, Greece**
  Quantification of the photoreceptors of healthy retinas in rat by flow cytometry (405)
- Cornea / Ocular Surface: **Manuela LANZINI, Chieti, Italy**
  In vivo confocal microscopy in the diagnosis of corneal conjunctivalization (6232)
- Glaucoma: **Michael INBAL, Haifa, Israel**
  Interactions between trabecular meshwork cells and lens epithelial cells – a possible mechanism in infantile aphakic glaucoma (4455)
- Immunology/Microbiology: **Raquel GINEYS, Paris, France**
  Interest of an interferon-gamma release assay for diagnosing tuberulosis-related ocular inflammation (6423)
- Lens and Cataract: **Carla MARQUES, Coimbra, Portugal**
  Protein quality control and ubiquitin proteasome system: implications on cataract (464)
- Molecular Biology/Genetics/Epidemiology: **Marzena GAJECKA, Poznan, Poland**
  Genetics of high myopia in Polish families (6353)
- Neuro-ophthalmology/Strabismology/Paediatric/History: **Eleni PAPAGEORGIOU, Larissa, Greece**
  Driving performance in patients with homonymous visual field defects and healthy subjects in a standardized virtual reality environment (4421)
- Pathology/Oncology: **Francesca URBAN, Padova, Italy**
  Photodynamic therapy of circumscribed choroidal hemangioma: comparison of dosage and timing (6263)
- Physiology/Biochemistry/Pharmacology: **Alexandre FERNANDES, Coimbra, Portugal**
  25-Hydroxycholesterol increases IL-8 production in the RPE by activation of PI3K and p38 MAPK pathways (584)
- Retina/Vitreous: **Christoph EHLKEN, Freiburg, Germany**
  EphB4 is expressed in preretinal neovascularization in a mouse model of oxygen-induced retinopathy (652)
- Vision Sciences/Electrophysiol./Physiological Optics: **Archana PRADEEP, Leicester, UK**
  Can amblyopia treatment be optimised? (5224)

TFOS awards 2008

The following three researchers have received a travel award from the Tear Film and Ocular Surface Society for the three best abstracts submitted to EVER 2008 by young researchers in the cornea section:

- **Ammar MIRI, Nottingham, UK**
  Long term results of Limbal stem cell transplantation in ocular surface disease (5333)
- **Waldir NEIRA, Helsinki, Finland**
  Corneal morphology, topography and sensitivity in a family with inherited recurrent corneal erosions (556)
- **Liza VERA, Rouen, France**
  Outcome of transplanted mesenchymal stem cells in the alkali burned cornea (542)

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October 1-4, 2008
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Keynote Lectures

EVER 2008

ABSTRACTS

October 1-4, 2008
Portoroz, Slovenia

A.E.R.

3001

Much ado about nothing

Gijs VRENSEN
Zeist

May I introduce myself? I am a lens, one of the two you have. I look like a discus with my front less curved than my back. In good condition I am crystal clear and nearly colourless. When adult my diameter is 10mm, in the center I am 4mm thick and my weight is 250mg. I have a protected life, swimming in a small nicely warm pool, with water containing everything I need for living. I am hanging on thin strings in a trampoline. My back is supported by a huge soft waterbed. In front a round coloured iris is protecting me from too much sunlight. My only activity is regularly changing, in harmony with my fellow lens, my front and back curvature. As you see I am not very fascinating and I am surprised that my master and so many of his colleagues are spending so much time to me. Much ado about nothing!!!

However, when looking around I see many young and old people wearing glasses, for reading and far vision. Big business; so many shops selling these glasses in expensive mounts. Moreover, when my master is consulting the homepages of the WHO it comes out that I am still the main cause of blindness world wide. In my master's country lens blindness, also called cataract, is rare due to the fact that 130,000 of my fellow lenses are taken out per year and replaced by plastic lenses put in the thin bags surrounding us. Some 13,000-26,000 of them are frustrating this surgery and their renewed cloudy backs are eliminated by laser bombardment. Imagine the enormous financial burden for this simple but very common treatment of cataract and after-cataract. Much ado about nothing???

I am not as dull as I look at first glance. I am the only organ with no blood supply and no innervation. Food is coming in from the pool along small spaces between my fibers and my waste products are leaving through the fibers back to the pool. My center does not receive food at all. My most common cells: the fibres, are not shedded and I still contain all the fibers formed during my life span. For transparency my fibers have to loose their nuclei without dying; an unprecedented process. I am changing my curvatures without disturbing my internal structure. It is not surprising, however, that with all my metabolic and physiological handicaps, I become brown and opalescent in the end and am no longer able to help my 'old' master with reading. I am unique in many other aspects. So it is not surprising that many scientists got intrigued by my ingenuity to remain clear and active for nearly my whole life span. Much ado about nothing. No!!!

3002

Anton Banko, the Slovenian inventor behind the success of Charles Kelman

Marko HAWLINA
University Medical Centre, Eye Clinic, Ljubliana, Slovenia

Behind the success story of phacoemulsification that started with Charles Kelman, there was an ingenious engineer that helped him to create the first clinically useful apparatus. Anton Banko was born in a Slovenian family in Istria, very close to actual venue of EVER meeting. He studied engineering and electrics in Ljubljana and later moved to United Sates where he worked in the field of ultrasound instruments for dental use Cavitron company as the director of research and development. Charles Kelman turned to him with a request to construct an ultrasound device for cataract removal and their first joint US patent No. 3589363 was filed on 25th July 1967. A year later, Anton Banko established his own company in New York, named Surgical Design, and the company produced a series of very reliable and successful phaco machines that are still used worldwide. Anton Banko continued to develop many other patents used in ocular surgery including instrument for vitrectomy that he patented in 1969 after which a combined Mackool/Heslin Ocusystem machine was designed. Sadly , he died of incurable disease soon after the success of his company which since then is led by his son William. Anton Banko's wish to donate one of the machines to the University Eye Hospital in Ljubljana was conweyed by his family. Due to his legacy, surgeons from Slovenia started to use phacoemulsification as early as in 1989 after training in the wetlab of Surgical Design company. Anton Banko remains one of the giants of instrumentation in ocular surgery with Slovenian origins.

▪ 3003

The taming of the shrew or corneal transplantation: past, present and future

Uwe PLEYER
Department of Ophthalmology, Charité, Humboldt University, Berlin

Keratoplasty has definitely its paradoxes. It has been the first successful transplantation in man and is with approx. 100. 000 grafts/year easily the most frequent allograft in human medicine. At the same time it is still the least understood form of transplantation in respect to its biology. It is both, the most successfull as well as probably the most underestimated procedure regarding its risks in clinical transplantation. Indeed, the common assumtion, that corneal transplantation is a safe procedure with good prognosis may have hindered more intensive effort of research in this field.

This lecture aims to highlight significant milestones in the rich history of corneal transplantation, and to pay tribute to the many inspired and dedicated individuals involved in the development of keratoplasty. There are still limitations to corneal transplantation, and corneal allograft rejection still poses the greatest challenge to the modern corneal surgeon. Therefore, particular emphasis will be paid to recent efforts and developments to overcome this challenge.

4001

A new era for age-related macular degeneration: insights pertaining to a key role for the complement system

Gregory HAGEMAN
Department of Ophthalmology and Visual Sciences at the University of Iowa, Iowa City, Iowa

Age-related macular degeneration (AMD) is characterized by a progressive loss of central vision attributable to degenerative and, in advanced cases, neovascular lesions in the macula. As the leading cause of irreversible vision loss in the developed world, AMD affects an estimated 25% of individuals over the age of 75.

A host of new discoveries has begun to provide a much clearer picture of the relevant cellular events, genetic factors, and biochemical processes associated with early AMD. Among the first was the discovery that a variety of complement components, complement activators, and complement regulatory proteins are molecular constituents of drusen, a hallmark risk factor for AMD. These observations formed the basis for the concept that drusen are a byproduct of chronic, local inflammatory processes characterized, in part, by robust activation of the complement cascade along the RPE-choroid interface. Strong support for this new paradigm emerged from subsequent discoveries that revealed a highly significant association between AMD and variations in several complement-associated genes: Factor H (CFH), Component 3 (C3), and Factor B (CFB). Haplotypes defined by polymorphisms in these genes confer an increased risk for, or protection from, developing AMD. Moreover, a large deletion encompassing two CFH-related genes -- CFHR1 and CFHR3 -- defines one of the CFH protective haplotypes. Similar variations in CFH and CFH-related genes are also associated with seemingly unrelated systemic diseases, perhaps offering an explanation for some or the previously established risk factors for AMD.

Acta Ophthalmologica

■ 4002

Unraveling the genetics of exfoliation glaucoma

Fridbert JONASSON
Department of Ophthalmology, Reykjavik

Purpose To give an account of our recent discovery (2007) of the association of lysyl oxidase like 1 (LOXL1) sequence variants and exfoliation glaucoma (XFG) as well as later replications in other populations.

Methods We did a genome-wide association study on open angle glaucoma cases and controls using the Illumina 300 chip. This chip includes probes for 317.000 single – nucleotide polymorphisms (SNPs), that tag, as highly correlated surrogates about 80% of the 2.1 million known common SNPs in the Caucasian genome. For diagnosis of exfoliation syndrome a peripheral band or central shield of exfoliative material on the anterior lens capsule was required.

Results When we had done 195 open angle glaucoma cases high genome wide significance was achieved on chromosome 15q24.1 an association later found to be confined to XFG only. This SNP (rs2165241T) was located in the first intron of the LOXL1 gene. We then added 11 correlated SNPs that are not on the Illumina chip and found that two non-synonymous variants in the first exon of LOXL1 can jointly account for all the observed association (R141L, OR 2.5; G153D, OR 20.1). Combined the variants explained 99% of the population attributable risk for exfoliation glaucoma.

Conclusions These findings have now largely been confirmed in numerous American, Asian, Australian and European studies, and in all instances do these polymorphisms in the LOXL1 gene confer risk to XFG. LOXL1 is cross linking enzyme responsible for elastin polymer deposition in ocular tissue. The LOXL1 discovery is the first big hit in the search for genetic background for exfoliation glaucoma. These findings may soon influence monitoring of glaucoma suspects in the clinic targeting persons with the high risk haplotypes.

5001

Regional immunity of the eye: T lymphocytes and ocular pigment epitherial cells

Manabu MOCHIZUKI
Dept of Ophthalmology & Visual Science, Tokyo Medical and Dental University, Tokyo

Intraocular inflammation is mediated by activated CD4+ T lymphocytes. This notion was classically demonstrated by experimental autoimmune uveoretinitis induced by retinal antigens. In human, activated CD4+ T lymphocytes also play the essential role in the pathogenesis of uveitis. Such examples are Vogt-Koyanagi-Harada (VKH) disease and human T-cell leukemia virus type 1 (HTLV-1) uveitis. VKH disease is a classical autoimmune disease specific to melanocytes and activated CD4+ T lymphocytes sensitized to melanocyte-associated antigen, tyrosinase, are infiltrated in the eye, resulting in ocular inflammation. HTLV-1 uveitis is an intraocular inflammation caused by inflammatory cytokines produced by HTLV-1-infected CD4+ T lymphocytes infiltrating in the eye. Not only these diseases but also many other inflammatory disorders in the eye are mediated by activated CD4+ T lymphocytes. However, the eye has a unique regional immune defense system that protects the eye from sight-threatening inflammation mediated by activated CD4+ T lymphocytes. Recent studies of our group together with many others indicate that the aqueous humor, the corneal endotherial cells, the ocular pigment epitherial cells of the iris, ciliary body and retina, the vitreous have unique capacity to suppress activated CD4+ T lymphocytes infiltrating in the eye and down-regulate intraocular inflammation. The immune suppression against infiltrating CD4+ T lymphocytes is caused by both these ocular resident cells and regulatory T cells induced by ocular resident cells through various unique molecules, such as B7-2, CTLA4, TBF-β, thrombospondin 1, or CTLA-2α. One of the most amazing features of this regional defense system in the eye is that molecular mechanisms of each cells and tissues are adapted to its anatomical characteristics and allowing the defense system to exhibit its capacity most efficiently at their site in the eye. For instance, the iris pigment epitherial cells surrounded by aqueous humor down-regulate activated T lymphocytes via cell-to-cell contact mechanisms, but not soluble factors. On the other hand, the retinal pigment epitherial cells surrounded by cells in the retina and choroid exhibit their immunoregulatory function by soluble factors. In this lecture, the molecular mechanisms of the local defense system in the eye, with particular attention to ocular pigment epitherial cells, will be discussed based on our recent studies.

Ophthalmic Research
Journal for Research in Experimental and Clinical Ophthalmology

5002

Functional analysis of mutants of the optineurin gene, associated with some forms of glaucoma

Dbala BALASUBRAMANIAN - L. V. Prasad Eye Institute, Hyderabad, India
M CHALASANI M - L. V. Prasad Eye Institute, Hyderabad, India
SWARUP G - Centre for Cellular & Molecular Biology, Hyderabad, India
AGARWAL N - National Eye Institute, Bethedsa, USA

Purpose Mutations in the gene OPTN are associated with normal tension and open angle glaucomas. We have studied the effects of some of these mutations on the cellular biology of retinal ganglion cells, and tried to infer the role of the protein optineurin.

Methods We transfected plasmids expressing normal or wild-type (WT) and E50K, R545Q, H26D, and H486R mutant optineurin into a variety of cells such as HeLa, COS-1, retinal pigment epithelial (RPE), and the rat retinal ganglion cell (RGC) line RGC-5, and followed their effects on cell survival by morphologic observation of cells. Expression of optineurin and its mutants was monitored by immunofluorescence staining of cells and by Western blotting.

Results The E50K mutant of optineurin, which is associated with the severest phenotype, was seen to selectively induce the death of retinal ganglion cells but not of the other cell lines tested. Neither the wild type cDNA nor the other mutants have any such effect. This cell death induced by E50K OPTN was inhibited by the antioxidants N-acetylcysteine and Trolox. E50K was seen to generate reactive oxygen species (ROS), which were reduced by antioxidants. Coexpression of manganese superoxide dismutase with the E50K mutant abolished ROS production and inhibited cell death.

Conclusions E50K optineurin is a gain of function mutant, which has acquired the ability to induce cell death selectively in retinal ganglion cells. This cell death was mediated by oxidative stress. The present findings suggest the possibility of antioxidant use for delaying or controlling some forms of glaucoma.

6001

Recognition and treatment of herpes dimplex keratitis

Peter LAIBSON - Wills Eye Institute, Philadelphia

Although the incidence of ocular herpes simplex virus infection has not diminished in recent years, we are encountering fewer severe problems such as necrotizing stromal keratitis and diffuse disciform keratitis which may necessitate penetrating keratoplasty. The earlier recognition of herpes simplex viral keratitis and the better management utilizing oral antivirals and topical corticosteroids is probably responsible for this improved outlook of herpes simplex keratitis. Early recognition and management of acute and chronic herpetic keratitis, as well as the management of keratoplasty for herpes will be reviewed.

Courses

EVER 2008

ABSTRACTS

October 1-4, 2008
Portoroz, Slovenia

▪ 3211
Introduction ; the principles of OCT

DE SMET MD
Antwerp

ABSTRACT NOT PROVIDED

▪ 3212
Contribution of OCT to evaluate macular disease in JIA associated uveitis

BODAGHI B (1), DUCOS G (1), KODJIKIAN L (2), TERRADA C (1), TRAN C (1), CASSOUX N (1), LEHOANG P (1)
(1) Ophthalmology, Paris
(2) Ophthalmology, Lyon

Purpose To examine the frequency and characteristics of macular lesions observed in Juvenile Idiopathic Arthritis (JIA) uveitis, using Optical Coherence Tomography (OCT).

Methods In this cross-sectional study, 38 consecutive patients were recruited from a tertiary referral center in uveitis. All eyes with JIA uveitis underwent complete ophthalmic examination including OCT 3. Exclusion criterion was the inability to obtain OCT scans. Flare and visual acuity were also analyzed by using linear regression.

Results We analyzed foveal thickness (FT) and central foveal thickness (CFT) using the software mapping, to describe macular lesions in 61 eyes. Maculopathy was observed in 51 eyes (84%), compared to 12% in the literature (P<0.0001) and comprised four types: perifoveolar thickening in 45 eyes (74%), macular edema in 29 eyes (48%), foveal detachment in 11 eyes (18%), and atrophic changes in 6 eyes (10%). Only 4 eyes did not demonstrate any lesion.

Conclusion Among children with JIA-uveitis, macular involvement is frequent, and characterized by perifoveolar thickening and serous retinal detachment. OCT is a non-invasive instrument. It may easily show this maculopathy, which could impair visual function, and conditioned a therapeutic intensification.

▪ 3213
OCT imaging in uveitis: advantages and limits

HERBORT CP (1, 2), DE SMET MD (3, 4)
(1) Centre for Ophthalmic Specialised Care, Lausanne
(2) University of Lausanne, Lausanne
(3) Dept of Ophthalmology, University of Amsterdam, Amsterdam
(4) ZNA, Middelheim, Antwerp

Optical Coherence Tomography (OCT) has gradually invited itself into everyday practice. The imaging quality is steadily improving with new generations of instruments giving fascinating insight into the retina.Although OCT investigation gives stunning pictures of the retina it is basically imaging those structures for which imaging access was already possible. The novelty is, with the new machines especially, the degree of precision of the information we can gather: A corollary to this first point, is the fact that we can get this information instantly without invasive procedures. For conditions such as choroidal neovessels, much closer follow-up has allowed, in parallel with the availability of potent intravitreal anti-VEGF therapy to improve drastically the management of AMD cases. In inflammatory diseases the availability has changed our attitude in the management of CME, increasingly based on OCT profile rather than strictly functional parameters. In diabetic maculopathy also OCT came along with the advent of new performing therapies the effect of which can so be optimally verified. One drawback of OCT is the fact that information is lost or OCT is impossible when turbid media are present. It has also to be acknowledged that information on the underlying choroid is limited. Many cases will be presented with discussion especially on inflammatory and AMD.

▪ 3214
Advantages and limits of OCT for inflammatory macular edema

BOUCHENAKI N (1, 2)
(1) Geneva
(2) Lausanne

ABSTRACT NOT PROVIDED

■ 3215
OCT in diabetic macular edema

ABU EL ASRAR AM
Ryadh

ABSTRACT NOT PROVIDED

■ 3216
Comparison of microperimetry and OCT retinal thickness in uveitis

TAKEUCHI M
Department of Ophthalmology, Tokyo Medical University, Tokyo

ABSTRACT NOT PROVIDED

■ 3217
Advances in optical coherence tomography for age-related macular degeneration

NERI P
Ancona

ABSTRACT NOT PROVIDED

■ 3218
Enhanced, OCT-assisted management of choroidal neovessels in AMD

HERBORT C
Lausanne

ABSTRACT NOT PROVIDED

▪ 3241
Kaplan-Meier analysis and Cox proportional hazards regression

KIVELÄ T
Department of Ophthalmology, Helsinki University Central Hospital, Helsinki

Purpose To highlight basic concepts related to time-to-event data.

Methods Non-mathematical description of the Kaplan-Meier product-limit method and Cox proportional hazards multiple regression with examples from recent literature.

Results Kaplan-Meier analysis and Cox regression are nonparametric techniques with wide applicability in ophthalmic research. They are appropriate when time-to-event data are analyzed (e.g. time to loss of vision, bleb failure, graft rejection) as outcome measure. They are especially efficient when follow-up times vary, which is common in clinical research. The data needed are time to event or last follow-up, last status (e.g. experienced the event, under follow-up, lost to follow-up, died) and explanatory or confounding variables (e.g. sex, age, type of glaucoma). Subjects who did not experience the event are "censored" at last follow-up. Censoring must be independent of the probability of experiencing the event, and the subject must remain at risk of the event after censoring. Cox regression additionally requires that the hazard be proportional (i.e. hazard ratio is constant over time). Kaplan-Meier analysis produces stepped curves which show the cumulative probability of experiencing the event as a function of time by study group; groups can be compared using the log-rank test or equivalent. Cox regression provides a numerical hazard ratio (e.g. increased or decreased risk of the study group to experience the event relative to the control group), which is adjusted for the effect of other variables included in the regression model.

Conclusion After this talk, participants should be able to recognize time-to-event data, interpret studies which use Kaplan-Meier and Cox regression analysis, and understand when they benefit from these methods in their research.

▪ 3242
Neural networks compared with Cox regression

DAMATO B (1), TAKTAK A (2), ELEUTERI A (2)
(1) Ocular Oncology Service, Royal Liverpool University Hospital, Liverpool
(2) Dept of Clinical Engineering, Royal Liverpool University Hosp

Purpose Survival prediction is useful in patient care and research. Most studies rely on Cox analysis and Kaplan-Meier curves whereas we have preferred neural networks. The aim of this presentation is to compare these methods and to discuss the advantages and limitations of each.

Methods This presentation will be based on our experience with uveal melanoma. A neural network was trained with data from 1780 patients and evaluated with data from another 874 patients. Clinical, histopathological and cytogenetic data were included in the model. All cause mortality was reported, both for patients and for the matched general population.

Results Cox analysis assumes linear correlations between variables and proportional hazards throughout the follow-up period. Kaplan-Meier analysis requires large patient categories, so that the precision of any prognostication is reduced. Neural networks overcome these limitations. Our model does censor non-metastatic deaths so that melanoma-related mortality is not exaggerated in groups of patients with significant competing risks.

Conclusion Neural networks allow large numbers of variables to be included in predictive models with relatively small numbers of patients, thereby improving prognostication. Nevertheless, care must be taken when interpreting survival results to avoid serious misconceptions about the natural history of a disease and the impact of treatment.

▪ 3243
Cumulative incidence analysis and relative survival

KIVELÄ T
Department of Ophthalmology, Helsinki University Central Hospital, Helsinki

Purpose To highlight concepts related to competing events in time-to-event data sets.

Methods Introduction to cumulative incidence and relative survival analyses and competing risks proportional hazards regression with examples from recent literature.

Results Kaplan-Meier and Cox regression analysis were designed to study mortality. They return biased estimates in the presence of competing events that render subjects immune to the event of interest (e.g. one is no longer at risk of vision loss, bleb failure or graft rejection after dying). Kaplan-Meier can then be supplemented with cumulative incidence analysis and Cox with competing risks regression. The data needed are time-to-event or last follow-up, last status (e.g. experienced an event, under follow-up, lost to follow-up) and explanatory or confounding variables. Subjects who experienced a competing event are treated as such and subjects who did not experience any event are "censored" at last follow-up. A set of stepped curves is produced which show the cumulative incidence of each event as a function of time by study group; groups can be compared using dedicated tests. Competing risks regression provides a hazard ratio, adjusted for the effect of other variables in the model. Relative survival is an alternative to cumulative incidence method when analyzing mortality. It does not require that the status at last follow-up be known. Survival of the study group is compared with that of the underlying population. The difference is equivalent to the cumulative incidence of disease-specific death, but cumulative incidences of competing events are not available.

Conclusion After this talk, participants should be able to recognize competing events, assess whether Kaplan-Meier and Cox regression were appropriate methods and know alternatives to them.

▪ 3261
History

GOLNIK K
Cincinnati Eye Institute, Cincinnati

The two most common causes of acute visual loss and unilateral optic disc swelling are acute optic neuritis (AON) and Nonarteritic anterior ischemic optic neuropathy (NAION). Important historical points include patient age, presence of pain, and predisposing medical conditions (diabetes, hypertension, hypercholesterolemia, sarcoidosis, recent viral infections/illnesses, other autoimmune conditions). In patients over 50 years of age, symptoms of giant cell arteritis (scalp tenderness, headache, jaw claudication, weight loss, fatigue, fever) must be discussed. Details of the onset of visual loss may be important because occasionally more chronic loss of vision is suddenly discovered when the good eye is occluded. Finally, one must be sure that this is a completely isolated, unilateral visual problem by ascertaining whether any other symptoms exist.

▪ 3262
Examination of the patient with visual loss and unilateral disc swelling

KAWASAKI A
Neuro-Ophthalmology, Lausanne

This presentation will show multiple examples of disc swelling and the clues one must use to decide its cause.Several congenital conditions (tilted disc, hypoplasia, disc hamartoma, drusen) have an elevated or even swollen-looking appearance which may, at first glance, be mistaken for acquired disc edema. Acquired swelling of the optic disc represents axoplasmic stasis due to obstruction of orthograde axoplasmic transport. A variety of insults (compression, ischemia, inflammation, metabolic derangement, toxicity and malignancy) to the proximal portion of the optic nerve can disrupt axoplasmic flow , so disc swelling (edema) is a rather non-specific finding. It is presence of other accompanying fundus abnormalities which is helpful for distinguishing the mechanism of disc swelling, and these can be divided into disc-related signs and retinal signs and will be discussed.It is also helpful to examine the contralateral disc. For example, a small or absent cup suggests a structural risk for ischemic injury. Of note, papilledema due to increased intracranial pressure is rarely a cause of unilateral disc edema (less than 5% of cases).

▪ 3263
Ancillary testing and differential diagnosis

BORRUAT FX
Hôpital Ophtalmique Jules Gonin, Lausanne

The most frequent mechanisms leading to acute visual loss in the setting of a unilateral swollen optic disc include : ischemia (anterior ischemic optic neuropathy, arteritic versus non-arteritic) inflammation (demyelinative disorder or other inflammatory diseases), and infection (Lyme, syphilis, Bartonellosis). Less frequent causes include: infiltration (lymphoma, leukaemia, metastasis), paraneoplastic mechanisms, unilateral papilledema, pseudopapilledema (drusen), hereditary (Leber's optic neuropathy). Ancillary testing will be directed according to the presumed mechanism. Apart from a complete visual function examination (visual acuity, color vision, visual field) and pupillary testing, various tests are available including : retinal angiography (fluorescein, indocyanine green), electrophysiology (VEP, mfERG), to name a few.

▪ 3264
History

BOSCHI A
Neuro-ophthalmology, Brussels

ABSTRACT NOT PROVIDED

■ 3265

Examination of the patient with visual loss and normal fundus

KAWASAKI A
Neuro-Ophthalmology, Lausanne

This presentation will discuss certain examination clues that help to distinguish visual loss from retinal disease from visual loss due to optic nerve disease when the fundus appears normal. Chief among these is the relative afferent pupillary defect. The standard clinical technique for detecting an RAPD is the alternating light test and neutral density filters can be used to quantify the amount of pupillomotor asymmetry. Another useful examination technique is measuring the time it takes to recover central visual function, e.g. acuity, following exposure to a bright light. This is the principle of the photostress test and it is very useful for distinguishing maculopathy. The recovery time is prolonged in a variety of macular disorders but are normal in optic neuropathies. Other specific findings such as a carotid bruit which hints to a specific etiology, e.g. retinal emboli from carotid artery plaque will be discussed.

■ 3266

Ancillary testing and differential diagnosis

LEE A
University of Iowa, Ophthalmology, Iowa

ABSTRACT NOT PROVIDED

3311
Corneal bacterial diseases

CREUZOT CP, BRON AM
Department of Ophthalmology, University Hospital, Dijon

Purpose To present the main causes of corneal bacterial diseases and suggest an appropriate management. Bacterial keratitis is the most common cause of infected corneal ulceration.

Methods The epidemiology of corneal bacterial diseases and their link with different risk factors will be studied. The initial presentation is important to determine the potential stain responsible for the infection and to assess the overall severity of the disease. Local and general criteria evaluations lead to a proper management. Bacterial identification plays a key-role in the etiological diagnosis.

Results Contact lens wear, trauma, preexisting ocular disease and corneal surgery are the main risk factors for corneal bacterial disease. Specific signs to identify bacteria remain rare but the circumstances (contact lens wear, aspect of the infiltrate) can help to determine the first line treatment. However laboratory methods remain the only way to diagnose a corneal bacterial disease with certainty. The aspect of the infiltrate, the intraocular involvement and an immunosuppressed patient may influence the outcome. The treatment is based on an initial broad-spectrum antibacterial therapy with secondary adaptation to the identified bacteria.

Conclusion Multiple microorganisms are involved in corneal diseases. The local and systemic risk factors have to be identified to treat these diseases in emergency still considered as a leading cause of visual loss.

3312
Epidemiology of corneal viral infections

LABETOULLE M
Ophthalmology, Bicêtre Hospital, South Paris University, Kremlin-Bicêtre

The three main causes of viral keratitis are Herpes simplex virus (HSV), varicella-zoster virus (VZV) and adenovirus (ADV). Corneal HSV infection is a frequent cause of severely impaired visual acuity. Despite the effectiveness of currently available antiviral drugs, the incidence of herpetic corneal events does not tend to decrease in the general population, as recently showed in a nationwide epidemiological study performed in France. On the other hand, corneal transplantations relative to herpes keratitis tend to become rarer thanks to the effectiveness of preventive oral treatment. Management of herpes keratitis could thus be improved by a better knowledge of epidemiological data. For example, children and atopic patients are now identified as groups of patients with increased risk of severe herpetic disease. The epidemiology of VZV-related keratitis may drastically vary in the future, due to the generalization of the vaccination against chickenpox/herpes zoster, with a probable increase in the next decades, followed by a progressive and durable decrease. Finally, outbreaks of ADV-related keratitis are now less frequent than fifty years ago, thanks to the more rigorous hygiene in the general population.

Commercial interest

3313
Herpetic keratitis

BOURCIER T
Ophthalmology, Strasbourg

ABSTRACT NOT PROVIDED

3314
Parasitic corneal infections

GICQUEL JJ (1, 2)
(1) Ophthalmology, Poitiers
(2) Division of Opphthalmology and Visual Sciences, Nottingham

The exposure of the eye directly to the environment renders it vulnerable to a number of uncommon infectious diseases caused by parasites. Once anatomical barriers are breached, host defences are often insufficient to prevent the infection from spreading localy. A fast identification and treatment of the involved microorganisms are necessary. Contact lens wear is associated with keratitis caused Acanthamoebae. Parasitic infections may also arise following bloodborne carriage of the microorganism to the eye or adjacent structures.

3315
Fungal infections

KESTELYN P
Gent

ABSTRACT NOT PROVIDED

3316
Infectious crystalline keratopathy and its management

DUA HS (1), SAID DG (1, 2)
(1) Ophthalmology and Visual Sciences, University of Nottingham, Nottingham
(2) Research Institute of Ophthalmolgoy, Cairo

Purpose Infectious crystalline keratopathy (ICK) is defined as microbial infection of the cornea in the absence of the host inflammatory response. It presents as slowly progressive crystalline opacities resembling needles, snowflakes or ferns and are filamentous or branching in pattern within the cornea stroma.

Methods Pathogenesis: Streptococcus viridans is the most common cause of ICK but a range of fungi and bacteria have been isolated from cases of ICK. They are located within the corneal stroma within the interlamellar planes. The pattern of spread of bacteria within corneal tissue is determined by the compactness of the corneal stroma. Another common feature is reduced corneal sensation, abrogating the triple response reflex at the limbus and hence the lack of the host response.The diagnosis of ICK is made on history and examination as microbiological diagnosis by culture of scrapes is difficult. Histology of biopsy specimen confirms diagnosis.

Results Medical treatment with broad spectrum topical anti-microbial agents is initiated. Any concomitant use of topical steroids should be discontinued. If no resolution of infection occurs, surgery in the form of lamellar or penetrating keratoplasty or superficial keratectomy is required. The successful use of excimer laser therapeutic keratectomy and Nd:YAG laser in the treatment of ICK has been demonstrated in single case reports but these techniques need further evaluation.

Conclusion The diagnosis of ICK is largely clinical. It is difficult to treat medically often requiring surgical intervention. Poor corenal sensation and steroid use are important predisposing factors.

▪ 3321
Introduction to tests and ISCEV standard

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ABSTRACT NOT PROVIDED

▪ 3322
Electroretinography

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Purpose To illustrate the value of electroretinography in clinical practice.

Methods A case presentation format will be used to illustrate how pattern electroretinography, full-field flash electroretinography and multifocal electroretinography can be used in clinical practice.

Results As will be shown by the cases to be discussed, each of the electroretinography techniques has a specific role to play in making a better diagnosis.

Conclusion All electroretinography techniques have a specific role to play in the evaluation of retinal disease.

▪ 3323
Pattern electroretinography and imaging of the macula

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Purpose Pattern electroretinogram (PERG) is retinal response to contrast stimulation that originates from inner retina, mostly from ganglion cells. PERG may help to answer frequent diagnostic ambiguities between macular and optic nerve diseases and can serve as a link between flash and multifocal ERG and VEP.

Methods Current trends with emphasis on PERG recording in relation to mfERG, flash ERG and VEP, perimetry, microperimetry and scanning laser ophthalmoscope imaging including autofluorescence of the RPE and OCT will be reviewed in representative clinical cases.

Results Global retinal function is well assessed by flash evoked ERGs, but these may be normal in macular disease. PERG and multifocal ERG in combination with autofluorescence imaging and OCT may delineate macular diseases in very early stages. OCT may reveal transversal loss of photoreceptors which correlates well with PERG amplitude. In differential diagnosis, optic nerve diseases usually do not affect multifocal ERG but can affect PERG, especially its N95 component. Combination of reduced N95 component and delay in VEP is strongly suggestive for optic nerve or ganglion cell disease in which autofluorescence imaging would usually be normal.

Conclusion By judging the cause of visual loss, PERG in combination with mfERG and morphological features by RPE autofluorescence and OCT with psychophysical methods usually leads to correct diagnosis.

▪ 3324
Making the diagnosis

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ABSTRACT NOT PROVIDED

■ 3331

Clinical desicion for and with MRI

PLANT G
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ABSTRACT NOT PROVIDED

■ 3332

Imaging posterior visual pathways

SIBTAIN N
London

ABSTRACT NOT PROVIDED

3351
Diagnosis of intraocular and conjunctival tumours

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Purpose To summarise clinical methods used to diagnose eye cancer.

Methods Personal experience of the author and other members of the European Ophthalmic Oncology Group.

Results Conjunctival tumours are generally excised based on provisional clinical diagnosis or cosmetic considerations or, if they are extensive, atypical or part of systemic disease such as lymphoma, biopsied to obtain a histopathologic diagnosis. Additional methods to diagnose and stage conjunctival tumours are high frequency ultrasonography (US) or ultrasound biomicroscopy (UBM) to noninvasively measure their thickness, in vivo confocal microscopy or impression cytology to chart their extent, and exfoliative cytology to get a provisional diagnosis. Ciliary body tumours are visualised by radical biomicroscopy, transillumination and indirect ophthalmoscopy with scleral indentation, supplemented with high frequency US or UBM. Binocular indirect ophthalmoscopy and US form the basis or diagnosing choroidal tumours. In addition to fluorescein and indocyanine green angiography, optical coherence tomography to detect minor subretinal fluid and autofluorescence to detect orange pigment are useful adjuncts in telling a small melanoma from a nevus. The mnemonic "To Find Small Ocular Melanomas" (from Thickness >2mm, subretinal Fluid, Symptoms, Orange pigment, Margin touching disc) is also useful in this respect. Clinical diagnosis of medium-sized to large melanomas is 99% accurate, whereas fine needle aspiration or vitrectomy biopsy is used to diagnose atypical tumors and for prognostic purposes.

Conclusion Conjunctival tumours are almost always diagnosed histopathologically, whereas diagnosis of uveal tumours is usually based on clinical examination. While clinical diagnosis is usually reliable, biopsy of uveal tumours is increasingly used for prognostic purposes.

3352
Management of uveal tumors

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Purpose In this presentation, we will overview the management of uveal tumours, focussing on melanomas, metastases, lymphomas and haemangiomas.

Methods As with other diseases, proper management relies on full systemic and ocular assessment. Accurate measurement of tumour dimensions is especially important. Trans-retinal or trans-scleral biopsy may be needed for diagnosis or to grade the degree of malignancy. Uveal melanomas can be treated by: radiotherapy, delivered with plaque, proton beam or stereotactic methods; local resection, performed trans-retinally or trans-sclerally; phototherapy using a diode laser, with or without a photodynamic agent; and enucleation. Metastases and lymphomas usually respond to external beam radiotherapy. Haemangiomas resolve after one or two sessions of photodynamic therapy. Prognostication is important, especially in the case of melanoma and this requires both histology and cytogenetics. It is essential to address psychological issues to improve well-being as much as possible.

Results Outcomes are measured in terms of vision, local tumour control, ocular conservation, survival and quality of life. Such results are more meaningful if analyzed according to clinical, histological and cytogenetic baseline variables, depending on the underlying condition. Pathological studies are especially important and require a a specialized pathologist, with good facilities and the support of a highly-skilled team.

Conclusion The management of patients with uveal tumour requires access to a wide range of therapeutic modalities, close collaboration with the pathologist, the support of a multidisciplinary team, and an infrastructure for performing continuous outcomes analyses and research.

3353
Management of retinal tumors

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The course will include the management of retinoblastoma and the treatment of retinal angiomas.Practical management of retinoblastoma will be described.The techniques of treatment include enucleation, radiotherapy by external beam or proton beam, plaque brachyterapy , chemoreduction and chemothermotherapy, laser treatment and cryotherapy. The techniques will be detailed and the indications will be given. Advance unilateral retinoblastoma is often an indication for enucleation. Conservative management is performed as often as possible especially in bilateral retinoblastoma. We shall give the methods to avoid extra ocular retinoblastoma like orbital recurrence or metastasis. We shall describe the rules for follow up of the patients after treatment and for screening for early diagnosis in familial retinoblastoma. Guidelines for genetic counselling will be also given.Retinal capillary hemangangiomas can be unique or multiple in case on Von Hippel Lindau disease. Treatments of the angiomas include laser therapy and cryotherapy for bigger angiomas Vitrectomy with endolaser can be needed in rare instances and radiotherapy has been used in selected cases.Cavernous hemangiomas of the retina are rare; they usually are stable with no need for therapy.

3354
Management of conjunctival tumors

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ABSTRACT NOT PROVIDED

■ 3355
Lid tumors

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ABSTRACT NOT PROVIDED

■ 3356
Orbital tumors

PRAUSE J
Eye Pathology Institute, University of Copenhagen, Copenhagen

ABSTRACT NOT PROVIDED

Oral Presentations

EVER 2008

ABSTRACTS

October 1-4, 2008
Portoroz, Slovenia

4111
Diabetic macular edema. Clinical characterization

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The most frequent cause of progressive visual loss due to diabetes is diabetic macular edema. There is retinal edema when there is any increase of water in the retinal tissue resulting in an increase in its volume, i.e., thickness. In diabetes, the inner Blood-Retinal Barrier (BRB) opens resulting in increasing movements of fluids and molecules into the retina. In a situation of open BRB there is extracellular retinal edema and the situation of immune privilege is altered, creating the conditions for a systemic inflammatory repair response.When the BRB is open, the retinal edema accumulation follows Starling's law. With an open BRB any loss of equilibrium between hydrostatic, oncotic and tissue pressure gradients across the retinal vessels contribute to increased water movements and more edema formation.We are able to measure changes in retinal thickness and identify, using OCT, the evolution of macular edema. It is possible to follow closely changes in retinal edema and to characterize diabetic macular edema considering:1. The distribution of the edema. Is it focal or diffuse?2. Is it recent or chronic?3. Is the foveola preserved or is it involved and how much?4. Is the BRB open (vascular leakage)?5. Are there signs of retinal pigment epithelium (RPE) dysfunction? Diffuse edema with RPE signs of damage?6. Are there OCT "cysts"? A good indicator of low tissue pressure.7. Are there signs of vitreoretinal traction on OCT?8. Are there signs of capillary closure and ischemia in the fovea?9. Are HgA1C values higher than 8%?10. Is the blood pressure higher than 130/80mm/Hg even after medication?

4112
New developments in OCT evaluations

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Diabetic macular edema (DME) is one of the most common causes for visual loss (Ciulla et al., Diabetes Care, 2003). DME is characterized by an abnormal increase of the retinal thickness (RT) due to the accumulation of liquids in the retinal tissue, consequence of the first response to the inflammatory process occurring in diabetic retinopathy (DR). It is therefore considered one of the most important indicators of DR progression. Other indicators, such as microaneurysms and retinal leakage, were also observed and quantified in a prospective longitudinal 3-year follow-up study involving type 2 diabetic patients with nonproliferative DR. Patterns of progression were established based on these ophthalmic indicators (Lobo et al., Arch Opthalmol., 2004). OCT plays an important role in the assessment and quantification of DME. Stratus OCT version established a 9 area map for RT, being the central area of 1000µm in diameter. However, there is a lack of detailed information when studying DME. This problem was addressed by the use of an atlas of the human macula in a recent work from our group, where the merging of radial and circular scans was made possible (Bernardes et al., IOVS, 2008). Recently, Carl Zeiss introduced Cirrus HD-OCT, a Fourier domain OCT, allowing to achieve more detailed information of the macular area, performing either 512×128 or 200×200 B-scans, and allowing to export an eye fundus image for reference. It is now possible to assess local RT and correlate it with any imaging modalities available.

4113
Perspectives for detection of photoreceptor changes

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CHNO des XV-XX, Ophthalmology, Paris

ABSTRACT NOT PROVIDED

4114
Role of inflammation in blood-retinal barrier breakdown: animal models

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Purpose Animal models are valuable tools to study the pathogenic mechanisms of many diseases. Diabetic retinopathy is a low-grade chronic inflammatory disease. Nitric oxide (NO) is involved in leukostasis and blood-retinal barrier (BRB) breakdown in the early stages of the disease. However, the role of the different NO synthase (NOS) isoforms was not elucidated. We aimed to clarify the involvement of constitutive (eNOS, nNOS) and inducible NOS (iNOS) isoforms and the mechanisms underlying NO-mediated leukostasis and BRB breakdown, by using an experimental model of diabetes and iNOS KO mice.

Methods Diabetes was induced by streptozotocin in normal and KO mice (2 weeks of diabetes). Normal mice were treated with L-NAME (NOS inhibitor). Vessel leakage was assessed with Evans blue. Leukostasis was quantified in flat-mounted retinas and in vivo. ICAM-1, occludin, ZO-1 and nitrotyrosine levels were assessed by Western blotting or immunohistochemistry.

Results Diabetes increased the permeability of BRB and leukostasis, which were reduced by L-NAME. Similar effects were observed in diabetic iNOS KO mice. In diabetic mice, the immunoreactivity of tight junction proteins, occludin and ZO-1, decreased, whereas ICAM-1 protein levels increased. Those effects were prevented by L-NAME and in diabetic iNOS KO mice. Diabetes also upregulated all NOS isoforms and increased nitrotyrosine levels in normal mice, but did not significantly increase eNOS and nNOS, and nitrotyrosine levels, in iNOS KO mice.

Conclusion These data demonstrate that iNOS plays a predominant role in leukostasis and BRB breakdown. The mechanism involves ICAM-1 upregulation and tight junction proteins downregulation. Support: FCT, Portugal

▪ 4115
Inflammatory markers in diabetic macular

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Purpose Complications of diabetic retinopathy, such as macular edema, appear to be generated by multiple inflammatory factors that affect the retinal microcirculation. To elucidate the cell types and mechanisms underlying diabetic complications, human retinal microvascular pericytes (HRMP), monocytes (THP-1), and retinal endothelial cells (HREC) were treated with either high glucose, TNF-_- or IL-1_, and protein secretion was measured in the presence or absence of dexamethasone (DEX). In addition, retinal levels of several inflammatory proteins were measured in an animal model of diabetes over a 3 month study period.

Methods Cells were incubated for 5 hr (THP-1) or 24 hr (HRMP, HREC) with medium, TNF-_- (10 ng/ml) or IL-1_ (10 ng/ml), high glucose (25 mM) in the presence or absence of dexamethasone (10 nM–1 µM). Sprague Dawley rats were rendered diabetic by intraperitoneal STZ administration (65 mg/kg; blood glucose >220 mg/dl after 48h) and age-matched control rats were sacrificed 7 days, 4 weeks, and 1 month after STZ injection. Eyes were enucleated, snap frozen in liquid nitrogen and stored at -70°C. In both cell and retinal assays, protein levels (89 for human, 68 for rat) were measured by Rules Based Medicine using their Luminex-baed human and rodent antigen panels.

Results Compared to control responses, TNF-_ or IL-1_ induced a five-fold or more increase in several inflammation-associated proteins in each cell type. The number of mediators and extent of increased secretion were greatest in HRMP (≥ five-fold increase in 33 proteins with TNF-_ and 29 proteins with IL-1_). In HRMP and THP-1 cells, DEX inhibited the secretion of several inflammation-associated proteins in a dose-dependent manner. The IC50 for DEX inhibition ranged from 2 nM for some proteins to 1 µM for others, and this differential effect was dependent on cell type and inflammatory stimulator. Of 68 proteins measured in diabetic rat retinae, 9 were significantly elevated at 3 months including beta-2 macroglobulin, eotaxin, FGF-2, MCP-1, MCP-3, M-CSF, NGAL, osteopontin, and TIMP-1. At this time, there was a reproducible but not significant decrease in VEGF expression.

Conclusion Our results support the hypothesis that the early stages of diabetic retinopathy are associated with a subclinical inflammatory response and point to microvascular pericytes as a primary source of these mediators.

▪ 4116
Treating inflammation in DME. Combination treatments

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ABSTRACT NOT PROVIDED

4121
History of amblyopia

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Purpose Review the history of amblyopia.

Methods Analysis of original and secondary contributions in the history of amblyopia.

Results Traditionally amblyopia has been classified into different subgroups according to the major disorder which is responsible for its occurrence; accordingly, we distinguish among strabismic amblyopia, anisometropic amblyopia, isoametropic amblyopia and deprivation amblyopia. Since strabismus is the most visible disorder leading to amblyopia, the history of strabismus diagnosis can be roughly included in the history of amblyopia in the clinical context. It is known that Hippocrates described strabismus and differentiated it into comitant and non-comitant. Later Paulus of Aegina and Ambroise Pare not only diagnosed the disorder, but also attempted to treat it. One of the first explanations of the amblyopia mechanisms was given by de la Hire who suggested that in strabismus the most sensitive part of the retina is eccentrically displaced to an abnormal position. This idea was later supported by Johannes Muller. The first treatment of amblyopia was attempted in 1743 by George L. de Buffon, who covered the better eye and suggested the use of glasses for the weaker eye. In the 1930s orthoptic programs were introduced and in the 1950s pleoptic techniques began to be used. Finally, the experiments carried out in the 1960s and 1970s by Hubel and Weisel suggested that the neural basis for amblyopia was related to a massive reduction in the binocular neurons and a shift in the ocular dominance of neural activity towards the unaffected eye.

Conclusion Although our present understanding of the underlying mechanisms of amblyopia is much greater, our treatment methods are still rooted in history.

4122
Form deprivation amblyopia - a treatable cause of blindness

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Purpose Form deprivation amblyopia is associated with the obstruction or deformation of the passage of light causing degraded images on the retina. This lack of normal visual experience delays or blocks the visually driven development. If the obstacle is removed within the critical period the developing visual system has the capacity to regain visual function. Left untreated the deprivation and blocked visual experience may cause severe visual impairment and blindness.

Methods To review our current understanding of the pathophysiology and risk factors in form deprivation amblyopia and to evaluate the effectiveness of treatment. The main conditions obstructing light passage during early development of vision will be described. Form deprivation amblyopia and its functional consequences are defined. Factors of importance for a satisfactory long term visual outcome are evaluated.

Results Valid experimental and clinical models of form deprivation amblyopia are reviewed with focus on the role of visual deprivation per se and unequal visual input to the visual cortex, the primary site of functional change. Recent clinical observations of the visual outcome following early surgery of congenital dense bilateral and unilateral cataracts are used to evaluate the factors involved.

Conclusion Form deprivation amblyopia is a complex condition with a hallmark of impaired visual acuity. For a satisfactory visual outcome early detection and intervention is important.

4123
Occlusion therapy

BERK AT
Dokuz Eylul University, Pediatric Ophthalmology, Izmir

Purpose To present recent researches regarding the efficacy of ambliyopia treatment with patching.

Methods Various treatment options are reviewed, results from randomized clinical trials and controversies in the field will be discussed.

Results The evidence based knowledge for ambliyopia treatment is rapidly evolving. Indications of patching, adverse effects of occlusion treatment and compliance for patching and how compliance can be maximized, treatment factors including type and dose of treatment, method of treatment termination, age effect on treatment will be covered during the panel .

Conclusion Ambliyopia is still the leading cause of visual impairment in children, but it is treatable with several different treatment modalities and occlusion is one of the widely used and well known.

4124
Medical treatment

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Purpose To present an update on medical treatment of amblyopia and to review recent progress in this field.

Methods Various treatment modalities are reviewed, with particular emphasis to dopaminergic agents. The effect of cytycoline through various ways of administration will be discussed in detail.

Results Evidence will be brought of improvement in visual function attributable to medical treatment alone or in association with part-time occlusion. Potential adverse effects will be discussed, as well as characteristics of visual function modifications obtained. Possible guide-lines for medical treatment of amblyopia will be offered.

Conclusion It appears that medical treatment can be usefully included in the armamentarium for amblyopia therapy, particularly in difficult cases. Recently published animal experimental data on substances capable of delaying plasticity of the visual system in adults, will be hopefully transferred shortly to humans.

4131
Inflammation in AMD pathology

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Age-related macular degeneration (AMD) is a progressive retinal disease that leads to substantial irreversible vision loss in elderly patients. Two clinical categories of AMD are distinguished: the "dry" atrophic form and the exudative neovascular or "wet" form. There is neither a preventive therapy nor a cure for both forms, although recent efforts succeeded in a more effective treatment of the wet AMD with PDT and anti-VEGF drugs. AMD is a multifactorial pathology which involves complex interaction of metabolic, genetic and environmental factors, with major biochemical-clinical abnormalities seen in four functionally interrelated tissues: photoreceptors, retinal pigment epithelium, Bruch's membrane and choriocapilaries. Four processes specifically contribute to the development of AMD pathology: lipofuscinogenesis (in RPE cells), drusogenesis (with drusen located between RPE and Bruch's membrane), inflammation (local) and choroidal neovascularization (in wet form). Although the role of immune system and inflammation has been implicated in AMD pathogenesis for many years, an impetus to intensify the research in this direction gave a recent discovery of polymorphisms in genes that encode for elements of the complement system, including factor H (CFH; Y402H), factor B, and complement component 2. An increased activity of the complement alternative pathway due to the lack of or insufficient control by CFH appears to contribute to AMD progression via immunologic mechanism which drives inflammatory response. An arising question is whether blockade of overactive complement system will be a therapeutic strategy safe for patients and effective to prevent or slowing down the macula-devastating and vision-threatening disease. Supported by grant no. 503-1023-1 from Medical University of Lodz.

4132
Signaling pathways in innate immunity

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Inflammation has a key role in the pathogenesis of AMD. This lecture will review the recent progress in understanding the different host-defence mechanisms against pathogens and self-based danger signals involved in the activation of innate immunity. The innate defence system utilizes pattern recognition receptors (PRR) to respond to a variety of pathogen-associated (PAMP) and danger-associated (DAMP) molecular structures. Along with the well-known complement and scavenger receptor systems, Toll-like receptors (TLR) and NOD-like receptors (NLR) have also a crucial part in host-defence and these receptor systems can be activated both by PAMPs and DAMPs. Pattern recognition receptors are located either in cell surface, such as TLR2 and TLR4, or in intracellular locations, e.g. TLR3, TLR9 and all NLRs. PRRs show some specificity to ligands and also in downstream they activate different signaling pathways, most common of which are NF-kB and IRF-dependent pathways inducing inflammatory responses.Retinal pigment epithelial cells (RPE) have an important role in eye host-defence, both at apical and basolateral surfaces. Most of the TLRs are expressed in RPE cells, especially TLR3 and TLR4, and they can participate in photoreceptor outer segment recognition. TLR3 can also suppress angiogenesis. The functions of NLRs, e.g. those forming inflammasomes, are still unknown, although the danger-type of activation signals, such as oxidative stress and potassium efflux, are present in retinal pigment epithelium. It seems that the activation of innate immunity system via DAMPs and PRRs may have a central role in the pathogenesis of AMD.

4133
Complement factor H and factor B expression in RPE cells

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Purpose Age-related macular degeneration (AMD) is the leading cause of untreatable blindness in the developed world. The pathogenesis of AMD is not fully understood. Recent evidence suggests that local inflammation in particular complement activation plays an important role. We aim to understand how complement activation is regulated at retina/choroidal interface.

Methods The expression and distribution of complement factor H (CFH) and factor B (CFB) in mouse ocular tissues were examined by immunohistochemistry. Regulation of CFH and CFB gene expression by various cytokines or photoreceptor outer segments (POS) was investigated in vitro in cultured RPE cells. Changes in CFH or CFB gene expression after treatment were evaluated by RT-PCR.

Results In normal mouse eyes, CFH was detected in corneal epithelial cells, ciliary body, RPE cells, Bruch's membrane and choroidal vessels. There is no significant change in either the expression level or the distribution pattern of CFH in ocular tissues of different ages of mice. CFB was exclusively detected in RPE cells in normal mice. The expression of CFB in RPE cells increases with age. In vitro in RPE cultures, the expression of CFH was negatively regulated by cytokine TNF-alpha and IL-6, whereas the expression of CFB was positively regulated by TNF-alpha and IFN-gamma. Short-term incubation of RPE cells with POS did not alter the expression of CFH or CFB, whereas long-term incubation of RPE cells with POS significantly down-regulated CFH expression but up-regulated CFB expression.

Conclusion Complement regulatory factors CFH and CFB are produced locally in the retina/choroidal interface by RPE cells. The production of CFH and CFB in RPE cells is regulated differently by various cytokines and oxidized POS.

4134
Inflammatory gene defects in AMD

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Inflammatory markers have been raported in AMD patients at the serum, gene an tissue levels. Of the inflammatory cytokines especially IL-6, IL-8 and IL-10 have been associated with AMD. Inflammatory cytokines are multifunctional molecules potentially stimulating macrophages and other inflammatory cells and choroidal neovascularization (CNV) in AMD lesions. The cytokines a modulate the expression of other inflammatory markers and are associated e.g with elevated levels of CRP in AMD. Targeting these pathways with non-steroidal anti-inflammatory agents may be used in future pharmacologic treatments for AMD before and after CNV formation. This presentation reviews current knowledge of inflammatory cytokines in relation to the RPE and AMD in general.

4141
Sustained BMP signaling induces the lens placode

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Purpose Fate maps at late gastrula and head fold stages show that prospective olfactory and lens placodal cells are intermingled in a domain of the anterior border region between the neural plate and the future epidermis. During embryonic development Bone Morphogenetic Protein (BMP) signals represent one class of secreted signals that are implicated in lens specification. When and how BMP signals is involved in the initial specification of the lens placode remains to be defined.

Methods We have established explant and whole embryo assays of placodal cell differentiation in the chick embryo, and analyzed a panel of markers that are expressed in differentiated olfactory and lens placodal cells.

Results We provide evidence that cells in the anterior border region have become specified as olfactory and lens placodal cells at the late gastrula stage, and that BMP signals are required and sufficient to induce olfactory and lens placodal cells from these progenitor cells. We also provide evidence that time of exposure of progenitor cells to BMP signals plays a key role during the differential specification of olfactory and lens placodal cells. By the neural fold stage, the generation of lens cells requires continued exposure to BMP signals, whereas the generation of olfactory placodal cells has become independent of further exposure to BMP signals. Moreover, prolonged exposure of BMP signals promotes the generation of lens cells at the expense of olfactory placodal cells.

Conclusion Our results provide evidence that the specification of the lens placode requires sustained BMP signaling. Thus, our results support the emerging idea that time of exposure of progenitor cells to patterning signals play important roles during cell fate specification in different tissues in vertebrate embryos.

4142
A role for canonical WNT signaling in lens development

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Purpose To investigate Wnt signalling in lens development we conditionally deleted β-catenin (CatnβEx3-6) or mutated exon3 of β-catenin (CatnβEx3) or truncated adenomatous polyposis coli (Apc580S) to inactivate or activate the pathway in different cellular compartments of the murine lens.

Methods Cre deletor lines that express Cre in fibers only (MLR39) or in fibers and epithelium (MLR10), were used to conditionally mutate floxed CatnβEx3-6, CatnβEx3 and Apc580S alleles in developing mouse lens from E13. Lenses from mutant and wild-type mice were analyzed by histology, immunofluorescence and PCR arrays.

Results MLR10 intercrosses result in microphthalmia; MLR39 intercrosses show no ocular abnormalities at weaning. Mice with loss of β-catenin in fibres (MLR39Cre/CatnβEx3-6) develop cataract in later life. Analyses of MLR10-derived mutant mice at E13.5 show that loss of β-catenin inactivates Wnt signals and results in loss of lens cell progenitors, with decreased E-cadherin, cyclinD1 and cMyc expression, reduced BrdU and phosphohistone3 (pH3) labeling and premature cell cycle exit (p57Kip2). As well as Wnt signal effects, loss of β-catenin deregulates adherens junctions resulting in loss of hexagonal fibre structure. By contrast, activating mutations of Wnt pathway (CatnβEx3, Apc580S) result in increased epithelial proliferation (BrdU, cyclinD1, PH3), apoptosis (TUNEL) and inhibition of fibre differentiation (β-crystallin, p57Kip2). Pathway specific PCR arrays confirmed modulation of Wnt signaling in each lens mutant and show altered expression of Notch pathway, indicating these pathways operate as part of a network.

Conclusion These data show Wnt signals play key roles in regulating proliferation and differentiation of lens epithelial cells and that the pathway is tightly regulated.

4143
TGFbeta/Smad signalling, transdifferentiation and matrix contraction

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Purpose Matrix contraction is a key process in posterior capsule opacification (PCO) formation. Conventional wisdom suggests that TGFβ/Smad signaling, via Smad4, regulates transdifferentiation, which in turn gives rise to matrix contraction thus contributing to PCO. The relationship between TGFβ2 induced transdifferentiation of human lens cells and matrix contraction was tested.

Methods The human lens cell line FHL 124 was used. AlphaSMA and Smad4 knockdown was achieved using siRNA; efficiency was tested at message and protein level using QRT-PCR and western blots respectively. Contraction was assessed using a patch contraction assay, following a 24hr period of serum starvation, cells were maintained in the following conditions for 1–3 days: Control medium (CM) ± 100μM RGDS (Fn/Fn receptor inhibitor); 10ng/ml TGFβ2 ± RGDS; CM ± siRNA–alphaSMA; 10ng/ml TGFβ2 ± siRNA–alphaSMA; CM ± siRNA–Smad4; 10ng/ml TGFβ2 ± siRNA–Smad4.

Results TGFβ2 significantly increased expression of malphaSMA (197.7 ± 6.2%) and mfibronectin (197.4 ± 20.4%). SiRNA against alphaSMA and Smad4 significantly inhibited message and protein levels in the presence and absence of TGFβ2. Patch assays cultured for 3 days with TGFβ2 showed significant contraction. Neither inhibition of Fn/Fn receptor interaction using RGDS or knockdown of Smad4 or alphaSMA could prevent TGFβ2 induced matrix contraction. Interestingly, RGDS treatment and alphaSMA knockdown lead to a significantly enhanced rate of TGFβ induced contraction. AlphaSMA and fibronectin expression was suppressed in Smad4 knockdown cells.

Conclusion TGFβ induced transdifferentiation is not critical for matrix contraction, thus regulation appears to be via Smad independent pathways.

Commercial interest

4144
TGFbeta signalling through Smad-independent mechanisms in human lens cells

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Purpose Previous work has shown that TGFß can induce matrix contraction and is likely to be regulated by Smad-independent pathways. The present study investigated the role of the classical MAPK signalling and Rho kinase signalling pathways in TGFß mediated matrix contraction.

Methods Cells from the human lens line FHL 124 were employed. Contraction was assessed using a patch assay, whereby the area covered by cells, was measured using imaging techniques. ERK activation was evaluated using western blot methods. To study SMAD2/3 distribution immunocytochemistry was used. Following a 24hr period of serum starvation, cells were maintained in the following conditions: Control medium +/– 10μM MEK inhibitor (U0126); 10ng/ml TGFß2 +/– U0126; Control medium +/– 10μM Rho kinase Inhibitor (Y–27632); 10ng/ml TGFß2 +/– Y–27632. The experimental duration for Smad2/3 staining was 2 hrs; western blots, 30mins & 24hr; patch contraction assays, 2-3 days.

Results Addition of 10ng/ml TGFß2 lead to a significant elevation of P-ERK levels following both 30 min and 24hr periods of exposure. Addition of 10ng/ml TGFß2 to patch assays caused a significant contractile event to take place. Maintenance of cultures in the presence of 10μM U0126 or Y–27632 had no significant effect on patch area when added to control medium; however, when added in the presence of TGFß2, contraction was inhibited. With respect to cell population all groups were similar. Immunocytochemistry for SMAD2/3 showed clear nuclear translocation in response to 10ng/ml TGFß2; this signalling event was unaffected by U0126 and Y–27632.

Conclusion MAPK and Rho kinase signalling play important roles in TGFß mediated matrix contraction of human lens cells.

Commercial interest

4151
Monitoring retinal ganglion cells in vivo

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Progress in imaging techniques will considerably increase our knowledge on retinal cell pathophysiology and death during optic nerve disesases as a whole. Experimentally, current in vivo imaging using the green laser reflectance mode of the SLO allows noninvasive microscopic-scale definition of the nerve fibers. However, loss of the axons is a late and irreversible event, thus imaging the retinal ganglion cells themselves would be preferable in order to detect diseased states at an earlier stage. Retrogradelly-labelled RGCs can be conveniently seen in vivo, but such imaging require invasive procedures, the effect of which on RGC physiology remains uncertain. The recent development of molecular imaging of apoptotic ganglion cells is promising. The cSLO also allows in vivo imaging of other cellular compartments that are relevant for glaucoma, for instance microglial cells. In humans, current techniques allow imaging of the nerve fiber layer with a relatively low resolution. The GDx evaluates the nerve fiber layer thickness through light polarisation, and high resolution OCT through mapping of its thickness around the optic nerve. Yet, it is likely that these systems lack sensitivity for detection of the early loss of the NFL, and even more for early dysfunction of RGCs. Presently, adaptive optics does not appear to be a technique of choice for the NFL, but technological progress may prove this assertion to be wrong.In the future, techniques allowing increased contrast of fibrillar structures such as en face OCT may prove of interest.

4152
Determining rates of visual field progression in glaucoma

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Purpose To provide practical guidelines on detecting rates of visual field progression in glaucoma

Methods Using a mixture of real patient data, computer simulation and statistical analysis, the frequency of visual field examinations for detecting various rates of visual field change were determined.

Results Our results show that the ability to detect rates of visual field change depends critically on the magnitude of the change we wish to detect and the variability of visual fields. They also show that performing only one visual field per year will lead to failure to detect very significant visual field loss. The statistical power to detect clinically meaningful rates increases with 2 or 3 examinations per year

Conclusion This study provides guidance to general ophthalmologists and glaucoma specialists on detecting rates of visual field progression in glaucoma.

Commercial interest

4153
Is brimonidine better at stabilizing visual field than timolol?

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Purpose Alpha-2 adrenergic agonists are neuroprotective in animal models of focal cerebral ischemia. Brimonidine protects the retinal ganglion cell (RGC) from secondary degeneration following partial crush injury to the rat optic nerve and in an ocular hypertensive rat model. The mechanism for this effect is up-regulation of brain-derived neurotrophic factor in RGC and the retina. Brimonidine activates the alpha-2 adrenoceptor at 2 nM. Topical administration of brimonidine produces pharmacologic drug concentrations in the vitreous (100-170 nM) in humans that provides a drug delivery route to the RGCs sufficient to bind and activate the alpha-2 adrenoceptor. In this way, brimonidine could function to maintain the health of the optic nerve independent of its ability to reduce intraocular pressure (IOP)

Methods The Low-pressure Glaucoma Treatment Study (LoGTS) is a triple masked, randomized, multicenter clinical trial of the efficacy of monotherapy with brimonidine versus timolol eye drops to alter the course of low-pressure (normal-tension) glaucoma (untreated IOP < 22 mmHg). The primary outcome was visual field progression analyzed using point-wise linear regression analysis. This methodology required a minimum of four visual fields to obtain and compared the slope of decibel sensitivity of each test location to all previous examinations. Field progression was defined as a negative slope > 1.0 decibel/year with a significance P£0.05 for the same three or more test locations on three consecutive examinations (i.e., over an 8 month interval).

Results Previously published articles contains a detailed description of the study methods and baseline patient characteristics and baseline visual field and IOP asymmetry. The current presentation will discuss LoGTS outcomes.

Commercial interest

4154
The future of neuroprotection in glaucoma therapeutics

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Purpose Give an overview on the future of neuroprotection in light of the announcements concerning the memantine phase 3 clinical trial.

Methods Allergan recently unmasked the second memantine phase 3 clinical trial examining the efficacy and safety of oral memantine for the treatment of glaucoma.

Results While the study failed to meet its primary endpoint to sufficiently replicate the results of the first phase 3 trial; additional data analyses are ongoing. What have we learned about studing neuroprotection in this pioneering effort?

Conclusion An update on the status of the glutamate hypothesis and the implications for future neuroprotective therapies in glaucoma will be discussed.

Commercial interest

■ 4161

Gene transfer of disease regulated promoters during experimental autoimmune uveitis

CHTARTO A
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ABSTRACT NOT PROVIDED

■ 4162

Identification and characterization of novel disease genes for Leber Congenital Amaurosis (LCA)

COPPIETERS F
Gent

ABSTRACT NOT PROVIDED

■ 4163

Study of candidate genes for ocular anterior segment dysgenesis (ASD)

D'HAENE B
Gent

ABSTRACT NOT PROVIDED

■ 4164

Osmotic stress regulation of aquaporin 4 expression in a human retinal pigmented epithelial cell line

JANSSENS S
Brussels

ABSTRACT NOT PROVIDED

■ 4165

Study of the role of P2Y6 receptors in the development of experimental autoimmune uveitis

JUDICE DE MENEZES RELVAS L
Brussels

ABSTRACT NOT PROVIDED

■ 4166

AAV mediated SOCS1 gene expression in ARPE cells in an immune rejection model of xeno-graft for AMD diseases

KOCH P
Brussels

ABSTRACT NOT PROVIDED

■ 4211

European vision research - An independent point of view

VON BONHORST C
Consultant, Brussels

ABSTRACT NOT PROVIDED

■ 4212

International research funding advocacy: The US experience

ANGLE J
Executive Director, ARVO, Rockville, Maryland

ABSTRACT NOT PROVIDED

■ 4213

Advocating for research funding: The India experience

BALASUBRAMANIAN D
LV Prasad Eye Institute, Hyderabad

ABSTRACT NOT PROVIDED

■ 4214

The role of the European Vision Institute (EVI) for supporting vision research in Europe

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ABSTRACT NOT PROVIDED

4221
Papilledema due to cerebral venous thrombosis

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Purpose Review the clinical features and the most effective method of diagnosis of cerebral dural venous sinus thrombosis (CDVT). Treatment procedure of the predisposing factors and of the cerebral thrombosis will be briefly discuss.

Methods Recent litterature is considered

Results CVDT is a challenging condition because the variability of clinical presentations. It might mimic many neurological disorders such as, meningitis, intracranial hypertension, encephalopathy and stroke. However, the most common pattern of presentation is with a pseudotumor cerebri like syndrome: headache, nausea, vomiting, papilledema, optic-nerve related visual loss, and VI nerve palsies. CVDT can present at all ages, but is seen more in young and middle-aged women.The most frequent predisposing factor is a hypercoagulable state, although contiguous infection, like mastoiditis or middle-ear infections, and neoplasms should be excluded.MRI with gadolinium and MR venography are a safe and effective method for visualizing cerebral venous thrombosis. Treatment should be firstly direct toward any underlying medical condition, and any offending drug should be discontinued. Anticoagulation should be started with IV heparin, and usually followed by warfarin. Acetazolamide might be used to treat elevated intracranial pressure and mild field defect. Those with progressive or severe visual loss, despite medical therapy, should undergo optic nerve fenestration or other shunting procedure.

Conclusion One should keep in mind the possibility of CDVT in every patient with new-onset headache of any type, particularly if worsening despite analgesic. Earlier the diagnosis, earlier the treatment, better is the outcome.

4222
Hypertensive retinopathy mimicking papilledema

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ABSTRACT NOT PROVIDED

4223
Pituitary apoplexy

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Hemorrhage or infarction of a pituitary tumor is termed pituitary apoplexy. Most patients experience abrupt onset of severe headache, altered mental status and visual changes. Visual loss may be unilateral or bilateral and the severity is variable. Ophthalmoplegia, usually due to compression of the ocular motor nerves in the cavernous sinus, may also be unilateral or bilateral. The 3rd nerve is most commonly affected. The clinical picture of acute 3rd nerve palsy associated with severe headache may be mistaken for aneurysmal subarachnoid hemorrhage Precipitating factors for pituitary apoplexy include hypotension, Valsalva maneuvers, malignant hypertension, pregnancy or exogenous estrogen administration and anticoagulation. Cranial MRI is the diagnostic test of choice. Morbidity and mortality are related to the abrupt onset of panhypopituitarism, particularly cortisol insufficiency. Acute management includes systemic corticosteroids in stress dosages (e.g., hydrocortisone 100 mg IV every 6-8 hours), control of hemodynamic parameters (e.g.blood pressure) and correction of any metabolic derangements. Surgical decompression is usually performed as soon as the patient is stable.

4224
Wernicke encephalopathy

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Wernicke's encephalopathy is an acute neurological disorder caused by thiamine (Vitamin B1) deficiency and characterized by the clinical triad of ophthalmoplegia, ataxia and mental confusion. Ophthalmoplegia commonly takes the form of horizontal and/or vertical gaze palsy often accompanied by bilateral abduction deficits. Upbeat nystagmus is characteristic. Mental status changes may be mild therefore unappreciated. MRI abnormalities (periaqueductal area, midbrain tegmentum, mamillary bodies and dorsomedial thalamus) can be found in up to 60% of patients who are imaged within 2 weeks of symptom onset. The condition is life-threatening but early therapy with intraveinous or intramuscular 100mg thiamine with glucose supplementation can reverse symptoms and signs within hours.

■ 4225

Acute painful ophthalmoplegia: infectious considerations

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Acute painful ophthalmoplegia may be caused by a number of processes including inflammation (giant cell arteritis, sarcoidosis, thyroid eye disease, idiopathic), vascular (aneurysm, hemorrhage, thrombosis, ischemia, fistula), tumor, and migraine. However, infectious causes (fungal, bacterial) of ophthalmoplegia may be life-threatening if the diagnosis and treatment is delayed. Presenting symptoms and signs, differential diagnosis, and the appropriate treatment of these infectious entities will be discussed.

4231
Existence of limbal epithelial crypt within the infant limbus

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Purpose The Limbal Epithelial Crypt (LEC) has been suggested to be the limbal epithelial stem cell niche and the limbus has been shown to demonstrate regional variations in association with the LEC. Our aims were to 1) to determine the existence of LEC in the infant age group and 2) compare and contrast the corneo-scleral tissue between infant and the adult by use of immunofluorescent imaging.

Methods Donor eyes were processed and snap frozen in liquid nitrogen. Using a Leica cryostat machine, corneo-scleral sections were prepared and examined under microscopy for presence of LEC structures. Limbal sections were fixed, and stained with a range of current postulated markers of stem cells and cell differentiation by standard immunofluorescent imaging techniques.

Results Immunostaining in the infant group demonstrates that both limbal and corneal epithelium consist of cells that are characteristic of cells with less differentiated nature. No classical adult LEC was discernable in corneo-scleral rims of a 2 year old or a 4-month old infant. However, adult LEC immunofluorescence, demonstrate similar characteristics to the infant limbus.

Conclusion We hypothesize that the absence of classical adult LEC in infants suggests that LEC may arise during the natural human growth, and may act as a repository for limbal epithelial stem cells in the human adult.

4232
Microarray study of limbal epithelial crypt demonstrates its putative limbal stem cell niche characteristics

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Purpose We have discovered a novel anatomical structure at the limbus, termed the Limbal Epithelial crypt (LEC). Previous anatomical and immunohistological studies suggest its potential as the limbal stem cell niche. We aim to characterise the differential gene expression of the LEC by microarrays with a view to finding putative stem cell marker(s).

Methods Frozen tissue blocks of corneoscleral buttons dissected from cadaver eyes were cryosectioned. These tissue sections from different ocular surface regions were laser microdissected. Extracted RNA was amplified & hybridized to microarray chips. Raw data obtained with Genepix Pro6 software was filtered, normalized & analysed on BASE, TMeV & Jexpresspro software. Unpaired T-Test, Significance Analysis of Microarrays and k-means clustering were performed on the data. Quantitative gene expression analysis (qPCR) was performed on the genes of interest.

Results 150 differentially expressed genes in the LEC were obtained($p \leq 0.01$). These genes were clustered according to stem cell related functions. qPCR was performed on the Integrin Beta 1 binding protein gene (ITGB1BP1). The protein expressed by this gene specifically binds to Beta 1 Integrin (ITGB1) which is a cell adhesion molecule, is predominantly an inhibitor of cell proliferation and has a role in maintaining stem cells in their niche. These genes were significantly expressed in the LEC (P=0.03).

Conclusion The constituents of the LEC are stem cells with neighbouring niche cells, hence representing a Limbal Epithelial Stem Cell niche.

4233
Limbal microenvironment can induce transdifferentiation of hair follicle stem cells into corneal epithelial-like cells

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Purpose To investigate the plasticity of murine vibrissa hair follicle (HF) stem cells regarding differentiation into corneal epithelial-like cells through modulation by limbus-specific microenvironmental factors.

Methods HFs were isolated and the dissociated bulge stem cells enriched by clonal expansion, and subcultivated on various extracellular matrices (collagen type IV, laminin-1, laminin-5, fibronectin) in DMEM/F12 medium supplemented with different conditioned media (CMs). CMs were derived from central and peripheral corneal fibroblasts and limbal stromal fibroblasts. Growth potential and cellular phenotype were evaluated by light and electron microscopy, real-time-PCR and immunohistochemistry using antibodies against stem cell (CK15, integrin α6) and differentiation markers (CK12) or (CK10).

Results Laminin-5 and collagen IV promoted rapid cell adhesion, proliferation, and generation of confluent, regularly arranged epitheloid cell sheets, whereas laminin-1 and fibronectin adversely affected these cell properties. Addition of CMs differentially influenced cellular phenotype and differentiation. Limbal fibroblast CM induced differentiation of cuboid cells showing ultrastructural characteristics of a corneal epithelial phenotype. Moreover, it markedly increased the number of CK12 immunopositive cells while decreasing expression of CK10 opposed to the other CMs.

Conclusion Hair follicle stem cells are capable of differentiating into corneal epithelial-like cells in vitro when exposed to a limbus-specific microenvironment. Therefore, the HF may be an alternative therapeutic source of multipotent stem cells for generation of autologous epithelial cell sheets for ocular surface reconstruction.

4234
The effect of spongy layer (sl) isolated from amniotic membrane on ocular cells growth

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Purpose The extraembryonic coelom or spongy layer (SL) is the gelatinous, biochemically complex layer, which functions as a physical boundary between the vascular chorion and avascular amnion membrane (AM). SL often remains associated with the AM and is partially but variably removed during preparation for transplantation. We have shown that SL contains a similar profile of potentially beneficial factors as AM, but at considerably higher levels, which may explain in part the observed clinical variation. However, the effects of SL on ocular cell growth have yet to be established

Methods Soluble proteins were extracted from freeze-dried SL to generate a soluble (sSL) and an insoluble structural SL fraction (iSL). Cultured corneal epithelial cells (CEC), keratocyte derived fibroblasts (KDF) and lymphocytes were stimulated with sSL and iSL fractions at varying dilutions, and the effects on cell proliferation (WST-1) and cytotoxicity were measured.

Results At physiological concentration (16mg/ml) iSL killed all cell types within a few hours. Serial dilution of iSL (16mg/ml,8mg/ml,3.2mg/ml,0.32mg/ml) reduced rate of death, but death still occurred. Stimulation with sSL killed CEC at all concentrations, whilst the most dilute sSL fraction promoted KDF growth.

Conclusion SL exerts a powerful cytotoxic effect on ocular and immune cells. However, the depot of factors contained within the SL may over time be released over time to promote cell growth. Therefore in the current situation where SL is typically ignored during AM preparation for transplantation, may have significant implications for the clinical efficacy of AM.

4235

Distribution of BIG-H3 protein in primary and recurrent granular corneal dystrophy

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Purpose Granular corneal dystrophy (GCD) is a hereditary disease involving the formation of opaque granular deposits in the corneal stroma. In the present project we investigated the distribution of big-h3 protein in the cornea of primary GCD (PGCD), recurrent GCD (RGCD) and following epithelial debridement of RGCD.

Methods The distribution of big-h3 protein was studied in 2 PGCDs, 2 RGCDs, and in epithelial debridement specimens from 2 RCGD corneas. The corneas were fixed in 4% paraformaldehyde at 4°C and embedded in LR white under UV light. The primary antibody big-h3 was located by secondary, goat anti-rabbit antibody conjugated with gold.

Results In normal cornea moderate distribution of big-h3 was observed. In PGCD and RGCD corneas, strong labelling for big-h3 was observed in deposits, within very thin microfilaments (nm) and at the inter-lamellar junctions. Labelling was significantly higher in GCD Descemet's membrane compared to normal Descemet's membrane. Very strong labelling was observed in the deposits and in the cytoplasm of epithelial cells, of debridement specimens.

Conclusion Big-h3 protein, of epithelial origin, is thought to diffuse into the stroma to form stromal deposits. The presence of aggregates of the protein around keratocytes suggests that it is also produced by these cells. The presence of granular deposits and big-h3 protein suggested that the protein migrated from limbal epithelium during resurfacing of host epithelium.

4236

Anterior segment imaging with fourier-domain optical coherence tomography system compared to time-domain OCT

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Purpose To compare anterior segment measurements and morphology obtained from two anterior segment optical coherence tomography systems

Methods 30 eyes of 30 healthy volunteers were recruited for the study. Central corneal thickness (CCT), trabecular-iris angle (TIA) and angle opening distance (AOD 500) at the nasal and temporal angles were measured three times during one visit with two systems: Visante OCT (Carl Zeiss Meditec, Inc, Dublin, California, USA) and RTVue FD-OCT Corneal Anterior Module system (Optovue, Inc. Fremont, CA, USC). Anterior segment morphology was assessed and compared.

Results Mean values of CCT, TIA and AOD by Visante OCT and RTVue FD-OCT were as follows: automatic CCT 535 ± 33,07 µm, 538 ± 31,82 µm; manual CCT 545 ± 30,91 µm, 542 ± 30,57 µm; nasal TIA 34,7± 9,5, 35,2 ± 8,9; temporal TIA 35,3 ± 8,5, 35,5 ± 9; nasal AOD 435 ± 95 µm, 444 ± 98 µm; temporal AOD 443 ± 103 µm, 452 ± 99 µm. There was no significant difference between mean values and they were highly correlated. Morphologic analysis of two OCT systems proved that Visante OCT has lower resolution, but in one anterior chamber image, all the anterior chamber structures are visible, while RTVue provides very precise information about small fragments of anterior chamber.

Conclusion RTVue FD-OCT provides accurate anterior segment parameters measurements and shows agreement wit OCT Visante.

4241
Role of gap junction proteins in primary fiber cell elongation

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Purpose During lens development, the elongation of primary fiber cells is the first crucial step after formation of the lens vesicle. According to characterized mouse mutants, this step depends on the activity of at least three genes: Maf, Pparbp and Gjf1, which we reported recently to encode a new connexin. In all these mutants, lens development is inhibited because the primary fiber cells do not elongate and the secondary fiber cells cannot form properly. The Gjf1 gene is altered in the mouse mutant Aey12 being characterized by microphthalmia, frequently associated with cataracts.

Methods To identify downstream targets of Gjf1, we performed expression profiling in Gjf1Aey12 mouse embryos at 10.5 days of development.

Results At this stage, the lens placode is beginning to form the lens vesicle and histological and morphological differences between wild-type and mutant eyes are not yet obvious. We assumed that differences in gene expression might precede the morphological Aey12 phenotype. 31 genes were identified as up-regulated. Among them, Fhod1 shows the highest level of induction; it encodes a Formin homology-2 domain encoding protein. Another interesting up-regulated gene is Rai16 (coding for the retinoic acid induced protein 16) providing a new link between lens development and retinoic acid signaling.

Conclusion Since retinoic acid was shown recently to be necessary for lens differentiation in quails (Maden et al., 2007), the analysis of our Aey12 mutant might contribute to a better understanding of the role of retinoic acid and connexins during early lens development in mammals.

4242
Cholesterol oxides, signal transduction and cell dysfunction in the lens: a bizarre love triangle

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Purpose Cholesterol oxides was implicated in the development of cataract. The purpose of this study is to elucidate the molecular mechanisms underlying cholesterol oxide-induced cell dysfunction in the lens.

Methods Lens epithelial cells (LEC) were incubated with 7-ketocholesterol (7-KC) and 25-hydroxycholesterol (25-OH). The effects of cholesterol oxides on cytoskeleton were evaluated by immunofluorescence microscopy. Activation of p38 MAPK and Akt was detected by Western Blot. LC3 processing was detected by Western Blot and immunofluorescence confocal microscopy and autophagy was assessed by the LC3 I/LC3 II ratio.

Results Cells treated with 25-OH show increased migration and formation of lamellipodia. These effects are reversed by inhibitors of PI3K and p38 MAPK. Consistently, 25-OH induces activation of Akt and p38 MAPK in LEC. On the other hand, treatment of LEC with 7-KC decreases Akt levels and up-regulates autophagy. The increase in autophagy following treatment with 7-KC is prevented by overexpressing a constitutive active Akt. Chemical inhibition of PI3K or overexpression of a dominant negative Akt also leads to stimulation of autophagy.

Conclusion 7-KC stimulates autophagy in LEC by promoting degradation of Akt and activation of mTOR. The two different cholesterol oxides (7-KC, 25-OH) have opposite effects in the regulation of Akt, resulting in increased autophagy (7-KC) and increased cell migration (25-OH). Accumulation of cholesterol oxides in lens may thus account for loss of cell transparency by interfering with cell migration and by deregulating autophagy in LEC.Supported by FCT grants POCI/SAU-MMO/57216/2004 and POCI/SAU-OBS/57772/2004.

4243
SUMOylation during nuclear degradation in lens fibre cells

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Purpose To investigate the role of SUMO (small ubiquitin-related modifier) in organelle elimination and nuclear reorganisation during lens fibre cell differentiation.

Methods Antibodies raised against the small protein modifiers SUMO were localised by indirect immunofluorescence and laser scanning confocal microscopy in cryo-sections of bovine lenses. The localisation of these antibodies was correlated with other antibodies targeted to several nuclear compartments previously shown to be rearranged during nuclear elimination in the lens (Gribbon et al. EJCB 81:557-66).

Results In the lens epithelium and most recently differentiated fibre cells SUMO is present in a single small bright (as yet undefined) compartment in the nucleus and as a diffuse, fine punctate nucleoplasmic distribution. In the nuclei of deeper fibres the SUMO becomes associated with nucleolar caps, these caps are distinct from those containing proteins from other nuclear bodies; eg. coilin from Cajal bodies. Finally in the very last intact nuclei SUMO becomes associated with the nuclear membrane, and or the lamina, and or nuclear pores.

Conclusion The post-translational modification of proteins by SUMO can have many consequences including the regulation of protein-protein interactions, inhibition of transcription and regulation of enzyme activity. SUMOylation can occur on many, both cytoplasmic and nuclear proteins but little is known about its role in cell differentiation. Interestingly in the context of lens development SUMO has been implicated in the cellular responses to hypoxia - a metabolic stress that has been suggested to be involved in lens fibre cell differentiation.

4244
New blood for hemoglobin in the lens: roles in stem cell differentiation and fibre cell organelle loss?

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Purpose Evidence is emerging for haemoglobin (Hb) expression outside the vascular system. We previously demonstrated Hb expression in the mouse lens during post-natal development and cataract progression. Here, we extended this work by carrying out a comprehensive spatio-temporal analysis of Hb subunit expression during mouse lens development and maturation.

Methods We used RT-PCR, Western blotting and immunofluorescence to analyze Hb expression in mouse eyes (E16.5 to 9 wks). We also used a sensitive heme assay to test for the presence of heme in the lens by colourimetric assay and histological staining of paraffin-embedded sections.

Results Hb subunits were expressed in lens epithelial cells and cortical lens fibre cells. However, the heme assay revealed negligible levels of this prosthetic group in the lens. Hb immunofluorescence was also observed in other regions of the developing eye including the cornea, the retinal ganglion cell layer and the retinal pigment epithelium. Finally, we also observed Hb expression in early embryos by microarray and during differentiation of embryonic stem (ES) cells into embryoid bodies (EBs) in vitro.

Conclusion These results suggest a paradigm shift: Hb subunits are expressed in the eye during development and in the adult and, therefore, may have novel roles in ocular development, physiology and pathophysiology. The absence of heme from the lens indicates that at least some of these functions may be independent of oxygen metabolism. The pattern of expression of Hb in lens epithelial cells and cortical lens fibre cells may indicate an involvement for Hb subunits in lens epithelial cell differentiation into lens fibre cells and/or lens fibre cell organelle loss.

4251

Functional correlates of abnormally increased annular fundus autofluorescence in different retinal dystrophies

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Purpose To examine the functional significance and stability of annular fundus autofluorescence (AF) abnormalities in patients with different retinal dystrophies.

Methods One hundred patients were ascertained who had a parafoveal ring of high density AF. Seventy five had a clinical diagnosis of retinitis pigmentosa (RP) or Usher syndrome with good visual acuity; 20 of 75 had serial AF imaging. Twenty five others included cases of cone or cone-rod dystrophy (GUCA1A, RPGR, RIMS1) and "cone dystrophy with supernormal rod ERG" (KCNV2). International-standard full-field and pattern ERG (PERG) testing was performed. Some patients underwent fine matrix mapping (FMM).

Results Results: a) The AF ring radius correlated positively with PERG P50 in non-syndromic RP (R=0.79, p<0.0005, N=50) and in Usher syndrome (r=0.77, p<0.0005, N=25). The ring encircled areas of preserved photopic function. Serial AF revealed progressive ring constriction in 10 of 20 cases. b) In the 25 patients with cone or cone-rod dystrophy, AF rings resembled those seen in RP or encircled areas of central atrophy. There was an inverse relationship between P50 and ring size in those with detectable PERGs. High density arcs corresponded with gradients of sensitivity change. There was evidence of AF ring expansion in some cases.

Conclusion Conclusions: Parafoveal rings of high density autofluorescence are non-specific manifestations of retinal dysfunction associated with gradients of sensitivity change. High density rings progressively constrict in a high proportion of patients with RP and good visual acuity. Progressive ring expansion may occur in different forms of cone and cone-rod dystrophy.

4252

Summary of the findings of the RLBP1 mutations affecting the visual cycle known so far with extremely prolonged dark adaptation in the RP of Bothnia type

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Purpose The retinal diseases in the RP group associated with affected recycling of retinoids in the visual cycle is now being recognized in populations worldwide. The RLBP1 mutations are here summarized and the phenotype known so far is presented.

Methods A presentation of literature in the RLBP1 mutations and the phenotype of Bothnia Dystrophy (BD) with ophthalmologic findings and full-field electroretinography (ERGs) findings after 24 hours of dark adaptation are presented.

Results The phenotype (BD) in this group is described, an early progressive maculopathy, retinitis punctata albescens (RPA) as well as peripheral retinal degenerative changes is found. An extremely prolonged dark adaptation (24h) in the BD disease is presented and the full-field ERG (24h) show the rod b-wave and the mixed rod-cone a-wave responses reached normal but delayed amplitudes in the ERGs, the increase of the oscillatory response up to normal level was found and no recovery of the cone response was found.

Conclusion The phenotypes of RLBP 1 mutations worldwide and in Sweden show similarities in the expression and may be represented by the phenotype of BD. The unique findings of extremely prolonged DA and a significant and additional capacity of recovery of rod function and activity in the inner retinal layer and a continuous but slow regeneration of rod photopigment seems to occur at least up to 24h. The visual process in the RPE is retarded but also the Müller cells of the retina seem to be involved. The findings support an extremely slow synthesis of photopigments and an irreversibly disturbed cone function early in BD.

4253

Improving the diagnostic potential of the photopic electroretinogram (ERG) with refined mathematical tools

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Purpose Examine if the use of refined mathematical tools increases the understanding and diagnostic potential of the photopic ERGs.

Methods Analyses were performed on normal and pathological photopic ERGs (background of 30 cd.m-2; flash intensities ranging from -0.8 to 2.84 log cd.sec.m-2 in 15 steps; n>100). Mathematical instruments included: 1- the Continuous Wavelet Transform (CWT)2- The Reiman Integrator and 3- the Photopic Hill Gaussian:Logistic ratio [GL=Gb/(Gb+Vbmax)]claimed to weight the contribution of the OFF and ON pathways to the photopic ERG.

Results 1- CWT revealed 3 distinct frequency domains within the 10-50 msec poststimulus time interval, namely: 20-40 Hz, 90-150 Hz and 200-300 Hz that appeared to be independently modulated by flash intensity and/or pathology. 2- Integration of the OPs accurately reconstructed the broadband ERGs (r>0.90), irrespective of CWT. 3- In our cohort of RP patients (n=50), the GL ratio was 0.43 ±0.23, compared to 0.60±0.08 in normal (p<.05).

Conclusion 1-CWT dissects the ERG into its primary components, a method that should allow a more accurate quantification of ERG responses. 2- Strong evidence supports the concept that the b-wave results from the integration of the OPs. The value of the integration constant (1 sec) is close to the time constant of the Muller cell membrane suggesting that the latter could be at the origin of this integration. 3-The broader GL distribution obtained from our RP cohort suggests that in some the OFF retinal pathway is primarily affected while in others the ON is. It remains to be determined if the latter represents two stages of the same disease process or two different disease paths. Supported by CIHR and Réseau Vision.

4254

Erg explorer: a software for post-processing, analysing, and reporting of electrophysiological data

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Purpose For clinical routine and clinical trials it is important to provide structured, consistent reports of electrophysiological data. Also, there is the need for further processing of raw data. Moreover, the connectivity to different electrophysiological systems is a major requirement. We will present a system that is capable of reading raw data, evaluate and process it, to present it in a graphical report and to make it available for data management systems or statistical software packages.

Methods The application is based on Java Enterprise Edition. Algorithms can easily be added by dropping a new plug-in into the system. Algorithms like FFT, frequency filters, curve fitting, detrending, intensity-/response-function, a-wave slope detection, and SNR estimation are implemented. The application allows a flexible design of reports based on customizable templates. Templates according for ISCEV standards are included. It also allows exporting data into different formats including Excel or CSV. Currently we are providing an interface for the Espion E2 system, interfaces for LKC UTAS and Roland Consult Reti-port are being developed.

Results The use of open source frameworks allows for easy adaptation of new algorithms for post-processing electrophysiological data, the integration of new standards, outstanding reporting features and interfaces to existing devices or applications.

Conclusion The application is successfully used in routine clinical examinations. Further features are also currently being developed, like the integration of additional electrophysiological systems and the implementation of new algorithms, e. g. wavelet analysis and noise estimation. An auxiliary accomplishment may be the establishment of a DICOM standard.

4255

Improvement of visual acuity and visual evoked patterned potentials done at different spatial frequencies after rehabilitation in 45 subjects affected by Cerebral Visual Impairment.

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Purpose To analyze improvement of visual acuity(VA) and visual evoked patterned potentials (pVEP) in children diagnosed by MR as cerebral visual impaired (CVI) after rehabilitation (refractive correction and occlusion terapy).

Methods In 45 CVI infants(mean age 5.6)we analysed VA and pVEPs improvement after 1 year of follow up. Teller Acuity Cards and/or optotype were used for decimal visual acuity. P-VEPs were recorded at Oz,O1,O2, referenced to Fz. At least two spatial frequencies (among 300',120',60',30',15').Statistical analysis were made between VA and pVEP improvement.

Results VEP and VA percentage of success was 100% and 89% respectively at the beginning; after 1 year VA percentage of success rised 100%. Mean VA before treatment was 2,29/10(0.2-10); after treatment was 3,61/10(0.1-10). VA improvement was statistically significant(z=0,00)VA improvement occurred in 68,89%, while 31,11% were unimproved. Improved VEP were 80% and unimproved 20%. We considered improved VEP when children were able to detect lower spatial frequencies or when, in the same spatial frequency, we found higher amplitudes and reduced latencies.Differences between VEP amplitude and latency were not statistically significant in all frequencies but in L60' (T-test L60':0.02).There was an association between VA improvement and therapy,(Pr = 0.02)There wasn't association (Pr = 0.76) between VEP improvement and therapy. There wasn't correlation between VA and VEP improvement.

Conclusion We found an improvement both in VA and VEP.VEP improvement is independent of therapy,VA improvement is correlated with therapy.

4256

Flash vep anomalities in infants with delayed visual maturation (dvm)

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Normally eye contact and responsive smile in infants develop within 3 to 8 weeks postnatally. Delays may be due to ocular/eye diseases, neurological conditions or have unknown etiology.The flash visual evoked potential (fVEP) shows a typical potential pattern development in infancy(Kraemer & Sjöström ISCEV 1996) reflecting maturation of the afferent visual pathways. The unspecific pathways develops first as the 'late potential', eventually forming the P1 potential. The later retino-geniculo-cortical afferents development, i.e. the specific or primary pathway, is simultaneous with the development of conscious cortical vision. It is reflected in the VEP as development of the 'N1'-potential and in behaviour as eye contact and responsive smile.We have followed infants referred to us due to lack of normal visual development. Besides traditional clinical examinations we also included fVEP and ERG examinations, preliminary first reported at ISCEV 1997 (Kraemer).The fVEP in DVM children were all pathologic at first session, except in those that had developed eye contact before visit. The main finding was lack of normal N1 potential, sometimes combined with latency increase of P1 and/or other wave form pathology. Many of the children later developed eye contact, some as late as a year postnatally, and simultaneously also a N1 potential in the fVEP. The DVM etiology most often was cerebral palsy conditions of various types and degrees, however other conditions also were found. Examples of these cases will be shown as well as possible neurophysiological explanations to the altered VEP activity.

4257

Protection of the photoreceptors in ROP (retinopathy of prematurity)

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Purpose Interventions with putative protective effects on the immature photoreceptors are part of the clinical care of preterm infants. In rat models of ROP, the early status of the photoreceptors predicts ROP outcome, and modification of the energy demands of the developing photoreceptors affects ROP outcome. In prematurely born subjects with thoroughly documented newborn care, we studied the relation of photoreceptor status and ROP outcome.

Methods Retinal function and vasculature were characterized at pre- and post-term ages. Parameters of phototransduction and of post-receptor activity were derived from ERG a- and b-waves. The integrated curvature of the arterioles was used to quantify the retinal vasculature. The main newborn interventions, including oxygen limits, were categorized.

Results In infancy, the small ERG responses reflected immaturity of the photoreceptors and differed significantly between those who developed ROP and those who did not. The higher the integrated curvature the more severe the ROP. The magnitude of the ERG abnormalities varied significantly with the severity of ROP and integrated curvature. The putatively protective clinical interventions were significantly associated with better photoreceptor function and better ROP outcome.

Conclusion Protecting the immature photoreceptors appears to improve ROP outcome. Future interventions that target the photoreceptors may prevent ROP.

■ 4261

Functional MRI of the superior colliculus in dissociated vertical deviation

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ABSTRACT NOT PROVIDED

■ 4262

Analysis of a potential new model for neurovascular coupling in retina and its relation to the retinal relaxing factor

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ABSTRACT NOT PROVIDED

■ 4263

Utility of FISH in diagnosis and therapy of ocular melanocytic lesions

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ABSTRACT NOT PROVIDED

■ 4264

Modulation of wound healing after glaucoma surgery

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ABSTRACT NOT PROVIDED

■ 4265

Anti-PLGF, a safer alternative to anti-VEGF in the treatment of AMD?

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ABSTRACT NOT PROVIDED

■ 4266

Inflammatory cytokines in the tears of patients with vascularized corneas

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ABSTRACT NOT PROVIDED

■ 4267

Cultivated stem cell transplantation for the treatment of limbal stem cell deficiency

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ABSTRACT NOT PROVIDED

4311
Pharmacological vitreous remodelling through non-enzymatic disruption of the protein matrix

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Purpose To study the impact of inhibiting lysyl oxidase enzyme on vitreous extracellular matrix (ECM) proteins. Lysyl oxidase (LO) plays a critical role in the formation and repair of the ECM by oxidizing lysine residues and initiating covalent cross-links that stabilize fibrous proteins throughout the body. The LO activity in the eye could be an important aspect of vitreous embryogenesis and aging.

Methods Eyes (E8) of chick embryos were injected with beta-aminopropionitrile (BAPN: selective inhibitor of LO) or with saline. Eyes were fixed in glutaraldehyde 2% for TEM, in paraformaldehyde 3% for immunohistochemical staining or the eyes were lysed and prepared for immunoprecipitation (coll II) followed by mass spectrometry (MS: Fourier transform,MALDI-TOF/TOF and Orbitrap).

Results Microscopy showed a homogenous collagen network in the vitreous core and dense collagen fibers in the periphery of saline treated eyes. BAPN treated eyes showed a small triangular area of collagen meshwork immediately behind the lens and scarce collagen fragments in the periphery. Immunohistochemistry revealed positive staining for opticin in the vitreous periphery and for collagen IX in the vitreous centre and periphery in saline treated eyes. Immunostaining was negative for opticin and collagen IX in the BAPN treated eyes. MS identified a dose dependant signal shift in the treated samples for opticin, decorin and collagen IX.

Conclusion Inhibiting lysyl oxidase enzyme in the embryonic chick vitreous has a disrupting impact on its ECM assembly as shown by histology. The effect of BAPN on the vitreous ultrastructure could be related to the loss of decorin, opticin and collagen IX as suggested by MS and immunohistochemistry.

4312
Regulators of angiogenesis in the vitreous

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Purpose Preretinal neovascularisation is a form of angiogenesis i.e. growth of new blood vessels (into the vitreous) from the pre-existing vessels (the retinal vasculature). The vitreous contains pro- and anti-angiogenic molecules and normally the balance favours an anti-angiogenic state. However in diseases such as proliferative diabetic retinopathy, excess pro-angiogenic molecules, e.g. VEGF, stimulate preretinal neovascularisation. Anti-angiogenic molecules identified in the vitreous to date include PEDF, thrombospondin-1 and endostatin, but their relative importance in inhibiting preretinal neovascularisation remains unclear. Here we show that an endogenous glycoprotein of the vitreous called opticin has potent anti-angiogenic properties, and provide evidence that it has a pre-eminent role in inhibiting pre-retinal neovascularisation.

Methods Opticin null mice were generated and bred onto a C57/BL6 background. The opticin null mice and wild-type mice +/- intravitreal injection with recombinant opticin (at P14) were investigated using the oxygen-induced retinopathy model (75% oxygen from P7-12, and analysis at P17 by serial histological sectioning).

Results The opticin null mice demonstrated increased preretinal neovascular nuclei per cross section (109 +/- 6 S.E) compared to wild-type controls (73 +/- 3) ($P < 0.0001$). The opticin injected wild-type eyes showed a decrease in preretinal neovascular nuclei per cross-section (38 +/- 3) compared to eyes injected with PBS alone (76 +/- 4) ($P < 0.0001$).

Conclusion Opticin inhibits preretinal neovascularisation in a dose-dependent manner. This is the first time that a knockout mouse has demonstated increased neovascularisation using this model. Opticin, or molecules derived from opticin, represent potential therapeutics.

4313
Biochemical markers in the vitreous

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Purpose Prealbumin is a 55kDa protein (transthyretin) which plays an important role in the plasma transport of retinol in complex with retinol-binding protein. It is also synthesized by the retinal pigmentepithelium (RPE) but the functional significance of ocular prealbumin is still unclear. In this study, we wanted to explore the use of prealbumin as a biochemical marker in human vitreous fluid in various conditions.

Methods Prealbumin concentration was assayed in vitreous fluid using a BN II nephelometer (Dade Behring). Cadaver eyes (n =59) served as a reference. Vitreous fluid was investigated in 64 patients where therapeutic vitrectomy was indicated: 9 eyes were operated on for retinal detachment less than 1 week old, 25 eyes for longstanding retinal detachment (more than 1 week old), another 13 for proliferative diabetic retinopathy, 17 patients had vitreoretinal retraction at the macula, and in 1 case floaterectomy was performed.

Results In the reference group, median prealbumin value was 6.0 mg/l (IQR: 2-19.8 mg/l); total protein: median 567 mg/l; IQR: 271-996 mg/l). For patients operated for retinal detachment, prealbumin values were lowest in patients with retinal detachment less than 1 week old (median: 3 mg/l, IQR: 0-12 mg/l) and highest for patients with longstanding retinal detachment (median: 17 mg/l, IQR: 1-25 mg/l)($P<0.05$).

Conclusion Prealbumin is abundant in human vitreous fluid. In pathological conditions, prealbumin values may vary. No correlation was found between prealbumin levels and total protein levels in vitreous fluid. In particular, patients with longstanding retinal detachment showed highest prealbumin values. This might be due to increased synthesis of prealbumin by RPE cells. Prealbumin concentrations in the vitreous may be used as a marker for retinal dysfunction.

4314
Enzymatic vitreolysis promises and potential pitfalls

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ABSTRACT NOT PROVIDED

■ 4315

Micro Incisional Vitrectomy (MIVS): a new device for trocar insertion

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Purpose Despite its clinical advantages, MIVS poses significant challenges in performing airtight incisions especially dealing with 23-gauge system. Aim of this paper was to assess the feasibility of performing 23-g MIVS using an injector system for trocar insertion.

Methods 60 consecutive eyes of 56 patients underwent 23-g pp vitrectomy and gas endotamponade for the treatment of Regmatogenous Retinal detachment and Diabetic Prolipherative Retinopathy by the same surgeon (SD). 30 eyes were operated on with standard one-step 23-g and 30 using a prototype of injector holding the same 23-g trocar cannula system. The trocar squeezed into the plunger of the injector. The device had a metallic terminal oriented with a fix angle, allowing the insertion in the settled direction, able to fix the globe and displace the conjunctiva at the same time.Main outcome measure were sclerotomies airtightness, surgical time and complications.

Results In the 30 eyes operated with the 23-g ones step system 9 sclerotomies were sutured, in 5 refilling was required. Mean surgical time were 54 minutes. In the 30 eyes operated with the new device, the inserter was easy to apply in all cases and was useful especially in the nasal quadrant. Also dealing with sunken eyes the inclination of the system 5-10° tangential to the sclera was easily achieved. No suture was placed, refilling was needed in 3 cases. Mean surgical time was 45 minutes. No complications due to these device were highlighted.

Conclusion The new injector was safe and effective. The device facilitates the insertion manoeuvre allowing easier and quicker trocar positioning helping the airtight wound construction. MIVS success lie in the surgeon's skill but also in the development of the technology and instrumentations.

▪ 4321
The ophthalmological approach

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Purpose Patients with unvoluntary eye movements frequently consult an ophthalmologist. A correct diagnosis of the type and etiology is important.

Methods A clinical approach with selected technical examinations is mandatory for a correct diagnostic approach.

Results Isolated ophthalmological and combined neurological elements can be identified to guide the further approach.

Conclusion A practical work-up of a patient presenting with nystagmus will be presented. Frequently the collaboration with the neurologist is important.

▪ 4322
Genetic determinants of abnormal eye movements

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Purpose To describe the phenotypes and genotypes of genetically determined disease leading to nystagmus.

Methods A case presentation format will be used to illustrate different genetically determined conditions leading to nystagmus. Both clinical and electrophysiological phenotypes as well as genotypes will be discussed.

Results Phenotypes and genotypes of genetically determined nystagmus are very different. An important distinction to be made is the one between stationary and progressive diseases. Indeed, such distinction is important as the visual outcome varies considerably between those different conditions.

Conclusion Very diverse conditions may give rise to genetically determined nystagmus. Genetics and visual electrophysiology allows an important distinction between progressive and stationary conditions.

▪ 4323
The neurological approach to ocular instability

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Purpose Several neurological conditions can cause acquired instable eyes, nystagmus being certainly the most common finding in this setting.

Methods Nystagmus is an involuntary repetitive to-and-fro movement of the eyes, initiated by a slow ocular drift. The slow phase can be followed by a rapid return (in jerk nystagmus) or a repetitive slow phase only (pendular nystagmus).

Results A simple diagnostic algorithm of neurological nystagmus and other causes of ocular instability will be presented.

Conclusion Neurological nystagmus is only one of the aspects of acquired instable fixation. A precise clinical description of nystagmus is conditioning the subsequent diagnostic and management algorithm.

▪ 4324
The role of electrophysiology

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ABSTRACT NOT PROVIDED

4331
Zonal differentiation of the epithelium including the lid wiper at the human lid margin

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Purpose The lid margin represent the "other end" of the tear film and appear critically important for ocular surface integrity, in addition to the glandular structures that produce the tears. It guarantees the thin expansion of the tear film with every blink and prevents the leakage of tears over the lid border. However, the differentiation of the lid margin zones is insufficiently known as yet.

Methods The upper and lower lid margin in human whole-mount specimens from ten body donors was investigated in serial section histology and compared to the image by in-vivo confocal microscopy in four eyes with a Heidelberg retina tomograph and Rostock cornea module (RLSM).

Results At the inner lid border, following the keratinised epidermis of the free lid margin, a narrow zone (100-150µm) of para-keratinised squamous epithelium represented the muco-cutaneous junction (MCJ) corresponding to the line of Marx. This was followed by a much broader zone of epithelial thickening (50-100µm) that formed a kind of cushion, reclined sharply at the inner lid border and represented the so called lid wiper which extended for about 1mm and finally transformed into the epithelium of the sub-tarsal fold. MCJ and lid wiper extended all along the lid margin from nasal to temporal in upper and lower lid. Details of the epithelial structure as well as the underlying dermal papillae in these zones were also detectable by RLSM.

Conclusion Due to its location and structure, the lid wiper appears as the structure that actually spreads the tear film and is distinct from the MCJ/line of Marx. Better knowledge of the lid margin structure and its different zones appears important for the understanding of ocular surface disease, in particular the dry eye disease.

4332
Structure of the lid margin in laboratory animals

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Purpose The eye lid margin is of great importance for the spreading and the limitation of the tears. The so called lid wiper which is a specialized zone at the inner lid border directly apposed to the corneal surface for spreading the preocular tear film has, at present, only been described for the human conjunctiva. We have investigated common laboratory animals (rat and rabbit) for the presence of such a zone.

Methods Conjunctival whole-mount specimens and total bulbi were investigated by serial section histology in ten rats (DA and Lewis) and in ten rabbits (NZW and Chinchilla).

Results The stratified squamous keratinised epidermis of the free lid margin showed a sharp transition with loss of the keratin layer at the level of the meibomian glands. Close to the inner lid border it was replaced by a small zone of an optically denser epithelium covered by para-keratinised cells. This area represented the mucocutaneous junction (MCJ) equivalent to the line of Marx in the human.The MCJ rapidly transformed into a thickened 8-12 cell layered stratified epithelium of that formed a cushion-like epithelial elevation, reclined sharply towards the inner lid border and hence formed a typically relatively sharp lip-like edge. The lid-wiper epithelium showed species-specific differences in morphology (cuboidal with goblet cells in the rabbit versus squamous without goblet cells in the rat) but it extended all along the lid margin in both species.

Conclusion At the inner border of the upper and lower lid of rat and rabbit, several zones of different morphology occur similar to the human including a lid-wiper structure. Since lid wiper epitheliopathy was shown as a sensitive early indicator for human dry eye syndrome its investigation may be useful for future research in dry eye models of laboratory animals.

4333
Compartmental factors influencing tear film osmolarity

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Purpose To illustrate how compartmental factors could influence the distribution of tear osmolarity at the ocular surface in normals and dry eye.

Methods Mathematical modelling using parameters in the literature.

Results Tear film hyperosmolarity is a final common pathway causing ocular surface damage in dry eye. Modelling predicts that tear osmolarity is higher in the tear film than the meniscus, which may influence the distribution of ocular surface damage and the initiation of symptoms caused by hyperosmolarity. Once tear film break up occurs within the blink interval it is likely that this differential is amplified locally. The model allows the effect of compartmental factors on tear osmolarity to be addressed, including: regional differences in air flow and surface temperature, variations in ambient temperature and humidity, imperfect tear mixing, differential corneal and conjunctival exposure and individual differences in reflex tear flow, evaporation rate and blink interval. We hypothesise that interactions between these factors determine the dry eye phenotype in an individual. Additional considerations suggest that events at the ocular surface differ in aqueous-deficient and evaporative dry eye.

Conclusion Hyperosmolarity at the ocular surface is affected by multiple factors, each of which may make different contributions to distribution and severity of surface damage in a given individual. This may determine the phenotype, frequency and severity of dry eye in a population.

4334
Lid wiper epitheliopathy, ocular surface and tear film in symptomatic contact lens wearers

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Purpose Lid wiper epitheliopathy (LWE) as well as lid parallel conjunctival folds (LIPCOF) are related to dry eye symptoms in contact lens weares and are thought to be caused by mechanical forces during blinking. This study investigates whether any correlations are detectable between LWE and LIPCOF and the ocular surface and tear film in soft contact lens wearers.

Methods 38 subjects were classified asymptomatic and 23 symptomatic by the Contact Lens Dry Eye Questionnaire. Pre-lens break-up time, ocular hyperaemia, corneal staining, LWE and LIPCOF were assessed in the right eyes of 61 (23 males, 38 females; mean age = 32.1 ±11.4yrs) experienced lens wearers. Pre-ocular fluid was sampled using Schirmer strips pressed onto the temporal conjunctiva, and from harvested contact lenses. Mucins were assessed in dot-blots and in Western blots after electrophoresis on 1% agarose or 4-12% NuPAGE Gels.

Results LWE and LIPCOF were significantly increased in the symptomatic group ($p<0.03$). Significant correlations were found between LWE and both temporal LIPCOF ($r=0.67$, $p<0.001$), and nasal LIPCOF ($r=0.39$, $p<0.001$), and between LWE and bulbar hyperaemia ($r=0.28$, $p<0.001$). MUC5AC reactivity was significantly decreased in symptomatics ($p=0.050$). MUC4 was negatively correlated to temporal LIPCOF and LWE ($r=-0.47$ and -0.46; $p<0.01$), MUC16 and MUC5AC correlated with corneal staining ($0.36<r<0.53$;$p<0.04$)

Conclusion Symptomatic contact lens wearers exhibit significantly more LWE and LIPCOF, and decreased MUC5AC reactivity. Decreased mucins are associated with LWE and LIPCOF severity. Correlations between LWE and LIPCOF may reflect their common frictional origin. Increased friction might follow from insufficient mucins at the ocular surface.

■ 4335

New surgical techniques for reconstruction of the lid margin

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The lid margins are extremely important to the health of the ocular surface. They play a major role in the distribution of the tear film over the eye. It is therefore important that disease of the eyelid margins be controlled before significant scarring of the ocular surface occurs. Two or three rows of eyelashes are present in the upper eyelid margin and one or two rows of eyelashes in the lower one. The tarsal plates include the meibomian glands. The objectives of eyelid margin surgery are both functional and cosmetic.Structural eyelid margin defects should be corrected with surgical techniques that return the anatomy to as close to normal as possible. Upper eyelashes should be preserved during the surgical procedures because defects of eyelashes in the upper eyelid are very visible. Restoring normal three dimensional anatomy (good lid contour, continuity of the lashes, etc) allows the eyelid margins to keep their functions for ocular surface protection and tear film distribution and gives optimal cosmetic result. In the time we will have in this session, we will seek to focus on the up to date surgical techniques that can be employed to correct inherited or acquired eyelid margin structural defects.

4341
Genetic epidemiology in age-related cataract research

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Purpose Age-related cataracts are the major cause of blindness worldwide. However, the contribution of genetics to their etiology is largely unknown. In contrast, the congenital and juvenile forms of cataracts are mainly caused by de-novo or hereditary mutations leading to severe changes in the structure and/or function of the corresponding proteins – as it is obvious from the dominant mode of inheritance of most of the mutations.In addition to rare mutations, these cataract-causing genes have also polymorphic sites in their regulatory and coding sequences (single nucleotide polymorphisms, SNPs); they might contribute to minor changes in the structure and/or function of the corresponding proteins. These alterations could be cataractogenic per se (in a mild form) or they might lead to an increased sensitivity of the proteins to environmental stress.

Methods In a new population-based study in Augsburg (Germany), which will be finished in summer 2008, ~3000 probands have been asked for cataracts; the answers are being validated and further specified by the treating ophthalmologists.

Results 16 SNPs from known cataract causing genes (coding for crystallins, connexins and transcription factors) have been identified to be informative without violation of the Hardy-Weinberg equilibrium. They will be tested with respect to their association with age-related cataracts by logistic regression allowing for adjustment with respect to age, gender and other confounding effects.

Conclusion The results will be presented and discussed.

4342
Genetics in exfoliation syndrome and age-related cataract

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Purpose To describe the recent discovery of the association of Lysyl Oxidase Like 1 (LOXL1) gene polymorphisms with exfoliation syndrome as well as similar study on age-related cataract.

Methods For phenotyping of exfoliation syndrome (XFS) and exfoliation glaucoma (XFG) peripheral band and/or central shield of exfoliative material on the anterior lens capsule was required and in case of glaucoma glaucomatous optic neuropathy. For phenotyping we excluded all exfoliation suspects. The phenotyping of cataract included cortical and nuclear cataract by type and grade using the Japanese Co-operative Cataract Epidemiology Study Group system. Our genome wide association study on open angle glaucoma included XFG. For both studies we used the Illumina 300 chip including over 300,000 single – nucleotide polymorphisms (SNP´s).

Results When we had done 195 open angle glaucoma cases high genome wide significance was achieved on chromosome 15q24.1 in the LOXL 1 gene, later identified to be confined to XFG only. Combined, the identified DNA sequence variants explained 99% of the population attributable risk for exfoliation glaucoma. Having done 234 cases of age-related cataract we still have not achieved a high genome wide significance although there was a modest signal associated with the LOXL1 polymorphisms.

Conclusion Exfoliation glaucoma and age-related cataract have in twin studies both been found to have strong hereditary components. We did discover a major genetic risk factor for XFG/XFS, have however, so far, been unable to identify a highly significant single nucleotide polymorphism for age-related cataract. The risk factors for cataract may include many modest genetic risk factors together with environmental risk factors.

4343
Genetic epidemiology studies of cataract in a population-based biobank

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Purpose To describe genetic epidemiology studies of cataract in the Marshfield Clinic Personalized Medicine Research Project (PMRP)

Methods The PMRP is the largest population-based biobank in the US. Nearly 20,000 adults aged 18 years and older have participated, with stored DNA, plasma and serum samples, and access to the Marshfield Clinic medical records. Subjects complete a brief questionniare that includes questions about smoking and alcohol intake. Height and weight are measured and body mass index is calculated. A candidate gene study of age-related cataract has been completed and a genome-wide association study (GWAS) of age-related cataract is currently underway. Cataract cases are identified through diagnostic codes for cataract and procedure codes for lens extraction. Exclusionary diagnoses and procedures include congenital cataract, after-cataract, traumatic cataract and steroid-induced cataract. Controls are identified by the absence of any of the inclusion diagnoses and procedures in the context of an eye exam in subjects aged 50 years and older in the previous five years. Cataract location (cortical, nuclear, PSC) is identified through manual chart abstraction and natural language processing of dictated notes.

Results In the candidate gene study of 1618 cataract surgery cases and 495 controls aged 60+, a SNP in the CRYGB gene proposed for study by Dr. Jochen Gray was found to be significantly associated with cataract surgery for females only. Electronic algorithms to accurately identify cases and controls for the GWAS study will be presented.

Conclusion It is possible to conduct scientifically rigorous genetic epdiemiology studies of cataract in the context of a group medical practice. Care needs to be taken to accurately classify case and control status.

4344
Risk factors for cataract in India: the INDEYE study

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Purpose To describe the prevalence of lens opacities and to assess risk factors in older people in India.

Methods People aged 60 years and older identified using random cluster-sampling in 2 study centres in north and south India, attended an eye examination. Digital images of lens opacities were graded using the Lens Opacity Classification System III. To identify lifestyle and environmental factors associated with lens opacities, assessment of different potential risk factors was performed, with a focus on cooking fuels, tobacco and alcohol use, sunlight exposure, diet and antioxidant blood levels.

Results 2821 people in north India and 3079 in south India attended an eye examination. The prevalence of any cataract was 73.6% and similar in the two centres (p=0.2). Type of cataract differed in prevalence between the centres: nuclear 60.0% in north India, 48.0% in south India; posterior subcapsular 26.5% in north India, 21.7% in south India; cortical 9.6% in north India and 12.8 % in south India. Prevalence of any cataract rose with age (54.9%, age group 60-64 years; 90.3%, age group 70 years and older, p<0.001) and was higher in women than in men (76.7%, women; 70.1%, men, p<0.001). Similar patterns with age and gender were observed for each type of cataract.Among risk factors, tobacco use, exposure to cooking fuels and antioxidants levels were significantly associated with cataract (p<0.001).

Conclusion Cataract prevalence, especially posterior subcapsular cataract, is very high in older Indians compared to comparable age groups in western populations.Factors as tobacco use, exposure to cooking fuels and low antioxidant blood levels may in part explain the high prevalence of cataract in this population.

■ 4345

Multivitamin-mineral supplementation and age-related cataract. The Italian-American controlled clinical trial

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Purpose To evaluate if a multivitamin-mineral supplement at RDI dosage can prevent incidence and progression of age-related cataract.

Methods Randomized, double blind, single centre clinical trial. 1020 participants of Italian descent living in Parma, 55 to 75 years old, were assigned to placebo or to a daily tablet of Centrum. Lens status was assessed at baseline and at yearly follow-up visits by lens photography.Primary outcome was a prespecified increase from baseline in N, C, or PSC opacity grades or cataract surgery. Secondary outcomes were increase in type-specific opacity grades, cataract surgery, and visual acuity loss > 15 letters.

Results After an average follow-up of 9 +- 2.4 years there was a decrease in total lens events in participants assigned to Centrum (HR 0.82, 95% CI 0.68-0.98, P = 0.03). Nuclear events were significantly less common (HR 0.66, 95% CI 0.50-0.88, P = 0.004) and PSC events significantly more common (HR 2.00, 95% CI 1.35-2.98, P =< 0.001) in participants taking Centrum. No statistically significant treatment effects were seen for cortical opacities, moderate visual acuity loss, or cataract surgery.

Conclusion Lens events were less common in participants who took Centrum, but treatment had opposite effects on the development or progression of N and PSC opacities. This and the absence of effect on a functional outcome does not allow us to recommend the use of RDI nutritional supplement to affect the risk of cataract development (Ophthalmology 115;599,2008).

4351
Mathematical models of intraocular pressure measurements and ocular rigidity

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The term ocular rigidity is widely used in ophthalmology. Generally it is assumed as a measurable physical parameter related to biomechanical properties of the whole eye globe. Formulas for clinical tonometry and tonography methods include the concept of ocular rigidity. Unfortunately ocular rigidity represents an elusive concept that means many things to many people. First of all, there is no consensual view on ocular rigidity in ophthalmology. The most of the formulas for ocular rigidity are based on discrete or continuous tonometric measurements in living or enucleated human eyes. Surprisingly ocular rigidity is measured in different units and has a different meaning by different authors.Finally, there is no clear consent between biomechanical engineers and ophthalmologists on the concept of ocular rigidity. In biomechanics parameters for the elasticity and viscoelasticity are accepted, which represent mechanical properties of a tissue an can consider its morphology. These are for example: Young's moduli of the sclera, Poisson's ratios of the cornea etc. Ophthalmological concepts on ocular rigidity are based on the consideration, that biomechanical properties of the corneoscleral shell are involved in the pressure-volume relationship of the eye globe. Ocular rigidity defined in such a way climes to describe the total response of the eye without detailed considerations on its morphologic and material properties. In the proposed review several formulations of ocular rigidity are analysed and classified. It is attempted to link these conceptions with each other.

4352
Ocular rigidity and hydrodynamics of the human eye

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Purpose The intraocular pressure (IOP) is the primary mechanical load to several ocular structures. It fluctuates over time as a result of a dynamic equilibrium between the systems of aqueous and blood flow. The purpose of this study is to characterize the eye's pressure volume relationship and quantify hydro and haemodynamic parameters in the living human eye.

Methods An invasive manometric dynamic measurement procedure was developed and used in a series of healthy and pathological eyes measured intraoperatively before cataract surgery. Different measurement protocols involving injection of predetermined doses of saline and monitoring the IOP in a time-resolved manner, allow the measurement of ocular rigidity, outflow facility and pulsatile ocular blood flow. In addition, a new non-invasive ultrasound based technique enabled us to visualize and define the elastic properties of the ocular globe and periocular structures.

Results Measurements in humans indicate that the above techniques are safe and effective. A non-linear pressure-volume relationship is established. The ocular pulse amplitude (and therefore pulsatile ocular blood flow) is shown to correlate with IOP.

Conclusion A model that incorporates ocular rigidity is proposed in order to describe and quantify the relationship between hydrodynamic and hemodynamic parameters of the human eye. These measurements along with the use of new non invasive techniques may improve our understanding of the relationship between these parameters and their significance in health and disease.

4353
Biomechanics of the eye tunic, especially the sclera and the cornea

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Purpose The biomechanics of the cornea is not only important for IOP-measurement but also for the outcome of refractive surgery. In recent studies, a thin cornea was also identified as an independent risk factor for the onset and progression of glaucoma. Besides, the rigidity of the sclera was proposed to play an important role in glaucoma and myopia.

Methods An overview of biomechanical properties of the cornea and the sclera, based on own research results and on recent literature references, was performed.

Results A stiffer cornea led to an overestimation of true IOP measured by applanation tonometry. The stiffness of the cornea increased by age compared to a decreasing corneal thickness. The Ocular Response Analyzer (ORA) measures the viscosity of the cornea. Paradoxically, ORA measurement revealed a reduction of corneal hysteresis with age which may indicate that corneal hysteresis is not equal to stiffness. In glaucoma the scleral and corneal rigidity increased in contrast to a reduced corneal hysteresis (CH) which may indicate that a damping effect of these tissues is reduced in glaucoma patients. Conversely, a more flexible and distensible sclera, lamina cribrosa and cornea were proposed to be beneficial to protect against experimentally induced IOP-spikes.

Conclusion A biomechanical concept of the eye tunic (cornea, sclera and lamina cribrosa) may further help to explain the relationship between IOP measurements, refractive surgery and glaucoma.

4354
Assessment of ocular responce analyzer advantages for IOP measurements in children with progressive myopia

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Purpose To study IOP in children with progressive myopia and myopic adults 4-9 years after photorefractive keratectomy (PRK) using ORA (Reichert) and to assess the influence of corneoscleral biomechanics on IOP measurement results.

Methods Corneal-compensated IOP (IOPcc), corneal hysteresis (CH), factor of corneal resistivity (FCR), IOP by Goldman (IOPG), corneal thickness and axial length were measured in 34 children (75 eyes) with low (27 eyes), moderate (31 eyes) and high (17 eyes) progressive myopia and 8 patients (16 eyes) with emmetropia or low hyperopia aged 7-17, and 17 adults (28 eyes) with moderate and high myopia 6.5±0.2 years after PRK and 8 adults (16 eyes) of the same age (36.6±2.0 years) and myopia degree who had no refractive surgery.

Results An insignificant (within the age norm) relative increase of IOPcc has been detected in children with moderate (17.6±0.7 mmHg) and high myopia (17.8±0.8 mmHg) as compared with low myopia (16.4±0.6). Values of IOPcc seem to provide a more exact reflection of the ophthalmic tonus in myopic eyes than IOPG. CH proved to be lower in moderate (10.9±0.3 mmHg) and high myopia (10.7±0.4 mmHg) than in low myopia (11.2±0.3 mmHg) and emmetropia (12.4±0.7 mmHg), while FCR remains practically unchanged. So, CH is related to biomechanical properties of sclera. In the late period after PRK, IOPcc (14.9±0.4 mmHg) and FCR (8.9±0.2 mmHg) are lower than without refractive surgery (resp. 18.4±0.8 and 10.5±0.4 mmHg), while CH shows an identical drop in both cases (resp. 9.4±0.2 and 9.8±0.4 mmHg) compared to norm, which testifies to surgically induced biomechanical changes of the cornea.

Conclusion ORA reduces the impact of corneoscleral biomechanical properties on IOP measurements.

4355

The estimation of intraocular pressure after refractive surgery. Statistical and simulation data

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Purpose To estimate the change in intraocular pressure (IOP) measured by either Maklakov tonometer or by Goldmann tonometer after refractive surgery for myopia and hypermetropia. In contrast to Goldmann tonometer, which measures the IOP by estimating the force needed to apply for prescribed deformation of the cornea, with Maklakov tonometer IOP is measured by estimating the diameter of the circular contact area of the cornea and the flat bottom of a tonometer.

Methods Numerical simulations have been carried out using finite element package ANSYS. The eye shell is modeled as two joint shells (cornea and sclera) with different mechanical properties. The results of mechanical simulation and statistical data were compared. For statistics the measurements of IOP were made for both eyes of 110 patients before and one month after corneal refractive surgery

Results Applanation tonometry after refractive surgery for both myopia and hypermetropia shows reduction of IOP, since in both cases the bending stiffness of the cornea decreases. For some parameters of refractive surgery for myopia (with decreasing corneal thickness less than 0.1 mm) the reduction of IOP is correlated with central corneal thickness. But in general the current model predicts nonlinear relations between new central corneal thickness and IOP reading

Conclusion All parameters of refractive surgery (the depth, the width and the place of ablation, the thickness of flap for Lasik surgery) have an effect on IOP reading obtained with both Goldmann and Maklakov tonometry. The results obtained by Goldmann tonometer are significantly more sensitive to all parameters of refractive surgery than those found with the Maklakov tonometer with load 10 g.

4356

The mechanical response of lamina cribrosa to the elevated intraocular pressure

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Purpose To consider the different mechanical aspects of the development of glaucomatous atrophy of the optic nerve fibres.

Methods The Lamina Cribrosa (LC) is modelled as a continuous anisotropic plate with radial and angular nonuniformity.The solutions for LC with different degrees of nonuniformity can help reveal the structure of the LC, for which the glaucomatous damage is most probable to develop. In the second model, LC is assumed to be of multilayer shell of revolution with elastic ties between the layers.The varying of the LC strain of the optic nerve disk after decompression surgeries due to a dissection of the sclera channel paries is analyzed.The nonlinear shell theory is used to analyze deformations of the LC.

Results The calculations of the stresses and deformations in the LC show that the shear deformation of the vertical element of the LC could cause the atrophy of the optic nerve fibres.Buckling in the nonaxisymmetric state in the neighborhood of the edge could also cause edemas at the periphery of the LC and the atrophy of the optic nerve fibres.It is shown, that after decompression surgeries the shape of the LC deflection becomes more shallow, its relative value decreases, as a result of the sclera refinement. However the absolute LC deflection increases.

Conclusion All considered models confirm the mechanical genesis of glaucoma and help to evaluate the deflection of LC in normal state and after decompression surgeries.

■ 4361
The EBO heritage: past, present and ... Concordia

KIVELÄ T
Helsinki

ABSTRACT NOT PROVIDED

■ 4362
The role of supranational societies in education

SPIVEY B
San Fransisco

ABSTRACT NOT PROVIDED

■ 4363
Future strategies of EBO

HAWLINA M
Ljubljana

ABSTRACT NOT PROVIDED

■ 4364
New strategies of SOE uniting the european national societies

SEREGARD S
Stockholm

ABSTRACT NOT PROVIDED

■ 4365

European network on education in ophthalmology

TASSIGNON MJ
Antwerp

ABSTRACT NOT PROVIDED

▪ 4411
Towards a blood test for diabetic retinopathy

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Purpose Diabetic retinopathy (DR) is the leading cause of blindness among adults of working age in the UK. Early detection and appropriate management can prevent severe visual loss in 95% of cases. However, current screening methods are costly and suffer from subjective grading. Nucleic acids have been shown to circulate in plasma, with levels raised in conditions of cell death such as cancer and trauma. This study aimed to quantify circulatory retinal-specific nucleic acids, and to evaluate potential for their use in the assessment of DR.

Methods Diabetic patients (n = 106) and healthy controls (n = 24) were recruited from the Diabetes and Ophthalmology departments at St Thomas' Hospital. RNA was extracted from whole blood, with quantitative real-time RT-PCR used to quantify mRNA levels for rhodopsin and RPE65, two proteins expressed exclusively in the retina. Beta-actin mRNA was used for normalisation.

Results Rhodopsin, RPE65 and beta-actin mRNA were detected in 100% of subjects. Circulating rhodopsin and RPE65 mRNA levels were higher in diabetic patients than healthy individuals ($p < 0.02$). Circulating rhodopsin mRNA was raised in all DR groups compared to healthy individuals, irrespective of presence or severity of DR ($p < 0.02$). With respect to healthy controls, circulating RPE65 mRNA levels were higher in diabetic patients with background and proliferative DR ($p < 0.02$). Patients with active proliferative DR (neovascularisation, vitreous and pre-retinal haemorrhage, or retinal detachment) possessed higher RPE65 mRNA and lower rhodopsin mRNA levels than those with quiescent disease ($p < 0.01$).

Conclusion There is significant potential for use of these markers to screen for the presence of DR in diabetic patients in a quantitative manner using a blood test.

▪ 4412
Autofluorescence and microperimetry in clinically significant diabetic macular edema

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Purpose Clinically significant diabetic macular edema (CSME) shows variable retinal structural and functional impairment. The aim of this study was to assess the correlation between different macular parameters, mainly fundus autofluorescence (FAF) and macular sensitivity, in diabetics with CSME.

Methods Sixty diabetic patients with untreated CSME (104 eyes) underwent: best corrected visual acuity determination (BCVA, logMAR), slit lamp biomicroscopy, fluorescein angiography, OCT, FAF and microperimetry.

Results Thirty eyes had normal FAF , whereas 74 increased (IFAF) pattern. Retinal sensitivity over areas with IFAF was significantly lower than over areas with normal FAF ($p<0.001$). Cystoid OCT-pattern correlated to both presence and dimension of IFAF ($p<0.05$), whereas sponge-like and subfoveal neuroretinal detachment did not. BCVA did not correlate either to FAF pattern or area of IFAF.

Conclusion Functional impact of CSME correlate with IFAF and is better determined with macular microperimetry rather than VA. Increased FAF seems to be a relevant characteristic of cystoid CSME. New structural and functional parameters should be used to better predict the prognosis of (treated and untreated) eyes affected by CSME.

▪ 4413
Segmentation of spectral domain OCT volume scans of patients with no or minimal diabetic retinopathy

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Purpose A comparison of thickness measurements of segmented spectral domain optical coherence tomography (OCT) derived topographic maps of patients with no or minimal diabetic retinopathy (DR) versus healthy controls.

Methods Ninety-nine patients, 44 with type 1 DM, and 36 with type 2 DM, with no or minimal DR underwent full ophthalmic examination, fundus photography and spectral domain OCT (3D OCT-1000, Topcon). Following automated segmentation the mean thickness was calculated for 6 layers: 1/ Retinal Nerve Fibre Layer (RNFL), 2/ Ganglioncell layer (GCL) + Inner Plexiform Layer (IPL), 3/ Inner Nuclear Layer, 4/ Outer Plexiform Layer, 5/ Outer Nuclear Layer + Inner Segments (photoreceptor), 6/ Outer Segments (photoreceptor), in the ETDRS defined regions of the macula and compared to 76 age and sex matched healthy controls.

Results The total retinal thickness in the diabetic patients was reduced compared to the healthy controls. In the diabetic patients both the mean RNFL and the mean OPL were significantly ($p<0.05$) thinner.

Conclusion The decreased total retinal thickness in diabetic patients with no or minimal retinopathy may be due to a selective loss of thickness in several retinal layers and supports the concept of early DR as a neuro-degenerative disease.

▪ 4414
Risk markers for progression of mild nonproliferative retinopathy to clinically significant macular edema in type 2 diabetic patients

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Purpose To determine risk markers for the development of clinically significant macular edema (CSME) needing photocoagulation treatment in type 2 diabetic patients with mild nonproliferative retinopathy (NPDR), during a 7-year period.

Methods Fifty-one type 2 diabetic patients with mild NPDR, followed-up for 2 years as controls of diabetic retinopathy clinical trials, were selected. Patients underwent ophthalmological examinations every 6 months, including stereoscopic color fundus photography, fluorescein angiography and vitreous fluorophotometry, and were metabolically controlled. These patients were thereafter followed-up for the next 5 years by conventional general and ophthalmological care.

Results At the end of the 7-year follow-up period, 8 patients developed CSME, needing photocoagulation treatment. These patients presented a higher microaneurysm (MA) formation rate at the first year of follow-up ($p<0.001$), a higher blood-retinal barrier (BRB) permeability value ($p=0.042$), an abnormal foveal avascular zone (FAZ) contour on fluorescein angiography ($p=0.009$) and a higher HbA1C level at baseline ($p=0.001$).

Conclusion Microaneurysm formation rate higher or equal to 3 MA/year, BRB permeability values over or equal to 4.0 nm.s-1, evidence of abnormalities in the FAZ, and hemoglobin A1C levels at baseline, are risk markers for progression of NPDR to CSME in patients with type 2 diabetes.

▪ 4415

Screening diabetic retinopathy using a wide field imaging system

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Purpose The wide field (200°) imaging system (Optos, Great Britain) using a scanning laser ophthalmoscope (SLO) enables to visualize a large part of the retina including the periphery. The present study was designed to evaluate the imaging system for screening purposes in diabetic retinopathy.

Methods The SLO system was used in diabetic patients in stationary care. Screening for diabetic retinopathy was performed: An undilated and dilated retinal biomicroscopy was performed by a senior ophtalmologist. An undilated SLO image was taken by an orthoptist in training. The images were reviewed by a resident masked to results of the previous retinal biomicroscopy. The results of the clinical examination were compared with the results of the SLO image analysis.

Results A total of 251 patients were evaluated (n=503 eyes). Of the retinal lesions detected on the undilated SLO images, the undilated retinal biomicroscopy missed 24% and the dilated retinal biomicroscopy 11%. None of the retinal lesions detected with the undilated retinal biomicroscopy were missed on the SLO images.

Conclusion The diagnostic rate of diabetic retinopathy using undilated SLO images was significantly higher when compared with the diagnostic rate of undilated and dilated retinal biomicroscopy. Further work is necessary to evaluate the diagnostic yield of the wide field SLO system in comparison with standard non mydriatic retinography procedures.

▪ 4416

Is diabetic retinopathy an inflammatory, oxidative stress, genetic, mediated process ?

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Purpose Diabetic Retinopathy (DR)neurovascular degenerative process of systemic disease is one of the main causes of blindness in adults(20-70 years).Multifactor machanisms with growing evidence of hyperglycaemia induced inflammation and oxidative stress with genetic influence can lead to retinal cell apoptosis in early STZ diabetic rats. Expression of inflammation and oxidative stress markers and their genetic phenotypes in diabetics under treatment and in controls were studied.

Methods Transmembrane Reductase (TMR), Erythropoeitin (EPO) activity and Haptoglobin (Hp) genotypes were determined in 60 type 2 diabetics, 26 with and 34 without retinopathy (mean age 64.2 ±11.64 years) of both sexes and in 44 non diabetic controls. TMR (mmol/l cell/h) was determined by spectophotometry, EPO(mIu/ml) by ELISA and Hp genetic phenotypes using polyachrilamide gel electrophoresis. Student t test, ANOVA,χ2 and Pearson correlation was used.

Results TMR activity was high in retinopathy subjects (5.29 ± 2.11 vs 4.11 ± 1.51 in controls p=0.016). EPO serum levels were high in retinopathy patients (15.15 ± 11.14 vs 9.47 ± 6.57 in controls p=0.043).Hp 2.2 allele genotype predominance in diabetics with retinopathy (40.9%).Hp 2.1 genotype higher incidence in diabetics without retinopathy (70.6%) p=0.028).

Conclusion High inflammatory/oxidative activity expressed by TMR,EPO,Hp and other markers in diabetic retinopathy,supports our hypothesis. EPO has also antiapoptotic, cell regenerative angiogenic properties. Its up-regulation in retinopathy could be endogenous auto-protective mechanism.

▪ 4417

Enhanced levels of VEGF and reduced levels of VEGFxxxb in the vitreous of patients with retinal vein occlusion

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Purpose To investigate the role of VEGF and VEGFxxxb in the pathogenesis of Central Retinal Vein Occlusion (CRVO) and Branch Retinal Vein Occlusion (BRVO).

Methods In a cross sectional study we analyzed the vitreous of patients with CRVO (ischemic and non-ischemic) and BRVO. A group of patients with vitrectomy not due to CRVO/BRVO served as control. The vitreous of 25 patients with CRVO, of 28 patients with BRVO and of 32 patients with no sign of CRVO/BRVO were analyzed using ELISA for VEGF and VEGFxxxb.

Results The ratio CRVO/controls for VEGF was 5.5, and 2.5 in BRVO/controls. In comparison the VEGFxxxb ratio in CRVO/controls was 0.19, and 0.85 in BRVO/controls.

Conclusion Total VEGF levels in patients with CRVO and BRVO are significantly upregulated compared to controls. The finding of a significantly down-regulated antiangiogenic VEGFxxxb in patients with CRVO is similar to the altered balance of the splice variants found in vitreous samples of patients with proliferative diabetic retinopathy.

4421

Driving performance in patients with homonymous visual field defects and healthy subjects in a standardized virtual reality environment

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Purpose The aim of this study was to assess whether visual field-related parameters per se are able to predict driving performance of patients with homonymous visual field defects (HVFDs) and healthy controls in a standardized virtual reality (VR) environment.

Methods Thirty-two patients with HVFDs due to cerebro-vascular lesions and 32 healthy control subjects underwent testing on a driving simulator under two levels of traffic density. Driving performance was defined as the frequency of accidents under VR-conditions. From the binocular visual field, as measured with kinetic perimetry, we assessed the area of sparing within the affected hemifield (A-SPAR) and the perimetric reaction time (RT).

Results Frequency of traffic accidents was best explained by traffic density, age of individuals, A-SPAR and RT. This model explained 78% of the total variability (Radj2 = 0.78). All factors were significant. The effect of traffic density explained 63.4 % of the total variance. Age, A-SPAR and RT were minor effects explaining only 2.7%, 2.0% and 0.9% respectively.

Conclusion The extent of the visual field loss is weakly related to driving performance. This finding suggests that – at least for this group of patients – the visual field-related parameters should not be taken as the sole indicator of fitness to drive. Some patients with HVFDs demonstrated sufficient compensatory driving behavior during the simulated test ride, presumably due to eye and head movements. Driving performance declined slightly with age; these changes were exacerbated in the presence of cerebro-vascular disease.

4422

Reading strategies in nystagmus

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Purpose To understand how individuals with infantile nystagmus read in view of the sensory motor deficits associated with this condition.

Methods Eye movement recordings were carried out in healthy (n=7), IIN (n=7) and albino voulnteers (n=7) during reading for distance (1.2m) and near (0.33m) at five gaze positions (-20°, -10°, 0°, 10° and 20°). Reading speeds (RS) and beating pattern were derived from these recordings. Visual acuity (VA) was also measured over the same eccentricities and distances. The nystagmus volunteers underwent a further fixational task (-30° to 30°) to derive the waveform characteristics of nystagmus.

Results RS were significantly ($p<0.05$) slower in nystagmus volunteers when compared to age and IQ matched controls. VA is a good predictor of RS in IIN ($R2 = 0.48$, $p<0.05$) but not albinism ($R2 = 0.08$, $p<0.05$). Right beating waveform was associated with faster RS and left beating with slower RS ($p<0.05$). Intensity had a significant effect on RS in IIN ($p<0.05$); however, it was a poor predictor of RS ($R2 = 0.12$).

Conclusion We describe, for the first time, that visual acuity is a reliable measure of RS in IIN but not albinism. However, intensity does not predict RS. Therefore oculomotor recordings and VA measurements should be supplemented with reading tests to assess functional visual improvements. Furthermore, the direction of the fast phase and/or slow phase significantly affects RS. This could be because reading is an asymmetric task (English reading is from left to right). This has important implications because the null region does not always exhibit right beating pattern and faster RS. Therefore therapies aimed at broadening or shifting the null should be evaluated against whether such interventions will improve functional vision.

4423

The extraocular muscles in Amyotrophic Lateral Sclerosis (ALS)?

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Purpose To investigate the morphology, fiber type composition, contractile proteins, extracelluar matrix (ECM), innervation and capillarisation, of the extraocular muscles (EOM) of patients deceased with ALS, in order to evaluate the possible involvement of EOMs in this disease.

Methods EOM and limb muscle samples obtained from 5 ALS patients and age matched controls at autopsy were processed for immunocytochemistry, with monoclonal antibodies against myosin heavy chain isoforms; laminin chains (Ln) α1, α2, α4, α5 and β2; etc. Hematoxylin and eosin, NADH-TR, acetylcholinesterase and alpha-bungarotoxin were also used.

Results The EOMs of ALS patients appeared remarkably unaffected, in strong contrast to the limb muscles. Wider variation in fiber diameter than normally seen in EOMs, including apparently atrophic and hypertrophic groups of fibers, was noted. MyHC embryonic was only present in sporadic fibers and the pattern of distribution of MyHC slow-tonic was also affected. In most ALS cases, Ln α4, α5 and β2 isoforms were lost from the basement membrane of the EOM fibers . The laminin content of the neuromuscular junctions was altered, Ln α2 and β2 isoforms were missing in perineurium and endoneurium and Ln α5 was absent in endoneurium. In capillary and blood vessels, Ln α4, α5 were maintained whereas Ln β2 was absent.

Conclusion The changes observed in EOMs with ALS suggest that they are not completely spared in this motoneuron disease although they are significantly less affected that limb muscles. The altered contractile protein content and structure-specific changes in the composition of the ECM are likely to be functionally relevant. Further studies are underway to determine the functional implications of our findings.

4424

A comparison of clinical and eye movement characteristics between albinism and idiopathic infantile nystagmus with and without mutations in the FRMD7 gene

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Purpose Nystagmus consists of involuntary to and fro oscillations of the eyes. The differences between nystagmus associated with albinism and idiopathic infantile nystagmus (IIN) are unclear. Recently mutations in a novel gene called FRMD7 have been found to underlie a significant proportion of X-linked IIN. Phenotypic variations in eye movements between FRMD7 and non-FRMD7 types have also been recently described. We have compared clinical and eye movement characteristics between albinism and IIN with and without mutations in the FMRD7 gene.

Methods Clinical features and eye movement were recorded from 37 albino subjects, 83 subjects with the FRMD7 mutation and 45 subjects without the FRMD7 mutation.

Results Mean visual acuity was significantly worse in albinos compared to IIN patients ($p<<0.0001$). Although there was no significant differences between the groups ($p>0.05$) for nystagmus amplitude or foveation, the frequency of nystagmus was significantly slower in albinism ($p<<0.0001$). In addition, nystagmus associated with albinism was significantly more likely to be jerk nystagmus rather than pendular nystagmus compared to FRMD7 group ($p<<0.0001$). The most common waveform associated with albinism was pure jerk nystagmus, whereas non-FRMD7 was more likely to be associated with jerk with extended foveation.

Conclusion Contrary to available literature, nystagmus associated with albinism shows distinct differences to IIN both with and without FRMD7 mutations. This suggests the possibility of different underlying mechanisms to albinism and IIN in generating eye oscillations although these are yet to be elucidated

▪ 4425
Torsional optokinetic nystagmus in strabismus

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Purpose Torsional optokinetic Nystagmus (tOKN) in patients with strabismus since childhood has not been previously evaluated.The authors investigated the optokinetic response in horizontal, vertical and torsional directions in strabismus patients and in age-matched normal volunteers.

Methods Monocular torsional, horizontal and vertical eye movements were recorded in 16 subjects with childhood strabismus and 15 normal volunteers.Constant velocity horizontal (nasalward and temporalward) and vertical(upward and downward) OKN stimuli were used at 10°/s, 20°/s and 40°/s.Torsional(intorsion and extorsion)OKN stimuli were rotated at velocities of 40° and 400°/s.

Results OKN responses from strabismus patients produced significant asymmetric responses in horizontal and vertical directions. The nasalward response was significantly greater than the temporalward and upward response was greater than downward. A significant high incidence of absent tOKN was present in both intorsion and extorsion. Eight of the 15 patients tested did not respond to any stimulus in either direction in their non-dominant eye and 4 showed no response in their dominant eye.

Conclusion Torsional OKN is dramatically affected in the presence of strabismus with a high incidence of no response. The possibility of a lack of development in the binocular cortical structures that respond to torsional motion could explain these findings.

▪ 4426
Optical Coherence Tomography testing : possible biomarker value in multiple sclerosis?

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Purpose To assess retinal nerve fiber layer thickness (RNFLT), macula volume (MV) and visual acuity (VA) in multiple sclerosis (MS) eye , with or without optic neuritis (ON).

Methods Optical coherence tomography (OCT) measures of the RNFLT and MV were studied in 14 patients with primary progressive multiple sclerosis (8 male / 6 female - mean age 47 yrs) and 12 patients with secondary progressive multiple sclerosis (5 male / 7 female - mean age 41 yrs). From the group with secondary progressive dissease 8 had history of ON.Control group consisted of 12 healthy control(3 male / 9 female - mean age 49 yrs) underwent RNFLT and MV OCT testing.

Results Of the patients eyes not affected by ON, mean RNFLT and macula volume were reduced when compared with control values.The mean RNFLT and MV were significantly decreased in secondary progressive MS group, but not in primary progressive MS, when compared with controls. Decreased RNFL and MV significantly correlated with decreased VA and visual field mean deviation. RNFL loss was most evident in the tmeporal quadrant, where significant reduction was seen in secondary compared to primary progression MS, and primary progression MS versus control group.

Conclusion Progressive MS is manifesting more marked decrease in RNFLT and MV. OCT is promissing to detect subclinical changes in RNFL and MV, and could possibly considered as potential biomarker of reinal / brain involvement in MS.

▪ 4427 / 433
The lot of shaken baby syndrome (SBS) cases: Follow-up of visual outcome and congnitive function

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Purpose To study long-term outcome of SBS on visual and cognitive functions.

Methods Case series of 10 children (7 M, 3 F) with confirmed SBS has been examined and followed-up. All chldren underwent a fundus evaluation by indirect ophtalmoscopy and wide-field digital ophtalmic camera (RetCam II) in the acute phase and until retinal hemorrhage resorption. The assessment was repeated at follow-up combined with ocular motility evaluation, visual field (BEFIE test), visual acuity by preferential looking tecnique (teller acuity cards), refractometry, cognitive-behavioural evaluations (Griffiths scales, Child Behaviour Check List), and family stress measurement (Parenting Stress Index).

Results Mean age at acute episode of SBS: 6 months (range 2-20). Mean age at last follow-up evaluation: 27.6 months (range 4.5-41). At last follow-up evaluation: 1 out of 6 had a decreased visual acuity (cortical visual impairment), 3 out of 6 had mild-severe visual field deficits, 3 out of 6 has strabismus. None of the cases showed significant refractive errors. Due to age or severity of impairment and delay in global development, in any of the cases we were able to perform a recognition acuity test by symbols or E-charts. Cognitive and behavioural assessment demonstrated global delay and impaiments in speech/language development and attention problems.

Conclusion SBS is characterized by severe long-term sequelae both in visual and cognitive function. Several visual impairments are observed, mainly related to cortial injury of visuo-spatial area. Although follow-up is difficult due to family history, there is strong indication for global assessment until scholar age where other impairments are demonstrated.

4431

The role for stimulus timing in local retinal responses: global propagation of retinal inhibition, in space and time

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Purpose Stimulus timing strongly influences visual responsiveness, a dramatic example being the exquisite neural sensitivity to certain spatiotemporal patterns in photosensitive epilepsy. Local inhibition is a widely recognized property of mammalian retinal function. One signature of such adaptive inhibition is the reduced local response to a second flash. Here we studied global propagation of retinal inhibition, in space and time, as a function of temporal stimulus properties.

Methods We have used a scanning laser ophthalmoscope based system interfaced with multifocal electroretinography to extract local retinal responses by means of standard reverse correlation techniques across 19 independent locations in 11 subjects.

Results Specific manipulations of previous stimulus history and timing revealed invariable shifts of the balance between excitation and inhibition. Local responses were significantly inhibited, by the presentation of flashes within a preferred temporal window at other locations, depending of local flash modulation rate. Asymmetries were observed for P1, but not for the N1 component contribution, showing a retinal origin beyond the photoreceptor level.

Conclusion These findings confirm that responses to even apparently homogeneous patterns may systematically shift depending on stimulus timing and that human retinal networks can globally adapt with exquisite temporal sensitivity, with local responses influencing far responses in space and time even when local stimulation patterns are independent.

4432

Electrophysiological measurement of macular pigment distribution using annular stimuli: implications for colour vision testing

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Purpose To quantify macular pigment optical density (MPOD) and distribution using steady-state VEPs and to optimize the koniocellular selectivity of large chromatic gratings.

Methods Blue/Green (B/G) gratings were generated within 1 circular and 3 concentric annular fields (maximum radius 9°). All 4 fields were modulated simultaneously, each at a different temporal frequency. Onset-offset VEPs were recorded as the luminance ratio between adjacent chromatic components within each field changed from 0.25 to 0.85 in 11 automated steps. Fourier analysis showed that the first harmonic was minimised at each subjects' isoluminant ratio, as verified using flicker photometry. MPOD was computed at each retinal location relative to the most eccentric annulus. The stimuli were adjusted to compensate for the MP profile, allowing generation of a B/G grating that was isoluminant over the whole of the 18° stimulus area. The optimised B/G field was used to probe koniocellular function using onset-offset VEPs and psychophysical temporal tuning characteristics.

Results Results: MPOD values computed from VEP estimates of B/G isoluminance correlated with those derived from minimum flicker measurements ($r=0.94$, $p<0.005$, slope=0.80). Large B/G gratings comprising of concentric annuli and optimised to compensate for MP, elicted large chromatic-specific onset VEPs of negative polarity. Temporal tuning characteristics to the same stimuli were low-pass, in keeping with the low temporal resolution of the koniocellular system.

Conclusion The steady-state VEP can be used to determine MPOD at different retinal eccentricities. Macular pigment profiles may be used to optimise the koniocellular selectivity of large B/G stimuli.

4433

What limits chromatic sensitivity in normal and colour deficient observers?

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Purpose Variability in chromatic sensitivity was assessed in normal trichromats (n=133) and in subjects with deutan (n= 106) and protan (n=48) deficiency. The purpose of this study was to quantify variability within normal colour vision and to determine how this impacts the assessment of minimum colour vision requirements within occupational environments.

Methods Rayleigh matches were modelled with the aim of explaining the locations of match midpoints and ranges. Model parameters included the wavelength of peak sensitivity of cone photopigments, the photopigment optical density and the noise amplitude in the red/green colour channel. In order to avoid the suprathreshold, perceptual effects of extreme L:M cone ratios on colour vision, selective postreceptoral amplification of cone signals is needed. The noise is also amplified and this causes corresponding changes in red/green threshold sensitivity.

Results We measured midpoint and matching range in anomaloscope matches and red/green and yellow/blue thresholds under conditions that isolate the use of colour signals. A subset of subjects with deutan deficiency that exhibited less common Nagel matches were selected for genetic analysis of their cone pigment genes to predict the corresponding peak wavelength separation of their two, long-wavelength cone pigments.

Conclusion The model predicts accurately the midpoint and the range for the spectral differences specified by the genes. The model also predicts the "normal" matches made by some subjects that rely on two hybrid genes and therefore exhibit red/green thresholds outside the normal range, typical of mild deuteranomaly. The anomaloscope is therefore not by itself sufficient to classify with certainty the colour deficiency involved.

4434

Acquired colour vision deficiency in subjects with ARMD and Diabetes

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Purpose Age Related Macular Degeneration (ARMD) is the leading cause of blindness in the developed world in people over the age of 50. Its prevalence increases with age as does diabetes. Such conditions affect the metabolic stability of the retina, resulting in non-inflammatory damage to retinal structures, and finally retinopathy. These changes to the visual pathway result in colour vision loss and in general, diminished visual performance. The aim of this study was to quantify accurately using sensitive visual tests the severity of visual loss in subjects with ARMD and diabetes.

Methods We investigated a large number of ARMD and Diabetic subjects with varying degrees of retinopathy and assessed their colour vision, achromatic high contrast acuity and flicker sensitivity under photopic and mesopic viewing conditions.

Results Results show a loss of chromatic sensitivity in both the red-green and yellow-blue channels, more pronounced under mesopic viewing condition. It was observed that chromatic loss was not localised to the site of retinopathy but affected peripheral retina also. Flicker sensitivity and contrast acuity loss were also observed in all subjects diagnosed with the above conditions. Preliminary findings show that significant loss of chromatic and flicker sensitivity precedes structural changes in the retina as revealed in conventional fundus imaging.

Conclusion The results so far suggest that loss of chromatic sensitivity is the most sensitive measure for detection of early damage in subjects with eye disease and can be used to detect and to monitor the progress of disease or the outcome of treatment.

4435
Chromatic VEP in colour deficient children

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Purpose To compare chromatic VEP response to isoluminant red-green stimulus in children with congenital red-green colour deficiency with a control group of 30 children with normal colour vision.

Methods 15 children (7-18 years) with congenital colour vision deficiency (8 in deutan and 7 in protan axis) and 30 healthy children (7-19 years) were included in the study. Colour vision was assessed with Ishihara plates, Nagel Anomaloscope, Mollon-Reffin Minimalist test, Farnsworth-Munsell D-15 saturated and desaturated test and Farnsworth-Munsell hue 100 test. VEP were recorded to isoluminant red-green stimulus. The stimulus was a 7 deg large circle composed of horizontal sinusoidal gratings, with spatial frequency 2 cycles/deg and 90 % chromatic contrast. VEP were recorded from Oz (mid occipital) position. Children were tested binocularly. Latency and amplitude of positive (P) and negative (N) wave were measured and so was mean amplitude (N-P wave).

Results N wave was present in 24/30 children with normal colour vision (110 ± 25.1 ms; 9.7 ± 4.8 μV) and only in 1/15 child with colour vision deficiency (93 ms; 3.2 μV). P wave was present in 30/30 children with normal colour vision (138 ± 21.1 ms; 21.1 ± 13.5 μV) and in 13/15 children with colour vision deficiency (131.9 ± 6.1 ms; 19.4 ± 10.7 μV). In healthy children waveform changed from predominantly positive to negative wave with increasing age, whereas in colour deficient children no obvious waveform changes were observed.

Conclusion VEP response to isoluminant chromatic stimulus showed different characteristics in children with congenital colour vision deficiency compared to children with normal colour vision.manca.tekavcic-pompe@guest.arnes.si

4436
New approach to establish safe colour vision limits for occupational environments

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Purpose Concern has been expressed that current colour vision (CV) standards in occupational environments tend to screen for normal trichromacy and may not therefore relate directly to actual CV requirements within specific working environments.

Methods The new approach of establishing CV limits for specific occupations involves:- measuring chromatic sensitivity and investigating the variability amongst normal trichromats- accurate assessment of the severity of CV loss- identifying the most important colour-critical tasks at the work place when no redundancy is involved and discrimination of colour differences is most difficult- simulating the most critical colour-based tasks identified- correlating the level of chromatic sensitivity and the subject's performance of these tasks.

Results A large number of normal trichromats and colour deficient observers have been examined on the CAD (Colour Assessment & Diagnosis) test. The test provides an accurate measure of the severity of CV loss (for red-green and yellow-blue discrimination) and diagnoses the class of deficiency involved. The findings from this study so far have produced minimum CV requirements in two specific occupational environments. These limits specify the level of chromatic sensitivity loss below which colour deficient subjects no longer perform the most demanding colour related tasks with the same accuracy as normal trichromats.

Conclusion The new approach provides evidence-based guidelines for minimum CV standards that can be implemented through objective testing without having to rely on either arbitrary limits or normal trichromacy. Further, this approach can be extended to other occupational environments where colour is important for carrying out visual tasks.

4441
Introduction to straylight as quality measure for ophthalmic procedures

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Purpose Often patients complain about halos, glare, hazy vision and blinding at night, but while doing regular tests like visual acuity, contrast sensitivity and slit lamp examination little unusual can be found. Most probably, the patient's complaints are caused by increased large angle light scattering in the eye media which can not be detected by common tests, but straylight degrades the image projected on the retina, thus decreasing the quality of vision. Usually the variable for increasing ocular straylight is the crystalline lens and a cataract may cause a significant increase. Increased ocular straylight may also be caused by refractive surgery and pathological changes.

Methods A forced choice psychophysical assessment technique was developed ("Compensation Comparison"), which resulted in a commercial product (C-Quant from Oculus). The task of the patient is to make 25 short observations, comparing flicker strength in two half fields, and indicate with push buttons wich half field flickers most strongly. The straylight value is obtained including a reliability estimate. Added value in comparison to visual acuity was assessed in 2400 subjects in the European GLARE study.

Results Straylight gives the part of the point-spread-function outside 1 degree. In contrast, visual acuity and contrast sensitivity relate to the psf within 0.3 degrees. Consequently, straylight assesses a part of the visual spectrum that is missed with the classical visual function measures. Patient studies have been performed on normal aging, cataract and cataract surgery, refractive surgery, YAG capsulotomy, etc. In all those studies straylight was often much increased, corresponding to complaints, while visual acuity was good.

Conclusion Straylight is important to assess quality of vision.

Commercial interest

4442
Scattered light and visual acuity after Descemet-stripping with endothelial keratoplasty

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Purpose The lamellar interface and anterior host cornea after posterior lamellar keratoplasty scatter more light than normal corneas. In this study, we examined the relationship between forward-scattered light, back-scattered light, and visual function after Descemet-stripping with endothelial keratoplasty (DSEK).

Methods Nineteen eyes of 17 patients received DSEK with the donor prepared by a microkeratome; all eyes were pseudophakic postoperatively. Eyes were examined before and at 6 months after surgery. Best-corrected high-contrast visual acuity (HCVA) was measured by electronic-ETDRS and low-contrast visual acuity (LCVA) was measured by using a 10% contrast chart. Intraocular forward light scatter was measured by using a stray-light meter (Oculus C-Quant) and back-scattered light was measured in anterior, middle, and posterior thirds of the cornea by using a custom slit-lamp scatterometer. Generalized estimating equation models were used for statistical analyses to account for possible correlation between fellow eyes of the same patient.

Results HCVA improved from 0.46 ± 0.26 logMAR (20/58) before DSEK to 0.28 ± 0.15 logMAR (20/38) at 6 months ($p<0.001$, n=19), and LCVA improved from 0.88 ± 0.26 logMAR (20/152) before DSEK to 0.62 ± 0.19 logMAR (20/83) at 6 months ($p<0.001$). At 6 months after DSEK, forward light scatter correlated with HCVA ($r=0.67$, $p<0.001$) and with LCVA ($r=0.75$, $p=0.006$). Back-scattered light from the anterior, mid, or posterior cornea were not correlated with forward scatter or with HCVA or LCVA ($p>0.2$).

Conclusion Visual outcomes after DSEK are associated with the forward-scattered light induced by the host cornea and lamellar interface, although not with the back-scattered light visible on slit-lamp examination.

4443
In-vitro characterisation of corneal scatter in rabbit corneas following PRK

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Purpose The present work pertains to the measurement of light scatter in rabbit corneas after Excimer laser treatment, to the microscopic characterisation of the corneal irregularities and to the development of a mathematical model of light propagation through the post-laser treatment cornea, based on the statistical properties of the scattering structures.

Methods Fourteen rabbits underwent photorefractive keratectomy (-6D). Nine to twelve weeks postoperatively, after confocal imaging, animals were sacrificed and the corneas were excised. The intensity and angular distribution of scatter was measured by enclosing the excised rabbit corneas between two glass elements to form a triplet lens. This lens was used with a CCD camera to record images projected on a computer screen. Scatter intensity and distribution was calculated by measuring the intensity in small dark disk concentric with a series of bright disks. After the scatter measurement, the corneas were examined histologically. The structures observed using the confocal microscope -corresponding to refractive index (and therefore optical path difference) variation were fitted with a fractal surface band-pass filtered in the Fourier domain.

Results Scattered light is characterised by a narrow forward distribution. Scatter is dominated by the subepithelial structures having sizes of the order of 50-150 microns. The modelling of scatter by means of a spatially filtered fractal surface corresponding to OPD results to predictions in accordance to the experimental data.

Conclusion Forward scatter following PRK can be attributed mainly to the subepithelial irregular layer. The angular distribution of scatter is in accordance to the size of structures observed microscopically in this layer.

4444
Glare test as indicator for cataract surgery

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Purpose The concept of glare, as determined by the Oculus C-Quant device, can be useful in clinical practice as additional parameter to guide the surgeon in its decision for cataract surgery. Before to decide upon pathological conditions of glare, benchmarks of what is considered normal should be available.

Methods The C-Quant device was calibrated in the Department of Ophthalmology of the Antwerp University Hospital in order to achieve benchmarks of what is "physiological" glare.

Results Based on the results of the Gullstrand Benchmark study, glare in our "normal" population was found slightly higher than in other settings. Glare was also measured prior to each cataract operation as well as after cataract surgery.

Conclusion Two conclusions can be drawn: it might be important to calibrate each individual machine before testing pathology, and glare is generally increased prior to cataract surgery and decreased after successful cataract surgery.

4445
Pseudophakic dysphotopsia - Counting the stars

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Purpose To demonstrate the use and potential for two very disparate measures of glare and dysphotopsia

Methods We report the development of a system of measuring pseudophakic dysphotopsia dependent on patient recognition of photographic plates. The photographs are structured such that type and intensity of varied dysphotopsia can be assessed. The photographs have been used in preliminary studies to assess prevalence of dysphotopsia and also to compare the amount in patients with different intraocular lenses. In a parallel study C-Quant measures of stray light were obtained on 106 patients referred to the cataract clinics. In addition to tests of visual acuity and contrast sensitivity (LogMar and Pelli-Robson), cataract morphology was assessed using the Oxford cataract grading system. The paper examines associations and differences between the visual and clinical measures and using latent class analysis explores subgroups of different patient profiles

4446
Reliability results of straylight measurements using the C-Quant

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Purpose Assessment of repeatability and reproducibility of straylight measures with the C-Quant straylightmeter (Oculus AG, Germany), effect of age on reliability measures and correlation of measures determined with new methods of scatter determination.

Methods Results from different studies will be presented. For repeatability assessment, 20 eyes (age 26.9±2.7 years) were examined with the C-Quant, taking 10 consecutive readings. 5 subjects were also examined on 5 consecutive days to assess reproducibility. Repeated measures from 84 subjects, age range 19-86 years, were analysed to assess the effect of patient's age. Software was developed to quantify scatter from centroid patterns obtained using a clinical aberrometer(WASCA, Zeiss) based on previous work by Donnelly & Applegate, and 3 values were obtained on 10 eyes. 3 measures were also made with the C-Quant. Preliminary results comparing the C-Quant and the StarLight hallometer will also be presented.

Results Results failed to show differences between readings taken within the same session (mean SD 0.07, $p>0.05$) or between sessions (mean SD 0.05, $p>0.05$). Variability of intrasession measurements was not significant for subjects of different age ($p=0.094$). After removal of incomplete patterns, good correlation was achieved between psychometric and objective measures despite small sample size ($n=6$; $r= -0.831$, $p=0.040$).

Conclusion The C-Quant straylightmeter is repeatable and reliable for retinal straylight assessment on human eyes. Age does not decrease repeatability eventhough they feel more insecure about their ability to perform the test. Psychometrical determination of straylight showed remarkably high correlation with objective measures of scatter on young healthy subjects.

4451
Effects of repetitive IOP measurements

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Purpose The purpose of this study was to evaluate the effect of repetitive applanation tonometry measurements on IOP and aqueous humor volume in the anterior chamber.

Methods This is an ongoing study where four healthy volunteers have participated so far. Consecutive repeated series of six measurements with Goldmann applanation tonometry (GAT) and applanation resonance tonometry (ART) were made alternately on both eyes for one hour. Using an Oculus Pentacam, the anterior chamber of the left eye was photographed before the measurements and then consecutively for 20 min. Finally, one additional measurement was performed with both GAT and ART.

Results In this abstract we present the results from the first four subjects. The results show that there was a significant reduction in IOP on the right eye both with GAT and ART. After one hour of measurements, IOP was reduced by 5.5 mmHg (range 4.3-7.2 mmHg) for GAT and 3.1 mmHg (range 1.0-4.1 mmHg) for ART. The decrease in aqueous humour volume after IOP measurements was less than 10 % for all subjects.

Conclusion Although Bechrakis showed as early as 1966 that repetitive measurements result in significant IOP reduction, the mechanism behind this is still matter of debate. Our preliminary results confirm the occurrence of IOP reduction after repetitive measurements, but indicate that it could not be explained by the decrease in volume of the anterior chamber.

4452
Risk factors for progression in glaucoma. The Groningen Longitudinal Glaucoma Study

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Purpose To investigate risk factors associated with visual field progression in glaucoma.

Methods 221 patients with a reproducible glaucomatous visual field defect at baseline were followed prospectively with perimetry (HFA 30-2). Three criteria for progression were used: the EMGT algorithm (GPA), a non-parametric algorithm applied to mean deviation (MD; NPA) and MD slope. For progression according to GPA, the last field had to be labelled as possible or likely progression. For progression according to NPA, the last two or more consecutive fields had to have an MD value worse than the worse baseline MD value. Risk factor analyses were performed using Cox proportional hazard models (dependent variables: classification by GPA and NPA) and multiple linear regression (dependent variable: MD slope).

Results Mean follow-up was 5.4 years; on average 7.2 reliable fields were available. Mean MD at baseline and MD slope during follow-up were -9.9 dB and -0.26 dB/yr for OD and -9.0 dB and -0.21 dB/yr for OS. Of 167 eligible right eyes, 45 showed progression with GPA and 69 with NPA. For OS, these numbers were 36 and 67 of 167. Mean IOP during follow-up (per mmHg increase; GPA: HR 1.13, P=0.014; NPA: HR 1.10, P=0.016; MD slope: -0.042 dB/yr/mmHg, P=0.002) and disease stage (early versus moderate/severe glaucoma with MD = -6 dB as cut-off point; GPA: HR 1.88, P=0.034; NPA: HR 2.05, P=0,001; MD slope: -0.20 dB/yr, P=0.010) were found to be significant risk factors. Less convincing associations were found for family history of glaucoma and age. Highest IOP ever measured, myopia, sex and cardiovascular disease were not associated with progression.

Conclusion Higher mean IOP during follow-up and worse disease stage at baseline were associated with progression.

4453
HLA class I haplotypes and progression of primary open angle glaucoma

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Purpose Patients with primary open-angle glaucoma (POAG) with HLA class I haplotypes (A9-B12, A2-B40, A1-B8) associated with this disease could have a fast disease progression than patients who wouldn't present these haplotypes.

Methods Anatomic and functional evaluation of 25 patients (six of them with one of the haplotypes associated with glaucoma) followed, in the Glaucoma Outpatient Clinic of the University Hospital of a Brazilian Medical School, for ten years after the typing of their HLA antigens in order to compare with the previous conditions.

Results There was observed a higher increase in the cup/disc ratio in patients with HLA haplotypes associated with POAG predisposition (P=0.01248, comparing with patients of different ages; and P=0.0047, comparing with patients of the same age group), however it wasn't observed significant differences, between these and the others patients with glaucoma, in functional damage progression (evaluated by Humphrey perimetry) neither in losses in retinal nerve fibers layer (evaluated by optical coherence tomography).

Conclusion These results show the association of class I HLA haplotypes with faster progression of anatomic alterations of the optic nerve head in patients with glaucoma.

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Lamina cribrosa and peripapillary scleral histomorphometry in myopic and non myopic glaucomatous chinese eyes

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Purpose To study the glaucomatous optic nerve head in Chinese eyes.

Methods The histomorphometric investigation included a Normal group (non-highly myopic eyes) of 40 human globes enucleated due to a malignant choroidal melanoma, a Glaucomatous group (non-highly myopic eyes) of 55 eyes enucleated due to painful secondary angle-closure glaucoma, and a Highly Myopic Glaucomatous group of 26 glaucomatous globes with an axial length >26.5 mm. Anterior-posterior histological sections through the pupil and the optic disc were morphometrically evaluated and compared.

Results The lamina cribrosa was significantly (P<0.001) thicker in the Normal group than in the Glaucomatous group, in which it was significantly (P<0.001) thicker than in the Highly Myopic Glaucomatous group. The lamina cribrosa thickness decreased significantly (P<0.001) with increasing axial length and presence of glaucoma (p<0.001). The peripapillary scleral thickness close to the optic nerve scleral canal and just outside of the optic nerve meninges decreased significantly with increasing axial length (P=0.04 and P=0.02, respectively). The peripapillary scleral thickness did not vary significantly between the Glaucomatous group and the Normal Group. The distance between the intraocular space and cerebrospinal fluid space was (p<0.001) shorter in the two glaucomatous groups than in the Normal group.

Conclusion Lamina cribrosa thickness and peripapillary sclera thickness decreased significantly with axial length, in addition to a glaucoma-related thinning of the lamina cribrosa. Within non-highly myopic eyes, the peripapillary sclera thickness did not vary significantly between glaucomatous eyes and normal eyes.

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Interactions between trabecular meshwork cells and lens epithelial cells – a possible mechanism in infantile aphakic glaucoma

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Purpose Infantile aphakic glaucoma may develop as a postoperative complication of early childhood cataract surgery. Its causes and mechanisms to date are poorly understood. Our goal is to study the mechanisms leading to trabecular meshwork (TM) dysfunction and glaucoma following the cataract removal. We focus on deciphering the interactions between TM cells and lens tissue or conditioned medium by analyzing changes in TM cells co-cultured with lens epithelial cells (LECs), or cultured in the presence of factors found to be secreted by LECs.

Methods These interactions are studied by analyzing for morphological alternations, and differential gene and protein expression.Factors secreted by LECs are analyzed using cytokines array membranes.

Results TM cells grown in the presence of LECs exhibited structural changes (mainly volume and size enlargement and decreased cell-cell interactions), as well as altered protein expression (mainly cytoskeletal), and gene expression (such as genes related to cell morphogenesis and inflammatory response). Several cytokines were found to be elevated in the medium of LECs, and of the co-culture, but not in the medium of TM cells, suggesting their role in the changes observed in TM cells co cultured with LECs; co-culture of TM cells in the presence of these cytokines will be further performed.

Conclusion Many of these changes were reported in primary open-angle glaucoma, suggesting the possible role of LECs in the development of aphakic glaucoma.

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Circulating ether-lipids as an early marker of POAG

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Purpose Neuronal tissues such as the retina contain high amounts of particular phospholipids named "ether-lipids". Since abnormal blood levels of ether-lipids have been associated with several neurological disorders, we wanted to check whether ether-lipid levels were modified and associated with the severity of POAG.

Methods Blood samples were collected from 41 healthy subjects and 64 POAG patients. Following lipid extraction from erythrocytes, total phospholipids including ether-lipids were isolated using silica cartridges. The fatty acid profile of phospholipids was determined using capillary column gas chromatography (GC). The individual molecular species of phospholipids and ether-lipids were quantified by tandem liquid chromatography-mass spectrometry.

Results The levels of ether-lipids were significantly decreased in glaucoma patients and especially the choline ether-lipid sub-class. The Mean Deviation (MD) value from Humphrey perimetry was negatively correlated to erythrocyte levels of total choline ether-lipids (r^2=0.99). The linear regression model predicted that total choline ether-lipid levels started to decrease about 20 years prior to clinical symptoms.

Conclusion Although the mechanisms responsible for the reduction of erythrocyte levels of ether-lipids in POAG patients remains unclear, the known functions of ether-lipids in the protection against oxidative stress make these results very consistent with the pathogenesis of glaucoma.

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Correlation of optic disc morphology and ocular perfusion parameters in patients with primary open angle glaucoma

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Purpose Little information is available about the relationship between glaucomatous visual field defects and reduced blood flow in the optic nerve head. It is still not clear, if impaired circulation is a causative factor in the disease process, or if it is secondary as a result of loss of axons in the optic nerve head. In the present study vascular parameters were correlated against structural damage of the optic nerve head and functional damage.

Methods 103 patients with primary open angle glaucoma, documented visual field defects and optic disc morphology changes were examined. Blood flow parameters were assessed using Laser Doppler Flowmetry, Laser Doppler Velocimetry, and the Retinal Vessel Analyzer. To evaluate the morphology of the optic nerve head, a fundus photograph was taken. For determination of the degree of visual field damage, automated perimetry was performed.

Results The degree of optic nerve head damage was significantly correlated with the intensity of visual field loss. Decrease in retinal vessel diameter was only slightly correlated with the degree of glaucomatous optic neuropathy and visual field defect. Reduced optic nerve head blood flow was, however, strongly correlated with the degree of visual field loss and morphological optic disc damage.

Conclusion The data of the current experiment indicates that blood flow in the optic nerve head is strongly associated with the degree of visual field damage, whereas retinal vessel diameters show only little association with the degree of visual field damage.

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Frequency of melanocytic conjunctival lesions in an ocular oncology unit

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Purpose Pigmented lesions of conjunctiva account for 50% of conjuntival tumors.The purpose of this study was to evaluate the frequency of incidence,clinical characteristics and distribution of these pathologies in a referral oncology unit.

Methods Retrospective observational cases series of patients with diagnosis pigmented conjuntival lesions were studied at the Ocular Oncology Unit of Valladolid Clinical Hospital dated from January 1992 until June 2008.Clinical chart of consecutive cases were reviewed through evaluation of the clinical features. Demographic data (age,sex,background) and clinical features (shape,location,ocular and extraocular extension) have been registered in a data base design in AccessXP and statistical SPSS 15 analysis.

Results 314 cases were diagnosed with conjuntival tumors, 149 (47%) corresponded to melanocytic tumors; mean age was 42 years, and 52% were females. 73.2% were benign tumors, 22.1% precancerous and 4.7% malign. Comparing clinical characteristics of PAM and melanoma we found significant clinical differences (p<00,5) regarding clinical presentation, 100% melanomas presenting as a growing lesion;limbal involvement was 42.9% for melanoma and 62% for PAM;Corneal involvement was 28.5% for melanoma compared to 17.2% of PAM and 2% of Nevus. All nevus were circumscribe lesions,38% of PAM were diffuse/multicentrics and 42,9% de melanomas were multicentricts;Mean age at diagnosis was 38 years for nevus,53.5 for PAM and 61.3 for melanomas.

Conclusion Pigmented lesions were more frequent tumor in our serie.Most of them benign.Clinical characteristics were related with precancerous or malignal lesions were growing onset,multicentric lesion with corneal and limbal involvement and older age.

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Results of treatment of conjunctival melanoma in 61 consecutive patients

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Purpose Analysis of patients with conjunctival melanoma.

Methods Retrospective analysis of 61 consecutive patients with histopathologic diagnosis of conjunctival melanoma treated between 1991-2007 at the Department of Ophthalmology and Ocular Oncology of Jagiellonian University in Krakow. There were 30 (49.2%) women and 31 (50.8%) men in mean age of 57.6 years (25-89).

Results The tumors involved in 29 cases right eye and in 32 cases left eye. 26 (42.6%) melanomas were located in temporal quadrant; 37 (60.6%) tumors involved limbus and 22 (36.1%) bulbar conjunctiva; in 2 (3.3%) patients tumors infiltrated tarsal conjunctiva. 53 tumors (86.9%) were pigmented, 5 (8.2%) - amelanotic and 3 tumors (4.9%) - mixed. In 59 (96.7%) patients the tumors were nodular and in 2 (3.3%) diffuse, superficial. In all cases surgical excision was performed and in 44 (73.13%) cases adjunctive Ru-106 brachytherapy. In 20 (32.7%) cases recurrence of melanoma necessitating secondary treatment was observed. The mean time to recurrence was 24.65 months (2-91). In 5 (8%) cases documented metastasis occurred. Among all patients 5 (8%) died because of metastatic disease, 3 because of other reasons. 6 cases were lost to follow-up because they moved to other countries.

Conclusion Conjunctival melanoma most commonly occurs in form of a melanocytic, nodular tumor localized in corneal limbus and bulbar conjunctiva. Local recurrence of the tumor may be expected despite the surgical excision combined with adjunctive therapies.

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Collective of patients with conjunctival melanoma treated at the Jules Gonin Eye Hospital (Lausanne)

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Purpose Since 1985, a new therapeutic strategy for the conservative treatment of conjunctival melanoma has been developed at the Jules Gonin Eye Hospital (Lausanne). In order to evaluate its long-term results, we had to identify and classify our patients.

Methods We looked retrospectively in our clinical and histopathological databases for all cases of conjunctival melanoma treated in Lausanne since 1985.

Results 189 patients were identified. We studied patients' parameters, clinical presentation and histopathological characteristics of all consecutive conjunctival melanoma cases.

Conclusion A database of 189 conjunctival melanoma patients treated with the same therapeutic strategy since 1985 was established. This collective will allow for further studies with regard to the long-term results of the Lausanne conservative therapeutic strategy of this rare ocular tumour.

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Genetic predisposition to uveal melanoma

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Purpose Uveal melanoma is a rare tumor with exceptional familial or bilateral cases. The possibility of genetic predisposition has been evoked.We have tried to identify patients with history compatible with genetic predisposition of uveal melanoma and to perform genetic testing.

Methods Between 1994 and 2008 we have registered for all our uveal melanoma patients the history of personal and/or familial previous cancer. According to the antecedents, selected patients were seen for genetic counselling and were offered blood test.

Results 1665 patients treated in our institution for uveal melanoma had registered personal and familial history of previous cancer. 152 patients had previous cancer: 35 breast cancers, 9 gynaecological cancers, 21 digestive cancers and 87 other locations. 34 of them had a cancer before the age of 50; 23 patients had a familial history of uveal melanoma; 39 patients had a familial history of cutaneous melanoma; 276 patients had a familial history of breast cancer; 40 patients had a familial history of pancreatic cancer; 822 patients had a familial history of other cancers.143 patients had a genetic counselling, 81 patients had blood sampling and genetic testing was performed on BRCA1and or BRCA2 for 27 patients and p16-CDK4 for 18 patients. All the results were negative.

Conclusion Further studies should be performed to determine the genes possibly implied in a predisposition to uveal melanoma.

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Surgical treatment of severe choroidal detachment after brachytherapy for choroidal melanoma

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Purpose Choroidal detachment is a rare but potentially serious complication of plaque radiotherapy of choroidal melanoma. We present a patient who was successfully treated by trans-scleral drainage over the pars plana using an unconventional technique.

Methods A 69-year-old man was referred to our service for an infero-nasal, collar-stud melanoma in the left eye. On ultrasonography, the tumour measured 14.1 x 11 mm, with a thickness of 5.8 mm. The patient was treated with a 20 mm ruthenium plaque. Two weeks after the plaque removal, the patient was referred back to our service with a painful eye and ocular hypotension. Ophthalmoscopy showed severe choroidal detachments. The patient was managed expectantly, but the pain became uncontrollable. The supra-choroidal fluid was drained through a circumferential deep scleral incision over the pars plana and under a lamellar scleral flap hinged posteriorly. A high intraocular pressure was maintained with infusion, using a 6 mm cannula placed in an area between the choroidal detachments. The patient was on warfarin and this was not discontinued before the surgery.

Results Postoperatively, the eye was comfortable, the intraocular pressure returned to normal and the choroidal detachments did not recur.

Conclusion Our technique has several advantages over previously described methods. First, it avoids the risk of retinal tear, because of the pars plana location of the incision. Second, the scleral flap facilitates wound closure, also avoiding the risk of retinal prolapse. Third, it does not require the warfarin therapy to be stopped. We propose this technique as a relatively safe and effective treatment for severe, painful and persistent choroidal detachment after plaque radiotherapy of choroidal melanoma.

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A clinical pathway for episcleral brachytherapy

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Purpose To develop the clinical pathway of episcleral brachytherapy as developed in our center.

Methods 1 .- Recruitment multidisciplinary team2 .- A critical review of clinical practice guidelines applicable3 .- Combining the expertise of professionals with revisions to guidelines previously outlined and the rest of literature applicable4 .- design of the clinical pathway and indicators for evaluation

Results The clinical pathway designed consists of 3 tables: time from diagnosis until they have all the data for treatment, during treatment and variances on the pathway and the establishment of indicators to assess the degree of compliance with the pathwayi. - Number of patients included in the pathway in relation to that should have been includedii .- Number of patients with variances from the clinical pathwayiii .- Total number of variancesiv .- Survey of patientsv. - Survey of professionals

Conclusion The establishment of the delimitation of functions through a clinical pathway has served the research team, who is also the team that develops clinical treatments in our center, to narrow the deadlines for action of each specialty and the order in which they must be made. The research team is inclined to clinical pathways of more immediate usefulness for clinical practice the existence of guides in the scientific literature. An improvement that could be done would be the computerization of the pathway.Acknowledgments:This work has been financed partly by a grant of the Junta de Castilla y León (Order SAN/1829/2007 of November 13, BOCYL of November 15, 2007)

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Impact of continuous myopic defocus on the refractogenesis and myopia progression

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ABSTRACT NOT PROVIDED

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Myopic macular degeneration: classification and treatment

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Purpose There is no accepted method for the control of progressive high axial myopia, the phenotype of Degenerative Myopia. Myopic Macular Degeneration was studied and classified by clinical presentation, structural features and responses to certain natural and therapeutic changes.

Methods Two hundred eyes, with 9.0 D to 24.O D of axial myopia, were evaluated in terms of their clinical presentations, axial length and Optical Coherence Tomography images. The changes occurring with vitreous detachment, macular buckling, vitrectomy and the treatment of exudative complications were also evaluated.

Results Vision loss progressed with the length of the eye, the shape of the posterior pole and the age of the patient. The macular degeneration was classifiable into: Atrophic, Exudative, Cicatricial and Neural-disruptive stages.Macular buckling stabilized axial length and corrected some features of macular traction. Vitrectomy and membrane peeling relieved other aspects of macular traction, but gave no restraint to axial myopia progression.Photo-dynamic-therapy and intra-vitreous anti-VEGF injections controlled exudative macular complications.

Conclusion The stages of Myopic Macular Degeneration were: Atrophic, Exudative, Cicatricial and Neural-disruptive. Progression was related to time, axial length, posterior pole anatomy and vitreous detachment. Macular buckling limited axial myopia progress and modified schisis and other neural-disruptive features. It remains to be shown that such surgery can prevent myopic macular degeneration and preserve macular function. Additional vitreous surgery may be required for macular holes, detachments and pre-retinal fibrosis.Exudative changes were found to respond to treatments for the comparable stage of age-related macular degeneration.

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Pharmacological control of myopia - current options and future possibilities

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Purpose To review current pharmacological options for myopia control and explore future options. The underlying cause of both myopia and associated retinal complications is excessive ocular growth, which is a logical target for pharmacological intervention.

Methods This presentation will review relevant research using animal models for myopia as well as clinical myopia research.

Results The first attempts to control human myopia with drugs date back to the middle of the 19th century and involved topical atropine, an antimuscarinic drug. Possible reasons for why it remains the only drug in wide-spread use for myopia control today, despite its significant adverse ocular side-effects, will be considered along with general and drug-specific clinical issues associated with long-term use of topical ophthalmic formulations. Other plausible pharmacological treatment options will also be explored.

Conclusion Progress in developing acceptable drug treatments for myopia control has been disappointing, especially given the near epidemic levels of myopia in some countries. However, the increased attention paid to the translation value of biomedical research may help to change this situation.

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Derangement of pigment epithelium derived factor (PEDF) activity in progressive myopia

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Purpose To study the Tenon's capsule ultrastructure and PEDF metabolism of the sclera and Tenon's capsule in progressive myopia.

Methods Transmission electron microscopy, western blot analysis and immunohistochemistry using polyclonal antibodies against PEDF molecule, nucleotide sequence of PEDF mRNA and histochemistry with Kongo red staining specific to amyloid structures have been used to study 140 samples of 106 eyes of patients aged 7-22 with progressive myopia of 5.5-31.0 D and 29 eyes of patients aged 7-23 with emmetropia or low hyperopia (control group). The samples were obtained during scleroplasty, squint and eye trauma surgery.

Results Myopic samples of the Tenon's capsule showed a looser and less regular organization of collagen fibrils, and a fall of the mean fibril diameter (d=75.7±7 nm) as compared to control samples (d=87±9 nm). These structural abnormalities are similar to those of highly myopic sclera. Soluble PEDF level decreased 2-3 times, while accumulation of insoluble PEDF around fibroblasts was found to correlate with the formation of amyloid-like fibril structures and an increased PEDF stability to hydrolysis. In PEDF's mRNA obtained from myopic sclera 3 point mutations were revealed. All these substitutions change conservative amino acid residues near the serpin loop and can affect the conformation and stability of PEDF molecule.

Conclusion Serious defects of extracellular matrix organization and disorders in PEDF metabolism in the highly myopic Tenon's capsule were detected.These disorders may contribute to myopia progression and development of its complications.

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Use of imposed myopic defocus to control the progression of myopia

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Purpose Animal studies suggest that axial elongation of the eye is controlled by pathways that detect hyperopic defocus (growth-promoting) and others that detect myopic defocus (growth-inhibiting). The inhibitory pathways generate more powerful signals, and brief periods of imposed myopic defocus block the axial elongation induced by otherwise constant hyperopic defocus. An intervention to prevent myopic progression based on these findings was trialled in a Sydney paediatric ophthalmology practice.

Methods The study was approved by the ANU Human Ethics Committee. Informed consent was obtained from the parents of 30 progressing myopes. Participants removed their corrections for 30 minutes per day, replacing them with +3D glasses. During this period, they were encouraged to avoid nearwork. Participants were followed for two years, with initial and final cycloplegic retinoscopy, and subjective refraction and axial length measured at 4 monthly intervals.

Results Complete data was obtained for 20 participants. In 13 cases, there was sufficient pre-trial data on subjective refractions to compare pre-trial progression with progression during the trial. Of the 26 eyes available for this analysis, progression was reduced by over 80-100% in 7 eyes, by 60-80% in 7 eyes, by 40-60% in 5 eyes, by 20-40% in 1 eye, and by less than 20% in 6 eyes. In 16/26 eyes, the estimated reduction in progression was at least 1D over the two years.

Conclusion These results are consistent with other data on the impact of imposed myopic defocus in humans. However, an RCT in Singapore using monocular rather than binocular treatment has given negative results. A school-based trial of binocular treatment has now commenced in Guangzhou in collaboration with Professor Mingguang He of the Zhongshan Ophthalmic Centre.

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Time spent outdoors can prevent the development of myopia

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Purpose To examine the relationship between the development of myopic refractive error and near-work and time spent outdoors.

Methods The Sydney Myopia Study is a school-based study using a random cluster design stratified by socio-economic status. Over 4,000 Australian school-aged children from two age groups had a comprehensive eye examination including cycloplegic autorefraction. Parents and students completed questionnaires on relevant lifestyle factors. Myopia was defined as spherical equivalent ≤-0.5D in at least one eye. 1,765 children with a mean age of 6.7 years (75.3% response rate) and 2367 with a mean age of 12.7 years (75.3% response rate).

Results There were no consistent associations between refraction and measures of activity in the 6 year-old sample, where the myopia prevalence was 1.3%. It was significantly higher in the 12 year old sample at 12.7%. In this age sample, higher levels of outdoor activity (sport and leisure activities) were associated with more hyperopic refractions and lower myopia prevalence. Students who combined low levels of near-work with high levels of outdoor activity had the most hyperopic mean refraction (+0.56D; CI 0.38-0.75), while those who performed high levels of near-work but had low levels of outdoor activity, had the least hyperopic mean refraction (+0.27D; 95% confidence interval, CI, 0.02-0.52). The lowest odds ratios for myopia, after adjusting for near-work, parental myopia and ethnicity, were found in groups performing the highest levels of outdoor activity. There were no associations between indoor sport and myopia.

Conclusion Increasing time spent outdoors was associated a lower prevalence of myopia in the 12 year-old sample. This may form the basis of a public health approach to the prevention of myopia.

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Atropine and plus lenses in the control of myopia - results from clinical trials

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Purpose A safe and effective treatment that can control or slow the progression of myopia, which typically occurs during childhood, would be a significant advance in the management of myopia. The findings of recent clinical trials evaluating the use of antimuscarinic agents atropine and pirenzepine as well as optical modalities such as progressive addition lenses for controlling the progression of myopia in children are reported.

Methods Randomized controlled trials with comparisons of the effectiveness of interventions such as atropine, pirenzepine and progressive addition lenses to decrease myopia progression in myopic children were reviewed.

Results Topical atropine was well tolerated and effective in slowing the progression of low and moderate myopia and ocular axial elongation in children. Pirenzepine gel was also effective and relatively safe in slowing myopia progression during a 1-year treatment period. Progressive addition lenses did not, or at best marginally slowed the increase of myopia and axial elongation.

Conclusion Trials of progressive addition lenses on myopia progression have yielded disappointing results. To date, only pharmacological intervention with atropine and pirenzepine appear to have some consistent effect on reducing the progression of myopia. However, the long-term safety and efficacy profiles of these drugs are not known. As such, well-designed clinical trials with longer duration of treatment and follow-up are required.

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Pseudoexfoliation in the Reykjavik Eye Study: 5-year incidence and changes in related ophthalmological variables

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Purpose The objective of this study was to examine the 5-year incidence of definite and possible pseudoexfoliations (PEX) in a randomized sample, and changes in related ophthalmological variables.

Methods The Reykjavik Eye Study is a randomized population-based study of 1045 persons 50 years and older. It included keratorefractometry, air puff tonometry, Scheimpflug photography of the anterior segment, fundus photograph, and slit-lamp examination. 88% of survivors participated in the 5-year follow-up study.

Results Incidence PEX was found in 3.5% of all right eyes. Females have a twofold risk of 5-year incidence compared with males (p=0.05). Increasing age was also linked to the incidence of PEX by an average of 5% between the 10-year age-groups (p=0.022). 68%, of those right eyes that did not have PEX at baseline remained the same 5 years later, whereas 11% were deemed to have progressed to possible PEX and 2% had progressed to definite PEX. 47% of the right eyes diagnosed with possible PEX at baseline, were not found to have signs of PEX after 5 years. 21% continued to be diagnosed as possible PEX and 5% progressed to definite PEX. Five year incidence cases of PEX showed a significant increase in IOP (p=0.007). Cup/disc ratio increases for all participants, significantly more for those that already had PEX at baseline.

Conclusion The diagnosis of definite PEX holds well over five years, but not possible PEX. The incidence of PEX increases with age, and is more common in females. The results indicate that the increase in IOP that usually accompanies PEX develops in the same period as the PEX changes become visible. The increase in cup/disc ratio seem to accelerate after the PEX changes have established and not before.

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Histological analysis of sensory receptors in human extraocular muscles

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Purpose Recent publications have promoted the view that tendon receptors at the distal insertion of extraocular muscles (EOMs) provide more adequate proprioception than the muscle spindles, yet some uncertainty remains. The purpose of this study was therefore to analyse the morphological features of the muscle spindles and their potential proprioceptive capacity.

Methods Samples of human EOMs were selected from stock and all sections containing muscle spindles were selected for further analysis. The age of the subjects ranged from 6 months to 90 years and both sexes were included. No previous history of binocular anomalies or neuromuscular disease had been recorded. An image analysis system (Imaris Imageaccess) was attached to a light microscope (Nikon Optiphot) in order to obtain a more detailed analysis.

Results Digital three dimensional reconstructions of the most prominent morphological features were obtained from serial sections of 35 spindles. These features included narrow periaxial spaces, fragmented intrafusal fibres and other peculiar features which could potentially interfere with the functional principals upon which this type of mechanoreceptor is based. The digital reconstruction provided additional information about variations in spindle shape which most likely would have been missed by conventional light microscopic observations.

Conclusion The proprioceptive capacity of the muscle spindles in human extraocular muscles has previously been questioned based on the presence of several peculiar morphological features. The current study confirmed these observations and has added credence to the notion that the muscle spindle in human EOMs in not the main source of proprioception. A similar study of the tendon receptors is now in progress.

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Crosstalk between Hsp70 molecular chaperone, lysosomes and proteasomes in autophagy-mediated proteolysis in human retinal pigment epithelial cells

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Purpose The pathogenesis of age-related macular degeneration involves chronic oxidative stress, impaired degradation of membranous discs shed from photoreceptor outer segments and accumulation of lysosomal lipofuscin in retinal pigment epithelial (RPE) cells. It has been estimated that a major part of cellular proteolysis occurs in proteasomes, however the importance of proteasomes and the other proteolytic pathways including autophagy in RPE cells are poorly understood. In the present study the role of Hsp70 molecular chaperones, proteasomal and lysosomal proteolytic pathways were evaluated in human RPE cells (ARPE-19).

Methods The Hsp70 and ubiquitin protein levels and localization were analyzed by western blotting and immunofluorescense. Confocal and transmission electron microscopy were used to detect cellular organelles and to evaluate morphological changes.

Results The proteasome inhibition evoked the accumulation of perinuclear lysosomal vesicles/residual bodies positive for ubiquitin and the lysosomal membrane protein LAMP-2, and a robust accumulation of Hsp70 protein and ubiquitin-protein conjugates. We found that the accumulation of lysosomal/residual bodies was reversible, a cessation of proteasome inhibition led to clearance of the deposits via a mechanism that probably includes autophagy.

Conclusion We show novel connection of Hsp70 molecular chaperones, proteasomes and autophagy in regulation of protein turnover in human retinal pigment epithelial cells that may thus open new insights to understand degenerative processes in retina cell pathology.

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A 3 year retrospective case series of temporal arteritis in Portsmouth, United Kingdom

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Purpose To investigate the incidence,socioeconomic status and inflammatory markers of patients with biopsy proven Temporal(Giant Cell)Arteritis(GCA)in Portsmouth, United Kingdom.

Methods A single-centre retrospective study assessed patients referred for Temporal Artery biopsy.Serum platelet count,Erythrocyte Sedimentation Rate (ESR)and C-Reactive Protein(CRP)were analysed. Socioeconomic status was investigated using index of deprivation scores from the national database and compared to a cataract surgery group(control). Patients received high dose oral prednisolone or intravenous methylprednisolone initially,followed by oral prednisolone.Telephone survey follow-up for biopsy positive patients assessed smoking history and subjective visual improvement following treatment.

Results 70% of biopsies were negative. Biopsy positive age adjusted incidence was 29.3/100000.93% of cases referred were subsequently diagnosed with GCA on clinical grounds.Mean platelet count was 359.7(B-ve)vs.438.8(B+ve)($p \leq 0.001$),mean CRP 50.75(B-ve)vs.98.0(B+ve)($p \leq 0.001$)and mean ESR was 53.9(B-ve)vs.69.9(B+ve)($p \leq 0.018$). Insignificant differences in socioeconomic status were found in biopsy positive group compared to controls(p=0.112).33% of biopsy positive patients sustained Visual loss, all patients reported unchanged Visual function, irrespective of treatment regime.

Conclusion Biopsy +ve GCA was associated with significant elevations in serum platelet count,ESR and CRP levels compared to B-ve GCA. The incidence in Portsmouth appears higher than other Caucasian populations. GCA appears unrelated to socioeconomic status in this cohort. A large proportion of biopsies were negative or inconclusive – warranting a strict referral pathway to ease pressure on Ophthalmic services.

5125
Clinical Assessment of Disc at Risk

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Purpose Diagnostic agreement among clinicians is fundamental to a clinical diagnostic criterion. We assessed the inter-observer variability among examiners for the clinical entity popularly called Disc at Risk, a risk factor for non-arteritic ischemic optic neuropathy (NAION).

Methods Examiners graded a randomized series of 40 monoscopic optic nervehead images, yes or no, as to whether each individual image merited the clinical diagnosis of a Disc at Risk. Ten academic ophthalmologists including (7 neuroophthalmologists) Group 1 and Group 2, 51 comprehensive ophthalmologists familiar with NAION participated.

Results Good agreement was found for Group 1 at lower cup-disc ratios, (CD ratio) reaching 100% for horizontal CD ratios below 0.27. Agreement fell sharply at horizontal CD ratios 0.28 and above. Disagreement was high in horizontal CD ratios from 0.38 to 0.47 (26 Yes responses to 44 No). When vertical or when horizontal and vertical ratios were combined percent agreement followed a similar pattern. For comprehensive ophthalmologists (Group 2) percent agreement was consistently less than Group 1. Agreement varied from 26 to 74% across the full range of horizontal CD ratios.

Conclusion Poor agreement among comprehensive ophthalmologists over a wide range of CD ratios, undermines the creditability of the assessment in regular clinical practice. Even though skilled practitioners of Group I demonstrated better agreement than did comprehensive ophthalmologists, lack of agreement was evident over a broad range of common CD ratios. As a result, the diagnosis of a Disc at Risk is rendered suspect in many instances even by this specialist group.

5126
Douglas Argyll Robertson (1837-1909) – what did he do other than describe the Argyll Robertson Pupil?

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Purpose To study medical achievements of Douglas Argyll Robertson in ophthalmology.

Methods The data dealt with in this paper is analysed both from the historical and present-day perspectives.

Results Douglas Argyll Robertson (1837-1909) was the first surgeon in Scotland to practice entirely in the field of ophthalmology. In this he was no doubt encouraged by the memory of his father, John Argyll Robertson, who was one of the founders of the Edinburgh Eye Dipensary but who had died when his son was only 18 years of age. Douglas completed his medical education under von Arlt in Prague and Albrecht von Graefe in Berlin. Argyll Robertson made major contributions to ophthalmic surgery. He introduced extracts of Calabar bean (Physostigma venenosum), in the treatment of glaucoma. He also described in cases of spinal cord disease that there may be loss of the light reflex of the pupil but retention of its movement in accommodation. This condition was named the "Argyll Robertson pupil" and as a clinical sign is almost always indicative of neurosyphilis. His other contributions include: lupus of the eyelid, aetiology of glaucoma, melanotic tumor, diphtheritic ophthalmia, sympathetic ophthalmia, retinitis pigmentosa, hypertrophy of the lacrimal gland, senile entropion, hydrophthalmos, asteroid hyalitis, pulsating exophthalmos, conjunctival filiariasis, albuminuric retinitis, miner's nystagmus and microphthalmos. Argyll Robertson is also credited with being the first to recommend trephining the sclera in those cases of glaucoma where extensive degenerative changes in the iris made an iridectomy impracticable.

Conclusion As we approach the centenary of his death Argyll Robertson deserves to be celebrated for more than his pupil.

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Binocular vision disturbances and eye movement restrictions in patients with thyroid associated ophthalmopathy(TAO)

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Purpose To investigate the incidence and associations of various types of double vision and limitations of gaze among patients presenting with ocular complaints related to thyroid associated ophthalmopathy.

Methods We included 325 patients (268 female and 57 male) aged 42 to 78 (mean 51.1 +/-5.2) referred with ocular symptoms and the diagnosis of TAO. 156 sex and age matched, healthy volunteers served as a control group. Eye movements restrictions were investigated and recorded in the four point scale. The degree of exophthalmos was recorded, as well as the degree of horizontal and vertical disparation.

Results 59.8% of patients reported significant double vision. 96% of patients complaining of double vision trported that it is intermittent,(29% in primary gaze position and 67% in other than primary). The most common limitation of eye movement was elevation(49%). There is a significant correlation between clinically significant double vision and vertical disparation (P=0.30) as well as asymmetrical exophthalmos (p=0.34). There is no correlation between the amount of exophthalmos and double vision.

Conclusion Diplopia is an extremely common presenting sign of TAO. Most patients are troubled by diplopia in different than primary gaze direction. Asymmetrical exophthalmos, and asymmetrical vertical eye muscle involvement are the most significant factors associated with symptomatic diplopia.

5131
Corneal cross-linking for keratoconus

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Purpose to point out the efficacy and safety of collagen cross linking of the cornea as a parasurgical treatment of keratoconus

Methods corneal cross linking has been performed on 50 patients from 17 to 35 years old with topographical and clinical evolutive keratoconus

Results Cross linking treatment has been proven to strengthen the weak corneal structure by increasing collagen cross links, wich are the natural anchors within the cornea.These anchors prevent the cornea from bulging out and becoming steep and irregular.Several aspects of the procedure will be considered including ultrastructural and histological behaviour of the corneal collagen after this photodynamic procedure.

Conclusion The procedure seems to be safe and effective in increasing stiffness of the cornea.More studies are needed to clarify the intrinsic mechanisms of the procedure

5132
New insights in amniotic membrane transplantation

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The amniotic membrane (AM) has been used for almost a century in reconstructive surgery of various parts of the human body, including bladder, and vagina. More recently, it has found application for treating ocular burns and ocular surface disorders, including conjunctivital and corneal defects. One placenta can provide material sufficient for more than 20 surgeries. Limbal epithelial cells are also cultured and expanded on denuded AM. Until now there have been very few studies on the proteins present in AM and responsible for its anti-inflammatory, anti-scarring and anti-angiogenic properties. A better knowledge of the biochemical composition and function of the AM will help develop standardised AM, both for culture and surgery as well as later on synthetic membranes. Thru a review of published studies and of the research performed at the Division of Ophthalmology and Visual Sciences we will focus on the necesity of using standardized membranes for both limbal epithelial cells culture and surgery.

5133
The use of femtosecond laser in corneal transplantation

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Purpose Femtosecond laser (FSL) devices, based on the physical phenomena of ultrashort laser pulses in the sub-picosecond range of duration, have gained significant interest in ophthalmology thanks to their potential for high-precision microsurgery, particularly in applications involving the transparent tissue of the cornea that take the greatest advantage of these attributes. The potential advantages and limits in using FSL in the field of corneal grafts are presented

Methods FSL is applied in performing deep lamellar (DALK), penetrating keratoplasty (PK) and arcuate keratotomy (AK) in human eyes. Clinical and histological analysis was performed.

Results FSL technology enables multiple cut configurations and customized-shaped PK, DALK and AK are feasible techniques. PK with complex wound shapes including top-hat profile and orientation teeth and notches can be performed. FSL-deep lamellar dissection both for DALK and endothelial transplantation presents a good morphology of the dissection plane. The graft geometry in DALK for keratoconus, in contrast, shows limits related to the posterior stromal bed shape. Transmission electron microscopy revealed precise geometry and good quality of the cuts. Customised shaped paired AK can be successfully performed to treat high post-keratoplasty astigmatims.

Conclusion Femtosecond laser technology may offer further promising approaches towards customized trephination, and dissection procedures in the field of corneal transplantation.

5134
Deep anterior lamellar keratoplasty

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Despite the long term risk of endothelial rejection, full-thickness corneal transplantation is still considered the gold standard surgery for replacing a diseased cornea. Deep anterior lamellar keratoplasty (DALK) is not a new procedure, but in the past, its use has been of limited popularity owing to the challenging, lengthy and tedious surgery involved. With the advent of newer surgical techniques and instruments for performing lamellar corneal surgery, DALK has gained in popularity. This presentation discusses the techniques for performing the procedure as well as the clinical outcomes, especially focusing on Big bubble DALK. Results will be compared with the outcomes of penetrating keratoplasty (PK). Results suggest that DALK is the logical choice in the surgical management of corneal stromal disease, in presence of a functional endothelium.

5135
Options in endothelial transplantation

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Purpose To reduce DSAEK surgery time using pre-cut tissues.In addition real time valuation of specific parameters like cell density,endothelial mortality rate and finally thickeness of the posterior corneal lamella.

Methods Corneo scleral discs were fixed in an artificial anterior chamber AC and Moria One microkeratome (Moria S.A., Antony, France) with a 350-micron Carriazo-Barraquer-type head was used to the prepare the lamellar corneal tissues.The artificial AC was cushioned with EUSOL-C (AL.CHI.MI.A.S.r.l,Ponte S.Nicolò,Italy).The sectioned tissues were stored at 4°C;post-cut and 24 hours pachymetry was repeated. Before the cutting,post-cut,at 4 and 24 hours cell viability and the same time cell morphology was measured with an inverted microscope.Cell density was measured at beginning and at the end of time course.Following this preliminary study,40 tissues were assigned for transplantation.

Results Endothelial cell mortality was observed,which was characterized by trypan blue-positive cells diffused in the whole endothelial surface and corneal folds.The pattern of damage was typically due to mechanical factors associated to the passage of the microkeratome head.Cell morphology was well preserved at the end of the storage period at 4°C in EUSOL-C. We find a regular endothelial mosaic and absence of significant pleomorphism and polymegathism. An increase (approx.20%) in corneal thickness was observed at the end of time course. Finally no cases of graft dislocation or primary graft failure were observed.

Conclusion The results have demonstrated the reproducibility of the procedure.In this way is possible to provide tissues ready to use,within 24h, and at the same time to certify tissue quality to prevent the primary graft failure and graft dislocation.

5141
UVR-effects in human versus animal eyes: more contradictions or more similarities?

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Purpose To compare the characteristics and time scales of UV-radiation effects in the eye, especially the lens, investigated and documented in human and various animal species. The target is to test the predictability potential of animal experiments for characterization of human UV-risk scenarios.

Methods Experimental studies on UV-effects to the cornea and lens in mice and rats are critically compared to epidemiological studies on UV- effects to the human eye.

Results Animal studies provide a broad spectrum of data on genetical and environmental factors leading to various types of cataracts and corneal alterations. Many patho-physiological factors are identified. Epidemiological studies in humans identify other noxious factors but the most important difference seems to be the time scale and thus the age-related difference in UV-sensitivity of the lens and the anterior eye segment.

Conclusion Future studies should focus more on species- and age-related sensitivities of the lens to UVR effects and on the influence of systemic effects, also in relation to ocular immunology.

5142
UVR exposure of the lens in the mammalian eye, species difference

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Purpose To determine the absorption properties of the anterior segment of the mammalian eyes and relate those changes to aging mechanisms of the anterior segment and to possible consequences of cataract formation.

Methods A simple method has been developed to determine the optical properties of the anterior segment of the intact eye. This consists of a probe which is inserted into the posterior sclera and detects light passing through the anterior segment. The probe is connected to a CCD spectrophotometer via a fiber optic bundle. Digitized data is collected and analyzed by a laptop computer.

Results The absorption and transmission characteristics of mammallain anterior segments vary markedly with species and age. This has implications for photochemical and other light studies in both the lens and retina. The anterior segment of nocturnal animals, such as the rodent, transmit light down to 300 nm, but as they age this increases to 310-320 nm. Diurnal mammals, such as the rabbit, guinea pig and cow contain large amounts of NAD(P)H, which absorbs all of the UV-B and most of the UV-A.The yellowing of the primate lens results in a progressive decrease in the amount of blue light reaching the retina. The young lens absorbs primarily UV-A, whereas with age, there are increases in absorptions at 320 nm and out to wavelengths as long as 550 nm. The position of cortical cataract may be due to the optical characteristics of anterior segment.

Conclusion The optical characteristics of the lenses of various animal models have markedly different UVR absorption properties. These qualities are critical to consider when using animal models to study aging mechanisms and cataract formation in the lens.

5143
Oxidative stress in lens epithelial cells after UVR exposure

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Purpose The lens epithelium is the primary target in solar photooxidation. Thioltransferase is a repair enzyme capable of reactivating oxidized critical proteins and enzymes in the cells.

Methods Primary lens epithelial cell cultures from wild type and thioltransferase knockout mice were exposed to various doses of UV radiation or hydrogen peroxide. The short-term reaction pattern of several glutathione-related enzymes were investigated, as well as long-term growth rate and cell adhesion.

Results UV radiation induces a reaction pattern comparable to that of hydrogen peroxide, with initial increase or decrease in activity of antioxidative enzymes, and a subsequent recovery within 1-2 hours. Low dose UVR exposure induces cell stimulating effects similar to treatment with low peroxide concentration.

Conclusion Oxidative stress from peroxide and UVR might be channeled through same oxidant cellular pathway.

5144
The lens response to daily in vivo exposures to UVR

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Purpose Epidemiological data indicate correlation between life long exposure to ultraviolet radiation and cortical cataract. There is no experimental data on the effect of daily repeated in vivo exposures of the eye to UVR. This experiment was designed to verify whether the dose additivity for UVR exposures holds through periods of time up to 30 days.

Methods Eighty rats were conditioned to a rat restrainer five days prior to exposure. All animals were divided into 4 exposure period classes of 1, 3, 10 and 30 days of exposure to UVR. Each exposure period class of 20 animals was randomly divided into five cumulated UVR dose sub-groups. Eighteen-week-old non-anesthetized albino Sprague-Dawley(SD) rats were exposed daily to UVR-300 nm for 15 minutes. One week after the last exposure, animals were sacrificed. The lenses were extracted for macroscopic imaging of dark-field anatomy and degree of cataract was quantified by measurement of intensity of forward lens light scattering. Maximum tolerable dose (MTD2.3:16), statistically defined standard for sensitivity for threshold for UVR cataract, was estimated for the periods of exposure and plotted with a linear regression as a function of days during which dose was accumulated.

Results All exposed lenses developed anterior subcapsular cataract with varying appearance depending on the period of days exposed to UVR. Small single doses of UVR accumulated to cause cataract during the periods up to 30 days. MTD2.3:16 for 1, 3, 10 and 30 days of repeated exposures was estimated to 4.7, 4.74, 4.8 and 6.0 kJ/m2, respectively.

Conclusion The tolerance to UVR-B for 18 week old SD rat increases with increasing number of days being exposed. With lower single dose and longer duration for daily exposure the lens is more tolerant to UVR.

5145
Systemic inflammatory response after ocular in vivo UVR-300 nm exposure

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Purpose To investigate if unilateral in vivo UVR-B exposure of one eye affects the contralateral eye in a co-cataractogenic, sympathetic reaction and to determine if an inflammatory response is involved in the pathogenesis.

Methods C57BL/6 mice were unilaterally exposed in vivo to UVR-B for 15 minutes. Groups of 24 animals each received 0x/ 2x/ 3x/ or 4x cataract threshold equivalent dose. 48 hours following UVR - B exposure cataract morphology was documented in dark field illumination photography and light scattering was quantified, in both lenses in vitro. Serum levels of pro-inflammatory cytokines IL-1ß, IL-6 and TNF-α were analyzed with ELISA. Immunohistochemistry was performed for inflammatory infiltration in exposed and contralateral eyes.

Results UVR-B exposure induced cataract in all exposed lenses. There was additionally a significant UVR dose dependent increase of light scattering in contralateral not exposed lenses. Inflammatory infiltration was detected immunohistochemically in the anterior segment of both eyes. IL-1β serum concentration increased with increasing UVR-B exposure dose. There was a similar trend for serum IL-6 but not for TNF-α.

Conclusion Unilateral UVR-B exposure increases light scattering also in the contralateral eye and triggers a systemic inflammatory response mediated by IL-1β and possibly IL-6. Age related cataract is almost exclusively a bilateral event. Since a systemic inflammatory response might be an important factor in cataractogenesis our results might initiate new strategies in the prevention of the disease.

5146
Prevention of UVR cataract with Vitamin-E

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Purpose To analyze the potential of Vit-E for cataract prevention

Methods The experimental animal was 6 weeks old albino SD rat. Animals supplemented with Vit-E received a daily dose per os for 4 w prior to exposure. Oxidative stress was induced by in vivo unilateral exposure to ultraviolet radiation (UVR) around 300 nm. Forward light scattering was measured in the lens 1 w after exposure. I: 40 animals were divided into supplementation (100 IU/day)/no supplementation groups. In all animals, one eye was exposed to 8 kJ/m2 UVR. II: 80 animals were divided into two exposure groups, (5 min, 15 min). Each group was divided into supplementation (100 IU/day), no supplementation subgroups. In all animals, one eye was exposed to 8 kJ/m2 UVR. III: 100 animals were divided into 5 dose groups (0, 5, 25, 50, 100 IU/day). All animals were unilaterally exposed to 8 kJ/m2 UVR. IV: 40 animals were divided into supplementation (20 IU/day)/no supplementation groups. Each group was subdivided into 5 dose subgroups. MTD(2.3:16) was estimated for both supplementation groups and the protection provided by Vit-E was calculated as MTD(2.3:16) ratio between supplementation and no supplementation.

Results I: Vit-E supplemented animals had a higher content of Vit-E and expressed less light scattering than non-supplemented animals. II: Vit-E suppressed additional light scattering expressed after 15 min exposures as compared to 5 min. exposures. III: Vit-E suppressed the UVR induced light scattering exponentially declining as a function of increasing supplementation. IV: Vit-E supplementation provided a protection factor of 1.4.

Conclusion Vit-E suppresses oxidative stress from in vivo exposure to UVR.

5151
Perfusion pressure and blood flow: difference and relevance

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Purpose Maintenance of appropriate levels of regional blood flow play an essential role in the maintenance of a stable internal environment of an organism. The relative contributions of the different mechanisms vary between and within vascular beds. The ability of vascular beds, especially those not or not particularly responsive to neuronal regulatory mechanisms, to maintain, within certain limits, an independence of regional blood flow from local perfusion pressure is called autoregulation.

Methods A proper appraisal of local perfusion pressure is mandatory if one is to understand blood flow and the effects of its perturbation. When speculating about ocular perfusion pressure, it has become customary to estimate mean blood pressure within the ophthalmic artery and to subtract the value of intraocular pressure, assumed to be equal to venous pressure. This concept, likely to be adequate under steady state condition in healthy eyes, may not hold under stress conditions or therapeutic interventions, as well as in disease states. Examples are manifold.

Results Simple starvation may put a burden on the circulation to maintain the supply of metabolites, possibly solved by increasing transmural capillary filtration pressure. In glaucoma, an increased venous pressure has been described and, indeed, more force must be applied to the eye to induce retinal venous pulsations. These conditions are simple examples where our current approach in estimating ocular perfusion pressure is probably incorrect.

Conclusion The regulatory responses of ocular vascular beds have not yet been elucidated in full detail, and care must be applied when speculating about ocular perfusion pressure, and many of our current assumptions with regards to autoregulation in the ocular circulation may need a very critical scrutiny.

5152
Impact of glaucoma medications on IOP, blood pressure and perfusion pressure: relevance for the daily practice

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Higher it will be the Perfusion pressure and higher it will be the blood flow in a determined body district.How it has been determined by several population-based studies, low levels of diastolic ocular perfusion pressure (DOPP) are associated with an increased prevalence and incidence of POAG. As a matter of fact, the Baltimore eye study has shown that when DOPP decreases below 50 mm Hg the prevalence of POAG increases; similar results were obtained in the Egna-Neumarkt in Europe, in the Projecto VER in Mexico, and in the Barbados Eye Study in Caribbean.In the Barbados eye study DOPP was 63 ± 14.9 mmHg in healthy subjects, and 53.8 ± 14.9 mmHg in POAG patients. As a general indication, it can be concluded that when DOPP is lower than 55 mm Hg there is an increased risk to develop POAG.In the present lecture it will analyzed the relationship between BF and POAG, and the correlation between circadian fluctuation of BF and the extent of damage in POAG patients. Twenty-four hour Blood pressure and IOP will be detailed evaluated in the study of pathogenesis of glaucoma.Moreover it twill be analyzed the behavior of 24-hour IOP and blood pressure in normal-tension glaucoma patients.It will be also analyzed the influence of hypotensive drugs for glaucoma on BF and circadian IOP and blood pressure. The mean aim of the present lecture will be to give a comprehensive evaluation of the importance of the monitoring of blood pressure and IOP over the twenty-four hour, in order to evaluate the risk of progression of each POAG patients, but also to know the effect of hypotensive glaucoma therapy not only on IOP but also on diastolic ocular perfusion pressure.

5153
Blood flow and metabolism measurements: are they ready for the clinic?

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Purpose A growing number of epidemiological studies clearly identified reduced ocular diastolic perfusion pressure as a significant risk factor for open angle glaucoma (POAG), suggesting that optic nerve ischemia and hypoxia may play a role in the etiology and pathogenesis of POAG.

Methods Advances in ultrasound, laser computerized image analysis and Doppler technologies, within the last two decades have made it possible to objectively measure ocular hemodynamics. Each technique, however, examines different facets of the vascular system focusing on varying anatomical location of blood vessels and providing differing hemodynamic outcomes.

Results My talk will cover the pros and cons of the existing technologies for measuring ocular blood flow. Focusing on color Doppler imaging, scanning laser ophthalmoscopy with fluorescein, scanning laser ophthalmoscopy with indo-cyanine green, Heidelberg retinal flowmetry, laser Doppler flowmetry, retinal vessel analyzer (RVA) as well as the new generation of technologies aimed at measuring oxygen saturation in the optic nerve head and retina.

Conclusion At present no single technique can accurately assess all relevant vascular beds. More development and emphasis is necessary. This presentation will also focus on possible clinical utilization of ocular blood flow and metabolism measurements.

5154
Available educational material from the European Glaucoma Society on ocular blood flow techniques

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One of the major aims of the European Glaucoma Society is to provide education on glaucoma. Recently, an educational DVD was developed thanks to a joint effort of experts in the field. This DVD provides a comprehensive overview of various techniques that are used in the field of glaucoma. In the chapter on ocular blood flow, the following techniques are described: color Doppler imaging (CDI), retinal vessel analyzer (RVA), laser Doppler flowmetry (LDF) and confocal scanning Doppler flowmetry (HRF). The physical principles, the measured vascular beds and parameters, the clinical protocol, as well as the advantages and disadvantages are discussed and illustrated.

5161
Epidemiology of conjunctival melanocytic neoplasms

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Purpose To summarise the epidemiology of conjunctival melanocytic neoplasms.

Methods Review of population-based data on 85 patients with primary conjunctival melanoma (CM) and recently published literature.

Results CM accounts for 5-7% of ocular melanoma in Europe. Its age-adjusted incidence has increased 2-fold in North Europe (Finland, from 0.40 to 0.80/million) and North America (USA, from 0.27 to 0.54) during the last 25 y. In both regions, age-adjusted incidence is higher in men. Different rates between regions result from differences in registries, ethnicity and solar radiation. Age-adjusted incidence of CM is 3-fold in non-Hispanic Caucasians and 2-fold in Hispanics relative to Asians, African Americans and American Indians; among non-Hispanic Caucasians it increases 2.5-fold from 48 deg. (e.g. Paris) to 21 deg. (e.g. Mecca) of latitude. CM is rare below 30 y of age (age-specific incidence, 0.06) but increases steadily thereafter (0.48, 1.05 and 1.57 for 30-49, 50-70 and >70 y, respectively). Median age at diagnosis is 58-60 y. Most CM arise in limbal (57-64%) followed by bulbar (12-13%), palpebral (7-9%) and caruncular (3%) conjunctiva. Tumor-specific 5-and 10-y mortality estimates are 14-20% and 29-38%, respectively. Non-limbal location, increasing tumor thickness and local recurrence are consistently associated with higher mortality. Clinically detectable primary acquired melanosis (PAM) and nevus precede or accompany CM in 57-61% and 7-23% of patients, respectively. Median age at diagnosis of PAM is 56 y. The risk of malignant change is not precisely known and depends heavily on subtype of PAM, ranging from 10 to 90%.

Conclusion Recent studies provide epidemiological data on CM which are remarkably consistent. The epidemiology of conjunctival nevi and PAM is less precisely known.

5162
Pathology of conjunctival melanocytic neoplasms

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Purpose To describe the classification, grading and staging of conjunctival melanocytic proliferation.

Methods We have audited our experience with conjunctival melanomas, using a novel mapping system and have found shortcomings in the current Tumour Node Metastasis (TNM) staging system. We have also reviewed our cases of intra-epithelial melanocytic neoplasia and confirmed other authors' impressions that conjunctival 'primary acquired melanosis with atypia' is histologically similar to cutaneous in situ melanoma. To improve objectivity in the reporting of conjunctival intra-epithelial melanocytic neoplasia, we propose a scoring system based on pattern of melanocytic infiltration, density of melanocytes & degree of cellular atypia.

Results The term 'conjunctival melanosis' should be used only to describe the slit-lamp appearance of hyperpigmentation. Histologically, this abnormality should be categorized as 'hypermelanosis' or 'melanocytosis.' Hypermelanosis can either be primary or secondary to ocular or systemic disease. Benign melanocytosis comprises conjunctival melanocytic hyperplasia and naevi. Malignant melanocytosis is essentially melanoma, which is primary (in situ or invasive) or secondary (i.e., spreading to conjunctiva from adjacent tissues) or rarely metastatic. We suggest that the TNM staging system for conjunctival melanoma should be revised to: (1) include a Tis stage; (2) take account of superficial extent, invasion of adjacent tissues and caruncular involvement, in stages T1 to T3II; and (3) to sub-categorize T3V disease so that there is better correlation with likely mortality.

Conclusion We have revised the classification of conjunctival melanocytic proliferations & improved the grading and staging of melanoma. These developments should be useful in treatment & research.

5163
Treatment of conjunctival melanocytic neoplasms: the Paris experience

DESJARDINS L
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ABSTRACT NOT PROVIDED

5164
Treatment of conjunctival melanocytic neoplasms: the Liverpool experience

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Purpose To audit the results of treatment of conjunctival melanoma in Liverpool.

Methods Patients treated between 1993 and 2006 were identified by searching the Ocular Oncology Service database and pathology archives. The casenotes were reviewed. Patients were included if their conjunctival tumour was histologically diagnosed as invasive melanoma. Tumour extent and location were defined using a mapping system we developed. During the course of this study, cryotherapy was abandoned in favour of topical chemotherapy for intra-epithelial melanocytic neoplasia and brachytherapy for invasive disease.

Results Forty patients with invasive conjunctival melanoma were initially treated at our centre and another 36 were referred to us for salvage therapy after a surgical intervention elsewhere (11 with no visible tumour, 9 with intra-epithelial disease and 16 with invasive melanoma). The patients we initially treated all retained the eye, most without significant visual loss. Recurrence occurred in six patients, none of whom had adjunctive brachytherapy. Four patients died of metastasis, all with caruncular involvement. After salvage therapy in 16 patients referred with recurrent or persistent invasive disease, two eyes were lost and five patients died, only one of whom had caruncular involvement.

Conclusion Excision of invasive conjunctival melanoma with adjunctive brachytherapy and topical chemotherapy achieved high rates of local tumour control with little ocular morbidity. Without caruncular involvement, disease-specific mortality was rare unless the patient was referred with invasive disease after a surgical procedure elsewhere. Our results suggest that inexpert surgical intervention increases the risk of local tumour recurrence and metastatic death.

■ 5165

Combined treatment of conjunctival melanomas. The experience of the Jules-Gonin Eye Hospital of Lausanne

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Purpose The recurrence rate of conjunctival melanomas following a monotherapeutic approach (surgery, irradiation or Cryoapplication) is as high as 50%. The etiology of this high recurrence rate is partially related to the biological characteristics of the PAM and partially to the anatomic properties of the various parts of bulbar, limbus and tarsal conjunctiva.

Methods We developed a combined therapeutic strategy which associates surgical excision with Gamma or Beta brachytherapy, proton beam irradiation, and Cryotherapy with liquid nitrogen under pressure. This combined therapeutic modality is used in all the cases of primary and recurrent conjunctival melanomas which was referred in Jules-Gonin Eye Hospital, during the last 20 years (190 cases).

Results Therapeutic results depend on the extension and location of conjunctival melanomas. Definitive loss of local tumour control is rare and occurs in cases in which both of the leads are invited by the tumor as well as in cases which present an unpigmented recurrence.

Conclusion Positive results may be obtained by the use of a combined therapeutic modality of surgical excision irradiation and Cryotherapy for the treatment of selected cases of conjunctival melanomas.

■ 5166

Conjunctival melanoma : the Curie experience

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Purpose To evaluate the treatment of conjunctival melanoma at the Institut Curie in term of local recurrences, ocular preservation, distant metastasis and survival

Methods Retrospective study of patients with conjunctival melanoma treated for their first tumoral localisation between January 2000 and December 2005. The clinical records, histologic features, ocular treatments were rewiewed. The rate of local recurrences, ocular preservation, regional and distant metastasis, and survival were recorded.

Results During the study period, 91 patients were referred for conjunctival melanoma. 67 of them were treated for a first occurrence of malignant melanoma (38 women and 29 men). The mean age was 62 years (25 – 90). 32/67 patients (47 %) presented a primary acquired melanosis (PAM). Most cases (55 patients) were treated by surgical excision and adjunctive radiotherapy (Iodine plaque, protonbeam or external beam irradiation), 5 cases were treated by surgery alone, and the last 6 by surgery and adjunctive cryotherapy or adjunctive topical chemotherapy. 3 patients were lost of follow-up. With a mean follow-up of 52 months (15-101months) 20/64 patients developped at least one local recurrence (between 1 and 7 recurrences). 16 of them presented a PAM. An enucleation was finally necessary for 1 patient and an exenteration for 2 patients. 7 patients developped metastatic disease (all but one presented a PAM) and 6 of them died.

Conclusion Local recurrences, metastatic disease and tumor related death appear to occur at higher frequency when melanoma is associated with PAM. This risk must be taken into account in the therapeutic approach of conjunctival melanoma.

▪ 5211
Experimental principles and indications of internal limiting membrane peeling

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Purpose The removal of the internal limiting membrane (ILM) has become a widely accepted option in macular surgery. We will present the fundamental and clinical features to assess the influence of this technique in the management of surgical macular diseases.

Methods The internal limiting membrane peeling is considered as an option to the commonly accepted treatment of macular hole surgery but its place remains under debate. Different studies were performed to assess the influence of ILM peeling on the outcome of macular hole, epiretinal membrane or macular edema. However they frequently combined different factors as well as different surgical techniques.

Results The ILM should constitute a scaffold for glial cell proliferation if not removed. It should increase the rate of success and decrease the rate of late opening of macular hole but it remains speculative and controversial at the moment. About all the studies assessing the efficacy of ILM peeling in macular hole surgery are retrospective. All the studies about ILM peeling in macular edema or epiretinal membrane are non randomized study. The peeling of ILM is possible without any staining. However, the difficulty to peel it without trauma of the retina and even more the putative toxic risk of the different dyes to facilitate its removal are of concern.

Conclusion The ILM peeling represents an interesting option in the treatment of macular hole surgery but its place needs to be defined more clearly. In the future, we have to define "individual" treatment considering all influencing factors (size, onset, stage of macular hole) to choose a "tailored" treatment.

▪ 5212
Visualization drugs for vitreoretinal surgery

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Purpose To discuss data on the potential or real toxicity of intraocular visualization drugs, based on animal and human studies.

Methods The course will be based on last experimental and clinical data available in the literature or from our studies.

Results There is a larger choice of visualizations drugs with a clear benefit of helping the surgeon. Each of them has its own advantages and risks. The decision to use or not these drugs should also take into account the goal for which they may be used and the expected benefit from it.

Conclusion Visualizations drugs, as most drugs, may represent risks that have to be weighed up against awaited benefits.

▪ 5213
Experimental and clinical studies of transconjunctival vitrectomy 20G, 23G and 25G

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Purpose Microincision transconjunctival vitrectomy has gained popularity in the recent years. This surgical innovation needs to be evaluated in prospective and controlled studies.

Methods A prospective study concerning 23-Gauge vitrectomy (with cryoapplication and gas tamponade) in 20 patients with retinal detachment and 4 patients with acute endophthalmitis was performed and litterature data (Pubmed database research) was analyzed.

Results Performance of microincision transconjunctival vitrectomy may be maximized with use of high duty cycle, largest internal diameter (23G), a sharp guillotine and a high cut rate. Sclerotomy construction is a key point of this technique. In retinal detachment surgery on a selected population, the rate of anatomic reattachment and visual recovery were similar between 23G PPV and 20G PPV. In one patient 23G PPV was complicated by a choroidal detachment secondary to a displacement of the infusion cannula. The redetachment in one 23G case was secondary to a sclerotomy related retinal tear. Microincision transconjunctival vitrectomy for acute endophthalmitis is feasible but has limited capacities as compared with 20G technique.

Conclusion The main advantage of sutureless vitrectomy remains the confort of patient after complicated surgeries, but this point should be analyzed with quality of life. This trend toward smaller incisions will lead to improvement of instrumentations, better understanding of the surgical techniques (wound construction, performance of vitreous cutters). 23G PPV is suitable for patients with retinal detachment treated with PPV-cryo-gas technique. Sutureless vitrectomy is usefull only in selected cases of acute endophthalmitis .

▪ 5214
Vitrectomy cryo gas for the treatment of pseudophakic retinal detachment

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Purpose The management of pseudophakic rhegmatogenous retinal detachment (PsRD) has represented a challenge for vitreoretinal surgeons for many years. Different surgical techniques have been used to manage PsRD including pneumatic retinopexy, scleral buckling (SB) and primary pars plana vitrectomy (PPV) with or without SB. Recent advances in the vitrectomy technique and instrumentation have contributed to the expanding role of PPV as a first-line surgical treatment in cases of PsRD.

Methods A potential advantage of PPV is removal of posterior capsular and vitreous opacities for better visualisation of the peripheral retina and the use of wide-angle viewing systems and microscopic inspection of the fundus periphery with internal illumination and scleral identation during PPV. This allows for an accurate diagnosis of retinal breaks, their prompt treatment and thus high initial anatomical success.

Results A meta-analysis of published studies suggested that PPV with or without SB is more likely to achieve favorable anatomical and visual outcomes than conventional scleral buckling alone in uncomplicated PsRD. Recently published prospective or randomized clinical trials also found that primary PPV alone is at least as effective as scleral buckling for the treatment of PsRD. The Scleral Buckling versus Primary Vitrectomy in Rhematogenous Retinal Detachment study, found no difference in visual acuity between PPV and SB alone in pseudophakic eyes, but anatomic outcomes were better in the PPV group.

Conclusion Primary vitrectomy without scleral buckling provides a high anatomic success rate in eyes with PsRD and is associated with few complications.

▪ 5215
Combined surgery (phacovitrectomy)

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Purpose To review the results and complications of combined phacoemulsification and vitrectomy in phakic patients.

Methods Retrospective review of 412 consecutive phakic patients who underwent phacoemulsification and vitrectomy for primary rhegmatogenous retinal detachment (RRD) (71), stages 2 to 4 full thickness macular holes (FTMH) (86), idiopathic epiretinal membrane (ERM) (237), diabetic macular edema (DME) (18) .

Results Lens opacity was absent or mild in 85% of patients. Reattachment rates for primary RRD after one procedure were 86% and final reattachment rates were 95% . Macular hole closure rate was 95% for holes under 500 microns. There was significant improvement in the median logMAR visual acuity from 1.6 preoperatively to 0.48 postoperatively for the retinal detachment patients ,from 0,59 preoperatively to 0,28 for the idiopathic epiretinal membrane , from 0,93preoperatively to 0,4 in full thickness macular holes and from 0,96 to 0,60postoperatively in diabetic macular edema. Postoperative complications included fibrinous uveitis (2%), IOL/iris capture secondary to gas overfill (1.1%), and posterior capsule opacification (8%).

Conclusion Combined phacoemulsification and vitrectomy is a safe and desirable option in the management of phakic patients with vitreoretinal pathologies that warrant vitreous surgery, even in the absence of significant lens opacity.

5221
Critical flicker fusion frequency in age-related macular degeneration

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Purpose To discuss the influence of AMD on critical flicker fusion frequency (CFF)

Methods CFF was measured centrally for red, green and blue signal and in 10° excentricity with a red signal. 33 patients with non exsudative AMD and a visual acuity (VA) of 20/100-20/20, 12 patients with exsudative AMD (VA: 20/100-20/25) and 45 age-matched healthy eyes (VA: 20/32-20/20) were included.

Results CFF decreased in eyes with non exsudative AMD (red 1,6Hz p=0,01, green 1,6 Hz p=0,04, blue 2,1 Hz p=0,01). The difference between central and peripher CFF increased (red-red 10°, 1,0 Hz p=0,01). Differences between different colours were low and reached no significance. In eyes with exsudative AMD CFF showed lower values (red 2.2 Hz p=0.02, green 3.3 Hz p=0.001, blue 2,9 Hz p=0.02, but in spite of increased difference between central and peripher CFF had no statistical significance. (red-red 10° , 1,3 Hz p=0,25). Eyes with exsudative AMD showed a 1.0 Hz (p=0.02) higher difference between CFF with a red and a green signal than healthy eyes. Sub-group analysis of patients with non exsudative AMD and visual acuity better than 20/32 (n=20) and healthy eyes showed no difference. Patients with non exsudative (n=13) and eyes with exsudative AMD (n=7) and VA between 20/200 and 20/40 reached equal CFF values.

Conclusion CFF was decreased in non exsudative and exsudative AMD. The difference between central and peripher CFF increased in exsudative and nonexsudative AMD. Exsudative AMD has a stronger impact on a green than on a red signal. CFF is not able to distinguish between groups of equal visual acuity and therefore not applicable as a diagnostic test.

5222
The spatial and neural deficit of human amblyopia

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Purpose Human functional imaging studies confirm deficits of V1 identified from animal models and suggest additional extrastriatal areas of dysfunction. This study aims to investigate spatial visual and neural deficits in human amblyopia.

Methods Participants were 6 adults (mean age=20±2 years) with amblyopia; anisometropia (n=2); mixed (n=4) and 3 normal adults (mean age=31±4 years). Cortical activation for each eye was measured using functional magnetic resonance imaging (fMRI) and psychophysical methods. Stimuli included four attributes of spatial vision known to be deficient in individuals with amblyopia: visual resolution, contrast sensitivity, vernier acuity and global motion. In each subject, retinotopic mapping experiments were also performed to establish locations of different visual areas and to act as regions of interest. All paradigms used a block design: 18 seconds stimulus 'on' alternated with 18s 'control', stimulus subtending 15x15 degrees and flickering at a temporal frequency of 8 Hz. The scans were performed on a Siemens Trio 3.0 Tesla System at Royal Holloway University.

Results All participants with amblyopia had residual amblyopia following treatment. Mean logMAR visual acuity was 0.24 (sd 0.06) and -0.08 (sd 0.06) for amblyopic and fellow eyes respectively. Mean visual acuity for the normals was -0.06 (sd 0.06). Global motion was reduced significantly in the amblyopic (p=0.04) and fellow eyes (p=0.05) of observers compared to the normals; amblyopic eye: 54%(25%); fellow eye: 41%(16%); normals: 25%(7%).

Conclusion Amblyopic observers show significant deficits of global motion for amblyopic and fellow eye stimulation. This is suggestive of extrastriatal deficits of amblyopia in addition to those in V1.

5223
Contact lens wear in strabismic and non-strabismic young patients: sensorial and oculomotor study and quality of life outcome

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Purpose The main aim of the study was to compare sensorial and oculomotor examinations in a sample of strabismic young patients corrected with eyeglasses and secondarily fitted with contact lenses. The second aim was to evaluate the quality of life.

Methods Forty-eight patients were included (8 to 19 years-old) in Tours University Hospital from June 1st 2005 to May 31st 2007. Oculomotor and sensorial examinations were performed.

Results Thirty-seven patients had a mean follow-up of 17.6 months. Twenty-six patients had strabismus. Contact lens wear was stopped in 22.9% cases. In esotropic patients, the decrease of horizontal deviation angle in distant vision with lens was significantly more important when the initial angle measured with eyeglasses was more than 8 dioptries. The contact lens spherical power was significantly higher than the eyeglasses power. We did not find significant difference of quality of life in strabismic young person and the control group.Those results show that contact lens wear can uncover residual accommodation and can decrease the horizontal deviation angle in distant vision when the initial angle is higher than 8 dioptries.

Conclusion Contact lens fitting has to take part in the global medical management of strabismus, especially in young patients willing to give up wearing eyeglasses.

5224
Can amblyopia treatment be optimised?

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Purpose To investigate the efficacy of an educational program in improving the compliance with patching treatment.

Methods A randomised control trial was conducted with 29 amblyopes receiving no educational program and 31 receiving educational program.The compliance was measured using occlusion dose monitors for the entire patching period of 12 weeks. Our secondary aim was to look at the dose effect response for longer effective hours of patch wear.

Results We found that patients who received the educational program complied more and dropped out less (p=0.02).We also found a significant dose effect relationship in strabismic and mixed group with a greater improvement in visual acuity with longer hours of patching :greater than 6 hours (p= 0.0001).We did not find any significant relationship in anisometropes.

Conclusion An educational program would reduce poorly compliant patients and drop outs in amblyopia treatment.

■ 5225

Evaluation of contrast sensitivity on monocularly - deprived subjects

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Purpose It is widely accepted that monocular deprivation results to improved visual performance of the non-pathological eye. The aim of the study was to investigate the effect of monocular deprivation on the contrast sensitivity performance of the fellow eye.

Methods Sixteen subjects (mean age: 28.0 ± 7.9) with monocular deprivation volunteered to participate in the study. Eleven more subjects (mean age: 28.1 ± 3.6) served as the control group. Best-corrected visual acuity was -0.15 ± 0.09 and -0.16 ± 0.08 logMAR, correspondingly. Best-corrected contrast sensitivity was evaluated using vertical sinusoidal gratings (2 Hz square-wave reversal) displayed on a Sony GDM F-520 CRT display at 200cm distance, by means of a VSG2/5 stimulus generator card (CRS, Rochester, UK). Seven spatial frequencies (1, 2, 4, 8, 12, 16 and 24 c/deg) were tested. The average of three thresholds was taken. Performance of the control group was tested both monocularly (dominant eye) and binocularly.

Results Binocular viewing improves contrast sensitivity by about 3.5 dB in control subjects. Contrast sensitivity was found to be higher (4.6 dB on average) for monocularly-deprived subjects, compared with the dominant eye of the control group. However, the effect was spatial frequency-dependent: the difference was more pronounced for low and high spatial frequencies.

Conclusion Monocularly-deprived subjects show higher contrast sensitivity compared to monocular values of normal young subjects. The improved performance of the non-pathological eye of patients with monocular deprivation may be a result of the neuronal synaptic plasticity of the visual cortex.

5231
The basics of wavefront aberrometry

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Wavefront technology has been first used by astronomers for years in order to reduce higher order aberrations induced by the earth's atmosphere, it has been introduced into clinical eye care recently.
 Ophthalmological practice involves performing a full subjective refraction. The sphere, cylinder and axis of astigmatism are measured. We are only correcting two components of a whole host of refractive components of the optics of an eye. These two components (sphere and cylinder) constitute by far the majority of the optical aberration of an eye.
 Even a basic exam yields important information about optical quality. However, all ophthalmologists have been faced with patients reporting visual acuity (or contrast sensitivity, glare, etc.) at levels much lower than would be expected from an eye exam.
 Wavefront aberrometry measures aberrations over the entire eye taking into account not only spherocylindrical refractive error, but also spherical aberration, trefoil, coma, secondary astigmatism as well as other "higher order" aberrations described by Zernike polynomials. Higher order aberrations are thought to contribute to more than 20% of the total number of aberrations in a normal eye an increase with pupil size. In the majority of normal patients, these high order aberrations play a minor role, however, in cases of refractive surgery, keratoconus and orthokeratology, they can induce a number of visual disturbances.
 We will define higher-order aberrations and show how to measure them, giving you a basic working knowledge of wavefront sensing (also known as aberrometry).
 We will show how wavefront sensors work, what are Zernike polynomials, what they tell us and we will show present and future clinical applications of wavefront aberrometry.

5232
Custom wavefront optimization of intraocular lens asphericity

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Purpose To investigate the optimal amount of ocular spherical aberration (SA) in an intraocular lens (IOL) to maximize optical quality.

Methods In 54 eyes of 27 patients, implantation of aspheric IOLs was simulated with different amounts of SA to produce residual ocular SA from -0.30 microm to +0.30 microm. Corneal wavefront aberrations up to 6th order were computed from corneal topographic elevation data. HOAs were measured with the Imagine Eyes IRX3 wavefront aberrometer. The PSF was calculated for the residual ocular higher-order aberrations (up to the 6th order)with fully corrected 2nd-order aberrations. 14 patients were implanted with the Tecnis (AMO)IOL and 13 with the SN60WF (Alcon France).

Results The amount of optimal SA could be predicted based on other HOAs of the cornea. The amount of ocular SA varied among subjects and could be predicted based on corneal HOAs.

Conclusion Selection of an aspheric IOL should be performed according to corneal HOAs.

5233
Retinal images using adaptive optics

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Purpose To image cells of the retina using adaptive optics.

Methods Imaging the human retina in vivo is affected by the eye's natural aberrations, which limit the resolution of retinal images. Measuring these aberrations, including the high order ones, is possible using wavefront sensing techniques.

Results A review of the rapid progress in this field is given. Once the aberrations are known, adaptive optics methods, developed for astronomical observing in the past 15 years, can be applied in order either to improve retinal imaging or to give hyper-vision to the subject. Progress in this domain is reviewed, and some original results are reported with a new instrument.

Conclusion Applications are discussed, including a possible three-dimensional, high-resolution method to image the human retina in vivo.

5234
Cone mosaic imaging using an adaptive optics flood illumination camera system

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Purpose The objective of this study was to develop an adaptive optics (AO) retinal imaging system and conduct in vivo pilot tests in a group of healthy eyes and in several pathological eyes. The experiments aimed at determining the device ability to image cone photoreceptors in presence of a variety of refractive errors.

Methods We examined 20 healthy eyes and 3 eyes with inherited maculopathy using the instrument. The AO system was based on a 52-actuator electromagnetic deformable mirror and a 1024-lenslet Shack-Hartmann wavefront sensor (respectively mirao52e and haso32e, both Imagine Eyes, France). The device was completed with a modified Badal arrangement in order to compensate for possibly large defocus errors. A super luminescent diode operating at 750nm was focused at the retina and the wavefront sensor. Additionally the retina was illuminated by a 3°x3°produced by an electroluminescent diode at 850nm. The center of this field was located at 3° off the fovea. The images were detected using a low-noise CCD camera (Ropper Scientific, USA).

Results Cone photoreceptor mosaics were imaged in the eyes with spherical refraction ranging between –7D and +4D and astigmatism up to 4.5D. The AO correction residual error ranged between 0.08 and 0.2µm in all tested eyes. The imaging resolution was estimated to be better than 5µm in all cases. The mosaic was visible over the entire 3°x3° field in several eyes.

Conclusion It appeared that the retinal isoaplanetic field width was at least 3° experimentally in several tested eyes. This study demonstrated the feasibility of cellular retinal imaging in eyes with relatively large refractive errors using a compact AO instrument.

Commercial interest

5235
Optical aberration measurements in dog and cat eyes: interest & limit

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Purpose To measure the ocular optical aberrations in dog and cat using a wavefront aberrometer based on Hartmann-Shack technology.

Methods Two dogs and one cat were sedated (Medetomidine, 0.1 mg/kg) and their right eye (RE) pupils were artificially dilated (tropicamide). Wavefront aberrations were measured using an irx3 aberrometer (Imagine Eyes, Orsay, France). Prior to each measurement, the eye was aligned with the instrument optical axis by centering both the eye pupil and Purkinje images. The Hartmann-Shack spot images were produced by an array of 1024 microlenses that defined a 7.2x7.2 mm square area in the pupil plane. In preliminary tests, spot image histograms were optimized by adjusting the sensor acquisition time. Wavefront aberrations were then repeatedly measured 10 times in each animal's RE. Spherical defocus, astigmatism and Zernike coefficients up to the 8th order were finally analyzed.

Results The optimal acquisition time was 10 ms for all animals, instead of 33 ms when measuring human eyes. Refractive errors could be analyzed in a 6 mm pupil diameter in all cases. The dilated pupil often exceed the sensor area. The average refractive errors in dog #1, dog #2 and the cat were +2.9D(-2.0D)111°;-0.8D(-0.8D)126° and +3.3D(-2.1D)98°, respectively while their Root Mean Square (RMS) higher-order aberrations amounted to 1.9, 1.1, and 2.1 µm RMS respectively. Standard deviation in sphere and cylinder was 1.0D in the cat and less than 0.5D in both dogs. Standard deviation in the higher-order RMS was 0.8 µm in the cat and less than 0.5 µm in both dogs. The observation of individual data revealed that a significant part of this variability was due to blink-related changes in aberrations.

Conclusion Ocular optical aberrations can be easily measured in dog and cat using a Hartmann-Shack aberrometer with reduced image acquisition time. The tested animals had relatively large higher-order wavefront aberrations when compared to date measured in healthy human eyes. Measurement reproducibility was notably affected by tear layer effects. This variability could probably be reduced using a larger sensor area, specific head contention device and artificial tears. This new diagnostic technique is easily feasible without any use of anaesthesia and provides less variability and more detailed information than skiascopy. Wavefront aberrometry could be useful in both research and clinical applications.

5236
Effects of higher-order wavefront aberrations on the eye's depth of focus

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Purpose To evaluate the impact of higher order aberrations (HOA), defined by individual Zernike polynomial coefficients, on the eye's depth of focus using an adaptive optics (AO) system.

Methods A crx1 AO visual simulator (Imagine Eyes, France) was used to introduce different amounts of individual 3rd and 4th order HOA in 10 healthy eyes. These HOA included coma (Z(3,-1)) and trefoil (Z(3,-3)) at magnitudes of +/-0.3 µm, and spherical aberration (SA) (Z(4,0)) at magnitudes of +/-0.3,+/-0.6 and +/-0.9 µm through a fixed 6-mm pupil diameter. A through-focus response (TFR) curve was assessed by recording the percentage of optotype letters of fixed 20/50 size that the subject could identify while these letters were presented at various target distances. Testing was performed under cycloplegia. For each applied HOA, the subject's depth of focus (DoF) and center of focus (CoF) were computed as, respectively, the half-maximum width and the midpoint of the TFR curve.

Results The introduction of SA resulted in linearly shifting the CoF by 1.3 D for each 0.5 µm of wavefront. The shift was hyperopic with positive SA, myopic with negative SA. The simulation of either positive or negative SA also had the effect of enhancing the DoF, up to a maximum increase of 2 D with 0.6 µm of SA. The enhancement became smaller when the SA was further increased. Trefoil and coma appeared to neither shift the CoF nor significantly modify the DoF.

Conclusion AO technology allowed us to selectively test the visual impact of several HOA on the DoF. The introduction of SA significantly shifted and expanded the subjects' overall DoF. This technique could help in designing optimal corrections for presbyopia and allowing patients to preview refractive surgery outcomes.

Commercial interest

5241
Immunological similarities between the eye and the brain

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ABSTRACT NOT PROVIDED

5242
Neuroophthalmological findings of sarcoidosis and Vogt-Koyanagi-Harada syndrome

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Besides common ocular manifestations neurologic involvement including optic nerve disease, cranial nerve palsies and disorders of the hypothalamus and pituitary gland was also identified in 12% of patients with sarcoidosis. Facial nerve palsy is the most common but usually self-limited neurological manifestation. Optic nerve involvement is the most common neuroophthalmic manifestation. Papilledema, compressive, ischemic, or neuritic optic neuropathy due to granulamatous infiltration of any part of the optic nerve may be seen. Lacrimal gland involvement is also common and is usually asymptomatic. Extensive granulomas may lead to diplopia. Orbital symptoms may mimic other inflammatory syndromes.Like sarcoidosis Vogt-Koyanagi Harada is a disorder characterized with bilateral, granulomatous panuveitis associated with central nervous system and auditory manifestations. At prodromal stage lumbar puncture reveals a pleocystosis, ultrasonography shows diffuse thickening of the choroid tissue. At this stage patients typically report severe headaches, nausea, meningismus, dysacusia, tinnitus, and may even have fever, orbital pain and photophobia. Prodromal phase usually lasts for several days, which may persist for several weeks. It is followed by acute uveitic phase, characterized by bilateral choroiditis, vitritis and papillitis. After that chronic phase is seen with vitiligo, poliosis and resolution of exudative retinal detachments. Neuroophthalmological manifestations may help in diagnosis of rare disorders like Sarcoidosis and VKH syndrome.

5243
Multiple sclerosis & Behçet disease

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Purpose To discuss uveitis associated with multiple sclerosis and Behcet disease

Methods Literature review

Results Uveitis is an uncommon manifestation of MS occurring in around 1% of patients. MS uveitis is more common in females between 20-40 years of age. Intermediate uveitis and retinal periphlebitis are the most common forms of intraocular inflammation associated with MS. Isolated anterior uveitis, more commonly granulomatous, is also seen. The onset of uveitis may precede the diagnosis of MS by several years. The presence of retinal periphlebitis shows a strong correlation with progressive neurological dysfunction.Uveitis is a common manifestation of Behcet disease occurring in around 70% of patients whereas neurological involvement develops in around 5%. Both uveitis and neurological involvement are more common in males, and the typical age of onset is in the 3rd or 4th decade of life. There are mainly two types of neurological involvement. Around 70% of patients have parenchymal involvement which is characterized by an aseptic meningoencephalitis involving the brainstem structures. Around 30% of patients with neurological involvement have dural sinus thrombosis. The most common form of ocular involvement in Behcet disease is nongranulomatous panuveitis and retinal vasculitis with a relapsing and remitting course.

Conclusion While uveitis is uncommon in multiple sclerosis, it is one of the most frequent manifestations of Behcet disease. Clinical findings and course of the disease help in the differential diagnosis.

5244
Herpes virus infections

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The Herpes simplex virus (HSV) is characterized by its neurotropism and the balance between latent infection and reactivation. Studies on human post-mortem tissues showed that HSV is widely distributed in the population, with a preferential location within the trigeminal ganglions (innervating the cornea), but also in the superior cervical ganglions (innervating the iris) or in brain/medullar tissues (innervating the retina). It is thus logical to observe in patients some association between neurological and ophthalmologic infection. Whereas retinitis, and in a lesser extent uveitis, may be classically associated to meningitis or meningo-encephalitis, such association is rarer for herpetic keratitis or conjunctivitis, despite their superior frequency. This discrepancy is probably explained by sites from which virus reactivates, with a higher risk of encephalitis when reactivation occurs in the brain, comparatively to the trigeminal ganglion for example. Ideally, complete work-up of presumed herpetic retinitis should include neurological examination, brain imaging, and lumbar puncture. In some cases, HSV (or VZV) are found in the cerebrospinal fluid, showing that viral reactivation is not only localized in ocular tissues.

Commercial interest

■ 5245

Susac's syndrome

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Susac's syndrome is a primary vasculitis of the central nervous system. It is a microangiopathy affecting the brain, the inner ear and the retina. Its clinical presentation usually consists in behavior and memory disturbances, hearing loss and visual loss due to multiple branch arteries occlusions. It affects mostly women between 18 and 40 years of age. There are no specific radiological or laboratory abnormalities. Lumbar puncture reveals non specific minimal pleocytosis and elevation of proteins. The differential diagnosis includes granulomatous angiitis of the central nervous system and Cogan's syndrome. The pathogenesis is unknown but immune complex and antibody-mediated endothelial damage are possible mechanisms. There is no universally recognized therapy, but immunosuppressants are frequently used.

■ 5246

Primary intraocular and CNS lymphoma

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ABSTRACT NOT PROVIDED

5251
Corneal biomechanical properties and IOP measurements by ocular response analyzer (ORA)

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Purpose To describe the method of operation of the Reichert Ocular Response Analyzer (ORA) and the importance of corneal biomechanical properties in clinical practice.

Methods The engineering and physics concepts behind the operation of the Ocular Response Analyzer will be introduced. The measurement parameters provided by the instrument will be introduced and defined. Special emphasis will be placed on the importance of the Corneal Hysteresis and Corneal Resistance Factor measurements in the understanding of corneal biomechanical properties, and the clinical relevance of these parameters.

Results Relevant results from existing peer-reviewed literature will be presented.

Conclusion The Ocular Response Analyzer provides clinically useful indicators of corneal biomechanical properties.

Commercial interest

5252
The characteristics of corneal biomechanics and their correlations with other biophysical parameters

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Purpose To assess the characteristics of corneal biomechanics; corneal hysteresis (CH) and corneal resistant factor (CRF) and their correlations with other biophysical parameters in healthy subjects.

Methods 150 healthy subjects had an IOP measurement with ORA. CH and CRF were analyzed based on age, race, sex, refractive error, corneal thickness and visual field parameters. Diurnal variability and short time variability were also examined. Patients with corneal pathologies were excluded. Regression analysis and Pearson correlation were used to assess the correlation between different parameters. Student test was used to assess the difference. Anova test was also applied to examine the differences in diurnal and short time variability.

Results CH was lower in advanced age. CRF was higher in the elderly. There was no difference in corneal biomechanics between males and females. CH and CRF seemed lower in black race then Caucasian. There was a positive correlation between CH, CRF and CCT. We couldn't show any diurnal variability.

Conclusion The characteristics of CH and CRF in healthy subjects will be discussed.

5253
Corneal biomechanics and IOP measurements: the implications for glaucoma management

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Whilst the effects of variations in central corneal thickness and corneal curvature on intraocular pressure measurement are well known, it has only been recently possible to measure corneal biomechanical properties in vivo. Reichert has produced an instrument, the Ocular Response Analyzer (ORA; Reichert Corporation; Depew, USA), that measures the corneal response to indentation by a rapid air pulse. The instrument generates a measure of corneal viscoelasticity, corneal hysteresis, which is a direct measure of the cornea's biomechanical properties. This parameter may more completely describe the contribution of corneal resistance to IOP measurements than CCT alone. This talk will consider the effects of corneal parameters, including biomechanics, on intraocular pressure (IOP) measurement. The potential role of corneal biomechanics as an indicator of globe structural integrity will be discussed.

5254
Corneal hysteresis and resistance factor in normal, keratoconus suspects and true keratoconus eyes

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Purpose To compare corneal hysteresis (CH), corneal resistance factor (CRF) in normal, keratoconus suspects and true keratoconic eyes.

Methods Data were collected from normal, keratoconus suspect and true keratoconus eyes. Corneal hysteresis, corneal resistance factor and collection of the aspect of the signal were obtained with the Ocular Response Analyser (ORA; Reichert Ophthalmic Instruments, Buffalo, NY).

Results The mean CH value was 11.2 ± 1.4 mm Hg (range :8.1-14.4) in normal eyes, compared with 9.8± 1.6 mmHg (range:12.6-6.1) in keratoconus suspect and 8.0 ± 1.3 mm Hg (range, 5.2-11.1) in true keratoconic eyes. The difference was statistically significant between groups ($P < 0.0001$, ANOVA test). Mean CRF values in the normal, keratoconus suspect and keratoconic eyes were respectively 11.2 ± 1.5 mm Hg (range, 7.7-14.6), 9.6± 1.7 mmHg (range 6 – 11.7) and 6.8 ± 1.4 mm Hg (range 3.5-10). These difference was statistically significant. The aspects and heights of the peaks were also different between the groups.

Conclusion Corneal hysteresis and corneal resistance factor were significantly lower in true and suspect keratoconic eyes than in normal eyes. The signal peaks was significantly lower in keratoconic eyes.

5261
Conjunctiva-associated lymphoid tissue (CALT) – the physiological protective MALT of the conjunctiva

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Purpose Conjunctiva-associated lymphoid tissue (CALT) is a part of the mucosal immune system – the local MALT of the conjuncitva. The presence of lymphatic cells in the conjunctiva is known for about a century but had remained controversial for a long time.

Methods Complete conjunctival sacs in a large number of rabbits and humans were investigated in combined studies of whole-mount observation together with histology, scanning and transmission electron microscopy and immunohistochemistry.

Results A diffuse lymphoid tissue composed of lymphocytes and plasma cells along with accessory cells of the immune system occurs in the sub-epithelial lamina propria with intraepithelial lymphocytes. Lymphoid follicles are regularly interspersed. These are less frequent and flat in elderly humans, but prominent in the rabbit. They show a typical structure, are composed of B-cells with parafollicular T-cells and high endothelial venules, and are covered by a specialised follicle-associated epithelium (FAE) devoid of goblet cells. This has specialised M-cells that contain groups of lymphocytes for uptake of antigens. Follicles frequently have a bright germinal center which indicates that antigens were in fact taken up and lymphocyte proliferation and differentiation was induced.

Conclusion The conjunctiva of the rabbit and human have typical components of a physiologically protective mucosal immune system in the form of diffuse lymphoid tissue and lymphoid follicles that form the efferent and the afferent limb, respectively, of an immune answer. CALT can hence detect antigens from the ocular surface, pre-sent them to lymphoid cells and generate protective effector cells and hence repre-sents a part of the mucosal immune system at the conjunctiva. (DFG KN 317/11)

5262
Eye-Associated Lymphoid Tissue (EALT) – the local branch of the physiological mucosal immune system at the ocular surface and appendage

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Purpose Eye-associated lymphoid tissue (EALT) is the local branch of the mucosal immune system located at the ocular surface proper and its mucosal appendage: the lacrimal gland, conjunctiva (as CALT), and lacrimal drainage system (as LDALT). It is equivalent and follows the nomenclature of other parts of the mucosal immune system such as GALT in the gut or BALT in the bronchial tract.

Methods We investigated complete tissues of the human, rabbit, rat and mouse including the lacrimal gland, conjunctival sac and lacrimal drainage system by morphology and molecular biology.

Results A diffuse lymphoid tissue was regularly found in the lacrimal gland of all species. In the conjunctiva, a typical mucosal immune system with similar characteristics occurs in human and rabbit and is also reported in several other species. The same is true for the lacrimal drainage system. Hence, a continuous mucosal immune system is present in the embryologically connected tissues of the ocular surface from the gland via its excretory ducts into the conjunctiva and through the lacrimal puncta into the lacrimal drainage system. These tissues share common antigens and protective factors as well as specialised vessels for lymphocyte recirculation and hence act together as an efficient functional unit for ocular surface defence. As a surprise, the conjunctiva of the common laboratory animals rat and mouse, however, contains almost no lymphoid cells.

Conclusion The ocular surface and appendage together form an Eye-Associated Lymphoid Tissue (EALT) that represents a part of the mucosal immune system of the body and provides cellular and secretory immunity. Deregulation of this system may explain important aspects of ocular surface disease.

5263
Malt lymphoma

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Purpose To review the histomorphology, immunophenotype and genotypic features of conjunctival "MALT" lymphomas.

Methods The conjunctival lymphomas represent the malignant end of the spectrum of lymphoproliferative lesions occurring in this site. The new W.H.O. Lymphoma Classification is the most suitable system for subdividing the conjunctival lymphomas, whereby the extranodal marginal zone B-cell lymphoma of MALT type (or "MALT lymphoma") represents the most common lymphoma subtype.

Results MALT lymphomas are characterized by mainly small B-cells in the marginal zone. Their immunophenotype is: CD20+, CD43 (+/-), BCL-2, IgM+, and a low Ki-67 growth fraction. A number of chromosomal changes have been described in conjunctival MALT lymphomas, and include trisomy 3, t(14;18), t(3;14), t(11;18), t(1;14) and loss of 6q23.3-24. Through differing pathways, these chromosomal alterations result in the dysregulation of NF-KB, and hence the uncontrolled proliferation of lymphocytes. In some geographical regions, there may be an association between these neoplasms and microorganisms, such as Chlamydia, Helicobacter as well as HCV. Management of patients with MALT lymphomas includes a thorough systemic medical examination to establish the clinical stage of the disease. The majority of patients with conjunctival lymphoma have Stage IE disease (Ann Arbor); however, systemic spread is not uncommon. Reported prognostic criteria for MALT lymphomas are few but include stage of disease at presentation; serum lactate dehydrogenase level; and tumour cell growth rate. A new more refined clinical staging system has been proposed by the TNM/AJCC committee and is to be published in its 7th Edition.

Conclusion Although the most common lymphoid neoplasm of the conjunctiva, there is still much to learn about MALT lymphomas.

5264
Mantle Cell Lymphoma in the Ocular Region

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Purpose To characterize the clinicopathological features of mantle cell lymphoma (MCL) in the ocular region.

Methods All lymphoid lesions were retrieved searching the Danish Ocular Lymphoma Database 1980-2007. Specimens were collected from Danish pathology departments and re-evaluated with a panel of monoclonal antibodies. For all patients with confirmed MCL the complete clinical files were collected and reviewed.

Results Twenty-one patients with MCL were identified comprising nine percent (21/230) of all lymphomas in the ocular region. There were 18 male and three female patients with an age range from 60 to 90 years (median 75 years). Ocular region MCL as first presenting symptom included 67% of the patients. Of these, 71% had bilateral involvement and all had lymphoma in more than one site within the ocular region. The orbit (71%) and eyelids (64%) were the most commonly affected sites. At the time of diagnosis 93% of the patients were in Ann Arbor stage III/IV, with bone marrow involvement (79%) and B-symptoms (50%). Median overall survival (OS) was 30 months and the five-year OS rate was 21%. Patients receiving anti-CD20 (Rituximab)-containing chemotherapy had a significant better 5-year OS rate (80 %) ($p < 0,027$) than patients in treatment regimes without Rituximab (5-year OS rate, 29%).

Conclusion MCL presenting in the ocular region has a male predominance and affects elderly patients. The orbit and eyelids were frequently involved. Patients with ocular region MCL as first presenting symptom had a high proportion of bilateral affection. Patients had advanced stage disease at diagnosis, multiple relapses and a low 5-year OS rate similar to systemic MCL. Treatment with Rituximab-containing chemotherapy improved survival significantly.

■ 5265

Current and possible future treatment of ocular adnexal lymphomas

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Purpose To review the current and possible future therapies of ocular adnexal lymphomas.

Methods Ocular adnexal lymphomas represent approx. 8% of all extranodal lymphomas. The majority of these can be classified as extranodal marginal zone (MALT) lymphomas, and are usually staged as Stage IE disease.

Results Recommended therapy in Stage IE tumours is low-dose radiotherapy, while disseminated disease (>Stage IIE) is treated with chemotherapy. Although often responding to initial therapy, the MALT lymphomas tend to recur in distant extranodal sites. Few biomarkers are available to aid prediction of either recurrence or systemic dissemination, which occurs in up to 25% of patients. The ocular morbidity associated with current therapies is not insignificant, and, therefore, more effective treatment is being sought.

Conclusion The newer treatment options, including rituximab and doxycyclin, will be discussed

5311
Dynamic vessel analysis for assessing endothel dysfunction of microcirculatory vessels – method, model and results

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Purpose To access the endothel function (flow induced autoregulation) provide a unique potential for vascular risk stratification,early recognition, diagnosis and treatment of big vascular heart and brain diseases by using the eye as a diagnostic window.It is assumed that Dynamic Vessel Analysis by DVA (Dynamic Vessel Analyzer Imedos GmgH Jena,Germany) is a practical and easy test for endothel dysfunction.

Methods DVA can access vessel functions by use of flickering light.Online measurements of the diameter enable a highly reproducible observation of local and temporal changes of big retinal vessels with high accuracy.For functional analysis the retina is stimulated by a 12.5 Hz monochromatic flicker light.The stimulation period amounts 20s.The vessel response before, during an after stimulöation is recorded.Vessel dialation is estimated.To understand and for clinical interpretation of the flickering vessel response model of vessel response to flickering light was developed.

Results In normal subjects flickering light induces an increase in vessel diameter. Reduced diameter dilatation is caused by exhausted regulative reserve (hypotonics) or by vascular dysfunction.The interpretation of the vascular dysfunction based on the following model:Flickering light is activating the neurovascular coupling, leading to a dilation of the capillaries and small arterioles.This causes an increase in flow leading to increased velocity in the bigger vessels indirectly.The flow induced autoregulation dilates the diameter of the big vessels by increasing nitric oxid NO via eNOS.Different experimental results support this model thesis.

Conclusion The vessel dilatation can be explained by eNOS.Endothel dysfunction reduces the flicker dilatation.

Commercial interest

5312
Measurement of time-resolved autofluorescence

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Purpose Functional alterations are first signs of reversible pathologic processes. Whereas microcirculation studies metabolism globally, autofluorescence of endogenous fluorophores has the potential for description of cellular basic processes. Therefore, a discrimination of fluorophores is required in the tissue.

Methods Besides excitation and emission spectra, the fluorescence lifetime after short-time excitation is a promising substance-specific mark. Using the opto-mechanical system of a HRA II (Heidelberg Engineering), a fluorescence lifetime mapper was developed. Picosecond pulse-lasers (448nm, 468nm, 100ps FWHM, 80MHz) can be used for excitation and the emission will be detected in 2 spectral ranges (490-560nm, 560-700nm). The dynamic fluorescence will be detected in time-correlated single photon counting (SPC 150, Becker/Hickl, Berlin). An on line image registration is realised by simultaneously detected infrared images during measuring time. Approximating the fluorescence decay by 3-exponential model function, images (lifetime and amplitudes), histograms, and cluster diagrams can be calculated for interpretation.

Results Examples are given for healthy subjects, AMD patients (non-exudative, exudative, geographic atrophy), diabetic retinopathy, and oedema. Measurements of excitation and emission spectra as well as lifetimes are performed of expected substances and of anatomical ocular structures for comparison.

Conclusion Fluorescence lifetime measurement at the eye is a new method for evaluation of functional metabolic state.

5313
Flicker-induced retinal vasodilataion - what does a reduced response mean?

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Purpose In the recent years much interest has been directed towards flicker-induced vasodilatation. Various studies were done showing reduced flicker responses in diseases such as diabetic retinopathy or glaucoma. The basis for this reduced flicker responses is, however, largely unclear.

Methods Papers published on this topic in the last years were reviewed. Specific emphasis was directed towards publications that deal with potential mechanisms underlying flicker-induced vasodilatation.

Results There is evidence from animal and human studies that flicker-induced vasodilatation is at least partially dependent on nitric oxide. In addition, there is evidence to assume that flicker induces changes in the retinal glucose metabolism and the ratio of cytosolic NADH/NAD+ are involved.

Conclusion Flicker-induced retinal vasodilatation appears to be partially endothelium-dependent. It is, however, likely that other factors are also involved Further research is required to characterize the mechanisms underlying flicker-induced vasodilatation in more detail. From a clinical point of view studies are needed to test the hypothesis that reduced retinal flicker responses are related to the prevalence, incidence and progression of ocular vascular disease.

5314
Is there a role for dynamic retinal vessel analysis in internal medicine?

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Purpose Human retinal vessels and their reaction to stimuli change during life and in disease due to physiological, genetic and pathological influences. Using the Dynamic Vessel Analyzer (DVA, Fa. IMEDOS, Jena) it is possible to assess changes in retinal vessel diameters in response to vasoactive stimuli in real time and non-invasively.

Methods Retinal arterial vessel reaction in the natural time course and to the average of 3 consecutive monochromatic flicker stimulations (530-600 nm, 12,5 Hz, 20 s) with a 80 s observation pause between stimulations was investigated in healthy volunteers of different age groups, obese patients, diabetes type 1 patients, systemic hypertensive patients and patients with lysosomal storage disease. Statistical data analysis of vessel reactions independent from the DVA program was performed.

Results There is a statistically significant difference in retinal vascular behaviour in different age groups in a healthy population. The same is true between a healthy population and each of the diseases investigated. Lysosomal storage disease however demonstrated an increase in dilation following flicker stimulation compared to normal persons.

Conclusion Flicker stimulation of the retina light evokes a prompt vessel reaction in all healthy subjects. We could demonstrate an age dependence of the retinal arterial reaction in medically healthy persons and in hypertension, diabetes and obese patients. From the increased reaction in lysosomal storage disease further understanding of different factors leading to the vascular reaction to stimuli may be derived. Application of flicker stimulus to retinal vessels represents a method to assess the endothelial function of vessels which is important to understand in systemic disease.

5315

New optical device for functional studies of the optic nerve head

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Purpose To develop a confocal ocular laser Doppler device for the recording of functional optic nerve head (ONH) blood flow responses to various physiological stimuli.

Methods The flowmeter consists of a self-aligned confocal system, a fundus illumination (green light) and CCD based observation unit, a target fixation system and a CCD camera to observe the pupil. This CCD allows monitoring of the position of the probing laser beam at the pupil to insure constant entrance point in successive measurements of ONH blood flow. The Doppler signal is digitized and a dedicated software operating on a portable computer calculates the relative velocity, volume and flux of the red blood cells in the ONH microcirculation. Synchronization of theses parameters with the heart pulse allows determination of the flow pulsatility. Flicker stimulation of the macular area can be performed at 2 wavelengths. Three measurements were performed at rest in each of 29 normal subjects to determine the variability of ONH blood flow parameters. Preliminary responses of these parameters to the breathing of various gases were obtained.

Results Variability of blood flow obtained from 3 successive measurements from the same site ranged from 0.5 to 33% (mean 11%, n = 29). The breathing of carbogen (95% O2, 5% CO2) for 5 min by subjects with optimal target fixation induced an increase of ONH blood flow of 28 +/- 16 (sd) % (p = 0.03, n = 11) in accordance with previously published data.

Conclusion This new confocal device combined with monitoring of the entrance site of the laser beam at the pupil provides laser Doppler blood flow data at the ONH that show a variability that makes the device potentially useful for physiological and clinical investigations.

5316

Optic nerve reflectance variations in the near-infrared during neural function

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Purpose Diffuse luminance flicker induces optic nerve head (ONH) reflectance changes, ChRonh, in humans, when Ronh is measured at visible wavelengths (Crittin and Riva, 2004). Intrinsic signal imaging in macaque retina and ONH has revealed also flash-induced infrared (840-900 nm) reflectance changes (Hanazono et al., 2007). Our purpose was to determine a) whether flicker-induced near-infrared ChRonh are detectable from the human ONH; b) is there a spatial distribution of ChRonh.

Methods Ronh was measured at 770 nm with a fundus camera based reflectometer. Neural activity was evoked by 535-nm diffuse (50 deg) flicker (various frequencies below 20Hz). 7 successive recordings were performed at 9 temporal sites, each consisting of a 20s baseline, a 60s flicker period and a 40s recovery. ChRonh (%) was defined as 100 x (Ronh,fl - Ronh,bl)/Ronh,bl, where Ronh,bl is the average response during the baseline (no flicker) and Ronh,fl is the response, averaged over time slots of 2s, during flicker. ONH regions containing visible vessels were avoided.

Results Flicker induced significant decreases in Ronh at most sites. These decreases presented a strong oscillatory behavior (period of about 8s), reached a maximum in less than 40s of flicker and were more marked at the rim. ChRonh was found to be frequency-dependent. Ronh during recovery also showed marked oscillations

Conclusion Flicker induces significant frequency-dependent decreases in near-infrared (770 nm) reflectance in the temporal region of the human ONH, confirming previous infrared optic nerve intrinsic signal reflectance findings in monkeys. Comparison with flicker-induced blood flow increases in the ONH, these decreases are most probably due to changes in blood volume during neural activity.

5321
The role of leukocytes in ischemia-driven neovascularisation

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Purpose Our research strategy has been to study VEGF-A and the adaptive response to ischemia, with the aim of better understanding the benefit that VEGF-A may bring to ischemic tissues, and to characterize the basis for the chaotic and poorly controlled neovascular response that usually accompanies ischemia in retinal diseases such as diabetic retinopathy.

Methods Mice genetically engineered with deletion of the VEGF164 isoform were examined during normal vascular development of the retina and following oxygen-induced retinopathy. Abnormal vascular growth and leukostasis were quantified. To study determinants of VEGF-A involved in leukostasis, VEGF-A mutants and VEGF-A signaling antagonists were injected intraocularly

Results Rather than focusing on the abolition of VEGF-A signaling in ischemic retinal disease, we have tried to find ways to normalize the adaptive response. We previously demonstrated that inflammation was critical for the abnormal vascular response in OIR. Here we found that inflammation was driven by VEGF164, and that a cluster of residues in the heparin-binding domain of VEGF164 were responsible for its heightened inflammatory activity compared to other VEGF-A isoforms. This region of VEGF164 imparts high affinity binding to VEGFR1

Conclusion Data suggest that reducing VEGF-VEGFR1 mediated inflammation, whilst preserving VEGF-mediated angiogenesis, may be a strategy to help transform the unwanted pathological response to ischemia into a desirable outcome whereby new vessels sprout into the area of need and nurture the ischemic retina.

Commercial interest

5322
Mechanisms driving neovascularisation and microangiopathy in DR: VEGF-triggers cell adhesion via endothelial- and leukocyte-induced pathways

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Purpose Our research strategy has been to study VEGF-A and the adaptive response to ischemia, with the aim of better understanding the benefit that VEGF-A may bring to ischemic tissues, and to characterize the basis for the chaotic and poorly controlled neovascular response that usually accompanies ischemia in retinal diseases such as diabetic retinopathy.

Methods Acute retinal inflammation was induced using VEGF-A and the mechanisms and consequences of retinal inflammation were examined in STZ-induced diabetes in mice and rats. Various antagonists of VEGF signaling and of leukocyte adhesion were examined.

Results VEGF-A induced upregulation of ICAM-1 on endothelial cells in a VEGFR2-dependent and Neuropilin-1 dependent manner. VEGF-A also triggered leuokocyte invasion via signaling through VEGFR1. These data predict that inhibiting the influx of leukocytes may demonstrate a benefit in DR, which was demonstrated by inhibition of ICAM-1 function following STZ-induced retinopathy

Conclusion Targeting of VEGF-induced inflammation or leukocyte adhesion via ICAM-1/LFA-1 may provide a means of normalizing the microvasculature in DR

Commercial interest

5323
Chemokines in proliferative diabetic retinopathy and proliferative vitreoretinopathy

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Purpose To determine levels of the chemokines I-309, MCP-1, MIP-1α, MIP-1β, MCP-3, MCP-2, ENA-78, GCP-2, IP-10 and I-TAC in vitreous and serum from patients with proliferative diabetic retinopathy (PDR), proliferative vitreoretinopathy (PVR) and retinal detachment with no PVR (RD) and expression of MCP-1, SDF-1 and the chemokine receptor CXCR3 in epiretinal membranes.

Methods Vitreous and serum samples were obtained from 57 RD, 32 PVR and 88 PDR patients. The levels of chemokines were measured by ELISAs. Epiretinal membranes were studied by immunohistochemistry.

Results MCP-1 and IP-10 were the only chemokines detected in vitreous. Levels and incidence of detection in vitreous were significantly higher than that in serum for MCP-1 ($p<0.001$ for both comparisons) and IP-10 ($p=0.0035$; <0.001, respectively). Levels were significantly higher in vitreous from patients with PVR and PDR compared with RD for MCP-1 ($p=0.0002$) and IP-10 ($p=0.0083$). Incidence of IP-10 detection was significantly associated with increased levels of MCP-1 in vitreous ($p<0.001$). MCP-1, SDF and CXCR3 were expressed by myofibroblasts and vascular endothelial cells in membranes.

Conclusion MCP-1, IP-10 and SDF-1 may participate in pathogenesis of PVR. Clinical Relevance: Chemokines and their receptors could be molecular targets for preventing angiogenesis / fibrosis in the eye.

5324
The role of arachidonic acid metabolites in DR

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Purpose The inducible enzyme cyclooxygense-2 (COX-2) and its metabolic products are important mediators for angiogenesis. We investigated the expression of COX-2 and its downstream enzymes microsomal prostaglandin-E synthase (mPGES)-1, cytosolic PGES (cPGES) and thromboxane synthase (TXS) and correlated it with vascular endothelial growth factor (VEGF) expression and level of vascularization in proliferative diabetic retinopathy (PDR) epiretinal membranes.

Methods Fourteen membranes were studied by immunohistochemistry.

Results Vascular endothelial cells expressed COX-2, mPGES-1 and VEGF in 75.6%, 64.3% and 50% of the membranes, respectively. TXS was expressed in stromal cells in 85.7% of the membranes. There was no immunoreactivity for cPGES. There were significant correlations between number of blood vessels expressing CD34 and the numbers of blood vessels expressing COX-2 ($rs = 0.858$; $p<0.001$), mPGES-1 ($rs = 0.743$; $p = 0.002$) and VEGF ($rs = 0.845$; $p = 0.001$) and the number of cells expressing TXS ($rs = 0.74$; $p = 0.002$). Number of blood vessels expressing VEGF correlated significantly with the numbers of blood vessels expressing COX-2 ($rs = 0.879$; $p<0.001$) and mPGES-1 ($rs = 0.942$; $p<0.001$) and the number of cells expressing TXS ($rs = 0.702$; $p = 0.011$).

Conclusion COX-2 and its metabolic products might contribute to PDR angiogenesis.

5325

The action of pro-inflammatory cytokines on retinal endothelial cell barrier permeability: protective effect of corticosteroids

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Purpose The pro-inflammatory cytokines interleukin-1β (IL-1β) and tumor necrosis factor-alpha (TNF-α) were found to be increased in the vitreous of diabetic patients and in diabetic rat retinas, and increased cytokine levels were correlated with elevated retinal vascular permeability. In this work, we investigated the mechanisms underlying IL-1β- and TNF-α-induced retinal endothelial cell permeability and evaluated the ability of a glucocorticoid, dexamethasone (DEX), to prevent changes in permeability.

Methods Primary cultures of bovine retinal endothelial cells (BRECs) were grown on transwell filters and exposed to IL-1β and TNF-α. BRECs permeability to 70 kDa RITC-dextran was measured. The content and localization of tight junction proteins was assessed by Western blotting and immunocytochemistry.

Results IL-1β and TNF-α increased retinal endothelial cell permeability in a concentration- and time-dependent manner, but TNF-α was more effective (increased permeability at a lower dose and shorter time-point). The increase in permeability was not due to changes in cell viability. IL-1β and TNF-α altered ZO-1 and claudin-5 content. TNF-α also decreased ZO-1 staining at the cell border. Pre-treatment with DEX prevented TNF-α-induced cell permeability, and the protective effect of DEX was partially abolished by the glucocorticoid receptor antagonist RU486.

Conclusion These data demonstrate that TNF-α and IL-1β potently induce endothelial cell permeability through alterations in tight junctions. Also, the study supports the potential therapeutic use of glucocorticoids to reduce retinal vascular permeability. Support: FCT (Portugal), NIH, JDRF and Allergan

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Circulating fibrocytes contribute to the myofibroblast population in proliferative vitreoretinopathy epiretinal membranes

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Purpose Fibrocytes, circulating cells that co-express markers of hematopoietic stem cells, leukocytes and fibroblast products, traffic to sites of tissue injury, differentiate into myofibroblasts and contribute to wound healing and fibrosis. We investigated the presence of fibrocytes and the expression of their chemotactic pathways CCL21 / CCR7 and CXCL12 / CXCR4 in proliferative vitreoretinopathy (PVR) epiretinal membranes.

Methods Sixteen membranes were studied by immunohistochemical techniques.

Results Cells expressing alpha-smooth muscle actin (alpha-SMA), a marker of differentiation of fibrocytes into myofibroblasts, were present in all membranes. Cells expressing the hematopoietic stem cell antigen CD34, the leukocyte common antigen CD45, CCR7, CXCR4, CCL21 and CXCL12 were noted in 50%, 75%, 68.8%, 100%, 80% and 93.8% of the membranes, respectively. Double immunohistochemistry indicated that all cells expressing CD34, CD45, CCR7, CXCR4, CCL21 and CXCL12 co-expressed alpha-SMA. The number of cells expressing CD34 correlated significantly with the numbers of cells expressing CXCL12 ($rs = 0.567$; $p = 0.022$) and CCL21 ($rs = 0.534$; $p = 0.04$).

Conclusion Circulating fibrocytes may function as precursors of myofibroblasts in PVR membranes.

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Therapeutic implications and perspectives

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Purpose Vascular endothelial growth factor-A (VEGF-A) has recentlybeen recognized as an important neuroprotectantin the central nervous system. Given its positionas an anti-angiogenic target in the treatment ofhuman diseases, understanding the extent of VEGF'srole in neural cell survival is paramount.

Methods We have examined if VEGF-A is necessary and sufficient for retinal neuroprotection in a model of ischemia-reperfusion injury.

Results VEGF-A effects on neurons have been documented in several experimmental systems, including now, the retina. VEGF-A's effects are likley mediated by direct signaling in neurons via VEGFR2.

Conclusion These findings have implications for both neural pathologies and for the use of potent VEGF-A antagonists in chronic ocular vascular diseases, such as diabetic retinopathy. Translateability of these animal findings to patients, and potential next steps will be discussed.

Commercial interest

5331

Selection and assessment of vital dyes to improve the endothelial quality control of organ cultured corneas

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Purpose In eye banks, corneal quality control requires an accurate endothelial cell density (ECD). ECs are counted after osmotic preparation (NaCl/sucrose) that makes cells visible. Nevertheless, endothelial images remain often poorly contrasted, non uniform, with a high background noise. Aim: to replace this technique by a non toxic 'endothelial dye'

Methods 30 dyes were pre-selected. Ability to stain EC was assessed on porcine, bovine and rabbit corneas. They were exposed (1 min) to pure or diluted dyes and observed under a light microscope using bright field and 4 standard fluorescent filters. Toxicity was assessed in vitro on EC cultures (live/dead assay, Hoechst Ethidium Calcein). Using the same assay, the less toxic dyes were further assessed on keratocytes cultures and on animal corneas organ cultured for 24H after exposure to dyes. Controls: exposure to BSS only or 3% H2O2

Results Only Ledermycin, Hemalun, Rose Bengal, Nuclear Red, Congo red, Evans Blue, and Chicago Sky Blue (CSB) stained ECs, and only the 3 diazoïc dyes (Congo red, Evans Blue, and CSB) stained EC borders using fluorescence (Em554/Ex568nm). Both blue dyes also stained the nuclei of dead cells. Hemalun and Rose Bengal were highly toxic. In vitro and ex vivo toxicity of CSB was negligible. The other dyes had an intermediate toxicity

Conclusion Diazoïc dyes and especially CSB could be non toxic dyes for ECs borders. They could improve the accuracy of ECD determination. Their ability to stain human endothelium and their safety (using an animal graft model) have to be assessed as well as their contribution in ECD determination versus the classical osmotic endothelial preparation

5332

Sclerocorneal limbus transplantation

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Purpose Discussion of the evolution of a technique suggested by José I. Barraquer in 1947, later completed by Strampelli and adopted and modified by other corneal surgeons. The original procedure was based on the clinical observation that regeneration of the corneal epithelial cells is dependant on the state of the limbus. This explained the bad prognosis of chemical burns and severe limbus trauma. At present it is well known that the stem cells located in the corneal limbus are responsible for epithelial regeneration. Penetrating keratoplasty limited to the cornea does not supply stem cells.

Methods The technique consists in obtaining and grafting limbus tissue, in form of an annular or partial conjunctivosclerocorneal limbal graft preferably from the fellow eye or a living donor, or an eye bank eye. A case of chemical burn operated in 1981 is presented to illustrate the original technique of Strampelli. To illustrate the modern approach a case of chemical trauma with superior and inferior symblepharon and total vascularized leucoma operated in 1999 (limbal donor graft)taking advantage of the modern advances available at present (improved instrumentation, pharmacological inhibition of homograft reaction)is shown.

Results The results were encouraging.The patient operated in 1981 died in 1988 with good vision (0.6).In the case operated in 1999, three months after the limbal transplant, re-epithelization of the cornea was correct and an 8 mm penetrating keratoplasty combined with cataract extraction and IOL implantation was performed. Corrected vision 5 years postoperatively was 0.35.

Conclusion Modern investigation and technology have converted a procedure based on surgical inspiration more than half a century ago into a valuable option in cases of irreversible damage of the corneal limbus.

5333

Long term results of Limbal stem cell transplantation in ocular surface disease

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Purpose To evaluate results of limbal stem cell transplantation (LSCT) in patients with ocular surface (OS) disease.

Methods The case records of 26 eyes of 25 patients who underwent LSCT with at least one year follow up were retrospectively reviewed. Aetiology, type of transplant procedure, intra and post-operative complications and final visual outcome were analysed. Surgical success of transplanted limbal epithelial stem cells was defined by the duration of maintenance of normal corneal epithelial phenotype after surgery. Failure was defined as the presence of abnormally high fluorescein permeability and late corneal epithelial staining, recurrence of conjunctivalisation, neovascularisation, and persistent epithelial defect. Functional success was assessed by National Eye Institute Visual Functioning Questionnaire 25(VFQ-25).

Results Survival of ocular surface transplantation in this study was seen in 23 procedures (82%) after 6 months and in 22 procedures (79%) after one year. An increase in visual acuity was observed after 21 limbal stem cells transplantations (75%).VFQ-25 results have showed remarkable improvement in terms of vision and daily activities of the patients.

Conclusion LSCT is an effective surgical procedure in the management of eyes prior to corneal graft surgery or as a combined procedure. Post-operatively non healing defects and vascularisation of the cornea may contribute to the occurrence of surgical failure and the need for further procedures.

5334

Quality of vision following penetrating keratoplasty and deep anterior lamellar keratoplasty for keratoconus

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Purpose The authors purpose is to investigate whether quality of vision in keratoconus patients after deep anterior lamellar keratoplasty (DALK) with and without descemet's membrane (DM) exposure, may be comparable with Penetrating Keratoplasty (PK).

Methods To investigate quality of vision after PK and DALK with and without DM exposure a files of 52 keratoconus patients were analysed. Patients were divided in 3 groups: group 1 (n = 16) DALK with DM exposure, group 2 (n = 22) DALK without DM exposure and group 3 (n = 14) PK. Visual function was assessed by Uncorrected Visual Acuity (UCVA) and Best Spectacle Corrected Visual Acuity (BSCVA), Low Contrast Visual Acuity (LCVA) and Pelli-Robson Contrast Sensitivity (PRCS).

Results UCVA was comparable among groups. BCVA, LCVA and PRCS were better in group 1 than group 2 ($p < 0.05$) and comparable between groups 1 and 3 ($p > 0.05$).

Conclusion Quality of vision after DALK is comparable to PK if the DM is exposed.

■ 5335

Impact of culturing on metabolic profile of human corneas

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Purpose The aim of this study was to examine possible differences in the metabolic profile between cultured and non-cultured corneas.

Methods Corneas from 12 donors were obtained post-mortem and introduced to the tissue culture for 8-20 days. The control corneal tissues were excised during enucleating of eyes with malignant melanoma in the retina from 4 patients and immediately frozen at -80 °C. The metabolic profiles of the samples were investigated with HR MAS (High Resolution Magic Angle Spinning) 1H NMR (Nuclear Magnetic Resonance) spectroscopy (14.1 T) operating at 600.132 MHz. All data obtained with both methods were analysed using special software for: (i) analysis of complex mixtures, (ii) principal component analysis – PCA, (iii) detailed statistical analysis.

Results Significant deferences in metabolic profiles between cultured and non-cultured corneas were detected. The levels of several metabolites in cultured tissues were increased in comparison to the control. It was also shown that the levels of some of metabolites in samples cultured for 9-14 days differed significantly from the samples kept for less than 9 days or 15-20 days.

Conclusion Corneal culturing results in the changes of the metabolic profile in tissue. The increase of the levels of the metabolites in organ within the second week of culturing may indicate increased enzymatic activity or/and increased response of cells toward stress factors in the tissue.

5341
MMP involment in TGFbeta-mediated matrix contraction: implications for PCO

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ABSTRACT NOT PROVIDED

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Promotion of ER stress: a potential therapeutic approach for PCO

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Purpose Posterior Capsule Opacification (PCO) remains a significant clinical problem following cataract surgery. Endoplasmic Reticulum (ER) stress has been shown to play a critical role in cell death and apoptosis. The aim of this study was to determine the relative effectiveness of ER stressors, thapsigargin (Tg) and arsenic trioxide (As2O3) on induction of cell death in human capsular bags.

Methods FHL124 cell survival was assessed by Coomassie blue staining after 4 days. Induction of ER stress genes was detected using real-time PCR and apoptosis assessed using the TUNEL assay. Human capsular bags were prepared from donor eyes and sealed with the Perfect Capsule device. The agents were again introduced to the bags for a 2 minute period prior to perfusion with EMEM alone. The bags were maintained in EMEM for 28 days and phase images were acquired throughout.

Results Tg and As2O3 application to FHL124 cells induced significant up-regulation of ER stress genes Bip, EIF2α, IRE1 and ATF6. FHL124 cells exposed for 2 minutes to both Tg and As2O3 for 4 days demonstrated reduced cell survival in a dose-dependent manner. Moreover, TUNEL assay data showed that both Tg and As2O3 could induce FHL124 cell death by apoptosis. Application of the 100uM Tg and 100mM As2O3 to capsular bags for a 2 minute period using the perfect capsule system resulted in a total loss of viable cells following the 4 week culture period.

Conclusion Thapsigargin and arsenic trioxide induce an ER stress in human lens epithelial cells, which is associated with a reduced cell survival and promotion of apoptosis. Using the perfect capsule system, a 2 minute exposure of either agent successfully killed all cells within the capsular bag and thus predicts putative therapeutic benefit in vivo.

5343
Sealed capsule irrigation to prevent posterior capsule opacification: Results of long-term clinical trials and laboratory studies

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Purpose We investigated long-term safety and efficacy of sealed capsule irrigation (SCI) during cataract surgery to prevent posterior capsule opacification (PCO).

Methods One eye of each of 17 patients (mean age: 70.1+/-9.7 years) who presented with bilateral cataracts was randomly chosen for SCI treatment. After phacoemulsification, the capsular bag was vacuum sealed with the PerfectCapsule device (Milvella) followed by SCI using distilled water for two minutes. No vacuum loss occurred during irrigation. Each patient's fellow eye served as a control. One hydrophilic acrylic intraocular lens model was implanted in all eyes. Five patients had to be excluded due to deep anterior chamber, small pupil or unilateral surgery. Follow-up examinations took place one day and one, three, six, 12 and 24 months after surgery. We evaluated safety parameters, anterior capsule (AC) overlapping and PCO.

Results Postoperatively, mean best corrected visual acuity, pachymetry, endothelial cell count, intraocular pressure, AC overlapping and PCO showed no statistically significant difference between SCI and the control group ($p>0.05$, Wilcoxon test).

Conclusion SCI is a safe procedure and enables the specific pharmacological targeting of lens epithelial cells inside the capsular bag. Using distilled water, however, it is not possible to reduce PCO development significantly. Thus, alternative substances should be evaluated.

5344
Intraocular lens features that affect PCO

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Purpose To review IOL features that affect PCO

Methods Review of clinical PCO studies using retroillumination imaging and objective quantification of PCO following cataract surgery and laboratory EM studies of IOL profile

Results The optic diameter, haptic design and IOL material all affect PCO performance but the optic edge profile is the most important. Electron microscopy shows IOL edge is of variable profile in so called 'square edge' IOLs and this can be explained by the inevitable interrelationship of the limitations that material imposes on engineering, early closure of the capsular bag around the IOL seems to be important in preventing leakage of LECs into the retro lenticular space soon after surgery that later proliferate and form clinical PCO

Conclusion PCO has a multifactorial pathogenesis. Improved IOL design can limit but does not prevent PCO

Commercial interest

■ 5345

Mechanism of PCO prevention in the bag-in-the-lens technique

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Purpose Since the technique of the bag-in-the-lens (BIL) implantation is based on performing a PCCC, the question can be raised whether we need the posterior capsule and in case it is removed whether this is safe for the eye.

Methods Fluorophotometry, review of the literature and retinal detachment rates after BIL implantation have shown that PCCC does preserve the anterior ocular barrier and probably even better than in case YAG capsulotomoy is needed as it is the case in the traditional lens-in-the-bag implantation technique.

Results The risk for retinal detachment is comparable with the lens-in-the-bag implantation at the short postoperative follow-up. However, since no Nd:YAG laser capsulotomy is necessary after BIL technique, the risk for retinal detachment after BIL is lower with time.

Conclusion At the long run, the BIL technique may even be safer for the eye than the lens-in-the-bag implantation.

Commercial interest

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Predictive value of a dexamethasone provocative test prior to intravitreal triamcinolone acetonide injection

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Purpose To investigate the diagnostic value of a topical dexamethasone (DXM) provocative test for steroid-induced ocular hypertension after intravitreal triamcinolone acetonide (IVTA) injection.

Methods Patients scheduled for IVTA received DXM 4x over 4 weeks. IVTA was injected in those with no or moderate DXM steroid response (6 mmHg≤IOP rise≤15 mm Hg). High DXM steroid responders (IOP rise>15 mmHg) received no IVTA and were subsequently excluded. IOP was measured at baseline, 4 weeks after DXM drops, and at day 1, weeks 1, 2, and 4, and months 3 and 6 following IVTA.

Results Thirty-six patients (36 eyes) were included. After the DXM test, 4 patients (11%) and 2 patients (5%) were moderate and high steroid responders, respectively. After IVTA, 12 patients (33%) and 4 patients (11%) were moderate and high steroid responders, respectively. The DXM test had a sensitivity of 25% (95%CI[0.07,0.52]), a specificity of 100% (95%CI[0.83,1.00]), a positive predictive value of 100% (95%CI[0.40,1.00]), and a negative predictive value of 62% (95%CI[0.44,0.79]) for a moderate to high steroid response after IVTA. The IOP rise after IVTA was significantly higher in previous topical DXM responders vs. DXM nonresponders, 17.0±7.8 mmHg vs. 5.0±4.4 mmHg, respectively (P=.005, Mann Whitney U).

Conclusion We found a low sensitivity, a high specificity, a high positive predictive value and a moderate negative predictive value for the topical DXM provocative test with regard to a steroid response after IVTA. These findings indicate that a topical DXM test is clinically useful in predicting steroid response after IVTA. However, a negative DXM provocative test does not rule out steroid response after IVTA.

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Increasing IOP decrease with sequential use of travoprost, travoprost/timolol fixed combination and travoprost/timolol fixed combination with adjunctive brinzolamide

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Purpose To investigate if combined intraocular pressure (IOP) lowering medication with travoprost/timolol (travg/tim) fixed combination and a carbonic anhydrase inhibitor, brinzolamide is superior to both travoprost monotherapy and trav/tim fixed combination therapy in POAG and OHT.

Methods Following a four-week wash-out period and using four-week treatment periods, 20 POAG or OHT patients were treated with evening travoprost 0.004%, then switched to evening travoprost 0.004%/timolol 0.5% fixed combination, and finally the treatment was combined with adjunctive twice-daily brinzolamide 1% ophthalmic suspension. Both eyes were treated but only one eye per patient, (the eye with higher mean diurnal IOP at baseline), was evaluated. IOP was measured at 8 a.m., 12 noon and 4 p.m. at baseline and at the end of each treatment period.

Results Mean diurnal IOP (mean (SD)) at baseline was 28.5(7.3) mmHg which decreased to 22.3(6.3) mmHg on travoprost, 19.2(3.4) mmHg on trav/tim fixed combination and 17.3(3.4) mmHg when the brinzolamide was added to trav/tim (ANOVA, contrast test, p<0.003 for all comparisons). The individual time point IOP values showed similar and significant stepwise differences.

Conclusion Adjunctive brinzolamide medication provided a clinically and statistically significant further IOP decrease in patients receiving evening-dosed trav/tim fixed combination. The trav/tim fixed combination was significantly more effective in IOP reduction than travoprost monotherapy. These results suggest that combined therapy with trav/tim fixed combination and brinzolamide is clinically useful for IOP lowering in primary open-angle glaucoma and ocular hypertension.

Commercial interest

5353

Effect of bimatoprost on patients with primary open-angle glaucoma or ocular hypertension who are nonresponders to latanoprost or timolol

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Purpose To test the efficacy of bimatoprost 0.03% in lowering intraocular pressure (IOP) in patients affected by primary open-angle glaucoma or ocular hypertension who did not respond to treatment with latanoprost 0.005% or timolol 0.5%.

Methods It was a retrospective case-note review study with minimum 6 months follow-up. Between May and October 2007, all patients who were not responsive to latanoprost or timolol (monotherapy) were prescribed bimatoprost. In all, 635 eyes of 330 patients (latanoprost, n=405; timolol, n=230) were included. Eligibility criteria: (1) Patients with original diagnosis of POAG, and (2) Nonresponsives- IOP reduction <20% on current treatment.Main outcome measure was IOP reduction.

Results IOP data (mean and standard deviation) were as follows: baseline = 24.85 ± 2.05 mmHg, after latanoprost =21.23 ± 1.6 mmHg, after timolol = 21.5 ± 1.66. When switched over to bimatoprost, mean IOP =18.39 ± 2.32 mmHg. There was statistically significant reduction in the IOP on bimatoprost when compared to baseline, latanoprost, and timolol (P<0.0001). 12.34% of latanoprost and 13.04% of timolol nonresponders did not respond to bimatoprost as well. While 12.72% patients reported significant conjunctival hyperaemia, only 6.96% had to stop the drug because of it.

Conclusion Bimatoprost is better in controlling intraocular pressures in those non-responsive to latanoprost or timolol. Conjunctival hyperemia remains the most important cause of stopping the use of bimatoprost.

5354

Safety of trabeculectomy with mitomycin C: The ReGAE (research into glaucoma and ethnicity) experience

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Purpose To describe the prevalence of surgical complications in patients undergoing trabeculectomy with mitomycin C (trab + MMC).

Methods A Review of an open consecutive prospective interventional case series performed by a single surgical team was undertaken. The case mix was a supra-regional complex mixture of primary, secondary and paediatric glaucoma. Complete and qualified success rates, and the prevalence of complications were calculated.

Results 382 eyes of 298 patients were included in the study. Mean follow up was 3.08 years. Mean age was 57.4 years (range: 6-87). At latest follow up qualified success (IOP ≤ 21mmhg with ≥1 ocular hypotensive agent) was 95.7% (360 eyes) and complete success (IOP ≤ 21mmhg without an ocular hypotensive agent) was 84.8% (319 eyes). Early postoperative complications ≤1 month of surgery were reported in 21 (5.5%) eyes. 7 (1.8%) eyes developed late surgery related complications >1 month of surgery. Clinically significant early hypotony (IOP <6 on 2 separate occasions and requiring surgical intervention) occurred in 17 (4.5%) eyes. 2 patients developed late hypotony including 1 case of hypotony maculopathy, and there was 1 case each of toxic anterior segment syndrome, corneal decompensation plus cystoid macular oedema (ICE syndrome patient), blebitis, endophthalmitis, aqueous misdirection, suprachoroidal haemorrhage, retinal tear, and epiretinal membrane. No patients developed choroidal neovascularisation or malignant glaucoma. 1 patient developed pulmonary oedema after general anaesthesia.

Conclusion Trab + MMC in a complex supra-regional case mix service is a highly effective and safe operation. Only 3 (0.8%) eyes developed irreversible vision loss > 2 lines Snellen.

■ 5355

Inhibition of vascular endothelial growth factor reduces scar formation after glaucoma filtration surgery

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Purpose In 30-50%, glaucoma filtration surgery fails due to excessive postoperative scarring. This study was designed to elucidate the role of vascular endothelial growth factor (VEGF) in fibrosis after glaucoma surgery. In addition, the effects of the monoclonal humanized VEGF-antibody bevacizumab (AvastinTM, Genentech) on fibroblast proliferation and outcome after trabeculectomy were studied.

Methods The effect of VEGF and bevacizumab on Tenon fibroblasts in vitro was determined using a Tenon fibroblast mediated proliferation assay. The effect of the antibody was also investigated in vivo in a rabbit model for glaucoma surgery by measuring intra-ocular pressure (IOP) and bleb area, and by (immuno-)histological analysis of inflammation and fibrosis. VEGF-concentration after bevacizumab-administration was measured in samples of aqueous humor by ELISA.

Results The proliferation of human and rabbit Tenon fibroblasts in vitro was stimulated by VEGF-delivery and inhibited by bevacizumab-administration. The antibody also significantly improved glaucoma surgery outcome, more specific the bleb area, in a rabbit model of trabeculectomy. Inflammation and collagen deposition were significantly reduced after bevacizumab treatment as compared to sham injections. VEGF was significantly reduced in aqueous humor after bevacizumab-administration.

Conclusion VEGF stimulates in vitro fibroblast proliferation suggesting that it plays a role in scarring after filtering surgery. Furthermore, the monoclonal humanized VEGF-antibody reduces in vitro fibroblast proliferation and improves surgical outcome in vivo in a rabbit model of trabeculectomy.

■ 5356

Micropulse diode laser trabeculoplasty for secondary corticosteroid induced glaucoma

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Purpose To evaluate the role of micropulse diode laser trabeculoplasty (MDLT) in the treatment of secondary glaucoma due to intravitreal injection of corticosteroid.

Methods Five consecutives patients previously treated with intravitreal triamcinolone (4mg) for refractory diabetic macular edema developed secondary glaucoma in the treated eye. Each eye underwent 360° micropulse diode laser trabeculoplasty (2000 mw power, 200 msec duration, 15% duty cicle, 300 µm diameter per spot). Patients were followed at 1, 7, 15, 28 days and monthly for 12 months.

Results Mean age of the patients was 56 ± 2 years. Mean baseline intraocular pressure (IOP) was 30 ± 3 mmHg. IOP significantly decreased at 7 days post operative (19 ± 4 mmHg; $p < 0.001$) and maintained at normal level in 3 of 5 eyes. After 28 days two eyes needed retreatment and IOP maintained normal in one eye during follow up. No pain or side effect was documented.

Conclusion Secondary glaucoma due to intravitreal injection of corticosteroid may be safely treated with micropulse diode laser trabeculoplasty.

5361
Different techniques to evaluate chromosome aberrations

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Purpose To review the demonstration of chromosomal alterations in uveal melanomas

Methods Uveal melanomas (UM) have an incidence of 6 per million per year, with presentation peaking at 60 years. Treatment is by various combinations of radiotherapy, local resection and phototherapy in 70% of patients, and by enucleation in 30%. Despite successful ocular treatment, 50% of UM patients develop metastatic disease. This occurs haematogenously, usually involving the liver, and almost always causing death within a year of the onset of symptoms. Long-term survival is rare. Clinical trials evaluating agents for systemic adjuvant therapy are difficult because of the rarity of UM & the reduced availability of molecular genetic testing.

Results In 1999 Prescher et al. reported that metastatic death occurs almost exclusively in patients with UM showing monosomy 3. Others also demonstrated a strong inverse relationship correlation between the presence of additional copies of 8q and survival. In contrast, patients with tumours having chromosome 6 abnormalities appear to have better prognosis. These analyses have been performed using FISH. Long-term data suggests that FISH, however, is not highly specific, and that approx. 5-10% of patients with disomy 3 UM develop metastatic disease. Newer methodologies are being tested on a research basis in the hope of using them as a diagnostic tool. These include multiplex ligation probe amplification (MLPA), array chromosome genomic hybridisation (aCGH), single nucleotide polymorphism (SNP) analysis and gene expression profiling.

Conclusion Newer methodologies will provide more details to chromosomal changes in uveal melanoma, and possibly molecular therapeutic targets to which new medications can be directed in adjuvant treatment of metastatic disease.

5362
Epigenetics, chromosome 3 and early detection of metastasis

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Purpose Uveal melanoma patients that present a tumor with monosomy 3 have a high propensity to develop metastases. Based on the two-hit hypothesis, one might expect that the remaining copy of chromosome 3 contains a genetically-modified gene and that loss of this gene is responsible for malignant progression. Identification of the gene and the genetic or epigenetic mechanisms that influence genes on chromosome 3 will enlighten the pathway(s) that determine uveal melanoma progression. In addition, studying epigenetics may result in useful molecular markers: whereas analysis of monosomy 3 is useful in primary tumors, it is useless in the detection of spreading tumor cells in the blood. We propose that a molecular marker in the form of a (tumor specific) genetic or epigenetic modification will be more helpful in this respect.

Methods We have analyzed genes on chromosome 3 for epigenetic regulation that may suffice in non-invasive testing for spreading tumor cells.

Results We have identified RASSF1a methylation as a predictor of metastasis in uveal melanoma based on analysis of uveal melanoma tissues. In order to detect disseminating tumor cells in the bloodstream of uveal melanoma patients we have developed a very sensitive assay for methylation of RASSF1a. The detection limit of RASSF1a methylation exceeds 1/10,000 and in combination with isolation cell-free DNA we are able to detect tumor DNA in the background of a vast excess of normal blood cells. With this assay we will test patient blood and validate the prognostic and diagnostic value of this marker.

Conclusion With this assay we will test patient blood and validate the prognostic and diagnostic value of this marker.

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Epigenetic alterations in uveal melanoma

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Purpose Epigenetic alterations are frequently observed in many tumors. Aberrant hypermethylation of CpG rich regions can silence gene expression and, therefore, can result in loss of function equivalent to a null mutation. Recently, regional hypomethylation of CpG rich regions that can result in activation of affected genes has gained increasing attention. Like somatic mutations epigenetic alterations may be used as molecular markers indicating the presence of cancer and minimal residual disease

Methods To study the epigenetic alterations in uveal melanoma we determined DNA methylation by direct sequencing and sequence-based quantitative methylation analysis (SeQMA) of PCR products from bisulfite treated genomic DNA from primary uveal melanomas, uveal melanoma cell lines, mononuclear blood cells and sperm samples of healthy donors.

Results We have found a frequent epigenetic mutation in the OXTR gene located within a minimal deleted region on chromosome 3p25-26 in uveal melanoma. Real-time RT-PCR showed that OXTR hypermethylation does not affect OXTR expression thus suggesting that this epimutation may affect expression of distant genes. We also identified a CT gene that is hypomethylated and consequently activated in about half of uveal melanomas. Interestingly, hypomethylation of this gene was biallelic.

Conclusion Therefore this alteration is unlikely to be the result of stochastic demethylation processes. We suggest that this region is actively demethylated or selectively protected from maintenance methylation during cell proliferation, or that hypomethylation of CT genes reflects the origin of the malignant cells from an unmethylated progenitor.

5364
Genomic profiling and identification of high-risk tumours in uveal melanoma by array-CGH analysis of primary tumours and liver metastases

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Purpose Current therapeutic efforts in Uveal Melanoma are directed toward detection of liver metastases at an earlier stage and adjuvant systemic therapy in high risk patients. Beside clinical and histological features, specific cytogenetic alterations, particularly monosomy 3 and gain of 8q, are strongly associated with metastasis.

Methods A series of of 78 ocular tumours (OT) (median follow-up 54 mo.)and of 66 liver metastases (LM), was analysed by CGH on a genome-wide BAC/DNA microarray (CIT, INSERM U830), with a 1 Mbase average resolution. Correlations were looked for between genomic profiles of OT and the metastatic status of patients, and a prognostic classifier was built, in order to identify tumour profiles of high risk patients.

Results Hierarchical clustering shows that status of chromosome 3 defines two groups of genomic profiles in OT and LM: group 1, with disomy 3, and group 2, with monosomy 3. Seven OT show a partial loss of chr 3, with a minimal deletion of 8.9 Mbase, distal to 3p25.3. Groups 1 and 2 can be subdivided in subgroups according to the presence of additional imbalances. Same genomic groups are found in OT and LM, but with different frequencies. The disomy 3 group represents 20% of metastases.A prognostic classifier including the status of chromosomes 3, 6p, 8p, 8q, 16q, and the position of breakpoint in 8q gains, leads to the best prediction performance in this sample (82%).

Conclusion Genomic profiling by array-CGH, combined with the allelic status of chromosome 3, should be a robust and reliable approach for identifying high-risk patients eligible for LM screening and adjuvant systemic therapy.

■ 5365

Identification of molecular markers associated with high metastatic risk in uveal melanoma

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Purpose Uveal melanoma occurs to the detriment of uveal melanocytes (located in the iris, ciliary body and choroid) and is the most common intraocular malignancy in adults, with 500-600 new cases every year in France. The survival rate for uveal melanoma has not increased significantly in the last 20 years.

Methods Gene expression profiling from the 63 tumours with a three years follow-up (33 of which have metastasized) have been already performed, and genes selection using significant analysis of microarays performed between primary tumours that have metastasized (meta1) and those that do not have metastasised (meta0) showed that 1210 probe sets are differentially expressed using a FDR cut off of 5%. Gene expression profiling from 115 liver metastasis have also been performed and compared with the primary tumors.

Results We used real-time PCR to validate, using a set of selected genes the microarray expression values. The results obtained with 14 uveal melanoma showed a complete concordance with the Affymetrix microarrays. We have already obtained a set of genes involved in cell migration differentially expressed between primary uveal tumors that have, or not, metastazised. These genes included the PTK2 focal-adhesion kinase, an important mediator of growth-factor signalling, cell proliferation, cell survival and cell migration. We will also focuss on NEDD9, a gene described by oncogenomic analysis as involved in melanoma metastasis. In our study PTK2 and NEDD9 expression are anticorrelated, (p=0,015), PTK2 is found more expressed in the meta1 group.

Conclusion we hope that deciphering the function of the selected genes will help to identify new pharmacological targets.

5411

Duration of retinal detachment and central retinal artery hemodynamics: repercussion on logmar visual acuity

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Purpose To analyze if duration of primary rhegmatogenous retinal detachment(RD) influences central retinal artery(CRA) hemodynamics with repercussion on LogMAR visual acuity (VA)

Methods Sixty six healthy patients between 42 and 70 years with unilateral RD candidates for scleral buckling(SB)surgery(PVR<C3)as a first and single surgical procedure were prospectively selected. Central retinal artery(CRA) Doppler sonography parameters:peak systolic(PSV) and end diastolic(EDV) velocities and resistive index(RI); and IOP were measured before SB. Pearson's correlations were evaluated between duration and each CRA parameter and also between both variables and LogMAR VA(preoperative, postoperative and the difference: postoperative minus preoperative)

Results Preoperative LogMAR VA showed significant($p<0.0001$) linear correlations with duration of RD($r=0.615$) and with CRA parameters: PSV($r=-0.485$), EDV($r=-0.592$), RI($r=0.509$). Postoperative LogMAR VA, with (all with $p<0.0001$) duration ($r=0.619$), and with CRA parameters: PSV($r=-0.637$), EDV($r=-0.711$), RI($r=0.630$). LogMAR VA Difference showed lower correlations with duration($r=0.085$, $p=0.0498$)and with CRA parameters: PSV($r=-0.266$, $p=0.031$), EDV($r=-0.236$, $p=0.057$)and RI($r=0.238$, $p=0.054$) than pre- and postoperative LogMAR VA.

Conclusion Duration showed a higher correlation with preoperative LogMAR VA and a lower correlation with postoperative LogMAR VA and with LogMAR VA difference than the CRA parameters.(Supported by FIS 04/0446)

5412

Use of PLGA microparticles for vitreous staining during anterior vitrectomy

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Purpose To demonstrate in vitro the potential use of FDA-approved PLGA poly(lactic-co-glycolic acid) microparticles to aid visualisation of vitreous during anterior vitrectomy following posterior capsule rupture and to compare with the use of triamcinolone suspension.

Methods 10-60um sized PLGA microparticles were fabricated using the single and/or double emulsion technique(s) and used i) untreated (ii) pre-treatment with sodium hydroxide (iii) surface adsorption of a protein/synthetic peptide. Particle size, shape, morphology and surface topography were also assessed using scanning electron microscopy (SEM).The efficacy of these microparticles to enhance visualisation of vitreous against triamcinolone suspension was assessed using a simple in vitro set-up exploiting human cadaveric vitreous.

Results Unmodified PLGA displayed a degree of hydrophobicity and also a high rate of dispersion following repeated wash cycles. Interestingly, surface modified PLGA microparticles demonstrated a significant improvement in its 'vitreophilic' properties and were comparable to a triamcinolone suspension.

Conclusion The use of modified biodegradable PLGA microparticles may represent a novel method of visualising vitreous and aiding anterior vitrectomy. This method may provide a distinct alternative for the visualisation of vitreous without the pharmacological effects of triamcinolone. Furthermore, such a technique allows the incorporation of drugs, growth factors and/or antibiotics within the microparticles which may be desirable in complicated cataract extraction. Animal models are required to assess in vivo biocompatibility of this method.

5413

Idiopathic epiretinal macular membrane and cataract extraction : combined surgery vs consecutive surgery

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Purpose To assess the functional and anatomical outcome of cataract and idiopathic epiretinal macular membrane extraction in combined and consecutive surgeries.

Methods A retrospective nonrandomized study of 174 epiretinal macular membranes (ERM) and cataract extractions in 1 or 2 sessions was undertaken in two academic centers. Combined surgery (n=109) and successive surgery (n=65) were performed between 2005 and 2006. All patients underwent ERM and internal limiting membrane removal. We compared the near and far visual acuity and the central macular thickness with OCT (Optical Coherence Tomography) for these procedures.

Results Mean follow-up was 8 months. The postoperative best-corrected visual acuities significantly improved in both combined (near and far vision: $p<0.0001$) and consecutive surgeries (near and far vision: $p<0.0001$) groups. Similarly, the postoperative macular thickness significantly decreased in both groups ($p<0.0001$). We noted no statistical differences between the visual acuity improvement in both groups (near vision $p=0.54$; far vision $p=0.38$).

Conclusion Combined and consecutive surgeries are effective procedures to treat idiopathic ERM. The functional and anatomical results are equivalent in these two procedures. However, combined surgery is more convenient for the patient.

5414

A new method for fixation and explantation of epiretinal implants

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Purpose In epiretinal prosthesis surgery the fixation of the implant on the retina is generally performed with retinal tacks in order to achieve a firm and a sufficiently close attachment to the ganglion cells. However, this fixation does not allow the removal of the implant without potentially causing major trauma. We therefore developed a new fixation method for the implant with the goal of enabling a safe and less traumatic explantation procedure.

Methods We implanted an inactive epiretinal device consisting of a polyimide strip and a calotte in 11 Göttinger minipigs. The concept of the new fixation method is to implant the tack first and fixate the implant on the tack with a silicone tube by using a special instrument developed for this purpose. Thus the implant is firmly attached to the retina and removal can be performed by simply splitting the silicone tube and lifting the implant from the tack while the tack remains in place.

Results All animals were implanted successfully without major complications. At the end of the observation periods the retinal tack and the silicone tube fixating the implant on the tack were still in position. The explantation procedure was accomplished easily and without any complications.

Conclusion This new implantation method ensures a firm fixation of the implant whilst also allowing explantation without trauma to the posterior eye segment.

5415
Perioperative bevacizumab injection: clinical and histological results

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Purpose To evaluate the safety and efficacy of Intravitreal Bevacizumab (IVB) injection as an adjuvant in the management of proliferative diabetic retinopathy (PDR) before or after planned vitrectomy.

Methods Prospective, interventional, consecutive case series of 58 eyes of 55 patients with PDR. The patients were divided in two groups: Group A (28 eyes) had IVB within 10 days before the surgery; Group B (30 eyes) had the IVB at the end of the surgery. A dose of IVB was of 2.5mg in 0.1 ml and was given under aseptic conditions. The specimens obtained from the both groups were evaluated by histological examination.

Results In Group A, 3 of 28 eyes (12%) had no significant reduction of neovascularisation; 8 of 28 eyes (28%) had a significant reduction in leakage and regression of tractional retinal detachment (TRD) with parallel improvement in visual acuity. Four (50%) of these 8 patients had recurrence of PDR within 10 weeks after the injection. In 2 patients, worsening of TRD was noted. In 11 patients, vitrectomy, delamination and endolaser laser were performed within 10 days. Post-operative bleeding was not noted in this group.In Group B, 7 out of 30 eyes (23%) had a re-bleeding within one month from the surgery. No difference in morphology was observed between the specimens of the two groups. An analogous staining pattern was observed between two groups when comparing markers for apoptosis (caspase), hypoxia (HIF1 and HIF2) and VEGF.

Conclusion IVB seems to be efficacious as an adjuvant treatment, if injected pre-operatively rather than post-operatively, for the management of PDR. IVB does not appear to cause any change in the light microscopic appearance or in the immunohistochemically-detectable expression of hypoxia or apoptosis markers.

5416
Standardized surgical procedure in complicated retinal detachment

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Purpose Within the last ten years the surgical procedures have been refined in patients with complex retinal detachments resulting in a better anatomical outcome. The reported reattachment rates vary from 54-96 %. Limited information about the final outcome of the complete cohort of complicated retinal detachment eyes after silicone oil removal is available. Several risk factors for redetachment have been identified: the number of previously unsuccessful surgeries, an incomplete removal of the vitreous base, the absence of an encircling element and the lack of a 360° laser retinopexy. However, the additional use of relaxing retinotomies, an encircling band and lens removal were up to the surgeons discretion. Based on the conclusions of these previous studies the present study investigated the impact of a standardized treatment approach on the anatomical and visual outcome in eyes with PVR grade C2 following unsuccessful retinal detachment surgery.

Methods The standardized treatment comprised of vitrectomy, placement of an encercling band, 360° laser retinopexy and silicone oil endotamponade in every eye combined with a small incision cataract surgery, if the patients were phakic. More than 50 eyes of 50 patients with failed prior scleral buckling procedure were included in this study.

Results Reoperations had to be performed in 25% of the eyes. The final reattachment rate 6 months after silicone removal was 95.8%. Macular pucker was found in 12%. 70% (43 patients) achieved a visual acuity of 20/200 or better.

Conclusion Standardized approach had no impact in the number of reoperation or the incidence of macular pucker. However it improves the final reattachment rate and consequently ameliorates the visual results.

5417
PASCAL Photocoagulator, is it better ?

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Purpose To demonstrate the advantages of the new PASCAL system over conventional laser

Methods Review of new laser modality

Results PAttern SCan Laser is a new retinal (amongst other things) photocoagulator which has many advantages over conventioal laser.It is a fully integradted laser system using frequency-doubled Nd-YAG diode pumped solid state laser with short 5532 nm pulses and can deliver anything from a sigle spot or a predetermined patternarray of up to 56 spots at the press of a pedal.

Conclusion PASCAL system delivers a comprehensive range of laser treatments in a considerably shorter time and more comfort and precision in comparison with conventional laser.

5421
Introduction

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ABSTRACT NOT PROVIDED

5422
Eye-derived systemic immune regulation : ACAID

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A form of systemic tolerance is created when antigenic material is placed in the anterior chamber of the eye, an immune privileged site. Termed anterior chamber associated immune deviation (ACAID), this form of tolerance insures that the systemic immune response to eye-derived antigens is devoid of T cells that mediate delayed hypersensitivity and antibodies that fix complement. ACAID arises when antigen is captured by intraocular antigen presenting cells, then carried to the spleen where a microenvironment is created that activates antigen-specific T cells to differentiate into regulatory cells that interfere with the induction of delayed hypersensitivity as well as its expression. Several cytokines and neuropeptides, constitutively present in the aqueous humor of the eye, imposes distinctive properties on antigen presenting cells, which play primary roles to the induction of ACAID. In this SIS, I would like to provide up-to-date information of what kinds of diseases ACAID can be effective for and whether human monocytes can acquire the specific functions as ACAID-inducing antigen presenting cells, in addition to molecules, cells, and concepts newly recognized as contributing to tolerance induction induced in ACAID. Evidence is given to support the idea that application of such information may lead to potential for therapeutic applications of ACAID mechanisms in prevention of progression of immune-inflammatory diseases in humans.

5423
Role of dendritic cells in the ocular immune response

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ABSTRACT NOT PROVIDED

5424
Macrophage modulation of inflammatory responses

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Purpose To give overview of the role of myeloid cells in homeostasis and more particularly their role in generating tissue damage as well as regulating immune responses within the retina.

Methods Reviewing the experimental evidence of homeostatic role of macrophage populations in the iris, choroid and retina of normal eye we will focus on the behviour and mechanisms of tissue damage during experimental autoinflammatory responses. In particular examining the interaction of myeloid cells in controlling inflamamtory responses during acute and regulatory phases (resolution) of disease.

Results The overall plasticity of macrophage populations and their intrinsic ability to respond to microenviromental signals (cytokines, chemokines and cognate receptor signalling) allows rapid responses to initiate yet limit tissue damage and generates targets to manipulate toward therapeutic gain.

Commercial interest

■ 5425

Role of ocular pigment epithelial cells in regional ocular immunity

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Purpose To whether soluble factors by retinal pigment epithelial cells (RPE) promote the generation of T regulatory cells in vitro.

Methods Primary cultured RPE cells were established from normal C57BL/6 mice. T cells were co-cultured with RPE, x-irradiated, and used as regulators (RPE Treg cells). Target bystander T cells were established from normal splenic T cells with anti-CD3 antibodies. T-cell activation was assessed for proliferation by [3H]–thymidine incorporation. Expression of cytotoxic T lymphocyte antigen-2α (CTLA-2α) and cathepsin L on RPE and T cells was evaluated with oligonucleotide microarray, RT-PCR, immune staining, western blots and flow cytometry. Recombinant mouse CTLA-2α and anti-mouse CTLA-2α abs were used for the assay. For induction of experimental autoimmune uveitis (EAU), mice were immunized with interphotoreceptor retinoid-binding protein peptide emulsified in complete Freund's adjuvant.

Results RPE converted CD4+ T cells into Treg cells by producing and secreting CTLA-2α, a cathepsin L inhibitor. CTLA-2α secreted by RPE cells selectively inhibited cathepsin L in the T cells and the cathepsin L-lacking T cells exhibited Treg phenotype, i.e. expression of Foxp3 and production of transforming growth factor beta (TGFβ). CTLA-2α enhanced their production of active forms of TGFβ. In addition, CD4+ T cells from EAU-induced cathepsin L knockout (KO) donors contained high population of Foxp3+ T cells and EAU in cathepsin L KO mice was significantly less than those in wild type mice. Furthermore, treatment with recombinant CTLA-2α significantly suppressed EAU.

Conclusion These results indicate that immunosuppressive factors derived from RPE participate in the establishment of immune regulation in the posterior segment of the eye.

5431

The Royal Victorian Eye and Ear Hospital (RVEEH) technique of DSAEK Triple

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Purpose Descemet stripping endothelial keratoplasty, together with cataract surgery, constitutes the DSAEK triple procedure. This remains an evolving technique, with new modifications continuing to simplify the technique and improve its reproducibility.

Methods At the Royal Victorian Eye and Ear Hospital (RVEEH), we have developed a sutureless technique of DSAEK triple using a glide to insert the donor lenticule. This procedure was performed in 4 eyes of 4 patients with Fuchs' endothelial dystrophy and cataract.

Results All surgeries could be performed successfully. No intraoperative complications were encountered in any of the cases. At mean follow up of 3 months, all grafts were attached, clear, and well-centered, with mean BCVA ≥6/18. There were no instances of graft dislocation or failure.

Conclusion The RVEEH technique of Sutureless DSAEK Triple procedure is effective, successful and easy to perform. The use of a glide eliminates the need for folding of the tissue and allows atraumatic transplantation of the donor lenticule.

5432

Full thickness cornea transplantation to lamellar bad managing extensive corneal perforations

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Purpose Present surgical techniques for managing extensive corneal perforations.

Methods In three eyes of the three patients full thickness to lamellar bad cornea transplantations were performed because of the cornea perforations. In all cases previous to corneal grafting amniotic membrane was transplanted in tectonic purposes since donor corneas were not urgently available. Surgical techniques of the amniotic membrane transplantation consisted of intrastromal fluffed–up and intrastromal blanket-fold multilayered amniotic membrane transplantations.Full thickness corneal grafts were decided because of the extensive descemet defects in the bad of the ulcers. Previously to the surgeries clinical diagnosis of ocular rosacea, herpetic keratitis and keratitis sicca were establisched in every consequent case. Additional sistemic treatment was administered for ocular rosacea and herpetic keratitis patients.

Results In all three cases multilayered amniotic membrane transplantation showed sufficient effect for restoration integrity of the globe for short period. Full thickness corneal transplantation to lamellar bad was effective surgical procedure. In one case double anterior chamber was observed for 1 month.

Conclusion 1.Multilayer amniotic membrane transplantation can be as the bridge to cornea grafting, in cases, when donor corneas are not urgently available. 2. For extensive corneal perforations full thickness cornea transplantation to lamellar bed is reliable method of treatment. 3. If corneal perforations are related to systemic disease it is necessary to administer appropriate regimen of the adjacent systemic medical treatment.

5433

Corneal thickness values in case of patients who underwent lamellar keratoplasty using various evaluation techniques.

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Purpose To analyze results of pachymetric measurements in patients after deep anterior lamellar keratoplasty (DALK) and endothelial keratoplasty (DSEK) using three techniques of pachymetry estimation.

Methods For the study 35 eyes after various lamellar keratoplasty were qualified. 20 eyes they who underwent DSEK (12 women and 8 men) and 15 after DALK (9 men and 6 women). The subjects age ranged from 23 to 92 years old (mean 45.0.1 years). The follow-up ranged from 9 to 31 months (mean 16.8 months). Patients underwent routine DSEK and DALK, using "big bubble" technique, surgery. Pachymetric values were achieved using three devices: ultrasonic pachymeter, specular microscope, Anterior Segment OCT. Pachymetric outcomes were analyzed and compared.

Results Total corneal thickness in case of patients who underwent DSEK surgery using ultrasound pachymeter ranged from 581 to 829µm (672.4 ± 89.1), specular microscope registered values from 518 to 719µm (575.4 ± 78.3), OCT Visante ranged from 575 to 911µm (690± 122.1). Total corneal thickness in patients who underwent DALK surgery using ultrasound pachymeter ranged from 382 to 571µm (487 ± 76.8), specular microscope registered values from 380 to 481µm (427 ± 84.2), OCT Visante ranged from 379 to 569µm (439± 143.1). Corneal thickness values received with the use of ultrasound and OCT values significantly differed form obtained using specular microscope.

Conclusion Specular microscope seems to omit graft thickness in corneal pachymetry evaluation, also pachymetric outcomes are underrated, even though is able to calculate endothelial cell density in patients who underwent lamellar keratoplasty.

5434

Factors influencing the outcome of the treatment of allograft corneal graft rejection

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Purpose To identify clinical characteristics of patients which influence the outcome of treatment of allograft corneal graft rejection.

Methods A retrospective chart review of 197 cases of corneal graft rejections was undertaken at the Royal Victorian Eye and Ear Hospital, Melbourne over a period of ten years from 1997-2007. Cases were divided into two groups according to the response to the treatment after allograft corneal rejection. Main parameters evaluated were demographic characteristics, primary indication of corneal graft and preoperative donor characteristics.

Results Corneal graft rejection was successfully treated in 163 cases and 34 cases failed to respond to therapy. Both the groups were age (p=0.12) and sex-matched (p=0.85). Keratoconus was more common as the primary indication for corneal graft in the group that had good response to the treatment (19% vs 5.9%; p= 0.08). Cases that failed to respond to treatment had higher number of recipient grafts > 9mm (9.4% vs 1.3%; p=0.04). Preoperative corneal neovascularization (adjusted odds ratio aOR= 4.8, p=0.03), and corneal edema at presentation of rejection episode (aOR=5.2, p=0.01) were associated with treatment failure.

Conclusion Preoperative corneal neovascularization and corneal edema were found to be associated with failure of treatment in cases with allograft corneal graft rejection.

■ 5435

An assessive model for corneal endothelium morphometry by diffraction

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Purpose Most in vivo measurements on the corneal endothelium morphology are done by specular microscopy. This is a time consuming process, due to the need of operator involvement. To assess alternative methods, an experimental optical setup for corneal endothelium morphometry by diffraction has been created.

Methods A phantom Polymethyl methacrylate (PMMA) cornea was created, having dimensions of a real cornea. The posterior surface of the phantom cornea was grated to allow for identification of a reflected far field (Fraunhofer) diffraction. The grating was manually etched under a microscope and consisted of a quadratic mesh with a periodicity of approximately 80 µm. The phantom cornea was fitted to a phantom anterior chamber. Because of differences in refractive indices, the phantom anterior chamber was filled with a water/sugar solution (61%) to fully emulate the relative reflection of the cornea-aqueous humor interface. Light from a He-Ne laser at 632.8 nm was modulated with achromatic lenses towards the phantom cornea at an incident angle of 45˚. The light reflected from the phantom cornea-aqueous humour interface was collected at the opposite 45˚ angle. The Fraunhofer diffraction pattern was recorded with a CCD chip.

Results Experiments showed that a diffraction pattern of the periodicities of the emulated corneal endothelium could be recorded.

Conclusion A simple optical setup was created and a grated emulated cornea was used to assess the possibilities of corneal endothelium morphometry using diffraction. Even with the low reflective power of the emulated cornea-aqueous humor interface, clear diffraction patterns could be recorded. The result is encouraging for further development of an optical system for in vivo morphometry on the corneal endothelium.

■ 5436

Optimisation of amniotic membrane (AM) denuding for tissue engineering

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Purpose Amniotic Membrane (AM) has gained increasing popularity as a useful carrier for ex-vivo expanded cells for tissue engineering, particularly in ocular surface reconstruction. However, current methods employed for denuding AM are highly variable and the consequent effects on the structural and molecular composition of the AM basement membrane (BM) are ambiguous. We compare the effects of the main denuding procedures, and propose a highly effective standardised alternative.

Methods AMs preserved for transplantation were denuded using published EDTA and Dispase-based methodologies and our novel thermolysin-based procedure. Scanning and Transmission electron microscopy and immunohistochemistry, for BM components (Collgens IV, and VII, laminin 5, and inegrins α6 and -β4) were used to assess effectiveness of denuding epithelium, whilst maintaining the integrity of the BM.

Results EDTA and Dispase-based denuding techniques resulted in the disaggregation and even destruction of the BM structure and molecular composition. Employing thermolysin effectively denuded epithelium whilst maintaining BM structural and molecular integrity.

Conclusion Current procedures for preparing AM are variable and often ineffective, resulting in non standard membranes. Our novel thermolysin-based technique effectively denudes the AM whilst preserving an essentially intact and consistent BM. Therefore, we propose this novel thermolysin procedure may potentially improve overall generation of tissue engineered constructs using AM.

5441
Morphological link between accommodation, presbyopia and cortical cataract

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Purpose Evaluation of the gross morphology, the cortical location and the fiber cell architecture of cortical opacities in the aging human lens.

Methods 39 human donor lenses were photographed in toto in frontal view using dark-field stereomicroscopy. 15 lenses were fixed, cut in axial slices and photographed the same way. Details of fiber cell architecture were investigated by fluorescent staining for membranes and by scanning electron microscopy.

Results Small focal and cuneiform cortical cataracts are discrete opacities located at a specific depth below the capsule, and extending from the equatorial region in anterior and posterior direction. A sharp border is observed, between the opacities with their disorganized fiber architecture and the deeper nuclear layers, which show a regular fiber pattern. This border is at a mean depth of 700 µm below the capsular surface. Close examination of the opacities revealed fiber folds, fiber undulations, fiber-to-fiber separations, fiber breaks, water lakes and fiber displacement. Because the lens cortex and nucleus have different viscoelastic properties in young and old lenses, we hypothesize that external forces during accommodation cause shear stress predominantly in this border zone.

Conclusion The location of the described changes suggests that mechanical forces may cause fiber disorganization, small cortical opacities, and, ultimately, cuneiform cataracts. Our hypothesis would be in line with recent findings by Truscott and co-workers about a two-compartmental organization of the human lens. They found biochemical arguments for a transport barrier developing at a middle age at the cortical/nuclear interface.

5442
The time of onset of inherited cataract

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Purpose The lens grows by addition of fibres to its surface, with the newest fibres just under the epithelium anteriorly and the capsule posteriorly. In slit-section the cortex shows 4 optical zones of dysjunction (C1 to C4) with differing light-scattering properties. We explore the clock-like implications of this arrangement and how the spatiotemporal distribution of opacities implies the timing of mutated gene expression and/ or the influence of modifying factors.

Methods Methods: A case report, literature review and proposal of a hypothesis

Results We have observed dot cataract in a mother (42 years) and 2 sons (16 and 11 years) expressing a dominantly inherited, activating mutation of the calcium sensing receptor (CaSR). In each patient, lens opacities were present in the deep and superficial cortex (C2, 3 and 4) but absent from C1 and lens nucleus.

Conclusion In our family, absence of opacities in the lens nucleus implies either that the mutated gene is not expressed pre-natally or that there is protection from the effects of the mutation in utero, which is lost post-natally. Absence of opacities in C1 implies the same for these young fibres and suggests that expression of disease (lens opacity) does not occur immediately after birth. We hypothesise that in our family, the expression of lens opacities once these fibres have entered C2, may be related to the switch from aerobic to anaerobic metabolism in the transitions from C1 to C2, to denucleation and loss of organelles and to other structural and functional changes which occur in this region. We suggest that the location and timing of appearance of inherited cataracts is related to the onset of gene expression and the presence of modulating factors which influence the effects of the mutated protein.

5443
Acute effects of the sigma- receptor agonist on human lens epithelial cells

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Purpose The aim of the present study was to examine the effect of the sigma-2 receptor agonist, Siramesine, on morphology, growth, cell death, lysosomal function and effects on extra-lysosomal proteolytic systems in human lens epithelial cells.

Methods Human lens epithelial cells in culture were exposed to siramesine and examined for morphological changes using Nomarski optics or calcein. Lysosomes were evaluated using acridine orange and MagicRed. Nuclear morphology was studied using Hoechst 33342 and propidium iodide. Enzymatic activities in living cells or cell lysates were studied using different fluorogenic substrates.

Results Siramesine at low concentrations increased the cytoplasmic proteolytic activity of the proteasome and the calpain system. Effects was also observed with respect to lysosomal morphology, acidity and function. Activation of caspase-3 and the appearance of nuclei with an apoptotic morphology were also found.

Conclusion Siramesine at low concentrations affects lens epithelial cells with perturbation of the major proteolytic systems, lysosomal morphology and results in caspase activation and cell death. Siramesine may be a promising substance for clinical studies concerning the treatment of PCO.

5444
In vivo high power infrared radiation exposure time dependence of lens light scattering

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Purpose To determine the exposure time dependence of lens light scattering after high power in vivo infrared radiation exposure of the eye.

Methods The experimental animal was 6 weeks old albino SD rat. Altogether, 12 animals were divided into four exposure time groups (5, 8, 13, 20 s). The animals were anesthetized with ketamine-xylazine, 95/14 mg/kg bodyweight, 20 min prior to exposure and both eyes were dilated with tropicamide 10 mg/ml. The infrared radiation source was a single mode CW fiber laser emitting at 1090 nm (Model SP-120C, SPI Lasers, UK) with the output power set to 6.2 W. The primary laser beam was focused just in front of the anterior focal point of the eye with an F# close to that of the rat eye so that a divergent beam entered the eye with a spot size of 3 mm in diameter inside the dilated pupil. This allowed for a homogenous intensity distribution within the lens and a large spot size on the retina. One week after exposure, the animal was sacrificed and the lenses were extracted for darkfield macroscopic imaging and measurement of intensity of forward light scattering.

Results The intensity of forward light scattering increased with increasing exposure time. The increase was well described by a 2nd order polynomial, omitting the 0:th and the first order term. The threshold exposure time, estimated as Maximum Tolerable exposure Time (MTT:2.3:16) was 4.8 s. Considering the power used, this corresponds to 30 J, thus delivered over 3 mm diameter which implies a radiant exposure of 4.2 MJ/m2.

Conclusion At 1 week after exposure to 6.2 W of 1090 nm, the intensity of forward light scattering in the lens increases with increasing exposure time and the threshold exposure time is 4.8 s.

■ 5445

In vivo assessment of blue light attenuation of the crystalline lens and tinted and not tinted intraocular lenses

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Purpose To compare lens absorption in vivo, as estimated by blue light luminance perception, of patients with tinted IOLs versus patients with clear IOLs, and with their status before cataract surgery.

Methods We tested 43 patients with variant density of nuclear senile cataract (18 had 0 to 1+ and 25 more than 1+), before and after lens extraction and IOL implantation. 21 received clear IOL and 22 the AcrySof® Natural (Alcon). The absorption of blue light was assessed by measuring the parafoveal relative sensitivity of blue-green radiation using Heterochromatic Flicker Photometry (MPS 9000 QuantifEYETM, ZeaVision©).

Results Preoperative results indicate that blue light attenuation is increasing with age. The postoperative results show that tinted IOLs absorb significantly more compared to clear IOLs ($p<0.001$). The difference in postoperative absorption with tinted IOLs from preoperative status was not statistically signifficant ($p=0.3$), and in the group of patients with 0 to 1+ cataract density the preoperative with the postoperative absorption was similar ($p=0.941$). On the contrary, the absorption of clear IOLs was significantly reduced postoperatively in the low cataract density group ($p<0.001$) and also in the total group of patients ($p<0.001$).

Conclusion The tint may simulate the aged crystalline lens of patients with low cataract density in blue light attenuation.This may offer protection to the retina from the photochemical damage caused by high energy short wavelength radiation.

■ 5446

Comparison of parameters in cataract surgery between coaxial microincision and standard coaxial incision

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Purpose To compare the outcomes of coaxial microincision cataract surgery (C-MICS) versus standard coaxial cataract surgery.

Methods In a prospective study, 60 eyes of 30 patients with corticonuclear cataract were selected to have a crystalline lens extraction through a temporal clear corneal incision using either C-MICS (30 eyes) or standard coaxial cataract surgery (30 eyes). C-MICS was performed through a 1.8 mm incision, and coaxial standard cataract surgery through a 3 mm incision. In all cases, hydrophilic intraocular lens was implanted. Collected parameters during the surgery were total surgical time, ultrasound time, and total balanced salt solution used. Preoperative and postoperative parameters collected were refraction, visual acuity, slit lamp exams and endothelial cell counts with corneal thickness evaluation.

Results There was no significant difference in postoperative parameters between the 2 groups. On the other hand, there was a significantly lengthening of surgical total time and ultrasound time in MICS group.

Conclusion Although ultrasound and total surgical time were significantly higher in coaxial microincision cataract surgery, this technique appears to be as safe and efficient than standard coaxial cataract surgery.

5451
Molecular genetic information - impact on the family

CHURCHILL A
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Methods This talk will focus on the impact being given a diagnosis of genetic eye disease has on families. The first part will consider ways in which information can be given and received using examples, including questions that arise from knowing this information and issues surrounding confidentiality and consent. The second part of the talk will concentrate on issues surrounding predictive and pre-natal genetic testing using examples from our Genetic Eye Clinic.

5452
Doctor, my baby doesn't fix and follow

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Purpose To describe the phenotypes and genotypes of genetically determined disease leading to either abnormalities of, or complete absence of visual development in the first few years of life.

Methods A case presentation format will be used to illustrate different genetically determined conditions leading to delayed or absent visual development. Both clinical and electrophysiological phenotypes as well as genotypes will be discussed.

Results Phenotypes and genotypes of genetically determined diseases leading to delayed or absent visual development are very different. An important distinction to be made is the one between stationary and progressive diseases. Indeed, such distinction is important as the visual outcome varies considerably between those different conditions.

Conclusion Very diverse conditions may give rise to genetically determined abnormal visual development. Genetics and visual electrophysiology allows an important distinction between progressive and stationary conditions.

5453
Genetic testing in retinal dystrophies

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Purpose To describe genetic testing in autosomal recessively inherited retinal dystrophies.

Methods Retinal dystrophies (RD) are a heterogeneous group of diseases characterised by progressive retinal degeneration leading to severe visual disability. The prevalence of RD is ~ 1/3500; of these up to 40% are presumed autosomal recessive (AR). AR inheritance is frequently seen in juvenile onset cases, but also presents in young adults. The heterogeneity of inherited eye disease can make differential diagnosis difficult. For a sporadic case in a young male the differential diagnosis may include autosomal recessive, X-linked or autosomal dominant RD. Although there are no treatments yet available for inherited RD, knowledge of the underlying genetic variation can be helpful for: clinical diagnosis in patients with signs and symptoms of disease; pre-symptomatic testing for individuals who do not have the disease, but given their family history, are at risk for the disease; carrier testing for individuals who may carry a gene mutation that can be passed on to their children; and may be useful if genetic therapy becomes a viable option. Methods: Testing strategies using novel technologies are now being adopted to increase identification of disease causing mutations. One major advance includes the use of high throughput sequencing platforms. The introduction of this technology is likely to overcome many of the problems associated with testing multiple patient samples and multiple genes, as well as providing the accuracy required in a diagnostic setting. Even these technologies will not identify all types of mutations, for example large deletions so other technologies will be required.

5454
Molecular diagnosis of X-linked retina diseases

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Purpose X-linked retinal dystrophies present as clinically severe in affected males, whereas heterozygous carrier females show a wide spectrum of clinical signs from normal to marked abnormalities. A range of phenotypes will be discussed, and phenotype/genotype correlation explored.

Methods Patient DNA was analysed for mutations in X-linked genes by a combination of PCR and sequencing. Clinical tests included fundus examination and ERG recordings.

Results Molecular screening has resulted in identification of the causative mutation in many cases. Interpretation of the pathogenicity of a sequence alteration can be problematic in the absence of a functional test for sequence changes. Examples of mutations identified will be presented with associated clinical outcomes, with particular emphasis on RPGR as a cause of retinitis pigmentosa, cone-rod dystrophy, or syndromic RP.

Conclusion A molecular diagnosis is often necessary to determine carrier status of at risk females in X-linked pedigrees. Phenotypes vary between and within families with mutations in the genes RPGR and RP2. However, phenotype and genotype can be correlated for X-linked congenital stationary night blindness caused by mutations in the NXY and CACNA1F genes.

5455
Testing and counselling in inherited optic neuropathies

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Purpose Inherited optic neuropathies are a diverse group of conditions presenting with mild to severe visual loss, colour vision deficits, central/ paracentral visual field defects, optic disc pallor and in many cases a positive family history. Modes of inheritance are dominant, recessive, X-linked and mitochondrial. The absence of a family history does not exclude this diagnosis as there are many apparently new mutations and sporadic cases. Examination of first-degree relatives may be essential if family history is in doubt. All of these conditions are untreatable but referral for genetic counselling, molecular diagnosis, low vision aids, school assistance and blindness registration may be of benefit to the patient and their family.

Methods Autosomal dominant optic atrophy (ADOA) and Leber's hereditary optic neuropathy (LHON) are the most common of these conditions. ADOA typically presents in mid to late childhood, with an insidious bilateral, symmetrical mild to moderate visual acuity loss, accompanied by dyschromatopsia, central/ centro-caecal field defect and optic disc pallor. LHON typically presents in early adult life with a sudden, asynchronous, consecutive, catastrophic loss of central vision progressing rapidly to profound visual loss. Visual recovery is most unusual.

Results At least three genes for dominantly inherited optic atrophy have been mapped (OPA1, OPA4 and OPA5), of which the gene has been identified in one (OPA1). A gene for recessive optic atrophy (OPA3) has also been identified. X-linked optic atrophy (OPA2) has been mapped but to date no gene has been identified. Mutations in mitochondrial DNA have been identified in Leber's hereditary optic neuropathy.

Conclusion Testing and counselling in the primary inherited optic neuropathies has positive benefits.

5461
Unusual patterns of orbital extension in periorbital squamous cell carcinomas

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ABSTRACT NOT PROVIDED

5462
Atypical inflammatory lesions in the orbit and adnexae

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Purpose The common use of an initial systemic steroid treatment trial in orbital and adnexal inflammatory disease is now more questionable and used less frequently. The increased availability of specialized oculoplastic and orbital surgeons has enabled us to biopsy masses of the orbit routinely in recent years. As a result unusual pathology appears more commonly than expected in previous years. We reviewed the diagnosis and presentation of unusual inflammatoty lesions of the orbit biopsied over the past 8 years in our oculoplastic and orbital clinic. Some interesting representative cases are presented.

Methods A search of the operation register and recorded diagnosis of pathology specimens was carried out and a retrospective review was made of all patients with unusual orbital inflammatory lesions presenting at the oculoplastic surgical service in Meir Medical Center between 1999 and 2008.All cases had CT imaging of the orbits and underwent biopsy of the lesion. Pathology examination was performed on all specimens following biopsy.

Results There were 5 cases of non caseating granulomas in the Orbit, 1 case of Churg Strausse syndrome, 2 cases of lymphoid hyperplasia, 1 case of infectious mononucleosis dacryoadenitis, 2 cases of Eosinophillic Granuloma, 1 case of malignant schwannoma, 2 cases of angiolymphoid hyperplasia, 1 case of Sclerosing type idiopathic orbital inflammatory disease and 1 orbital abscess with an unusual presentation

Conclusion We recommend biopsy of all orbital inflammatory masses before beginning treatment with steroids. Unusual pathology is more likely than expected and may have significant implications for the well being of patients.

5463
Diagnostic difficulties in orbital pathology

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Purpose To describe and discuss sources of difficulty in histopathological diagnosis in orbital pathology and the approach to problematic diagnostic cases.

Methods Review of case material in Manchester Royal Eye Hospital and Manchester National Specialist Ophthalmic Pathology Service Laboratory archives and review of the literature.

Results Problems may be due to inadequacies of the process of specimen submission/handling, eg inadequate clinical information, inadequate sampling or crush/cautery artefact in small biopsies. They may be due to insufficient or uncertain histopathological criteria, eg isolated or rare orbital presentation of systemic pathology (such as isolated orbital Wegener's granulomatosis), isolated presentation of metastatic malignancy with unknown primary site, anaplastic malignancy and other lesions of uncertain histogenesis, inflammatory lesion vs lymphoreticular neoplasm (such as lymphoid hyperplasia vs low grade B-cell non-Hodgkin's lymphoma and necrotizing inflammation vs T/NK cell lymphoma).

Conclusion Good communication between clinicians and pathologists is essential at all stages during the diagnostic process. Sound morphological assessment remains crucial. Immunohistochemistry plays a valuable part in assisting diagnosis of lesions of uncertain histogenesis and in lymphoreticular pathology. There is an expanding use of molecular genetic analysis. Electron microscopy has largely been supplanted by immunohistochemistry but still has a role to play. Despite the vastly increased technological armamentarium there remain lesions which are very difficult to diagnose or classify. The multidisciplinary team approach fosters interplay among the differing areas of clinical and diagnostic expertise and allows a rational approach to diagnosis and management of problematic cases.

5464
Unexpected orbital and adnexal masses: Experience of several cases

DRAY JP

ABSTRACT NOT PROVIDED

■ 5465

Some unusual vascular mass presentations in the orbit and adnexae

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ABSTRACT NOT PROVIDED

6111
Contribution of inflammation to the early stages of diabetic retinopathy

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Purpose Many biochemical and physiological abnormalities detected in retinas of diabetic animals are consistent with a potential role of inflammatory-like processes in the capillary degeneration.

Methods We have used drugs and genetically modified rodents to investigate the role of inflammation in the development of early stages of diabetic retinopathy, focusing especially on the diabetes-induced degeneration of retinal capillaries.

Results In animal models, vascular lesions characteristic of the early stages of diabetic retinopathy have been found to be inhibited by salicylates (which inhibit NF-κB and cyclooxygenase), a PARP inhibitor (which inhibits inflammatory responses apparently by regulating NF-κB), minocycline (which inhibits the generation of IL-1β), a topical inhibitor of cyclooxygenase, and by an inhibitor of iNOS. These studies demonstrate that inflammation plays a critical role in the development of early stages of diabetic retinopathy.

Conclusion The concept that localized inflammatory processes play a role in the development of diabetic retinopathy is relatively new, but evidence that supports the hypothesis is accumulating rapidly. This new hypothesis offers new insight into the pathogenesis of diabetic retinopathy, and offers a novel target to inhibit the ocular disease.

6112
Metabolic memory puzzle and progression of diabetic retinopathy

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Purpose Retinopathy is one of the most feared complications of diabetes. Good glycemic control can inhibit its development, but the effects of good glycemic control on the progression of retinopathy are not immediate. Diabetic patients may take years after re-establishment of good glycemic control to show signs of arrest of its progression. Further, good glycemic control after a profound period of poor glycemic control does not immediately benefit the progression of retinopathy, and the imprinted effects of prior glycemic control produce the long lasting benefits of good glycemic control, thus suggesting a 'metabolic memory' phenomenon.

Results Animal models of diabetic retinopathy, including dogs and rats, have duplicated this metabolic memory phenomenon. In rats, histopathology associated with diabetic retinopathy does not stop for at least six months when good glycemic control is initiated six months after induction of diabetes. Increase in retinal oxidative stress and peroxynitrite levels and activation of apoptosis execution enzyme-caspase-3 resist reversal after re-institution of good glycemic control. Hyperglycemia-induced inactivation of retinal glyceraldehyde dehydrogenase that is postulated to activate some of the key pathways associated with the development of diabetic complications remains inactive and covalently modified, and pro-inflammatory markers elevated.

Conclusion This suggests that the process of metabolic memory is complex, and multiple pathways contribute to this resistance of diabetic retinopathy to arrest. Understanding the mechanism responsible for the tendency of diabetic retinopathy to progress after reestablishment of good glycemic control should help reveal targets for therapies to prevent its progression.

6113
New insights into the pathogenic role of advanced glycation in diabetic retinopathy

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Purpose Retinopathy is the most common microvascular complication of diabetes. The clinicopathology of microvascular lesions and neuroglial dysfunction in the diabetic retina have been extensively studied, although the relative contribution of various biochemical sequelae of hyperglycaemia remains ill-defined. The formation and accumulation of advanced glycation endproducts (AGEs) is an important pathogenic pathway in the progression of diabetic retinopathy although some of the cellular and molecular pathologies initiated by these adducts in retinal cells remain unknown.

Methods This presentation will cover several aspects of AGE-linked retinal pathology and demonstrate opportunities for therapeutic intervention. The studies outlined will cover a wide range of molecular cell biology approaches using appropriate in vitro and in vivo model systems.

Results It will be demonstrated that AGEs form in vivo in the diabetic retina through the reaction of alpha-oxaloaldehydes leading to significant modifications of retinal proteins. Evidence will be presented to demonstrate that these AGEs act as significant effectors of retinal vascular and neuroglial cell dysfunction, leading to pro-inflammatory responses, growth factor imbalance and, ultimately, neurovascular lesions such as blood retinal barrier dysfunction and microvascular degeneration. The protective role of novel AGE-inhibitors will also be shown.

Conclusion Evidence now points towards a pathogenic role for advanced glycation in the initiation and progression of diabetic retinopathy and this review lecture will outline the current state of knowledge of AGE-related pathology in the retina at a cellular and molecular level.

6114
Caspase-1/interleukin-1beta signaling in diabetic retinopathy

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Purpose The pro-inflammatory cytokine, interleukin-1β (IL-1β), is known to induce vascular dysfunction and cell death. Previously, we have shown that caspase-1 activity is increased in retinas of diabetic and galactosemic mice, and diabetic patients. Therefore, we investigated the role of IL-1β and caspase-1 (the enzyme that produces it) in diabetes-induced degeneration of retinal capillaries.

Methods First, we determined the effect of agents known to inhibit caspase-1 (minocycline and tetracycline) on IL-1β production and retinal capillary degeneration in diabetic and galactose-fed mice. Diabetic and galactose-fed mice were injected intraperitoneally with minocycline or tetracycline (5mg/kg). Second, we examined the effect of genetic deletion of the IL-1β receptor on diabetes-induced caspase activities and retinal capillary degeneration using IL-1 receptor knock-out mice.

Results At 2 months of diabetes, minocycline inhibited hyperglycemia-induced caspase-1 activity and IL-1β production in the retina. Long-term administration of minocycline prevented retinal capillary degeneration in diabetic (6 months) and galactose-fed (13 months) mice. Tetracycline inhibited hyperglycemia-induced caspase-1 activity in vitro, but not in vivo. Mice deficient in the IL-1β receptor were protected from diabetes-induced caspase activation and retinal pathology at 7 months of diabetes.

Conclusion These results indicate that the caspase-1/IL-1β signaling pathway plays an important role in diabetes-induced retinal pathology and its inhibition might represent a new strategy to inhibit capillary degeneration in diabetic retinopathy.

■ 6115

PARP, Na+/H+-exchanger-1, and early diabetes-induced retinal changes

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Purpose To evaluate the roles for PARP and Na+/H+-exchanger-1 (NHE-1) in early diabetes-induced changes in the retina and retinal capillary cells

Methods Control (C) and STZ-diabetic (D) rats were treated with/without the PARP inhibitors, 1,5-isoquinolinediol (ISO, 3 mgkg-1d-1 i.p.) or 10-(4-Methyl-piperazin-1-ylmethyl)-2H-7-oxa-1,2-diaza-benzo[de]-anthracen-3-one (GPI 15427, 30 mgkg-1d-1), for 10 wks after 2 wks without treatment. Apoptosis was evaluated in flat-mounted retinas by TUNEL assay, and nitrotyrosine (NT), poly(ADP-ribose) (PAR), GFAP, BiP/GRP78 and GRP94 expressions by immunohistochemistry and Western blot analyses. Primary bovine retinal pericytes and endothelial cells were cultured with/without 0.6 mM palmitate, or in 5 mM or 30 mM glucose. Apoptosis was assessed by TUNEL and caspase-3 assays, superoxide production by ethidium fluorescence, and NT and PAR by immunocytochemistry.

Results In the PARP study, the number of TUNEL-positive nuclei was increased ~4-fold in D, and this increase was prevented in D+ISO and D+GPI 15427. PARP inhibitors counteracted oxidative-nitrosative and endoplasmic reticulum stresses, and glial activation. Palmitate dose dependently increased superoxide production in cultured retinal cells. GPI 15427, 20 microM, prevented FFA-induced increase in the rate of apoptosis, and alleviated NT and PAR accumulation in both pericytes and endothelial cells. In the NHE-1 study, the specific NHE-1 inhibitor cariporide (10 microM) prevented high glucose-induced apoptosis, and alleviated oxidative-nitrosative stress and PAR accumulation in bovine retinal pericytes. In vivo studies in the STZ-diabetic rat model are in progress.

Conclusion PARP and NHE-1 play an important role in early diabetes-induced changes in retina and retinal capillary cells.

▪ 6121
Modern exploration of choroidal inflammation

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Purpose The choroid is the site of intraocular inflammation as often as the retina. Because choroidal structures were not accessible to sensitive and performing investigational procedures, analysis of inflammatory events lagged behind. This was at the origin of the inadequate appraisal of choroiditis and the use of imprecise or vague terminologies such as "White Dot Syndromes".Thanks to indocyanine green angiography (ICGA), access to the choroidal compartment has been granted to the clinician and more precise information on inflammatory mechanisms has allowed to establish a classification based on disease behaviour as well as direct monitoring of disease evolution in the choroid.

Methods With the help of ICGA, choroiditis could be subdivided into at least two inflammatory patterns touching 2 different choroidal structures are occuring. Firstly, inflammation of the choriocapillaris causing non perfusion is very well recognised by its typical ICGA features and constitutes a group of diseases that are called inflammatory choriocapillaropathies, including MEWDS, APMPPE or multifocal choroiditis.

Results Secondly, there is a totally different type of choroiditis, with inflammation occurring in the choroidal stroma in form of a mostly granulomatous infiltration called stromal choroiditis. When the target is specifically in the choroid such as in VKH disease or Sympathetic Ophthalmia (SO) we speak of primary stromal choroiditis and when the choroid is just the structure where a systemic disease such as sarcoidosis elects to manifest itself we speak of secondary stromal choroiditis.

Conclusion Beside the fact that ICGA has helped us classify choroiditis based on disease mechanism, it also allows proper monitoring of disease activity reaching a high degree of accuracy.

▪ 6122
OCT, a value adding technique (VAT) in the appraisal of macular inflammation

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ABSTRACT NOT PROVIDED

▪ 6123
The role of gamma-interferon tests for suspected tuberculous ocular inflammation

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Purpose To evaluate the introduction of new T-cell based blood tests for tuberculosis infection in order to improve the diagnosis of ocular tuberculosis.

Methods Patients with presumed ocular tuberculosis from the Ocular Immunology Unit of the hospital of Reggio Emilia underwent both Mantoux skin tests and Gamma Interferon assays to confirm the diagnosis of tuberculosis.

Results 8 patients (7/8 male; mean age 58 yrs) were diagnosed with presumed ocular tuberculosis. Three patients presented with serpiginous retinochoroiditis and five with bilateral panuveitis. Four patients had undergone immunosuppressive therapy before the correct diagnosis was made. All the patients were positive both with Mantoux skin test and Gamma Interferon assays (ELISpot and QuantiFERON TB-Gold). They started the specific anti-tuberculous tritherapy, improving significantly in visual acuity and decreasing intraocular inflammation.

Conclusion These results confirm the feasibility of these new blood tests in routine clinical work-up. These new methods are important for the ophthalmologist in order to follow and evaluate developments in every method of detection of tuberculosis for the containment of this global public health epidemic.

▪ 6124
The role of interferon alpha in uveitis therapy

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Purpose Severe uveitis is potentially associated with visual impairment or blindness in young patients. Therapeutic strategies remain controversial. Efficacy of interferon alpha-2a (IFN-a2a) in severe uveitis, refractory to steroids and conventional immunosuppressive agents has been evaluated.

Methods Patients were included after a major relapse of uveitis occurring under corticosteroids and immunosuppressants. IFN-a2a (3 millions units three times a week) was administered subcutaneously. Efficacy was assessed by the improvement of VA, decrease of vitreous haze, resolution of retinal vasculitis and macular edema, and decrease of oral prednisone threshold.

Results Forty-five patients were included. Mean age was 30.6 years (range 8-58 years) and sex ratio (F/M) was 0.66. Uveitis was associated with Behçet's disease in 23 cases (51.1%) and with other entities in 22 cases (48.9%). Mean duration of uveitis before interferon therapy was 50.5 months and an average of 3 relapses under corticosteroids and immunosuppressants has been noted. Uveitis was controlled in 82.6% of patients with BD and 59% of patients with other types of uveitis ($p=0.07$). During a mean follow-up of 29.6 months, mean oral prednisone threshold decreased significantly from 21.5 mg/d to 9.8 mg/d ($p<0.001$). Interferon has been discontinued in 10 patients (22.2%) with BD and 4 patients without BD. Relapses occurred in 4 and 1 cases, respectively.

Conclusion Though our study carries several limitations, interferon-therapy seems an efficient strategy in severe and relapsing forms of BD but also other uveitic entities. However, it seems more suspensive than curative. Therefore, IFN-α2a may be proposed as a second line strategy after the failure of conventional immunosuppressants.

▪ 6125
The role of mycophenolate mofetil in uveitis therapy

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Purpose To summarize current evidences for mycophenolate mofetil (MMF) therapies in the treatment of uveitis. The review emphasizes the safety and efficacy of MMF in the treatment of inflammatory ocular diseases.

Methods The review describes published research since early nineties, and reports the experience of a tertiary-referral center.

Results Studies in other disciplines have proven the efficacy of MMF with a long-lasting remission in patients affected by Crohn's disease, severe atopic dermatitis, Wegener's granulomatosis, rheumatoid arthritis, pemphigus vugaris, and psoriasis. Recent publications have confirmed the satisfactory control of uveitis with MMF in a large cohort of patients. Severe ocular inflammations can also have late sequela, generated by the chronic damage to the retina: cystoid macular oedema (CMO) and choroidal neovascularization (CNV) can be late occurrences. MMF has been recently used for the control of such sequela, showing a promising role in the control of both CNV and CMO.

Conclusion Non-infectious uveitis is one of the leading causes of visual impairment in ophthalmology. Steroids can control such disease and its sequela, but a long-term therapy with steroids could lead to complications such as high blood sugar level, osteoporosis, blood cell abnormalities, cataract and glaucoma. MMF is a reversible, non competitive, selective inhibitor of the de-novo pathway of purine synthesis; mycophenolic acid has a strong effect to Type II isoform of inosine monophosphate dehydrogenase enzyme, providing a stronger cytostatic effect on lymphocytes than on other cells types, with minor action to Type I expressed in most other cells. The specific action of MMF on selected targets makes it a promising drug for the control of non-infectious intraocular inflammations.

▪ 6126
The role of TNF-alpha blockers in uveitis therapy

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Tumor necrosis factor (TNF)-α has been implicated as an important mediator in autoimmune ocular inflammatory disease pathogenesis as shown by animal studies and its detection in the ocular fluids of patients with uveitis. Blockade of TNF-α has emerged as one of the most promising therapies in autoimmune diseases including uveitis. Currently, there are three TNF-α antagonists: two monoclonal antibodies (infliximab and adalimumab) and a soluble receptor that binds soluble TNF-α (etanercept). Infliximab is a chimeric monoclonal antibody directed against TNF-α. It binds with high affinity to both the soluble and the membrane-bound TNF-α and inhibits a broad range of biologic activities of TNF-α. Several studies reported that infliximab therapy was rapidly effective and safe treatment for refractory noninfectious uveitis including childhood uveitis and is indicated as rescue therapy for relapses of ocular inflammation or as maintenance therapy when conventional immunosuppression fails. It also allowed a reduction of corticosteroids and immunosuppressive drugs required to control the disease. However, repeated infusions are required to maintain long-term remission. Moreover, infliximab administration is costly and requires hospital admission. Recently, adalimumab, fully humanized monoclonal anti- TNF-α antibody, was also found to be effective and safe therapy for the management of refractory noninfectious uveitis. Several studies reported that infliximab was more effective than etanercept in the treatment of refractory uveitis. Perhaps infliximab's ability to target membrane-bound TNF-α in addition to the soluble form may contribute to its increased efficacy in comparison with etanercept for uveitis.

6131
Corneal keratocyte density after mechanical versus femtosecond laser in situ keratomileusis

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Purpose To determine changes in keratocyte density three months after mechanical versus femtosecond laser in situ keratomileusis.

Methods This was a retrospective study in which 20 consecutive eyes received LASIK to correct a mean refractive error of -2,3+/-2,1 D sphere and -0,8+/-2,1 D cylinder, and 21 consecutive eyes received femtosecond laser to correct a mean refractive error of -1,8+/-3,5 D sphere and -2,2+/-2,9 D cylinder. Both groups were compared with a control group of 20 normal and healthy eyes with a mean refractive error -2,2+/-2,9 D sphere and -0,5+/-0,6 D cylinder. Corneas were examined by using confocal microscopy three months after the procedures. Keratocyte densities were determined in the anterior stroma, stromal bed, central and posterior stroma.

Results Keratocyte density in the anterior stroma and in the stromal bed was 500,8 +/- 108,4 cells/mm2 in the control group, 506,1 +/- 130,6 cells/mm2 and 475,9 +/- 147 cells/mm2 respectively in the LASIK group, and 446 +/- 120,7 cells/mm2 and 416,3 +/- 115 cells/mm2 respectively in the femtosecond group (p>0,05). In central and posterior stroma the difference was also not significant.

Conclusion Keratocyte density is decreased in the stromal bed after mechanical and femtosecond laser in situ keratomileusis as compared to controls, however, there is not difference between both procedures.

6132
Structural and optical changes in the eye after soft contact lens wear

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Purpose To investigate the magnitude and aetiology of structural and optical changes in the cornea after short-term hydrogel contact lens wear and to explore the effect of these changes on visual performance.

Methods Sixteen healthy subjects were fitted with a low-Dk hydrogel contact lens (CH) in one eye and a silicone hydrogel (SH) lens in the contralateral eye. Subjects wore the lenses for 1 month in daily wear (DW) and 1 week in extended wear (EW), with at least 1 week 'wash out' in between. All lenses were plano powered and were manufactured in matched designs with the same specifications. Measurements of corneal topography, corneal pachymetry (apical and peripheral), and corneal and ocular aberrations were performed at baseline and after lens wear using a Scheimpflug imaging system (Oculus Pentacam) and a Hartmann-Shack aberrometer (IRX3). Best corrected visual acuity (BCVA, logMAR) and contrast sensitivity measurements (CS, Pelli-Robson) were also performed.

Results The optical and structural changes in the cornea after 1 month of DW and 1 week of EW for both the CH and SH materials were of low magnitude. The topographic and pachymetric changes observed were not found to be significant (p>0.05, repeated measures ANOVA). After 1 month of DW, however, the corneal root mean square of quatrefoil aberrations was found to be significantly different after CH contact lens wear (mean difference -0.021 µm; 95% confidence interval for difference: -0.037 to -0.06 µm; p=0.003). BCVA and CS did not change significantly after lens wear.

Conclusion Our data showed that the CH and SH lenses tested do not significantly alter the structure or the optical performance of the cornea after one month of daily wear and 1 week of extended contact lens wear.

6133
Effectiveness of moisturizing daily disposable lenses with additives

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Purpose Recently, contact lens manfacturers are incorporating moisture additives in their contact lenses. Examples include povidone in 1-DAY ACUVUE MOIST lenses, polyvinyl alcohol (PVA) in DAILIES with AquaComfort lenses and hydroxypropyl-methylcellulose, polyethylene-glycol and PVA in the DAILIES AquaComfort Plus lenses. These two trials were aimed to compare the effectiveness of these additives to general lens performance.

Methods In the first trial, 20 investigators in the US and Germany enrolled 276 subjects currently wearing nelfilcon A with PVA (nefA+1) lenses in daily disposable modality of comparison to nelfilcon A with moisturizing additives (HPMC, PEG and PVA (nefA+3) for ten days. In the second trial, 14 investigators in Germany enrolled 314 current daily disposable wearers to wear nelfilcon A with moisturizing additives HPMC, PEG and PVA (nefA+3), and etafilcon A with added PVP (etaA+1) for one week each.

Results 273 subjects completed the first trial. Comfort upon insertion was rated 9.1 for nelfilcon A with moisturizing additives (nefA+3) and 8.7 for nelfilcon A lenses (nefA+1); comfort during the day was 8.7 and 8.7, respectively; end of day comfort was 7.9 and 7.2, respectively; overall comfort was 8.6 and 8.4, respectively. 309 subjects completed the second trial. Comfort upon insertion was rated 8.6 for nefA+3 and 7.6 for etaA+1; comfort during the day was 8.4 and 7.8, respectively; end of day comfort was 7.2 and 6.6, respectively; overall comfort was 8.4 and 7.5, respectively.

Conclusion Mean comfort ratings were significantly in favor of nelfilcon A with additives HPMC, PEG and PVA in both trials. Future innovations in daily disposable lenses with added moisturizes to last throughout the day should be expected.

Commercial interest

6134
Re-treatment after LASIK for correction of myopia and myopic astigmatism

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Purpose To evaluate the results of LASIK re-treatment for under-correction or regression after primary LASIK procedures for myopia and myopic astigmatism.

Methods Of 360 consecutive LASIK-treated eyes, for myopia and/or myopic astigmatism, 32 eyes of 34 patients were retreated and followed at 3, 6 and 12 months post retreatment. Re-treatment was performed by lifting the original flap after cutting the epithelium around the flap edge with a fine needle. Standard ablation was performed based on the patient's residual refraction.

Results 9.4% of eyes patients required retreatment. Prior to re-treatment the mean manifest spherical equivalent (SE) was –0.99 D ± 1.48 D (range from - 0.75 to -2.63). The mean sphere was - 0.79 D ± 1.20 D (range from –2.50 to -0.50) and the mean cylinder was –0.90 D ± 1.14 D (from –2.75 to 1.25). At 1 year follow up 56% of the eyes were within ± 0.50 D SE and 78% were within ± 1.00 D SE. 78% percent of the eyes examined at one year post re-treatment managed unaided vision of 6/9 or better. Peripheral epithelial ingrowth not requiring treatment, developed in two eyes. Second re-treatment for regression was performed in one eye.

Conclusion LASIK re-treatment for residual myopia, by lifting the original flap is an effective option. Refractive results are fairly predictable and refraction stabilizes by 3 months after re-treatment. Lifting the corneal flap after cutting the epithelium on the flap edges, is easy to perform and has a very low incidence of epithelial ingrowth.

6135

Refractive surgery using CustomVis Solid State Laser 213nm. One year post-op clinical evaluation supported by an experimental study

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Purpose To report our experimental and clinical findings using a solid state laser system 213nm in refractive surgery.

Methods 40 pigmented rabbits underwent myopic PRK using a solid state laser in one eye and excimer laser in the fellow eye. Rabbits were sacrificed immediately after the ablation, at 7days and at one, 3 and 12months after surgery. Corneal tissue was preserved for Light, Scan and Transmission electron microscopy.60 patients (115eyes) underwent PRK [mSEQ -4.43±1.81D] and 20 patients (40eyes) LASIK [mSEQ -5.55±1.52D] using CustomVis quintupled Nd:YAG Solid State laser at 213nm.

Results Experimental study: Immediately after the ablation, LM, scan and TEM microscopy revealed relatively smooth ablation surfaces in both groups. At 1,3 and 12m postoperatively, there was tissue appearance, typical for post-PRK samples, of all corneal layers in both groups.Clinical study: At one year follow-up for the PRK mRSEQ was -0.11±0.52D and mUCVA was 1.03. 39% gained more than 1 line, 48% had no loss or gain of lines and 12% lost more than 1 line. For the LASIK group at 12m the mRSEQ was 0.42±0.70D and the mUCVA was 0.94; 61% of eyes gained more than 1 line, 33.3% of eyes gained had no loss of lines and 5.6% of eyes lost more than 1 line. 67% of eyes were in the +/- 0.25 and 72% of eyes were in the +/-0.5 interval for the Lasik patients. For the PRK patients 49% of eyes were in the +/- 0.25 and 80% of eyes were in the +/-0.5 interval for the Lasik patients.

Conclusion Photorefractive keratectomy in rabbits with ultraviolet solid state and excimer laser revealed similar histopathological findings up to one year postoperatively. PRK and LASIK were both effective and safe in the correction of myopic astigmatism.

6136

Endothelial cell loss 9 years after PRK and LASIK and its importance for eye banks

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Purpose To measure changes in the endothelium of corneas 9 years after myopic PRK and LASIK to determine if these corneas are suitable donor tissue for posterior lamellar transplantation.

Methods Central endothelial photographs were taken before and at 9 years after PRK in 9 eyes of 6 patients and after LASIK in 20 eyes of 10 patients. Preoperative spheroequivalent refraction was -3.5 ± 1.7 D (range -1.25 to -5.75) in PRK eyes and -6.2 ± 1.4 D (range -4 to -9.25 D) in LASIK eyes with intended correction to emmetropia in all eyes. Endothelial cells were analyzed with the center method by the same masked investigator from the endothelial images after calibration for magnification. Comparisons were made by using generalized estimating equation models to account for any correlation between fellow eyes of the same subject.

Results Endothelial cell density at 9 years after PRK (2559 ± 423 cells/mm2) was not significantly lower than before PRK (2641 ± 340 cells/mm2, P=0.45, n=9). Endothelial cell density at 9 years after LASIK (2741 ± 308 cells/mm2) was lower than before LASIK (2925 ± 303 cells/mm2; P<0.001, n=20), representing an annual exponential cell loss of 0.7 ± 0.8%. This cell loss was not significantly different from the annual exponential cell loss of 0.6 ± 0.5 % during a ten-year period measured in 42 normal (unoperated) corneas of control subjects from a previous study (P=0.41, minimum detectable difference = 0.5%, α=0.05, ß=0.20).

Conclusion We found no effect of PRK or LASIK on the corneal endothelium 9 years after the procedure. Eye banks and surgeons can use donor corneas from PRK eyes and from LASIK eyes for posterior lamellar keratoplasty procedures.

6137

Intracorneal lenses for the treatment of presbyopia: visual outcomes and safety

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Purpose To investigate the visual outcomes and safety of Intracorneal lenses (Invue Lens, Biovision AG, Switzerland) for the treatment of presbyopia.

Methods This was a prospective clinical study. An intrastromal corneal tunnel was created using a microkeratome composed by a control unit, a suction ring and a cartridge. The lens was inserted within the cornea tunnel of the non-dominant eye of 45 presbiopian patients. Mean age was 52,33 years old ± 3,29 (25 males and 20 females). The follow-up was up to 12 months.

Results In the operated eye, mean uncorrected visual acuity for distance (UVA-D) preoperatively, one day, one week one month, three months,six months and 1 year after surgery was 20/20, 20/40, 20/40, 20/32, 20/32, 20/32 and 20/32 respectively, whereas for near (UVA-N) was 20/50, 20/40, 20/30, 20/30, 20/25, 20/25 and 20/30.Binocular far vision was not altered.Contrast sensitivity tests demonstrated a decrease in scotopic and mesopic conditions.Wavefront analysis demonstrated an increase in all high order aberrations, whereas maximum myopic effect was demonstrated in 3,5 mm zone,which corresponded in the diameter of the lens. No tissue alterations of the cornea were found using corneal confocal microscopy. No intra or post-operative complications were demonstrated up to one year after surgery.

Conclusion Intracorneal lenses for presbyopia seems to be a safe and effective method to correct presbyopia in patients aged between 45 to 55 years old; a target group which is considered too old for refractive laser surgery and too young for clear lens extraction. Longer follow-up and a larger population are necessary in order to draw more significant results of this new surgical approach for the treatment of presbyopia.

6141
Multifocality and focus shift IOLs - theoretical aspects

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Purpose The purpose of this talk is to review the clinically relevant optical properties of multifocal and accommodative intraocular lenses and the potential visual consequences. The intention is to develop a fundamental understanding for clinicians and those working with them.

Methods Critical evaluation of the optical, clinical and vision science literature. Topics covered will include principles of refractive and diffractive lenses, apodization, effect of pupil size, compromises in design, single and dual optic accommodative intraocular lenses, objective and subjective accommodation, depth of focus and theories of accommodation.

Results Design of multifocal lenses involves a compromise in image quality that does not always manifest itself visually but can be measured optically. Accommodative intraocular lenses are limited in the amount of accommodation they can restore by the longitudinal shift in the lens and also post operative changes in the capsule. Changes in the radii of curvature of the lens surfaces are much more efficient at producing alterations in lens power.

Conclusion All surgeons and associated workers need a knowledge of the optical principles of multifocal and accommodative intraocular lenses together with their visual consequences if they are to understand the cause of unwanted side effects. In addition, they will be better equipped to understand new developments in this rapidly changing field.

6142
Clinical use of multifocal and focus shift IOLs

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Purpose To compare the clinical experience with multifocal and focus shift IOLs in Austria, Germany and Spain.

Methods We give a summary of published and unpublished data, reviews and meta-analyses. Main outcome measures are uncorrected distance and near visual acuity, and reading speed under different light conditions as well as subjective patient satisfaction and spectacle independence. The focus will be on ReStor, ReZoom and Technis IOLs in the multifocal group, and ICU, BioComFold, AT-45 Crystalens in the focus shift group.

Results Multifocal IOLs can provide functional intermediate vision in bright light; under dim light the results vary depending on the IOL design. Hybrid design of the refractive-diffractive IOL can reduce the increased optical aberrations induced by purely refractive multifocal IOLs. Aspheric apodized diffractive IOLs can reduce stray light artefacts and can enhance distance vision performance for large pupils. Focus shift IOLs result in a moderate to no improvement for uncorrected near visual acuity and minor or no forward movement, on average corresponding to less than 0.5 diopters.

Conclusion Multifocal IOLs provide pseudo-accommodation and their optical quality has improved due to new design developments. Focus shift IOLs accommodate only by a minor amount abd give some pseudo-accommodation by mechanisms not clearly understood.

6143
Straylight effects in diffractive multifocal IOL compared to monofocal IOL

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Purpose To measure levels of intraocular straylight following cataract surgery and implantation of either the ReSTOR SA60D3 IOL or the SA60AT monofocal IOL.

Methods A newly developed straylight meter was used to objectively measure straylight in a prospective open observational case series at 6 months postoperatively in 66 eyes with the diffractive ReSTOR SA60D3 IOL (Alcon Laboratories) and in a control group of 40 eyes with the monofocal SA60AT IOL. A comparison with straylight levels in an age-matched population without cataract was performed.

Results The straylight levels in the ReSTOR SA60D3 IOL and in the control group with the monofocal SA60AT IOL were 1.20±0.16 logunits and 1.10±0.19 logunits. When the difference in mean level of straylight was adjusted for age by multivariate analysis of the combined pseudophakic groups, mean straylight levels were 0.078 logunits lower for the monofocal SA60AT IOL group as compared to the multifocal ReSTOR SA60D3 IOL group ($p=0.026$). Straylight levels in both pseudophakic groups were lower than those of the normal age-matched control group without cataract ($p<0.0001$).

Conclusion Levels of intraocular straylight log(s) were significantly lower ($p<0.0001$) for both types of IOL as compared to age-matched subjects from the normal population, with expected reduction of complaints of glare and halos and higher levels of contrast sensitivity.The mean level of intraocular straylight 6 months postoperatively was higher for subjects with a ReSTOR SA60D3 IOL as compared to subjects with a monofocal SA60AT IOL, with expected less gain in contrast sensitivity and less reduction of glare and halo complaints.

6144
Visiogen Synchrony dual-optic lens

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Purpose Currently available single optic accommodative IOLs have their limitatations in terms of maximal potential accommodative amplitudes. A dual optic system may theoretically have more accommodative power.

Methods The dual optic accommodative IOL Synchrony from the Company Visiogen (Irvine, Ca, USA) consists of a +30diopters anterior lens and a minus-lens of variable power (depending on emmetropisation). The IOL is made of silicone material.

Results Since more than 3 years this IOL is already under clinical investigation showing promising results. The lens has been implanted in several hundred patients in Europe and South America. A FDA study is currently running, in Europe the IOL is CE-marked Accommodative values around 1-4 dioptes have been measured and documented in patients.

Conclusion Longterm results indicate low posterior capsule opacification and stable accommodative abilities.

■ 6145

Innovative IOL accommodative technologies: NuLens and TekClear

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Purpose To develop intraocular lenses capable of changing the power of the lens or the power of the eye related to active ciliary body function.

Methods Clinical pilot study on a consecutive series of patients implanted with the Nulens accommodative IOL (NuLens Ltd) and TekClear positional pseudoaccommodative IOL (Tekia Inc). Follow up was 3-6 months. The tenets for the Helsinki declaration were followed in this investigation. Main outcome measures were improvement in near vision with distance correction and without near vision add, near vision add to reach best spectacle corrected vision for near, biometrical study of the IOL changes inside the eye at the postoperative.

Results The Nulens demonstrated a mean clinical accommodation of 8-10 diopters. TekClear demonstrated a mean near vision improvement of 1.25 diopters. Some variability was observed with both lenses. Biometrical investigation of both lenses when implanted inside the eye demonstrated a potential for accommodation of up to 17 diopters for the Nulens and up to 2.5 diopters for the TekClear.

Conclusion Real accommodation restoration up to 8 diopters is feasible with the Nulens IOL and a near vision gain of 1-2 diopters is possible with the TekClear IOL. In both cases, active ciliary body action was correlated with the near vision improvement observed in the patients.

Commercial interest

6151
Introduction

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ABSTRACT NOT PROVIDED

6152
Epidemiological study of the blindness burden in the state of AP, India

KHANNA R
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ABSTRACT NOT PROVIDED

6153
Molecular and functional genetics of inherited eye disorders in India

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Purpose To understand the genetics of ocular diseases in India by identification of the underlying genes, characterizing the functional effects of pathogenic or disease-associated variants in suitable systems and to develop applications of genetics in patient screening and counseling.

Methods Genetic analysis involves the screening of candidate genes, linkage and association studies on patients and families recruited for specific eye diseases including several Mendelian and complex diseases. Phenotypic correlations are drawn using clinical, histological and other data as applicable from medical records of patients.

Results Over the last 10 yrs, we have carried out studies on retinal dystrophies, retinoblastoma, congenital cataract, corneal dystrophies, anterior segemnt dysgeneses, congenital glaucoma, POAG, age-related macular degeneration and myopia. These studies have led to the identification of new genes and genetic associations, as well as delineation of mutational spectra for various Mendelian disorders. Functional and/or structural effects of disease-associated mutations are another area of activity and questions in this realm have been investigated for some proteins such as crystallins and optineurin.

Conclusion The challenge in the near future is to develop effective and relevant ways of translating genetic and molecular science towards the benefit of patients.

6154
Stem cell therapy at LVPEI

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ABSTRACT NOT PROVIDED

■ 6155
Clinical research and trials

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ABSTRACT NOT PROVIDED

■ 6156
Outreach programmes of LVP

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ABSTRACT NOT PROVIDED

■ 6157
"Vision care at all levels:
From bench to bedside to the community"- A working model by L. V. Prasad Eye Institute, Hyderabad, India

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Purpose Of the 50 million blind people in the world, 60% live in developing countries. The three major causes of blindness here (cataract, infection, uncorrected refractive errors) are needless, since they are treatable or avoidable. In order to do so, we need a program of outreach to the countryside and village communities, involve them as partners in the endeavor, and thus make it successful and sustainable.

Methods Over the last twenty years, the L. V. Prasad Eye Institute (LVPEI), a non-profit, non-governmental eye care centre at Hyderabad, India, has set up a multi-tier pyramid model to address this problem of winning over needless blindness. This pyramid connects a centre of excellence at Hyderabad on the top with tertiary eye care centres in two other cities, secondary care centres in 15 towns- each of which is served by 10 vision centres in villages, thus taking care of about 20 million people. Prescription of eyeglasses, drugs against infection, and cataract surgical care are delivered on a large scale through this pyramid approach. This model of translation from bench to bedside to the community appears to be replicable in other places and for other aspects of healthcare.

Results In basic and clinical research, LVPEI is involved in the molecular and functional genetics of some inherited forms of blindness, use of stem cells to reconstruct the damaged ocular outer surface, and biochemical aspects of cataract.

Conclusion This model of translation from bench to bedside to the community appears to be replicable in other places and for other aspects of healthcare. It also appears suitable for the goals of Vision 2020: The Right to Sight.

▪ 6161
Upper eyelid tumour

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Purpose To describe the clinical and histologic features of a rare eyelid tumour.

Methods A 56-year-old male patient presented with a nodular subcutaneous tumour in his right upper eyelid close to the eye brow. The lesion had been present for 2 years; there was no pain or inflammation but a slow increase in size.No other significant ocular abnormality was noted, and the patient's general health was good without any medication.On MRI, the tumour presented as a circumscribed non-infiltrating pseudocystic mass, 20mm in diameter in size and located in the subcutis.

Results Histopathology showed a loose myxoid stroma with low cellularity and occasional small blood vessels. A distinct capsule or pseudocapsule was not identified. Near the periphery some fat lobules were seen. The mucoid ground substance stained lightly with Alcian blue. The tumour cells were sparsely distributed throughout the tumour without any particular pattern; most appeared spindle-shaped with an inconspicuous nucleus and no mitotic figures. Several mast cells were identified. Together with immunohistochemical findings (CD34+, SMA-, Desmin-), the diagnosis of myxoid spindle cell lipoma was made.

Conclusion To our knowledge, no tumour has been documented in the literature that was histologically really similar to the one present in our patient. There was only very little normal adipose tissue, and a floret-like nuclear pattern typical for pleomorphic lipoma (but also seen occasionally in normal orbital fat) was not observed. Even though the distinction from other lesions might in some cases be somewhat academic the differential diagnosis includes herniated orbital fat, other lipoma variants such as myolipoma and the hitherto mentioned pleomorphic lipoma, other myxoid tumours, and obiously malignant lesions such as (especially myxoid) liposarcoma.

▪ 6162
Natural killer/T-cell lymphoma with primarily orbital involvement: case report

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ABSTRACT NOT PROVIDED

▪ 6163
Topical 5-FU vs. mitomycin C in conjunctival squamous cell tumours

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ABSTRACT NOT PROVIDED

▪ 6164
Change of the diagnosis after retinal involvement in "CNS lymphoma"

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ABSTRACT NOT PROVIDED

■ 6165

Choroidal collision tumour

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ABSTRACT NOT PROVIDED

■ 6166

Fundus autofluorescence imaging of choroidal tumors

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Purpose To investigate the different pattern of fundus autofluorescence imaging of choroidal tumors generated with short-wavelength and near-infrared

Methods Thirty-one eyes of 31 consecutive patients affected by choroidal tumor performed standard fundus autofluorescence with short-wavelength (SW FAF) and fundus autofluorescence with near-infrared (NIR FAF). Fundus photography, A and B scan ultrasound and OCT were performed. Autofluorescence features of choroidal tumor and overlying retinal pigment epithelium (RPE) were correlated with clinical features.

Results Twelve of 31 choroidal tumors were choroidal melanoma, 8 choroidal nevus, 5 circumscribed choroidal hemangioma and one was choroidal granuloma. Different pattern of SW FAF and NIR FAF were detected related to the presence of pigment, drusen, RPE atrophy and hyperplasia, RPE detachment and subretinal fluid over or around the lesion.

Conclusion Standard autofluorescence (SW FAF) and NIR FAF provide different information on intrinsic autofluorescence of choroidal tumor and on the related RPE and retinal changes

■ 6167

Panoramic ICG and angiography in ocular oncology: new observations

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ABSTRACT NOT PROVIDED

▪ 6211
Diabetic retinopathy : facts and resources

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Diabetic retinopathy (DR) is the most frequent ocular complication in patients with diabetes and the main cause of blindness in the working age population in industrialized and developing countries. The most important risk factors that contribute to the pathogenesis of DR are chronic hyperglycaemia, hyperlipidemia and hypertension. Epidemiologic data show that each year 12 percent of new cases of legal blindness are attributed to diabetic retinopathy (DR) and that its prevalence increases with both increased duration of diabetes and the age of patients. Of insulin-dependent patients with diabetes for 30 or more years, 12% are blind. Diabetic macular edema (DME) is a frequent manifestation of DR and the leading cause of legal blindness in patients with type 2 diabetes. Over a 10-year period, non clinically significant DME and clinically significant DME will respectively develop in 14% and 10% of known diabetic patients. Approximately half of patients with DME will loose two or more lines of visual acuity within 2 years. Overall social costs (expenditures and lost productivity) caused by DR are about $174 billion in the USA. Approximately 20% of health care expenditures for persons with DM (50% with DM as a co-morbidity), 10% of expenditures for complications of DM and 15% of expenditures for health care for DM are ophthalmic. Therefore, DR accounts for significant economic costs that can be reduced with early diagnosis, achieved with screening methods. Screening of DR allows for timely treatment, vision preservation and consequent saving costs. Implementation of screening systems in different environments worldwide is the first necessary step in order to prevent blindness caused by diabetes mellitus.

▪ 6212
Methods of screening

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Diabetic retinopathy (DR) is one of the leading causes of adult blindness in working age population worldwide due to its late diagnosis and treatment. In effort to early detect DR, before visual loss, international guidelines for DR screening recommend an annual fundus examination for all diabetic patients. A variety of techniques can be used to detect and classify DR, including direct and indirect ophthalmoscopy, stereoscopic color film fundus photography, mydriatic and nonmydriatic (NM) digital color and monocromatic photography. Although ophthalmoscopy is the most commonly used technique to screen for DR, it has poor sensitivity when performed by nonophthalmologists in nonmydriatic conditions. The sensitivity of direct ophthalmoscopy in detecting proliferative DR is about 50% when performed by non-ophtahlmologists in NM conditions. Seven-field stereoscopic color fundus photographies have been considered as reference standard for diagnosing DR in randomized clinical trials. But this method is time consuming with uncertain practicity for widespread screening programs. Several studies have reported sensitivity and specificity in detecting DR and diabetic macular edema (DME) using limited number of fundus fields, proposing an alternative method for diabetic retinopathy evaluation to the ETDRS 7 fields. Recently introduced telemedicine screening programs based on digital images have the potential to allow for increased detection of DR, resulting in timely treatment and preservation of vision. Also important cost savings have been reported with DR screening, either by manual (human) or automatic (computer-based) grading. Therefore, there is a critical need for a sensitive, specificic and cost-effective screening method.

▪ 6213
Timing of diabetic retinopathy screening

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ABSTRACT NOT PROVIDED

▪ 6214
The Moorfields diabetes survey: lessons learnt

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Purpose The purpose of this talk is to describe the lessons learnt from the Moorfields Diabetes Survey and the Tower Hamlets Diabetic Retinopathy Screening Programme in order to emphasise the importance of good communication between components of screening.

Methods The Moorfields Diabetes Survey highlighted that most patients in eye clinics have diabetes related complications, but little understanding of diabetes itself and its relevance to eye disease. In order to help these patients, it was essential to understand how diabetic retinopathy screening could help with the detection, the education and the referral of patients with diabetic eye disease requiring treatment. The screening episode consists of proper identification of the target population and appropriate funding for the whole service, a robust call-recall system, a protocol driven screening episode and the timely treatment of sight threatening retinopathy. All elements must have in-built quality assurance.

Results In England, the National Screening Committe's guidelines govern the screening process. Although it provides strict quality control and reporting guidance, there is considerable freedom for the individual programs to set up the best service for their population. Tower Hamlets is one of the most deprived boroughs of the UK and as such, faced a difficult task to build a programme to such standards. To identify and keep track of the highly mobile population, deal with several religious requirements are the first challenges, followed by obtaining enough funding for the screening, the educational activities and for the treatment of retinopathy.

Conclusion A well-trained and committed workforce working in good partnership between primary care and the treatment centre has made this possible.

6231

In vivo confocal microscopy of abnormal cornea: a clinical and pathological correlation

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Purpose To establish correlations between in vivo confocal microscopic (IVCM) images with histopathology of various ocular surface disorders.

Methods 50 patients with various ocular surface/corneal diseases scheduled to undergo biopsy, impression cytology or surgery such as keratoplasty were clinically examined and assessed by IVCM with emphasis on area of pathology. The tissue obtained was then oriented and studied by light and/or electron microscopy. The microscopic anatomy was then correlated with the IVCM findings to establish a pathological basis for the observations. Conditions studied included corneal degenerations & dystrophies, conjunctival tumours, conjunctivalisation of the cornea and others. The Rostock Cornea Module (RCM) attached to HRT II machine from Heidelberg Engineering was used for IVCM.

Results By precise histological characterization of tissue changes we have been able to assign diagnostic criteria to IVCM features such as hyper and hypo reflective dots and shapes, linear straight and branching images and smaller dendritic figures. A diagnostic feature of intraepithelial neoplasia by IVCM has been established. A distinct pre Descemet's layer, termed the posterior stromal layer has also been defined. Subepithelial bright shadows in advanced Fuch's endothelial dystrophy have been identified as fibroblasts. Other interesting correlations are emerging.

Conclusion High quality in vivo corneal confocal microscopic imaging can highlight pathological changes comparable to those found in histopathology slides in a way that can help establishing diagnostic confocal microscopic criteria obviating the need for histopathology and biopsy in some cases.

6232

In vivo confocal microscopy in the diagnosis of corneal conjunctivalization

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Purpose The diagnosis of corneal conjunctivalization (CC) due to limbal stem cells deficiency(LSCD)is usually based on clinical features and on impression cytology (IC) which provides ex vivo morphology and immunoistochemical features of the corneal epithelium. The aim of this study was to validate laser scanning in vivo confocal microscopy (IVCM) as a new method to assess CC, based on the morphology of epithelium in central cornea and microstructural analysis of the limbal architecture

Methods 15eyes of 15patients with suspected CC were enrolled. All patients underwent IVCM (HRT2-Heidelberg Eng.)on the central cornea and limbus. CC was defined as presence of monolayered epithelium with goblet cells and subepithelial fibrovascular tissue. These findings were related with limbal alterations. Patients underwent IC of the central cornea to evaluate epithelial features in a masked fashion by mean of PAS and immunofluorescence CK12 staining. The epithelia were then classified into corneal,conjunctival and mixed pattern and the diagnostic hypotheses of in vivo and ex-vivo findings were compared .

Results The diagnostic hypotheses were concordant in 87% of the cases. In 3 we found corneal epithelium with corneal morphology by IVCM, no goblet cells and k12 positive cells by IC. In 2 we found an epithelium with conjunctival morphology by IVCM, presene of goblet cells and ck12 negative cells by IC.In 5 we found mixed epithelia with both methods.The last two cases were discordant.IVCM showed limbal alterations in the cases of mixed and conjunctival epithelium.

Conclusion IVCM is a useful non invasive method to help the diagnosis of LSCD and CC which well correlates with IC allowing also the analysis of the limbal structure.

6233

Antimicrobial peptides expression in activated human corneal keratocytes

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Purpose The eye despite being a delicate structure,has evolved many protective mechanisms.Antimicrobial peptides(AMPs) and Toll-like receptors(TLRs)have an important role in the ocular defense system.However during an infection or trauma, the innate defense system is breached.In this instance,keratocytes and fibroblasts aids in wound healing as well as provide a second line of defense.Little is known about AMP expression by TLR signalling pathways in corneal fibroblasts.This study therefore demonstrates the mRNA expression of both novel and known AMPs in various fibroblast phenotypes(myofibroblasts and keratocytes).In addition, AMPs were also shown in microbial ligand and/or pro-inflammatory cytokine stimulated human corneal fibroblast cultures (HCFC).

Methods Fresh Keratocytes and HCFC were cultured and collected at different stages of growth and/or after stimulation with microbial ligands. Total RNA was extracted and cDNA was synthesized for semi-quantitative gene expression studies. Polymerase chain reaction (PCR) amplified product were analyzed on ethidium bromide stained 1% agarose gels.

Results Constitutive expression of Thy-1(CD-90), vimentin, keratocan and alpha SMA was shown in all cultures.Keratocyte phenotype marker CD-34 showed decreased expression from 1st to 4th passage.Positive expression of Human beta defensin 109, Liver-expressed AMP(LEAP-2) and cathelicidin/LL-37 was demonstrated in cytokine and microbial ligand stimulated HCFC.

Conclusion Reminiscent with previous studies,we have demonstrated the mRNA expression of novel and known AMPs in corneal fibroblast mediated by TLR dependent signalling mechanisms. This result warrants the further study to fully understand the role of AMPs in ocular wound healing.

6234

Diagnostic and therapeutic applications of alcohol delamination (ALD) of the corneal epithelium

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Purpose Application of a weak alcohol solution to delaminate the corneal epithelium was first popularised for LASEK (Laser subepithelial keratomielusis). We subsequently reported successful results using ALD for the treatment of recurrent corneal erosion syndrome. In this study we explored the uses of this technique for other therapeutic and diagnostic indications.

Methods Eight patients were studied. In 3 the indication was for diagnosis only, in 3 it was for diagnosis and treatment and in 2 for treatment only. Following slitlamp evaluation, a 6mm well was placed over the site to be delaminated and 20% alcohol applied for 30-40 seconds following which the alcohol was removed and the cornea washed before peeling off the loosened epithelial sheet, which was spread on paper and covered with fixative for light and/or electron microscopy.

Results Of the 3 that had ALD for diagnosis, clinical suspicion of conjunctival intraepithelial neoplasia was confirmed in all 3 with preservation of cell morphology and orientation. 3 patients had chronic epitheliopathies manifesting as persisting epithelial defects and sick corneal epithelium. One showed epithelial cell apoptosis and the other 2 showed non specific or conjunctival features. All conditions resolved with visual improvement. Two symptomatic patients, 1 with extensive basement membrane dystrophy and the other with recurrence of granular dystrophy in the epithelium of a graft, showed improvement after ALD. Histology confirmed the diagnosis.

Conclusion ALD is a simple, safe and effect intervention for removal of an intact epithelial sheet that can be histologically examined with proper tissue orientation facilitating accurate diagnosis. It also serves as a therapeutic intervention.

6235
Amniotic membrane transplantation (AMT): Implications for corneal wound healing

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Purpose When transplanted as a graft AM is incorporated into the cornea. Our aim was to ascertain by immunohistology the fate of the incorporated membrane over time.

Methods Corneal buttons from 8 eyes treated by AMT for bullous keratopahty and subsequently had penetrating keratoplasty were examined by electron microscopy and by immunohistology with markers for keratocytes (CD34), fibroblasts (vimentin) and myofibroblasts (SMactin). Time from AMT to PK was between 2 to 32 months

Results Amnion tissue was covered with stratified corneal epithelium with well-defined hemidesmosomes. At places a fluid cleft was seen between amnion and underlying Bowman's zone. Transformed keratocytes/fibroblasts could be seen migrating from the anterior stroma, through breaks in the Bowman's zone, into connective tissue of the amniotic membrane. Immunohistology showed that the cells populating amnion stroma were CD34 negative but positive for vimentin and smooth muscle actin. In 2 samples where corneal transplants were performed more than 1 year following AMT, some cells in the amniotic stroma showed CD34+ staining

Conclusion The amniotic basement membrane facilitates epithelial cell migration and adhesion. Corneal stromal keratocytes can migrate through breaks in Bownans zone, into the amniotic tissue thus integrating it with the host. Despite the presence of large fluid clefts between amniotic membrane and Bowman's zone, the overlying epithelium remained compact. Repopulation of the amniotic stroma by corneal keratocytes allows for rebuilding of corneal stroma with an indication that over time they may revert to the resting keratocyte immunophenotype.

6236
Comparison between liposomes spray and non preserved tears substitutes in patients with meibomian gland dysfunction

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Purpose Many elderly people present with lachrymal film lipid phase disorder caused by a meibomian dysfunction. During a prospective randomised study performed in Poitou-Charente, we compared the use of vegetal liposomes in spray (intended for stabilizing the lipid phase) against one of the gold standard lachrymal substitutes.

Methods 50 patients aged 75 years old or older with a functional dry eye syndrome due to a meibomian dysfunction were studied between March and June 2007 in the department of ophthalmology of St Louis Hospital. The first group was treated with vegetal liposomes spray (Vyséo®) (3 sprays /day, eyelids closed). The control group received lachrymal substitutes (Refresh Tears® (Polyvynilic alcohol and Polyvidone) 1 eyedrop 6 tid). The following criteria have been studied: inflammation of the eyelids edge, lid-parallel conjunctival folds (LIPCOF), break up time (BUT), Schirmer I, best corrected visual acuity (BCVA) and Root Mean Square (RMS) with the Imagine Eyes IRX3 wavefront aberrometer. The statistical analysis was done with Prism for Windows.

Results The improvement of inflammation at the eyelids edge, LIPCOF, BUT, and RMS was significantly higher in the group treated by Vyséo®. The Schirmer I had not been modified in neither of the two groups. The best patients' satisfaction and ease of use scores were found in the Vyséo® group.

Conclusion Vegetal liposomes spray is easy to use for elderly patients with meibomian dysfunction and provide them with effective long term discomfort relief.

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In vitro evaluation of adhesion of adipose-derived adult stem cells to chitosan for the treatment of ocular surface pathologies

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Purpose To analyze the ability of adhesion of adipose-derived adult stem cells (ADAS) to porous materials made of chitosan for the future design of biodegradable autologous membranes for the treatment of ocular surface pathologies

Methods We used porous chitosan scaffolds prepared by cold neutralization in a 4% chitosan aqueous solution at acid pH, some of the materials were treated with argon plasma to favour cell adhesion. ADAS cells were obtained after adipose tissue processing from patients undergoing liposuction surgery. 5,000 cells were seeded per each scaffold in DMEM/F12 medium and cellular growth was analyzed on these materials by scanning electron microscopy (SEM) after ten days in culture.

Results Adhesion was observed and cell growth was optimal on the surface of non-plasma-treated biomaterials. Chitosan scaffolds treated with argon plasma showed better adhesion properties. Extracellular matrix production was also observed

Conclusion 4% chitosan biomaterials allow for adhesion, proliferation and extracellular matrix production of ADAS cells. Biocolonization of these biomaterials with ADAS cells will imply the future design of biological autologous membranes containing cells from the very same patient that would act as patches for the treatment of ocular surface pathologies for which current treatments show certain risks such immune rejection, infections or low effectivity.

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No consequence of dietary omega-3 polyunsaturated fatty acid deficiency on the severity of scopolamine-induced dry eye

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Purpose Epidemiological studies suggest that dietary omega-3 polyunsaturated fatty acids (PUFAs) may protect against prevalence of dry eye. This work aimed to evaluate whether a dietary deficiency in omega-3 PUFAs may increase the severity of dry eye in a scopolamine-induced rat model.

Methods Three consecutive generations of Lewis rats were bred under diets deprived of omega-3 PUFAs. Dry eye was experimentally induced by continuous scopolamine delivery in female animals from the third deficient generation and in female Lewis rats fed with a balanced diet. After 14 days of treatment, the clinical signs of ocular dryness were evaluated in vivo using fluorescein staining. MHCII and the mucin Muc5AC were immunostained on eyeball cryosections. Lipids were extracted from the exorbital lacrimal glands and phospholipid fatty acids were analyzed by gas chromatography.

Results The percent of fluorescein stained area to total area of the cornea was significantly increased in scopolamine-treated animals when compared to not implanted animals. Scopolamine treatment decreased Muc5AC immunostaining and tended to increase MHCII immunostaining in the conjunctival epithelium for both diets. In exorbital lacrimal gland phospholipids, arachidonic acid (AA) and the delta5-desaturase index were significantly increased by scopolamine treatment for both diets. There was no significant diet-difference in scores of fluorescein staining, Muc5AC and MHCII immunostaining. The omega-3 PUFA deficiency induced a significant increase in AA in the exorbital lacrimal gland.

Conclusion Our data suggest that, unexpectedly, an omega-3 PUFA deficiency did not increase the severity of dry eye in the rat.

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Cyanoacrylate tissue gluing in corneal perforations associated with herpetic keratitis

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Purpose To evaluate the success of cyanoacrylate tissue adhesive for the management of corneal perforations associated with herpetic keratitis.

Methods Forty six eyes of 46 patients with microbiologically proven herpetic keratitis associated with corneal perforation were included in a retrospective analysis. N-Butyl cyanoacrylate tissue adhesive and bandage contact lens were applied in addition to antiviral therapy. Outcome measure was the preservation of the structural integrity of the globe.

Results After glue application, the corneal perforation healed with scar formation in only 12 (26%) eyes. Keratoplasty had to be performed in 32 eyes (70%) due to failure of the glue. Fourteen (31%) eyes required multiple applications of tissue adhesive. Two eyes underwent enucleation and 1 eye became phthisical.

Conclusion Glue application for corneal perforation in cases of herpetic keratitis is not effective and most cases require a corneal graft to maintain the ocular structural integrity.

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Red eye multimedia teaching tool

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Purpose Since 2004, the Eastern Europe and Middle Eastern External Eye Disease Group has been actively involved in creating various educational programs and tools, targeted at general medical public as well as at ophthalmology residents, younger ophthalmologists and family medicine specialists, regarding diagnosis and treatment of various external eye diseases.

Methods The Eastern Europe and Middle Eastern External Eye Disease Group has designed new computer-based Red Eye Multimedia Teaching Tool, which uses interactive approach, thus enabling active participation of students in teaching process.

Results Red Eye Multimedia Teaching Tool focuses on training in establishing correct diagnosis, as well as choosing the most appropriate therapy for the most common external eye diseases: bacterial, viral and allergic conjunctivitis, as well as dry eye.

Conclusion The newest multimedia teaching tool focuses on diagnosis and treatment of most common external eye diseases, namely bacterial, viral and allergic conjunctivitis, as well as at dry eye. Its interactive approach enables each student to tailor the teaching process to its needs, interests and level of previous knowledge. It is expected to be used by ophthalmology residents, as well as family medicine physicians and other interested medical staff.

▪ 6241
Lutein supplementation - the rationale

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Purpose Photo-oxidation is believed to play a role in age-related macular degeneration (AMD). Macular pigment (MP), consisting of lutein (L), zeaxanthin (Z) and meso-Z, protects the retina from photo-oxidative damage. We review this rationale and critically appraise the current evidence-base germane to the use of supplements containing the macular carotenoids in patients with, or at risk of developing, AMD.

Methods The evidence supporting a role for MP in the prevention of AMD is primarily available from observational studies and interventional (supplementation) studies. We present data from the following observational and interventional studies: Age-Related Eye Disease Study (AREDS, I and II); Lutein Antioxidant Supplementation Trial (LAST); LUtein Nutrition effects measured by Autofluorescence (LUNA); Carotenoids in Age-Related MAculopathy (CARMA).

Results The AREDS I demonstrated that patients with AMD exhibited a 25% risk reduction in progression to advanced AMD when supplemented with zinc plus antioxidants. The LAST reported that visual function improved with L supplementation alone, or with L supplementation in combination with other antioxidants. The LUNA study reported a significant increase in MP optical density with 12 mg L and 1 mg Z, combined with co-antioxidants ($p > 0.05$).

Conclusion In conclusion, we await the outcomes of several randomized controlled trials before a truly meaningful comment can be made upon the potential beneficial effects of supplemental L, Z and meso-Z in patients with AMD. However, the benefits of the macular carotenoids, if any, relate to the ability of these compounds to protect against chronic and cumulative retinal damage and, therefore, the putative protective effect of this pigment may need to be exerted in the young and middle age.

▪ 6242
Lutein supplementation - the mechanisms

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Lutein and zeaxanthin are responsible for the formation of the macular pigment. There is a decrease of macular pigment density with increasing age. There are several studies showing that loss of macular pigment density is associated with an increased risk of age related macular degeneration (AMD). Therefore macular pigment density seems to have a protective effect of the macular from developing AMD. The best characterized role of lutein/zeaxanthin in the protection is the ability to absorb damaging blue light. Furthermore it is known from several in vitro and chemical investigations that lutein/zeaxanthin have anitoxidative properties. Based on the fact, that oxidative plays a major role in the pathogenesis, lutein/zeaxanthin could also protect the macular from damaging free radicals. A natural response of oxidative stress is the process of inflammation. Based on genetic studies and morphological studies AMD revealed the involvement of a subclinical inflammation in AMD pathogenesis. Lutein/zexaxanthin have anti-inflammatory properties. This fact may explain the recently described inhibition of choridal neovascularisation in an experimental model of wet form of AMD. Taken together lutein/zexaxanthin are ideal candidates to protect the macular from damaging blue light, oxidative stress and subclinical inflammation. Based on these findings lutein/zeaxanthin seem to be ideal substance to prevent and stop progression of AMD.

▪ 6243
Reducing mitochondrial dysfunction and ganglion cell death: focus on use of α-lipoic acid

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Purpose Retinal ganglion cell axons within the globe enriched with mitochondria. Good evidence exists to suggest that when mitochondria are drastically impaired as might occur in retinal ischemia or glaucoma, ganglion cell apoptosis occurs. Thus agents targeted specifically at enhancing ganglion cell mitochondrial energy production and/or scavenge free radicals (known to be generated by dysfunctional mitochondria) might therefore be useful to treat a disease like glaucoma. One such substance is possibly α-lipoic acid.

Methods Rats were injected intraperitoneally with either vehicle or α-lipoic acid (100 mg/kg) once daily for 11 days. On the 3rd day, ischemia was delivered to the rat retina by raising the intraocular pressure above systolic blood pressure for 45 min. The electroretinogram was measured prior to ischemia and 5 days after reperfusion. Rats were killed 5 or 8 days after reperfusion and the retinas were processed for immunohistochemistry and for determination of mRNA levels by RT-PCR. Insults were also delivered to retinal cells in culture (anoxia, light) and the influence of α-lipoic acid examined.

Results Ischemia-reperfusion affected the electroretinogram and caused a decrease in nitric oxide synthase and Thy-1 immunoreactivities and retinal ganglion cell-specific mRNAs. Exposure of retinal cells to light or anoxia caused a loss of cell viability. α-Lipoic acid attenuated all these effects.

Conclusion The results show that α-lipoic acid provides protection to the retina and their ganglion cells from ischemia-reperfusion injuries. It also blunts any loss of retinal neurons in culture caused by anoxia or light. Since α-lipoic acid can be tolerated when taken orally its use for treating e.g. glaucoma is worthy of consideration.

▪ 6244
Role of oxidative stress in glaucoma

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Purpose Glaucoma is the second major cause of permanent blindness worldwide. It is a group of chronic progressive neuropathies of the optic nerve with a loss of visual field resulting from the death of retinal ganglion cells. There are a lot of risk factors known like genetic susceptibility factors, elevated intraocular pressure (IOP), increased age, myopia and vascular diseases but the real pathophysiology is still unknown.

Methods In the past several experimentel and clinical studies showed that oxidative stress is involved in this complex process.

Results First of all, mitochondria seems to be genetically vulnerable in glaucoma patients as well as damaged by elevated IOP. In the anterior segment trabecular meshwork cells show oxidative DNA damage as well as increased aging and lipid peroxidation. In addition aqueous humor has an reduced antioxidative status. In the posterior segment retina and the optic nerve are involved by an reduced antioxidative status, increased lipid peroxidation and increased apoptosis.

Conclusion In summary, oxidative stress is one of the major players in the glaucoma disease and should be taken into the therapeutic management .

6251
Retinal microvascular signs as biomarkers of cardiovascular disease

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Purpose To review associations of retinal microvascular signs and cardiovascular disease.

Methods The retina is a unique site where the in vivo microvasculature can be directly observed and monitored repeatedly over time. Assessing the characteristics of the retinal small arteries and arterioles offers a surrogate means to evaluate associations of changes in the microcirculation in other organs that may be associated with systemic conditions in vivo. Recent advances in retinal photographic imaging techniques have facilitated the development of computer-assisted methods to measure and quantify subtle variations and abnormalities in the retinal microvasculature. These quantitative assessments have been applied to large populations, of both adults and children, and in community and clinic settings.

Results Existing data now convincingly show links between a range of retinal microvascular signs to both clinical and subclinical ocular, cerebro-vascular, cardiovascular and metabolic outcomes. This presentation will outline the major retinal vascular imaging methods used in large population based studies and provide an overview of novel methods under development.

Conclusion Retinal microvascular signs can be biomarkers of cardiovascular disease as well as ocular diseases, independent of traditional risk factors.

6252
Spherical equivalent versus AL/CR ratio - a tool for classifying refractive error

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Purpose To demonstrate that refractive development in children can be analysed in terms of three phases of development, defined in plots of cycloplegic spherical equivalent refraction (SER) versus the ratio of the axial length to the corneal radius (AL/CR ratio), rather than as a unitary process of emmetropisation.

Methods Schools were randomly selected, with stratification by SES. Partipation was sought from students in Year 3 (age 6-7) and Year 7 (age 12-13). Participation was high (>75%). Cycloplegic SER (autorefraction), AL and CR (IOL Master) and height were measured in over 4000 children, giving two representative cross-sectional samples.

Results Plots of SER versus AL/CR ratio were triphasic, consisting of a hyperopic wing (SER >2D, an internediate sone (SER between ~0-0.5D and 2D) and a myopic wing (SER <0-0.5D) The relationship between differences in SER and AL changed between the phases (>2D/mm in hyperopic and myopic wings, but <1D/mm in the the intermediate zone). Correlations between SER, AL and height decreased across the three phases.

Conclusion We interpret these plots as defining a developmental trajectory for refractive development. In the first year of life, rapid adjustment of AL to CR produces leptokurtic distributions of SER and AL/CR, at mildly hyperopic mean SER. Children with SER >2D after the first few years of life may be unable to emmetropise. The impact of continuing increases in AL on SER is reduced by compensatory reductions in lens power, in an anti-emmetropic phase. For SER of <~0-+0.5D, lens power changes cease, and further AL increases lead to myopia. The utility of analysis in terms of these phases is illustrated by the systematic changes in relationships between SER, AL and height. This analysis may have wider application.

6253
The predictive risk factors and grading of pathologic myopia for retinal photographs

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Purpose To determine the predictive factors and grading for pathologic myopia in several population-based studies.

Methods More than 12,000 fundus photographs are available from large population-based studies in Singapore including the Singapore Cohort Study of the Risk Factors for Myopia (SCORM) of 1,600 children and SIMES ofMalays aged 40 to 80 years. Refractive error measures were performed using the Canon RK-F1 machine and fundus photographs using the Canon CR6-45NM non-mydriatic camera. The number, type and position of the following will be assessed: staphylomas, lacquer cracks, cytotorsion of optic disc, Fuch's spots, choroidal neovascularization, lattice degeneration, and B peripapillary atrophy. In SCORM, the predictive factors including age of onset of myopia will be assessed. Additionally, genome-wide analyses (GWA) studies using the Illumina Sentrix HumanHap 550K BeadChips were performed in 1043 SCORM samples.

Results The different grades of pathologic myopia with severity of refractive error or axial length will be correlated. In 679 children in SCORM with myopia and 100 with emmetropia, the prevalence of lattice degeneration was 0.15%, there was increased PPA-to-disc area ratio with increased axial length and smaller cup-to-disc ratios in myopes compared with emmetropes. The GWA scans were run on 969 buccal-derived and 74-saliva derived) after excluding 82 samples.

Conclusion Myopia has a huge burden because high myopia is associated with potentially visually disabling ocular pathology. Further research should identify the environmental and genetic risk factors for pathologic myopia.

6254
The measurement of light intensities and effects on myopia development

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Purpose Given the protective effects of time spent outside against the development of myopia, the aim is to outline methods for assessing time spent outside and light exposures in population studies of the risk factors for myopia.

Methods The questionnaire previously used in the Sydney Myopia Study was used as the basis for further refinement, by a WHO working group; Kathryn Rose (Australia), Seang-Mei Saw (Singapore), Terri Young (USA, Singapore), Mingguang He (China), Jane Gwiazda (USA), Yuddha Dhoj Sapkota(Nepal), Solange R. Salomão(Brazil) and Leon Ellwein (USA). The questionnaire was field-tested at several sites. Light intensities at a variety of indoor and outdoor locations were sampled to predicted location during daylight hours.

Results Protection from myopia is associated with time spent outdoors, irrespective of whether sport was engaged in, and indoor sport is not protective. The existing questionnaire was therefore simplified to include questions which directly addressed the issue of how much time was spent outside and inside during daylight hours. Measurements of the light intensity at various indoor and outdoor locations showed that light intensity during daylight hours had high specificity and selectivity for estimating location. These measurements also showed that light intensities encountered during travel to and from schools were variable depending on the children walked or cycled, or traveled by train, bus or car. The questionnaire was modified to cover this issue.

Conclusion The development of a standard questionnaire for studies of time spent outdoors and the aetiology of myopia will facilitate international comparison of data. It is recommended that comparable information on ambient light intensities also be collected.

▪ 6255
Cornea biomechanical characteristics measured using the Ocular Response Analyzer in Singapore children

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Purpose To determine the corneal biomechanical parameters measured with the Reichert Ocular Response Analyser(ORA) in Singaporean children, and to assess their correlations with refractive error and biometry

Methods This was a cross sectional study of 271 subjects from the Singapore Cohort Study of Risk Factors for Myopia(SCORM). Corneal hysteresis (CH), corneal resistance factor(CRF), central corneal thickness(CCT) and intraocular pressure(IOPcc) were measured with the ORA. Spherical equivalent refraction, axial length, height, weight, and blood pressure were measured.

Results The mean age of the study population was 13.97±0.89years, the gender distribution was almost equal(138 males,50.9%),and the majority were Chinese.The mean CH and CRF were 11.78±1.55mmHg and 11.81±1.71mmHg. CH and CRF did not vary with age, sex or race. CH and CRF did not vary with myopia (p=0.79;0.83), or axial length (r=-0.11 and -0.05,p=0.08 and 0.40). Multivariate analyses were performed with CH, CRF or CCT as the dependent and age, gender, race, weight, IOPcc, CCT, SE refraction, and corneal curvature as covariates. CH was significantly associated with IOP (beta=-0.22(95%CI -0.27,-0.17)), CCT (beta=0.03(0.02,0.03)) and corneal curvature (beta=-1.13(-2.08,-0.19)). CRF was significantly associated with IOP, CCT and corneal curvature.(beta=0.08(0.02,0.14);0.03(0.03,0.04) and -1.39(-2.54,-0.23) respectively). The only factor predictive of decreased CCT was Malay or Indian race compared with Chinese.

Conclusion The CH and CRF values in our study on children are slightly higher than in adult studies. CH and CRF are not associated with refractive error or axial length. Flatter corneas are associated with lower CH and CRF readings

▪ 6256
Grading techniques for the assessment of retinal

GROSSO A
Torinese

Historical perspectiveBrief history of vascular measurement-Leishman-Kagan-Parr-Wisconsin (WESDR, ARIC, CHS)-CERA, MelbourneRetinal vessel measurement-Validation as epidemiological tool-Brief history of technology-Retinal arteriolar signs predict various vascular diseasesApplication of retinal vessel measurement to retinal diseases-Diabetic retinopathy, retinal vascular occlusive disorders, uveitis, age-related macular degeneration, glaucoma-Response to treatment (laser, VEGF inhibitors) Exploration of vessel measurement as a vascular test-Retinal microvascular evaluation to predict systemic diseaseChallenges regarding vessel measurementConclusion

6261

Infrared reflectance in choroidal melanoma and its correlation with fundus autofluorescence

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Purpose We have previously shown that fundus autofluorescence (FAF) improves visualization of lipofuscin (orange pigment) and subretinal fluid in pigmented choroidal melanomas in comparison with conventional fundus photography. The purpose of this study is to describe infrared reflectance (IRR) imaging findings in choroidal melanomas and compare them with those obtained by FAF imaging.

Methods Retrospective chart review of 7 consecutive patients with choroidal melanoma who underwent FAF and IRR photography. The correlation between IRR and FAF patterns and foci of orange pigment, hyperpigmentation, lipid exudates, fibrous metaplasia and subretinal fluid, was evaluated.

Results Orange pigment is hyperreflective in IRR imaging. IRR imaging highlights the presence of condensed clumps of orange pigment, presenting a good correlation with FAF imaging, but hardly detects diffuse fine lipofuscin. Hyperpigmentation is isoreflective with the normal fundus, showing low correlation with FAF, where they appear mainly hypofluorescent. Lipid exudates are hyperreflective in IRR imaging and difficult to distinguish from the orange pigment, creating a "confusion factor". Fibrous metaplasia is mainly hyperreflective while it is hypofluorescent in FAF imaging. Subretinal fluid is hardly visible in IRR imaging, while FAF imaging highlights its presence. The top of dome-shaped surfaces in the fundus is usually hyperreflective, creating a "noise factor" that doesn´t exist in FAF imaging.

Conclusion IRR imaging improves visualization of lipofuscin in choroidal melanomas in comparison with conventional fundus photography, but is inferior to FAF imaging.

6262

Follow up of a slowly growing melanocytic lesion during 12 years

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Purpose We report an atypical case of a very slowly growing and rather flat pigmented lesion in the posterior pole.

Methods A women 53 years old at presentation, was followed during more than 12 years for a posterior pole lesion. Periodical fundoscopy, fluoangiography, ICG angiography and ultrasounds were performed. After enucleation in 2008, the definitive diagnosis was made after histopathologic examination.

Results Visual decrease because of macular oedema in the left eye was the reason for referral. Fundus examination and fluo-angiography revealed a slowly enlarging subretinal lesion with abnormal pigmentation and leakage with signs of chronic neurosensory detachment; ultrasound examination showed a cystic lesion with macular oedema. The lesion increased very slowly in thickness until a maximum of 1.5mm. Finally a chronic retinal detachment caused an intractable neovascular glaucoma and necessitated enucleation in 2008.Histopathology showed a diffuse proliferation of small spindled melanocytes with bland, uniform nuclei lacking mitotic activity with some small nests of larger, haevely pigmented epitheloid melanocytes with nuclear pleimorphism, embedded in collageneous matrix. The cell proliferation marker Ki67 showed only rare tumor cells with immunoreactive nuclei,indicating a very low fraction of cycling tumor cells. Other immunohistochemical markers are currently performed in order to elucidate the biological behaviour.

Conclusion This case shows a unusually slowly growing lesion with classical histological features of melanoma and suggests the existence of a type of ocular melanoma of extremely low grade malignancy. Further phenotypical profiling is warranted in order to understand the cause of this "benign" behaviour.

6263

Photodynamic therapy of circumscribed choroidal hemangioma: comparison of dosage and timing

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Purpose To compare standard versus bolus photodynamic therapy (PDT) in the treatment of symptomatic circumscribed choroidal hemangioma (CCH).

Methods Twenty consecutive cases of CCH were included in this prospective randomized study. Each patient was randomly assigned to receive either standard PDT (10-minutes 6mg/mq2 verteporfin infusion; treatment at 15 min; 50 J/cm2; 83 sec) or bolus-PDT (6mg/mq2 verteporfin intravenously bolus in 2 min; treatment at 5 min; 100 J/cm2; 166 sec). All patients were treated with a single PDT application. Best correct visual acuity, fundus photography, optical coherence tomography, fluorescein and indocyanine green angiography were performed at baseline and at each follow-up examination. Retinal sensitivity was tested with microperimetry after treatment. Follow-up was longer than 24 months.

Results Mean follow-up was 28 ± 4 months. All cases (100%) showed clinical regression of the treated lesion, complete resolution of subretinal fluid and reduction of choroidal leakage on angiograms. Cases treated with bolus-PDT showed retinal pigment epithelium (RPE) hyperplastic changes over treated area. No similar RPE changes were found in patients treated with standard PDT. Two patients treated with bolus-PDT developed macular pucker, respectively 4 and 5 months after treatment. Microperimetry examination revealed areas of reduced sensitivity after bolus-PDT compare to standard PDT ($p<0.001$).

Conclusion Both standard and bolus-PDT seem effective in the treatment of symptomatic CCH. Bolus-PDT may cause reactive retinal changes impairing retinal sensitivity, whereas standard PDT never impairs (and sometimes restores) retinal function.

6264

Regulatory T-cells induce an immune escape in a murine model of primary intraocular B-cell lymphoma

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Purpose The role of regulatory T cells (Tregs) in the immune evasion of tumors is usually prominent. The aim of this study was to assess the presence and role of Tregs in a murine model of primary intraocular B-cell lymphoma (PIOL).

Methods We used a syngeneic model of PIOL in immunocompetent BALB/c mice. Immunohistochemistry and flow cytometric analysis have been performed to study the tumor growth and the immune infiltrate. Depletion of Tregs was achieved using intraperitoneal injection of anti-CD25 mAb (PC61). Splenectomy was performed to study the role of induced Tregs.

Results Tregs were recruited in PIOL eyes (16.2%) compared to control eyes (1.2%, $p<0.001$). The number of infiltrating Tregs was correlated with tumor burden ($r2=0.76$), and inversely correlated with CD4+ T-cells ($r2=-0.79$). Recruitment of Tregs was also observed in the spleen of mice bearing tumor (2.9%) compared to controls (2.1%, $p<0.001$), but not in the draining lymph nodes. Depletion of Tregs resulted in a significant decrease of tumor burden (53.8% in control mice compared to 37.7% in PC61 mice, $p=0.03$), and an increase of the immune infiltrate. Splenectomy experiments comfirmed the role of iTregs in tumor escape. Eventhough the number of tumor cells decreased, tumor growth could not be abrogated.

Conclusion We demonstrated that Tregs are recruited in the tumor microenvironment. Tregs limit the recruitement of CD4+ T-cells in the eyes and are thought to inhibit their effector functions. The mechanisms by which Tregs are generated could be similar to ACAID, yet in the posterior chamber. Several escape mechanisms are responsible for tolerance toward the tumor in the eye.

▪ 6265
Structural and cellular diagnosis of ocular surface squamous neoplasia using in-vivo confocal microscopy

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Purpose Aim of this study was to analyze in-vivo structural and cellular features of ocular surface squamous (OSS) neoplasia using clinical confocal microscopy (CM).

Methods Ten consecutive cases of OSS neoplasia were investigated using in-vivo corneo-conjunctival CM (ConfoScan4, Nidek, Gamagori, Japan) with a 40X surface-noncontact objective. Data obtained using CM were also compared to standard histopathology or cytologic samples obtained by scraping technique.

Results CM analysis of OSS neoplasia showed good agreement with correspondent tumor cytology or histopathology, revealing some structural and cellular features of the lesions, including: loss of the normal epithelium structure in 10 cases (100%), high-reflective areas in 10 cases (100%), inhomogeneous cell density in 8 cases (80%), cells debris in 8 cases (80%), abrupt demarcation at the lateral edge of the lesion in 7 cases (70%), nodular zone of cell proliferation in 6 cases (70%), fibrovascular structures in 3 cases (30%), keratin pearls in 1 case (10%) and pre-Bowman space involvement in 1 case (10%). No anterior stroma involvement was documented. Cells anisocytosis, pleocytosis and anisonucleosis were also documented in 9 of 10 tumors (90%).

Conclusion In-vivo CM seems a reliable, non-invasive method useful for in-vivo diagnosis of OSS neoplasia.

▪ 6266
An unusual lid/orbital tumour in infants

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Purpose To present 3 cases of an unusual soft tissue lesion in infants with clinicopathological correlation.

Methods Case 1: A 2-year-old boy presented with a rapid growing lesion in his right lateral orbit. Case 2: A 5-year-old girl with a left superior orbital lesion close to lacrimal sac. Both cases had clinical appearances of a dermoid and excision was performed. Case 3: A 1-year-old boy presented with a 6 week history of an enlarging right medial canthal mass. CT scan showed a greatly expanded nasolacrimal duct. Endoscopy revealed a polypoid lesion and multiple biopsies were taken.

Results The specimens from cases 1 and 2 consisted of firm nodular tissue measuring up to 30 and 18mm in diameter respectively. Several biopsies (2-6mm) were submitted from case 3. In all cases histology showed plump spindle cells arranged in interweaving fascicles in a collagenous stroma. Variable amount of myxoid change was present. There was no necrosis or mitotic activity. Diffuse SMA and focal CD68 positivity were encountered. Negative markers were: CD34, S100, neurofilament, desmin, MyoD1 and myogenin. The overall features were those of a nodular fasciitis.

Conclusion Only four cases of orbital nodular fasciitis have been reported in children younger than 5 years. We report a series of further three cases in this age group, two masquerading as a dermoid, raising the awareness of this entity as a clinical differential diagnosis of rapidly growing lid/orbital lesions in infants.

▪ 6267
Foreign body conjunctival granuloma

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Purpose To present a case of a small inflammatory epibulbar mass developed soon after a branch of the tree injury.

Methods 57-years old healthy men presented to our Department with complaints of discomfort, foreign body sensation, mild tearing and redness of his left eye. The patient sustained branch tree injury two weeks before. Slit lamp examination demonstrated a small red mass measuring about 3mm in diameter, located at the 3 o`clock position, loosely connected with adjacent tissues. An excisional biopsy of the mass was performed and tissue was send to histopathology laboratory for microscopic analysis.

Results Microscopic examination revealed a massive infiltrate composed with multiple giant cell (of foreign body type) surrounding organic material (pieces of wood and plants) together with multiple plasma cells and lymphocytes. Focally neutrophils were also present. Histopathology diagnosis: foreign body conjunctival granuloma.Clinical differential diagnosis should considered: conjunctival benign lesions, Splendore-Hoeppli fenomenon, inclusion conjunctival cyst or nodular episcleritis.

Conclusion 1.Foreign body granuloma should be considered in differential diagnosis of conjunctival epibulbar lesions.2.Histopathology is crucial for proper and final diagnosis.

▪ 6311

Anti-PlGF (placental growth factor) as a safer alternative for anti-VEGF in the treatment of age-related macular degeneration (AMD)?

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Purpose To evaluate the efficacy and safety of PlGF blockage by inhibiting choroidal neovascularization (CNV) in a mouse model of AMD.

Methods A laser-induced CNV model was used in C57Bl/6 mice. Mice were injected intraperitoneally with 25 mg/kg of an anti-PlGF-antibody, an anti-VEGF receptor2 (VEGFR2) antibody, a combination of both, or a control antibody. The CNV lesions were evaluated on flat mounts and serial sections after 14 days, by immunostainings for endothelial and inflammatory cells (CD31 and F4/80 respectively). Ganglion cell survival was scored via NeuN and TUNEL staining after 2, 4, and 6 weeks in C57Bl/6 and Swiss mice with and without CNV lasering. Safety of anti-PlGF and anti-VEGFR2 on normal vascular development in the retina, kidney, and heart was assessed.

Results Anti-PlGF or anti-VEGFR2 comparably inhibited CNV by ± 50%. Moreover, a combination treatment of the optimal dose of anti-PlGF and a lower dose of anti-VEGFR2 further suppressed CNV to ± 70%, allowing to reduce the dose of anti-VEGFR2 by fourfold. Anti-PlGF did not inhibit vascular development in the retina, heart, or kidney, whereas a reduction of ± 40% was seen after anti-VEGFR2 treatment. Repeated anti-VEGFR2 injections induced an increase in ganglion cell apoptosis after 4 and 6 weeks of administration, whereas anti-PlGF did not.

Conclusion Anti-PlGF treatment inhibits CNV formation in a mouse model of AMD, and enhances the efficacy of anti-VEGFR-2, allowing the dose of anti-VEGF therapy to be lowered and the potential adverse effects to be minimized. Moreover and contrary to anti-VEGFR2, anti-PlGF is safe for the neuroretina and for the systemic and retinal vascular development.

▪ 6312

The in vitro effects of anti-angiogenic AMD treatments on human choroidal endothelial cells

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Purpose Age-related macular degeneration (AMD) is the most common cause of irreversible visual loss in elderly populations in the western world. Neovascularisation by choroidal endothelial cells (hCEC) causes AMD; however, the mechanisms responsible are not fully understood. Vascular endothelial growth factor (VEGF) is thought to be the most significant growth factor in AMD and subsequently, molecular inhibitors including pegaptanib (Macugen), ranibizumab (Lucentis) and bevacizumab (Avastin) have been developed as treatments for AMD.

Methods hCEC were isolated from cadaver eyes and cultured in EBM2-MV medium as previously published. hCEC proliferation after exposure to VEGF isoforms 165 and 121 and anti-angiogenic treatments was measured using the WST-1 assay. The effect of the VEGF isoforms and anti-angiogenic treatments on angiogenesis was assessed using a double layer Matrigel technique.

Results hCEC proliferation in response to VEGF 121 and 165 was found to be equivalent. Individually and in combination both Ranibizumab (Lucentis) and bevacizumab (Avastin) were effective in decreasing proliferation of hCEC. Pegaptanib (Macugen) was moderately effective in controlling the proliferation of hCEC stimulated by VEGF 165, but was ineffective against the stimulatory effect of VEGF 121.

Conclusion Although molecular inhibitors of angiogenesis have been shown to have a beneficial effect as treatments for AMD, direct comparison of the efficiency of the drugs is complicated, due to variations between trials and dosing regimes. In vitro testing of the drugs on the proliferation and angiogenesis of hCEC showed that the efficacy is in the order Lucentis>Avastin>Macugen, in line with the current clinical outcomes seen.

▪ 6313

Intravitreal bevacizumab versus triamcinolone acetonide for exudative age-related macular degeneration

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Purpose To compare an intravitreal high-dose injection of triamcinolone acetonide versus an intravitreal injection of bevacizumab for treatment of progressive exudative age-related macular degeneration (AMD).

Methods The comparative non-randomized retrospective clinical interventional study included 305 patients with progressive AMD, divided into a bevacizumab group of 36 patients (1.5 mg bevacizumab) and a triamcinolone group of 269 patients (about 20 mg triamcinolone). All patients were consecutively included, in the first phase of the study for triamcinolone, and in the second phase of the study for bevacizumab. Mean follow-up was 8.5 ± 6.8 months (2-35.7 months).

Results In the bevacizumab group, best visual acuity increased significantly (P<0.001) by 3.2±3.4 Snellen lines, with 25 (69%) eyes and 21 (58%) eyes, improving by at least 2 Snellen lines and 3 lines, respectively. In the triamcinolone group, the visual acuity change was not statistically significant whenever within the first 3 months. Maximal increase in visual acuity, visual acuity change at 2 months after injection, and the percentage of patients with an improvement by at least 2 Snellen lines and 3 lines were significantly (P<0.001) higher in the bevacizumab group than in the triamcinolone group. Intraocular pressure increased significantly (p<0.001) in the triamcinolone group, and did not change significantly (P=0.47) in the bevacizumab group.

Conclusion In exudative AMD, intravitreal bevacizumab (1.5mg) compared with intravitreal triamcinolone acetonide (about 20mg) results in a higher improvement of visual acuity and does not markedly influence intraocular pressure within 2 months after injection

▪ 6314

Intravitreal bevacizumab (Avastin®) in wet AMD: the OCT-assisted "wait and see" management

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Purpose To retrospectively review the evolution of our patients managed with the OCT-assisted "wait and see" approach after intravitreal bevacizumab (IB) injection.

Methods Charts of 46 consecutive patients affected by wet AMD that had received IB (1.25 mg) for recent CNV and completed ≥ 9-month follow-up were reviewed. The patients were divided into 3 groups, on the basis of the number of injections: "1 injection" (group 1), "2 injections" (group 2) and "≥ 3 injections" (group 3). Visual gain and loss were defined as improvement or worsening of 2 or more lines of BCVA, respectively. Injections were repeated in case of OCT worsening and decreased BCVA, confirmed by FA. Main outcome measures were the stability/improvement of the BCVA, and both the FA and OCT stability/improvement.

Results Sixteen patients needed only 1 injection (34.8%), 11 needed 2 injections (23.9%) and 16 (41.3%) patients ≥ 3 injections. In group 1, the median follow-up time, was 14 months, while, in group 2 and 3, it was 12 months. In group 1, 14/16 patients (87.5%) had stable/improved BCVA (P<.05), while in group 2 and 3, 9/11 (81.8%, P<.05) and 17/19 (89.5%, P<.05) patients had stable/improved BCVA, respectively. All the patients that had stable/improved BCVA had both stable/improved FA and OCT. No differences were observed between the outcomes of the groups (P>.05).

Conclusion In 1 patient out of 3 a single IB and in more than 50% of patients no more than 2 IB were sufficient to treat CNVs. Our data indicate that bevacizumab is effective even if administered on the basis of the CNV activity, and the scheme of 3 automatic initial injections proposed in trials using other anti-VEGF agents should be revised at least for bevacizumab. Further trials are mandatory to validate our data.

6315

Analysis of intravitreal ranibizumab injections effects on exudative reaction complicating subfoveal choroidal neovascular age related macular degeneration (AMD)

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Purpose To evaluate the effect of RANIBIZUMAB intravitreal injections(IVT) on exudative reaction secondary to retrofoveolar neovascular AMD,at short and long term evolution

Methods 110 eyes of 88 patients , 31 men,57 women, with retrofoveolar sub-retinal neovascularisation complicating AMD .65 were inaugural cases,23 previously treated by photodynamic therapy and/ or pegaptanib IVT. Patients received intravitreal ranibizumab injection, 3 times, every 4 weeks in an inductive treatment, the next injections depending on the follow-up results. First and 2 months' interval follow-up exam included ETDRS visual acuity (VA), complete ophthalmic examination, fluorescein (FA) and infracyanine (ICG) angiography, and optical coherence tomography (OCT). VA and OCT were done before each IVT.OCT was evaluated and compared time to time and cut to cut, FA and ICG analysis appreciate neovascular net's leakage and flow.

Results Exudation decreased intensely in all cases.Diffuse oedema was 70% reduced in 80% cases,cystoid oedema was 75% less in 65%, retinal serous detachment was 80% decreased in 78%.Angiographic leakage reduced about 70% in 72%.At ICG ,vascular flow wAS 2/3 time less in 55%. Best results noted than with PDT alone and/or pegaptanib IVT, and with no anastomosis lesions. Exudation scale was considered, compared with FA and ICG follow-up results and for next IVT criteria and indications. Inductive treatment was sufficient in 74 cases.

Conclusion The results, with indeed reduction of exudation on OCT, lack of fluorescein leakage, low neovascularisation's flow in ICG, suggest Ranibizumab IVT seem effective on exudative neovascular reaction complicating AMD and OCT be the main evaluation means.

6316

Lessons learned in setting up a reading centre network for high volume grading in Europe

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Purpose In 2004, the Verteporfin Photodynamic Therapy (VPDT) study was commissioned in the UK to assess patients with CNV undergoing PDT. A Reading Centre network (NetwORC UK) was established to independently grade 5000+ angiograms per year. Previous to this, there were no independent RCs in Europe capable of grading this volume.

Methods Three geographically distinct centres (Belfast, Liverpool and London) form NetwORC UK with a management facility (CARF) coordinating the administrative and technical aspects. A custom software platform was developed to manage the import, transmission and grading of images, collection of data between the three RCs, and ensure communication across separate IT networks. Quality assurance and concordance ensure grading is consistent across NetwORC UK.

Results Between October 2005 and October 2007, 12612 angiograms were graded and 6833 were baseline angiograms. The grading of angiograms is ongoing in NetwORC UK and will continue until the study ceases.

Conclusion A network structure has enabled grading of a large volume of images from the VPDT study. Regular training and concordance exercises have contributed to the success of this service. The authors recommend that the administration and management is separate from grading ensuring grading staff are dedicated to grading tasks. Therefore technical queries and software can be managed in one location, importing and exporting data can be centralised, vacation and sickness cover is easier to maintain, and unique training is offered by pooling staff from different locations. Regular monitoring of IT systems ensures data has integrity and dedicated IT personnel are essential. Future studies of this size will now be possible in Europe using NetwORC UK.

6317

Photodynamic therapy for choroidal neovascularization secondary to choroidal nevi

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Purpose To assess the efficacy and the safety of photodynamic therapy (PDT) for treatment of choroidal neovascularization linked to choroidal nevi.

Methods It is a retrospective study including choroidal neovascularization secondary to choroidal nevi treated by PDT for 1999 to 2005. PDT was performed according to the standard protocol used for treating choroidal neovascularization secondary to age-related macular degeneration (ARMD). Post-PDT follow-up was also done according to the guidelines used in ARMD. Moreover, tumors were controlled every 3 months.

Results Six choroidal neovascularizations secondary to choroidal nevi were included in our study. All nevi were localized in the posterior choroids. The median of their largest diameter was of 3mm and their thickness was <2mm in all cases. Neovascular membranes were "classic" in all cases, subfoveal in 2 cases, juxtafoveal in 3 cases and extrafoveal in 1 case. The sizes of choroidal neovascularization were ≤ 1-disk-diameter in half the cases. On average 3.3 sessions of PDT were necessary to obtain the stabilization of choroidal neoascularization. The mean follow-up was 35 months without any patient lost of follow-up. Visual outcomes were extremely variable. Large or retrofoveal choroidal neovascularization but also antecedents of atrophic ARMD were related with worse functional results. No growth of the nevi was observed.

Conclusion Choroidal neovascularization is considered to be a relative indicator of benignity of the naevus. However, it often marks a definitive turning point in the visual function. PDT appears as a safe and efficient procedure for treating choroidal neovascularization secondary to choroidal naevus with results similar to those observed in ARMD.

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Investigation of the effect of the Alcon AcrySof Natural (ANIOL) blue-filtering intraocular lens on macular pigment

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Purpose Photo-oxidation is believed to play a role in age-related macular degeneration (AMD). Macular pigment (MP), consisting of the carotenoids: lutein (L), zeaxanthin (Z) and meso-Z, protects the retina from photo-oxidative damage. This study was designed to test the effect of the Alcon AcrySof Natural (ANIOL) blue-filtering intraocular lens on MP.

Methods Forty four patients scheduled for cataract surgery were recruited into our study. These patients all had pre-operative best corrected visual acuity (BCVA) of at least 6/18 in the study eye. Patients were randomised to have either the standard Alcon AcrySof three-piece acrylic intraocular lens (AIOL) [controls] or the ANIOL. We measured the spatial profile of MP using customised heterochromatic flicker photometry (cHFP) pre-operatively and post-operatively, and at three, six and 12 months after surgery. BCVA was measured in the study eye at each visit and a blood sample was taken to control for changes in serum carotenoid levels.

Results The mean age (± SD) of our study group was 69 (± 11) years. The last patient study will be completed by 27th of June 2008 and randomisation and final study data will be available for analysis and presentation after this date. Preliminary analysis shows that the mean (± SD) MP optical density at peak (0.25o eccentricity) was 0.301 (± 0.159) before and 0.296 (± 0.142) after cataract extraction (Paired-sample t-test, p = 0.616).

Conclusion Customised HFP appears to be unaffected by lens opacity where BCVA is at least 6/18 and can be used to obtain reliable measurements of the spatial profile of MP in patients with cataracts. Further comment will be made following final study analysis in June.

Commercial interest

6321

RNase-7 expression mediated by IL-1 beta in human ocular surface cells via multiple signalling pathways

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Purpose Antimicrobial peptides are known to play an essential role in the host defense system. It was recently identified that the Ribonuclease(RNase)-7 posses a broad-spectrum microbicidal property against various pathogens.In this study our aims were a)to investigate the RNase-7 expression in ocular inflammation and/or infection and b)to identify the involvement of possible signalling pathways in interleukin(IL)1-beta mediated RNase-7 expression using SV40-immortalised human corneal epithelial cell line(SHCEL).

Methods a)Total RNA was obtained from impression cytology specimen of normals and diseased individuals. Quantitative polymerase chain reaction technique was used to analyze RNase-7 mRNA expression. b)SHCELs were treated with IL-1beta and inhibitors of signalling molecules both in time- and dose-dependent manner. Quantitation of both phosphorylated and total proteins was evaluated using Western blotting. The effect of IL-1beta and inhibitors on secretory cytokines in SHCELs was measured using BD-cytometric bead arrays.

Results The normalised expression of RNase-7 mRNA significantly increased in disease conditions (bacterial, viral, dry-eye and acanthamoeba keratitis). Inhibition of following signalling pathways: PI3K(phosphatidylinositol-3-kinase), MAPK(mitogen-activated protein kinase) and NF-kB(nuclear factor-kB) have reduced the RNase-7 gene expression. Significant changes in the secreted cytokines (IL-6, -8, -10 and-12p70) was also demonstrated.

Conclusion The first study which demonstrates the RNase-7 expression in the eye. The involvement of multiple signalling pathways in RNase-7 induction by IL-1beta may facilitate the development of novel approaches in enhancing antimicrobial defense and healing of the eye.

6322

Aquaporins expression on blood retinal barrier cells during experimental autoimmune uveitis

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Purpose To study the expression of aquaporins 1 and 4 on blood retinal barrier cells during EAU.

Methods Experimental Autoimmune Uveitis (EAU) was induced in C57Bl6 mice by immunization with interphotoreceptor retinoid-binding peptide 1-16. Four weeks later animal were sacrificed. The severity of the disease was graded and the expression of AQP1 and AQP4 were detected by immunofluorescence (IF). In vitro using ARPE-19 cells, basal expression of AQP1 and 4 was analysed by RT-PCR, Western blot(WB) and IF. The effects of IFN-gamma and TNF-alpha on AQP1 and AQP4 expression in ARPE-19 cells were determined by WB.

Results In controls animals, AQP1 expression was limited to the photoreceptor layer while AQP4 expression extended from the internal limiting membrane to the external limiting membrane. The patterns of AQP1 and AQP4 expressions were not changed during uveitis. Neither AQP1 nor AQP4 were found in RPE cells in controls or EAU animals. However AQP4 was expressed in ARPE-19 cells and its expression somewhat upregulated by IFN-gamma and TNF-alpha.

Conclusion The patterns of AQP1 and AQP4 expressions in the internal blood retinal barrier are not modulated during EAU. Besides, in vivo, the AQP1 or AQP4 expressions could not be detected on the external blood retinal barrier (RPE cells). In contrast, in vitro, AQP4 expression was detected in a human ARPE cell line and slightly increased by proinflammatory cytokines.

6323

Expression of galectin molecules in intraocular tissue and inflammation

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Purpose To study the role of Galectin molecules in intraocular tissue. We examined the expression of Galectin molecules in intraocular tissues in normal and inflammatory conditions.

Methods Lewis rats eye ball and cultured human retinal pigment epithelial cells were used for experiment. Expression levels of Galectin – 1, 3, and 9 were examined with immune staining for the proteins and in situ hybridization for the mRNAs in normal and inflammatory conditions. Expression levels of the mRNA from established retinal pigment epithelium (RPE) derived cells of ARPE-19 and hTERT were also examined with real time PCR

Results Galectin - 1in normal condition: the protein expression was detected in ciliary body, RPE, retinal outer and inner segments. In inflammatory condition, expression levels were not changed dramatically. Galectin – 3 in normal and inflammatory condition: ubiquitous expression was detected in almost all tissues of the eye (ciliary body, RPE and neural retinal layers). Galectin – 9 in normal condition: a little amount of expression was detected in ciliary body, choroid RPE, and some layers of neural retina. In inflammatory condition, expression levels increased in the above tissues. In cultured RPE cells expressed galectin molecules in normal conditions. When the cells were stimulated by proinflammatory cytokines, only expression of Galectin – 9 increased.

Conclusion Recently It is reported that Galectin – 9 and Tim – 3 bind and negatively regulates Th1 immunity. In intraocular tissue,Galectin – 9 also may play important roles for modulating intraocular immune responses.

6324

Expression pattern of antimicrobial peptides (AMPs) in acanthamoeba keratitis

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Purpose Acanthamoeba keratitis (AK) is a sight-threatening ocular infection, which is more likely in contact lens wearer. Antimicrobial peptides(AMPs)are cationic polypeptides with wide-spectrum activity against pathogens. We studied(1)the profile of AMP mRNA expression in ex-vivo impression cytology (IC) specimen from normals and 5 AK patients &(2)compared AMP gene expression between ex-vivo and in-vitro cell culture samples.

Methods a) IC samples were collected for Total RNA extraction and cDNA synthesis. Quantitative gene expression(qPCR)was employed to evaluate expression of Defensins,Cathelicidin,& Liver-expressed AMPs (LEAPs).b) Immortalised human corneal epithelial cell line (HuCL) was incubated with trophozoites of Acanthamoeba castellanii for 24 hours and the supernatant analysed by BD cytometric bead array for pro-inflammatory cytokines.The cells were processed for qPCR analyses.

Results Variable expression of AMPs was observed in AK patients.Eight AMPs,Human Beta defensins(HBD)1 to 3,Cathelicidin (LL37,LEAP 1 and 2 and DEF 109 were detected.Of these HBD 1 to 3 and DEF 109 were shown to be reduced and whereas LEAP 1 & 2 were induced in AK specimen. Similarly, increased mRNA expression of LEAP 1 & 2 was also demonstrated in Acanthamoebae treated HuCL cultures.Whereas, HBDs showed the baseline expression when compare to untreated HuCLs.

Conclusion This is a first study demonstrating AMP gene expression in AK. Differential expression pattern of these AMPs during AK may have important implications in understanding the pathogenesis of this blinding infection. Modulation of AMP defense barrier at the ocular surface or use of the AMP as a contact lens preservative agent may help to reduce the AK infections

6325
Profile of antimicrobial peptides (AMPs) at the ocular surface

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Purpose Purpose: Antimicrobial peptides are eukaryotic analogues of antibiotics and serve as early effectors of innate defence. Our aim was to profile the spectrum of AMPs at the ocular surface in health and disease.

Methods Methods: Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and real time PCR techniques with primers for 21 known AMPs were employed to evaluate gene expression on the following human ocular surface (OS) samples: a) Impression cytology specimen of normals and patients suffering from bacterial, viral keratitis and acanthamoeba keratitis and dry eyes. b) OS cells from cadaver donors and c) cultured corneal epithelial cells from limbal explants. Over one hundred samples were thus studied.

Results Results: AMP expression was observed in all the different groups of samples but was variable. Nine AMPs, namely Human Beta defensins (HBD) 1 to 4, Cathelicidin (LL37), Liver expressed antimicrobial peptides, LEAP-1 and -2, DEFB-109 and RNAse were detected. Of these, HBD3 was prominent in bacterial keratitis and LEAP 1 and LL37 in viral keratitis. LEAP 2 and LL37 showed an increased tendency of expression in dry eyes. DEFB-109 was the only AMP found to show decreased expression in the inflammatory conditions studied. RNAse, the most potent of all AMPs was found in abundance at the OS.

Conclusion Conclusions: The OS is endowed with a range of AMPs which contribute to defence against environmental microbes and also participate in other immune mediated, inflammatory and wound healing events. They hold promise as therapeutic agents against microbes and in modulation of inflammation and wound healing.

6326
Microbiological culture and panbacterial PCR yield of diluted or undiluted vitreous from vitrectomy are comparable in acute postsurgery endophthalmitis (FRIENDS group)

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Purpose To compare the diagnostic yield of microbiological analysis performed on diluted and undiluted vitreous samples from pars plana vitrectomy in patients with acute postcataract surgery endophthalmitis.

Methods Undiluted and diluted vitreous samples were harvested in 34 patients at the beginning of the vitrectomy, among the 57 vitrectomized patients (out of 100 patients presenting with an acute postcataract surgery endophthalmitis) included in the multicenter prospective study FRIENDS (2004-2005). Vitrectomy was performed after one (n=12) or two (n=22) antibiotics intravitreal injections. Each vitreous sample was divided into two parts for conventional culture (Brain Heart Infusion broth) and panbacterial PCR, respectively.

Results Microbiological analysis of both undiluted and diluted vitreous allowed a bacterial identification in 28 out of 34 cases (82.3%). Microbiological diagnosis using undiluted vitreous and conventional culture was negative in 32 cases and positive in 2 cases. In one case, there was a discrepancy between undiluted (culture negative) and diluted vitreous (S. epidermidis). Analysis of both undiluted and diluted vitreous using PCR was positive in 28 cases and negative in 6/34 cases. There was a discrepancy between both samples in three cases.

Conclusion Microbiological results combining PCR and cultures showed that diluted vitreous analysis may replace analysis of undiluted vitreous. The diluted sampling of vitreous, more easily performed and less iatrogenic, may be recommended when panbacterial PCR is used .

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Lack of association of the Toll-like receptor 4 gene polymorphisms Asp299Gly in Italian patients with Fuchs uveitis

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Purpose Fuchs uveitis is a chronic low grade intraocular inflammation of unknown etiology that is usually painless and characterized by the presence of persistent infiltrating cells in the anterior chamber and vitreous. One commonly occurring Single Nucleotide Polymorphism (SNP) in the human TLR4 gene (Asp299Gly) has been shown to be associated with increased risk of Gram-negative bacteremia in sepsis patients and with susceptibility to inflammatory bowel disease and autoimmune disease.

Methods 75 Italian patients with Fuchs heterochromic cyclitis and 210 healthy age and sex matched blood donors were genotyped for the Toll-like receptor 4 gene polymorphisms Asp299Gly gene by molecular methods.

Results The distribution of allele and genotype frequencies of the Toll-like receptor 4 gene polymorphisms Asp299Gly did not differ significantly between the patients with Fuchs heterochromic cyclitis and the healthy controls.

Conclusion Our data suggest that the Toll-like receptor 4 gene polymorphisms Asp299Gly in Italian patients with Fuchs uveitis is not associated with susceptibility of Fuchs uveitis Italian patients.

▪ 6331
The narrowing choice of keratoprostheses

LIU C
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There is a narrowing choice of keratoprostheses. The mainstream KPros include the age old osteo-odonto-keratoprosthesis (OOKP) which is capable of withstanding a hostile, dry ocular environment. Its derivatives (OOKP allograft, tibial bone KPro, Pintucci KPro, HAKPro) can be used when there is no suitable single rooted tooth available, but they do not match the longevity of the OOKP. For the wet blinking eye, it looks as though the Boston Type 1 KPro is favoured over the AlphaCor as the former gives much better vision and is no longer associated with corneal melts. Many "new" devices have failed the test of time. Yet others such as the Keralia are not yet established. The author surveys the changing scene in the world of KPros.

▪ 6332
Developing a recovery psychological model for patients undergoing KPro surgery

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Undergoing keratoprosthesis surgery is demanding Physically, Psychologically and Socially. Good outcomes, including improving Quality of Life, require that all these domains are considered during patient selection, surgery and during follow up.Evaluation of Psychosocial outcomes after medical events often limit themselves to areas such as Anxiety and Depression using an illness model rather than a Recovery Model, using quantitative rather than qualitative methodology, and thereby possibly limiting the information received and which could potentially be used to help patients adapt and cope.The Brighton OOKP service seeks to integrate patient experience to inform a Bio-psycho-social approach using Qualitative methodology to complement earlier quantitative work undertaken in the service. Integrating this information with the experience of the specialised clinical team and the wider literature in areas such as Resilience, Coping, and Social Support and drawing on the literature on sight loss/ recovery and living with changed appearance will contribute to the emergence of a Recovery Model for OOKP patients. This approach looks at processes which support or impede recovery and seeks to act upon them. Through this it is envisaged that the service will be better able to support patients as they consider, experience and live with a KPro such as the OOKP. This presentation will discuss progress to date.

▪ 6333
More than 50 years of experience with keratoprostheses

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We started to use acrylic corneal prostheses experimentally in 1955, principally in eyes considered functionally lost or after several attempts of other keratoplastic procedures had failed. In our first 15 cases a Dorzee prosthesis or a modified Dorzee prosthesis (Barraquer-Cardona) had been used, in three cases some useful vision was obtained for several months or even up to 4 years. However, the expulsion rate was high, mainly due to the lysis of the corneal borders around the prosthesis. The communication of Strampelli's first technique of osteo-odonto-keratoprosthesis, using a "live" support encouraged us to continue our experimentation. A case of bilateral blindness in a 50 year old patient, due to mine explosion in 1941 (Second World War) was first seen in 1965, 25 years after the accident. The right eye was lost due to retinal detachment, the left eye was aphakic, with opaque cornea due to explosion impacts and anterior synechiae due to old perforations. In 1965 osteo-odonto-keratoprosthesis, using Strampelli's first technique, was performed with good recuperation of vision (0.4) for 10 years. Different aspects and details of the case are presented and commented. Unfortunately in 1975 necrosis of the bone support developed and reconstructive keratoplasty had to be performed. The patient remained with very low visual acuity (0.03) and a very reduced visual field. The author considers that this result, obtained with the very limited facilities available more than 40 years ago, confirms and justifies that experimentation in this field must continue, making use of all technological, surgical, pharmacological and research facilities available today.

▪ 6334
Boston KPro experience in Barcelona

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Purpose To describe the indications, intraoperative complications, post-operative complications and anatomical and functional results of Type I Boston keratoprosthesis at our eye center in Barcelona.

Methods Retrospective interventional case series on 24 eyes of 22 patients who underwent Boston keratoprosthesis implant from May 2006 to May 2008.

Results The main indication for Boston keratoprosthesis implantation was a repeated failed graft (mean = 2.33 previous grafts). The most common principal pathologies were: bullous keratopathy, herpetic keratitis, aniridic keratopathy, corneal ectasia, calcific band keratopathy. No major intraoperative complications were noted and average time of surgery was 47 minutes. The mean follow-up time was 7.42 months. The major post-operative complications encountered were retroprosthetic membrane in 2 eyes, endophthalmitis in 2 eyes and corneal graft melting in 1 eye. The mean best corrected visual acuity improved from 0.015 pre-operatively to 0.1 post-operatively. Only one case of extrusion due to melting was encountered which was resolved by a reimplantation of the keratoprosthesis.

Conclusion Our short-term experience with the type I Boston Keratoprosthesis is a good alternative for patients with repeated graft failures. Improvement in visual acuity is immediate and only minor complications were encountered.

6335
Biosynthetic corneas - an update

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Purpose To present preliminary results on the implantation of biosynthetic corneal grafts into human corneas.

Methods Ten collagen biosynthetic corneas were implanted into human corneas by deep lamellar keratoplasty and have been followed for 6 months. Nine of the patients initially had keraatoconus and one had a scar following a bacterial keratitis. The eyes recieved a postoperative treatment of topical steroids and antibiotics for 1-2 moths. The patients were analyzed clinically, photographed, and tested for sensitivity. They were examined with pachymetry, in-vivo confocal microscopy, and anterior segment OCT.

Results Following implantation the sutures were removed typically after 5-6 weeks. During the 6 months follow-up the vision improved and the graft surface became more even. After 6 months nerves started to emerge and cellular invasion of the constructs could be identified to a varying degree. Some thinning of the grafts was identified which appeared to be an adaptation to the host corneal thickness. Of the 10 patients one suffered a minor bacterial keratitis at the edge of the graft and one patient was temporarily treated using an amniotic membrane coverage to achieve epithelialization of the surface.

Conclusion The constructs used were well-integrated into the recipient corneas. They are biocompatible without appearant untoward reactions. The surface is readily covered with epithelium and the nerves are staring to re-emerge. Thinning may be a concern but this can be adjusted for by altering the graft material.

6341

Retinal blood flow in patients with diabetes during normalized insulin and glucose plasma levels

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Purpose Ocular blood flow studies in patients with diabetes showed contradictory results. One of the reasons for these discrepancies is related to glycemic control, because glucose and insulin have been shown to induce ocular vasodilatation. Hence, we performed a study in diabetic patients measuring ocular blood flow during euglycemic euisoglycemic clamps.

Methods 16 patients with insulin dependent diabetes, no or mild non-proliferative diabetic retinopathy and serum cholesterol levels < 250 mg/dl and 16 healthy sex- and age-matched controls were included in the study. Retinal blood flow was measured in diabetic patients before the insulin morning dose and during euglycemic euinsulinemic clamps. For the assessment of retinal blood flow the Retinal Vessel Analyzer and bi-directional laser Doppler velocimetry were used. All veins entering the optic nerve head were measured to gain information on total retinal blood flow.

Results Plasma glucose levels decreased from 176±21 mg/dl before morning insulin to 102±4 mg/dl during the euinsulinemic clamp. Retinal blood flow was reduced significantly from 51.4±5.5 µl/min before the clamp to 42.1±5.2µl/min during the euglycemic euinsulinemic clamps ($p<0.01$). As compared to the healthy control group retinal blood flow was increased before the clamps, but not during euglycemic euinsulinemic conditions.

Conclusion The present study indicates that retinal blood flow is increased in diabetic patients during high blood glucose levels. Retinal blood flow values are, however, comparable to healthy controls during euglycemic euisoglycemic clamps.

6342

Retinal vessel pulse amplitude in health and disease

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Purpose End-organ microvascular diseases is a major cause of morbidity and mortality in the general population. There is however a lack of objective, quantitative methods for evaluation of microcirculation. We hypothesized that the systolodiastolic variation in vessel diameters may be an indicator of microvascular stiffness.

Methods The amplitude of systolodiastolic variations of the diameters of temporal arterioles and venules were recorded using the Retinal Vessel Analyzer (RVA®)in 37 normal eyes, 19 eyes of arterial hypertensive patients, 16 eyes that had recovered from CRVO and 9 fellow normal eyes. A minimum of 20 cardiac cycles were averaged.

Results In control eyes, the mean (±SD) pulse amplitude over the cardiac cycle was 1.9% (± 0.5) for arterioles and 3.3% (± 1.1) for venules. Reproducibility (mean (±SD) intersession difference; n=14) was 3% (± 0.4) for arterioles (ICCs:) and 2.5% (± 0.5) for venules, with ICCs of 0.94 (± 0.2) and 0.94 (± 0.3), respectively. There was a significant positive correlation between arterial pressure and venular relative pulse (r: 0.49; $p < 0.01$) but not with arteriolar pulse (r: -0.004; p= 0.9). The venular pulse amplitude was significantly lower in post-CRVO eyes (1.4% ± 0.9; $p<0.002$).

Conclusion Pulse amplitude of retinal venules, but not of arterioles, is positively correlated with arterial pressure, and negatively correlated with CRVO history. Additional basic and epidemiological studies are needed in order to determine if the measure of retinal vessel pulse amplitude is of interest for management or follow-up of cardiovascular and eye diseases.

6343

Is pulse-wave velocity in retinal arteries of healthy volunteers age dependent?

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Purpose Pulse wave velocity in large vessels has been extensively used in clinical practice as an indirect measure of arterial stiffness and an indicator of cardiovascular risk factors. Arterial stiffness increases with age and in coronary arterial disease. An in-vivo clinical method to characterise arterial stiffness of the central microcirculation was developed. Pulse wave velocity was measured in retinal arteries using the Dynamic Vessel Analyzer (DVA, Fa. IMEDOS, Jena).

Methods Time dependent alterations of retinal vessel diameter were examined continuously by DVA in a randomly chosen eye of 10 young (26,0(23,5; 27,0) [median(1. quartile;3. quartile)] and 10 senior (67,0(61,3; 69,5) years old) healthy volunteers.Two segments of a retinal artery were measured simultaneously. The phase delay between the pulsations of the segments and the distance between the segments were assessed. The data was filtered and analysed by methods of signal analysis.

Results There was a significant difference in pulse wave velocity between both groups ($p<0,01$, U-Test). It amounted to 21,5(17,9; 34,6) mm/s in young volunteers and to 243,8(186,1; 347,7) mm/s in seniors. Retinal arterial elasticity calculated on the base of these data amounted to 5,5(3,8; 12,5) Pa in young volunteers and to 607,5(329,8; 1426,8) Pa in seniors ($p<0,05$).

Conclusion An important clinical parameter, pulse-wave velocity, can be measured in the central microcirculation in-vivo using a commercially available medical device. Pulse wave velocity in retinal arteries increases significantly with age. This represents the age-dependent increase in retinal arterial stiffness which is part of the general aging processes in the human vasculature and might be the basis of age related ocular vascular disorders.

6344

Association between flicker-induced vasodilatation and flow mediated vasodilatation in patients with diabetes, systemic hypertension and hypercholesterolemia

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Purpose Flicker induced vasodilatation is reduced in patients with vascular related diseases. However, the reason for this diminished response is unclear, but may be related to endothelial dysfunction. Currently, the standard method to assess endothelial function in vivo is flow mediated vasodilatation (FMD). Thus, the present study was performed to investigate whether a correlation exists between flicker induced vasodilatation and FMD in patients with diabetes and patients with mild systemic hypertension and/or hypercholesteremia.

Methods In the present study 20 patients with insulin dependent diabetes, 40 patients with systemic hypertension (systolic blood pressure:140-159 mmHg; diastolic blood pressure 90-99 mmHg) and/or serum cholesterol plasma levels > 250 mg/dl and 20 healthy control subjects were included. The flicker response was measured using the Dynamic Retinal Vessel Analyzer. FMD was determined using a high resolution ultrasound system, measuring brachial artery diameter reactivity during reperfusion after arterial occlusion.

Results The flicker response of both retinal arteries and veins was significantly reduced in the two patients groups. Likewise, FMD was significantly reduced in patients as compared to healthy controls. However, only a weak correlation between flicker induced vasodilatation and FMD was observed.

Conclusion The study confirms evidence that flicker responses and FMD is reduced in the selected patients groups. Whether the weak correlation between FMD and flicker is due to the different stimulation type, the different vascular beds measured or other mechanisms has yet to be investigated.

6345
A new invasive method of measuring pulsatile ocular blood flow

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Purpose The purpose of this study is to demonstrate proof of principle of a new rigidity based invasive technique to assess pulsatile ocular blood flow in a wide range of clinically relevant IOP levels.

Methods An invasive manometric dynamic measurement procedure is employed, using a computer controlled device, comprising a pressure transducer and a microdosimetric pump. The anterior chamber is cannulated under topical anaesthesia with drops with a 21 gauge needle and the initial IOP is recorded. The IOP is artificially set to 10 mmHg and the eye is infused with predetermined volumes of BSS in a stepping sequence. After each infusion step, the IOP is continuously recorded for 2 sec, in order to calculate the pulsatile change in IOP. Ocular rigidity is measured from the pressure volume relationship in the stepping sequence. Pulsatile Ocular Blood Flow (POBF) is obtained through algorithms converting the IOP readings to the corresponding change of ocular volume derived from the rigidity diagram.Forty eyes of 40 cataract patients were measured with this technique. The study was approved by the Institutional Board and performed under the patient's informed consent. Systemic blood pressure and pulse rate were monitored during the measurement.

Results There were no complications related to the procedure. The average Friedenwald's Rigidity Coefficient was 0.0206 mmHg/µL (SD=0.0054). The corresponding POBF was 888(SD=185) µL/min at 15mmHg decreasing to 548(SD=146) µL/min at 40mmHg.

Conclusion The invasive method described is safe and effective. It can provide accurate estimates of POBF by incorporating the individual eye's measured rigidity coefficient. Moreover, POBF can be estimated in relation to the IOP.

6346
Retinal oximetry: clinical studies

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Purpose Disturbances in blood flow and oxygenation are believed to be involved in diseases such as diabetic retinopathy, retinal vascular occlusion and possibly glaucoma. The purpose of the studies presented here is to measure haemoglobin oxygen saturation (SatO2) in retinal vessels in patients with these diseases.

Methods Our retinal oximeter is based on a fundus camera, which is coupled with beam splitters and narrow band-pass light filters. The oximeter yields fundus images with 4 wavelengths of light simultaneously. Two wavelengths, 605nm and 586nm, are used for estimation of SatO2. Measurements were made on (A) 7 patients with CRVO, (B) 19 patients before and after glaucoma surgery and (C) 21 patient with diabetic retinopathy, who were compared with 20 healthy volunteers.

Results (A) Venous SatO2 was 53±9% in CRVO eyes and 65±4% in fellow eyes (mean±SD, p=0.015, n=7).(B) Glaucoma surgery has a minimal effect on SatO2 in both arterioles (2% rise, p=0.046, n=19) and venules (no change). IOP was lowered by 13mmHg.(C) SatO2 in retinal venules was 60±8% in healthy volunteers (n=20), 67±7% in patients with non-proliferative DR (n=12, $p<0.05$ compared to healthy) and 68±6% (n=9, $p<0.05$) in patients with proliferative DR after PRP treatment.

Conclusion Human retinal vessel oximetry can detect changes in various ocular diseases and this may help us understand the pathophysiology. The decreased venous SatO2 in CRVO is probably caused by decreased blood flow. A small change in SatO2 after glaucoma surgery may indicate a large change in oxygen delivery since blood flow may be increased with IOP lowering. Higher venous SatO2 in DR patients may for example be explained with arteriovenous shunting of blood.

Commercial interest

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The pulsatile ocular blood flow (POBF) in patients with sleep apnea syndrome (SAS)

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Purpose To determine the correlations of pulsatile ocular blood flow (POBF) and intra ocular pressure (IOP) with sleep apnea syndrome (SAS).

Methods The study design was cross-sectional. A total number of 26 patients, recruited into the study between January 2006 and February 2008, who underwent polysomnography were selected for the study. All of them were of European Caucasian Origin. The study participants were contacted by telephone and scheduled for eye examination. Sleep apnea syndrome was diagnosed if the apnea-hypopnoea index (AHI) was > 5, based on whole night polysomnographic recordings. Patients with sleep apnea syndrome using CPAP were excluded from the study. Each patient underwent a slit lamp and indirect ophthalmoscope evaluation of anterior and posterior segment as well as pulsatile ocular blood flow (POBF) examination. POBF was recorded in sitting position after instillation of one drop of Alcaine. In this study, only average POBF and IOP were included for the analyses.

Results Of them, 17 (65.4%) patients had sleep apnea syndrome (SAS) and 9 (34.6%) patients were healthy and served as the control group. The study revealed that the differences between rates of average POBF and IOP measurements in the SAS group and in the control group were not statistically significant either in the right or in the left eyes ($p> 0.05$)

Conclusion Although, experimental studies showed that POBF was lowered in hypoxia, in our patients there was no correlation between pulsatile ocular blood flow and sleep apnea syndrome. Further investigations, concerning vascular impairment, are needed to give evidence of the mechanism of the optic nerve damage in the SAS.

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Pharmacokinetics and ocular tissue penetration of VEGF trap after intravitreal injection in rabbits

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Purpose VEGF Trap is a potent antiangiogenic agent that binds and blocks the action of all VEGF-A isoforms and placental growth factor and, is active in numerous animal models of age-related ocular neovascularization and diabetic retinopathy, when administered either intravitreally or systemically. Moreover, systemic administration of VEGF Trap was active in reducing excess retinal thickness in a Phase I study in age-related macular edema. To understand the pharmacokinetics following intravitreal administration, VEGF Trap (500 mcg) was administered to both eyes of pigmented rabbits.

Methods Plasma and eyes were harvested from three animals/time point at defined times to 4 weeks after administration. Concentrations of VEGF Trap, free and bound to VEGF, were determined in plasma, vitreous, choroid, and retina by ELISA.

Results Maximal vitreal concentrations of free VEGF Trap were approximately 500 mcg/mL at 0.25 to 6 hours after injection. The drug was cleared from the vitreous in a first order process with a half-life of approximately 4.5 days. Vitreal VEGF:VEGF Trap complex reached a plarteau of 0.6 mcg/mL 10 days after administration. Drug was detected in both retina and choroid, and the elimination profile from these tissues approximated by that of the vitreous. Peak plasma total drug concentrations of 1.6 mcg/mL occurred at 10 days. At 4 weeks, the vitreal free VEGF Trap remained over 10-fold in excess of bound VEGF Trap and the complex levels were on a plateau.

Conclusion Given the vitreal half-life, free should remain in excess of bound for at least 3 additional half-lives (13.5 days), suggesting that eye VEGF production would be completely blocked for more than 6 weeks after adminstration of of 500 mcg/eye of VEGF Trap.

Commercial interest

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Retinal arteriolar vascular reactivity to incremental changes in hyperoxic stimuli during isocapnia

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Purpose To determine the relationship between the magnitude of retinal arteriolar vascular reactivity and incremental changes in hyperoxic stimuli whilst maintaining isocapnia.

Methods Twelve healthy, young adults (mean age 27 years, SD 4) participated in a gas protocol consisting of 4 phases at varying fractional expired oxygen levels (FeO2): baseline (15%), hyperoxia I (40%), hyperoxia II (65%), and recovery (15%). End-tidal carbon dioxide (ETCO2) was maintained at isocapnia throughout the experiment. Retinal arteriolar diameter, blood velocity, and blood flow were assessed non-invasively using the Canon Laser Blood Flowmeter during each of these phases.

Results Repeated measures ANOVA showed that there were significant influences of incremental changes in FeO2 on retinal arteriolar diameter ($p<0.0001$), blood velocity ($p<0.0001$), and blood flow ($p<0.0001$). Paired t-tests of these retinal hemodynamic parameters during each phase in the gas sequence showed they were significantly different ($p<0.05$) from each other, with the exception of baseline and recovery values. Incremental increases in FeO2 caused a linear decrease in group mean arteriolar diameter ($R2 = 1$, $p = 0.002$), group mean blood velocity ($R2 = 0.9968$, $p = 0.04$), and group mean blood flow ($R2 = 0.9982$, $p= 0.03$).

Conclusion Isocapnic hyperoxia elicits vasoconstriction and the reduction of retinal arteriolar diameter, velocity and blood flow in a dose-dependent manner over the range of FeO2 explored in this study.

Commercial interest

6351
The novel Col8a2G257D mutant mouse line Aca23 – a model for endothelial corneal dystrophies

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Purpose The purpose of this study was the morphological and genetic characterization of the novel eye-size mutant Aca23 in the mouse.

Methods The eyes of the mutants were described by histology and in situ hybridization. Visual properties were examined in the optokinetic drum. Linkage analysis was performed using single nucleotide polymorphisms and micro-satellite markers. The Aca23 mutation was identified by sequence analysis of positional candidate genes.

Results Aca23 (ACMaster abnormality) is a new dominant eye size mutant, which was recovered in an ENU mutagenesis program at the HMGU. The pathologic phenotype includes increased anterior chamber depths, longer axes, and reduced corneal thicknesses. Visual properties are not affected by these irregular eye size parameters. In genome wide mapping studies, Aca23 was linked to the distal part of chromosome 4 between the markers D4Mit249 and D4Mit73. A G=A point mutation was identified at cDNA position 770 of the candidate gene Col8a2, which belongs to the collagen superfamily. The transition results in a G257D amino acid exchange within the collagen triple helix repeat. Col8a2 is expressed in the posterior part of the cornea. These data suggest that effects on structure and elasticity of the corneal Descemet's membrane might cause the corneal thinning and anterior expansion in Aca23 eyes. Comparable pathologic abnormalities can be observed in human Fuchs' endothelial dystrophy of the cornea (FECD) and posterior polymorphous corneal dystrophy (PPCD).

Conclusion The mouse mutant described here offers a novel mutated allele of the collagen type VIII gene Col8a2 and represents a new model for endothelial corneal dystrophies.

6352
Hereditary opacification of the anterior and posterior cornea: a new corneal dystrophy?

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Purpose To describe an inherited, progressive corneal disorder observed in a small Swedish family.

Methods A mother and her son were initially examined for atypically-distributed bilateral corneal opacities. Three years later, re-examination of the mother and son and two additional family members was conducted using slit-lamp biomicroscopy and in-vivo confocal microscopy.

Results Flat, rounded opacities were initially observed in the peripheral cornea at the level of Descemet's membrane, in both the mother and son, while the mother exhibited additional round opacities in the central anterior cornea. Three years later the mother's corneas were unchanged while in the son the condition had progressed, with numerous opacities appearing in the central anterior cornea as in the mother. Opacities were examined with in-vivo confocal microscopy, which confirmed in both mother and son, that the corneal opacities were limited to the most anterior and posterior stroma with the central stroma remaining transparent. The size and morphologic features of the opacities in mother and son were remarkably similar at the microscopic level. The central anterior opacities occupied Bowman's layer and the anterior stroma and appeared to affect the subbasal nerves. No abnormalities were noted in the two additional family members who were younger siblings of the son. In all cases vision was unaffected and subjects remained asymptomatic.

Conclusion An atypical type of progressive corneal opacification with a dystrophy-like presentation has been examined. The location and progression of the corneal changes do not correspond to any known corneal dystrophies and may represent a new dystrophy.

6353
Genetics of high myopia in Polish families

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Purpose Myopia is the most common of all ocular conditions. In high myopia, genetic factors appear to play a predominant role. The purpose of this study is to verify the available data and to identify a new high myopia susceptibility locus (loci).

Methods Fifty two families with multiple members were diagnosed with high myopia (<-6 diopters) without other ocular or systemic features. Prior to the targeting genotyping, linkage to markers for the myopic genetic syndromes were tested and genotyping of high myopia associated loci was performed. Next, we performed genome wide screen with 1) fluorescent markers with an average spacing of 8 cM spanning all chromosomes and 2) Affymetrix Genome-Wide Human SNP Array 6.0 which contains 906,600 SNPs and 946,000 copy number probes.

Results All previously reported high myopia loci were excluded in Polish families. The genome-wide screen for a high myopia identified three novel loci. These loci are currently being verified using SNP array in the largest multigenerational family.

Conclusion We have identified, collected and characterized a large cohort of polish families with high myopia and excluded the principal genetic cause of this phenotype. These families will be instrumental in identifying one or more loci for genetic high myopia.

6354
DNA profile strongly associated with exudative age-related macular degeneration

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Purpose The genetics of age-related macular degeneration (AMD) is slowly unfolding with the recent discovery that single nucleotide polymorphisms (SNPs) in 4 genes, Complement Factor H (CFH), ARMS2/LOC387715, HTRA1 and Vascular endothelial growth factor (VEGF) independently confer a greater risk of disease. We have taken this further and analyzed a combined DNA profile for the SNPs in these 4 genes.

Methods Patients with exudative AMD (n=45) and age-matched controls (n=94) were genotyped for the CFH Y402H (rs1061170), ARMS2 A69S (rs10490924), HTRA1 -512 (rs11200638), and the VEGF +674 (rs1413711) polymorphisms, by RFLP, AS-PCR and randomized sequencing. Statistical analysis was carried out for each individual loci and into a combined DNA profile using the PHASE program.

Results Association of the VEGF +674CC genotype with AMD has been previously reported. We observed strong associations with AMD and the CFH-CC [OR=11.9 (4.5,31.3), p=0.0000000184], ARMS2-TT [OR=4.7 (1.6, 13.8), p=0.0023] and HTRA1-AA [OR=3.6 (1.3,10.1), p=0.0128] genotypes respectively. We also observed strong linkage disequilibrium between rs10490924 and rs11200638 (r2=0.9138), as seen in previous studies. However, possession of the 4 SNP DNA profile: CTAC (CFH/ARMS2/HTRA1/VEGF) is strongly associated with AMD [OR=63.0 (8.3, 475.4), p<0.00001].

Conclusion Past associations between CFH, ARMS2 & HTRA1 have already been reported, and this data further supports this. However, the possession of the CTAC 'at risk' DNA profile shows the potential combined effects of these three genes, and their strong association with AMD. It is now possible to identify those most at risk in the general population allowing lifestyle choices to be made that could reduce the overall risk of AMD.

▪ 6355
The role of factor h macular degeneration secondary to pathologic myopia

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Purpose To compare the frequency of genes associated with age-related macular degeneration (AMD), specifically the complement factor H alleles in patients with choroidal neovascularization (CNV) secondary to pathologic myopia (CNV).

Methods Patients with pathologic myopia (defined as axial length > 25.50mm or -6.00 dpt) were examined. The presence of choroidal neovascularization was confirmed by clinical examination and fundus photography; fluorescein angiography and autofluorescence images were analyzed when available. DNA samples from all study subjects were screened for variants in the CFH genes, commonly associated with age-related macular degeneration.

Results Seventy-three patients (47 female and 36 male; age 23 – 90 years; average: 59 years) were included into the study. Visual acuity ranged from 20/25 to count fingers in 1 meter. The frequency of the CFH Y402H as well as other common CFH polymorphisms in this cohort corresponded to that detected in the general population.

Conclusion Factor h variants commonly associated with AMD and other forms of CNV may not play a causal role in neovascular complications of pathologic myopia.

▪ 6356
Distribution and clinical peculiarities of monogenic retinal dystrophies at the Center for Ophthalmology, University of Tuebingen

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Purpose To investigate distribution and clinical peculiarities of monogenic retinal dystrophies (MRD).

Methods Patients, seen in Tuebingen Department of Ophthalmology in 1994-1999 and diagnosed with Macular dystrophy (MD), Stargardt disease (ST), Bardet-Biedl syndrome (BBS), Usher syndrome (USH) I and II, Central Areolar Choroidal Dystrophy (CACD) and Choroideremia (CHD) were selected from the database, containing 3787 records. Age, sex, diagnosis, age at first visual acuity (VA) decrease, at night blindness (NB), photophobia onset, types of visual field (VF) defects and mean age of onset (MAO), best corrected VA (BCVA) were analyzed. For VF assessment patients were divided into 2 groups: group 1: ST, MD, CACD; group 2: BBD, USH I, II, CHD.

Results Records of 259 patients were reviewed. Male/female ratio was 2:1. Mean age (MA) of the patients was 47 (SD=15,6). Prevalence of diagnoses were ST-34%, USH II-22%, MD-18%, CHD-14%, USH I-7%, BBS-5%. In 29% of all patients were first diagnosed at age between 21-30 years, when 29% of these patients noticed VF defects (MAO=26, SD=14.5) and 24% - VA decrease (MAO=25, SD=14). MAO of NB-23 years (SD=14.8), MAO of photophobia-26 (SD=15). Group 1 presented concentric constriction in 82%, central scotoma in 14 % and ring scotoma in 4%, group 2 - 29%, 57% and 14% respectively. 50% of all patients preserved BCVA at better eye at the level of 20/40 or higher, 31% had 20/40>VA>20/200, 12% had VA less or equal to 20/200. 7% were legally blind according to the German law, having VA<1/50 or VF<5°.

Conclusion The most prevalent diagnoses were ST, USH II, MD. Concentric constriction and central scotoma were decreasing the quality of life of MRD patients.

▪ 6357
Phenotyping parallel visual pathways in autosomal dominant optic atrophy

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Purpose To characterize different phenotypes of Kjer optic atrophy along different visual pathways.

Methods Novel computerized psychophysical assessment methods (CCT - Cambridge Colour Test and CSF - Metropsis Contrast Sensitivity Function Test) were used to evaluate visual function in a population of 13 subjects (26 eyes) from 8 families with Autosomal Dominant Optic Atrophy (ADOA). This evaluation was completed with electrophysiological assessment (Pattern ERG, Pattern and Multifocal VEP) and Automated Static Perimetry (ASP).

Results CCT shows evidence for severe damage of all cone populations ($p<<0.0001$), and of similar magnitude, implying concomitant damage of parvo and koniocellular pathways. Achromatic contrast sensitivity is severely impaired for all six spatial frequency channels studied ($p<0.002$), suggesting mixed magno/parvocellular impairment. A decrease of both P-50 and N-95 amplitudes of PERG is found ($p<<0.001$), while implicit times are normal. MfVEP results show significant impairment in amplitudes of the most central rings (1, 2 - $p<0.001$), with concomitant local increased implicit times, no significant changes being found at most eccentric rings. Pattern VEP impairment is consistent with these results. Amplitude values of MfVEP in visual quadrants are significantly correlated with the decreased retinal sensitivity obtained in the 4 quadrants by ASP.

Conclusion Our results suggest that all functional types of nerve fibers are damaged in ADOA, with a predominance of the parvocellular ones. Multimodal psychophysical and electrophysiological methods are good quantitative markers to understand the pathophysiology of damage of central and peripheral pathways in this condition.

6361
OCT and small melanocytic tumors

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ABSTRACT NOT PROVIDED

6362
PDT for amelanotic choroidal melanoma

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ABSTRACT NOT PROVIDED

6363
Modified enucleation for choroidal melanoma with large extrascleral extension

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Purpose To describe the technique and results of modified (enlarged) enucleation via lateral orbitotomy for choroidal melanomas with macroscopic periopticposterior extrascleral extension.

Methods 5 cases of choroidal melanoma with macroscopic periopticposterior entrascleral extension underwent modified enucleation via lateral orbitotomy. After lateral orbitotomy and orbital mass exposure with direct tumor visualization, a long optic nerve stump was cut and the orbital component of the tumor was completely (macroscopically) removed along with the globe in all cases. After haemostasis and orbital reconstruction an orbital implant was than placed. Follow up was longer than 12 months

Results After pathologic examination, the tumor result completely removed in 5 patients (100%). Excellent cosmetic outcome was achieved in all cases (100%) without operative or postoperative complications.

Conclusion Modified (enlarged) enucleation via lateral orbitotomy for choroidal melanomas with macroscopic perioptic/posterior extrascleral extension allows placement of an orbital implant avoiding the long healing process of orbital exenteration with excellent clinical and cosmetic outcome.

6364
A relevant panel of human uveal melanoma xenografts directly established from primary and/or metastatic patient's tumor for pharmacological preclinical assays

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Purpose Human cancer xenografts transplanted into immunodeficient mice constitute a useful preclinical tool for testing new agents and protocols and for further exploration of the biological basis of drug responses. The aim of this study was then to develop, establish, and characterize an in vivo panel of xenografts directly obtained from uveal melanoma patients.

Methods Samples obtained from primary tumors after enucleation or from liver metastases, were subcutaneously xenografted into immunocompromised mice. A characterization of the xenografts growing into mice was then performed and compared to originated tumors, including histopathological, genetic (karyotype or FISH, and CGH-array), and molecular assays.

Results Thirty-seven xenografts have been obtained among 95 patient's tumor sample transplantations in which 10 have still grown after at least three transplantations in mice and have been characterized. Pathological analyses of these ten xenografts confirmed the diagnosis of uveal melanoma and showed, for the five models derived from primary tumors, similar chromosome 3 status. Bcl-2 protein was overexpressed in all but 2 xenografts. NA17 and Melan-A antigen expressions were positive in all tested samples, tyrosinase antigen expression was positive in all but 2 xenografts, and MAGE- (1/2/3/4/6/10), LAGE-1, and MAGE-C2 antigens expression were negative in all studied cases.

Conclusion Our in vivo human uveal melanoma xenografts present the same histopathological and genomic characteristics of the patient's originated tumors. This observation supports the use of our panel for pharmacological preclinical evaluations that could serve as a bridge linking pre-clinical and clinical research, and drug development.

▪ 6365

Small, fatal choroidal melanoma: a retrospective study of patients treated in Liverpool

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Purpose To review the Liverpool experience of small, fatal uveal melanomas.

Methods We searched the database of the Liverpool Ocular Oncology Service for British patients dying from metastatic disease after treatment of a uveal melanoma having a basal diameter less than 10.0mm (i.e., 'small melanoma'). The cause of death was obtained from death certificates provided by the National Health Service Cancer Registry.

Results Of the 3186 patients first treated for uveal melanoma in Liverpool between January 1993 and July 2008, there were 994 (31%) with a small melanoma. In 803 of these patients residing in mainland Britain, the 15-year actuarial survival was 88.4%. The 35 patients dying of melanoma (19 female, 16 male) had a median age of 72 years at primary treatment (range 43-88). The tumours had a median diameter of 7.6mm (range 3.2-9.9) with nine measuring less than 7.0mm. The posterior tumour margin was located in iris in 1 patient, ciliary body in 6 patients and choroid in 29 patients. The initial management consisted of brachytherapy (14 patients), proton beam radiotherapy (9), enucleation (5), local resection (2), transpupillary thermotherapy (3) and observation (2). Histological studies had been performed in 11 tumours, 9 of which contained epithelioid cells. Cytogenetic data were available for four tumours, two of which showed monosomy 3. Three patients had developed local tumour recurrence after their initial treatment. The median time to death was 4.8 years (range 0.1 – 13.7). This survival time was longer than in fatal cases with a medium-sized or large tumour (Log rank, $p<0.001$).

Conclusion Multicentre studies are indicated to understand the metastatic process and how this is influenced by ocular treatment.

▪ 6366

Ten smallest melanomas that killed the patient – a very long-term analysis

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Purpose To characterise the nature and course of smallest uveal melanomas that were fatal in a very long-term follow-up study.

Methods Charts of 289 consecutive patients with choroidal and ciliary body melanoma treated in the Helsinki University Central Hospital district in 1962-1981 were used to identify and those ten patients who died from the smallest tumours during the subsequent 30-40 years. In this period, enucleation was the only treatment available.

Results Altogether 41 (14%) melanomas were <10 mm in diameter, and 10 (25%) of these were fatal long-term. For this size of tumour, the 5-, 10-, 15-, 20- and 30-year actuarial survival, which cancels the effect of other causes of death, was 90%, 85%, 80%, 80% and 70%, respectively. The 10 patients who died of melanoma were a median of 54 y (compared with 54 y for those who survived) old at treatment (range 33-73 vs. 30-74). The median tumour diameter was 7.5 vs. 8 mm (range 6-9 vs. 3-9), with 2 of 10 (20%) vs. 5 of 31 (16%) tumours measuring <7 mm. The median tumour height was 4 vs. 4.5 mm (range 2-8 vs. 1-11), with 2 of 10 (20%) vs. 7 of 31 (23%) tumours measuring less than 3 mm; thus, not all were "small" melanomas. 1 (10%) vs. 3 (10%) tumours extended to ciliary body and 0 vs. 1 extended extrasclerally; none of the patients developed local tumour recurrence. The median time to death was 6.7 y (range 1.2-33). The two smallest fatal tumors were 6 and 7 mm in diameter and 2 mm in height.

Conclusion The smallest ciliochoroidal melanomas that are fatal do not differ clinically at diagnosis from nonfatal melanomas in the same size range. A multicenter histopathologic and tumor cytogenetic analysis is necessary to characterise small melanomas as close to the time point when they acquire metastatic potential as possible.

6411

Mapping of photoreceptor dysfunction using high resolution, three-dimensional spectral optical coherence tomography

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Purpose To introduce a novel method of 3-D Spectral Optical Coherence Tomography (SOCT) data analysis called reflectivity maps.

Methods We introduced new software to perform segmentation of the junction between photoreceptor inner and outer segments (IS/OS) at 2-D tomograms. After segmentation, each cross-sectional image is transformed in such a fashion that posterior contour of the retina becomes a straight line but all radial distances within each cross section are preserved. It enables us to display the distribution of a back-reflected intensity taken only from individual retinal layers located at specific distance from the reference plane and create reflectivity maps. We analysed the reflectivity maps of the IS/OS layer of 56 patients with photoreceptor dysfunction in course of age-related macular degeneration, central serous chorioretinopathy, macular holes, retinal detachment, acute zonal occult outer retinopathy, multiple evanescent white dot syndrome, acute posterior multifocal placoid pigment epitheliopathy, drug-induced retinopathy and congenital disorders.

Results The reflectivity maps of the IS/OS layer displayed the areas of photoreceptor dysfunction.

Conclusion Subtle changes in the IS/OS reflectivity can be detected and presented as SOCT reflectivity maps. The maps reveal the areas of photoreceptor dysfunction and can be correlated with standard techniques like fluorescein angiography and electrophysiological examination. We believe that the use of 3-D analysis of segmented IS/OS layer in larger number of retinal pathologies may help in better understanding of photoreceptor dysfunction and allow for more accurate interpretation of the IS/OS layer on SOCT images.

6412

Assessment of macular pigment optical density (MPOD) among patients with wet age-related macular degenaration (AMD) in one eye and the dry form in the fellow eye

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Purpose To estimate the Macular Pigment Optical Density (MPOD) in patients with unilateral wet Age-Related Macular Degenaration (AMD), not taking any carotenoid supplements.

Methods The MPOD was measured in 20 patients (73.7±5.32 years) and in 20 healthy-retina subjects (71.6± 5.19 years) using Heterochromatic Flicker Photometry. Independent-samples t test was performed between patients' eye with dry AMD and controls' right eye.

Results No significant difference (mean difference: 0.01 (p=0.845)) was observed between the Macular Pigment Optical Density (MPOD) of the fellow dry AMD eye of patients with unilateral wet AMD (mean MPOD: 0.51 ± 0.16) and the eyes of age-matched control subjects (mean MPOD: 0.52 ± 0.15).

Conclusion Patients with unilateral wet AMD were not found to have less Macular Pigment than healthy subjects of same age. This finding suggests that MPOD might not be useful as prognostic factor for the progression of the disease at this high-risked group of patients.

6413

Assessment of fixation locus with microperimetry and OCT in patients with Stargardt disease

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Purpose Patients with maculopathies adapt to foveal vision loss by choosing an eccentric retinal area for fixation (preferred retinal locus; PRL). The aim here was to evaluate fixation patterns by microperimetry (MP) and to correlate the results with retinal morphology seen by optical coherence tomography (OCT) in patients with genetically confirmed Stargardt disease (mutations on both alleles).

Methods Fourteen patients with Stargardt disease were examined. In all patients, full ophthalmological examination, MP (Nidek Technologies MP1 Microperimeter), OCT (Topcon 3D OCT-1000) and autofluorescence imaging (Heidelberg Engineering HRA) were performed. The results of MP testing were superimposed on the fundus image with a rectangular grid of retinal thickness as measured by OCT.

Results In three eyes, fixation was central and stable. In 25 eyes, fixation was eccentric, with a superior shift in 20, a temporal shift in two, and a nasal shift in three eyes. The eccentric fixation was stable in nine, relatively unstable in 11, and unstable in five. The mean visual acuity (VA) in central fixation was 0.7 ±0.2, and in eccentric fixation 0.15 ±0.1. The mean macular thickness in central fixation was 212 ±11 µm, and in eccentric fixation 181 ±32 µm. A correlation between VA and macular thickness was seen ($r = 0.43$, $p = 0.02$).

Conclusion In early stages of Stargardt disease a stable central fixation with a VA range of 0.5-0.9, and a macular thickness range of 201-222 µm was seen. In eyes with loss of central function, a shift of fixation to PRL was seen, with a VA range of 0.01-0.4 and a macular thickness range of 118-228 µm.

6414

Macular retinal thickness in amblyopic and normal eyes of children evaluated with spectral domain OCT

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Purpose The purpose of this study was to investigate the macular retinal thickness, in relation to the axial length in amblyopic and normal eyes, using spectral domain OCT.

Methods Included amblyopic and healthy children underwent a standard orthoptic examination and were scanned with spectral domain OCT (3D OCT-1000, Topcon). The mean, nasal, temporal and foveal retinal thicknesses (RT) were used for analysis. We recorded the axial length using the IOL master (Zeiss). Nonparametric testing for paired data and correlations were performed using SPSS 14.0.2.

Results Fifteen amblyopic patients (7 male and 8 females, mean age 8.2 ± 2) and 13 healthy children (7 males and 6 females, mean age 8.3 ± 1.5) were enrolled in this study. Compared to their fellow eyes the amblyopic eyes were 0.3 (0.6 – 0.1) mm shorter ($p<.02$) and had a 2.6 (0.6 – 4.5) micron thicker mean RT ($p<.02$) and a 4.2 (1.0 – 7.4) micron thicker temporal ($p<.02$) RT. No significant differences were found in the nasal and foveal minimal RT. In the normal controls none of the parameters differed significantly between both eyes ($p>.05$). The longer eyes were significantly correlated ($r = 0.4$, $p<.04$) with a thinner RT in this control group. However, after correcting for the axial length, the amblyopic eyes still had a significantly thicker mean and temporal RT (differences 3.4 (0.7 – 6.1) and 3.1 (0.6 – 5.5) micron, $p<0.02$).

Conclusion Based on this study in 28 children, amblyopic eyes are slightly but significantly shorter and have thicker mean and temporal RT compared to their fellow eyes. The thicker RT in amblyopic eyes seems not to be explained by their shorter axial length.

6415

A new slitlamp mounted Fourier domain-OCT (SL-FD-OCT) for flexibility in daily clinical practice

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Purpose To demonstrate the flexibility and quality of a new SL-FD-OCT device, mounted on a slitlamp, in daily clinical practice.

Methods Images were made in patients, with different types of macular pathology, and 30 patients with AMD, treated with ranibizumab, with a newly developed FD OCT scanning device integrated into a common slitlamp. Scans were made through a handheld lens (Volk 60 D), while simultaneously the (lesion in the) retina could be observed, with the slitlamp. A color fundus photograph of the observed area was made at the same time (Topcon camera DC1, resolution = 3.24 Mp).For comparison, line scans were made in the same patients with the Stratus-OCT (Zeiss) and 3D-volume scans with the 3D-OCT-1000(Topcon). Scans made at approximately the same location were subjectively compared with respect to quality of the images.

Results With the new device scans, and photographs could be made without difficulty in all patients with a reasonably clear retinal image on slitlamp examination. The quality of the scans made with the new device is better than the Stratus-OCT,and slighly less than the 3D-OCT-100. In 30 patients with exudative AMD, treated with ranibuzumab, conclusions regarding the presence of leakage based on SL-FD-OCT images were in concordance with the conclusions based on 3D volumes with the 3D-OCT-100(Topcon).

Conclusion Quality of the scans made with the new device compare favourably with scans of the Stratus-OCT (Zeiss), and are slightly less than scans made with the 3D-OCT-1000 (Topcon). The ease of use and the instanteneous availablity of results of OCT examination, during a regular clinical examination, could be very usefull in daily practice.

6416

Use of intravitreal Ketorolac tromethamine for postoperative cystoid macular edema

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Purpose To investigate the effect of intravitreal ketorolac tromethamine in chronic post-operative cystoid macular edema.

Methods Six patients diagnosed with chronic post-operative CME non responsive in conventional therapies, were enrolled. 2 patients received 2 intravitreal injections of 300 μg (0.05ml) of ketorolac tromethamine (Toradol) with a 3-week interval, three patients received 4 consecutive injections of 500 μg (0.05ml) weekly and 3 patients received 4 consecutive injections of 500 μg (0.05ml) daily. Patients were followed by means of biomicroscopy, fluorescein angiography and optical coherent tomography. Follow-up lasted up to six months.

Results No adverse effect was noticed in any of the patients. A trend for visual acuity improvement and macular edema regression was noticed after initiation of the therapy. A rebound of the edema happened usually a week after the last injection. In the long follow-up regression of the macular edema was noticed in three out of six patients.

Conclusion This pilot study indicates a possible role of intravitreal injection of ketorolac tromethamine in patients with chronic postoperative cystoid macular edema. Further research is warranted in order to obtain conclusive results concerning doses and timing of injections.

6417 / 603

Orbital floor triamcinolone acetonide in the treatment of pseudophakic cystoid macular oedema

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Purpose To report the outcome of orbital floor triamcinolone acetonide (OFTA) in refractory pseudophakic cystoid macular oedema(PCMO) and to determine the visual outcome in these patients

Methods Six eyes of 6 patients with PCMO inadequately responsive to treatment combinations of topical steroidal and non-steroidal agents were retrospectively studied. All received 40mg (1ml) OFTA injection. Post-operative Visual acuity (VA), intraocular pressure (IOP) and OCT findings were assessed. Other potential complications were looked for retrospectively.

Results The average age was 72 years(+/-12 years). OFTA was given, on average, 4 weeks after a diagnosis of PCMO was made (range 0-6 weeks) and treated with topical anti-inflammatory agent combinations. The mean follow-up was 11.0 months (range, 5-18), and the mean improvement of VA after OFTA was Snellen, (6/18-6/12). This was noticed at a mean of 12 weeks (range 4-72). At last follow-up, five eyes showed an improvement of two lines or more, while in one eye vision was maintained at 6/24 which developed diabetic maculopathy and required grid laser. None of the patients developed post-treatment raised IOP or lost vision. There was a significant reduction of retinal thickness and cystoid space height (P = 0.003). The dosage of topical steroids was reduced or stopped altogether in all 6 eyes. There were no cases of injection-related retrobulbar haemorrhage, cellulitis, or globe perforation

Conclusion In cases of psuedophakic CMO, initial response to OFTA treatment was encouraging. Further larger long term studies are required to ascertain whether re-treatment is effective with subsequent orbital floor steroid injections. This is with a view to maintain the initial improvement.

▪ 6421

Ophthalmic microsporidiosis: Emerging pathogens or emerging awareness?

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Purpose We report and discuss an apparent increase in the number of ocular and adnexal microsporidial infections.

Methods We present cases of ocular microsporidial infection which were diagnosed by light (LM) and electron microscopy (EM) at our departments and review the literature.

Results Cases involved Encephalitozoon, Vittaforma, Trachipleistophora and Nosema sp. with infection of ocular surface, corneal stroma, canaliculi and nasolacrimal apparatus.

Conclusion Microsporidia are minute obligate intracellular parasites which infect via a polar tube. Human microsporidiosis is normally HIV/AIDS related, most infections being enteric with few ocular cases. With the success of antiretrovirals, the incidence of enteric microsporidiosis is now much lower. Ocular infection is now more prevalent and not usually HIV-associated. Our cases had infection of ocular surface, cornea and lacrimal canal/sac. The diagnosis was not initially considered clinically. LM may be diagnostic if characteristic refractile ZN-positive microspores are seen. If they are few or are not identified, LM is not diagnostic. LM does not permit speciation which usually requires EM. Diligent search for organisms may be necessary as distribution may be focal. Insufficient data exist to allow PCR-based diagnosis of most microsporidial species. Sources and mechanisms of infection remain speculative. Insect infection is abundant. Spores are present in water. Microsporidia are poikilothermic. Microsporidiosis occurs in animals. Does the eye's immune status and lower surface temperature favour opportunistic infection by organisms adapted to lower temperatures in insects? Are animals vectors? Is travel to "exotic" places a factor? Are microsporidia emerging pathogens or are they simply not recognised?

▪ 6422

Efficacy and tolerance of early high-dose corticosteroid therapy in Vogt-Koyanagi-Harada disease

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Purpose Early high dose corticosteroid therapy with "adequate" duration has become the mainstay therapy in Vogt-Koyanagi-Harada (VKH) disease. This work report the tolerance and side-effects in a small series of VKH patients having received "maximal" Inflammation Suppressive Therapy (IST).

Methods Medical records of VKH patients seen in the the COS uveitis clinic in Lausanne were analyzed. Standard care consisted in prolonged high IST including high dose oral prednisone (60-200 mg/day), slowly tapered, with or without initial 3-day megadose (500-1000 mg of methylprednisolone) intravenous pulse therapy with adjunction of immunosuppressive therapy if necessary. Follow-up time, total prednisone dose, duration of therapy, adjunctive immunosuppressive treatments, major side-effects, clinical outcomes were recorded.

Results Nine patients were included. Initial oral daily corticosteroid dose was above 60 mg of prednisone in all patients. Immunosuppressive therapy was used in 6 patients either to reinforce IST or to obtain a corticosteroid-sparing effect. Major side effects were recorded in one patient who developed a bilateral aseptic hip necrosis needing bilateral hip replacement. Clinical outcomes were favorable in 8/9 patients with no sunset-glow fundus at the one year follow-up visit and with 7/9 patients beeing treatment free after a slow, mostly indocyanine green angiographically controlled tapering over more than 2 years.

Conclusion High dose IST was relatively well tolerated and associated with favorable clinical outcome. Side-effects of maximal IST are not to be minimized, but seem however acceptable in view of the favorable outcome induced. Treatment duration was found to be much longer than usually recommended in textbooks.

▪ 6423

Interest of an interferon-gamma release assay for diagnosing tuberulosis-related ocular inflammation

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Purpose Tuberculosis-related ocular inflammation has many clinical presentations. Most of the time, bacteriological proof is not available and the diagnosis remains presumptive. Workup for another site of infection is seldom rewarding and tuberculin skin test (TST) results can be misleading. QuantiFERON-TB Gold test is an interferon-gamma release assay now currently available for tuberculosis screening.

Methods We made a review of the charts of the patients who had had a QuantiFERON-TB Gold test in the ophthalmology department in Pitié-Salpêtrière, Paris, France between January and October 2007.We included patients with intraocular inflammation who had the QuantiFERON test done before the TST was performed. We decided to conduct a full anti-tuberculosis therapeutic test in those patients who had a positive QuantiFERON-TB Gold test result.

Results We found 96 QuantiFERON-TB Gold test results. The mean age at presentation was 51 years (22-88, SD=17)and the F/M ratio was 60%. Patients exhibited all types of uveitis (anterior, intermediate, posterior, panuveitis) and some of them had scleritis. QuantiFERON-TB Gold turned out positive in 41 cases, among whom 33 had positive TST, 9 had negative TST and 9 had undetermined TST. Twenty-six patients received the treatment. At six months of follow-up, 16 of them had no intraocular inflammation.

Conclusion QuantiFERON-TB Gold test is a convenient ancillary test compared to TST (no control visit, no stimulation of the patient's immune system). It appears useful to help identify patients with tuberculosis-related ocular inflammation. Further studies are needed to determine whether we should use it instead of TST in this setting.

▪ 6424

Lyme borreliosis: different ocular aspects of the same disease in North-West of Italy

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Purpose To show different presentations of ocular Lyme disease in an endemic area (North-West of Italy)

Methods In last ten years, at Lavagna (Genova) uveitis referral centre, we examined about a hundred people affected by Lyme ocular disease (57 males and 45 females; mean age 42 +/- 3.2 years) and we were able to recognize some different ocular manifestations of this affection in 133 eyes.Diagnosis was made by means of ELISA or Western-Blot tests;sometimes by PCR test.Different systemic symptoms were present: 53% of patients had inflammatory arthropathy, 24% erythema migrans, 13% neuro-ophthalmologic findings.

Results Five main groups of Lyme disease ocular involvement were detected from our long-term study:1 - diplopia and periocular pain2 - diffuse or nodular episcleritis3 - acute anterior uveitis4 - retinal vasculitis and papillitis5 - retino-choroiditisGroup 4 and 5 were the more frequent bilateral presentation.Our study shows slit-lamp, FA, ICG-A and OCT pictures of these different Lyme disease presentations.Antibiotic treatment of early diagnosed infection allowed a complete recovery in 79 patients.

Conclusion Lyme ocular disease, because of its peculiar characteristic of being able to mimic a lot of ocular inflammations, may be underdiagnosed by ophthalmologists; aim of our work is to show and to point out some different ocular presentations of this disease

▪ 6425

Developments in diagnosing the tubulointerstitial nephritis and uveitis (TINU) syndrome

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Purpose Tubulointerstitial nephritis and uveitis (TINU) syndrome is a rare form of uveitis but there is reason to believe that this syndrome is underdiagnosed and renal manifestation may not be treated. Gold standard for diagnosisng TINU is invasive renal biopsy. Here, we show that performing beta-2 microglobulin analysis in urine and HLA typing is helpful to find otherwise undiagnosed TINU cases with subclinical forms of nephritis.

Methods Beginning January 2006 we prospectively obtained Ub2MG levels in all children with AU attending our pediatric uveitis clinic for the first time. Mandeville criteria were used to grade certainty of diagnosis. We compared with a healthy control group of children. HLA typing on patients with AU but no nephritis (n =28) by a Luminex-based PCR-SSO typing method was performed in another study. We compared frequencies to normal published controls and a published TINU cohort (n=20).

Results The simple screening method of determining urinary Beta-2-Mikroglobulin showed in up to 2/3 of children with new-onset AU subclinical renal manifestation. HLA Typing showed the TINU associated HLA DRB1*0102 in 12.5% of patients with AU with normal renal function opposed to 0.6% in healthy controls (p <0.0001; RR 14.3 (8.3-32.0)). The allele was even more frequent in patients < 20 years with AU with 40%.

Conclusion Determining the right uveitis subset is essential for therapy and prognosis, therefore TINU has to be kept in mind when considering differential diagnosis of AU. Urinary Beta-2 micorglobulin and HLA Typing can give helpful information to direct this process.

▪ 6426 / 673

Presentation of orbital aspergillosis

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Purpose To describe the presentation, diagnostic difficulties and treatment in three rare cases of aspergillosis of the (peri)orbita.

Methods Retrospective reportage of three patient histories.

Results The first patient, known with leukemia, presented with total vision loss and ophthalmoplegia. Clinical suspicion was raised for a sinus cavernosis and apex syndrome, but could not be revealed by imaging at first, but only later in the disease progression. The patient was treated with chemotherapy and Amfotericine, but died few weeks later.A second patient presented with complaints with bilateral decrease of visual acuity and sinusitis. No process could be revealed in the cavernous sinus, but bilateraly in the ethmoids. An endonasal ethmoidectomy was done, and oral steroids were given, with good result. A third patient was referred with diplopia since four days. CT-scan together with MRI made the suspicion of fungal disease with found after tumor excision of the sphenoid MRI showed at first desctruction of the sella floor, without intraorbital infection but forced duction invasion toh orbit. The patient was treated with amphotericin and itraconazole with vanishment of the infection in one month.

Conclusion These three cases with aspergillosis infection show that a combination of MRI and CT may be necessary to locate the infection but clinical suspicion and symptoms may be present before imaging can reveal them.

▪ 6427 / 674

Management of ocular disease in epidermolysis bullosa variant: Laryngo-onycho-cutaneous (LOC) syndrome

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Purpose To assess the long term outcomes of ocular surface reconstruction and immunomodulation in Laryngo-onycho-cutaneous (LOC) syndrome

Methods Prospective, interventional, case series

Results Four children with LOC were treated by multiple operations involving excision of ocular granulation tissue and amniotic membrane graft reconstruction. The clinical course was monitored for an average period of 4.7 years +/- 2 SD (range 3 to 7 years). In all patients, surgical intervention was successful in the medium term with regression of granulation tissue, visual improvement and symptomatic relief from ocular discomfort. Granulation tissue recurred in 8 months (3.7 SD). One patient received Thalidomide trial which stabilized systemic manifestations but had limited effect on ocular disease progression. Immunomodulation with Infliximab infusions stabilized ocular disease in all patients. All patients had stabilisation or slight improvement in vision.

Conclusion Ocular disease in LOC syndrome can be successfully managed with repeated amniotic membrane grafts and immunomodulation. The treatment is effective in maintaining the ocular surface integrity and managing the symptoms of ocular inflammation, although long term visual outcomes remain disappointing.

▪ 6431
IOL filters, is there an optimal absorption?

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Purpose To analyze the need for optical filtering in IOLs

Methods The spectral distribution of radiation from the sun, the action spectra for diurnal rhythm regulation and vision, and the action spectra for phototoxic effects in the aphacic and pseudophacic eye were analyzed.

Results Ultraviolet radiation (UVR), visible radiation and infrared radiation from the sun reaches the surface of the earth. In the aphacic eye, the retina is exposed to considerable amounts of toxic optical radiation. At the same time, optical radiation is required for vision and diurnal rhythm regulation. Therefore, an IOL needs to block toxic radiation while conserving enough light for vision and diurnal rhythm regulation. The cornea blocks out UVR below 290 nm and then gradually transmits more toward longer wavelengths. The aqueous humor and the vitreous provide some additional blocking of UVR up to 320 nm but then transmits large amounts of longer wavelength radiation up to 1400 nm. In the phacic eye, the crystalline lens, age dependently, blocks out UVR and short wavelength visible radiation. Diurnal rhythm is regulated by melatonin and the action spectrum for the regulation has a maximum around 450 nm. Scotopic vision has a maximum sensitivity around 505 nm and photopic vision around 555 nm. UVR is increasingly toxic towards shorter wavelengths. Visible light causes a retinal Type I phototoxicity with a maximum action around 505 nm and a Type II phototoxicity with a maximum action around 440 nm.

Conclusion It is possible and desirable to block the UVR hazard and the Type II phototoxic reaction with conserved diurnal rhythm regulation and scotopic and photopic vision with IOLs.

▪ 6432
Aspheric optics, theoretical considerations

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Spherical aberration is the largest higher-order aberration in the human eye and it is the only aberration with a nonzero population average. Furthermore, in contrast to other aberrations such as, e. g., coma, spherical aberration can be corrected by rotationally symmetric optical surfaces, so called aspheric optics. These facts form the basis for an increasing number of both IOL's and contact lenses which manipulate the spherical aberration in the eye. This talk will give a background on spherical aberration and state of the art aberration measurements in the human eye. Different aspects of ocular spherical aberration will be reviewed and the implications and possible visual benefits of correcting, or even inducing, spherical aberration will be discussed.

▪ 6433
Clinical experience in aspheric IOLs - a review of the world literature

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The natural crystalline lens continues to grow throughout life. In early adult life, the asphericity of the cornea and the lens more or less cancel each other out. Later in life, this balance is lost and older subjects experience poorer quality vision. During cataract surgery, there is an opportunity to redress this balance, or at least not add to the problem of positive spherical aberration by implanting IOLs with aspheric optics. Results from the emerging literature suggests that patients do have higher quality vision, including when an aspheric mulitfocal IOL such as the Alcon ReSTOR SN6AD3 is used. However, there may be problems with IOLs with deliberate negative spherical aberrations if decentration and tilt should occur. Also, the approach is one size fits all, and is not tailored to the optics of individual eyes. There is a great variation in corneal spherical aberrations in normal individuals.

▪ 6434
Purkinje based IOL centration

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Purpose Surgeon-controlled centration of IOLs might be an issue when introducing IOL optics yielding additional properties aiming at correcting spherical aberrations, astigmatism and accommodation or pseudoaccommodation.

Methods First and third Purkinje reflexes can be used during cataract surgery for the purpose of IOL alignment provided the IOL allows that freedom of action. The bag-in-the-lens (BIL) concept has been designed to add this dimension of freedom to the surgeon.

Results When using the Purkinje alignment method, a physiological nasally positioning of the IOL can be observed. Aberrometry shows an increased spherical aberration but no increase of other HO aberrations.

Conclusion Surgeon-controlled centration of IOL is possible with the BIL implantation technique. This opens new perspectives for further development and alignment of the optic.

Commercial interest

■ 6435

Long-term results of cataract surgery with implantation of a mechanically, reversibly adjustable intraocular lens: *Acri.Tec AR-1 PC/IOL

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Purpose To investigate long-term safety and function of a mechanically, reversibly adjustable intraocular lens in human eyes

Methods Clinical long-term monitoring of the initial 38 eyes of 38 patients with senile cataract after implantation of the *Acri.Tec AR-1 PC/IOL including a control group.

Results Median follow-up was 25 (range 6 to 52 months). Throughout the entire period of observation all eyes were behaving clinically in the same way as if implanted with a conventionel PC/IOL. 2 eyes were adjusted surgically 2 weeks after implantation. 19/38 eyes underwent Nd:YAG laser capsulotomy after a median period of 12 (range 6 to 43) months after implantation. Median change of spherical equivalent between 1 month and the last visit was 0 (range – 0.5 to + 0.5) diopters. At the last visit median best visual acuity was 0.7 (range 0.2 to 1.0) for eyes with the *Acri.Tec AR-1 PC/IOL and 0.8(range 0.3 to 1.0) for the control group. Both eyes having undergone adjustment surgery had visual acuity of 0.8 rsp 1.0 with stable refractions 45 rsp. 42 months after adjustment surgery.

Conclusion The *Acri.Tec AR-1 PC/IOL implanted into the capsular bag of adult human eyes is a safe PC/IOL. Refraction is predictably adjustable after implantation. It remains stable before and after Nd:YAG laser capsulotomy or after surgical adjustment of the refraction. This type of IOL may prove helpful especially in pediatric cataract surgery to avoid the development of amblyopia and in adults when precise refractive outcome is important either because of individual preference of the patient for a preferred refraction or because of intendend monovision to reduce spectacle dependence to a minimum.

Commercial interest

6441

Effect of dietary omega-3 and omega-6 fatty acids on IOP elevation, electroretinographic changes and retinal ganglion cell loss in a rat model of glaucoma induced by laser

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Purpose To test the efficacy of dietary omega-3 and omega-6 fatty acids in a rat model of glaucoma induced by laser photocoagulation.

Methods Rats were fed for 3 months with a diet containing either: 1) 17% of omega-3 fatty acids (10% EPA + 7% DHA), 2) 10% of omega-6 fatty acids (as GLA), or 3) a combination of both omega-3 and omega-6 fatty acids (10% EPA + 7% DHA + 10% GLA), by comparison with a control group of animals fed with a standard diet deprived of EPA, DHA and GLA. After 3 months of diet, glaucoma was induced in one eye of the animal by laser.IOP was regularly measured and the retinal function was evaluated by electroretinography (ERG) for 3 months. At the end of the experiment, the loss of the retinal ganglion cells in both operated and fellow eyes was evaluated after retrolabelling using Fluorogold.

Results A significant increase of IOP was observed in the laser treated-eyes: 49±16 mmHg compared to 11±1.2 mmHg in the fellow eyes, after photocoagulation. IOP elevation was similar in each group. The ERG b-wave amplitude was significantly reduced by approximately 70% 8 and 12 weeks in the laser treated-eyes.None of the diets efficiently prevented the loss of the retinal ganglion cells.

Conclusion Neither dietary omega-6 nor omega-3 fatty acids efficiently prevented the development of glaucoma in our rat model, as illustrated by the absence of effects against IOP elevation and loss of retinal ganglion cells. Further works are warranted to elucidate the mechanisms and consequences of the effects of omega-6 fatty acids on the retinal function as assessed by ERG.

6442

Effects of antioxidants on ocular blood flow in the LPS-induced inflammation model in humans

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Purpose We set out to investigate whether the AREDS medication is capable of normalizing retinal blood flow reactivity to systemic hyperoxia in a human lipopolysaccharide (LPS) model.

Methods The present study was a randomized double masked placebo-controlled parallel group study in 21 healthy volunteers. The infusion of LPS was used as a standardized experimental model of systemic inflammation associated with enhanced oxidative stress and widespread endothelial dysfunction in humans. Ocular hemodynamic measurements were performed before endotoxemia and 4 hours after the subjects had received an LPS bolus. At each of these time points the retinal vascular reactivity to hyperoxia was studied. After the first trial day the subjects had to take either the AREDS medication (n=14) or a placebo (n=7) for 14 days. Thereafter a second trial day was performed on which the time schedule exactly followed the first day as described above.

Results As expected LPS induced retinal vasodilatation ($p < 0.01$) together with an increase in retinal leukocyte density, which occurred because to systemic leukocytosis. The oxygen induced decrease in retinal blood flow was reduced after infusion of LPS ($p < 0.01$). This effect was partially restored after intake of the AREDS medication, but not after intake of placebo ($p = 0.04$) between groups.

Conclusion Our findings support previous data showing that LPS induces impaired endothelial function. This effect was significantly reduced by the AREDS medication. Our model may be used to study the effects of various antioxidants and the components of the AREDS medication on oxidative stress-induced vascular dysregulation in the human retina.

6443

No-induced retinal vasodilatation is maintained in type 1 diabetes

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Purpose Various studies have shown that retinal vessels in patients with diabetes mellitus have a reduced capacity to adapt to changes of perfusion pressure. The mechanisms lying behind this abnormal autoregulation have not been completely identified yet. Histomorphological changes of retinal vessels in diabetes could possibly reduce their capacity of vasodilation and vasoconstriction. To test this hypothesis we compared the response of retinal vessel diameters to systemic glyceryl trinitrate (GTN) in patients with diabetes and healthy controls.

Methods 20 patients with insulin dependent diabetes mellitus featuring no or mild non-proliferative diabetic retinopathy were included into this study. In addition, 20 healthy and age-matched subjects were included as controls. Retinal vessel diameters were measured before and immediately after sublingual application of 0.8 mg of the NO-donor GTN. The IMEDOS Retinal Vessel Analyzer was used for continuous measurement of diameters of retinal arteries and veins.

Results Oral application of GTN induced vasodilatation of retinal arteries and veins. This effect was not different between patients with diabetes and healthy controls. Systemic arterial blood pressure was reduced in both groups after GTN application, but to a comparable degree.

Conclusion The present study indicates that in patients with no or mild non-proliferative diabetic retinopathy the vasodilatory response of retinal vessels to a direct NO-donor is maintained. This indicates that abnormal retinal autoregulation in diabetes mellitus, as observed previously, is not a consequence of generally reduced retinal vascular reactivity.

6444

Intracameral moxifloxacin (Vigamox): in vitro safety on human ocular cells

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Purpose The 4. generation fluorochinolon moxifloxacin covers most isolates causing endophthalmitis. It is safe and effective for systemic and topical use, however only very limited data is available on prophylactic intracameral administration to prevent endophthalmitis. This study investigates the safety of Viagamox (moxifloxacin) for intracameral application in a cell culture model

Methods Endothelial toxicity of Vigamox (moxifloxacin) was evaluated in cultured human corneas. Toxic effects regarding primary human RPE, trabecular meshwork cells (TMC) and corneal endothelial cells (CEC) were evaluated after 24h and under conditions of oxidative stress. By treating cells with TNF-a, LPS and IL-6 the effects of moxifloxacin on viability under conditions of inflammation were investigated. Toxicity was evaluated by measuring the inhibition of cell proliferation (MTT). Cell viability was quantified by a microscopic live dead assay

Results No corneal endothelial toxicity could be detected after 30 days treatment with 500µg/mL moxifloxacin. RPE,TMC,and CEC showed adverse effects on proliferation and viability at concentrations higher than 150µg/mL moxifloxacin only. Preincubation with TNF-a, LPS, IL-6 or H2O2 and subsequent treat with moxifloxacin concentrations up to 150µg/ml for 24h had no significant effect on proliferation and viability

Conclusion Moxifloxacin concentrations up to 150µg/mL had no significant toxicity on RPE, TMC, CEC and human corneas. The MIC90 of moxifloxacin for common pathogens of endophthalmitis is known to be in the range of 0.25 - 2.5µg/mL. Therefore, intracameral use of moxifloxacin at concentrations up to 150µg/mL may be safe and effective to prevent endophthalmitis after intraocular surgery

6445

Lipid and fatty acid profile of the retina, RPE/choroid and lacrimal gland, and associations with dietary fatty acids in human subjects

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Purpose The contribution of dietary lipids to the accumulation of lipids in the retina during ageing and in the course of age related maculopathies remains under debate. Our objective was to establish associations between fatty acid profiles of ocular structures, and adipose tissue as a surrogate for the past dietary intake of the subjects.

Methods Lipids and fatty acids were analyzed by tandem thin-layer chromatography-flame ionization detection and gas chromatography-flame ionization detection from the neural retina, RPE/choroid, lacrimal gland and adipose tissue, collected from 19 women and 8 men, aged 59–95 years.

Results DHA concentrations in the neural retina were positively associated with those in cholesteryl esters (CE) from RPE/choroid, and negatively associated with DHA concentrations in phospholipids (PL) from RPE/choroid. DHA in orbital fat was positively associated with DHA in lacrimal gland, whereas no significant association was observed in the other ocular structures. Linoleic acid in orbital fat was positively associated with linoleic acid in the lacrimal gland, followed by neural retina and CE from RPE/choroid, and slightly correlated with PL from RPE/choroid. Other fatty acids that are exclusively of dietary origin such as trans fatty acids were detected in orbital fat, lacrimal gland, PL and CE from RPE/choroid.

Conclusion DHA in the neural retina was poorly associated with its dietary intake, on the contrary to others fatty acids like linoleic acid. Although epidemiological studies have reported the benefit of dietary DHA for the prevention of AMD, the relevancy for supplementing patients with DHA is questioned.

6446

Automatic estimation of the arteriolar-to-venular diameter ratio (AVR) in retinal images

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Purpose The Arteriolar-to-Venular diameter Ratio (AVR), a parameter derived from vessel caliber measurements in a specific region of retinal images, is used as a descriptor of generalized arteriolar narrowing. We developed a computerized system to compute AVR in a totally automatic way.

Methods Images are at first enhanced to highlight the vessel network, which is then traced by a vessel tracking algorithm. From the detected vessel structure, the position of the optic disc is derived and the region inside which the AVR data are to be measured is determined. Vessels within this region are classified as either arteries or veins, their caliber estimated and the AVR parameter is eventually computed. Results provided by the system have been compared with manually derived AVR values on 20 eye fundus images.

Results Mean and SD values from the two sets of measurements are the same, and automatic/manual ratios have an average value of 1 and 95% confidence interval of (0.98-1.02). The correlation coefficient between the two methods is 0.88. In only two images the ratio is appreciably different from unity, 1.14 and 0.89 respectively. A detailed analysis of these cases revealed that in each image the wrong classification of one vessel only was the cause for these unsatisfactory results. When these misclassifications are manually corrected, e.g. with a quick editing tool that can be easily made available to the user, the ratios become 0.95 and 0.99, respectively, and the overall correlation coefficient becomes 0.97.

Conclusion Additional evaluation on a larger set of images, acquired from subjects exhibiting wide variations of AVR, will be performed in order to fully assess the reliability and clinical applicability of this automatic procedure.

6447

Changes in ocular signs and symptoms when switching from preserved latanoprost 0.005% to preservative-free tafluprost 0.0015%: phase IIIb study in patients with open-angle glaucoma or ocular hypertension

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Purpose This open-label, multinational, phase IIIb study investigated the changes in ocular signs and symptoms when patients were switched from preserved latanoprost 0.005% to preservative-free tafluprost 0.0015% (q.d. at 20:00) for 12 weeks.

Methods Patients with open-angle glaucoma or ocular hypertension who had received latanoprost for at least 6 months and had at least 2 ocular symptoms or one symptom and one sign were enrolled (n=158). Change from screening in ocular symptoms and signs were the main endpoints. Data from the 6-week analysis are reported here.

Results After switching to preservative-free tafluprost, the proportion of patients with at least mild symptoms decreased: irritation/burning/stinging sensation 56.3% to 30.8%, foreign body sensation 46.8% to 25.6%, tearing 49.4% to 28.8%, itching 55.1% to 25.6% and dry-eye sensation 64.6% to 35.3%. Decreases in proportions for abnormal signs were: tear break-up time 94.9% to 76.9%, corneal fluorescein staining 81.6% to 52.6%, conjunctival fluorescein staining 84.2% to 53.8%, blepharitis 60.1% to 42.3%, conjunctival hyperaemia 84.2% to 69.2% and tear production 71.5% to 61.5%. All changes were statistically significant.

Conclusion Switching patients from preserved latanoprost to preservative-free tafluprost clearly reduced ocular symptoms and signs.

Commercial interest

6448

Comparison of Lucentis monotherapy vs. combination therapy for neovascular AMD

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Purpose To compare the efficacy of neovascular AMD(NAMD) treatment options by monthly Lucentis(L)(monotherapy), combination therapy utilizing RF-PDT(P), and Lucentis combined with Kenalog(LK).

Methods IRB-approved retrospective chart review of therapies administered only as-needed over 20 months. Inclusion criteria: active primary/recurrent subfoveal or juxtafoveal CNV (all types); Snellen BCVA ≥20/400. Exclusion criteria: f/u <3 months or noncompliance; subfoveal atrophy/fibrosis. Kenalog offered with Lucentis when active PED or subretinal fibrosis threatening fovea. RF-PDT combined with Avastin ± Kenalog(PA±K) or Kenalog alone(PK). Primary outcome measure: mean change in Snellen VA from baseline at last f/u. Secondary outcome measures: incidence of moderate/severe VA change; resolution of leakage; treatment-free interval.

Results 21 eyes received L; 16 eyes LK; 10 eyes RF-PDT (5 PA±K; 5 PK). Mean f/u was 8.8 (range 3–18) months. At last f/u, mean Snellen VA for L improved -0.25; RF-PDT remained stable +0.06 overall (although PA±K improved -0.135; PK worsened +0.27); LK worsened +0.13 logMAR units (p=0.02 for L vs. LK). VA loss <15 letters was greater for L>PA±K>LK>PK, occurring 91%, 80%, 75%, 60%, respectively. 14% L gained ≥30 letters. 20% PK lost ≥30 letters. Leakage resolved greater for L>PA±K>LK>PK, occurring 86%, 80%, 69%, 40%, respectively.

Conclusion At intermediate-term f/u, Lucentis monotherapy administered only as-needed had results similar to larger studies and was the most effective in maintaining or improving VA in NAMD. Lucentis monotherapy had the greatest leakage resolution and treatment-free interval. RF-PDT with Avastin was more effective than with Kenalog alone. Kenalog supplementation to Lucentis unlikely provided added benefit.

▪ 6451
Scientific Community - contact networking, research collaboration on a global scale

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Purpose In the era of globalisation and growing competitiveness research projects are conducted by big teams of scientists located in distant geographical locations. Management of collaboration of such diffused team is a big challenge even for experienced leaders, which requires a lot of efforts and careful logistics.

Methods Virtual Research Groups is an internet-based platform for management and conduction of multi-center research projects. The platform consists of four modules: research module, information module, communication module and administration module. The system allows complete supervision and control of investigators and approval of entered protocols if needed. Simple protocols can be set up easily by investigators but more complicated ones are custom-made and contain validation algorhytms. Statistical tools are available and are set up individually for the project according to the investigators requirements. Information module provides up-to-date literature on the subject of investigation along with information on available grants and other financial support, conferences and even suggestion on scientists whos profiles match the subject of investigation, who might be invited to join the group if expansion is desirable.Financial and scientific settlement of the project is one of the new features of the Virtual Research Groups.

Conclusion The platform can be equally used for spontaneous creation of research teams as well as for management of structured research consortia or multi-center clinical research

Commercial interest

▪ 6452
Open evaluation of science: can we simply say “no, thank you?”

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In today’s world of information doubling at faster rates because of rapid technological and biomedical advances nations must pay closer attention to the productivity and creativity that can be obtained from their universities. A professor’s intellectual property may have important patent consequences. Thus, universities must foster lines of communication that aid the professor in making critical decisions not only about the advance but its potential to generate a revenue stream. In the same light, universities must also be able to evaluate the contribution and the potential of a lab to make future contributions in an objective manner since all laboratories and projects cannot be funded in a nation/university due to the high cost of doing so. In the past, this evaluation has taken the form of a grant, which depends on peer evaluations. Now however, due to ever increasing flow of information, which generates new technologies, additional evaluation processes must be in place so the funding can be prioritized and revenue not wasted. This calls for a rapid evaluation process, taking advantage of the increase in informational flow. This process must be as objective as possible, providing documentation of the ability to generate successful projects without damaging continuing research and hurting the ability of high risk projects to reach fruition.

▪ 6453
Community Services enter professional territory - what is in there for us?

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International collaboration - a cornerstone of today’s research - requires state-of-the-art communication tools. There are a number of dedicated services for scientists in the internet which provide networking and social services, such as SciVee, SciLink, Community of Sciences and Index Copernicus, just to name a few of them. Each of them have unique functionalities which make the service useful and interesting. The ideal scientific service should provide maximum security and excellent networking capabilities. Scientists should be able to search for collaborators not only by specialty, keywords and geographical location, but also by special research skills and available lab equipment. It would be helpful if some kind of achievement evaluation could be added into the search service. The second important property of an ideal scientific service should be profiled information delivery which could save a precious researchers time. Last but not least a real collaboration tools should be added to enable online investigations. In my talk I will try to give an answer to the question “what is in there for us?”.

Posters

EVER 2008

ABSTRACTS

THURSDAY

FRIDAY

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October 1-4, 2008
Portoroz, Slovenia

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Philatelic aspects on WHO Year Glaucoma 2008

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Purpose WHO dedicates anno 2008 to Glaucoma. Here we like to present philatelic aspects from Hippocrates to modern Glaucoma Screening, spiced with issues of stamps in 2008.

Methods Collecting stamps.

Results To be seen.

Conclusion Philatelic/historical aspects of glaucoma may induce a humble view.

402
Ghrelin's MRNA levels in the developing rat's eye

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Purpose The aim of the present study was to investigate the expression of ghrelin the late phase of development of the rat eye.

Methods Wistar rats (n=16) were euthanized 22 days post-conception (n=8) or 15 days after delivery (n=8). The eye globes were enucleated and dissected, and the cornea, iris, lens, retina and sclera were microdissected. A portion of the gastric fundus was also collected. The lens could only be isolated 15 days after birth.To evaluate the levels of ghrelin mRNA in the distinct eye tissues and the stomach an equal amount of total mRNA of each sample (50ng) underwent two-step real-time RT-PCR with specific primers. Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) and β actin were used as internal controls. Data is presented as mean±SE in relative expression units. Comparisons were performed with two way ANOVA.

Results GAPDH and β actin mRNA levels differed between tissues, precluding their usage as internal control genes, nevertheless, β-actin levels were similar in the iris and retina and the expression of ghrelin normalized for β-actin did not differ at birth or 15 days after between iris (1.0±0.3 and 0.4±0.3, respectively) and retina (1.2±0.3 and 0.5±0.3, respectively). Absolute ghrelin mRNA levels were also not different at birth or 15 days after in each of the tissues evaluated but were higher in the retina (1.0±0.2) than in the cornea (0.4±0.1), sclera (0.5±0.1) and gastric fundus (0.3±0.1). The lens showed the lowest value of expression (0.1±0.0).

Conclusion Ghrelin is more expressed in the newborn retina than in the stomach, lens, cornea and sclera. The expression in the iris and retina is similar. The high expression of ghrelin in some tissues of the eye at these stages suggests it may have a role in the eye's development.

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Form-deprivation myopia in the guinea pig: scleral myofibroblasts and biomechanics

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Purpose To investigate the effect of induced myopia on cell populations and biomechanical properties of the sclera.

Methods Week-old guinea pigs (n = 29) were monocularly deprived (MD) of form vision for 14 days. Total cells and myofibroblast (contractile) cells were visualized using DAPI and α-smooth muscle actin (α-SMA) antibodies respectively in 20 µm thick scleral sections. Ocular biomechanics were investigated by raising the IOP to 50 mmHg for one hour in anaesthetized animals. Ultrasound biometry measures were made before, during (every 10 min) and after raising the IOP.

Results As expected, MD eyes developed significant axial myopia. Generally, MD had no effect on total cell number or myofibroblast number compared to control or normal eyes. However, in MD eyes a significant decrease in total cell number was observed between the optic nerve and 10° nasal (equivalent to human temporal myopic crescent). Overall, myofibroblasts accounted for 63.67 ± 1.65% of scleral cells (mean ± SEM: three groups combined; n = 30 eyes). On increasing IOP, there was significant elastic expansion of the vitreous chamber depth (VCD) in deprived and control eyes but not in normal eyes. The VCD creep response to increased IOP stabilized at equivalent lengths to MD and control eyes.

Conclusion A high proportion of scleral cells are myofibroblasts, but cell number is unaffected by MD. The biomechanical response of MD eyes differs from normal eyes, suggesting that something other than myofibroblast cell number controls axial length.

404
Contribution of Müller cells to blue light injury

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Purpose Excessive light causes both damage to the photoreceptors and pigment epithelium, and degenerative alterations in the inner retina, for example apoptotic death of ganglion cells and a decrease in the thickness of the inner plexiform layer. We investigated whether gliotic alterations of Müller cells may contribute to the light-evoked degenerative alterations in the inner retina.

Methods Retinas of adult rats were exposed to blue light for 30 minutes. At various time periods after treatment, retinal slices were immunostained against potassium and water channel proteins. Recordings of potassium currents were made in isolated Müller cells, and the swelling of Müller cell bodies was recorded in retinal slices.

Results After blue light treatment, Müller cells displayed hypertrophy and an increase in glial fibrillary acidic protein. The immunostaining of the glial water channel aquaporin-4 was increased in the outer retina while the immunostaining of the photoreceptor water channel aquaporin-1 disappeared. Blue light treatment resulted in a decrease and mislocation of the glial Kir4.1 protein in the whole retinal tissue, and a decrease in the potassium conductance of Müller cells. Hypoosmotic stress evoked a swelling of Müller cell bodies in blue light-treated retinas that was not observed in control tissues.

Conclusion Gliosis of Müller cells associated with a loss of functional Kir4.1 channels will result in a disturbance of the retinal potassium and water homeostasis contributing to the degenerative alterations of the inner retina after exposure to blue light.

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Quantification of the photoreceptors of healthy retinas in rat by flow cytometry

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Purpose The primary purpose of this study was to evaluate the potential to quantify photoreceptor population in the retina of healthy Spargue –Dawley rat in an accurate quantitative way by using flow cytometry. As far as we know, flow cytometry has not been used for photoreceptor quantification.

Methods Rats were killed and the eyes were enuclated to achieve retinal dissection. Tissue dissociation was accomplished with trypsin. Retinal cells were washed in PBS and permeabilized. The permeabilization was followed with the primary antibody incubation and then with the secondary antibody incubation.The analysis achieved in a flow cytometer. Flow cytometry was to measure physical and chemical characteristics in the photoreceptor population. Individual cells flow in suspension past one or more lasers scattering light and emitting fluorescence.

Results Quantification of photoreceptors was possible using flow cytometry. In this preliminary study, the photoreceptors had the 44,661 % in the hole mixed retinal population after anti-rhodopsin staying.

Conclusion Flow cytometry can be used to quantify the different neuronal populations in control healthy eyes and this verification will be very useful in the futture in studies in apoptosis or proliferation of these cells.

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Localization of cathepsin x in the mouse retina

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Purpose Cathepsin X is a recently identified member of the papain-like cysteine protease family that is expressed by many cell types. The in vivo functions of Cathepsin X are unknown. Hence, the aims of this study are to localize cathepsin X expression in the mouse retina and to compare the retinal morphology and ERG function of cathepsin X knock-out mice (Ctsx-/-) to congenic wild type C57Bl/6 mice (Ctsx+/+).

Methods Left eyes of adult mice were prepared for paraffin- and right eyes for cryo-sections. Histology was accomplished by Hämalaun-Eosin and PAS staining after depigmentation. Expression of cathepsin X and the proliferation marker Ki67 were investigated by immunohistochemistry. Retinal function was tested by ERG.

Results Cathepsin X expression in WT mice accumulates along the external limiting membrane. Additionally, a netlike pattern of cathepsin X was found around the neuronal cells in the inner nuclear and ganglion cell layer. There is no significant difference between cathepsin X knock-out and WT mice in retinal morphology, cell proliferation or ERG readings.

Conclusion We found prominent expression of cathepsin X in WT mice retina. Normal retinal morphology and ERG function in cathepsin X knock-out mice, however, suggest that other cathepsins might compensate for the loss of retinal cathepsin X.

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Cx43 internalization is mediated by the ubiquitin-binding adaptor protein Eps15 in retinal endothelial cells

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Purpose Intercellular communication through gap junctions (GJIC) is important in maintaining the integrity of the blood-retinal barrier. GJ are multimeric structures composed of proteins called connexins. Modifications on stability or subcellular distribution of connexins have a direct impact on the extent of GJIC. The purpose of this study is to investigate the molecular mechanisms involved in the regulation of connexin 43 (Cx43) stability at plasma membrane by eps15 in retinal endothelial cells.

Methods To investigate the interaction of Cx43 with eps15, Cx43 was selectively immunoprecipitated (IP), followed by western blot (WB) and probing with antibodies against eps15. To investigate the role of eps15 in Cx43 stability and subcellular distribution cells were transfected with a dominant negative form of eps15 or siRNA targeted against eps15, cell extracts were WB and probed with antibodies against Cx43. Alternatively, cells were fixed and simultaneously stained with antibodies against Cx43 and eps15, and imaged by confocal microscopy.

Results Data obtained in this study indicates that eps15 interacts with Cx43 mediating its internalization from the plasma membrane. When the normal function of eps15 is disrupted by the presence of a dominant negative form of the protein or through silencing of the eps15 gene with siRNA, Cx43 accumulates at the plasma membrane.

Conclusion Data suggests a novel protein interaction between Cx43 and eps15 that mediates the plasma membrane stability of Cx43. Disruption of this interaction may impact on GJIC, contributing to endothelial cell dysfunction associated with the breakdown of the blood-retinal barrier, as observed in diabetic retinopathy. Supported by POCI/SAU-MMO/57216/2004

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Spinule number per cone pedicle is a biomarker of predatory behavior in teleosts

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Purpose Teleots are a successful vertebrate group, constituting more than 50% of vertebrate species. These fishes are the only vertebrate group that presents spinules from the lateral dendrites of retinal Horizontal cells into cone pedicles. A way to study the degree of predatory behavior is measuring patterns of microwear on tooth surfaces. These patterns are related to trophic adaptations and produced by the abrasives in food, during feeding. The aim of this work was to compare the number of spinules per cone pedicle with tooth microwear parameters and predatory behavior, in three families of teleosts.

Methods Light-adapted fishes were sacrificed and their retinas processed for transmission-electron-microscopy studies. The number of spinules, per cone pedicle was measured. Several lower premaxillary teeth from each fish were used for microwear analysis with scanning electron microscopy. We measured the density, mean length, and breadth of micro-features, of the teeth.

Results The number of spinules per pedicle was two fold greater (≈9 spinules/pedicle) in the moronidae family that in the labridae and sparidae ones (≈4 spinules/pedicle). In turn, the dental microwear parameters presented an inverse relationship to the number spinules per pedicle. The density, mean length and breadth of teeth micro-features were lower in moronidae family than in labridae and sparidae ones.

Conclusion The amount of spinules per pedicle correlates positively with predatory behavior and negatively with dental microwear parameters. These data support the hypothesis that spinules and microwear are biomarkers of trophic adaptations in teleost fishes.Spanish Grants BFU2004-03727-C02-02 and 01/BFI and GV04B-521

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Receptor retinoid-binding protein (IRBP) binds cone outer segments differentially in light and dark

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Purpose Vision requires the continuous exchanges of visual cycle retinoids through the interphotoreceptor matrix (IPM). IRBP, which is synthesized by the rods and cones, is the major soluble protein component of the IPM. In the matrix, IRBP protects and targets retinoids trafficking between the photoreceptors, RPE and Muller cells.

Methods Organ culture of isolated Xenopus retina was used to characterize the cellular binding of recombinant full-length IRBP protein free of fusion tags. Xenopus was selected for these studies because of their large photoreceptors which are easily detached in both light and dark-adapted states. xIRBP was covalently bound to the fluorescent dye Alexa-647 at 1:1 molar ratio. Labeling had no effect on the retinoid ligand-binding properties of the protein. Xenopus retinas were detached and incubated with xIRBP-647 for 1 hour at room temperature in light and dark. The distribution of xIRBP-647 was studied by confocal microscopy in retinal flat whole mounts and cryosections.

Results In light, xIRBP-647 bound to cone outer segments with lighter labeling of the rod outer segments. Retinas incubated with the xIRBP-647 in the presence of a 50 fold excess of unlabeled protein showed reduced cone and rod outer segment labeling. In dark, outer segment binding was not appreciated. Positive staining near the level of the external-limiting membrane was noted in dark but not light.

Conclusion The binding of xIRBP-647 to cells of the isolated retina was different in light versus dark. Our data suggests that the direct interaction of IRBP with the outer segments and Muller cells plays an important role in retinoid trafficking in the the visual cycle.

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Selective estrogen receptor modulators regulate IL-6 inflammatory response in ARPE-19 cells

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Purpose Recent findings reveal that Toll-like receptors (TLRs) and innate immunity participate in the pathology of age-related macular degeneration (AMD). Many studies indicate that estrogens and selective estrogen modulators (SERMs) modulate inflammatory responses, but their effect on the development of AMD is weakly understood. In this study, we investigated the regulatory role of various SERMs (provided by Hormos Medical Ltd.) on IL-6 expression in human retinal pigment epithelial cells (ARPE-19).

Methods ARPE-19 cells were exposed to lipopolysaccharide (LPS; TLR 4 agonist) with simultaneous exposure to various SERMs and the secretion of IL-6 cytokine was analyzed by ELISA. The estrogen receptor alpha and beta were qualitatively measured by RT-PCR. To study the effect of various SERM treatments of estrogen response element (ERE) -mediated transcription, the ARPE-19 cells were transiently transfected with ERE-luciferase vector. The activity of ERE was measured by Luciferase assay.

Results Simultaneous exposures to LPS and SERM-320 reduced the IL-6 expression levels in ARPE-19 cells compared to LPS exposure alone. The RT-PCR analysis showed that ARPE-19 cells expressed estrogen receptor alpha but not beta proteins. Interestingly, SERM-320 did not increase the activity of ERE in ARPE cells. This reveals that SERM-320 is implicated in regulation of IL-6 expression, but is not mediated through estrogen response element.

Conclusion Our findings reveal that SERM-320 is a novel compound to suppress innate immunity response in human retinal pigment epithelial cells.

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Activation of autophagy induced by 7-Ketocholesterol and dysfunction of RPE in AMD

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Purpose Retinal pigment epithelial (RPE) cell death is a hallmark of age-related macular degeneration (AMD). Lysosomal impairment in RPE cells is one of the traits present in the pathology of AMD. Authophagy, a process whereby proteins and subcellular organelles are degraded in the lysosome is activated by several stress stimuli. RPEs internalize large amounts of oxidized lipids including 7-ketocholesterol, the most cytotoxic of oxysterols. The purpose of this study is to determine if exposing RPE to 7-ketocholesterol can act as a stimulus to induce autophagy and thus account to the dysfunction of the RPE.

Methods RPE cells where incubated with 7-ketocholesterol (20 ug/ml) for 6 or 12 h, or deprived from nutrients for 12h. To assess Macroautophagy cells were transfected with EGFP-LC3 plasmid. Formation of autophagic vesicles was assessed by confocal microscopy. LC3 processing was measured by western blot with antibodies against GFP. Chaperone mediated autophagy (CMA) was assessed by determining if chaperones interacted with Lamp2, performing Lamp2 immunoprecipitation.

Results 7-ketocholesterol induces the formation of autophagic vesicles and the processing of the LC3-I into LC3-II, both hallmarks of Macroautophagy, Moreover treatment with 7-ketocholesterol increases the interaction between Lamp2 and Hsc70, Hsp90 and Hsp40, suggesting that this cholesterol oxide also stimulates CMA.

Conclusion RPE cells undergo Macroautophagy and CMA activation when exposed to 7-ketocholesterol. At early stages both may act as a cell survival mechanism whereas prolonged exposure may result in macroautophagic cell death.

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The role of FGF2 in the in vitro proliferation and angiogenesis of human choroidal endothelial cells

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Purpose Age-related macular degeneration (AMD) is the most common cause of irreversible visual loss in elderly populations in the western world. The mechanism of this disease is not yet fully understood, although vascular endothelial growth factor (VEGF) is thought to be the most significant growth factor in AMD, other growth factors, including FGF2 also stimulates the proliferation of human choroidal endothelial cells (hCEC). These factors may explain the only partial success of current anti-VEGF AMD treatments.

Methods hCEC were isolated from cadaver eyes and cultured in EBM2-MV medium as previously published. hCEC proliferation after exposure to VEGF and FGF2 was measured using the WST-1 assay and angiogenesis assessed using a double layer Matrigel technique. Western blotting was used to examine the intracellular signalling stimulated by FGF2 and VEGF.

Results hCEC proliferation was increased in response to both FGF2 and VEGF. This effect was cumulative, indicating that these work through different intracellular signalling pathways. Western blotting identified common and differential intracellular signalling between the two growth factors.

Conclusion Currently VEGF is thought to be the most important growth factor which stimulates neovascularisation leading to AMD and treatments developed reflect this. However, these results show that FGF2 also stimulates neovascularisation and may play a role in AMD development. A treatment which targets downstream signalling common to both growth factors may provide a more targeted and therefore successful treatment.

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Development of immunostaining of cell cycle related proteins in flat mounted corneal endothelium

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Purpose Immunostaining of cell cycle proteins is necessary for the study of the proliferative status of corneal endothelial cells (EC). Most studies use cross sections, which offer direct access to intracellular antigens but allow visualization of only few cells, without giving a global view of an intact endothelium. We developed protocols for immunostaining of ECs of flat mounted corneas

Methods Studied proteins: 4 proteins with a known expression pattern (intra-membranous ZO-1, cytoplasmic α actin, nuclear hnRNP and H3 histone) and 8 others, already described within EC: 3 cell cycle inhibitors (P27, P21, P16); 3 proliferation markers (PCNA, MCM2, Ki67), cyclins D1, and E. Fresh and organ cultured (OC) human corneas were used. Fixation/permeabilization: paraformaldehyde (PFA), acetone, methanol, ethanol, Hg, Zn, acetic acid, triton, sodium docecyl sulfate, alone or in combination. Antigen retrieval: heating and biochemical or chemical agents. Patterns of expression were also compared between endothelium and epithelium

Results There was no universal protocol. Most of the time 0.5% PFA gave the best results, but for p21, and cyclins, specific protocols were necessary. Homogeneous staining was always obtained with a clear subcellular localization (nuclear or cytoplasmic). OC did not globally modify expression within EC whereas several nuclear or cytoplasmic translocations were observed within the epithelium

Conclusion The use of protocols specifically designed for the endothelium of whole intact flat mounted corneas would allow a better localization of cell cycle proteins. They will be especially useful during attempts to alter the cell cycle and trigger EC proliferation. Grant: Fondation de l'Avenir 2007 ET7-468

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Cell cycle genes expression in human corneal endothelium: study by microarray and qRT-PCR

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Purpose To use microarray and qRT-PCR to identify changes in cell cycle genes expression in human corneal endothelial cells (CEC) from " in vivo", post mortem, and organ cultured (OC) corneas, and also in confluent primary culture and immortalized CEC

Methods Total RNAs were extracted. "in vivo" corneas were obtained during penetrating grafts for keratoconus, immediately after trephination, post mortem corneas (body donation to Science) within 24H after death. OC corneas were stored for 15D. Descemet was peeled off to avoid contamination with other cell types. Biotin-labeled cRNA probe was synthesized from RNAs extract and hybridized to the pretreated Oligo GEArray Human Cell Cycle Microarrays, which covered 112 key genes of cell cycle. Microarrays were performed in duplicate. Gene expression of 'in vivo' CEC served as a reference. A difference >1,5 fold of the transcriptional level was considered significant. qRT-PCR were done on cyclin E1; cyclin D1; p16INK4a; p21CIP1 and p27Kip1 to confirm the microarrays

Results Compared to 'in vivo' CEC from OC corneas had 1 upregulated gene (CDK7) and 26 downregulated (CCNE1; CDKN1B; MCM2; RB1…), post mortem corneas had 2 up(CDC28; CDK7) genes and 16 downregulated (ATM; BAX; CDC16; CDKN1B…), primary culture had 1 up(CKS2) and 9 downregulated (BAX; CCNE1; CDK2; MCM2…), and the immortalized cell line had 16 up (ATM; CCNH; CKS2; MCM2…) and 2 downregulated genes (BAX; CDK5R2). qRT-PCR of the 5 aforementioned genes validated the Microarrays data

Conclusion Microarray seems to be a powerful tool to better understand the proliferative status of human CEC. It will help to choose the targets we need to alter in order to trigger CEC proliferation. Grant: Fondationdel'Avenir2007 ET7-468

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A novel cytocompatible thermoresponsive co-polymer for corneal tissue engineering

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Purpose Using thermoresponsive polymers as a substrate to expand healthy sheets of transplantable cells for the immediate cover of wounds is an attractive novel treatment for ocular surface reconstruction. However, the cytocompatibility of thermoresponsive polymer and the effect on cell expansion must be assessed. Changes in the expression of secretory proteins in response to different microenvironments can be used to determine a more precise suitability of polymers in cell culture at molecular level. We assess the specific cytocompatibility of a novel thermoresponsive co-polymer with the future goal of its use in corneal reconstruction.

Methods Protein was extracted from conditioned medium of SV-40 immortalised corneal cell line (CCL) cultured on both thermoresponsive polymer and tissue culture plastic. Proteins were separated by two-dimensional gel electrophoresis and the resulting spot map profiles were differentially compared. Differences in the protein profiles were characterised by mass spectrometry and western blot analysis.

Results Differential analysis of whole cell extract, and conditioned medium from CCL on plastic identified over 50 potentially secreted proteins. Mass spec characterisation confirmed these proteins as secretory, but also suggested healthy cell expansion was occurring. Comparison of CCL on plastic and thermoresponsive polymer revealed few differences suggesting the polymer did not effect cell expansion.

Conclusion Thermoresponsive polymer is cytocompatible for CEC cell growth. This novel co-polymer maybe a potential substrate for the future ex-vivo engineering of transplantable cell sheets, for improved corneal reconstruction

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Myofibroblast and smooth muscle actin in scarred corneal stroma

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Purpose Mohan et al, (2003) hypothesised that after corneal injury, the site of injury is invaded by myofibroblasts (MFBCs) derived from dividing keratocytes. We report here the distribution of myofibroblasts (MFBCs), and cellular location of α-- smooth muscle actin (α--SMA) in scarred cornea.

Methods Three penetrating keratoplasty buttons, two with post-zoster scarring and one with hypertrophic dendriform epitheliopathy, were fixed in: 1) 2.5% glutaraldehyde containing cuprolinic blue for ultrastructural studies and 2) 4% paraformaldehyde for immunogold localisation. Primary α--SMA and vimentin antibodies were localised by gold conjugates.

Results Large numbers of MFBCs were observed in the sub-epithelial collagenous pannus, posterior stroma and posterior collagenous layer in these corneas. The MFBCs were very large in size, lay in layers and occasionally fused with each other. Labelling for α-SMA was very strong in all MFBCs. Labelling of α-SMA was also observed in basal epithelial cells. MFBCs contained very prominent rough endoplasmic reticulum, vimentin filaments and large nuclei. Significantly, large proteoglycans (nm) and collagen fibrils (nm) were present around these cells.

Conclusion It has been suggested that cytokynes released from the overlying epithelium act to maintain the myofibroblast phenotype (Jester et al 1999a, 1999b). We hypothesise that MFBCs synthesise large amounts of proteoglycan which disrupt the organisation of collagen fibrils and lead to the opacities of scarred cornea. The finding of labelling for α-SMA in basal epithelial cells suggests that some epithelial cells may transform into MFBCs.

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Geometric characterization of anterior segment in the hen's eye

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Purpose To characterize the corneal geometry and the anatomical configuration of the anterior segment in the hen's eye

Methods 6 eyes of 3 brown leghorn hens with a mean age of 6 months were analyzed. The animals were anesthesized prior to the beginning of the measurements. In all cases, corneal geometry and anatomical configuration of the anterior segment were evaluated by means of the CSO and Visante OCT systems, respectively

Results Mean corneal curvature in the 3-mm central area was 69.35 ± 1.77 D, with a marked corneal astigmatism of a mean value of 3.00 ± 1.86 D. Mean corneal asphericity was -0.23 ± 0.41. Regarding central pachymetry, a mean value of 306.67 ± 46.76 microns was found. Anterior chamber had a mean diameter of 8.14 ± 0.13 mm and a mean associated sagittal depth of 2.33 ± 0.23 mm

Conclusion The hen's eye has a thin cornea, slightly prolate and with significant steepness, and an anterior chamber with a reduced diameter

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Two distinct populations of corneal epithelial cells with limbal stem cell characteristics in the mouse

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Purpose Purpose. To detect and isolate cells with stem cell (SC) characteristics in the limbus of the mouse.

Methods Methods. Limbal tissues from BALB/c mice were trypsin-dissociated and separated on a Percoll gradient. Several fractions were isolated and characterized by Real-time PCR for the presence of limbal SC markers and differentiation markers of corneal epithelial cells, by flow cytometry for the determination of the side-population (SP) phenotype and for growth properties in vitro.

Results Results. Cells retained in the 40% Percoll fraction and in the 80% Percoll fraction of the gradient were both enriched for populations with a high expression of SC markers ABCG2 and Lgr5 and also expressing the SP phenotype. However, the lightest fraction contained cells with the strongest spontaneous proliferative capacity and expressed the corneal epithelial differentiation marker K12. In contrast the densest fraction was K12 negative and contained small non-spontaneously proliferating cells, which instead were positive for p63.

Conclusion Conclusion. These findings demonstrate the presence of two distinct populations of corneal epithelial cells with limbal SC characteristics, based on differential expression of the keratin specific marker K12 and transcription factor p63, and suggest a difference in developmental stage of the two populations, with the K12-p63+ population being closer to the primitive limbal SC.

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Depth profile study of molecular collagen structure in normal human cornea

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Purpose To investigate the structure and organisation of corneal collagen as a function of stromal depth.

Methods A strip extending from limbus to limbus along the superior to posterior meridian was cut from a normal human cornea and 100µm serial sections, parallel to the surface plane of the tissue, were obtained. Wide angle x-ray diffraction experiments were performed in ID-13 at the European Synchrotron Radiation Facility (ESRF) using a 25µm square beam. Each section was scanned at 450µm or 500µm steps. Additionally, another thin vertical strip (1mm thickness) was mounted in such a way that the beam was scanning edge-on. Two scans were performed (1mm apart, each covering the depth of the cornea) from the anterior to the posterior surface at 25µm intervals. Data analysis provided information on the direction and degree of alignment of preferentially oriented collagen fibrils, as well as collagen intermolecular spacing (IMS).

Results IMS is relatively stable throughout the depth of the central cornea, but is decreased in the posterior peripheral cornea. The degree of preferential alignment of fibrillar collagen is lower in the peripheral anterior part. In addition, the previously well-documented tangential or annular collagen structure at the limbus is mainly restricted to the most posterior 100µm of stroma. At more superficial layers collagen preferred orientation tends to obtain an "x" shaped pattern, possibly forming part of the "anchoring fibril" structure alluded to previously in full-thickness averaged x-ray studies.

Conclusion The preferred directions of the lamellae and IMS are depth-dependent. The annulus at the limbus, which is thought to be implicated in the maintenance of corneal curvature, resides in the posterior limbus.

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Leber´s stellate neuroretinitis. A case report

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Purpose A 49 years old man was admitted in our hospital with a 4-day history on sudden loss of vision in the right eye.

Methods Completed ocular examination, including visual acuity, anterior ocular segment, pupillary light reflex, intaocular pressure, ophthalmoscopic examination, visual fields, fluorescein angiography, system examination, including computed tomography and serologic test were done.

Results We present a 49 years old man with sudden loss of vision who presented unilateral disc swelling. Five days later, the fundus examination reveled a macular star, and peripapillary retinal detachment. The fundus findings were normalized in a few weeks, leaving behind only retinal pigment epithelial defects and an inferior visual field defect. Infectious aetiology and others causes were rejected.

Conclusion Leber´s idiopathic stellate neuroretinitis is un uncommon syndrome characterized by unilateral optic disc swelling followed by a macular star. It has a spontaneous resolution, and the aetiology is unknown.

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Evaluation of the retinal nerve fiber layer in patients with multiple sclerosis

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Purpose To evaluate the changes in one year in the retinal nerve fiber layer (RNFL) in patients with Multiple Sclerosis (MS) by means of ocular imaging technologies.

Methods Forty-two patients with MS (84 eyes) were enrolled in this study. None of the patients had an optic neuritis episode in at least 6 months prior to the inclusion, nor during the follow-up. All patients underwent a complete ophthalmic examination that included visual acuity (logMAR), colour vision (Ishihara pseudoisochromatic plates), refractive evaluation, visual field examination, optical coherence tomography (OCT) and scanning laser polarimetry (GDx). All the patients were re-evaluated in a period of 12 months in order to quantify the changes in the retinal nerve fiber layer (RNFL).

Results All the parameters showed a decrease in the RNFL thickness during the 12-month follow-up greater than the decrease due to the age in healthy patients, although these changes were not detected by the standard automated perimetry. Differences were statistically significant (P<0,05, t test) in the mean and inferior RNFL thickness and macular volume provided by OCT and in the TSNIT SD provided by GDx. The greater differences were obtained in the mean RNFL thickness (87,86 µm vs 90,13 µm).

Conclusion Progressive axonal loss can be detected in the optic nerve of MS patients. Ocular imaging technologies are useful tools to evaluate structural abnormalities in the RNFL and changes in time.

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Unilateral optic neuritis as presenting feature of acute hemorrhagic leukoencephalitis

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Purpose We report a case of 23 year-old previously healthy female with acute hemorrhagic leukoencephalitis AHLE (Hürst disease) leading to lethal outcome within two weeks after presentation with unilateral visual loss and moderate upper respiratory tract infection with leukocytosis.

Methods At presentation, VA was 0.3 RE and 1.2 LE with centrocecal defect on right eye, positive RAPD and dyschromatopsia. Optic nerve on fundus examination was normal. Neurological examination revealed right sided hyperreflexia and diminished right plantar response. Initial MRI revealed few focal periventricular hyperintensive lesions consistent with demyelination.

Results Treatment started with 1g metilprednisolon i.v. for 3 days with good initial effect. Third day of treatment, VA in right eye was normal (1.2), RAPD was negative and dyschromatopsia improved. Three days later, altered consciousness with seizures developed, subsequently followed by right hemiparesis and coma. Cerebrospinal fluid pleocytosis was present. Follow- up MRI, obtained 4 days after initial one, revealed large areas of hemorrhagic necrosis in the left hemisphere.Despite continued high dose steroid treatment,antiviral prophylaxis and plasmapharesis, the disease progressed to death within days.

Conclusion Acute hemorrhagic leukoencephalitis AHLE (Hürst disease) is a rare fulminant demyelinating disorder characterized by a fulminant clinical course due to hemorrhagic necrosis of the white matter associated with high rate of mortality. We present a case of this severe disease in which optic neuritis was presenting focal neurological deficit.

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Effect of different antioxidants in experimental alcoholic optic neuropathy

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Purpose To establish the possible beneficial effects of three synthetic antioxidants: S-adenosil-L-methionine (SAMe), N-acetyl-L-cysteine (NAC) and Ebselen in optic nerve damage following chronic ethanol feeding in adult rats.

Methods Twenty male Sprague-Dawley rats (five groups of four animals each) were fed a liquid, ethanol-containing diet with littermates given isocaloric amounts of ethanol-free diet serving as controls. Antioxidants were administered by dissolving them in the liquid diet at 0.4 mg/ml (SAMe), 0.163 mg/ml (NAC) and 5.33 mg/ml (Ebselen). After 6 weeks, optic nerves were obtained and parameters that are relevant for the modulation of oxidative stress, such as antioxidants -GSH content and Glutathione-peroxidase (GSH-Px) activity- and lipid peroxidation-derived end products -malondialdehyde (MDA)- were determined. Comparisons between groups were done using Student´s t-test for grouped data and one-way ANOVA. Differences were considered significant at p<0.05.

Results N-acetyl-L-cysteine and Ebselen were able to normalise MDA content and to restore GSH content and GSH-peroxidase activity, to values not significantly different from those of controls (p>0.05). Treatment with SAMe slightly improved values of some parameters, although no statistically beneficial (p<0.05 versus control).

Conclusion These results support the use of NAC and Ebselen for the treatment of chronic alcohol-induced optic nerve damage.

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Bilateral internuclear opthalmoplegia in a patient with Devic's neuromyelitis optica

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Purpose To present a clinic case of Devic's neuromyelitis optica (NMO) with bilateral ophtalmoplejia internuclear (OIN) , which is an extremely extraordinary association.To explain the reason why an episode of ophtalmoplejia internuclear appears in the context of a NMO case.To expose the visual involvement in NMO.

Methods We studied and observed the clinical evolution of a patient diagnosed of NMO. The profile started with headache and sudden loss of visual acuity in right eye (RE), counting fingers at 1metre. She related neurologic symptoms as paresthesias 18 months ago. At the evaluation with visual field, eye fundus, Ishihara test was diagnosed of retrobulbar neuritis RE. We treated the patient with metilprednisolone and immunosuppressant drugs. She got better. After the childbirth, new neurologic symptoms that remined to transverse myelitis appeared. After a new treatment with metilprednisolone and plasmapheresis, she got better but a sudden bilateral OIN appeared

Results The patient had a limitation in the movement of the eyes in addution and a bilateral nistagmus in abdution. The patient didn´t have a good reponse to the treatments. At present, she continues being admitted to hospital with paresis of legs and right arm. Double vision and OIN disappeared gradually. However, the patient has a residual exoforia in RE with nistagmus in abdution in left eye.

Conclusion The MNO prevalence is lower than a case for million inhabitants, and it is not used to affect the encephalon trunk. To diagnose NMO are required two major criteria and at least two of the three minor ones, and this patient fullfills the diagnosis criteria.

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Binocular vision disturbances and eye movement restrictions in patients with thyroid associated ophthalmopathy(TAO)

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Purpose To investigate the incidence and associations of various types of double vision and limitations of gaze among patients presenting with ocular complaints related to thyroid associated ophthalmopathy.

Methods We included 325 patients (268 female and 57 male) aged 42 to 78 (mean 51.1 +/-5.2) referred with ocular symptoms and the diagnosis of TAO. 156 sex and age matched, healthy volunteers served as a control group. Eye movements restrictions were investigated and recorded in the four point scale. The degree of exophthalmos was recorded, as well as the degree of horizontal and vertical disparation.

Results 59.8% of patients reported significant double vision. 96% of patients complaining of double vision trported that it is intermittent,(29% in primary gaze position and 67% in other than primary). The most common limitation of eye movement was elevation(49%). There is a significant correlation between clinically significant double vision and vertical disparation (P=0.30) as well as asymmetrical exophthalmos (p=0.34). There is no correlation between the amount of exophthalmos and double vision.

Conclusion Diplopia is an extremely common presenting sign of TAO. Most patients are troubled by diplopia in different than primary gaze direction. Asymmetrical exophthalmos, and asymmetrical vertical eye muscle involvement are the most significant factors associated with symptomatic diplopia.

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Bilateral visual loss and paraplegy in a patient with metastaic carcinoma of stomach

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Purpose We present a case report of bilateral visual loss and paraplegy in patient with metastatic carcinoma of stomach.

Methods 64-year old male presented with painless visual loss on right eye, and one week later, he was blind on both eyes with no light perception and amaurotic pupils. One year earlier he was diagnosed with primary metastatic carcinoma of stomach and was treated by Xeloda and Docetaxel. Fundi revealed bilateral hyperemic disc oedema. Solu-Medrol 1 g i.v. for three days had no effect.

Results CT and MRI of brain showed no lesion that would explain his visual loss. Scotopic and photopic electroretinography was normal.Visual evoked potentials (VEP) on flash stimulation were nonrecordable. Specific onco-neurologic antibodies in CSF and serum were negative:anti-Ri(ANNA-2),anti-Yo,anti-CV2(CRMP5),anti-amphiphysin,anti-Mal,anti-Hu(ANNA-1),anti-Ma2(Ta-). One month after onset of blindness, he had acute neurological deterioration with paresis of left leg and retention of urine which was diagnosed as Brown-Sequard syndrome. MRI of spinal chord showed intramedular lesion between Th 6-10. Oligoclonal bands in serum and CSF were identical, indicating systemic inflammation. Serum was sent for testing NMO-IgG,but results are in process. Patient was restarted on high doses of Solu-Medrol i.v. Slight improvement of vision was noted after few days of therapy, and flash-evoked VEP was barely detectable. The discs were no longer swollen and appeared pale.

Conclusion This unusual case of bilateral blindness due to optic neuropathy might be linked to atypical presentation of neuromyelitis optica or to paraneoplastic optic neuropathy caused by yet unknown antigen.

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Clinical variability in a three-generation family with Duane's syndrome

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Purpose The majority of Duane syndrome cases are sporadic in origin with only 2-5% patients showing a familial pattern. Only a few large families have been reported. The purpose of this study is to report the clinical presentations, abnormalities of ocular motility, and strabismus in 3 generations of a family with Duanes syndrome.

Methods 22 members of a family of three generations (age range 6 years to 70 years) were examined. Detailed ophthalmologic assessment included assessment of vision, binocularity, and video recordings of ocular motility.

Results Unilateral Duane syndrome type 1 was noted in the left eye of a lady in the first generation of the pedigree.In the second generation, of the 4 subjects examined, two females had esotropia with diplopia, one male had minimal bilateral abduction deficit with endpoint nystagmus and one sibling was normal. 12 subjects from the third generation were examined. Two of them had unilateral Duane's syndrome. Two children had minimal abduction deficit with endpoint nystagmus. Three subjects had esotropia and diplopia requiring surgery. The mother of one of the affected subject had normal eye movements.

Conclusion This large family with Duane syndrome appears to have a dominant form of inheritance with variable penetrance and expressivity. The skipped generation indicates unaffected carrier state. The variable phenotypic expression seen in this family suggests that classical Duane syndrome could be one end of a spectrum of eye movement disorders comprising esotropia, abduction deficits and globe retraction; the other end being normal ocular motility.

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Strabismus, epilepsy vs. motor & neurological disorders in quadriplegia

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Purpose To correlate strabismus and epilepsy with the severity of the motor and brain disorder in spastic quadriplegic children.

Methods 52 quadriplegic children (2-9 years of age) participated in this study. Strabismus (Krimsky test), gross motor function (GMFCS) were estimated and EEG and brain MRI were also performed.

Results 29 children were premature and 23 were full terms. 30 out of 52 (57.69%) had epilepsy, 29 out of 52 (55.76%) had strabismus (19 (36.53%) esotropia & 10 (19.23%) exotropia). 73.07% of the children had moderate to very severe motor disorders. 32 children (61.53%) had periventricular leukomalacia and 20 (38.47%) had various brain damages.

Conclusion Epilepsy and strabismus are very common in quadriplegia and there is a statistically significant relationship between epilepsy, strabismus and neurological and brain damage.

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Treatment of acquired periodic alternating nystagmus with memantine

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Purpose To report a patient with acquired periodic alternating nystagmus secondary to sarcoidosis successfully treated with memantine

Methods A 43 year old man had a four year history of acquired horizontal periodic alternating nystagmus (PAN) with oscillopsia secondary to sarcoidosis. Visual acuity (VA) was measured and eye movement recordings were performed with an infra-red eye tracker (Eyelink I, 250 Hz) before and after treatment with 5 mg memantine per day

Results The visual acuity (VA) was 6/36 in the right eye and 6/24 in the left eye during maximum nystagmus amplitude. The duration of the right beating and left beating phases was 105-110 seconds and of the quite phases was 4-5 seconds. During the quiet phase the nystagmus was insignificant. On memantine the patient became significantly less symptomatic. The right visual acuity improved to 6/6 and the left to 6/4 during the entire cycle of PAN. Before treatment the nystagmus reached a maximum intensity of 11.9°/sec (frequency 3.6 Hz and amplitude 3.3°) during right beating periods and 14.0°/sec (frequency 3.5Hz and amplitude 4.0°) during left beating. Again the quiet phases in between were insignificant in terms of nystagmus. After treatment of 5mg of memantine per day the intensity was reduced to a maximum intensity of 0.41°/sec (frequency 1.54 Hz and amplitude 0.26°) during right beating period and 0.54°/sec (frequency 1.28 Hz and amplitude 0.42°) during left beating.

Conclusion We showed for the first time that memantine can reduce PAN dramatically (4% of the original amount). Treatment with memantine should be investigated systematically in PAN.

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Third nerve palsies without pupil involvment can still be surgical

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Purpose To emphasise the importance of maintaining a high index of suspicion of a surgical cause of a partial third nerve palsy even when pupil is not involved. To highlight an unusual presentation of a pituitary tumour.

Methods Case Report

Results A 15 year old presented to the emergency department one evening after noticing he had a "droopy eyelid". He reported being under a lot of stress whilst revising for exams and described some occasional mild tension type headaches. Of note two weeks before this presentation he had "fainted" in the school playground, it had felt that this episode required no further investigation at the time. There was no other history ellicited. Also of note was that he denied any diplopia or visual symptoms.On presentation, he had a right sided partial ptosis. Visual acuity was normal. Both eyes were normal. On examintion of the ocular movements he had diplopia on upgaze especially in abduction. He had no past ocular or medical history. Goldmann fields were normal. When he was seen it was noted thet he was over 6 feet tall yet his parents were of average height.On discussing the case with radiologists and paediatricains great emphasis was placed by them on the lack of pupil involvement, it was then assumed therefore that it would be unlikely that there would be any brain lesion. However, he did go on to have an MRI scan the next day which revealed a large pituitary mass which protruded laterally hence the third nerve involvment. As of when this abstract was submitted he is awaiting neurosurgical work up.

Conclusion Importance of high index of suspicion of surgical cause of third nerve palsyy depsite pupil involvement.To Highlight an unusual presentation of pituitary tumour

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f-Visual evoked potentials (f VEPs), nystagmus vs. motor & neurological disorders in quadriplegia

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Purpose To correlate flash VEPs and nystagmus with the severity of the motor and brain disorder in spastic quadriplegic children.

Methods 52 quadriplegic children (2-9 years of age) participated in this study. Flash VEPs (ICEVE), and brain MRI were performed, also nystagmus (clinical evaluation) and gross motor function (GMFCS) were evaluated.

Results 29 children were premature and 23 were full terms. 15 out of 52 (28.84%) had normal f VEPs and 37(71.15%) had abnormal. epilepsy, 13 (25%) had nystagmus (horizontal). 73.07% of the children had moderate to very severe motor disorders. 32 children (61.53%) had periventricular leukomalacia and 20 (38.47%) had various brain damages.

Conclusion Affected flash VEPs and nystagmus are common in quadriplegic children. There is a statistically significant relationship between VEPs, nystagmus and neurological and brain damage.

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Pupil light reflexes mediated by outer retinal versus inner retinal photoreceptors in normal subjects and patients with neuroretinal visual loss

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Purpose This study was designed to translate recently published physiological behavior of the melanopsin-expressing retinal ganglion cells to the clinical setting.

Methods 43 normal eyes were tested by recording the pupil light reflex to a Ganzfeld red (620nm+/-20nm) and blue (480nm+/-20nm) light stimulus at 3 light intensities (1, 10, and 100 cd/m2) under mesopic conditions. The pupil responses of the normal subjects were compared to patients with outer retinal disease and patients with optic nerve damage.

Results In normal eyes at lower intensities, blue light evoked much greater pupil responses compared to red light when matched for photopic luminance. A disparity between the transient and sustained pupil contractions was greatest at the lowest light intensity and decreased with increasing light intensity. Patients with primarily rod dysfunction showed reduced pupil responses to low intensity blue light stimulation.. A patient with genetically confirmed achromatopsia showed selective reduction of the pupil response to high intensity red light stimulation. Patients with optic neuropathy tended to have reduced pupil responses to all light conditions.

Conclusion Pupil responses that differ as a function of light intensity and wavelength support the hypothesis that selected stimulus conditions can produce pupil responses that may reflect phototransduction mediated by either rods, cones, or intrinsic activation of melanopsin-expressing retinal ganglion cells. The pupil light reflex may be used to differentiate diseases affecting either the outer or inner retina.

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The lot of shaken baby syndrome (SBS) cases: Follow-up of visual outcome and congnitive function

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Purpose To study long-term outcome of SBS on visual and cognitive functions.

Methods Case series of 10 children (7 M, 3 F) with confirmed SBS has been examined and followed-up. All chldren underwent a fundus evaluation by indirect ophtalmoscopy and wide-field digital ophtalmic camera (RetCam II) in the acute phase and until retinal hemorrhage resorption. The assessment was repeated at follow-up combined with ocular motility evaluation, visual field (BEFIE test), visual acuity by preferential looking tecnique (teller acuity cards), refractometry, cognitive-behavioural evaluations (Griffiths scales, Child Behaviour Check List), and family stress measurement (Parenting Stress Index).

Results Mean age at acute episode of SBS: 6 months (range 2-20). Mean age at last follow-up evaluation: 27.6 months (range 4.5-41). At last follow-up evaluation: 1 out of 6 had a decreased visual acuity (cortical visual impairment), 3 out of 6 had mild-severe visual field deficits, 3 out of 6 has strabismus. None of the cases showed significant refractive errors. Due to age or severity of impairment and delay in global development, in any of the cases we were able to perform a recognition acuity test by symbols or E-charts. Cognitive and behavioural assessment demonstrated global delay and impaiments in speech/language development and attention problems.

Conclusion SBS is characterized by severe long-term sequelae both in visual and cognitive function. Several visual impairments are observed, mainly related to cortial injury of visuo-spatial area. Although follow-up is difficult due to family history, there is strong indication for global assessment until scholar age where other impairments are demonstrated.

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Morphofunctional correlates in rhegmatogenous detachment of the retina

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Purpose To detect the selective reduction of retinal neurons' activity in retinal detachment (RD) of different duration and after the reattachment surgery (RS).

Methods We created earlier two protocols for 8-30Hz flicker ERG testing in photopic (Ph) and scotopic (Sc) conditions using EP-1000 TOMEY system. Standard and Ph/S flicker ERGs were examined in 9 healthy subjects and in 18 patients with rhegmatogenous RD (groups ≤1m, 1-2m, >2m duration) in eyes with myopia before, 1w, 1m after the RS.

Results The comparing of Ph/Sc flicker and standard ERGs showed that in the RD group 1, the Sc system function was relatively more impaired than the Ph, confirming literature histological data about rods' alterations in the earlier period after RD. In RD<1m, ERGs at 8-10Hz were more reduced than at higher frequencies. Our data showed the greater functional changes in photoreceptors for ≤1m, in cones and bipolar cells - for 1-2m, and moderate general alterations of retina function in the group 3 before the RS. After the RS, the general decrease of all ERGs was found, but the cone-ERG a-wave and Ph 8-12Hz flicker ERGs, which amplitudes showed the moderate increase during the follow up. It was more typical for RD duration < 1m, and a recovery was the worst in 1-2m RD.

Conclusion The flicker ERGs of broad frequency range seems to provide functional correlates of morphological alterations in RD, and may be useful in indirect estimation of retina recovery after the RS. In myopic eyes, even the earlier RS does not result in immediate recovering of retinal function. Earlier signs of restoration are characteristic only for the cone's function, and they are more manifested after the RS for less than 1m RD.

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Microperimetry, PERG and mfERG in patients with Stargardt dystrophy

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Purpose The aim of our study was to evaluate retinal function in patients with genetically determined mutation in the ABCR gene by correlating retinal morphology with functional and electrophysiological tests.

Methods 12 patients (10F, 2M, VA: 0,2±0,2) were included in the study. The central 10º visual fields were tested with Octopus M2 TOP and microperimetry (MP1, Nidek technologies), that enables one to compare central retinal sensitivity and fixation patterns in relation to the fundus image. PERG and mfERG were recorded in all the patients according to the ISCEV standards.

Results mfERG showed reduced responses mostly in the inner three rings (ring 1: 33,9% of mean normal value, ring 2: 35,4%, ring 3: 57,5%, ring 4: 75,5%, ring 5: 84% of mean normal value). There was good correlation between mfERG and pattern P50 (r=0,7, p=0,0001) and N95 responses (r= 0,6, p=0,004). mfERG appears more sensitive for central retinal testing than pattern ERG. There was a high correlation found between microperimetry (MP) and static perimetry (MD, r = 0.6, p=0.008). Shift of fixation to the preferred retinal locus(seen on MP) was found in 8 out of 16 eyes tested with VA 0,2 and less. In patients with absolute central scotoma and shifting of fixation, scotoma may erroneously be interpreted as eccentric when seen only with static perimetry.

Conclusion In patients with visual acuity 0,2 and lower, the fixation shift to the preferred retinal locus was observed. Cautious interpretation of the static perimetry and mfERG as well as PERG is needed in patients with eccentric and nonstable fixation.

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Cone electroretinograms to blue flashes on various backgrounds

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Purpose To observe the S-cone and LM-cone responses of the photopic electroretinogram (ERG), to study their interactions, and to define under which stimulus conditions the ERG waveform reflect the function of the S-cone as well as the L- and M-cone systems.

Methods The photopic ERG was recorded from 10 control subjects in a full-field stimulator (Diagnosys LLC, Littleton, MA). Responses were elicited with intensity series (0.004 to 1 cd*s/m2) of the blue (449 nm) stimuli on a 100 ph cd/m2 amber background (=40 sc cd/m2), as well as on a 100 ph cd/m2 green and a 40 sc cd/m2 red backgrounds.

Results The S-cone response appeared at the implicit time of 43 ms, with lower stimulus intensities on the amber, green and red backgrounds. With higher stimulus intensities (0.028 cd*s/m2), it showed with a similar implicit time, but as a second peak subsequent to the LM-cone response (b-wave). With a further increase in intensity (0.15 cd*s/m2), the S-cone response passed into the i-wave of the LM-cone system. The LM-cone response appeared as a double peak (first peak: 24 ms; second peak: 28 ms) on an amber background at intensities from 0.028 cd*s/m2 and above. On a green background, the first peak was more prominent, while on a red background, the second peak dominated the LM-cone response. This pattern of double-peak appearance might indicate that the first peak originates mostly from the L-cone system and the second peak from the M-cone system.

Conclusion The S-cone response can be elicited with various backgrounds as a single peak to a blue flash at lower intensities, while with brighter intensities it probably interacts with the LM-cone system. The double peak of the LM-cone response is an interesting finding, which might indicate selective monitoring the L- and M-cone systems.

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Multifocal ERG and OCT in unexplained visual loss

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Purpose To determine the value of multifocal ERG (mfERG) and optical coherence tomography (OCT) in the evaluation of patients with unexplained visual loss.

Methods mfERG and macular OCT were obtained from six patients with unexplained visual loss (normal ophthalmoscopy, fluorescein angiography, full-field ERG and brain CT scan) and four age and sex matched controls.

Results Patients BCVA ranged from 20/32 to 20/125. When comparing to controls, patients showed significantly depressed mfERG amplitudes in rings R1 (121.7 vs 64.8; p 0.01) and R2 (42.6 vs 19.5; p 0.02). Foveal thickness, as measured by macular OCT, was also reduced, although not significantly (p 0.1).

Conclusion Multifocal ERG allowed localization of the visual dysfunction to the central macula, in cases with hitherto unexplained visual loss.

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Objective assessment of chromatic and achromatic pattern adaptation reveals the temporal response properties of different visual pathways

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Purpose To investigate the temporal response properties of magnocellular, parvocellular and koniocellular pathways using contrast increment/decrement visual evoked potentials (VEPs).

Methods Static achromatic and isoluminant chromatic gratings were generated on a monitor (Michelson contrast 0.05 to 0.6). Chromatic gratings were modulated along R/G or subject-specific tritanopic confusion axes, established using a minimum distinct border criterion. Isoluminance was determined using minimum flicker photometry for a 1-degree field. Achromatic and chromatic VEPs were recorded to contrast increments and decrements of 0.1 superimposed on the static gratings. Field size for Tritan gratings was restricted to 3-degrees to minimize the effects of luteal pigment.

Results Achromatic increment/decrement VEPs were positive in polarity and largely unaffected by high levels of static contrast at low spatial frequencies. Responses to finer achromatic gratings showed marked attenuation as static contrast was increased. Chromatic VEPs to R/G or Tritan chromatic contrast increments were of negative polarity and showed progressive attenuation as static contrast was increased. Chromatic contrast decrement VEPs were of positive polarity and less sensitive to pattern adaptation.

Conclusion The relative contribution of sustained and transient response mechanisms to achromatic processing is spatial-frequency dependent. Chromatic contrast increment VEPs are highly sensitive to pattern adaptation consistent with high stimulus selectivity and the sustained temporal response properties of the parvocellular and koniocellular pathways.

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Pupil reactions in children with strabismic amblyopia in dependence of deviation value

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Purpose To reveal the difference between pupil reactions in amblyopic children with and without menifest deviation

Methods 51 patient with amblyopia aged 7-12 y.o. were examined on the elaborated upillography device. There were 22% with amblyopia of high degree (average visual acuity and 64% of low and 14% of middle degree. Children had hypermetropic refraction;central monocular fixation in 27,eccentric in 18 cases. 32% of cildren had strabismus of different kind others had no manifest deviation (68%). The changes of pupil parameters during investigation of direct and consensual reaction on flashlight test and accommodative-convergence response were conducted. With the help of elaborated device and corresponding software for pupillography method and STATISTICA for Windows 98.

Results The significant difference was found in groups with and without manifest strabismus during direct fleshligh, the amplitude was larger in those who had manifest viation. The amplitudes of pupil constriction in consensual reaction on flesh light test were also larger in amblyopic patients without deviation, P<0,05. Latencies of pupil striction was almost equal on both eyes in patients without deviation but were significantly different in those, who had manifest deviation. After accommodative-convergence response average value of pupil recovery was larger in patients without deviation in comparison with.

Conclusion Patients without manifest deviation have disorders in reaction of pupil to direct flesh light test and accommodative response on the near object. Patients with deviation have consensual pupil reaction disorders that indicate on involvement of afferent but and efferent pathways of eye motility in such cases.

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Visual development in premature infants without serious events in their pre – and perinatal period.

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Purpose To follow the visual development of premature neonates without serious health problems.

Methods 49 premies (GA 26<β<35 & BW 890<β<2240gr), with no neurological and ophthalmological lesions, participated in this study. Brain ultrasound, fundoscopy, cycloplegic refraction and assessment of the visual function (VFA-K test) were performed in 10th and 16th adjusted month of age. All the babies had a psychokinetic assessment (twice) (DENVER test).

Results 41 out of 49 neonates had GA <32 weeks .and 30 out of 49 had BW <1500 gr. 26 neonates had normal brain echo and 23 appeared with mild enlargement of brain ventricles. During the 1st examination, 3 neonates appeared with refractive error >1.00 D, 4 had strabismus, 4 had mildly abnormal VFA-K test score and 10 had reduced DENVER score. During the 2nd examination, the results were the same apart from an improvement in VFA-K and DENVER score.

Conclusion In the vast majority of the premature infants with no serious health problems, the visual function develops normally.

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Accommodation insufficiency in children: are exercises better than reading glasses?

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Purpose Purpose: The aim of the present study is to investigate which mode of therapy is the most effective in the treatment of accommodative insufficiency (AI). The two methods compared was plus lens (+1.00D) reading addition (PLRA) or spherical flipper (± 1.50D).

Methods Methods: Twenty four subjects (mean age 10.3 years, 2.5 SD) participated. All subjects were diagnosed with AI. Ten subjects were treated with PRLA and 9, out of 14, subjects completed spherical flipper treatment. The treatment time was 8 weeks.

Results Results: There was a statistical significant improvement in the accommodative amplitude with both regimes of treatment. However, accommodation did not reach normal values after only 8 weeks of treatment. The analysis between the two therapies did not reveal any statistical significant difference although spherical flipper treatment was found to have an overall larger effect.

Conclusion Conclusions: The results of the present study show that both methods improve accommodative amplitude but there were no significant difference between the two methods.

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Ametropia in children with regressed retinopathy of prematurity

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Purpose Main aims of this study were:(1)To identify the pattern of refractive changes in children with different degrees of pre-threshold retinopathy of prematurity (ROP). and (2)To establish whether long term follow-up is necessary for these children?

Methods ROP screening notes of all premature babies born between Jan 2001 to Jan 2005(5 years) within a defined geographical area (Leicestershire) of the UK and fulfilling the national ROP screening guidelines were reviewed retrospectively. According to the severity, we graded the pre-threshold ROP as follows: (1)Grade1- Any disease restricted to zone 3 or Stage I or II in zone 2, (2)Grade2- Stage II+ or III disease in zone 2, and (3) Grade3 - Stage III+ disease in zone 2 Any zone 1 disease. Eyes of matched eyes were used as controls (same gestational age and weight matched children who were premature but without ROP). Cycloplegic refraction data (minimum follow up period- 24 months) on these children were then collected through the clinic notes. The results were compared statistically.

Results Refractive status results (at 24 months age) were available for 116 eyes in 62 children (Electronic search + Case notes review). Eyes were assigned to our predefined grades: Grade1:60 eyes(32), Grade2:34 eyes(18), and Grade3:22 eyes(12). The results of cyclopegic refraction (Mean spherical equivalent, Range) were as follows: Grade1:0.59(-1.75 to +3), Grade 2: -0.04(-4.5 to +2.25), and Grade 3: -1.59 (-7.5 to +1.75). Statistically, refractive outcome of Grade 2 and 3 ROP children were different from controls.

Conclusion In pre-threshold ROP, the trend of myopia is directly proportional to the severity of ROP. We recommend that regular follow up is necessary for Grade 2 and 3 ROP babies but no follow up required for babies with Grade 1 disease.

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Straylight and the two domains of visual optics; small angle (0-1 degree) and large angle (1-90 degree)

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Purpose Retinal straylight is the cause of important visual disturbances such as glare hindrance and contrast loss. It results from light scattering in the optical media, over angles of 1 to 90 degrees. So, it addresses part of the visual function not accessible with other means, such as visual acuity, contrast sensitivity and optical techniques. How independent are those two domains?

Methods A forced choice psychophysical assessment technique was developed for objective and at the same time functional assessment of straylight ("Compensation Comparison", implemented in a commercial product, C-Quant from Oculus). Maximum likelihood estimation is performed, fitting a psychometric function to patient responses for 25 short comparisons, including a reliability estimate of the obtained straylight value. The outcomes were compared to classical visual function measures (visual acuity and contrast sensitivity) in 2400 subjects in the European GLARE study. Literature models for different aspects of the optical irregularities in the eye media were used to understand the independence between the two domains of the psf.

Results Straylight typically originates from irregularities in the optical media of small characteristic size (collections of particles sized 10 micrometer and below), as opposed to disturbances to the central part of the psf (<0.1 degrees), originating from large scale irregularities (refractile humps and bumps extending over 100 micrometer and more). As a consequence straylight is sensitive to disturbances like early changes to the lens, corneal haze, PCO, multifocal IOL artifacts, corneal scars, vitreous turbidity, etc.

Conclusion Straylight assess a domain of visual function not accessible with classical and optical means.

Commercial interest

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Variability of pupil behaviour due to different retinal's illumination levels

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Purpose To get the knowledge about how can pupil size be manipulated, in an artificial way, by using optical filters, with different absorbances, in order to change the level of retinal's illumination. This knowledge will allow the obtaining of an artificial myosis or mydriasis, with an optimal non-invasive technology, so that will be applied in several ways.

Methods The transversal study included data from 56 eyes of 28 subjects. To measure the different pupil size was used a digital binocular infrared pupillometer, which simulated 3 different light's conditions: high mesopic (4lux), low mesopic (0,4lux) and scotopic (0,04lux). The obtained pupil size measurements, without filter, were compared with the results after the insertion of the different optical filters used: 16 filters with different transmittances (from 82% to 5%).

Results Only in high mesopic (4lux) condition, the results showed significant differences between the pupil size measurements without and with different transmittance optical filters. The mean variation was between 10% and 14% depending on the filter which was used.

Conclusion The existence of a physiologically visual system limit for myosis in scotopic condition was confirmed, due to the lower amount of light in retina. Only in high mesopic condition, significant differences were obtained in the pupil size results with filter.

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A screening test for visual disorders based on Rarebit perimetry

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Purpose To evaluate the clinical usefulness of a newly developed screening program, the VisuBit™ Quick test, based on the Rarebit perimetric technique (Frisén 2002).

Methods Twenty-one subjects (32 eyes), 6 males and 15 females, median age 47 years (27-67), were examined using the VisuBit Quick and Full test, both including the Fovea test (4x3°visual field) and the Field test (30x20° visual field). Two subjects had amblyopia in one eye, one of these had normal visual acuity in the other eye and one had a history of central serous retinopathy in one eye, 2 subjects had a history of optic neuritis in both eyes and 2 had glaucoma in both eyes. All other eyes were healthy and had normal visual acuity.

Results The correlation coefficients between number of unperceived stimuli in the Quick and the Full test were 0.95 in the Fovea and in the 0.86 Field test. In the Quick Field test more than 4 unperceived stimuli predicted a subnormal result (MHR < 90%; Martin & Wanger 2004) in the Full Test. In the Fovea Test more than 2 unperceived stimuli predicted a subnormal results (MHR < 97%; Nilsson et al 2007). The positive and negative predictive values for the Quick Fovea test were 0.95 and 0.77, respectively. Corresponding values for the Quick Field test were 0.95 and 0.85.

Conclusion The findings in this pilotstudy indicate that this implementation of the Rarebit perimetric technique may be useful for rapid screening for visual disorders.

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Quantification of sphero-cylindrical defocus using refractive data

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Purpose To compare various indices calculated using refractive data to quantify defocus.

Methods Subjective refraction, pupil diameter (Colvard) and asphericity (Orbscan) were prospectively recorded in 200 healthy eyes (including ametropia) of 121 patients. Refractive data were expressed by a sinusoidal curve in one plane (power / meridian) and by a vector in a 3D dioptric power space. The three Cartesian coordinates of the vector respectively represented the spherical equivalent, WTR/ATR component (0°/90° Jackson), and oblique component (45°/135° Jackson). The defocus was quantified by the root-mean-square (RMS) value of the power curve and the length of the vector. Correlations between uncorrected visual acuity (UCVA) in LogMAR units and principal parameters including defocus indices and refractive parameters were analyzed.

Results The length of the power vector and the RMS index provided the highest correlation with UCVA ($rs=0.90$ $p<0.001$ and $rs=0.88$ $p<0.001$, respectively), whereas the correlation was less strong for subjective spherical equivalent ($rs=0.70$ $p<0.001$) and subjective cylinder ($rs=0.30$ $p<0.001$). Correlation was poor for the pupil diameter ($rs=0.20$, $p<0.001$); sex and asphericity coefficient showed no significant correlation ($rs<0.08$ $p>0.20$) with UCVA.

Conclusion The length of the sphero-cylindrical vector is clinically relevant to quantify the defocus with the aid of a single index using both spherical and astigmatic components of refraction. The UCVA is mainly explained by the ametropia.

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Wavefront aberration measurements in dog and cat eyes using an aberrometer designed for human eyes

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Purpose To measure the ocular optical aberrations in dog and cat using a wavefront aberrometer based on Hartmann-Shack technology.

Methods Data were obtained from eyes of two normal sedated dogs and one normal sedated cat in accordance to the ARVO statement for the use of animals in ophthalmic and Vision research. Wavefront aberrations were measured using an irx3 aberrometer (Imagine Eyes, Orsay, France). Spherical defocus, astigmatism and Zernike coefficients up to the 8th order were analyzed.

Results The optimal acquisition time was 10 ms for all animals. Refractive errors have been analyzed in a 6 mm pupil diameter in all cases. The refractive errors in dog #1, dog #2 and the cat were +2.9D(-2.0D)111°;-0.8D(-0.8D)126° and +3.3D(-2.1D)98°, respectively while their Root Mean Square (RMS) higher-order aberrations amounted to 1.9, 1.1, and 2.1 µm RMS respectively. SD in sphere and cylinder was 1.0D in the cat and less than 0.5D in both dogs. SD in the higher-order RMS was 0.8 µm in the cat and less than 0.5 µm in both dogs.

Conclusion Ocular optical aberrations can be measured in sedated dog and cat using a Hartmann-Shack aberrometer with reduced image acquisition time. The tested animals had relatively large higher-order wavefront aberrations when compared with healthy human eyes. Measurement reproducibility was affected by tear layer effects. This variability could be further reduced using a larger sensor area, specific head contention device and artificial tears. The measured range of aberrations could be corrected using available adaptive optics technology in order to image retinal cells in living dogs and cats. Financial interest disclosure: B. Lamory and N. Chateau are employees of Imagine Eyes

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Higher-order wavefront aberrations and accommodative response variations with phenylephrine 5%

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Purpose To study the effects of phenylephrine 5% topical administration on accommodative response and optical aberrations variation.

Methods The research followed the tenets of the Declaration of Helsinki . 28 eyes from 14 volunteers with spherical equivalent defocus error between –2D and +1D, no eye disease history and between 20 to 25 years of age, underwent wavefront measurements with a Shack–Hartmann wavefront aberrometer which included a movable accommodative target. Wavefront data was acquired while applying 6 different increasing accommodative stimuli, from 0 D to 5 D by steps of 1 D, before and after pupil dilation with Phenylephrine 5%.

Results The dilation using Phenylephrine 5% was found to larger lag errors in the accommodative response of about half of the subjects. The total RMS amount of aberrations above defocus remained stable during accommodation with and without dilation. Spherical aberration was positive in average in the non accommodated eye and changed toward negative values with increasing accommodation ($p<0.05$). Cylinder axis came closer to 90° as accommodation increased ($p<0.05$). Although vertical coma did not significantly vary with accommodation, horizontal coma increased significantly with accommodation ($p<0.05$). These changes in aberrations with increasing accommodation were similar on average in both pupil conditions.

Conclusion Phenylephrine 5% modifies the accommodative focus response of a significant proportion of young adult eyes. Wavefront aberrations above defocus undergo similar variations in both natural and dilated pupil conditions. However the total RMS error of aberrations above defocus remains relatively constant when the eye accommodates.

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First results in repeated functional testing in low vision patients with retinitis pigmentosa

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Purpose We created a visual function test, the Graz mobility (GM) test to document visual progress in artificial vision. In previous studies our low vision test adequately graded the low vision of patients with retinitis pigmentosa (RP). However in repeated testing the learning effect could contaminate the visual results after implantation. The aim of this study was to investigate the constancy of the performance and to record behavioural changes in repeated testing in low vision RP patients.

Methods 8 low vision RP-patients with a visual acuity from hand motion to 20/800 were tested repeatedly in 1, 2, 3 and 6 months time intervals. The GM test consisted of four different, structurally similar mazes with 11 obstacles. The subjects passed through each course several times. A people tracking system with an integrated trajectory projection system was established to record horizontal and vertical scanning movements of people during the test. Passage time, walking speed, number of contacts, frequency of scanning movements and average scanning angle were recorded.

Results In repeated testing significant changes of the passage time were observed once the patients became familiar with the mobility test. The maximum learning effect was achieved within the first test session and was never exceeded in the following sessions. However further changes in the remaining parameters were observed in each patient, displaying behavioural changes correlating to the level of comfort during the task performance.

Conclusion The GM proves to be reliable for repeated testing in low vision patients and the learning effect will not contaminate the results of visual function changes. Furthermore behavioural changes can be objectively assessed.

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Accommodative function in school -age children with poor reading skills

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Purpose Prior findings suggest correlation between reading problems and accommodative function, but few studies have assessed accommodation in children with poor reading skills. Our aim was to characterize monocular accommodative amplitude, relative accommodation and binocular accommodative facility in a population of healthy, non-dyslexic primary school children with reading difficulties.

Methods We conducted a cross-sectional study on 87 poor readers and 32 control children (all 8-13 years of age) in grades three to six recruited from eleven elementary schools in Madrid, Spain. In each subject with best spectacle correction, negative relative accommodation and positive relative accommodation were measured using a phoropter, monocular accommodative amplitude was determined using the minus lenses method, and binocular accommodative facility was measured using the Bernell Acuity Suppression Slide (VO/9) and a ± 2.00 D accommodative demand during 1 minute.

Results Monocular accommodative amplitude was significantly lower ($p < 0.001$) in the group of poor readers (right eye 9.1 D ± 2.3, left eye 9.0 D ± 2.3) than in the control group (right eye 10.5 D ± 1.7, left eye 10.5 D ± 1.7). Binocular accommodative facility values were significantly lower ($p<0.05$) in the poor readers (4.9 cpm ± 3.1) than controls (6.3 cpm ± 2.9). Negative and positive relative accommodation values were similar in both groups of children.

Conclusion This study provides data on the accommodative capacity of a population of children with reading difficulties. Our findings suggest a reduced monocular accommodative amplitude and binocular accommodative facility such that this function should be assessed by an optometric clinician in children whose reading level is below average.

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Objective measurement of near and distance visions by optokinetic response determination

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Purpose To evaluate the efficacy of using optokinetic nystagmus (OKN) suppression and induction method as an objective measurement of visual acuity at near and distance.

Methods Eighty-three eyes of 83 patients were examined from December 2007 to February 2008. The visual stimuli were presented on a 17-inch monitor screen located 40cm from subject for measuring visual acuity at near and on a 127-inch projector screen located 3m for visual acuity at distance. Eye movement were recorded by infrared oculography and analyzed. The correlation between objective visual acuities at near and distance and subjective visual acuities at near and distance were evaluated. And the reproducibility of objective visual acuity measurement was also investigated.

Results Linear regression identified that objective visual acuities measured by using OKN suppression and induction methods were found to be correlated with subjective visual acuities(r2; induction method at near: suppression method at near: induction method at distance: suppression method at distance = 0.641:0.685:0.566:0.724, P<.05). And the objective visual acuity measurement showed high reproducibility(intraclass correlation; induction method at near: suppression method at near: induction method at distance: suppression method at distance = 0.963:0.994:0.945:0.988, P<.05). The suppression method is useful in patient with visual acuities better than 20/120 while the induction method is useful in patient with visual acuities worse than 20/120.

Conclusion The objective near and distance visual acuities measured by presenting optokinetic stimuli on 17-inch monitor screen located 40cm from subject and on a 127-inch projector screen located 3m were highly correlated with subjective near and distance visual acuities.

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Effect of the interposition of optical filters with different visible light transmittances in mesopic and scotopic condition pupil size

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Purpose To determine how can the pupil size, in mesopic and scotopic condition, be affected by the interposition of optical filters. Also, the variability of the effect of these optical filters due to each filter's different visible light transmittance.

Methods The transversal study included data from 56 eyes of 28 subjects. To measure the different pupil size, in high mesopic, low mesopic and scotopic condition, was used a digital binocular infrared pupillometer. The obtained pupil size's measurements, without filter, were compared with the results after the insertion of the different optical filters used: 16 filters with different transmittances (from 82% to 5%).

Results Some filters, 5 of the 16, with different transmittances, 63%, 17%, 8%, 6% and 5%, caused significant variations in the pupil size in mean mesopic condition. The 2 highest transmittance's filters, 63% and 17%, between these 5 filters, which produced significant results ($p<0.00$, high mesopic condition, 4.0lux), were the ones that led a higgest pupil size variation, in the 3 different light conditions.

Conclusion The influence of some optical filters in pupil size variation, was confirmed. This effect on pupil size was significant only in high mesopic condition, and it was independent of each filter's different visible light transmittance.

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A comparison of intermediate and near visual outcomes and reading ability in patients bilaterally implanted with bifocal ZM900, ReSTOR IOLs and with multifocal ReZoom IOLs

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Purpose To compare intermediate and near distance visual outcome, reading performance, level of satisfaction and quality of vision at intermediate and near distance in patients bilaterally implanted with diffractive (AMO Tecnis ZM900 or Alcon ReSTOR) and refractive (AMO ReZoom) multifocal IOLs (MIOL).

Methods This study enrolled 71 cataract patients, 26 of whom received ZM900 diffractive IOL bilaterally (Group A), 22 of whom received ReSTOR diffractive IOL bilaterally (Group B) and 23 of whom received ReZoom refractive IOL bilaterally (Group C). Best distance-corrected intermediate and near visual acuity (BCDIVA - BCDNVA), defocus curve, binocular vision, reading speed, contrast sensitivity and Visual Function-7 (VF-7) modified questionnaire scores for intermediate and near distance everyday activities were assessed a month after surgery. Inclusion criteria were: age range 50-80 years, no concomitant ocular diseases and no intraoperative complicances.

Results BCDIVA and BCDNVA were better in group A and B than in group C. Group A achieved better contrast sensitivity than group B and C. Reading speed and VF-7 questionnaire scores were comparable in all groups.

Conclusion Intermediate and near distance performances were acceptable in all groups but diffractive IOLs proved slight1y better than refractive IOLs at near distance. Particularly, diffractive ZM900 IOL obtained better resu1ts than the other lenses. In our opinion the modified prolate aspherical surface of this lens could explain this phenomenon.

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Electrogenesis of the retina in proceeding glaucomatous optical neuropathy

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Purpose to investigate some branches of the pathogenetic mechanisms of eye function's disturbance in patients with the glaucomatous optic neuropathy(GON) with normalized intraocular pressure(IOP)

Methods 12 p-s(23 eyes) with primary open angle glaucoma(POAG) of I-IIIa study and normalized IOP by conservative treatment or after operation and 7 healthy volunteers were investigated.Standard (ISCEV) methods of record of the electroretinogram (ERG) and the original method of the oscillatory potentials (OPs) recording in light adaptation were used. Oscillations O1,O2 and O3 of the flicker 30Hz ERG were filtered on frequencies of 80 and 120Hz(MBN's equipment). Heidelberg retinal tomography(HRT), central field perimetry(CFP) on 30(Humphry) also were used

Results The correlation between decreasing of O3 and increasing of excavation of the optic nerve disc by HRT-data was obtained.Attenuation of amplitude of cones' oscillations O1 and O2 was linked with magnification of the degree of CFP's declension from the age norm (PSD). Decreasing of O1-oscillation amplitude was linked with the increasing of average elevation of CFP threshold mean(MD)

Conclusion 1.The genesis of the O1, O2 and O3 in flicker 30Hz ERG is differ in comparing with the genesis of OPs registered in dark adaptation, and is linked with the light on and dark off-channels of the cone retinal system. 2.Appearing indices of the retinal ischemia O1, O2 and O3, picked out from the flicker 30Hz ERG, show the link with the functional state of the retinal neurons in the light on- and dark off-channels of midget pathway. The O3-oscillation displays the neuronal links disturbance of the ganglion cells that is proving the degree of apoptosis' evolution

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Effect of litter size and birth weight on naturally occurring myopia in the Labrador retriever

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Purpose To evaluate early environmental influences (e.g. litter size, birth weight, birth season) on adult refractive error in dogs. A previous familial aggregation analysis has shown that the distribution of refractive error in a large family of pedigree Labrador Retrievers has a significant genetic component, but that litter size and other residual/ environmental factors also have significant effects.

Methods Refractive error was measured by cycloplegic retinoscopy in both eyes of 166 dogs, 1-8 years of age and free of ocular pathology, from a large family of pedigree Labrador Retrievers. All dogs originated from the same breeding colony. The early records of these dogs included information on birth weight, maternal litter cohort, litter size and neonatal weight gain, measured daily for the first 6 weeks. These factors were analyzed to investigate their effect on adult refractive error.

Results The average adult spherical equivalent refraction (SER) was -0.44D (-5.38D to +1.65D, n = 166): 35% were myopic (SER ≤ -0.50D), 58% emmetropic (SER = -0.49 to +0.99) and 7% hyperopic (SER ≥ +1.00D). Mean birth weight was 421±57g. Higher birth weight was weakly (R=0.3) correlated with more hyperopic adult refractions. Relative to large litters (≥ 7), dogs from small litters (< 7) gained more weight within the first 6 weeks of life and were on average 0.43D more myopic.

Conclusion The dog provides a unique model for studying a wide range of environmental influences on the development of naturally occurring, high prevalence, low degree myopia.

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10 years followup in children affected by various eye diseases: sensibility and specificity of VA, fundus and 30 Hz and mixed response electroretinogram done during anaesthesia as predictors of visual outcome

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Purpose This study aimed to define the relationship between 30 herz and mixed maximal response electroretinogram, recorded under anaesthesia, and the visual outcome in subjects affected by various retinal and/or optic disk affections.

Methods We present a review of 87 among 260 children examined under anaesthesia. All subjects(mean age 3,12)underwent ERG without adaptation, in a mid luminance, at 30 hertz and mixed maximal response. Results were matched with fundus findings and the visual acuities. Multiple statistical analysis comprehending student's t test for independent samples was used for comparisons between groups. A P value of less than 0.05 was assumed to indicate statistical significance.

Results Diagnosis linking fundus findings and ERG were: 7 Leber dystrophy, 12 ROP, 20 retinal dystrophy, 6 ny, 5 CVI, 2 Joubert syndrome, 1 Retinoblastoma, 5 ON coloboma, 1 Morning glory syndrome, 12 pale papilla, 2 congenital cataract associated with retinal anomalies, 14 not defined. Mean VA was 1,94 in right eye, 2,04 in the left. Significant correlations and "p" values were found between 30 hz amplitude, a and b amplitudes, b latency and visual acuities. ROC curves were statistically significant in latency and ampitudes in a and b waves.

Conclusion Our work indicate a correlation between fundus findings, ERG and visual outcome. When we are unable to perform a correct diagnosis by visit and instrumental methods in awake conditions, a brief anaesthesia allow to obtain results otherwise arduous.

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Retinal thickness vs. retinal sensitivity at the central human macula

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Purpose To assess the detailed correlation between retinal thickness and retinal visual function in the central 300 µm human macular area.

Methods Twenty-four eyes with clinically significant macular edema (CSME) (12 eyes with and 12 eyes without central foveal involvement) underwent retinal thickness measurement (RT) and retinal sensitivity, performed by Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA, USA) and MP1 (Microperimetry, Nidek, Japan) systems, respectively. The average retinal thickness in the 300 µm diameter area, centered in the fovea, was computed and correlated with the central MP1 value. RT could also be locally correlated with MP1 values in areas of 30 µm in diameter centered at each stimulus site. Precise correspondence between stimuli and RT locations was ensured by bringing into co-registering the fundus image references from both modalities.

Results A moderate correlation was found between RT and central MP1 value (R=-0.578, p=0.003). The correlation decreases when analysing, separately, eyes with or without central foveal involvement (p>0.05 for both groups) being stronger for the CSME eyes with central involvement.

Conclusion Cirrus HD-OCT high resolution mapping allows to correlate structure and function at detailed level in the central fovea. It became possible to demonstrate the lack of direct correlation RT/MP1 and the reason why an apparent correlation exist when considering all cases of being part of the same group.

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Lens cellular culture models obtained after cataract surgery: interest in cytogenetics analysis

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Purpose To model two new techniques of lens cellular culture after cataract surgery, depending of the technique used, in order to study cytogenetics characteristics

Methods Two techniques were provided to obtain lens cells during cataract surgery according to the technique used. Twenty phacoemulsification from patients (range 15 to 83 years-old) allowed to collect anterior capsules were collected during capsulorhexis before. Capsules were applied in thin layer on slides. Then they have been set in culture. Thirty posterior phacophagia (range 1 month-old to 8 years-old) allowed to collect liquids and were then cytocentrifuged. The cells centrifugated were set in culture. A cytogenetic analysis was performed with the lens cells and blood. An informed consent was obtained from the patients.

Results Twelve of the twenty capsules could lead to lens culture. The culture centrifugated cells of eighteen phacophagia could be used to perform a cytogenetic analysis and found a regular karyotype according to the blood results. The lens is specially exposed to UV rays and cytogenetic anomalies could be induced and then identify.Other applications could be applied with these lens cells as study of lens pharmacological effects of drugs.

Conclusion The techniques described are simple to perform and could be used in different applications. The cytogenetic analysis we used is one of those and confirms the interest to compare blood and tissue results.

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Application of agar sandwich technique for morphologic studies of anterior lens capsule

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Purpose Preparation of the anterior lens capsule for morphological studies is difficult due to its transparency, small size and delicacy. During preparation the capsule curls upon itself, causing various artefacts in capsule thickness and epithelial cells organization. The samples can also be easily lost. To overcome these problems, the agar sandwich technique was introduced.

Methods The capsules were obtained during routine cataract surgery and immediately fixated in 10% paraformaldehid for 1 to 2 hours. The agar sandwich consisted of 8mm wide agar disc and agar in liquid state, to be poured over the disc. The discs were pre-prepared and stored in alcohol, while the liquid phase was stored cold in syringe and melted for each case. With the aid of laboratory microscope pre-fixated capsule was gently straightened on the agar disc, mounted in the agar sandwich and fixated overnight. Fixation was followed by standard procedure for light or electron microscopy samples.

Results Anterior lens capsules from different cataracts were included in the study. Once positioned in the sandwich, the capsule remained in its shape throughout the preparation. The agar sandwich did not interfere with the standard Hematoxilyn-Eosin staining or cutting. Agar was clearly seen around the capsule on light microscopy samples. The appearance of basement membrane remained unchanged. However, for epithelial cells preservation the pre-fixation and gentle handling of the sample were crucial.

Conclusion The agar sandwich technique is a not-complicated technique, which turned out as an effective method in processing of the anterior lens capsule samples. In combination with pre-fixation no interfering with histological section or interpretation was noted.

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The acutely isolated human anterior lens capsule as a tool to study the physiology of human lens epithelial cells

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Purpose The defects in functional characteristics of lens capsule epithelial cells, can lead to the formation of the cataract, especially as cortical cataract. In the germinative zone of the lens the same progenitor cells, which also form the epithelil cells, differentiate also into the fiber cells, which make up the inside of the lens and through their activity also keep the lens clear. When their function is impaired the nuclear cataract ensues. We set out to make a preparation of the human anterior capsule from cataract surgery, which would allow functional studies of the physiology of capsule epithelial cells from patients with different types of cataract, using cell physiological methods.

Methods We used the entire anterior capsules, with the cells still attached. Cell contacts were preserved and allowed the communication between the cells. In addition all the contacts to the basement membrane were largely preserved although some parts of the capsule were denuded of the epithelium – possibly due to manipulation during the surgery itself, or to epithelial cell apoptosis. The remaining cells were viable and the capsules usable for experimentation for at least a day when kept in a tissue culture incubator. For experimentation using an inverted microscope, the capsules were weighed down with a harp as the one used for electrophysiological experiments. In a series of pilot experiments the lens epithelial cells were loaded with fura-2.

Results They exhibited normal [Ca2+]i responses to agonist application such as Ach.

Conclusion We conclude that this preparation represents a useful tool to study many aspects of the lens epithelial cell physiology.

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New non-contact biometer

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Purpose To evaluate and compare axial length (AL), anterior chamber depth (ACD), lens thickness (LT), and central corneal thickness (CCT) measurements assessed by optical biometry (OB), ultrasound biometry (UB), optical low coherence reflectometry pachymetry (OLCR-P), and by a new prototype applying optical low coherence reflectometry biometry (OLCR-B).

Methods OLCR-B (Haag-Streit), OLCR-P (optical low coherence reflectometry pachymetry; Haag-Streit), OB (IOLMaster, Zeiss), and UB (Tomey AL-3000) were performed in 35 eyes of 20 patients with incipient cataract. Among the patients were 13 women (age 60-88) and 7 men (age 53-90). There were no exclusion criteria. Bland-Altman analysis was performed to investigate agreement of AL, ACD, LT and CCT measurements between the devices. Correlation between the techniques was also determined using linear regression. All measurements were performed according to the manufacturers recommendations.

Results The mean AL was for OLCR-B 24.35 mm ± 2.32 (SD), OB 24.33 mm ± 2.41, and UB 24.03 mm ± 2.27; the mean ACD for OLCR-B 3.10 mm ± 0.51, OB 3.15 mm ± 0.52, and UB 3.09 mm ± 0.47; the mean LT for OLCR-B 4.71 mm ± 0.42, and UB 4.73 mm ± 0.49; the mean CCT for OLCR-B 543 mm ± 44, OLCR-P 536 mm ± 32, and UB 541 mm ± 41. Bland-Altman analysis and linear regression showed high correlation between the devices.

Conclusion OLCR-B, OLCR-P, OB and UB give comparable results in patients with incipient cataract. The advantages of the OLCR-B prototype are the non contact method, the exact measurement of AL, ACD, LT and CCT on the same interferometry method and hence the short duration of the measurements.

Commercial interest

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Anterior chamber morphometric estimation in patients they who underwent CTR implantation using Anterior Segment OCT and ultrasound biomicroscopy

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Purpose To estimate anterior chamber morphometric parameters (depth and volume) in case of patients they who underwent cataract surgery with posterior intraocular lens and capsular tension ring (CTR) implantation, using Anterior Segment OCT (OCT Visante) and ultrasound biomicroscopy (UBM).

Methods Studied group consisted of 23 persons 12 women and 11 men, aged from 79 to 52 years old (mean 63.9 years). BCVA ranged from 0.2 to 1.0 (mean 0.6). Anterior chamber depth and width were measured at first using Anterior Segment OCT (OCT Visante) than with the use of ultrasound biomicroscopy (UBM). Anterior chamber volume was calculated.

Results Anterior chamber depth measured using Visante OCT ranged from 4.34mm to 4.79mm (mean 4.61 ± 0.17) and in case of UBM ranged from 4.17mm to 4.92mm (mean 4.57 ±0.28). Anterior chamber volume measured using Visante OCT ranged from 230,42µl to 339,91µl (mean 278,2 ± 31,32) and in case of UBM ranged from 212,75µl to 330,51µl (mean 269,23 ±36,77).

Conclusion Anterior Segment OCT is more precise in anterior chamber estimation also allows to enlarge measured area. As a non contact device is easier and faster to performe, however picture's width in case of ultrasound biomicroscopy is larger.

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Glucose-6-phosphate dehydrogenase (G6PD) deficiency and senile cataract in a sardinian population, Italy

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Purpose There is still no general agreement on the role of G6PD deficiency in the pathogenesis of cataract. Although G6PD deficiency has been correlated with cataract in some studies, other reports have showed no correlation. The purpose of this study was to determine the prevalence of G6PD deficiency in male patients of Sardinian origin with senile cataract and to compare it with the prevalence rate of G6PD deficiency in the general population of the same area.

Methods Erythrocyte G6PD activity was determined using a quantitative assay in 1628 male patients with cataract. The control group consisted of 1646 apparently healthy male patients from the same area described in a former study. Student's t test was used to determine differences between groups.

Results G6PD deficiency was found in 134 (8.2%) patients with cataract and in 120 (7%) control subjects. Differences between cases and controls were not statistically significant (P=0.78).

Conclusion The results of this large study suggest that male patients with G6PD deficiency in the Sardinian population do not have a higher risk of developing presenile cataract.

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Protein quality control and ubiquitin proteasome system: implications on cataract

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Purpose Accumulation of damaged or abnormal proteins is cytotoxic and is causally related to various age-related diseases, including cataract. The objective of this study is to investigate the effect of 19S regulatory complexes on the fate of damaged proteins.

Methods The denaturation of firefly luciferase (a model protein) was performed at 43°C during 10 min in the presence of Hsp90 and denaturation of luciferase was monitored by the loss of its enzymatic activity. Luciferase activity in the cells was determined to monitor the refolding of denatured luciferase at 30°C in the presence or absence of ubiquitination system.

Results The data showed that heat-denatured luciferase was preferentially ubiquitinated and degraded by the UPP as compared with the native form. Inhibition of the ubiquitination or proteolysis enhanced renaturation. The 19S regulatory complex enhances renaturation of denatured substrate in the presence of ubiquitinating activity. The data also suggested that recognition of a poliubiquitinated substrate requires that polyubiquitin chain interact with specific domains of the 19S cap of the proteasome and this interaction play an important role on the fate of denatured proteins. Additionally, the data shown that are critical lysines in the ubiquitin moiety are required for an efficient and productive interaction with proteasome.

Conclusion Failure in the protein quality control system is likely to have important implication in loss of lens transparency and cataract formation.

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Spontaneous cataract formation in DBA/2J mice

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Purpose DBA/2J mouse develop spontaneously changes in anterior chamber like pigment dispersion syndrome, iris atrophy, posterior synechiae leading to IOP increase. Additionally, there are observations suggesting cataract formation. The aim of this study was to describe features of cataract formation in DBA/2J mice. Moreover, presence and pattern of the L- kynurenine aminotransferases (KAT I , II and III) immunoreactivity in the cataractous lens of DBA/2J mice was investigated.

Methods Immunohistochemistry was conducted using polyclonal antibodies against KAT I, II and KAT III on 18 cataractous lenses of 8-, 11- and 24-month old DBA/2J mice (6 in each group). All the sections of the lens were stained with Periodic Acid – Schiff (PAS), and normal anatomy of the anterior segment of the eye was confirmed. Moreover, all the animals subjected to the study were examined using slit lamp and anterior chamber photography.

Results As observed clinically, the animals developed cataract during aging. PAS staining revealed presence of lens opacification. Immunohistochemical analysis revealed presence of KAT I, II and KAT III in the extracellular structures of cataract showing specific pattern of the stain. In cortical cataract the immunoreactivity was observed on cortical lens fibres. In nuclear cataract, KAT II revealed stronger and diffused staining than KAT I. Additionally both KATs showed more pronounced staining at the edge of small clefts.

Conclusion Manifestation of L-kynurenine aminotransferases in extracellular matrix during cataract formation in DBA/2J mice suggests that products of L-kynurenine pathway might be involved in mechanisms of cataractogenesis in this animal model.

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Effect of glutathione with sea tangle extract on prevention of selenite-induced cataract formation in rat eyes

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Purpose To evaluate antioxidative and preventive effects of sea tangle extract on selenite-induced cataract formation.

Methods Eighty SD rat pups were randomized into 8 groups. Group 1, not injected any reagent (normal); In group 2-8, selenite(15μmol/Kg, s.c.) was injected on day 11. In group 2 (control) and group 3, normal saline (i.p.) and ascorbic acid (i.p.) was injected on days 3–31; In group 4-8, sea tangle extract (i.p.) was injected on days 3–31 with concentration of 12.5, 25, 50, 100, 200mg/Kg, respectively. Development of cataract was assessed and photographed weekly under slit lamp photo. After 31st day, rat lenses were analyzed for antioxidant enzymes, glutathione peroxidase (GPx), superoxide dismutase and malondialdehyde. Furthermore, amino acid analysis of sea tangle extract was performed.

Results Significant differences ($p < 0.05$) were seen in cataract development by the 8 groups. No rats developed cataract in group 1; Dense nuclear cataract was developed 8 of 10 and 4 of 10 rats in each group 2 and 3; Group 4-8 developed nuclear cataract with proportion of 6/10, 3/10, 2/10, 1/10 and 6/10 rats. In sea tangle injected group (group 4-8), levels of GPx were higher than those in ascorbic acid and control group. Especially, group 7, injected with 100mg/kg of sea tangle extract showed significantly high level of enzyme. Results of amino acid analysis showed sea tangle includes glutamate-glycine-cysteine, major constituents of glutathione(GSH).

Conclusion The glutamate-glycine-cysteine in sea tangle is supposed to increase the level of lens GSH and this may contribute to lowering cataract development. This study strongly supports the activity of sea tangle as an endogenous antioxidant and anticataract agent.

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Modifications in conjunctival and limbar epithelium after micro-incision cataract surgery (MICS). Impression cytology study

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Purpose To know if the exposition of the conjunctiva during the micro-incision cataract surgery (MICS) and the energy released during the phacoemulsification produce alterations in the goblet cell population and nucleus / cito plasm relation in the different areas of the conjunctiva of these patients.

Methods 32 patients scheduled for MICS surgery were included in this study. The cataract grade, phacoemulsification power, phacoemulsification time and time of the exposition of the conjunctiva were registered during the surgery. Goblet cell count, epithelial cell morphology and inflammatory cells were studied by conjunctival impression cytology before and after the surgery, at one and three months. The conjunctival samples were obtained from the nasal area, temporal area, and the phacoemulsification incision area.

Results Mean age of the patients was 67-years old. Mean phacoemulsification power was 6 %, and the "phaco" time was 30 seconds. Mean time of the exposition of the conjunctiva was 9 minutes and 30 seconds. Analysis by impression cytology of the ocular surface showed a goblet cell population pre-operative of 408/mm2 in the nasal area, 317/mm2 in the temporal area, and 343/mm2 in phacoemulsification incision area. Goblet cell count in the three different places decreased significantly after MICS surgery: p=0.038, p=0.018, and p=0,001 respectively.

Conclusion Impression cytology showed a significant reduction in the goblet cell populations after MICS in the three studied areas of the conjunctiva.

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Ophthalmologic surgeries in the one-day surgery unit. A descriptive study evaluating 13 years of activity

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Purpose A descriptive, retrospective study about the surgical activity at the One-day surgery Unit (ODSU) of the Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, during the years 1995 to 2007.

Methods To review the surgical activity of the ODSU, the following variables were analyzed: sex, age, diagnosis, risk of anaesthesia and applied anaesthesia, surgical technique, intra- and postoperative complications, medication, morbidity, criteria of discharge from hospital, waiting list time as well as the grade of information given to the patient, comfort, sanitary attention, and grade of satisfaction. These data were obtained from a personal questionnaire and a phone call and were statistically analyzed by the StatView program.

Results During the period of 1995 to 2007 13.585 surgical interventions were realized at the ODSU, among those 4.734 ophthalmologic surgeries (34, 8%).The average age of the patients was 56, 53 years. The 56 % were males. In the 22, 9% of the cases the employed anaesthesia was retrobulbar. The surgical techniques were: phacoemulsification and IOL 3550 (26, 1%), extracapsular cataract extraction 256 (1, 8%). In the 95% of the cases the patients were discharged from hospital, the remaining 5% is composed of non intervention, ocular hypertension, infection, retrobulbar haematoma and fever. The grade of general satisfaction was qualified as high (85%), with the acceptance to return to the ODSU in the 76% of the cases

Conclusion The ODSU offers a safe, fast and comfortable alternative to classic hospitalisation.

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The incidence of endophthalmitis after cataract surgery-a retrospective study: evaluation of risk factors and impact of the introduction of intracameral cefuroxime

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Purpose Postsurgical endophthalmitis is an inflammatory reaction of the ocular tissues of infectios or non infectious origin as a consequence of the ocular surgery.Determine the most frecuent causes of endophthalmitis.

Methods Retrospective observational study registrating the cases of endophthalmitis after phacoemulsification among the surgeries practiced during the period of 1993 to 2007 in the Hospital Clinico Universitario Lozano Blesa Zaragoza, Spain.

Results The study included 92 eyes with postsurgical endophthalmitis, an incidence of 0,4%. In the 65% of the cases the microbiological samples were positive, the most frequent findings were gram positive bacterias. The type of anaesthesia, the location of the incision, the use of sutures, the type of IOLs and the existence of a systemic disease seem not to be significant risk factors for developing endophthalmitis

Conclusion Posterior visual acuity depended mostly of the virulence of the germ causing the infection. The use of intracameral cefuroxime was associated wit a significative descense of the percentage of endophthalmitis.

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In vivo thermographic analysis of clear corneal incision during phacoemulsification: comparison for coaxial, microcoaxial and bimanual techniques

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Purpose To measure the wound corneal temperature of clear corneal incisions (CCIs) during phacoemulsification (PKE) using different surgical techniques: standard coaxial, microincision coaxial and microincision bimanual.

Methods Human corneal emissivity was determined on corneal graft with the "Black Tape" method. After validation of the method on porcine corneas, the temperature of 35 CCIs was recorded continuously during PKE (7 coaxial with 1.8 mm incision, 14 coaxial 2.2 mm, 8 coaxial 2.75 mm, and 6 bimanual 1.3 mm) using portable laser targeted infrared thermometer.

Results No thermal differences were observed within the three groups in PKE mode 1 (nucleus sculpting and grooving) (p=0.56) and in PKE mode 2 (nuclear fragments phacoemulsification) (p=0.32). Bimanual 1.3 mm CCIs's temperature was lower than the three other groups during irrigation-aspiration mode (p<0.05).

Conclusion Clear corneal microincisions did not induce temperature increase of CCIs during phacoemulsification compared to larger incisions.

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Morphologic changes in haptoglobin knockout mice, typical for anterior segment dysgenesis, may be linked to diminished expression of C-Maf

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Purpose To study the ocular phenotype of mice that lack Haptoglobin (Hpko) and investigate whether these changes correlate with the expression of C-maf. C-maf is known to be expressed in embryonic life and to be involved in the development of the lens and anterior segment

Methods Hpko mice and wild type(WT)littermates were histological investigated at embryonic day(E)12,15 and 18 and postnatal day(P)1,4 and 21. The expression of C-maf was studied at mRNA level by rt-PCR. C-maf expression in eyes was compared in adult mice between clinically blind versus not-blind Hpko and WT mice and in embryos at E12,between offspring from clinical blind versus not-blind Hpko mothers

Results Eyes of Hpko mice were histological normal at E12 compared with WT mice. At P1 eyes of Hpko mice were significantly smaller (mean 29%); in 55% of mice the lens was not yet separated form the cornea. At P21 12% of the eyes from Hpko mice still showed contact between lens and cornea; anterior senychiae were present in 42% of the eyes,whereas these structural abnormalities were never observed in WT eyes.The ocular C-maf mRNA expression at E12 was significantly lower in Hpko embryos as compared to WT embryos (P<0.05). C-maf expression levels in eyes of Hpko non-blind mothers were intermediate

Conclusion Haptoglobin knockout mice exhibit developmental disorders that are similar to those observed in developmental glaucoma. There is a delay in development of the anterior segment structures, which start during late embryonic life and continue after birth. C-maf expression is diminished at E12 and this may be linked to the aberrant anterior chamber development

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Single nucleotide polymorphisms of the tenomodulin gene (TNMD) in age-related macular degeneration

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Purpose TNMD is an X-chromosomal gene, which encodes a putative angiogenesis inhibitor, a type II transmembrane glycoprotein, which has proven to be expressed in retina. Associations of single nucleotide polymorphisms of TNMD with the prevalence of age-related macular degeneration (AMD) was examined.

Methods The study population comprised of 38 men and 65 women with exudative AMD, 16 men and 23 women with dry AMD and 35 men and 75 women without AMD (controls). Patients with choroidal neovascularization attributable to AMD were diagnosed by fundus photographs and fluorescein angiography in the Department of Ophthalmology at Kuopio University Hospital. There were no signs of AMD in the control group as visualized in fundus photographs. In both groups, selection criteria required subjects to be over 65 years of age and diabetes mellitus was considered an exclusion criterion.

Results Men with rs5966709-G genotype had higher prevalence of AMD (exudative and dry form combined) than subjects with rs5966709-T-genotype (69% vs 47%, p=0.045). However, the difference in the prevalence of exudative and dry form of AMD was not statistically significant (p=0.061, p=0.179). Among women the subjects with rs2073163-CT-genotype had lower prevalence (28%) of exudative form of AMD than other genotypes (49% and 59% for subjects with rs2073163-CC- and rs2073163-TT-genotypes, correspondingly, p=0.028).

Conclusion The rs5966709-G genotype of TNMD is a modest AMD risk factor for men, while rs2073163-CT-genotype might be protective for women in exudative AMD.

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A novel OPA1 mutation in a patient with severe, acute and late-onset Autosomal Dominant Optic Atrophy

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Purpose We report the first case of acute and late-onset Autosomal Dominant Optic Atrophy with a novel mutation. Autosomal Dominant Optic Atrophy (ADOA) is an inherited primary optic neuropathy that leads to reduced visual acuity. ADOA has often been associated with mutations in OPA1 gene. OPA1 encodes a large dynamin-related GTPase, involved in mitochondrial structure, mitochondrial DNA maintenance and apoptosis regulation.

Methods We conducted direct DNA sequencing of the entire coding sequence and the exon/intron junctions of OPA1 gene.

Results A 62-year-old woman noticed blurred vision with a central scotoma. Visual loss was sudden, painless and severe in her right eye. Papillary edema was noted. Left visual loss occurred one year after initial presentation. The ophthalmoscopic feature of our patient was diffuse optic disc atrophy. MRI examination confirmed the diagnosis of isolated bilateral optic neuropathy. We did not found any neurological, metabolic, toxic, or ophtalmic causes. One novel heterozygous missense mutation in exon 27 was characterized. This mutation has not been previously reported, was absent in 400 control chromosomes and affected highly conserved amino acids.

Conclusion The age of onset, like ADOA penetrance must be accepted to be more variable than initially thought, including late-onset cases. The presence of an OPA1 mutation reveales that this sporadic late-onset and acute case of optic neuropathy is related to ADOA. This result shows that the mutation screening of OPA1 gene could be justified in every case of optic nerve atrophy with no clear cause.

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Ophthalmological findings in childhood onset myotonic dystrophy type 1

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Purpose Myotonic dystrophy type 1 (DM1) is an autosomal dominant multisystemic disorder, characterised by increasing severity and anticipation (progressive expansion of the repeat size and earlier onset in successive generations). It is caused by an expanded cytosine-thymine-guanine (CTG) triple repeat expansions in the myotonic protein kinase gene located on chromosome 19. Muscle wasting, myotonia and cataract are features of classical DM1, while congenital and childhood DM1 are also present with CNS involvement and cognitive impairments. The aims of the current study were to describe ophthalmological findings in individuals with childhood onset DM1, to correlate the ophthalmological findings with the size of the CTG expansions, inheritance and the age of onset and presenting clinical symptoms.

Methods Sixty- two children and adolescents were eligible for the study and 49 accepted to participate. All had clinical symptoms <10 years of age and were diagnosed with >40 CTG repeats <18 years of age. According to the age of onset and presenting clinical symptoms, the subjects were divided into three subgroups: I/ severe congenital II/ mild congenital and III/ childhood DM1.

Results High hyperopia, heterotropia, subnormal VA, motility abnormalities and nystagmus were common features of congenital onset DM1. No cataract was found and ptosis was rare while pseudoptosis and motility disorders occurred frequently among individuals with high number of CTG repeats.

Conclusion Ophthalmological pathology was common and individuals with severe congenital DM1 were present with the highest frequency. Number of CTG repeats affected the motility and pseudoptosis while inheritance had no influence on ophthalmological abnormalities.

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Genetic analysis of families with autosomal recessive retinal dystrophies

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Purpose To screen candidate gene loci in families with autosomal recessive RP

Methods We used an approach of screening for homozygosity at candidate gene loci in affected individuals. 34 families with autosomal recessive RP (ARRP) or related phenotypes were included in the study of which 25 families were consanguineous, and all families had 2-4 affected offspring. Patients and family members were clinically evaluated and blood samples were collected for DNA extraction after obtaining consent. Microsatellite markers flanking 23 known candidate genes for retinal dystrophy were genotyped in available members of all families. Microstallite markers selected were located in a 5.0 cM interval of the candidate gene. Families in which homozygosity was present and specific for all affected members at a candidate gene locus were further screened for mutations in the relevant gene. Coding regions of the genes were amplified using exon-specific primers and subjected to direct sequencing.

Results Screening of 23 gene loci revealed homozygosity shared by affected individuals in 10 out of 34 families. Homozygosity was detected at 2-6 informative markers at each locus. The candidate gene loci are: ABCA4 (1p22.1), RPE65 (1p31), CRB1 (1q31), CNGA1 (4p12), PDE6B (4p16.3), TULP1 (6p21.3), RP1 (8q12.1), RGR (10q23), NRL (14q11) and RLBP1 (15q26). Putative pathogenic sequence changes were found in the probands upon screening the TULP1, ABCA4 and RPE65 genes. Screening of other candidate genes is in progress.

Conclusion This approach enabled a rapid preliminary screen of known loci in recessive RP and may be suitable for identifying the disease locus in small consanguineous families.

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Three Families with Best's Disease and Normal Electro-oculogram Recordings

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Purpose To describe 3 families with Best's disease with normal electro-oculogram (EOG) and without VMD2 mutations.

Methods Evaluation of the patients included visual acuity, fundus and autofluorescence (Heidelberg Retinal Angiograph), Goldmann visual fields, optical coherence tomography (Zeiss, OCT3), full field (ISCEV protocol) and multifocal electroretinograms, and EOG (ISCEV protocol). The diagnosis of Best's disease was based on autosomal dominant inheritance, typical yellowish, autofluorescent material in the central macula accumulating beneath the retinal pigment epithelium, and decrease of the EOG Arden ratio.

Results Among the 1130 families with various retinal dystrophies followed up in Montpellier, 40 (3.5%) were found with vitelliform macular dystrophy. Best's disease was observed in 20 of them while 13 families had adult macular vitelliform dystrophy and 7 had reticular dystrophy. In the group with Best's disease, a normal EOG was recorded in 3 families. None of these 3 families carried mutations in VMD2 or RDS, and linkage to the VMD2 locus was excluded in one of them.

Conclusion In patients with Best's disease and VMD2 (bestrophin) mutations, the decreased response of the EOG is attributed to an abnormal transepithelial chloride transport. However, the observation of families with normal EOG and no VMD2 mutations suggests that other genes are responsible for Best's disease which could not impair the ionic transport but yet lead to similar subretinal deposits.

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Ocular phenotype of CORD5, an autosomal dominant cone-rod dystrophy associated with a Q626H mutation in the PITPNM3

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Purpose The aim of the study was to describe the phenotype of CORD5, an autosomal dominant retinal dystrophy with a mutation Q626H in the PITPNM3/Nir1 gene encoding the PITPNM3 protein.

Methods The study included 33 individuals from two different families, all heterozygous for a Q626H mutation in the PITPNM3/Nir1 gene. Ophthalmological examination including kinetic perimetry, and in selected cases adaptometry, colour vision tests, OCT and electrophysiological studies were performed. In some case the data was obtained from medical records.

Results A majority of patients presented symptoms with subnormal visual acuity and light sensitivity from childhood. Signs of macular degeneration were observed early as well. There was a progressive decrease of visual acuity leading to legal blindness in early adulthood in some cases. Electrophysiological testing showed a progressive loss of photoreceptor function restricted to the cones. There seems to be a difference regarding severity of clinical manifestations between the families.

Conclusion Our observations and electrophysiological findings indicate a phenotype in CORD5 with loss of photoreceptor function restricted to the cones. An intra-familial and inter-familial difference regarding severity of clinical picture was noted.

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Cone dystrophy with supernormal rod response – case report

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Purpose Our purpose is to present a case demonstrating a novel, rare retinal disorder, called "cone dystrophy with supernormal rod response".

Methods A 31-year-old female patient has been suffering from colour vision disturbances since her childhood. Her best corrected visual acuity is 0.2 in both eyes. Beyond routine ophthalmological methods we performed electrophysiological examinations, colour vision tests, dark adaptation, optical coherence tomography, fluorescein angiography and molecular genetic testing.

Results Examinations revealed colour vision disturbances, OCT showed macular thinning, FLAG demonstrated enlarged foveal avascular zone. Electroretinography showed extinguished cone function, preserved rod response and supernormal maximal b-wave. Genetic tests confirmed mutation of the KCNV2 gene.

Conclusion „Cone dystrophy with supernormal rod response", known from recent literature, is a rare retinal disease, with the affection of the KCNV2 gene in the genetic background. Its stationery character is rare amongst cone dystrophies, congenital achromatopsia is the only one to have similar manifestation.

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X-linked retinoschisis

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Purpose To expose a case of X-linked retinoschisis and to correlate findings obtained by Optical Coherence Tomography (OCT) images with visual acuity and macular lesions.

Methods We present a case report of a male child diagnosed of X-linked Retinoschisis at the age of 6.About his family background, we know that his aunt has three sons diagnosed of the same disease.At the age of 18, his visual acuity was 0.5 for right eye and 0.1 for left eye by Snellen scale. The visual acuity did not change along all these years.

Results Cystic appearing macular lesions were observed both clinically and by tomography images.Cystic spaces on the foveal region, (as the image of a "cart wheel"), and peripheral retinoschisis were observed in the fundus examination.Optical Coherence Tomography showed cystic foveal blocked images located within the inner nuclear layer.

Conclusion The exposed disease has a very low prevalence (1 to 2 cases each 30000 inhabitants).The findings obtained by OCT images let make a diagnosis of localization within retina layers and also let follow up the macular lesions evolution.

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Spectrum of TGFBI gene mutations among Polish patients with corneal dystrophies

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Purpose To report the clinical and molecular findings in Polish patients with stromal corneal dystrophies caused by TGFBI gene mutations.

Methods Patients with clinically diagnosed granular (n=14; 9 unrelated families) and lattice (n=2; 2 unrelated families) corneal dystrophies participated in the study. Corneal phenotypes were assessed by slit lamp and confocal microscopy in vivo. Genomic DNA was obtained from blood samples and exons 4, 12-14, known to contain mutation hot spots, were PCR amplified and sequenced on both strands.

Results Molecular genetic testing revealed a heterozygous R555W (exon 12) mutation in eight (5 families) patients diagnosed with granular Groenouw type I corneal dystrophy. In one patient a heterozygous R124H mutation (Avellino corneal dystrophy, GCD type II) was found. In three families with "atypical granular" dystrophy affecting mainly the anterior stroma no mutation was detected in the analyzed regions. Heterozygous T538R (exon 12) and H626R (exon 14) mutations were identified, respectively, in two patients diagnosed with lattice corneal dystrophy.

Conclusion Our results show that TGFBI gene mutations located in exons 4, 12 and 14 are frequently (8/11, 72%) found in Polish patients with corneal dystrophies of granular and lattice type. This indicates that a relatively straightforward molecular analysis can be a practical use in diagnosis of these conditions and associated genetic counseling.

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Ophthalmic skills – Confidence and knowledge of recently graduated doctors

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Purpose Undergraduate medical education in ophthalmology is not standardized in the UK. The purpose of the study was to determine Foundation Year 1 Doctors (FY1) confidence in their own ophthalmic clinical knowledge and skills.

Methods Questionnaires were distributed to FY1 at a University Hospital in the United Kingdom. A total of 15 questions were asked and topics ranged from self-confidence in ophthalmic skills to ones regarding management of common ophthalmic conditions that present to an Accident and Emergency department.

Results A total of 20 doctors completed the form. More FY1 felt more confident measuring visual fields (80%) than visual acuity (70%). Only one (5%) was confident in measuring pupillary reflexes. 85% felt that they were not confident in using an ophthalmoscope or needed practise. Even though most were confident in measuring visual fields and 90% could identify a homonymous hemianopia, only 15% could identify a valid cause. Safe management questions were answered poorly with less than 50% correct responses in most questions. 70% indicated an interest in more teaching on practical skills and clinical scenarios in ophthalmology.

Conclusion There is a lack of confidence amongst FY1 in clinical skills and in particular with the use of the ophthalmoscope. The majority of FY1 questioned wanted more ophthalmology tuition.

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Use of mobile-learning amongst ophthalmic tutors and medical students

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Purpose As the use of SMART PHONE [mobile + personal digital assistant (PDA)] technology is on the increase, this study tried to analyze the attitude towards mobile learning amongst ophthalmic tutors and medical students and the impact of learning styles on the uptake of newer learning technologies

Methods Fourth year medical students undertaking their ophthalmology attachment and clinical tutors provided information about their views on their use of mobile technologies. Use of mobile (m-learning) environment was compared with an assessment of the individual index of learning styles (ILS)

Results The mean age of the tutors was 40 years (n=17) and medical students was 26 years (n=46). The students were significantly younger than the tutors ($p<0.001$, chi square). Students and tutors had a fairly well balanced score (1-3) on the two dimensions of the ILS scale. Students with moderate preferences for visual learning were more likely to enhance their clinical training and electronic-based learning ($p=0.003$), download course materials ($p=0.001$) and access health and related information ($p=0.004$) using smart phone technology. Similar correlations were not found with other dimensions of ILS. There was no similar correlation found between tutors and ILS on any dimension. Medical students appeared enthusiastic to use the new PDA based technology whilst tutors, in general, were wary of such technology for use by medical students or themselves

Conclusion Medical students had a more positive outlook towards m-learning with visual learners more likely to use smart phone technology. Tutors attitudes, however, were more reserved towards a potentially useful mode of learning

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EyeDiagnostics – a collaboration tool in eye care

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Purpose An Internet-based system for inter-professional collaboration between opticians/optometrists and ophthalmologists was developed and tested during 2007-2008. The purpose of the current study was to describe the main screening findings and the actions taken, based on the test results.

Methods State-of-the-art non-mydriatic fundus cameras and visual field testing equipment were installed and the opticians were offered targeted training in the use of these instruments. The examination results were uploaded to EyeDiagnostics server and evaluated by ophthalmologists.2301 subjects,63% women and 37% men, age 24 to 91 years (median 63, IQ 53-73), have been examined by one of 55 different opticians and the findings evaluated by one of two experienced ophthalmologist.

Results 63% (1 335) of the examined subjects showed no abnormalities. In 30% (675) a follow-up examination was judged to be indicated, which could be performed by the optician. 7% (159) of the tested subjects were referred to ophthalmic health care for treatment or further examinations.

Conclusion Modern technology in communication, fundus imaging and visual field examination have made it possible to reach a large number of people with advanced ophthalmic testing. This increase in diagnostic facilities can be expected to reduce workload in medical ophthalmic care, since many subjects, e.g. with family history of glaucoma, can be screened and followed using the EyeDiagnostics system.

Commercial interest

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Ophthabase: a generic extensible patient registry system

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Purpose To allow analyses on large amounts of patient datasets as well as to assemble populations of patients for clinical trials it is of great importance to have a robust and easily accessible patient registry system. Problems regarding technological and organisational aspects are usually reappearing among such systems. To enhance reusability we are pursuing a generic approach for our system, using a standardized model as a basis for free specifications of data definitions.

Methods The system is a Web application based on the Java. The model containing the data definitions is based on the CDISC Operational Data Model (ODM), a common standard for interchange of clinical data. The ODM-file is parsed at compile-time to generate the persistence layer, as well as templates for the Web-masks, reports, search-forms and interfaces. The application includes reusable aspects, e.g. auditing mechanisms, user management and input validation.

Results The generic system was successfully used in Tuebingen to construct a concrete patient registry called Ophthabase. Although created for ophthalmology, the generic concept allows creation of almost any kind of patient registry. The patient registry can easily be modified by editing the ODM-file. The generated system is less error-prone during system development, since data modelling is separated from technological concerns.

Conclusion The generic concept will be extended in the future to further augment the patient registry systems, e.g. by adding sophisticated search routines, analytic functionality or optional pedigrees. Multi-centre data interchange will be possible based on Web Services using a mediator-server able to match ODM-models of different patient registries. The ODM-file can also be used to configure clinical trial systems.

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Prevalence of age-related macular degeneration in the AGES - Reykjavik Study

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Purpose To determine the prevalence of age-related macular degeneration in the Age, Gene/Environment Susceptibility - Reykjavik Study.

Methods The random sample includes individuals born between 1907 and 1935 who were recruited to participate from 2002-2006. 5272 participated in the 3rd follow-up visit which included an eye examination. After a maximum dilatation of the pupil all had a digital fundus photography centered on the macula. The photographs were graded by masked graders at the Wisconsin Ocular Epidemiology Grading Center using a modification of the Wisconsin Age-related Maculopathy Grading System.

Results The participants were 67 years and older. There were 5138 right macular fundus photographs gradable for early age-related maculopathy (ARM). The prevalence of early ARM was 18.3% (95% CI 17.3-18.9). Among the participants 4.4% (95% CI 3.9-4.7) had late age-related macular degeneration (AMD). For pure geographic atrophy (GA) there were 5036 gradable photographs of the right macula and the prevalence was 2.1% (95% CI 1.7-2.3). Those with GA and also exudative AMD (mixed type) are not included in this category. For exudative late AMD there were 5152 gradable photographs of the right macula and the prevalence was 2.3% (95% CI 1.9-2.5). GA, when present, was located in the centre circle (foveal area) in the vast majority of cases.

Conclusion We found a steep age-related increase in the prevalence of age-related maculopathy in this elderly white population and geographic atrophy was usually located in the foveal area. The prevalence was similar for both late types of age-related macular degeneration.

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Anthropomorphic measurements and general and ocular parameters in adult Chinese. The Beijing eye study

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Purpose To determine whether anthropomorphic measurements are associated with ocular and general parameters.

Methods The population-based Beijing Eye Study, which included 4439 subjects (age: 40+ years) out of 5324 subjects invited to be examined in the year 2001, was repeated in 2006 with 3251 (73.2% of 4439, or 61.1% of 5324) subjects participating. The anthropomorphic measurements body height and weight, socioeconomic variables, and ocular parameters were evaluated.

Results Out of the 3251 subjects included in the study, measurements of body height and weight were available for 3214 (98.9%) subjects. In multivariate analysis, body height was significantly associated with the systemic parameters higher level of education (P=0.004), higher income (P<0.001), lower body mass index (P<0.001), lower systolic blood pressure (P=0.012), higher diastolic blood pressure (P<0.001), male gender (P<0.001), lower age (P<0.001) and living in an urban region (P<0.001), and with the ocular parameter of a deep anterior chamber (P<0.001).

Conclusion In adult Chinese, body length is associated with higher level of education, higher income, lower systolic blood pressure, higher diastolic blood pressure, lower body mass index, in addition to living in an urban region and to be male. From an ophthalmic point of view, tall subjects had deeper anterior chambers. Since the socioeconomic, systemic and ocular parameters examined influence occurrence and therapy of ocular diseases, these data may helpful in the assessment of risk factors and in the diagnosis and treatment of ocular diseases.

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The ocular findings among young males: a 12-year prevalence study of the military service in Poland

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Purpose To determine the prevalence of ocular diseases among young males and to assess the main ocular causes reflecting discharge from military service in Poland.

Methods A retrospective review of the medical records, of the 105017 men preliminary examined to military service during the period 1993-2004. All of them were of European Caucasian origin. Sample size for the study was calculated with 99% confidence, within an error bound of 5%. Data regarding the vision status was assessed in 1938 eyes of 969 subjects. Based on the age of subjects they were divided into two groups; group I aged 18-24 and group II aged 25-34.

Results Presenting visual impairment (VA <20/40) followed by color vision defects was the commonest ocular disorder and accounted for 13.21%. There were statistically significant differences of uncorrected visual acuity as well as of rates of particular refractive errors, in between age groups (p<0.05). Orthoptic problems, including various types of strabismus, were recorded in 3.61% subjects. Totally, 302(31.17%) males failed their medical examination and were temporally or permanently discharged from duty. Of them 52 (17.22%) subjects were discharged due to various ocular disorders. High refractive errors followed by chronic and recurrent diseases of posterior eye segment were the commonest ocular causes and accounted for 38.46%.

Conclusion Prevalence of ocular disorders among young males in unselected military population was closer to the results obtained in other population-based studies comprising both males and females in the same age group. High refractive errors followed by chronic and recurrent diseases of posterior eye segment are important causes of medical discharges from military service.

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Philatelic aspects on WHO Year Glaucoma 2008

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Purpose WHO dedicates anno 2008 to Glaucoma. Here we like to present philatelic aspects from Hippocrates to modern Glaucoma Screening, spiced with issues of stamps in 2008.

Methods Collecting stamps.

Results To be seen.

Conclusion Philatelic/historical aspects of glaucoma may induce a humble view.

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Correlation of optic disc morphology and ocular perfusion parameters in patients with primary open angle glaucoma

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Purpose Little information is available about the relationship between glaucomatous visual field defects and reduced blood flow in the optic nerve head. It is still not clear, if impaired circulation is a causative factor in the disease process, or if it is secondary as a result of loss of axons in the optic nerve head. In the present study vascular parameters were correlated against structural damage of the optic nerve head and functional damage.

Methods 103 patients with primary open angle glaucoma, documented visual field defects and optic disc morphology changes were examined. Blood flow parameters were assessed using Laser Doppler Flowmetry, Laser Doppler Velocimetry, and the Retinal Vessel Analyzer. To evaluate the morphology of the optic nerve head, a fundus photograph was taken. For determination of the degree of visual field damage, automated perimetry was performed.

Results The degree of optic nerve head damage was significantly correlated with the intensity of visual field loss. Decrease in retinal vessel diameter was only slightly correlated with the degree of glaucomatous optic neuropathy and visual field defect. Reduced optic nerve head blood flow was, however, strongly correlated with the degree of visual field loss and morphological optic disc damage.

Conclusion The data of the current experiment indicates that blood flow in the optic nerve head is strongly associated with the degree of visual field damage, whereas retinal vessel diameters show only little association with the degree of visual field damage.

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Effect of eye NGF application on NGF-receptor expression in visual cortex and geniculate nucleous of rat with glaucoma

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Purpose Glaucoma (GL) is an ocular disorder characterized by retinal ganglion cells loss and deficits of brain visual pathways. We have shown that eye topical application of nerve growth factor (NGF), a signaling molecule involved in neuroprotection, can reach brain NGF-responsive neurons. In this study, we investigated whether (i) experimentally-induced GL alters the presence of NGF and its receptors in the geniculate nucleus (GN) and visual cortex (VC); (ii) and whether application of NGF eye drops influences these biomarkers.

Methods GL was induced in rats with hypertonic saline injected into the right episcleral vein. After seven weeks, glaucomatous and control rats, untreated and treated with eye NGF application, were sacrificed and the presence of NGF, the expression of NGF-receptors in brain visual areas determined using structural, biochemical and molecular analyses.

Results GL reduces the concentration of NGF in the CSF, GN and VC, enhances the presence of the NGF/TrkA receptor in the GN, decreases this receptor in the VC. The NGF/p75 receptor is unaffected in the GN and down-regulated in the VC. In glaucomatous rats, topical eye NGF application for 35 consecutive days, enhances the concentration of NGF in the CSF, normalizes its presence in the VC and GN, and induces up-regulation of NGF/TrkA receptor

Conclusion Our findings suggest that, GL induced by elevated intraocular pressure significantly impairs the presence of NGF and NGF receptors in the VC and GN. It remains to be established whether NGF application could provide a functional benefit for the protection of GN and VC damaged neurons. Supported by CNR and by "Fondazione Bietti" Roma", Grant N° RF-FGB-2005-150198

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Aqueous humour ghrelin levels of eyes with and without glaucoma

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Purpose Ghrelin is a recently described acylated peptide, which works as a somatosecretagogue and modulates smooth, skeletal and cardiac muscles contraction, including that of the eye's muscle. Our purpose was to determine the levels of ghrelin and des-acyl-ghrelin in human aqueous humour collected from control and glaucoma patients undergoing cataract surgery.

Methods Blood and aqueous humour samples were collected from 24 patients (9 with open angle glaucoma and 15 from age matched cataract patients with no associated disease). The samples were analysed by ELISA to determine the levels of ghrelin and des-acyl-ghrelin.

Results There was a significant reduction of ghrelin levels in the glaucoma patients group, when compared to control (2.28±1.04 vs 4.26±2.56 fmol/ml, respectively), while those of des-acyl-ghrelin were similar (19.19 ± 6.64 vs 18.83 ± 4.92 fmol/ml, respectively). Both levels were not correlated to the duration of fasting. The ratio blood/aqueous humour of ghrelin and des-acyl-ghrelin were similar in all the groups.

Conclusion Ghrelin aqueous humour levels are significantly reduced in glaucoma patients, while the levels of des-acyl-ghrelin are maintained. So the intraocular secretion of ghrelin may be impaired in glaucoma patients, even if they have normal IOP levels.

▪ 505
Reliability and diagnostic significance of frequency doubling visual field testing

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Purpose The aims of this study were to compare results of Frequency Doubling Perimetry (FDP) with the gold standard of Humphrey Visual Field Testing (HVF). To determine the reliability and repeatability of FDP, and whether referrals had diagnostic significance.

Methods Notes collected of patients referred from the community because of abnormal visual fields, tested by FDP. Information gathered on proforma included reason for referral, place of referral, number of defects in both eyes, whether they were repeatable, consistent with HVF, reliability, follow-up and diagnosis.

Results 49 case notes were collected and reviewed, 98 eyes included. 31 females (63%), 18 males (37%). Mean age 59.5. All patients were referred because of VF defect. In 21 patients (43%), this was the only reason for referral.FDP showed poor consistency with HVF. This may be because it detects field loss earlier in the disease process.However, there was a lack of repeatability in FDP testing.In 29% of referrals, tests were not repeated, even though each test takes less than 90 seconds. FDP showed high reliability, possibly because it is a shorter test, simpler to perform and requiring less concentrationMost patients were discharged at first or second appointment.Patients were seen an average of 2.6 times.The number diagnosed with glaucoma are very low (3), and the number labelled 'glaucoma suspects' higher (6). These patients are unlikely to have been detected without this technology.

Conclusion In our study, FDP showed poor correlation with HVF.The lack of repeatability between field defects in FDP casts doubts on its validity of screening for glaucoma.Most patients were not diagnosed with glaucoma, ocular hypertension or glaucoma suspects following assessment.

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Study of suspicious subjects of suffering glaucoma evaluated by means of HRT, OCT and GDx-VCC. Representation by means of Venn's diagram

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Purpose To compare the diagnostic coincidence of the confocal laser HRT3, the optical tomography of coherence Stratus OCT 3000 and the laser polarimetry GDx-VCC, to discriminate against healthy eyes and glaucomatosos in subjects suspicious of suffering glaucoma.

Methods There were studied 312 eyes of 312 consecutive patients sent by ophthalmologists from the centers of speciality, for suspicion to be able to suffer glaucoma, (pressure intraocular> 21 mmHg, suspect optic nerve head morphology and / or standard automated perimetry).There were realized to each of them a clinical photographic study of the optic nerve head and of the retinal nerve fiber layer, and, an analysis by means of HRT, OCT and GDx-VCC. There was valued the classification obtained by each of the analyzers of image and was represented by means of Venn's graphs.

Results They found more positive cases in the evaluation of the optic disk that in the study of the retinal nerve fiber layer so much in global like in the intersection of 3 tests, but fundamentally at the cost of the diagnostic criterion GPS of the HRT. The monochromatic photography studio of the retinal nerve fiber layer detects major number of positive cases, followed by OCT and finally by GDx.

Conclusion The diagnostic criteria Moorfields Regression Analysis of the HRT3 and of the OCT presents the results nearest to the clinical photographic evaluation; finding a high diagnostic coincidence of the different analyzers of image.Key words: suspect of suffering glaucoma, HRT, OCT, GDx.

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Diagnostic ability of glaucoma probability score to discriminate between healthy individuals and glaucoma suspects

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Purpose To evaluate the diagnostic performance of the contour-line independent glaucoma probability score (GPS) classification obtained with the Heidelberg retina tomograph (HRT) 3 to differentiate between healthy and suspected glaucoma subjects (SG).

Methods 62 normal eyes and 48 SG (normal standard automated perimetry, intraocular pressure higher than 21 mmHg, and retinal nerve fiber layer defects measured with Stratus optical coherence tomography or scanning laser polarimetry GDx VCC) were included. The receiver operating characteristic (ROC) curves were plotted for the GPS numerical values and compared with HRT3 stereometric parameters.

Results GPS nasal and the FSM discriminant function had the best ability to differentiate between healthy and suspected glaucoma eyes. The areas under the ROC curve were 0.830 and 0.818, respectively. Sensitivity was 47.9% for GPS nasal at a fixed specificity of 90%.

Conclusion GPS had a good diagnostic ability to discriminate between normal and SG. There are structural changes at early stages of the disease that can be quantified by means of GPS.

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Diagnostic distribution according to the clinical guide of practices of the Finnish Society of Ophthalmology represented by HRT and OCT

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Purpose To know the diagnostic coincidence of the level of excellent quality of the "Guide of Clinical Practices of the managing of the glaucomatous patient" of the Finnish Society of Ophthalmology, of the confocal scanning laser HRT and of the optical coherence tomography Stratus OCT 3000.

Methods There were included 312 consecutive patients sent by suspicion to suffer glaucoma (pressure intraocular > 21 mmHg, suspicious optic nerve head morphology and standard automated perimetry).There was realized a clinical complete study including optic disk stereophotography and of retinal nerve fiber layer, and, an analysis by means of HRT and OCT. Your distribution was valued depending on the above mentioned diagnostic clinical level and your coincidence by HRT and OCT.

Results To being classified by the above mentioned diagnostic clinical level finds a major number of normal and glaucomatous cases (175 and 113), with minor number of suspicious subjects, in comparison to the cases catalogued by the HRT and OCT, (166, 87 and 59 respectively).

Conclusion In spite of obtaining a high coincidence, certain disparity exists; in such a way that the employment of analyzers allows to obtain quantitative parameters that detect the presence of structural damage; but they must not be valued of isolated form, needing a valuation it combines of all of them to increase your diagnostic efficiency close to the clinical evaluation.Key words: clinical guide, glaucoma, HRT, OCT.

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Optic disc and retinal nerve fiber layer analysis in perimetrically unaffected eyes of glaucoma patients: an optical coherence tomography study

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Purpose To evaluate whether optical coherence tomography (StratusOCT) may detect early changes in perimetrically unaffected (PU) fellow eyes of glaucomatous patients by analysis of retinal nerve fiber layer (RNFL) thickness and optic nerve head (ONH).

Methods 37 glaucomatous patients with unilateral field loss and 34 age-matched controls were recruited. In glaucoma patients, PU eyes and the affected ones were analyzed separately. For each group, mean values (±SD) of age, mean deviation, pattern standard deviation, as well as RNFL thickness parameters and ONH measurements were calculated. Comparisons between fellow eyes of glaucoma patients and between healthy and PU eyes of glaucoma patients conducted with t test and Mann-Whitney U-test, respectively. Number of clock-hour sectors flagged with probability levels <5% or <1% were collected and differences between healthy subjects and PU eyes of glaucoma patients evaluated on Fisher exact test.

Results Global (Average Thickness) and sectoral parameters (Inferior and Nasal Average), Max-min, as well as 2- and 6-o'clock sectors resulted significantly thinner in PU eyes than in control group, whereas ONH analysis did not provide any significant difference between the two groups. Proportion of eyes with clock-hour position flagged with probability <5% or <1% was not significantly different between healthy and PU eyes.

Conclusion PU eyes of glaucoma patients represent a group at risk to develop functional impairment over time since an early RNFL thinning was identified on OCT.

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Realationship optical coherence tomography and short-wavelength automated perimetry in glaucoma patients

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Purpose To correlate the main indices of short-wavelength automated perimetry (SWAP) with the peripapillary retinal nerve fiber layer (RNFL) thickness measured with optical coherence tomography (OCT) in glaucoma patients.

Methods 66 eyes of 66 glaucoma patients were prospective and consecutively selected. All of them had intraocular pressure >21 mmHg, and reproducible glaucomatous visual field loss in standard automated perimetry. SWAP test were performed with a Humphrey perimeter and the 24-2 full threshold algorithm. Pearson correlations were calculated between SWAP indices (mean deviation and pattern standard deviation) and OCT parameters.

Results Mild significant ($p<0.05$) correlations were observed between SWAP indices and some OCT parameters. The strongest correlations were found between the RNFL thickness in the vertical axis (superior and inferior pole thickness) and mean deviation of SWAP. Pattern standard deviation did not correlate with any OCT parameter. Average thickness and superior quadrant thickness had the strongest correlations with mean deviation of SWAP (both 0.36).

Conclusion RNFL thickness measured with OCT showed mild correlations with SWAP indices in glaucoma subjects.

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Correlation of GDx VCC with standard automated perimetry in glaucoma diagnosis

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Purpose To evaluate the correlation between GDx VCC parameters with global indexes of standard automated perimetry (SAP).

Methods 417 eyes of 417 patients were included. They were divided into 60 normal, 218 ocular hypertensive, 68 preperimetric glaucoma, and 71 glaucoma. Correlation between GDx VCC parameters and global indexes of SAP (MD and PSD) was calculated in all groups.

Results There was no significant correlation between GDx VCC and SAP between GDx and SAP in normal patients. Significant correlations were found for some parameters of GDx VCC and MD, being low for ocular hypertensive eyes and preperimetric glaucoma, and moderate-low for the glaucoma group. We only found significant correlations for a few parameters of GDx VCC and PSD in the glaucoma group, being the correlation coefficients low.

Conclusion GDx VCC shows weak-moderate correlations with SAP. The correlations were higher for MD than PSD.

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Central corneal thickness effect on GDx VCC parameters

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Purpose Evaluate the effect of extreme central corneal thickness in RNFL parameters measured by GDx VCC.

Methods A total of 131 eyes of 131 subjects were included divided into 60 control and 71 glaucoma patients. All of the glaucoma eyes had reproducible defects on standard automated perimetry. Central corneal thickness was measured with an ultrasonic pachymeter. ROC curves were plotted in the sample subgroups with exteme pachimetry values (outside mean ± 2SD) and were compared with ROC curves of the subjects in the normal pachimetry range (mean ± 2SD).

Results No differences were found in the areas under the ROC curve of the parameter of the GDx VCC in thinnest and thickest subgroups when compared with the mean pachymetry group.

Conclusion Central corneal thickness has no influence in RNFL measurements of GDx VCC.

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Variability of color doppler imaging parameters and consequences for sample size calculations

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Purpose The aims of this study were: 1) to determine the intra-observer variability of color Doppler imaging (CDI) measurements, 2) to compare the difference in variability of these measurements in healthy controls versus glaucoma patients, and 3) to provide calculations of minimum sample sizes for future CDI studies.

Methods Patients with normal tension glaucoma (n=28), primary open angle glaucoma (n=19) and age-matched healthy controls (n=22)underwent CDI on two occasions one month apart. Variability in CDI measurements was quantified using (within-subjects) coefficients of variation. Based on this variability, minimum sample sizes were calculated to guide the design of future studies comparing CDI between and within groups.

Results In general, within-subject coefficients of variation for measurements one month apart were comparable to previously reported short-term variations. Variability was higher in glaucoma patients than in healthy controls. The minimum sample size required for glaucomatous study populations is larger than for healthy controls. Smaller patient groups are required to detect change using the peak systolic velocities than using end diastolic velocities. Studies using a cross-over design require smaller sample sizes than studies with a pre-post or parallel design.

Conclusion This study provides extensive information on long-term intra-observer variability of CDI measurements in healthy controls as well as glaucoma patients. Moreover, sample size calcualtions are provided for studies involving glaucoma patients as well as healthy individuals using three different study designs.

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Functional activity of the retina before and after IOP normalization in glaucoma

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Purpose To study dynamics of bioelectrical activity of the retina before and after normalization of intraocular pressure (IOP) in primary open angle glaucoma (POAG).

Methods 20 normal subjects and 68 patients with different stages of glaucoma (early–I, advanced – II, late – III) and high level of IOP were included in our study. IOP ranged from 27 to 36 mmHg. All patients underwent complete eye examination, HRT II imaging, ERG including full-field, flicker, pattern ERG (PERG), oscillatory potentials (OP), long-duration flash ERG, chromatic macular ERG to red, green and blue stimuli (MBN, Russia).

Results Different decrease of ERG amplitudes were detected depending on the stage of POAG. Subnormal flicker, as well as subnormal macular ERG to red and green stimuli, diminished or unrecordable off-response were observed in all stages of POAG with increased IOP. A pathological configuration and decreased amplitudes of OPs, prolonged N95-component of PERG and subnormal full-field ERG was revealed in advanced and late stages of glaucoma. After reduction of IOP significant increase of amplitude values and shortening of implicit time (IT) were observed in early and advanced stages of POAG ($p \leq 0,05$), whereas those in late stage of POAG showed slight positive dynamics.

Conclusion ERG symptoms in POAG have high value for assessment the functional state of the retina and optic nerve, determination of degree of IOP normalization and must be used in treatment control.

▪ 515
Corneal central and temporal thickness in rabbits

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Purpose Rabbits are largely used in experimental eye research, including investigations related to glaucoma. Thus, it is important to know some clinical parameters of this animal, such as corneal thickness.

Methods Thirty eyes of 15 albinal Norfolk rabbits were evaluated, under anesthesia. Central and temporal corneal thickness were measured by ultrasonic pachimetry.

Results For the right eyes the mean values of central and temporal corneal thickness were 393.40 micra (sd=18.25) and 389.07 micra (sd=22.36), respectively. For left eyes the mean values were - central corneal thickness: 398.73 (sd=23.75) and temporal corneal thickness: 382.53 (sd=26.03).

Conclusion It is necessary to consider the corneal central thickness in the evaluation of ocular pressure values in rabbits.

▪ 516
Variation of intraocular pressure (IOP) & central corneal thickness (CCT) in neonates

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Purpose To record the variation of IOP and CCT during the neonatal period. Also, to investigate the relationship between IOP & CCT.

Methods 52 neonates, pre- and full terms, with GA 24 to 40 weeks (31.9 w) and BW 720 – 3180 gr (1913 gr) participated in this study. IOP measurement was done by Tono-Pen applanation tonometer and CCT measurement was done by Accutome ultrasound pachymeter only to the right eye. All the measurements were done between 15.00 and 17.00 am. Babies who had undergone an eye operation, babies with eye dysplasias or anomalies, or using corticosteroids recently, were excluded from the study.

Results Average CCT= 651,02 μm (STD= 63,19138) (min 528- max 750 μm) and the average IOP= 9.12 mmHg (STD= 2,931129). More specifically, in neonates with GA < 32 w, average CCT= 677.25 μm (STD= 51,13031) and average IOP= 9.4 mmHg (STD= 2,79). In neonates with 32<GA<37 w, average CCT= 638,5 μm (STD= 69,57379) and average IOP= 8.95 mmHg (STD= 2,601282). Finally, in neonates with GA > 37 w, average CCT= 613 μm (STD= 44,38919) and average IOP= 8,15 mmHg(STD= 3,275286).

Conclusion CCT is reduced as the neonate grows, while the IOP is increased. Finally, lower IOP is accompanied by thinner CCT.

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Comparison of Tono-Pen Avia with Goldmann applanation tonometer

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Purpose 1. To compare the IOP readings taken by Tono-Pen Avia (Reichert) With the GAT. 2. To assess the influence of central corneal thickness (CCT) on these measurements

Methods Prospective, controlled study including one eye at random of 30 glaucomatous patients and 30 healthy subjects. Patients with previous refractive surgery or corneal pathology were excluded. GAT measurement was followed by Tono-Pen Avia after a 10 min break. Only Reading with 95% statistical confidence index were taken into account. Pachymetry measurements were done at the end of the examination. Pearson correlation coefficient to assess the correlation between GAT and Avia tonometer. The agreement between IOP readings from GAT and Avia was assessed using the Bland-Altman plots

Results Mean IOP in glaucoma was 18.3 ± 6.7 mmHg with GAT and 16.7 ± 4.7 with Avia. Mean IOP in control group was 16.4 ± 3.8 mmHg with GAT and 15.2 ± 4.2 mmHg with Avia. Mean CCT was 545 ±101.2 µ in glaucoma and 546.7 ± 99.4 µ in control group. There was no correlation between CCT and the IOP readings with GAT or Avia in both groups($p<0.05$)

Conclusion Tono-Pen Avia is a very easy-to-use handheld applanation tonometer that functions in any position especially for in-bed or wheelchair patients. It can be used for screening purposes providing a lower IOP value than GAT and indicating a need for further investigation in suspect cases

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Physiological short-term variability of ocular pulse amplitude (OPA) measured by dynamic contour tonometer (DCT) in healthy subjects

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Purpose The Pascal® dynamic tonometer is a new non-applanation contact tonometer designed to be largely independent of the structural properties of the cornea. It measures the systolic and diastolic IOP and their difference to determine OPA. By recording the pulsatile component of ocular blood flow (heart pulse as a function of time) the OPA could provide an indirect measurement of the choroidal perfusion. It has been suggested that OPA could be an indirect risk factor for glaucoma progression. We aimed to assess the short-time variability of OPA in healthy persons

Methods The left eyes of 30 healthy subjects were included in this prospective study. The IOP was measured twice by Goldmann applanation tonometers (GAT) followed by 3 consecutive measurements by DCT 10 min later. Pachymetry, arterial blood pressure and pulse rate were measured after IOP measurements. These measurements were repeated with an interval of fifteen days at the same hour of the first measurements. The mean value of each parameter was taken into account for the statistical analysis. Student Test was used to assess the difference and the Pearson correlation was used to assess the correlation between the various parameters

Results The mean age was 41 ± 12 years. The mean IOP at the first visit was 13.6 ± 2.9 mmHg by GAT and 14.3 ± 2.2 mmHg by DCT. The mean OPA was 2.4 ± 0.9 mmHg (0.8 to 4.3 mmHg) at the first visit.The mean IOP at the second visit was 13.4 ± 3.2 by GAT and 15.0 ± 2.5 mmHg by DCT. The mean OPA was 2.6 ± 1.0 (0.9 to 5.8) mmHg at the second visit.

Conclusion There was no significant difference in both OPA measurements. This parameter remains stable in a short-time interval in healthy subjects.

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Comparison of the Schioetz indentation tonometer with the Tonopen® tonometer and the influence of two different anaesthetic techniques on the IOP in the porcine eye

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Purpose The aim of this study was to examine the accuracy of the intraocular pressure (IOP) reading of two portable tonometer in the porcine eye in situ. The influence of two anaesthetic techniques on the IOP was analysed.

Methods Experiments were conducted in 20 healthy domestic white pigs. After a standard premedication 9 pigs were investigated under a total IV propofol anaesthesia (A) and 11 pigs under an isoflurane inhalation anaesthesia (B). IOP was measured at two different time points: prior to anaesthesia (time 1) and 15 minutes after induction of anaesthesia (time 2). To compare IOP measurements obtained with the digital Tonopen® with those of Schioetz tonometry, one single measurement, generated by Tonopen® tonometer was compared with a single reading from Schioetz tonometer in 11 pigs at time point 1 and 2 (isoflurane anaesthesia).

Results A significant decrease in IOP of 13.8 % (A) and of 10.2 % (B) was measured in comparison to baseline IOP prior to general anaesthesia. There was a high significant ($r = 0.68$; $p<.05$) correlation at time 1 between the Schioetz and the Tonopen® tonometer but no significant correlation at time 2.

Conclusion The significant IOP-lowering effect of inhalation and total intravenous anaesthesia has to be considered in animal models. We point out that there are established methods for clinical measurements of the IOP but the user should be aware that there are differences in measured IOP when methods are compared.

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Intraocular pressure variation during different surgical procedures in rabbit eyes.

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Purpose To analyse intraocular and infusion line pressures during vitrectomy and cataract extraction (manual extracapsular extraction, phacofragmentation and phacoemulsification) in rabbit eyes.

Methods Twenty-two rabbits were submetted to vitrectomy (25 eyes) and cataract extraction (42 eyes) - extracapsular approach (14 eyes), phacofragmentation (14 eyes) and phacoemulsification (14 eyes). Their intraocular pressures were recorded through an antertior chamber cannula connected to a computed polygraph. Infusion line pressure was monitored only during vitrectomy and phacofragmentation.

Results Intraocular pressure spikes above 100 mmHg and sometimes almost reaching 200 mmHg were observed in this study. Phacoemulsification showed the greatest variation and phacofragmentation the smallest. The minimun pressures in all surgeries were around 0 mmHg. Infusion line pressure showed smaller variations than intraocular pressure.

Conclusion During surgical procedures in rabbit eyes, such as vitrectomy, extracapsular cataract extraction, phacofragmentation and phacoemulsification, there is a great intraocular pressure variation. Intraocular pressure did not show a good relation to infusion line pressure.

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Invasive measurement of outflow facility in the living human eye

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Purpose To measure the pressure-volume relationship (ocular rigidity) and outflow facility in the living human eye using a manometric device.

Methods Fourty cataract patients (aged 63 (13)) were enrolled in the study. An invasive manometric intraoperative dynamic measurement procedure was employed, using a computer controlled device, comprising a pressure sensor and a dosimetric pump. The anterior chamber of the eye is cannulated through a 21 gauge needle, under topical anaesthesia with drops and the initial IOP is recorded. The IOP is artificially set to 10 mmHg and the eye is infused with microvolumes of BSS. The IOP is recorded for 2 seconds after each infusion step in order to calculate the average IOP and its fluctuation during this interval. At 40 mmHg, the infusion stops and the sensor records the IOP decay curve for 60 sec. The ocular rigidity coefficient is calculated by the IOP-volume relation in the stepping sequence corrected for the volume loss from the outflow pathways. A model incorporating the value of ocular rigidity was developed to calculate the outflow facility from the outflow sequence. The study was approved by the Institutional Board and performed under the patient's informed consent.

Results The average rigidity coefficient of Friedenwald was of 0.0206 (sd 0.0042)µl -1. A nonlinear pressure volume relationship is found. The outflow facility was measured to be 0.31(sd 0.08) µl/min/mmHg. There were no complications related to the procedure.

Conclusion This invasive method of measuring ocular rigidity and outflow facility is safe and effective. Accurate measurements obtained with this method, avoiding the errors of tonography, may provide a normal database of these parameters in living human eyes.

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An opto-mechanical device for the measurement of ocular rigidity and intraocular pressure

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Purpose The purpose of the present study is to demonstrate pilot measurements of ocular rigidity and intraocular pressure (IOP) with a minimally invasive opto-mechanical device.

Methods The device consists of a glass lens that is used to contact and deform the corneal surface, while the force required for this deformation is measured by means of a load cell. An infrared LED is used to illuminate the area of deformation. The area of deformation is measured by sensing the reflected light by means of a quadrant photodiode. All signals are simultaneously recorded for post-processing. A nomogram (look-up table) developed using enucleated rabbit eyes is used to convert force-area data to IOP. Twenty right eyes of twenty healthy young subjects were enrolled in the initial evaluation of the instrument's measurement. In addition, intraocular pressure provided by the instrument was compared to GAT.

Results Twenty young ocular-disease-free persons (6 men and 14 women) with a mean age of 30 + 6,2 (mean + standard deviation(SD)) performed a measurement of ocular rigidity and IOP with the above-mentioned instrument. The average ocular rigidity was 0.562 + 0,254 mmHg/ uL (mean + SD) which in Friedenwald's notation corresponds to 0,0157 + 0,0071. The average IOP estimated was 21 + 9.3 mmHg (mean + SD). Average IOP using GAT was 18,5 + 3,8 mmHg.

Conclusion The calculated values of ocular rigidity are comparable to values reported in the literature. Measurement of rigidity in a simple and non-invasive manner may improve our understanding significance of this parameter in health and disease.

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The impact of common classes of topical antiglaucoma medications on central corneal thickness

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Purpose Recent studies have shown that prostaglandin analogs (PGA) may induce biochemical (via FP receptor and MMP-2 activation) and morphological (via collagen type I contraction) changes in corneal stroma thus affecting central corneal thickness (CCT). Beta-blockers (BB) and topical carbonic anhydrase inhibitors (CAI) were found to have rather no effect on CCT. To investigate the influence of common classes of topical antiglaucoma medications used either in monotherapy or combined therapy on CCT.

Methods In a retrospective study 487 eyes from consecutive 260 patients (148F/112M) with open angle glaucoma were examined. Depending on the topical treatment they were classified into 7 groups: A/ PGA (n = 212), B/ BB (n = 54), C/ CAI (n = 36), D/ PGA + CAI (n = 25) E/ PGA + BB (n = 23) F/ BB + CAI (n = 54), G/ non-treated (n = 83). The CCT was measured using ultrasound pachymetry Tomey AL-2000. The central corneal power was measured with the Topcon keratometer. ANOVA analyses were used for statistical analysis.

Results There were no statistically significant differences between CCT of all groups (F=1,06, p=0,3931); the lowest values were in the eyes treated with PGA + BB (535,9 nm SD 31,4) and the highest in the eyes treated with PGA + CAI (571,3 nm SD 46,3). The mean CCT in group A was 550,4 (SD 40,8), group B 552,5 (SD 34,7), group C 562,6 (SD 40,2), group D 571,3 (SD 46,3), group E 535,9 (SD 31,4), group F 559,5 (SD 32,5), group F 557,5 (SD 42,2) nm.

Conclusion In this study CCT appears not to differ in eyes treated with different classes of antiglaucoma medications either in monotherapy or combined therapy. CCT of treated glaucoma eyes does not differ from CCT of untreated glaucoma eyes.

▪ 524
The incidence of glaucoma following paediatric cataract surgery

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Purpose Aphakic glaucoma is a well-recognised complication of surgery for congenital cataract, however there are wide variations in its reported prevalence. In this study, we investigated the incidence of glaucoma and the visual outcome following surgery in paediatric cataracts.

Methods A 10-year retrospective case-note review of children who had cataract surgery by the same surgeon for congenital or secondary cataract. The diagnosis of glaucoma was based on the clinician's decision to initiate treatment for raised intraocular pressure.

Results Sixty-six eyes of 49 patients were identified, comprising; 57.1% (28/49,40 eyes) with congenital cataract, 26.5% (13/49,18 eyes) with cataract secondary to uveitis, and 10.2% (5/49) with traumatic cataract. 12.1% (8/66) of eyes had an intraocular lens inserted at the time of surgery. Of those with congenital cataract, surgery was performed at a median age of 101 days (range 5-5089). 7.5% (3/40) of these eyes developed glaucoma. The mean interval from surgery to the diagnosis of glaucoma was 3519 days.The age of the patient at surgery was not found to be a significant risk factor for glaucoma (student-t test, p=0.18). There was a mean follow-up of 2108 days with no significant difference in the length of follow-up between the groups. Of the patients with uveitis, 53.8% (7/13) developed glaucoma in the operated eye, with two eventually requiring aqueous shunt devices.

Conclusion We found a lower prevalence of glaucoma following surgery for congenital cataract than previously reported. However, glaucoma is significantly more likely following surgery for secondary cataract, particularly that associated with uveitis.

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Compliance and knowledge about glaucoma in austrian patients

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Purpose To document the rate of non-compliance and patients' attitude towards and knowledge of glaucoma in Austrian patients.

Methods Prospective observational case series. One- hundred consecutive glaucoma patients of an Austrian outpatient glaucoma department were included in the study. Patients were already under medical treatment for glaucoma. Personal characteristics, presence of systemic disease, compliance with glaucoma medication, and glaucoma-related attitudes were ascertained by means of a predetermined questionnaire with 40 questions. Patients were subsequently assessed for the ability to correctly instil placebo eye drops. Non-compliance was defined as omitting glaucoma medication more than once a week. Univariate and logistic regression was used to examine how patient characteristics and knowledge were related to reported compliance

Results Average age was 63.6 years (range 19-88). Overall, 89% (n= 89) of patients reported to be compliant. Knowledge about the disease was associated with higher compliance (RR 3.05, 95% CI 1.7-9.6). Forgetfulness was the most frequently cited reason for non-compliance (20%). Although 84% patients believed glaucoma medication to be efficient, only 26% could give a simple correct definition of glaucoma. 29% had a positive family history for glaucoma.

Conclusion Despite the comparatively high compliance rate of Austrian patients with their glaucoma medication, knowledge of glaucoma remains poor in long term glaucoma sufferers.Patient compliance to glaucoma treatment could be improved mainly by increasing patient knowledge of the disease.

▪ 526
Is audible alarm useful in increasing adherence?

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Purpose To investigate if objectively monitored adherence to travoprost administered once daily in the evening, improves if the alarm function of the monitoring device is activated.

Methods Thirty-nine glaucoma patients were enrolled. Inclusion criteria were topical medication with once daily, evening administered travoprost 0,004% (Travatan, Alcon, Forth Worth, Texas, USA). Adherence to travoprost was monitored with an electronic monitoring device (Travalert Dosing Aid, TDA, Alcon, Forth Worth, Texas, USA). In the initial 3-month period no alarm function was used, but in the second 3-month period it was activated. Patients were instructed to instill travoprost at 9 p.m. Adherence was defined with instillation of travoprost at 9 p.m. (+/-2 hours) as recorded by the device. Non-adherence for the study period was defined as the ratio (%) of the non-adherent days and all study days.

Results Thirty-four participants completed both study periods. Adherence was 81.6 % in the first, and 85.3 % in the second phase. Non-adherence was 18.4 +/- 18.9 % in the first period and 14.7 +/- 18.9 % in the second period (Wilcoxon signed rank test, p=0.059).

Conclusion Though the adherence was very good already in the first phase, it improved further when the audible alarm signal became activated. The improvement, however, did not reach the statistically significant level.

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Electronic compliance monitoring in glaucoma patients used to topical therapy

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Purpose Individual compliance of glaucoma and ocular hypertensive patients with Brimonidine was studied with regards to total dose, dosage intervals, coverage, drug waste, attempts per application and risk factors for low compliance.

Methods Thirty-eight men and 26women aged 70 ±11 years [42-89] received conventional Brimonidine vials (Alphagan®, Allergan™) equipped with a microprocessor-controlled monitoring device capable to record date and time of each eye drop application with a known detection sensitivity for eye drop applications ~ 99%. 48 glaucoma and 16 ocular hypertensive patients used to eye drop therapy for 11 ±8 years [1-35] were enrolled and randomly assigned to Brimonidine therapy b.i.d or t.i.d daily for 4 weeks.

Results Electronic records revealed a mean of 1.4 applications per day (range: 0.7-2.2) for patients assigned to Brimonidine 2x daily with a mean treatment interval of 18.2 hours (range: 11.2-38.4 h). Patients on Brimonidine 3x daily showed a mean rate of 1.8 applications per day (range: 1.0-2.7) and a mean treatment interval of 12.4 h (range: 9.1-39.7 h). 10 patients ceased therapy before completing the 4 weeks period, therein 4 with side effects and 6 patients having emptied the bottle prematurely.

Conclusion Almost 10 percent of the patients emptied their vial in less than 4 weeks by using more than one drop per application and thereby do need refills more often than usually calculated. Our data confirm the need for larger studies on individual compliance with topical ocular therapy in glaucoma. Electronic compliance monitoring may be a useful tool in ophthalmic practice to recognize low-compliant patients.

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A patient preference comparison of two fixed combinations, brinzolamide 10 mg/ml+timolol 5 mg/ml suspension and dorzolamide 20 mg/ml +timolol 5 mg/ml solution in patients with open-angle glaucoma or ocular hypertension

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Purpose To assess patient preference and comfort of Brinzolamide 10 mg/ml+Timolol 5 mg/ml Suspension (Brinz/Tim) compared to Dorzolamide 20 mg/ml+Timolol 5 mg/ml Solution (Dorz/Tim; COSOPT®) after topical ocular administration of a single drop.

Methods This was a double-masked, randomized, active-controlled, cross-over, multi-center study. Patients were randomly assigned to receive a single drop in both eyes of either Brinz/Tim or Dorz/Tim on day 1 followed by a single drop of the other medication on day 2. Immediately after dosing, the patients completed an ocular discomfort assessment (on a scale of 0-9; 0 = no discomfort; 9 = substantial discomfort). On day 2 the patients also responded to a preference question.

Results Of the 129 patients enrolled, on day 1, 63 received Brinz/Tim and 66 received Dorz/Tim. Of these patients, 106 (82.2%) expressed a drop preference and met all inclusion/exclusion criteria (PP population). Brinz/Tim was preferred by 84 patients (79.2%) while 22 patients (20.8%) preferred Dorz/Tim ($P < 0.0001$). The mean discomfort scores (± SE) were 1.5 ± 0.2 for Brinz/Tim and 3.3 ± 0.2 for Dorz/Tim. Brinz/Tim was significantly more comfortable than Dorz/Tim ($P < 0.05$).

Conclusion Brinz/Tim was preferred by more patients than Dorz/Tim. Patients also responded that Brinz/Tim was the more comfortable medication. This significant advantage in comfort may promote patients compliance with respect to the chronic use of their IOP-lowering medication.

Commercial interest

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Phase III, 24-month study investigating the efficacy and safety of tafluprost vs latanoprost in patients with open-angle glaucoma or ocular hypertension

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Purpose This double-masked, active-controlled, parallel-group, multinational, multicentre, phase III, 24-month study, conducted in 49 centres across 8 countries, investigated the efficacy and safety of tafluprost 0.0015% vs latanoprost 0.005% (once-daily at 20:00) in 533 patients with open-angle glaucoma or ocular hypertension.

Methods The primary endpoints were change from baseline IOP after 24 months (1.5 mmHg non-inferiority limit [tafluprost-latanoprost]) and safety.

Results Both treatments yielded a substantial IOP reduction, that was sustained for 24 months (tafluprost -7.1 mmHg; latanoprost -7.7 mmHg; n=402). Non-inferiority was shown with ANOVA and almost reached with ANCOVA (upper limits of the 95% CI for the treatment difference were 1.38 and 1.52, respectively; RM models). Most ocular adverse events were mild and comparable between groups (48% vs 44%).

Conclusion This 24-month phase III study demonstrated that both tafluprost and latanoprost yielded a substantial reduction in IOP that was sustained for 24 months, and a similar safety profile.

Commercial interest

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G-probe: results of use on eyes with visual functions with patients in Armenia

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Purpose G-probe cyclophotocoagulation(IRIDEX laser systems) on blind eyes has allowed us to develop differentiated approaches to the treatment considering the etiology and optimum dosages.The objective we had defined was to utilize the accumulated experience and apply the given technique also on eyes with visual acuity.

Methods During 3 years there were 10 eyes under our supervision with neovascular glaucoma after diabetic retinopathy or vein thromboses.IOP was 45.4 mmHg.In 9 cases visual acuity as light perception;1 patient had account of fingers on distance 50cm without correction.2 patients had undergone vitrectomy.Technique:position-supine; anaesthesia retrobulbar injection Sol.Lidocaine 2%-3.0;optimum dosages (power-duration-number of coagulants):NVG after vein thromboses:1000-1750mW(inclusive)-1000msec-minimum 24;NVG after diabetic retinopathy:1750-2500mW-2000msec-minimum 25.After TSCPC subconjunctival steroids injection was done.

Results Visual acuity after TSCPC at 8 patients increased to account of fingers on distance 1m;1 case-account of fingers on distance 2m;1 case-account of fingers on distance 2m with correction (+4.0D)20/200.In 3 cases a year after the condition had stabilized, we performed glaucoma surgery,in 1 case combined operation-cataract and glaucoma surgery,in 1 case-panretinal photocoagulation.All patients were under dynamic supervision.IOP after 3 years was 23.5 mmHg.1 patient after TSCPC and glaucoma surgery is preparing to keratoplasty.

Conclusion The results received by us are quite encouraging in terms of stabilization of intraocular pressure, painful syndrome, and also preservation of vision acuity.The given technique can be recommended as preparatory for the subsequent interventions for "refractory" patients.

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Contact transcleral ciliary body photodynamic treatment with verteporfin in cases of refractory glaucoma

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Purpose Previous animal studies showed that contact transcleral ciliary body photodynamic treatment with verteporfin is a safe procedure for temporarily reducing IOP. The purpose of this study is to investigate safety and efficacy in cases of refractory or absolute glaucoma.

Methods 8 patients, 8 blind painful eyes of with absolute glaucoma (6 neovascular, 1 Sil Oil, 1 refractory), with mean IOP 37±12 mmHg, were treated. Verteporfin bolus infusion of 6 mg/m^2 body surface area over 1 minute was done prior to irradiation, realized with a triple optic fiber connected to a 689nm diode laser. Energy at each fiber's tip was 80mW and irradiation time 3min per spot. 12 spots over 360 degrees (12min) were done. Eye drops with dexamethasone and tobramycin qd for 4 days were prescribed. Follow up consisted of daily slit lamp examination and IOP measurements with Goldman Tonometer during the first week, then weekly during the first month, then monthly. Photography was used to document clinical findings.

Results Significant mean IOP reduction of 25% for 2 weeks was observed in all cases. IOP returned to pre-treatment values during the third week in 4 cases, during the 2nd month in 2 cases and 3rd month in 2 cases. Conjunctival oedema and anterior chamber reaction were mild and lasted 24-48 hours. No serious adverse events were observed and patient's discomfort was limited.

Conclusion Our findings suggest that contact transcleral ciliary body photodynamic treatment with verteporfin with the above mentioned settings is safe and efficient in short term in cases of refractory or absolute glaucoma.

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Ocular adverse effects of the pneumatic trabeculoplasty in patients' treatment with open angle glaucoma

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Purpose To valuate the ocular adverse effects of the pneumatic trabeculoplasty in patient affected by open angle glaucoma. The subjective and objective troubles of the ocular surface have been valued during and after the execution of the procedure.

Methods 50 patients have been recruited (25 men and 25 women, inclusive age between 30 and 55 years) affected by open angle glaucoma in topical pharmacological treatment with beta-blockers. The patients in treatment with prostaglandin have been excluded. The treatment has been performed on day 0 and 7 only on 1 eye while the other one has been used as check. The ocular surface has been observed before and after the treatment relatively to the reported symptoms (burning, pain, ocular disconfort, lacrimation, visual alteration during the treatment, itch) and the signs (conjuntival hyperaemia, haemorrhage). After the treatment the patients have continued to instill only the hypotensive therapy.All the patients were controlled for 30 days.

Results The following side effects have been reported: conjuntival hyperaemia (75%), pain (50%), ocular disconfort (90%), visual alteration (90%), hemorrahe (0,25%), lacrimation (20%), itch (20%)

Conclusion Modest and transitory simptoms and signs have shown the treatment to be safe, both during and after it. With the exception of a case of subconjuntival hemorrhage, spontaneously resolved after 7 days.

▪ 533
The reasons of unsuccessful antiglaucoma operations

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Purpose The study was to determinate the level excessive scarring in zone of antiglaucome operations.

Methods This study 48 eyes of 46 consecutive patients with medically uncontrolled glaucoma after filtration surgery underwent reconstruction of filtration zone. IOP decompensation happened between 6 mount and 6 years after filtration surgery. Mean preoperative IOP was 35.7± 8.4 mm Hg.

Results After reconstruction of filtration zone in 9 causes (18,7%) aqueous humor outflow started after revision filtration bleb, 23 causes (48%) after reconstruction scleral spit. In other causes we had to cut up zone of trabeculectomy hole. In 8 causes (16%) excessive scarring in zone of trebeculectomy hole was mean reason for IOP decompensation.

Conclusion The mean reason of IOP decompensation after antiglaucoma operation is excessive scarring in zone of scleral spit (48%) and filtrations bleb (18,7%).

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Subconjuntival injection of bevacizumab in side of filtering bleb in the end of trabeculectomy : first experience

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Purpose To evaluate safety and local effects of -in the end of trabeculectomy Avastin injection on filtering bleb vascularisation and bleb failing trend.

Methods 1 male patients 65yo with a clinical history of pharmacologically uncontrolled primary open angle glaucoma in right eye (IOP 36 mmHg,CCT=525 µ)underwent to trabeculectomy without use of antiproliferative agents. A traditional surgical approach with a 12 o'clock scleral wedge(4 x 4 mm) and a double Nylon 10/0 made sclerocorneal suture using modified Meduri's technique was performed.At the end of the surgery ,0.05 ml of bevacizumab (Avastin 25 mg/ml , Roche) were injected in the subconjutival space above the sclera wedge.The IOP and bleb vascularisation have been recordered in the post op each day during the first week and one time a week in the following three months.A digital camera mounted on slit lamp was used for images acquisition.

Results IOP was stable on 9 mmHg during the first three weeks , increasing to 16 mmHg during the follow up and stable until the end of the study despite removing Meduri' sclerocorneal sutures . No complications were seen in the anterior chamber . Filtering bleb did not show any sign of inflammation or swelling with a " quite " vascularisation as clinical marker during the follow up .

Conclusion Our short experience demonstrates the safety of subconjuntival injection of Avastin and effects on bleb's vascularisation regardless of incidence of bleb failure. Further investigations in multicentric randomized studies on larger sample size are necessary to confirm current results.

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Long-term results of combined cataract and non perforant sclerectomy surgery supplemented with antimitotics: prospective study

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Purpose Prospectively to evaluate the long-term results of phacoemulsification plus non perforant sclerectomy (PNPS) supplemented with antimetabolites and without implant.

Methods Prospective, non-randomized study that comprised all consecutive patients who underwent PNPS in our unit from January 2004 up to now. We analysed those patients with a minimum of follow-up of one year.

Results 42 eyes of 42 patients suffering form open angle glaucoma were included. Mean follow up was 17.4 (SD: 5.6) months (range 12 to 24 months). 85.5% has best corrected visual acuity (BCVA) ≥ 0.5; 73.8% ≥ 0,7 and 28.5% , 1. After the first year or the follow-up the intraocular pressure (IOP) decreased by 49.3% and after the second year by 45.4% with or without medication. The decrease of the number of medications was statistically significant in all follow-up periods. The number of complications was low and they were no severe. Total success was higher when MMC was used than when 5-Fluorouracil was applied.

Conclusion PNPS supplemented with antimetabolites reduces significatively the IOP in the long-term, allows a rapid BCVA recovery, and has a low number rate of complications and they were no severe.

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Control of filtering bleb scarring trough tissue bioengineering

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Purpose To evaluate the effects on intraocular pressure (IOP) reduction and bleb morphology of a new biodegradable collagen implant iGen TM, a porous matrix reducing scar formation after glaucoma surgery.

Methods We conducted a prospective interventional case series in 18 eyes of 18 patients with uncontrolled primary open-angle glaucoma. We performed limbal-based deep-sclerectomy with implantion of the device in the scleral bed. We performed a complete ophtalmic examination, ultrasound biomicroscopy (UBM) and Visante anterior segment Optical Coherence Tomography (OCT) at each follow up visit, scheduled 1 day, 1 week, 4 and 12 weeks post-operatively.

Results Postoperative IOP decreased significantly ($p < 0.001$) from a preoperative mean value of 25.1 ± 5.9 mm Hg (n = 2.73 glaucoma medications) to a postoperative mean value of 8.0 ± 1.1 (n = 0), 8.3 ± 1.2 (n = 0), 11.5 ± 3.0 (n = 0) and 14.1 ± 3.7 mm Hg (n = 0.28) at 1 day, 1week, 4 and 12 weeks respectively. Characteristic imaging parameters of successful bleb were frequently observed (14/18 patients): high and hypoechoic bleb with UBM; thin and hyporeflective bleb wall, multiple subconjunctival fluid spaces and hyporeflective deep bleb tissue with OCT. Bleb height and trabeculocorneal membrane thickness are correlated with low IOP ($r = 0.91$ $p < 0.01$, $r = 0.90$ $p < 0.001$) with UBM examination. Thin bleb wall, large subconjunctival fluid spaces and low reflectivity of bleb tissue are associated with lower IOP ($r = 0.81$ $p < 0.01$, $p < 0.001$ and $p < 0.001$) with OCT examination. No post-operative complications were reported.

Conclusion In our series, deep-sclerectomy with iGen TM implantation seems to be an effective and well-tolerated method to lower IOP and avoid conjunctival scarring.

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In vitro evaluation of adhesion of adipose-derived adult stem cells to chitosan for the treatment of ocular surface pathologies

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Purpose To analyze the ability of adhesion of adipose-derived adult stem cells (ADAS) to porous materials made of chitosan for the future design of biodegradable autologous membranes for the treatment of ocular surface pathologies

Methods We used porous chitosan scaffolds prepared by cold neutralization in a 4% chitosan aqueous solution at acid pH, some of the materials were treated with argon plasma to favour cell adhesion. ADAS cells were obtained after adipose tissue processing from patients undergoing liposuction surgery. 5,000 cells were seeded per each scaffold in DMEM/F12 medium and cellular growth was analyzed on these materials by scanning electron microscopy (SEM) after ten days in culture.

Results Adhesion was observed and cell growth was optimal on the surface of non-plasma-treated biomaterials. Chitosan scaffolds treated with argon plasma showed better adhesion properties. Extracellular matrix production was also observed

Conclusion 4% chitosan biomaterials allow for adhesion, proliferation and extracellular matrix production of ADAS cells. Biocolonization of these biomaterials with ADAS cells will imply the future design of biological autologous membranes containing cells from the very same patient that would act as patches for the treatment of ocular surface pathologies for which current treatments show certain risks such immune rejection, infections or low effectivity.

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No consequence of dietary omega-3 polyunsaturated fatty acid deficiency on the severity of scopolamine-induced dry eye

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Purpose Epidemiological studies suggest that dietary omega-3 polyunsaturated fatty acids (PUFAs) may protect against prevalence of dry eye. This work aimed to evaluate whether a dietary deficiency in omega-3 PUFAs may increase the severity of dry eye in a scopolamine-induced rat model.

Methods Three consecutive generations of Lewis rats were bred under diets deprived of omega-3 PUFAs. Dry eye was experimentally induced by continuous scopolamine delivery in female animals from the third deficient generation and in female Lewis rats fed with a balanced diet. After 14 days of treatment, the clinical signs of ocular dryness were evaluated in vivo using fluorescein staining. MHCII and the mucin Muc5AC were immunostained on eyeball cryosections. Lipids were extracted from the exorbital lacrimal glands and phospholipid fatty acids were analyzed by gas chromatography.

Results The percent of fluorescein stained area to total area of the cornea was significantly increased in scopolamine-treated animals when compared to not implanted animals. Scopolamine treatment decreased Muc5AC immunostaining and tended to increase MHCII immunostaining in the conjunctival epithelium for both diets. In exorbital lacrimal gland phospholipids, arachidonic acid (AA) and the delta5-desaturase index were significantly increased by scopolamine treatment for both diets. There was no significant diet-difference in scores of fluorescein staining, Muc5AC and MHCII immunostaining. The omega-3 PUFA deficiency induced a significant increase in AA in the exorbital lacrimal gland.

Conclusion Our data suggest that, unexpectedly, an omega-3 PUFA deficiency did not increase the severity of dry eye in the rat.

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Cyanoacrylate tissue gluing in corneal perforations associated with herpetic keratitis

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Purpose To evaluate the success of cyanoacrylate tissue adhesive for the management of corneal perforations associated with herpetic keratitis.

Methods Forty six eyes of 46 patients with microbiologically proven herpetic keratitis associated with corneal perforation were included in a retrospective analysis. N-Butyl cyanoacrylate tissue adhesive and bandage contact lens were applied in addition to antiviral therapy. Outcome measure was the preservation of the structural integrity of the globe.

Results After glue application, the corneal perforation healed with scar formation in only 12 (26%) eyes. Keratoplasty had to be performed in 32 eyes (70%) due to failure of the glue. Fourteen (31%) eyes required multiple applications of tissue adhesive. Two eyes underwent enucleation and 1 eye became phthisical.

Conclusion Glue application for corneal perforation in cases of herpetic keratitis is not effective and most cases require a corneal graft to maintain the ocular structural integrity.

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Red eye multimedia teaching tool

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Purpose Since 2004, the Eastern Europe and Middle Eastern External Eye Disease Group has been actively involved in creating various educational programs and tools, targeted at general medical public as well as at ophthalmology residents, younger ophthalmologists and family medicine specialists, regarding diagnosis and treatment of various external eye diseases.

Methods The Eastern Europe and Middle Eastern External Eye Disease Group has designed new computer-based Red Eye Multimedia Teaching Tool, which uses interactive approach, thus enabling active participation of students in teaching process.

Results Red Eye Multimedia Teaching Tool focuses on training in establishing correct diagnosis, as well as choosing the most appropriate therapy for the most common external eye diseases: bacterial, viral and allergic conjunctivitis, as well as dry eye.

Conclusion The newest multimedia teaching tool focuses on diagnosis and treatment of most common external eye diseases, namely bacterial, viral and allergic conjunctivitis, as well as at dry eye. Its interactive approach enables each student to tailor the teaching process to its needs, interests and level of previous knowledge. It is expected to be used by ophthalmology residents, as well as family medicine physicians and other interested medical staff.

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Analysis of corneal epithelial cells with confocal microscopy after lamellar keratoplasty

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Purpose the purpose of this study was to analyze morphometry of corneal epithelial cells in normal eyes and after anterior lamellar keratoplasty using confocal microscopy.

Methods The combination of the Heidelberg Retina Tomograph II and the Rostock Cornea Module (HRT II/RCM) was used to evaluate the corneal epithelium of 10 eyes of patients who had undergone anterior lamellar keratoplasty (ALK group) and 10 normal eyes (control group). Three epithelial layers per cornea were examined: superficial cell layer, wing cell layer, and basal cell layer. A morphometric analysis software was used to determine area, perimeter, circularity, and Feret diameter of the corneal epithelial cells.

Results The mean basal cell area in the central zone was significantly higher ($p< 0.001$) after ALK than in the control group. After ALK, the mean basal cell area decreased with post-operative time ($rS = - 0.42$; $p = 0.039$) but it did not return to normal 24 months after transplantation. Comparison of both groups showed significant differences in cell perimeter, circularity, and Feret diameter of basal cells ($p< 0.001$). Similar differences were found in wing cell layer. Only few superficial cells could be analyzed on corneal graft (no statistical analysis could be done).

Conclusion This study imaged the living human basal epithelium of lamellar grafts, analyzed its structure and highlighted changes in epithelial cells density and morphology. We found an increase in basal cell density between 12 and 30 months. This could be explained by reinnervation of the cornea. Indeed, corneal nerves provide important protective and trophic functions.The basal cell area seems to be a relevant morphometric parameter to assess the corneal epithelium.

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Outcome of transplanted mesenchymal stem cells in the alkali burned cornea

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Purpose Mesenchymal stem cells show promising results in cell therapy for many medical fields. We aimed to study their fate when transplanted in the inflammatory corneal environnement: survival, migration towards the injured tissues, differenciation.

Methods Plastic-adherent, mononucleate cells derived from the bone marrow of New Zealand White rabbits, were transfected with Green Fluorescent Protein (GFP) and expanded in cultures. These MSCs were injected either directly in the stroma, or in the sub-conjunctival space, six hours after the alkali burn of the center of the cornea. Immunohistochemistry and immnunofluorescence were performed one week to four weeks after the transplantation.

Results MSCs were detected by fluorescence microscopy at 7 days and 14 days after transplantation, whatever the site of injection. They were not present in our cut sections after two weeks. After the sub-conjunctival injection, they were mostly localized at the limbus and the peripheral cornea. When transplanted directly in the stroma, they were more dispersed and remained at the site of injection. Fourteen days after transplantation, more than 90% of the MSCs expressed the a- smooth muscle actin marker, like residual keratocytes .MSCs never integrated the epithelial layers and did not express cytokeratins.

Conclusion These results suggest that MSCs transfected with GFP can migrate towards the damaged tissue when injected in the sub-conjunctival space and survive during at least two weeks. They engraft to stromal cornea and differenciate rapidly into myofibroblasts. These MSCs are not able to differenciate into epithelial cells in our model.Their differenciation into myofibroblasts suggests that they might be involved in the stromal wound healing.

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Experimental models of orthotopic limbal transplantation in the mouse. Evaluation of allo- and xenograft survival and characterization of cytokine response

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Purpose To establish and characterize experimental model of orthotopic limbal allo- and xenotransplantation in the mouse. Evaluation of graft survival and detection of intragraft cytokine response.

Methods Syngeneic (BALB/c donors), allogeneic (B6 donors) and xenogeneic (rat Lewis) orthotopic limbal transplantation was performed in BALB/c mice. Recipients with intact or removed corneal epithelium were used. Limbal graft survival and reepitelization of the cornea were scored clinically (opacity, oedema, neovascularization) or by the presence of graft donor cells as detected by the Real-time PCR. Expression of genes for IL-2, IL-4, IL-10, IFN-γ and nitric oxide (NO) in the graft was detected by PCR.

Results Significant differences in opacity, oedema and neovascularization were observed in syngeneic, allogeneic and xenogeneic limbal grafts and in the recipients´ corneal epithelium. The strongest rejection reaction was induced by limbal xenograft. No xenogeneic cells were detected in the graft 2 weeks after transplantation. The rejection reaction was accompanied by an abundant cytokine and NO response in the graft.

Conclusion The experimental limbal transplantation in the mouse can be a useful model to characterize rejection reaction and to test various immunosuppressive treatments after limbal tissue or limbal stem cell transplantation.

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Effect of VEGF blockade on corneal graft neovascularization and rejection in rats

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Purpose To evaluate the effect of anti-vascular endothelial growth factor antibodies directed at VEGF 164, 120, 121 and 165, administered by subconjunctival injections (SC), on neovascularization and rejection after penetrating keratoplasty (PK) in rats

Methods Twelve Lewis rats were grafted with corneal buttons from Brown Norway rats and were divided in 2 treatment groups (G) just after surgery (day 0). G1 received saline SC injections (0.02ml/inj, n=6) every 3 days from D0 to D21 and G2 received SC injections of anti-VEGF (0.02ml/inj, 10µg/ml), with the same regimen. Rejection clinical scores were based on corneal oedema (0 to 3) and transparency (0 to 4). Surface and extension of neovascularization were scored clinically (0 to 4) and then quantified using lectin immunostaining on flat-mounted buttons

Results At D21, the mean rejection scores were significantly higher in G1 compared to G2. Rejection rates were 83% in G1 vs. 50% in G2 ($p<0.05$). Neovessels scores were 4±0 in G1 vs. 2.5±0.54 in G2 ($p<0.001$). On flat-mounted corneas the mean ratio of vessels area/clear cornea was 58% in G1 vs. 36% in G2 ($p=0,003$).

Conclusion The sub conjunctival administration of anti-VEGF antibodies not only reduces neovessels growth but also prevent rejection after PK.

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Cis-urocanic acid, a novel anti-inflammatory and cytoprotective drug, decreases effectively UVB-induced IL-6 secretion and cytotoxicity in human corneal and conjunctival epithelial cells in vitro

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Purpose Urocanic acid (UCA) is a major UV-absorbing chromophore in the epidermis and has been suggested to act as one of the initiators of UV-induced immunosuppression. The anti-inflammatory and cytoprotective effects of cis-UCA were studied in human corneal and conjunctival epithelial cells in response to UVB-irradiation in vitro.

Methods Human corneal epithelial cells (HCE-2) and human conjunctival epithelial cells (HCEC) were exposed to 10, 100, 1000, and 5000 µg/ml concentrations of cis-UCA (BioCis Pharma, Turku, Finland) with and without UVB-radiation (4 x Philips TL 20W/12 lamps; total irradiation dose 153 mJ/cm2). Secreted interleukin-6 (IL-6) levels were analyzed with ELISA assay. Cell viability was measured by a colorimetric MTT (3-(4,5-dimethyldiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay.

Results The 100 µg/ml and 1000 µg/ml concentrations of cis-UCA significantly suppressed IL-6 secretion induced by UVB-irradiation in both cell types. In addition, the same concentrations improved the viability of the UVB-irradiated cells when analyzed by MTT assay. No significant alterations in IL-6 expression levels or viability were observed in response to 10, 100, and 1000 µg/ml cis-UCA only, while 5000 µg/ml cis-UCA evoked cytotoxicity in both cell types.

Conclusion Our findings suggest that cis-UCA is a promising novel drug to suppress UVB-induced inflammation and cellular damage in human corneal and conjunctival epithelial cells.

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The effect of UVA and UVB irradiation of the rabbit cornea on matrix metalloproteinase 2 and 9 expression in the corneal epithelium

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Purpose Matrix metalloproteinases (MMPs) synthetisized by corneal cells are primarily responsible for degrading and remodeling corneal stromal extracellular matrix. They participate in various pathophysiological processes in the cornea, including corneal wound healing and ocular diseases. Purpose of this study was to investigate the effect of UVA and UVB rays on the expression of matrix metalloproteinases (MMP-2 and MMP-9) in the corneal epithelium.

Methods In the first group of rabbits the corneas were irradiated with UVA lamp (365 nm, once a day during 4 days, a dose per day 1.01 J/cm2). In the second group of rabbits the corneas were irradiated with UVB lamp (312 nm, once a day during 4 days, a dose per day 1.01 J/cm2). Matrix metalloproteinases MMP-2 and MMP-9 were examined on cryostat sections immunohistochemically using mouse monoclonal anti-MMP-2 and anti-MMP-9 antibodies.

Results Immunohistochemical examination showed that UVA rays did not change the expression of MMPs studied in the corneal epithelium. In contrast, UVB rays induced the increased expression of MMPs in corneal epithelial cells. From both enzymes investigated in corneas irradiated with UVB rays the expression of MMP-9 was more pronounced than the expression of MMP-2.

Conclusion Comparing the effect of the same doses of UVA and UVB rays on the normal rabbit cornea, UVB rays /not UVA rays/ evoked the increased expression of MMPs in the corneal epithelium. To investigate the importance of these findings is the aim of our next study.

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Temperature- and osmosensing by the human corneal endothelium through activation of TRPV channels

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Purpose The human corneal endothelium is essential for the physiology and transparency of the cornea. This is sustained by a number of different regulatory mechanisms and response to various stimuli. Exposure to hypotonic challenge and temperature changes may have major impact. This study was undertaken to identify such possible stimuli pathways in human corneal endothelial cells (HCEC).

Methods The functional expression of putative temperature- and osmosensing ion channels was investigated by measurements of intracellular free Ca2+ ([Ca2+]i) with fura-2 and automated patch-clamping (microchip technology). Highly selective agents were used to identify TRPV channel subtypes in an immortalized HCEC population (HCEC-SV40) and two subcloned cell lines (H9C1, B4G12).

Results The TRPV1 selective agonist capsaicin (20 µM) increased [Ca2+]i and non-selective cation channel outward currents. Cells pre-treated with the antagonist capsazepine (10 µM) did not show any Ca2+ responses. Similar results were obtained with the TRPV4 selective agonist 4α-PDD (5 µM) and the TRP channel blocker ruthenium red (10 µM). In addition, exposure to hypotonic challenge (150 mOsm) led to an increase in [Ca2+]i whereas the isotonic baseline (control) was stable. Furthermore, temperature rises from room temperature to 40-43 °C led to an increase in [Ca2+]i in HCEC-SV40 and H9C1.

Conclusion There is functional expression of TRPV channels in HCEC. Therefore, these cells are able to react to temperature rises by activating of TRPV channels. In particular, TRPV1 and TRPV4 may be functionally expressed which are known as heat receptor and osmosensor respectively. These findings may have direct clinical implication (eye banking procedures, keratoplasty).

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The effect of corneal hydration on corneal ablation rate at 193nm and 213nm

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Purpose The ablation rate of corneal tissue depends primarily on the fluence of the laser and corneal hydration. It was the purpose of the study to compare the dependence of the ablation rate on corneal hydration for two different laser wavelengths (193 and 213-nm).

Methods ArF Excimer laser (Allegretto, Wavelight) with a wavelength of 193nm and Nd:YAG CustomVis laser with a wavelength of 213nm were used for the study. Corneal discs were harvested from porcine eye within 24 hours post-mortem. Corneal epithelium was removed with a blunt spatula. The disks received ablation equivalent to the ablation of 100 microns at a circular zone having a diameter of 7mm. Before and after ablation, each disk was weighted and subsequently dried in order to calculate its dry mass and therefore hydration during ablation. In order to test the ablation rate at different hydrations, the disks were ablated at different time intervals fooling their preparation. The hydration ranged from 66 to 80% w/w.

Results The ablated mass showed a positive linear correlation with hydration for both lasers. The corresponding normalised dry mass, which is more critical for the accuracy of refractive corrections, exhibited a negative linear correlation with hydration with similar slopes for the two lasers tested (-0,0651 for the 193nm and -0,0568[hydration-1] for the 213nm).

Conclusion Results of this study reveal the similar behaviour in the dependence of ablation rate from the hydration of cornea at the 193- and 213-nm laser wavelengths.

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Refractive changes after pterygium surgery

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Purpose To study the relationship between pterygium size (extension, width) and corneal astigmatism in eyes with unilateral primary pterygium. To evaluate the effect of successful pterygium surgery on corneal topography

Methods Computerized corneal topography was performed on 105 eyes with pterygium before and 3 months after successful excision and limbo-conjunctival autograft surgery.

Results The degree of corneal astigmatism significantly correlated with the extension of pterygium on the cornea. With-the-rule astigmatism was the more frecuently finding.

Conclusion Corneal topographic changes caused by the pterygium are almost reversible after surgical treatment. Successful pterygium surgery significantly reduces topographic astigmatism, SRI, SAI, and corneal flattening. However, precise prediction of these refractive changes is not always accurate.

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Confocal microscopy after descemet stripping automated endothelial keratoplasty (DSAEK): morphological findings in short term follow up

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Purpose To evaluate the clinical findings, visual outcomes, and confocal microscopic corneal features after DSAEK in Fuchs endothelial dystrophy.

Methods A 70-year-woman patient with pseudophakia and Fuchs endothelial dystrophy underwent small-incision DSAEK surgery. Best spectacle corrected visual acuity (BSCVA) was 1.30 (20/400) logMAR (Snellen) before treatment. Confocal scanning microscope (ConfoScan 4, Nidek Technologies, Padova, Italy) was performed before surgery procedure, after 7 days, at 1 and 6 months after DSAEK. Images of corneal structures, including endothelium, donor and recipient stroma were obtained. Endothelium density was evaluated using manual count and 40x probe.

Results BSCVA improved at 0.3 (20/40) log MAR (Snellen) at 6 months. No astigmatism change was recorded at the end of follow-up. Endothelial cell density was about 850 cells/mm2 after 6 months surgery procedure. Interface and donor stroma reflectivity were highest at 7 days showing progressive decrease over time.

Conclusion The DSAEK procedure represents a promising alternative to conventional penetrating keratoplasty (PK) for patients with Fuchs' dystrophy. Confocal microscopy is able to detect precise evaluation of corneal features, interface morphologic characteristics and reflectivity to improve therapeutic choice and to understand the pathophysiology of visual recovery.

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Donor tissue detachment after descemet stripping automated endothelial keratoplasty (DSAEK): a 35 mhz probe ubm study

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Purpose To evaluate the UBM role in cases of donor lamella detachment after DSAEK using a 35 MHz probe and immersion technique.

Methods Two patients ,a 68 yo woman and a 70 yo man,underwent to uncomplicated DSAEK for bullous keratopathy.An initial corneal clearing was observed in the first 48 hours followed by a progressive increase of corneal oedema causing a difficult evaluation of donor lamella and anterior chamber structures. In one case,an acute glaucoma occurred.Ecographic evaluation was performed with 35 MHz probe and immersion technique(Hi Scan Ecographer,Optikon 2000,Rome,Italy).Six scans centered on the cornea and 30 degrees angled were aquired in order to obtain a topographic map.

Results UBM allowed to distinguish between two morphological patterns according to donor lamella's position: partial detachment(PD)(double chamber appearance without lammela's dislocation)or total detachment(TD)if associated to donor graft dislocation. In the case complicated by acute glaucoma , a pupillary block caused by a PD was seen. The main UBM findings were:donor lamella tickening with high hyporeflectivity of recipient stroma due to oedema .

Conclusion The donor lamella detachment is the main complication of DSAEK procedure . Posterior lamella and anterior chamber evaluation may be difficult in this cases due to corneal oedema.UBM allows to distinguish between partial and total detachment of posterior lamella and main related complications;trought a topographic map,it offers informations usephul to the reattachment surgical strategy.

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Ultrastructural organisation of arthritis corneal stroma

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Purpose Normal corneal stroma consists of uniformly organised collagen fibrils regulated by corneal proteoglycans. The focus of the study is the ultrastructural organisations of the collagen fibrils and proteoglycans in patients suffering with corneal melting due to rheumatoid arthritis (RA).

Methods Corneas of two patients (ages 50 & 61 years) suffering from RA were fixed in 2.5% glutaraldehyde containing cuprolinic blue in sodium acetate buffer. The tissue were dehydrated in a graded series of ethanol and embedded and polymerised in spurs resin. The sections were studied under an electron microscope.

Results The epithelial cells were degenerated and Bowman's layer was replaced by fibrous pannus containing large abnormal proteoglycans and lucent spaces. In the stroma, longitudinally running collagen fibrils were curled and fused to each other. In cross section, collagen fibrils were not rounded and were separated with large spacings. Large proteoglycans and lucent spaces were present throughout stroma. The Descemet's membrane was followed by posterior collagenous layer. Degenerated keratocytes were present in the pannus and throughout the stroma.

Conclusion The collagen fibrils and proteoglycans were severely degenerated which resulted in the disorganisation of the corneal stroma. We believed that due to the disease, alteration in keratan sulphate and chondroitin sulphate might occur which possibly affected the structure of the corneal proteoglycans (lumican, keratocan and mimican) which were responsible for the collagen fibrils organisation.

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Optimisation of diagnostic strategy in severe ocular sicca syndrome

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Purpose To define the interest of phenol red thread in diagnosis of ocular sicca syndrome, and to estimate the agreement with the Schirmer I test.

Methods The PRT test was performed before (PRT1) and after (PRT2) the Schirmer I test, in both eyes of 72 patients complaining of ocular dryness secondary to Sjögren's syndrome, 71 patients with Sicca Asthenia Polyalgia Syndrome and 40 healthy volunteers. Only the lowest result for each test was used in statistical analysis and cut-off values were determined using the Receiver Operating Curve procedure. Groups were matched by age and sex.

Results The ROC procedure showed weak sensitivity/specificity couples whatever PRT1 cut-off value. A cut-off value of 15mm for PRT2 provided the best ratio between sensitivity and specificity (68% and 90% respectively) and 10mm for Schirmer I test permitted a sensitivity of 77.80% and specificity of 82.50%. Maximal agreement between PRT2 and Schirmer I test was found for a PRT2 value of 15mm with however a mean agreement (Kappa index~ 0.5); however none of PRT2 test alone or Schirmer I test alone was better than the other for diagnosis of ocular sicca syndrome. In contrast, the combination of Schirmer I test (≤10mm), PRT2 test (≤15mm) and negative"deltaPRT" (PRT2 < PRT1) permitted to increase sensitivity and specificity to 92% and 95%, respectively.

Conclusion Schirmer I test must certainly be used firstable in diagnostic step. However PRT2 and negative « deltaPRT » permit classification of patients « forgotten » by Schirmer I test. Finally, association Schirmer I test, PRT2 and negative « deltaPRT » offers characteristics of diagnostic test (high specificity (90%) and sensitivity (85%)) with a high positive predictive value (73, 3%) for SGS.

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Comparison of real intraocular pressure (IOP) during LASIK versus Epi-LASIK

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Purpose To compare real-time intraocular pressure (IOP) in LASIK versus Epi-LASIK in porcine eyes during flap creation using the Moria 2 microkeratome and the Moria Epi-KTM epikeratome.

Methods Interventional, prospective study of two keratomes: Moria Group (M2) and epipolis laser in situ keratomileusis Group (MEpi-K). These devices were used to create a lamellar corneal or epithelial flap respectively in freshly enucleated porcine eyes. The IOP changes induced by the procedures were recorded using manometry by direct cannulation with a reusable blood pressure transducer connected to the anterior chamber.

Results 7 eyes were included for M2 Group and 10 for the MEpi-K Group. In the M2 Group the IOP increased during suction phase to a mean value of 122.53±30.40 mm Hg and to 160.52±22.73 mm Hg during cutting phase (mean time: 21.42±7.48 and 15.71±1.88 secs respectively). In the MEpi-K Group, mean IOP increase was 100.66±18.60 mm Hg during suction phase, 91.38±17.79 mm Hg during cutting phase and 74,37±12.70 during low-back phase (mean time: 25.79±3.44, 33.68±2.81 and 29.74± 3.11 secs respectively). IOP values in both groups showed statistical significant difference in all comparison ($p<0.01$).

Conclusion Real-time IOP can be measured during flap creation process using direct manometry in the anterior chamber. Our results show a significant increase in IOP during the surgical procedure in both groups although the IOP increase reached with MEpi-K epikeratome seems to be lower than M2 microkeratome.

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Analysis of visual outcome with rigid contact lenses in keratoconic eyes

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Purpose To analyze the variation of best corrected visual acuity (BCVA) obtained with rigid gas permeable (RGP) lenses in keratoconic eyes compared to best spectacle-corrected visual acuity (BSCVA).

Methods We prospectively recorded visual acuity data (BSCVA and BCVA with RGP), subjective refraction, keratometric readings and lens geometry in 135 eyes of 78 patients with keratoconus. Acuity data was converted into LogMAR units for statistical analysis. BSCVA was compared to BCVA with RGP lenses, and the differences were correlated with all parameters.

Results The decimal BSCVA and decimal BCVA with RGP lenses was 0.36 (0.44 LogMAR, 20/56) and 0.70 (0.15 LogMAR, 20/29), respectively. The mean difference after RGP lens fitting was +2.83 lines ±2.55 (range 0-11.6). The gain was superior to 1 line in 70%, 3 lines in 40% and 6 lines in 16%. The difference was correlated with the BSCVA ($rS=0.90$ $p<0.001$), mean keratometry ($rS=0.33$ $p<0.001$), subjective cylinder ($rS=0.26$; $p<0.001$). The difference remained unaffected by age and sex ($p\geq0.31$). The difference was correlated with the lens radius rO ($rS=0.27$; $p=0.002$) and the lens power ($rS=0.25$; $p=0.003$). The lens diameter did not affect the variation in visual acuity ($rS=-0.04$; $p=0.62$).

Conclusion There was a significant increase in visual acuity with RGP lenses compared to BSCVA: the lower the initial BSCVA, the better the gain with RPG lenses. The gain was independent of the patients' age. The eccentricity of the keratoconus did not influence the visual outcome with RGP lenses.

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Corneal morphology, topography and sensitivity in a family with inherited recurrent corneal erosions

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Purpose To assess changes in morphology, corneal topography and sensitivity in a family with inherited recurrent corneal erosion syndrome.

Methods Eighteen family members, 9 affected and 9 unaffected eyes were examined. The affected members represented the different stages of corneal pathology from a nearly normal cor-nea to anterior stromal fibrosis of the central cornea with discrete corneal irregularities. To evaluate the corneal morphology and nerve structure, the eyes were examined under a corneal confocal microscopy (CCM, ConfoScan 3, Corneal Confocal Microscope. Nidek Technologies). Videokeratography (VK) was evaluated with the Tomey TMS – 2N (Topog-raphic Modelling System). Corneal mechanical sensitivity was measured with modified Noncontact gas Esthesiometer (NE) (Belmonte modified noncontact esthesiometer, Coop-erative Research Center for Eye Research and Technology).

Results CCM detected morphological changes in the epithelium and stromal nerves in 5/9 affected eyes. Haze formation with altered keratocytes could be found in the anterior stroma in all affected eyes. Except for two eyes (one affected and one unaffected), all VK showed irregular astigmatism. Corneal sensitivity was significantly lower in affected patients ($p<0.01$). Age and corneal sensitivity showed no correlation.

Conclusion The decreased sensitivity in the affected eyes seems to correlate with the low number of subbasal nerves reported by CCM. Yet, another possibility is that corneal haze masks the nerves. Correlation between VK and CCM findings in patients was not found. NE revealed a decreased corneal sensitivity in the affected members.

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Comparison of metabolic profile of normal and keratoconus corneas using HR MAS 1HNMR spectroscopy and HPLC

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Purpose The aim of this study is to examine possible differences in the metabolic profile between keratoconus and normal corneas.

Methods Samples of corneas with keratoconus were obtained during the transplantation surgery from 3 patients (age: 22-27 years). The control corneal tissues were excised during enucleating of eyes with malign melanoma in the retina from 4 patients (age: 65-72 years). The samples were immediately frozen at -80 °C. The metabolic profiles of the samples were investigated either with HR MAS (High Resolution Magic Angle Spinning) 1H NMR (Nuclear Magnetic Resonance) spectroscopy (14.1 T) operating at 600.132 MHz and HPLC (High Performance Liquid Chromatography). All data obtained with both methods were analysed using special software for: (i) analysis of complex mixtures, (ii) principal component analysis – PCA, (iii) detailed statistical analysis.

Results In all samples, 9 amino acids were detected with HPLC, and 19 metabolites (including amino acids) with HR MAS 1H NMR spectroscopy, respectively. PCA analysis of NMR spectra showed no grouping pattern between the keratoconus and control samples. Detailed analysis of data obtained with NMR spectroscopy and with HPLC revealed no significant differences in amino acid profiles between keratoconus and control corneas.

Conclusion The study presents metabolic profiles of human cornea examined with new approach combining NMR spectroscopy and HPLC. Significant differences in the metabolic profiles of corneas with keratoconus and healthy corneas examined with both methods were not revealed. Small number of samples analysed in this study represents a limitation of the results, and further investigation will be performed to focus on particular metabolites.

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Keratoconic corneas after ferrara rings implantation: histopathological findings

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Purpose To describe the histopathologic changes in human ectasic corneas, induced after implantation of intracorneal ring segments.

Methods Ten eyes (7 advanced keratoconus, 2 post-lasik ectasia and 1 marginal pellucid degeneration) recieved corneal implants (Ferrara-Keraring like) for treatment. Due to a poor refractive out-come they had penetrating keratoplasty.

Results Conventional histology on all specimens after hematein-eosin stain, showed no inflammation signs and hypoplasia of the corneal epithelium immediately surrounding the channel.

Conclusion Histopathologic changes seem to be complety reversible after implant removal. Longer follow-up is necessary to determine whether they accelerate corneal thinning or inflammation response.

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Tufting enteropathy: ocular surface and conjunctival markers

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Purpose to describe clinical impairment and ocular surface anomalies in a case of tufting enteropathy (intestinal epithelial dysplasia) and to characterized conjunctival markers

Methods We studied a case of a 5 year-old girl presenting a tufting enteropathy which is a rare congenital disease with persistent diarrhea. Systemic anomalies were associated. She presented a tearing since 8 months-old. At 5 years old she developed a marked keratitis with itching and blepharospasm non-responding to treatment. At fundus a unilateral coloboma was noted. Conjunctival impression cytology specimen were processed and markers were analyzed using flow cytometry and were expressed by determining the percentage of cells expressing the markers. CC chemokine receptor 4 (CCR4), CC chemokine receptor 5 (CCR5) expression and HLA-DR were studied. Conjunctival biopsies were studied in optical microscopy.

Results Markers obtained with conjunctival impression cytology specimens were described showing CCR4 CCR4 was overexpressed related to the Th2 inflammatory pathways. More than 60% are associated with a non specific keratitis. Allergic and dry eye syndrome could be both implicated in the mechanism of the keratitis. Conjunctival biopsy showed acute inflammation of the conjunctiva with epithelial cells exfoliation. This typical aspect of the conjunctiva could be related with the observed disorganization of surface enterocytes with focal crowding forming tuft.

Conclusion A better understanding of ocular surface disorders in tufting enteropathy might help to elucidate the molecular mechanisms of corneal and intestinal epithelial diseases.

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The roles of T and natural killer cells in a pig-to-mouse corneal xenotransplantation

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Purpose To determine the role of T cells and natural killer (NK) cells in mediating corneal xenograft rejection of a pig-to-mouse model.

Methods Pig corneas were orthotopically transplanted to C57BL/6, Balb/c-nu and CB.17 SCID mice with or without NK depletion. NK cells were depleted by an intraperitoneal injection of anti-NK1.1 mAb three days before and one day after transplantation. Graft survival was clinically assessed by slit-lamp microscopy, and median survival times (MST) were calculated. The rejected grafts were histologically evaluated.

Results The pig corneal xenografts were acutely rejected by C57BL/6 mice (MST 7.00±0.61 days), while Balb/c-nu and CB.17 SCID mice rejected pig corneas in more delayed fashion (MST 14.00±0.77 and 15.00±0.58 days, respectively). NK depletion failed to a further prolongation of the pig corneal xenograft survival in Balb/c-nu mice. The rejected grafts in C57BL/6 mice were heavily infiltrated with inflammatory cells, the majority of which were macrophages. Many CD4+ T cells were observed, but either CD8+ T cells or NK cells were rarely found. In contrast, the grafts in Balb/c-nu mice had markedly decreased inflammatory infiltration with small amounts of macrophages and CD4+ T cells, and the infiltration was further reduced in CB.17 SCID mice.

Conclusion Acute rejection of the pig corneal xenografts in mice is not solely a consequence of an adaptive immunity although CD4+ T cells play an important role in the graft rejection. Other innate immune effectors than NK cells seem to be involved in the rejection of a pig-to-mouse corneal xenotransplantation.

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Study of the corneal endothelial infection after Herpes simplex virus type 1 (HSV1) in a murine model: comparison between in situ confocal microscopy (ISCM) and immunofluorescent analysis on histological sections

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Purpose To compare images obtained with ISCM of cornea and immunofluorescence analysis in a mouse model of HSV1 ocular infection (keratouveitis), with the aim of assessing inflammatory reaction (macrophages, lymphocytes and polymorphonuclear cells) and apoptosis during acute infection.

Methods Fifty mice were analyzed using ISCM of left infected corneas, 6 days after HSV1 inoculation. The corneas were then flat mounted, and stained using immmunofluorescence for viral infection, inflammatory markers (macrophages, lymphocytes, PMNs) and apoptosis.

Results ISCM showed multiple retrocorneal cellular precipitates on the inner face of the cornea, with a cluster distribution, and multiple hyper- and hypo-reflective cells randomly distributed all over the endothelium. Histological analysis proved precipitates to be centered by infected endothelial cells and macrophages. Besides, hyper- and hypo-reflective ISCM signals could correspond to either lymphocytes or PMNs, which were found on flat corneas to be scattered onto the endothelium cells, or to apoptotic cells. Most of them corresponded to lymphocytes closely localised near infected endothelial cells (ongoing study).

Conclusion As ISCM images observed in our mouse model were very similar to those observed in human clinical practice with IVCM, our results provide precious information on the biological meaning of clinical observations. In the future, IVCM could be routinely used to monitor herpetic infection in pre-clinical studies, for example in experiments assessing the efficacy of new antiviral strategies.

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Tear meniscus height and lipid layer pattern in seasonal allergic conjunctivitis patients outside the season

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Purpose to exam whether the previously published tear film abnormalities in allergic season remain outside the season in patients with seasonal allergic conjunctivitis (SAC).

Methods Thirty seven subjects' (21 female, 16 male, mean age 27.2 ± 6.5 years) right eye were examined. Twenty three normal subjects and 14 asymptomatic allergic patients with positive allergic prick test were examined outside the season. All allergic patients had allergic symptoms at least during two earlier ragweed seasons. The tear film lipid pattern and tear meniscus height (TMH) were determinate with Keeler Tearscope Plus. The lipid pattern and the tear meniscus were recorded five times in each subject after a blink and three independent observers evaluated the photos. The lipid pattern was graded according to the user manual of Keeler Tearscope Plus. The non invasive tear break time (NIBUT) was also measured.

Results The mean TMH were 0.204 ± 0.048 and 0.234 ± 0.101 mm in normal and allergic patients, respectively. The lipid patterns were in normal range in control and allergic patients except 1 normal and 1 allergic participant. There were no significant differences in TMH and lipid patterns between allergic and control subjects. The mean NIBUT were 17.0 ± 8.4 and 21.5 ± 10.1 seconds in normal and allergic group, and did not correlate with TMH and lipid pattern.

Conclusion Outside the ragweed season the patients with SAC had healthy tear film status similar to normal patients. The allergic ocular inflammation during the season did not induce traceable tear film abnormalities outside the season.

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Occult traumatic nasolacrimal duct obstruction causing anophthalmic socket contraction presenting 20 years later

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Purpose To highlight undiagnosed nasolacrimal duct obstruction as a cause of multiple problems related to conjunctival cicatrisation of the anophthalmic socket and the importance of early diagnosis and treatment in their prevention.

Methods Case report with high resolution digital clinical photography.

Results We present a 43 year old Asian gentleman, who sustained penetrating trauma to the right globe and midface in 1984. At the time, he underwent primary repair of the globe, followed by enucleation. Over the next ten years, he suffered myriad problems with recurrent entropion and trichiasis of upper and lower lids, a dry socket with an uncomfortable artificial eye and chronic mucoid discharge. Twenty years later his initial diagnosis was revisited. On examination, he had a contracted socket with mucosal keratinisation, cicatricial entropion of the eyelids, forniceal shortening and mucoid discharge. There was also nasolacrimal duct obstruction with an occult mucoceole. He underwent external dacrocystorhinostomy with correction of the entropions and anophthalmic socket refashioning. He remains symptom free twelve months following surgery.

Conclusion Contracted anophthalmic sockets can occur spontaneously or secondarily to a disease process. These may lead to changes in tear composition and have pro-inflammatory effects on the ocular surface. We hypothesise that the chronic toxic tear film secondary to the mucocoele led to chronic conjunctivitis with cicatrisation over time and multiple structural lid & socket problems that ensued. This case highlights the importance of looking for occult causes of chronic cicatrisation in the anophthalmic socket.

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The use of intralesional injection of 5 fluorouracil to induce regression of recurrent pterygium

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Purpose To investigate the benefit of intralesional injections of 5FU for the treatment of recurrent pterygium

Methods Retrospective case note review of patients following surgical excision for pterygium identified 6 patients with recurrence treated with 0.1-0.2ml (2.5-5mg) of intralesional 5 FU post operatively. The time to recurrence, post recurrence injections, grade of pterygium pre and post treatment and time to regression were identified.

Results The study group consisted of 5 male and 1 female patients, affecting 6 right eyes. 3 patients developed primary recurrence. The other 3 patients had previous surgery with recurrence followed by further surgical excision and repeat recurrence. The average grade of recurrence was 3.5. All 6 patients showed regression of the fibrovascular tissue following intralesional 5FU injections with an average dose of 0.1-0.2 ml (2.5-5mg). 5 patients required 3 injections or less for regression, whilst one patient required 14 post recurrence 5FU injections. The average grade following regression was 1.7. This level of regression was maintained at an average of 9 months follow-up. No complications of 5FU were reported.

Conclusion The use of 5FU for the treatment of recurrent pterygium is safe and effective in limiting both progression and inducing regression of recurrent pterygium.

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Are Ocular Response Analyzer useful to measure corneal hysteresis in patients with intracorneal rings?

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Purpose Corneal hysteresis is a viscoelastic property characterized by the difference in behavior under loading and unloading. The aim of the study was to determine corneal hysteresis in different eyes: healthy eyes, keratoconic eyes and keratoconic eyes after intracorneal ring implants.

Methods This study comprised 95 eyes of 59 patients. The study population was divided into 3 groups. We analyze 30 healthy human eyes, 35 keratoconic eyes (Amsler grade II-III) and 30 keratoconic eyes after intracorneal rings implantation. Corneal biomechanical properties of these eyes were measured with the Ocular Response Analyser (ORA-Reichert) according to two parameters: corneal hysteresis (CH) and corneal resistance factor (CRF. The unpaired T student test was used for statistical analysis.

Results Mean CH and CRF in normal eyes (10.78 ± 1.6 (SD) mm Hg, 11.91 mm Hg ± 1.2) was clearly superior than in keratoconus group (8.01 ± 1.5 mm Hg, 7.32 ±1.8 mm Hg). However the difference of these parameters between keratoconus group without intracorneal rings and after corneal ring implantation (7.27mm Hg, 6.32 mm Hg) was not statistically significant ($p \leq 0.01$). Mean follow-up period was of one year.

Conclusion Corneal hysteresis and CRF values were significantly lower in keratoconic eyes than in normal eyes. But there is no marked differences if we compare these two biomechanical parameters in keratoconic corneas, before and after corneal ring implants. Improvements in the software accuracy of the ORA devices are needed to characterize corneal biomechanics.

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Assessment of visual outcomes of deep anterior lamellar keratoplasty (DALK)

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Purpose To evaluate visual outcomes following Anwar's 'Big Bubble' technique for deep anterior lamellar keratoplasty (DALK)

Methods Retrospective Case note review of all patients who were treated with DALK in a single university teaching hospital in the UK between January 2004 and December 2007. The main outcome measures were intra operative and postoperative complications, graft clarity and best corrected visual acuity.

Results The study group consisted of 37 eyes of 36 patients (21 male, 15 female). Average age of the cohort was 34.5 years (range: 16 -- 65), with a mean follow-up of 20.4 months (range: 6 -- 46) Keratoconus was the most common indication for attempted DALK (65%). Big bubble was achieved in 62% of cases with microperforations in 14%. A further 14% needed to have manual dissection. Clear Graft Host interface was achieved in 87% of cases where the big bubble was achieved and 76% gained best corrected visual acuity (BCVA) of >6/12.

Conclusion DALK offers visual outcomes similar to that of a penetrating keratoplasty and should be offered to all patients with a healthy endothelium undergoing corneal transplantation.

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In vitro contact angle and coefficient of friction profiles for daily disposable contact lenses

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Purpose To profile coefficient of friction (COF) and contact angle (CA) performance of popular daily disposable contact lenses many of which contain comfort additives. COF indicates the level of friction that may be experienced between a contact lens and ocular surfaces (corneal epithelium and palpebral conjunctiva). Small CA values indicate a more wettable lens surface.

Methods CA's and static and dynamic COF's were measured on commercially available nelfilcon A with PVA (NA); nelfilcon A with HPMC, PEG and PVA (NB); etafilcon A with added povidone (E); hilafilcon B (H); and omafilcon A (O) contact lenses. Lenses were removed from the original packages and measured for out of package (TO) or rinsed in PBS for 1 hour (T1) or 4 hours (T4) and measured. Unpaired t-tests with alpha <0.05 were used to compare between and within lenses and report statistically significant differences.

Results At TO, the CA's averaged NA (9.6), NB (11.4), E (39.6), H (11.2), and O (44.6). After rinsing the NA and NB lenses maintained the lowest CA's. The highest CA was with E at T4 (78.2). At TO, the lowest static and kinetuc COF's were measured on NA (0.006 and 0.027 respectively) while the highest static and kinetic COF's were measured on O (0.831 and 1.114). After rinsing, static COF's were statistically unchanged for NB and O (which contains no comfort additives) and all others increased at T1 and T4 from their T0 values.

Conclusion The contact angle and friction performance of daily disposable contact lenses was found to vary widely. Nelfilcon A with PVA were the most wettable as indicated by having the lowest CA. Nelfilcon A with PVA, PEG and HPMC showed low static and kinetic COF's that remained stable with rinsing.

Commercial interest

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Preliminary study of normal tear complement activation in patients with seasonal allergic conjunctivitis outside the season

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Purpose to determine whether there is a difference in complement activation level on the ocular surface and tear film stability between seasonal allergic conjunctivitis (SAC) patients outside the season and healthy individuals.

Methods outside the ragweed season asymptomatic ragweed pollen allergic patients with the diagnosis of seasonal conjunctivitis at least during two earlier seasons (n=14, mean age 25.79 ys; 5 male, 14 female) and healthy individuals (n=19, mean age 28.05 ys; 9 male, 5 female) were recruited. We collected tear samples with glas capillaries, measured C3a complement activation product with ELISA, and determined non-invasive break-up time (NIBUT) with Keeler TearScope Plus®.

Results the median (range) tear C3a levels were 9.80 (0.78–122.60) ng/ml in SAC patients, and 7.00 (2.00–35.14) ng/ml in the healthy individuals (p=n.s.). The C3a levels did not correlate with sex, age, and the number of seasonal conjunctivitis exacerbations, or NIBUT. The mean NIBUT was 21.50+/-9.41 seconds in allergic patients and 17.30+/-8.68 seconds in healthy individuals (p=n.s.).

Conclusion even though a broader complement activation range was detected in seasonal allergic conjunctivitis patients outside the season compared with healthy individuals, there was no significant difference between the two groups. Outside the season the tear film stability was also similar. We assume, the repeated allergic inflammation on the ocular surface did not manifest in tear film instability or increased complement activation in the asymptomatic period.

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Conjunctival impression cytology as a tool for clinical diagnosis, follow-up and treatment of a patient affected by severe keratoconjunctivitis

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Purpose To use Conjunctival Impression Cytology (CIC) as a tool for the diagnosis, follow-up and treatment decision of a patient affected by severe keratoconjunctivitis after exposure to alkali.

Methods A 48 year-old female patient affected by severe keratoconjunctivitis on her right eye after air exposure to alkali was monitored by CIC. Polyether sulphone filter papers were used to obtain samples from the superior (SB) and inferior bulbar (IB) conjunctiva from the affected eye and stained by PAS-Giemsa staining to reveal the status of goblet cell (GC) population. After observing a dramatic decrease of GC by CIC, we decided to perform a limbal-conjunctiva autograft transplantation from the healthy left eye (LE) to the affected right eye (RE).

Results CIC helped in the diagnosis, treatment and follow-up of a patient affected by severe keratoconjunctivitis after alkali exposure. The decision to perform a limbal-conjunctival autograft transplantation came after CIC results. This procedure resulted in a significant increase in GC density going from 30 cells / mm2 to 362 cells / mm2 on IB and from 0 cells / mm2 to 430 cells / mm2 on SB conjunctiva of the transplanted right eye, 1 month after the surgery.

Conclusion CIC is a very useful tool for the diagnosis and follow-up of cases of severe keratoconjunctivitis providing very relevant information about the status of GC and helping with the decision of the treatment to follow.

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Topical and subconjunctival bevacizumab in corneal neovascularization in keratoplasty patients

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Purpose To report the clinical use of topical and subconjunctival bevacizumab (Avastin) in keratoplasty patients with corneal neovascularization (NV).

Methods Retrospective case series: nine eyes of nine patients with corneal transplant and corneal NV were studied. NV was graded for depth (superficial, deep), extent (clock hours), centricity and intensity. Three patients received subconjunctival bevacizumab 2.5mg/0.1ml. Five patients were treated with topical bevacizumab 5mg/ml 4 times daily for 1 month. One patient first received injection, followed by topical bevacizumab. Follow up was up to 6 months.

Results Corneal NV partially regressed in 8 out of 9 patients. The extent decreased from 7.4±3.8 to 5.6±3.4 and from 8.7±5.8 to 5.3±4.5 clock hours after treatment in patients that received topical and subconjunctival bevacizumab respectively. The centricity changed only in one patient with eye drops. The greatest effect was seen in intensity with decrease from 2.6±0.5 to 1.4±0.9 and from 2.3±0.6 to 1±0.0 in topical and subconjunctival group respectively. One patient who received both subconjunctival and topical bevacizumab only showed response to topical treatment(decrease in intensity). NV regression was noticed 2 days after injection, response was maximal after 1 week, however NV regrowth started at 1 month follow up in all patients. Decrease in NV in topical group was seen after 1 week with maximum response after 1 month. One patient developed persistent epithelial defect 1 month after injection, no other adverse effects were noted.

Conclusion Topical and subconjunctival bevacizumab may be effective in inducing regression of corneal NV in keratoplasty patients. Further studies are needed to prove the effect and its duration.

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The pulsatile ocular blood flow (POBF) in patients with sleep apnea syndrome (SAS)

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Purpose To determine the correlations of pulsatile ocular blood flow (POBF) and intra ocular pressure (IOP) with sleep apnea syndrome (SAS).

Methods The study design was cross-sectional. A total number of 26 patients, recruited into the study between January 2006 and February 2008, who underwent polysomnography were selected for the study. All of them were of European Caucasian Origin. The study participants were contacted by telephone and scheduled for eye examination. Sleep apnea syndrome was diagnosed if the apnea-hypopnoea index (AHI) was > 5, based on whole night polysomnographic recordings. Patients with sleep apnea syndrome using CPAP were excluded from the study. Each patient underwent a slit lamp and indirect ophthalmoscope evaluation of anterior and posterior segment as well as pulsatile ocular blood flow (POBF) examination. POBF was recorded in sitting position after instillation of one drop of Alcaine. In this study, only average POBF and IOP were included for the analyses.

Results Of them, 17 (65.4%) patients had sleep apnea syndrome (SAS) and 9 (34.6%) patients were healthy and served as the control group. The study revealed that the differences between rates of average POBF and IOP measurements in the SAS group and in the control group were not statistically significant either in the right or in the left eyes ($p > 0.05$)

Conclusion Although, experimental studies showed that POBF was lowered in hypoxia, in our patients there was no correlation between pulsatile ocular blood flow and sleep apnea syndrome. Further investigations, concerning vascular impairment, are needed to give evidence of the mechanism of the optic nerve damage in the SAS.

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Pharmacokinetics and ocular tissue penetration of VEGF trap after intravitreal injection in rabbits

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Purpose VEGF Trap is a potent antiangiogenic agent that binds and blocks the action of all VEGF-A isoforms and placental growth factor and, is active in numerous animal models of age-related ocular neovascularization and diabetic retinopathy, when administered either intravitreally or systemically. Moreover, systemic administration of VEGF Trap was active in reducing excess retinal thickness in a Phase I study in age-related macular edema. To understand the pharmacokinetics following intravitreal administration, VEGF Trap (500 mcg) was administered to both eyes of pigmented rabbits.

Methods Plasma and eyes were harvested from three animals/time point at defined times to 4 weeks after administration. Concentrations of VEGF Trap, free and bound to VEGF, were determined in plasma, vitreous, choroid, and retina by ELISA.

Results Maximal vitreal concentrations of free VEGF Trap were approximately 500 mcg/mL at 0.25 to 6 hours after injection. The drug was cleared from the vitreous in a first order process with a half-life of approximately 4.5 days. Vitreal VEGF:VEGF Trap complex reached a plarteau of 0.6 mcg/mL 10 days after administration. Drug was detected in both retina and choroid, and the elimination profile from these tissues approximated by that of the vitreous. Peak plasma total drug concentrations of 1.6 mcg/mL occurred at 10 days. At 4 weeks, the vitreal free VEGF Trap remained over 10-fold in excess of bound VEGF Trap and the complex levels were on a plateau.

Conclusion Given the vitreal half-life, free should remain in excess of bound for at least 3 additional half-lives (13.5 days), suggesting that eye VEGF production would be completely blocked for more than 6 weeks after adminstration of of 500 mcg/eye of VEGF Trap.

Commercial interest

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Retinal arteriolar vascular reactivity to incremental changes in hyperoxic stimuli during isocapnia

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Purpose To determine the relationship between the magnitude of retinal arteriolar vascular reactivity and incremental changes in hyperoxic stimuli whilst maintaining isocapnia.

Methods Twelve healthy, young adults (mean age 27 years, SD 4) participated in a gas protocol consisting of 4 phases at varying fractional expired oxygen levels (FeO2): baseline (15%), hyperoxia I (40%), hyperoxia II (65%), and recovery (15%). End-tidal carbon dioxide (ETCO2) was maintained at isocapnia throughout the experiment. Retinal arteriolar diameter, blood velocity, and blood flow were assessed non-invasively using the Canon Laser Blood Flowmeter during each of these phases.

Results Repeated measures ANOVA showed that there were significant influences of incremental changes in FeO2 on retinal arteriolar diameter ($p<0.0001$), blood velocity ($p<0.0001$), and blood flow ($p<0.0001$). Paired t-tests of these retinal hemodynamic parameters during each phase in the gas sequence showed they were significantly different ($p<0.05$) from each other, with the exception of baseline and recovery values. Incremental increases in FeO2 caused a linear decrease in group mean arteriolar diameter ($R2 = 1$, $p = 0.002$), group mean blood velocity ($R2 = 0.9968$, $p = 0.04$), and group mean blood flow ($R2 = 0.9982$, $p= 0.03$).

Conclusion Isocapnic hyperoxia elicits vasoconstriction and the reduction of retinal arteriolar diameter, velocity and blood flow in a dose-dependent manner over the range of FeO2 explored in this study.

Commercial interest

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Short-term effect of topical dorzolamide hydrochloride on intrastromal corneal pressure “in vivo” in rabbit corneas

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Purpose To test if treatment with topical dorzolamide influences the intrastromal corneal pressure (ICP) “in vivo” in rabbit corneas.

Methods Interventional, prospective study. Topical dorzolamide (Trusopt 2% eye drops; Merck Sharp & Dohme, Spain) was administered in 7 eyes of New Zealand male rabbits three times daily for three consecutive days, and then the ICP changes were recorded with a reusable blood pressure transducer connected to the mid peripheral cornea. The ICP was measured in the same manner in 7 eyes of New Zealand male rabbits without any topical treatment (control group).

Results The ICP averaged -6.2±3.2 mmHg, -10±5.8 mmHg and -12.5±8.7 mmHg at 15, 30 and 45 minutes in the control group, respectively. In the study group (dorzolamide treated eyes), the ICP readings were 1.8±3.4 mmHg, -0.28±4.3 mmHg and -1.8±5.3 mmHg at the same time points, respectively. The differences in the ICP between both groups were statistically significantly different at all time points ($p=0.004$, $p=0.005$, and $p=0.02$, respectively).

Conclusion ICP is a valid and sensitive method to evaluate “in vivo” the endothelial function, and that it is more sensitive that other methods in detecting changes in the physiology of this structure with the use of topical dorzolamide.

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Ophthalmic timolol in a hydrogel vehicle leads to minor interindividual variation in timolol concentration in aqueous humor

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Purpose Ophthalmic timolol has been used for decades in the treatment of glaucoma and ocular hypertension, traditionally in aqueous 0.5% eye drops. Recently a timolol 0.1% hydrogel has been developed to improve systemic safety. The aim of the present study was to compare aqueous humor timolol concentrations after administration of 0.1% hydrogel and aqueous 0.5% timolol in patients scheduled for a cataract operation.

Results The concentration in the aqueous humor was 210 ± 175 ng/ml (mean ± SD) two hours after administration of timolol 0.1% hydrogel and 538 ± 304 ng/ml after aqueous 0.5% timolol. In the aqueous 0.5% timolol group more patients had unnecessarily high concentrations of timolol in the aqueous humor. Beta 1-receptors and Beta 2-receptors were practically 100% occupied after administration of both products. The hydrogel proved to be an excellent formulation in giving smaller inter-individual variation in penetration of timolol into the aqueous humor. Only a weak correlation was seen between corneal thickness and the aqueous humor concentration of timolol in the aqeuous 0.5% timolol group. A similar correlation was observed between age and concentration of timolol in the aqeuous 0.5% timolol group.

Conclusion In contrast to the conventional aqueous 0.5% timolol, 0.1% timolol hydrogel caused only slight inter-individual variation in timolol concentration in the aqueous humor.

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Dynamic retinal vessel reaction in diabetes type I

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Purpose Exposure of the retina to flickering light induces retinal vessel dilation in healthy subjects. Diabetes and related vascular disorders are able to change vascular endothelial function. Whether the dynamic reaction to luminance flicker stimulation in retinal branch arteries and veins differs between healthy volunteers and patients suffering from diabetes type I is investigated.

Methods 35 patients with insulin dependent diabetes mellitus type I (age (mean±SD) 50,9 ± 8,6 years old) and in 35 age and gender matched medically healthy volunteers were examined. Vessel diameters of retinal vessel segments were assessed by Dynamic Vessel Analyzer (DVA). After baseline measurement (50 s) monochromatic rectangular flicker stimulation (530-600 nm, 12,5 Hz, 20 s) was applied 3 consecutive times.

Results In most subjects fast vessel dilation compared to baseline and an ensuing reactive arterial constriction were observed. In detail we found:.....diabetes..... controlmean maximal arterial dilation,[%]:...2,3±1,8**...4,1±2,5time of max. arterial dilation during the stimulation,[s]:.....19,3±10,9*...14,2±3,4mean maximal venous dilation,[%]:.....3,4±1,8*...4,7±1,8 There were statistically significant differences between the two examined groups as marked with *($p<0,05$), **($p<0,01$) (T-test).

Conclusion Functional retinal arterial and venous reaction to flicker stimulation differs high significantly between diabetes type I patients and healthy subjects of the same age and gender. Maximal dilation as a response to the stimulus is not reached. These findings might be an indication for alterations in the vascular endothelium and vessel wall rigidity in diabetes, leading to impaired regulation following metabolic demand.

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The effect of four commercially available preserved and unpreserved prostaglandin analogues on human corneal epithelial and human conjunctival epithelial cells in vitro

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Purpose Four commercially available ophthalmic preparations of prostaglandin analogues: latanoprost, travoprost, bimatoprost, and the more recently developed prostaglandin analogue tafluprost as a BAC-free unit dose formulation, were tested for cytotoxicity using cell culture methods.

Methods The cells were exposed to eye drop concentrations diluted 0.1%-10% in culture medium without fetal bovine serum for one hour. Correspondingly, the cells were exposed to 0.00008%-0.005% BAC in serum-free medium for one hour. Cytotoxicity was assessed by measuring mitochondrial activity with the tetrazolium salt WST-1 assay for cellular growth and viability, and by measuring the lactate dehydrogenase (LDH) leakage in the culture medium.

Results The order of decreasing cytotoxicity of the tested drugs, assessed with the WST-1 test, was latanoprost > travoprost > bimatoprost > tafluprost. Conjunctival epithelial cells appeared to be more sensitive than corneal epithelial cells. The EC50 value of BAC, assessed with the WST-1 assay, was 0.0013% in corneal epithelial cells and 0.00047% in conjunctival epithelial cells. In corneal cells, only the commercial preparation of latanoprost with the highest concentration tested (10%) increased LDH leakage. In conjunctival cells, LDH leakage was also very minor and was statistically significant only after 3-10% travoprost and 10% latanoprost exposures.

Conclusion The cytotoxic effects of the commercially available formulations of latanoprost, travoprost, and bimatoprost were dependent on the BAC concentration of the eye drop. Preservative-free tafluprost had the least cytotoxic effects of the drugs tested.

Commercial interest

▪ 578

Retinal changes after acute increase of the intraocular pressure in adult mice

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Purpose To investigate the effects of increased IOP on the outer retina and its circuitry.

Methods Adult male swiss mice received a mean of 75 laser impacts (532 nm wavelength, 300 mW power, 0.5 second duration, 100 µm diameter spot size) over the limbar and episcleral veins of the left eye. Intraocular pressure (IOP) was measured with the Tonolab tonometer prior to and at 12 h, and 1, 2, 8 or 20 wks after lasering. Full field ERG responses were recorded from both eyes prior to and 1, 2, 8 or 20 wks after lasering. Mice were processed at 3 (n=5), 8 (n=4) or 12 (n=4) wks after lasering. Cryostat retinal sections were analized by fluorescent confocal microscopy.

Results Laser treatment induced an increase in mean IOP of 130% over baseline 12 hours after lasering but reached basal levels by 1 wk. Three wks after lasering, immunostaining with recoverin and transducin could not document any changes in the ONL, but both ON-rod bipolar and horizontal cells had lost their dendritic processes in the OPL. Sprouting of horizontal and bipolar cell processes were observed into the ONL. Eight weeks and 12 weeks after lasering, mice with severe impairment of their ERG (disappearance of b-wave) presented loss of photoreceptor cells. PKC showed morphologic changes of rod bipolar cells and Calbindin showed abnormal and diminished horizontal cells. Immunoreactivity for synaptophysin was decreased and no all the rod bipolar dendrites showed relationship with rod spherules.

Conclusion Increased IOP by laser photocoagulation of the perilimbar and episcleral veins in swiss mice results in changes of retina cell morphology and impairs retinal circuitries.

▪ 579

Early hydroxychloroquine retinal toxicity enhanced by laser flare-cell meter

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Purpose The aim of this study is the evaluation of the electro-oculogram (EOG) against the laser flare-cell meter methodology (LFM) in early detection of hydroxychloroquine retinal toxicity. Several studies have showed that hydroxychloroquine, an antiprotozoal drug used in the treatment of malaria and various rheumatic diseases, can cause severe visual loss due to a toxic effect on the outer retina and the retinal pigment epithelium (EPR).

Methods We enrolled 12 patients (3 males and 9 females) with rheumatoid arthritis (10 patients) and systemic lupus erythematosus (2 patients) in therapy with hydroxychloroquine without retinal toxicity, and 12 health controls (5 males and 7 females). EOG and LFM with a laser flare-cell meter instruments (FM-500, Kowa, Tokio, Japan).were performed in all patients and in health controls. The Student's t test and the Bartlett's correlation test was performed to compare the results of EOG and LFM with the hydroxychloroquine dose considering significant a $p<0.05$.

Results The Arden ratio was 188.75±48.94 in patients and 288.33±32.42 in controls ($p=0,262$); the LFM was 45.80±15.33 vs. 6.31±1.12 photons/ms($p<0.030$). The Bartlett's test showed a strong correlation ($p<0.022$) between the flare and the total hydroxychloroquine dose (394.16±53.84 mg).

Conclusion The flare is an index of anterior segment subclinical inflammation. The proteins level increase in many pathologies, especially in case of an alteration of pigmented cells of iris and ciliar body. These cells have the same origin of EPR and could be damaged by the hydroxychloroquine. In conclusion we can say that the laser flare-cell meter could be an easier, quickly and more sensibly exam than EOG to detect early hydroxychloroquine toxicity.

▪ 580

Dietary prevention of visual function and cognitive decline by omega-3 polyunsaturated fatty acids in senescence accelerated mouse P8 (SAM P8)

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Purpose Cerebral and retinal neurons contain high amounts of omega-3 polyunsaturated fatty acids and especially docosahexaenoic acid (DHA). DHA levels decrease in the aging brain together with the cognitive performances. We evaluated the effects of a dietary supplementation with DHA on mood, cognition and visual functionality in a mouse model for aging, the SAM P8.

Methods SAM P8 and control animals were fed from weaning until 12 months of age with a standard diet or a diet supplemented with DHA (6%). After 5 and 12 months of diet, we evaluated the scotopic ERG, the working memory and the despair behaviour. The fatty acid content of the retina and the brain were determined by gas chromatography.

Results DHA supplementation led to its significant incorporation in the retina and the brain. An age-related loss of the ERG b-wave amplitude was observed from 5 to 12 months of age in control SAM P8 whereas this visual impairment was prevented by DHA supplementation. Dietary DHA supplementation reduced the despair behaviour of control mice but not that of SAM P8.

Conclusion Dietary supplementation of DHA increased its retinal and cerebral incorporation. DHA successfully prevented the age-related loss of visual function in SAM P8 but did not improve the depression-like symptoms.

■ 581

Choroidal blood flow variations to gas in healthy young subjects before and after intermittent hypoxia

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Purpose To evaluate the effect of 14-day intermittent hypoxia on the response of the sub-foveal choroidal blood flow (ChBF) after gas inhalation, in healthy subjects. Recent studies have emphasized the effect of the obstructive sleep apnea (OSA) on CO2 vasodilatation and O2 vasoconstriction. A human model of OSA has been developed in our laboratory with healthy subjects submitting to intermittent hypoxia during 14 consecutive nights. The aim of our study was to determine if these subjects exhibit a dysregulation in ChBF response during and after exposition to intermittent hypoxia.

Methods The ChBF was measured before, at the end (D14) and 5 days after the period of exposition to intermittent hypoxia. ChBF was measured using laser Doppler flowmetry (LDF) in 6 healthy young volunteers exposed to night time intermittent hypoxia. We measured the variations in ChBF during 10 minutes of air inhalation (placebo), 100% O2, and carbogen (8% CO2) at each visit

Results The ChBF response to carbogen was considered as normal (increase of 11%) before the exposition to intermittent hypoxia, and was reduced at the end (+5%) and after the exposition (+5%). The response to 100% O2 in these subjects was not altered by the exposition to intermittent hypoxia. Using placebo, the ChBF remained unchanged at each visit. The sensitivity of the ChBF measurement was 6 %.

Conclusion Healthy subjects exposed to intermittent hypoxia exhibit an altered response of ChBF to carbogen. This CO2 responsiveness could be related to an alteration of the nitric oxide synthase expression.

■ 582

Lactate-induced retinal vasodilation implicates neuronal nitric oxide synthesis in minipigs

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Purpose To investigate the role of neuronal nitric oxide (NO) synthesis in the retinal vasodilatory response to lactate in minipigs

Methods Ten eyes of 10 minipigs were evaluated.After 1 hour of intravenous infusion of Nω-nitro-L-arginine methylester (L-NAME),an intravitreal juxta-arteriolar microinjection of 30µl of L-lactate 0.5 mol/l (pH= 7.4) was performed through a micropipette.Ten minutes later, an intravitreal juxta-arteriolar microinjection of 30µl of L-NAME 0.01 mol/l (pH= 7.4) was performed in all eyes but one which received balanced saline solution (BSS).Retinal arteriolar diameter changes were measured in vivo using a Retinal Vessel Analyzer.The animals' vital signs were monitored and systemic arterial pressure was maintained stable

Results Retinal arteriolar diameter decreased by 4.1% 1 hour after intravenous L-NAME infusion compared to baseline but the difference did not reach significance. Juxta-arteriolar injection of L-lactate induced a significant increase in retinal arteriolar diameter of 22.7% and 28.7% at 5 and 10 minutes respectively($p<0.01$). This was followed by a significant decrease of 8.6% 10 min after juxta-arteriolar injection of L-NAME($p<0.01$).Injection of BBS had no effect in the control eye and retinal arterioles remained dilated under the effect of L-lactate

Conclusion Juxta-arteriolar administration of L-lactate induced vasodilation despite inhibition of endothelial-derived NO by the continuous intravenous infusion of L-NAME. Moreover,juxta-arteriolar L-NAME microinjection significantly suppressed the vasodilatory effect of L-lactate.These data suggest that neuronal-derived NO is an important mediator of the lactate-induced vasodilation in minipigs

■ 583

Intracameral cefuroxime: evaluation of stability in normal saline and balanced salt solutions

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Purpose Intracameral cefuroxime use is an increasing practice to prevent post-operative bacterial endophthalmitis following cataract surgery. First objective is to test stability of cefuroxime solution up to seven days at +4 °C in normal saline solution (NSS). Second objective is to evaluate if cefuroxime may be stable when prepared and stored in a less described solvent: balanced salt solution (BSS).

Methods 0.4 mL syringes containing cefuroxime solution at 10 mg per mL are prepared in a laminar air flow by pharmacists. One set of 18 syringes is prepared with NSS, another set is prepared with BSS and stored in the same conditions (+ 4°C). Three syringes of each solvent are randomly selected every day after preparation (day 1) and tested for their cefuroxime content on day 1, 2, 3, 4, 5, 7. Cefuroxime content is measured by high performance liquid chromatography coupled with UV detection without any modification prior to injection.

Results In NSS a concentration of 9.1 mg/mL [8.8 – 9.4] is measured on day 7, that is statistically different from the concentration of 9.9 mg/mL [9.4 – 10.4] measured on day 1. In BSS a concentration of 10.4 mg/mL [10.2 – 10.7] is measured on day 7, that is statistically not different from the concentration of 10.6 mg/mL [10.4 – 10.8] measured on day 1.

Conclusion The decrease of cefuroxime concentration observed in NSS is not a subject of major concern due to its limited intensity (< 10%). Moreover, syringes are currently used before day 7 in practice. The good physico-chemical stability observed in BSS is promising but should be confirmed by microbiological tests.

■ 584

25-hydroxycholesterol increases IL-8 production in the RPE by activation of PI3K and p38 MAPK pathways

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Purpose Cholesterol oxides have been implicated in the overproduction of proinflammatory cytokines, such as IL-8. The purpose of this study is to establish whether cholesterol oxides increase IL-8 production in the RPE and elucidate the molecular mechanism underlying that increase.

Methods Cultured RPE (ARPE-19) cells were incubated with 7-ketocholesterol (7-KC) and 25-hydroxycholesterol (25-OH). Levels of phosphorylated Akt and p38 MAPK in the cells were determined by Western blotting. Levels of IL-8 mRNA were assessed by real-time RT-PCR. IL-8 protein levels in the medium were determined by ELISA.

Results 25-OH increases IL-8 gene expression and secretion in a time-dependent manner, whereas 7-KC does not have a significant effect on IL-8 production. This effect is not suppressed by antioxidants. Inhibition of the PI3K pathway using either chemical inhibitors or dominant negative forms of PI3K prevents the 25-OH-induced IL-8 production. Inhibition of the p38 MAPK only partially reverses this effect on IL-8 production. Consistently, 25-OH activates Akt in RPE cells, whereas only a modest increase on phosphorylated p38 MAPK is observed. Data further indicates that NF-kB is not involved in IL-8 production following treatment with 25-OH.

Conclusion 25-OH increases IL-8 production in RPE by a mechanism that requires activation of PI3K and p38 MAPK and does not involve oxidative stress. The effectors downstream of Akt and p38 MAPK remain unknown. This IL-8 increase may account for the proinflammatory properties of cholesterol oxides in retinal diseases, such as AMD.
Supported by FCT grants SFRH/BD/19039/2004 and POCI/SAU-OBS/57772/2004

■ 585

Flicker induced vasodilatation is reduced in chronic smokers

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Purpose Habitual smoking is a risk factor for a couple of vascular diseases, including ocular pathologies such as diabetic retinopathy or age-related macular degeneration. In the current study, we set out to investigate whether the regulation of retinal vascular tone is impaired in habitual smokers. For this purpose, vascular reactivity was tested using flicker light induced vasodilatation in smokers and in a non smoking control group.

Methods In this prospective, balanced, parallel group study, 24 chronic smokers (smoking at least 1 pack year) and 24 age and sex matched never-smoking volunteers were included. Flicker induced vasodilatation was determined using the Dynamic Retinal Vessel Analyser. Flicker light induced vasodilatation was expressed by percent change of baseline. Intraocular pressure was determined using applanation tonometry.

Results Intraocular pressure and mean arterial pressure were comparable in both groups. Stimulation with flicker light increased retinal venous diameter by +7.6+- 3.3 in non-smoking subjects. The flicker induced vasodilatation, however, was significantly diminished in chronic smokers (+4.9+- 2.4; $p<0.05$). Flicker stimulation did not affect mean arterial pressure or intraocular pressure.

Conclusion Our data clearly indicate that flicker response is reduced in chronic smokers compared to age matched healthy volunteers. This supports the hypothesis that chronic smoking leads to endothelial dysfunction in the eye.

▪ 601
Philatelic aspects on WHO Year Glaucoma 2008

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Purpose WHO dedicates anno 2008 to Glaucoma. Here we like to present philatelic aspects from Hippocrates to modern Glaucoma Screening, spiced with issues of stamps in 2008.

Methods Collecting stamps.

Results To be seen.

Conclusion Philatelic/historical aspects of glaucoma may induce a humble view.

▪ 602 / 6318
Investigation of the effect of the Alcon AcrySof Natural (ANIOL) blue-filtering intraocular lens on macular pigment

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Purpose Photo-oxidation is believed to play a role in age-related macular degeneration (AMD). Macular pigment (MP), consisting of the carotenoids: lutein (L), zeaxanthin (Z) and meso-Z, protects the retina from photo-oxidative damage. This study was designed to test the effect of the Alcon AcrySof Natural (ANIOL) blue-filtering intraocular lens on MP.

Methods Forty four patients scheduled for cataract surgery were recruited into our study. These patients all had pre-operative best corrected visual acuity (BCVA) of at least 6/18 in the study eye. Patients were randomised to have either the standard Alcon AcrySof three-piece acrylic intraocular lens (AIOL) [controls] or the ANIOL. We measured the spatial profile of MP using customised heterochromatic flicker photometry (cHFP) pre-operatively and post-operatively, and at three, six and 12 months after surgery. BCVA was measured in the study eye at each visit and a blood sample was taken to control for changes in serum carotenoid levels.

Results The mean age (± SD) of our study group was 69 (± 11) years. The last patient study will be completed by 27th of June 2008 and randomisation and final study data will be available for analysis and presentation after this date. Preliminary analysis shows that the mean (± SD) MP optical density at peak (0.25o eccentricity) was 0.301 (± 0.159) before and 0.296 (± 0.142) after cataract extraction (Paired-sample t-test, p = 0.616).

Conclusion Customised HFP appears to be unaffected by lens opacity where BCVA is at least 6/18 and can be used to obtain reliable measurements of the spatial profile of MP in patients with cataracts. Further comment will be made following final study analysis in June.

Commercial interest

▪ 603 / 6417
Orbital floor triamcinolone acetonide in the treatment of pseudophakic cystoid macular oedema

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Purpose To report the outcome of orbital floor triamcinolone acetonide (OFTA) in refractory pseudophakic cystoid macular oedema(PCMO) and to determine the visual outcome in these patients

Methods Six eyes of 6 patients with PCMO inadequately responsive to treatment combinations of topical steroidal and non-steroidal agents were retrospectively studied. All received 40mg (1ml) OFTA injection. Post-operative Visual acuity (VA), intraocular pressure (IOP) and OCT findings were assessed. Other potential complications were looked for retrospectively.

Results The average age was 72 years(+/-12 years). OFTA was given, on average, 4 weeks after a diagnosis of PCMO was made (range 0-6 weeks) and treated with topical anti-inflammatory agent combinations. The mean follow-up was 11.0 months (range, 5-18), and the mean improvement of VA after OFTA was Snellen, (6/18-6/12). This was noticed at a mean of 12 weeks (range 4-72). At last follow-up, five eyes showed an improvement of two lines or more, while in one eye vision was maintained at 6/24 which developed diabetic maculopathy and required grid laser. None of the patients developed post-treatment raised IOP or lost vision. There was a significant reduction of retinal thickness and cystoid space height (P = 0.003). The dosage of topical steroids was reduced or stopped altogether in all 6 eyes. There were no cases of injection-related retrobulbar haemorrhage, cellulitis, or globe perforation

Conclusion In cases of psuedophakic CMO, initial response to OFTA treatment was encouraging. Further larger long term studies are required to ascertain whether re-treatment is effective with subsequent orbital floor steroid injections. This is with a view to maintain the initial improvement.

▪ 604
Flame-shaped hemorrhage seen in diabetic retinopathy is indicative of macular ischemia

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Purpose To study oxygen saturation(OS) levels in the macula with non-proliferative diabetic retinopathy.

Methods 60 eyes of 46 diabetic patients were enrolled in this study. The eyes were divided into three groups based on additional fundus findings. 16 eyes had flame-shaped hemorrhages near the optic disk(group H). 20 eyes had soft exudates throughout thefundus(group E) and 24 eyes had neither flame-shaped hemorrhages nor soft exudates (group N). Patient`s age were 57±9.6, 58±8.5 and 54±16.2 years, respectively in each group. Exclusion criteria were eyes with macular edema treated with laser coagulation. The extent of capillary non-perfusion was evaluated using fluorescein angiogram divided into macula and 4 peripheral quadrants. The severity of non-perfusion was graded from 0 to 5 in a masked fashion. The OS level was measured only in the macular area using Fourier transform-based spectral retinal imaging (SRI) system (Retinal Cube;ASI Co.Israel).

Results The OS levels in the macula did not correlate with overall extent of capillary non-perfusions in the fundus. However group H showed a tendency to have lesser area of capillary non-perfusion when compared with group E or N. The OS levels of H,E and N group were 63±6.7,68±6.2,and 74±8.5% respectively. The difference between OS levels in group H and N and between group E and N were statistical significance ($p<0.01$ and $p<0.05$ respectively).

Conclusion The OS levels in the macular area of the retinas with non-proliferative retinopathy were lowest in the retinas with flamed-shaped hemorrhage. Surprisingly, the overall degree of capillary non-perfusion of the fundus did not correlate with macular OS level. Our study shows that flame shaped hemorrhages are indicative of macular ischemia.

▪ 605
Intravitreal bevacizumab for vitreous hemorrage

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Purpose Vitreous hemorrage is one of the major complications of ischemic retinopathies such as diabetic retinopathy. Our purpose was to describe the clinical outcome of patients who underwent a less invasive intervention than vitrectomy for therapy of persisting vitreous hemorrage

Methods Our clinical interventional case series study included 10 patients (n=11 eyes) who presented with vitreous hemorrage due to proliferative diabetic retinopathy (n=10 eyes)or ischemic retinal vein occlusions (n=1). The hemorrage had persisted for at least 3 months. Mean age was 62,1+/-14,5 years (median 58.4 years; range 45.8-90.8 years) and mean visual acuity was 1,65+/-0.97 logMAR. The mean intraocular pressure was 14.6+/-3.6 mm Hg. All eyes received an intravitreal injection of 1.25 mg bevacizumab, which was repeated in 2 eyes (17%). All patients were fully informed about the experimental character of the treatment and signed an informed consent.

Results At the end of follow-up at 3.9+/-2.3 months (range 1-6 months) after the first injection, the vitreous hemorrage had cleared without any further intervention in all but 1 (9%) eye. Visual acuity improved significantly (p=0.02) from 1.65+/-0.97 logMAR to 0.98+/-0.67 logMAR. The intraocular pressure remained in the normal range (mean 14.6+/-3.5 mm Hg) with no significant difference to the baseline values (p=0.94). We did not observe any sign of intraocular inflammation or other changes that could be regardesd as side-effects of the intravitreal injecion. 4 (36%) eyes underwent panretinal laser coagulation after clearing of the vitreous hemorrage.

Conclusion The present study may suggest to extend the intravitreal use of bevacizumab to persisting vitreous hemorrage due to ischemic retinopathies.

▪ 606
Electroretinography and macular edema in diabetic retinopathy

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Purpose To examine the electrophysiological symptoms in patients with preproliferative and proliferative diabetic retinopathy (PPDR, PDR) with macular edema (ME).

Methods 24 patients with type II diabetes were investigated. OCT presented a focal, diffuse and clinically significant ME. ISCEV standard ERG methods, as well as chromatic macular and multifocal ERG (mf ERG), long-duration flash ERG, pattern ERG (PERG) and retinocortical time (RTT) were performed.

Results ERG changes were similar in PPDR and PDR with ME. Full-field and flicker ERG were normal or subnormal depending on the localization of the pathological process in retina. The amplitude and interpeak latency of OPs were significantly changed. A different amplitude reduction of macular chromatic ERG to red, green and blue stimuli and prolonged b-wave latency to green and blue stimuli were revealed. The retinal density of bioelectrical activity and amplitudes of N1, P1 components were decreased. A long-duration flash ERG showed normal or subnormal ON-response and diminished OFF-response. The pathological macular and mf ERG were attended by pathological full-field and flicker ERG in certain cases. N95 component oPERG was changed in amplitude and implicit time. The RTT was prolonged in most of the patients.

Conclusion The ERG signs point to extent inclusion in pathological process of different retinal structures and layers. PERG and RTT changes indicate initial functional damage of the optic nerve. It is necessary to compare OCT and ERG data for understanding of mechanisms of visual disturbance in DR. The number of cases in which clinical and functional signs did not correspond to each other must be a subject to deep analysis before choosing a medical or laser treatment.

▪ 607
Posterior sub-tenon injection of triamcinolone acetonide as a pretreatment of focal laser photocoagulation for diabetic macular edema

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Purpose To determine whether a posterior sub-Tenon injection of triamcinolone acetonide (TA) before focal photocoagulation is a safe and effective treatment for diabetic macular edema.

Methods Sixteen eyes of 11 diabetic patients with unresolved diffuse macular edema were treated with a 20 mg sub-Tenon injection of TA 1 to 2 months before focal photocoagulation. Focal photocoagulation was applied only to microaneurysms, and grid laser photocoagulation was not performed. The main outcome measures were visual acuity (VA), the optical coherence tomographically (OCT)-determined central macular thickness (CMT), and the fluorescein angiographic appearance of the retina. Patients were followed for at least 6 months.

Results One month after the sub-Tenon injection of TA, the macular edema was resolved with a significant reduction of the CMT by OCT. The VA was slightly improved. Subsequent focal photocoagulation of the microaneurysms maintained the significant reduction of CMT for up to 6 months. A significant improvement of VA was observed in 37.5% patients at 6 months, and no patient had a decrease of VA.

Conclusion A 20 mg of sub-Tenon's TA injection prior to focal laser photocoagulation is a safe and beneficial treatment for diabetic macular edema.

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Calcium dobesilate prevents changes in tight junction proteins in the retina induced by diabetes

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Purpose Calcium dobesilate has been found to correct the excessive vascular permeability associated with diabetes in the retina of diabetic patients and in experimental diabetes. However, the molecular mechanisms underlying these effects are not elucidated yet. In this study, we investigated the potential protective effect of calcium dobesilate against changes in tight junction proteins (occludin, ZO-1 and claudin-5) induced by diabetes in the retina.

Methods Diabetes was induced by an intraperitoneal injection of streptozotocin (65 mg/kg) in two months old male Wistar rats (1 month diabetes duration). The animals were divided in three groups (7-8 animals/group): control, diabetic, diabetic treated with calcium dobesilate (100 mg/kg/day; orally given) during the last 10 days of diabetes. The protein levels and distribution of the tight junction proteins were evaluated by western blotting and immunohistochemistry, respectively.

Results Diabetes decreased occludin and claudin-5 protein levels (65.2 ± 7.6% and 63.2 ± 5.4% of the control, respectively) in the retina. ZO-1 levels were unchanged, but its distribution in retinal vessels was altered in the retinal vessels of diabetic animals. The treatment with calcium dobesilate prevented the changes in tight junction proteins induced by diabetes.

Conclusion In conclusion, calcium dobesilate is able to prevent changes in tight junction proteins in retinal vessels induced by diabetes, which may explain its beneficial effects against diabetes-induced blood-retinal barrier breakdown.Support: OM PHARMA, Switzerland

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Effect of diabetes mellitus on NGF and NGF-receptor distribution in retinal ganglion cells and vascularity in adult rats

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Purpose Recent studies reported that NGF exerts a protective action on cells of the visual system, including retinal cells, and that eye topical application of NGF can reach brain NGF-responsive cells. The aim of the present study is to investigate the response of NGF, NGF-receptor and VEGF in retinal cells in a rat model of DM.

Methods Adult SD rats were obtained from local animal facilities, maintained in a 12:12-hr light:dark cycle and had free access to tap water and food through out the experiments. Rats received a single intraperitoneal injection with 70mg/kg body weight of Streptozotocin (STZ) dissolved in PBS. Control rats received an equivalent volume of buffer solution. Animals were sacrificed with an overdose of Nembutal and pancreas, retina, optic nerve and lachrymal gland removed and used for biochemical, immunohistochemical, and molecular analysis. NGF was determined with "NGF Emax Immunoassay System" ELISA kit by Promega (USA). For histological and immunohistochemical analysis, eye globes were fixed in Bouin fluid. Twenty µm thick sections were cut with a cryostat at -20°C and immunostained for localization of NGF, NGF-receptors, or vascular endothelial growth factor.

Results DT lowers the presence of NGF in the whole retina and reduces the number of retinal cells, particularly in the retinal ganglion layer, and the presence of retinal vessels. NGF administration markedly reduces these deficits.

Conclusion The present findings support the hypothesis of a NGF role in retinal cell physiopathology and suggest that eye NGF application might be useful to prevent and/o reducing retinopathy induced by DT. *V. Colafrancesco has a fellowship supported by Bietti Foundation, Roma

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A pilot study of prevalence of diabetic retinopathy in diabetic patients using non-mydriatic retinography and telemedicine

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Purpose To asses whether the use of non-mydriatic retinography and telemedicine is an adequate method of screening DR in diabetic population

Methods We included all patients suffering from type I, type 2 noninsulin dependant and type 2 insulin dependant diabetes whose ocular fundus were examined in the specialist care center. A 3 field non-stereoscopic retinographies were taken both eyes and an ophthalmologist at hospital evaluated the presence of DR and its severity.

Results 81.2% of the subjects examined had no DR, 10.20% had mild non-proliferative DR, 7.24% had moderate non-proliferative DR and 0.15% had severe non-proliferative DR. The approximate prevalence of DR in area sanitaria 3 was 18.8%. 7, 12% of the examinations were invalid and the patients required mydriatic examination at hospital.

Conclusion The use of non-mydriatic retinography and telemedicine is an adequate method for the screening of DR in diabetic population.

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VEGF/Ang-2 imbalance: the crosslinking between methylglyoxal and vascular dysfunction in diabetic retinopathy

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Purpose Accumulation of methylglyoxal (MGO) in retinas of diabetic rats has been implicated in the formation of acellular capillaries, suggesting an important role for MGO in the vascular dysfunction observed in diabetes. In this study, we hypothesize that increased levels of MGO in retinal pigment epithelium (RPE) cells disturbs the balance VEGF/Ang2 secreted to the extracellular milieu, promoting apoptotis and low proliferation of endothelial cells.

Methods ARPE19 cells were subjected both to hypoxia and MGO, two main features of diabetic retinopathy (DR). The levels of VEGF and Ang2 secreted into the culture medium were assessed by ELISA. Retinal endothelial cells were subsequently treated with the pre-conditioned media of the ARPE19 cells, as well as with different ratios of VEGF and Ang2 recombinant proteins. Apoptotic cell death was determined by immunoblot against Bax and Bcl2, while endothelial cell proliferation was assessed by BrdU-incorporation and fibrin gel angiogenic assays.

Results MGO increases the levels of Ang2 and strongly decreases the levels of VEGF secreted by ARPE19 cells in response to hypoxia. VEGF downregulation appears to result from increased degradation of HIF1α and low HIF1 transcriptional activity. The VEGF/Ang2 imbalance generated by MGO significantly increases the expression of BAX and decreases the levels of Bcl2 of endothelial cells. Moreover, this imbalance also leads to decreased proliferation of the endothelial cells.

Conclusion The VEGF/Ang2 imbalance induced by MGO activates the apoptotic cascade and induces low proliferation of retinal endothelial cells, possibly leading to vessels regression in pathologies that favour accumulation of MGO and where hypoxia is also present, such as DR.

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Utility of retinal photography in the diagnosis of diabetic macular edema

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Purpose To determine the validity of the simple photography and stereo photography in the diagnosis of diabetic macular edema.

Methods Photographies were realized of 427 eyes of diabetic patients, previously dilated with tropicamide eye drops. The color and green filtered 45º and 30º photographies were centered on the posterior pole. Considering the difficulty of the detection of retinal thickenning on a flat photo, we decided to realize two photos to achieve stereopsis. This permits an easier perception of retinal thickening. Sensibility and specificity were compared of the photos to determine the validity in the diagnosis of diabetic macular edema. We used the optical coherence tomography (OCT) as the gold standard test.

Results We obtained approximately an 80% sensibility for the detection of diabetic macular oedema (45 º color photos,45 º green photos, 45 º stereoscopic green photos, 30 º stereoscopic color photos and 30 º stereoscopic green photos). With the 30 º stereoscopic green photos we achieved a sensibility of 94%.The specificity reached values close to 95%. The coefficients of interobserver agreement were at 80%.

Conclusion The stereoscopic color photos, the 30 º green photos and both the 45 º and 30 º stereoscopic green photos offer sufficient sensibility and specificity to be used for the diagnosis of diabetic macular edema.

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Evolution of the laser treatment of diabetic retinopathy (DR): from laser surgery to laser therapy

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Purpose To review benefits and collateral effects of conventional photocoagulation, the standard of care for DR, in comparison with newer laser techniques reported to provide comparable benefits with reduced treatment's hardship and side effects.

Methods Literature review and physical/technical considerations.

Results Conventional photocoagulation lowers the risk of severe visual loss, but is associated with long, painful, multiple treatments and with iatrogenic anatomical and functional damage. Light panretinal photocoagulation (PRP) has shown efficacy similar to that of conventional PRP with fewer sessions and complications. A patterned scanning laser (PASCAL) allows PRP with reduced surgeon's time, in 1 or 2 sessions, but still with discomfort and anatomical-functional damages due to the visible "burn" endpoint. Conversely, subthreshold diode-laser micropulse (SDM) PRP is a new laser therapy that comparably reduces the incidence of vitreous hemorrhage and vitrectomy with a gentle well tolerated treatment that does not cause iatrogenic vision deterioration or laser-lesions detectable at any time postoperatively.

Conclusion Retinal destruction has never been demonstrated to be a prerequisite for the therapeutic benefits. Whatever the elusive mechanisms of action of laser photocoagulation are, long term benefits can be provided either with high intensity/low density laser surgery or with low intensity/high density laser therapy. Non-laser treatments for DR are being tested, often with good, rapid, but also only transient effects. The combination of pharmacotherapy's short term beneficial effects with the long term benefits of a less damaging laser therapy appears as a new treatment paradigm that should undergo rigorous investigation.

Commercial interest

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Retinal fiber layer measured by oct in patients with type I diabetes without retinopathy

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Purpose To evaluate the changes in the peripapillary retinal nerve fiber layer (RNFL) thickness measured with optical coherence tomography (OCT) in patients with type I diabetes without retinopathy.

Methods Comparative cross-sectional study. Thirty eyes of 30 healthy subjects and 30 eyes of 30 patients with type I diabetes mellitus were studied. Ophthalmic examination of diabetic patients showed no retinopathy. One eye per patient was randomly selected for the study. All patients were examined by means of OCT.

Results The control group was formed by 9 women, 21 men, aged 18-38 yr (mean ± SD 28.7 ± 6.01). Diabetic patients were 9 women and 21 men, aged 25.02 yr (± 8.1). Mean period from the onset of diabetes was 14.2 years (SD 5.46). None of the diabetic group had changes at the fundus examination. The RNFL average thickness was 106.1 and 101.8 in the control and in the diabetic group respectively. A significant difference was found in the superior quadrant thickness where the measures were 136 vs 127 respectively (p=0.05).

Conclusion Our results suggest that RNFL changes assessed by OCT can be detected early in the course of type I diabetes.

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The difference in focal photocoagulation treatment decisions of clinically significant macular edema between different medical retina specialists

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Purpose To evaluate the difference in focal photocoagulation treatment decisions of clinically significant macular edema (CSME) between different medical retina specialists.

Methods Twenty five eyes of 16 diabetic patients with a clinical suspicion of CSME were examined by stereo slitlamp biomicroscopy to determine the exact location and extend of CSME. Results of these observations were drawn into a set of FA images (early / mid / late phase) and color fundus photographs. Based on these images, seven medical retina specialists, marked the position, pattern, and number of laserspots on the corresponding color photograph.

Results We found considerable differences between the medical retina specialists in treatment decisions with respect to the amount and localisation of the fictional laserspots.

Conclusion The focal photocoagulation treatment for CSME differs between medical retina specialists with respect to the amount and localisation of the laserspots. Therefore future studies concerning photocoagulation treatment outcome should define their treatment protocol precisely.

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Nerve fiber layer thickness measured with polarimetry (GDX) in patients with type I diabetes

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Purpose To evaluate the efficacy of GDX to detect loss of the retinal nerve fiber layer thickness in patients with type I diabetes without retinopathy.

Methods Comparative cross-sectional study. Thirty eyes of 30 healthy subjects and 30 eyes of 30 patients with type I diabetes mellitus were studied. Ophthalmic examination of diabetic patients showed no retinopathy. One eye per patient was randomly selected for the study. The nerve fiber layer thickness was measured with polarimetry (GDx).

Results The control group was formed by 9 women, 21 men, aged 18-38 yr (mean ± SD 28.7 ± 6.01). Diabetic patients were 9 women and 21 men, aged 25.02 yr (± 8.1). Mean period from the onset of diabetes was 14.2 years (SD 5.46). None of the diabetic group had changes at the fundus examination. No differences were found between control and diabetic group.

Conclusion GDx is not able to find differences in the retinal nerve fiber layer thickness in diabetic patients without retinopathy.

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Non mydriatic retinograph for the diagnosis and follow-up of diabetic retinopathy

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Purpose To determine the validity of the non mydriatic retinograph for the early diagnosis and follow-up of diabetic retinopathy

Methods 367 eyes of diabetic patients were examined using a non mydriatic retinograph. 45º and 30º pictures were taken of 9 fields, with and without pupilar dilation. Retina was examined in mydriasis with slit lamp biomicroscopy and conventional oftalmoscopy. Both methods were compared to determine their validity in the diagnosis and gradeing of diabetic retinopathy.

Results For the early diagnosis of diabetic retinopathy there was obtained a sensibility of 88-95 %, with a specificity of 96 %. 9,5 % of the photos were not valid. To obtain a good sensibility of the retinograph in establishing the grade of diabetic retinopathy, being comparable to the established one, the conventional exploration, it was necessary to realize photos in all the nine fields and with pupilar dilation. The sensibility of detecting edema was low

Conclusion The non mydriatic retinograph is a useful a tool for the screening of diabetic retinopathy in the population. Nevertheless, to determine the correct grade of the pathology, in order to permit a good follow-up of the retinopathy, the obtained sensibility was insufficient not being adequate to substitute the indirect oftalmoscopy and slit lamp biomicroscopy.

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Intravitreal pegaptanib sodium (Macugen) for diabetic macular edema

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Purpose To report the functional and anatomic outcomes resulting from the use of intravitreal pegaptanib sodium as primary therapy in patients with diabetic macular edema (DME).

Methods We conducted a retrospective outcome analysis, by optical coherence tomography (OCT) and best-corrected visual acuity (BCVA), of eyes with DME treated with primary intravitreal pegaptanib sodium (Macugen). Moreover, we evaluated the foveal transverse photoreceptor (PR) band integrity in the OCT images, at the time of the last follow-up visit.

Results Sixty-three eyes of 48 patients with a minimum of 6 months' follow-up (FU) were included for analysis. Intravitreal pegaptanib was found to produce significant improvements in mean BCVA ($p = 0.019$) and reductions in mean central macular thickness (CMT) ($p < 0.001$), as soon as the 6-weeks FU. Most eyes (60/63) required a mean of 3 repeated treatments, over a mean FU period of 6.7 +/- 1.2 months, to achieve significant improvements in mean BCVA ($p < 0.001$) and mean CMT ($p < 0.001$). In our series, the lower visual acuities tended to congregate in the group with the less-defined PR band ($p < 0.001$), and the lower CMT tended to congregate in the group with the best-defined PR band ($p=0.04$), even though the higher CMT did not tend to congregate in the group with the less-defined PR band.

Conclusion Our findings demonstrate that selective inhibition by intravitreal pegaptanib sodium of VEGF165 may produce a clinically meaningful and statistically significant benefit in the treatment of DME.

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Specificity and sensitivity of Heidelberg retina tomograph macular edema maps and the effect of exudate and hemorrhage

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Purpose To assess the specificity and sensitivity of the Macular Edema Module (MEM) of the Heidelberg Retina Tomograph (HRT, Heidelberg Engineering, Heidelberg, Germany) versus Stereoscopic Color Fundus Photographs (SCFP) for patients with different grades of diabetic macular edema (ME) and non-diabetic subjects. The effect of local exudates and hemorrhage on the specificity and sensitivity of MEM was also investigated.

Methods The study included 20 eyes of 20 normal subjects without diabetes and 60 eyes of 60 diabetic patients. Eyes of diabetic patients were classified as without ME (n = 20), with questionable ME (n =20) and with Clinically Significant Macular Edema (CSME, n =20). All participants underwent a full ophthalmological evaluation, plus SCFP and HRT II MEM assessment. The sectors with exudate and/or hemorrhage on the SCFP were removed from the CSME group to generate a modified group (n=20) with CSME and without exudate or hemorrhage.

Results In the normal subject group, the specificity of MEM was 92.2%. In the diabetes without macular edema group, the specificity of MEM was 91.7%. In the questionable ME group, the specificity of MEM was 93.1%. In the CSME group, the specificity of MEM was 87.3%, and the sensitivity for detecting CSME was 77.1%. In the modified group with CSME and without exudate or hemorrhage, the specificity of MEM was 85.7% and the sensitivity for detecting CSME was 96.9%.

Conclusion The determination of diabetic macular edema by MEM shows good to moderate sensitivity and very good specificity. Furthermore, removing the influence of the exudate and/or hemorrhage resulted in excellent sensitivity and very good specificity.

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TOPCON 3D OCT 1000 reproducibility in normal and diabetic patients

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Purpose TOPCON 3D OCT 1000 is a spectral domain OCT, used in our everyday's practice. There are many studies reporting reproducibility of commercially available time domain OCTs. The reproducibility of spectral domain OCTs is expected to be better. To our knowledge there are no reproducibility studies with TOPCON 3D OCT 1000. Our purpose was to evaluate its reproducibility in normal and diabetic patients.

Methods 10 normal maculae and 10 maculae with diabetic edema were scanned for 5 times. Data presented as retinal thickness and retinal volume were analyzed and statistically evaluated.

Results TOPCON 3D OCT 1000 shows excellent reproducibility in normal patients. Differences in measured parameters in patients with diabetic macular edema are not statistically significant.

Conclusion Retinal thickness and retinal volume measurements with TOPCON 3D OCT 1000 are very reliable, although care must be taken in interpreting small differences in pathologic conditions.

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Choroideal neovascularisation in age related maculopathy and high myopia. A Laser Flare-Cell Meter study

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Purpose We studied the subclinical ocular inflammation by laser flare-cell meter in patients with choroideal neovascularisation (CNV) in age related maculopathy (AMD) and in high myopia (HM).

Methods We enrolled 22 patients (12 males and 10 females) without diabetes, systemic inflammatory disease or previous ocular surgery or laser therapy, aged between 65 and 89 years (mean 78,2±6,3) with macular CNV. Twelve of these patients have an age related maculopathy (AMD) and ten have an high myopia (HM). The myopia was mean -14,25 D.We made an indocyanine angiography and measured the extension of neovascularization with the Heidelberg Eye Explorer analysis program.The flare was measured with laser flare-cell meter (FM-500, Kowa, Tokio, Japan) in both eyes of the same patient. Subsequently we compared the flare data of AMD-patients that had an CNV with an area similar of the CNV of the HM-patients.Statistical analysis was performed considering significant a p<0.05.

Results The flare in AMD and HM patients was 14,89±7,61 vs 8,00±0,86 photons/msec (p<0.013) and the CNV area was 4,03±2,236 vs 1,07±0,14 mm2 (p<0.001). We selected a sub-group of AMD-patients that had a CNV area similar to the CNV of HM-patients: 1.13±0.18 vs 1,07±0,14 mm2 (p<0.192) and the flare was 13,48±3,08 vs. 8,00±0,86 photons/msec (p<0.001).

Conclusion Our results show that sub-clincal inflammation in AMD with CNV is higher than in HM with CNV. Furthermore in AMD the flare is correlated with CNV (p<0.021)but not in HM. These data could be explain with inflammatory pathogenesis of CNV in AMD. whereas in HM the CNV could be related to a spontaneous ruptures of the Bruch's membrane.

▪ 622

Improvements in visual acuity within one year following intravitreal bevacizumab in neovascular age-related macular degeneration

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Purpose To evaluate the effects of intravitreal treatment with bevacizumab on vision and anatomic outcome in patients with neovascular AMD.

Methods Retrospective review of 153 eyes that received three or more intravitreal injections of bevacizumab (1.25 mg) for neovascular AMD over a one-year period. Patients underwent ophthalmological examinations, measurements of the best-corrected visual acuity (VA), fluorescein angiography and optical coherence tomography, at baseline and at monthly follow-up visits. Repeated injections were given in the presence of persistent leakage or retinal oedema. We analyzed the data obtained at three time intervals: 1 month (first evaluation) after the third injection, 6 months (second evaluation), and one year (third evaluation) after the onset of treatment. Changes from baseline in VA, central retinal thickness (CRT), and total macular volume (TMV) were analyzed using paired t-tests.

Results Mean baseline VA improved from 50.5 to 57.6 letters (P < 0.0001, N = 153) at first evaluation, 58.3 letters (P < 0.0001, N = 119) at second evaluation, and 59.5 letters (P = 0.002, N = 48) at third evaluation. Baseline mean CRT (344.6 µm) and baseline mean TMV (8.6 mm3) decreased at the first evaluation, to 219.0 µm (P < 0.0001) and 7.2 mm3 (P < 0.0001), respectively. No systemic or serious ocular side effects were noted.

Conclusion Intravitreal bevacizumab is an effective treatment for neovascular AMD, resulting in significant functional and anatomical improvement seen up to one year. After one year, VA in 27% of patients was improved by 15 letters or more, was maintained stable in 67% of patients, and was worsened by 15 letters or more in 6% of patients.

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A novel murine model of aging of the human retina

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Purpose Accumulation of lipids, and especially of cholesteryl esters, under the retinal pigment epithelium and within Bruch's membrane is a normal feature of aging and has also been observed in human eyes with age-related maculopathy. Our objective was to evaluate the retinal phenotype of apoB100,LDLR-/- mice, a model for lipid metabolism dysfunction and potentially of aging of the retina.

Methods ApoB100,LDLR-/- mice were studied at 7 and 14 months of age by standard scotopic and photopic electroretinography by comparison to control animals. Fundus images were obtained with a confocal SLO (Heidelberg Retina Angiograph). The integrity of the vascular system was investigated by means of fluoresceine and indocyanine green angiography. Sections of eye cups were stained by filipin to detect cholesterol deposits.

Results Both scotopic and photopic b-wave amplitudes were reduced in apoB100,LDLR-/- mice compared to control mice (Rmax=125 µV vs 208 µV for the scotopic b-wave amplitude at 7 months, and 83 µV vs 162 µV at 14 months). Similarly rods and cones sensitivity was 0.5log unit lower in apoB100,LDLR-/- mice at 14 months, compared to control mice. Although the retinal and the choroidal vascular systems were normal, apoB100,LDLR-/- mice displayed white auto-fluorescent dots in the retinal pigment epithelium layer which likely corresponded to cholesterol deposits.

Conclusion The present apoB100,LDLR-/- mouse, is one of the only models with neutral lipid deposits at the basement of RPE that can potentially be very useful to study the mechanisms of lipid deposition that occurs universally in human retina while aging.

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Intravitreal injection of bevacizumab to treat choroidal neovascularization with large submacular hemorrhage secondary to age-related macular degeneration

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Purpose To assess the effects of the intravitreal injection of Bevacizumab (Avastin) to treat choroideal neovascularization (CNV) associated with large submacular hemorrhage (LSH) secondary to age-related macular degeneration (AMD).

Methods Prospective interventional case series. Patients presenting occult subfoveal CNV with LSH greater the 50% of the entire lesion were recruited. The protocol required 3 monthly consecutive injections, followed by possible repeat injections on the basis of the morpho-functional responses related to OCT parameters, angiographic features and visual acuity over a 12-month follow-up.

Results Eight patients were enrolled in the study and prospectively followed up. Mean visual acuity and mean foveal thickness (FT) at the baseline were 0.72±0.35 (logMAR±SD) and 296±86µm SD, respectively. At three-month examination, mean visual acuity improved to 0.46±0.28 and mean FT decreased to 240±105µm SD. At 12-month examination, mean visual acuity was 0.48±0.32, and mean FT 238±50µm. A progressive resolution of macular bleeding was registered in 7 patients. No side-effect or complication was registered.

Conclusion Intravitreal bevacizumab can be considered a valuable treatment for subfoveal CNV with LSH secondary to AMD. A randomized clinical trial designed with a greater number of patients and a control group is needed to confirm our preliminary results.

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Intravitreal bevacizumab (Avastin) treatment in neovascular age-related macular degeneration: 6 months results

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Purpose To study the visual and anatomic outcome of the intravitreal bevacizumab injection in the treatment of neovascular age-related macular degeneration (AMD).

Methods 86 eyes of 79 patients (mean age: 74.9) who received one or more intravitreal bevacizumab injections for neovascular AMD and had a follow-up of at least 6 months were analyzed retrospectively. Visual acuity (VA), optical coherence tomography (OCT) macular thickness,pretreatments and number of the needed treatments were evaluated.

Results Results showed a mean visual acuity of 0.14 before the first intravitreal injection with bevacizumab. Six months after the first injection, patients VA increased by 0.18, i.e. they gain 0.04 lines of Snellen (P = 0,003). The mean number of treatments needed at this time was 3.3 (range: 1 to 5 injections). Central retinal thickness (CTR) assessed with OCT was 354±187 µm before the first treatment and decreased by 150±169 µm after 6 months (P < 0,001). 14% of the patients needed a treatment at the 6-months follow-up. One patient presented uveitis several days following intravitreal injection of bevacizumab.

Conclusion Six months follow-up of the intravitreal bevacizumab in the eyes with neovascular AMD showed stabilization of the visual acuity.

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Efficacy of pegaptanib sodium in occult or minimally classic

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Purpose Recent studies have highlighted the efficacy of Pegatanib sodium in sub-epithelial, occult, CNV seen in the early stages of the disease.

Methods This was a prospective study with a follow-up of 24 months. Patients underwent a complete examination including ETDRS visual acuity measurements, fundus photographs, FA and ICG-A and OCT, as well as treatment by intra-vitreous injection every 6 weeks.

Results 24 patients (16 women) presenting with exudative ARMD were chosen. The mean age was 76 years. 8 eyes had a sub-epithelial occult without classic neovascular lesion, or minimally classic. 8 eyes had a neovascular lesion of pre-epithelial type, predominantly classic. 4 eyes had a neovascular lesion of chorio-retinal anastomosis (CRA) associated with a PED. 4 lesions were fibro-vascular in type. At the end of the study, 100% of pure, occult type or « minimally classic » lesions presented with a loss of less than 15 letters of VA and in 25% of cases there was an improvement of 15 letters or more. Six out of eight treated patients did not lose any letter and five patients had an improvement of at least one letter. These patients had an initial VA of 20/100 or more. FA did not demonstrate any leakage in six cases, and OCT demonstrated an absence of intra-retinal edema in all cases. Out of the 16 patients who presented with a « predominantly classic » or with CRA or with fibro-vascular type lesion, only 3 had an improvement of at least one letter compared with 10 who had the loss of more than 15 letters of VA. Patients in younger age brackets had the better functional results.

Conclusion Treatment with Pegaptanib sodium is indicated preferentially for occult or minimally classic type lesions, which are recent and small.

▪ 627

No functional vision improvement after intravitreal ranibizumab injections (IVT) for retrofoveolarchoroidal neovascular age-related macular degeneration, why?

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Purpose To analyse the reasons of no improved functional vision in retrofoveolar choroidal neovascular AMD treated with ranibizumab IVT.

Methods 95 eyes of 80 patients,21 men,59 women,with retrofoveolar choroidal neovascular AMD treated by ranibizamab IVT.57 were inaugural cases ,38 previously treated by phototherapy and/or pegaptanib IVT.Patients received intravitreal ranibizumab injection,3 times,every 4 weeks in an inductive treatment,the next injections depending on the follow-up results.First and 2 months' interval follow-up exam included ETDRS visual acuity (VA),complete ophthalmic examination,fundus a utofluorescence(FAF),fluorescein (FA) and infracyanine (ICG) angiography,and time and/or spectral domain optical coherence tomography (OCT).VA and OCT were done before each IVT.FAF,OCT,FA and ICG analysis appreciate photoreceptor(PR),pigment epithelium(PE) layers,atrophic areas,neovascular net's leakage and flow.

Results Atrophic areas increased 20%,above all in predominant atrophic areas AMD, photoreceptor layer decreased in depth in 30%,pigment epithelium was 25% less dense in 42%,exudative reaction was 30% still present in 58%,neovascular net's flow and leakage was 45% left in 60%.Initial intense exudative neovascular AMD, most atrophic PE areas AMD,choroido-retinal anastomosis with neovascular AMD were predominantly concerned.Results are nevertheless better than PDT alone,than pegaptanib IVT on exudative reaction but obviously no,on PR and PE trophicity.AMD and/or ranibizumab IVT involvement is discussed.

Conclusion To consider all those notions is essential to choose the best therapeutic strategy, the most appropriate selective or no anti-VEGF, to go on in the understanding of AMD.

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To investigate the effectiveness of transpupillary thermotherapy (TTT) for neovascular age-related macular degeneration (ARMD)

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Purpose The effectiveness of TTT was investigated in terms of the change in Snellen visual acuity (VA) in patients having neovascular ARMD.

Methods A total of 84 patients with neovascular ARMD were recruited and the main outcome measures were Snellen VA both before and after TTT. Those with persistent oedema were retreated when assessed after 8 weeks with FFA or after subsequent visits.

Results No more than 1 Snellen line was lost in 44(68.8%) patients at 3 months, 41(71.9%) patients at 6 months, and 23 (53.5%) patients at 12 months. There was more than 2 Snellen lines lost in 20(31.2%) patients at 3 months, 16(28.1%) patients at 6 months and 20(46.5%) patients at 12 months. Only 24 patients required more than a single treatment.

Conclusion TTT treatment for neovascular ARMD shows the VA to be stable in the short-term as the majority had no more than a single Snellen line of VA loss. The limitations of this study are the mean follow-up of 6 months and no more than 50% having 12-month follow-up.

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Preliminary reading centre concordance in OCT grading in the UK IVAN Study

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Purpose To report on concordance of optical coherence tomography (OCT) grading in the Network of Ophthalmic Reading Centres UK (NetwORC UK). The present study looks at concordance of OCT gradings across the network for patients enrolled in the UK IVAN Study.

Methods A set of 5 patient scans (6 radial line scans and one 7mm offset scan using the Stratus OCT III (Zeiss, UK)) were graded by accredited graders at all three centres. Scans were exported as JPEG images with a corresponding PDF. Measurements for the Outer High Reflectivity Band (OHRB), Sub Retinal Fluid (SRF), Pigment Epithelial Detachment (PED), maximum height of largest cyst, maximum retinal thickenss (MRT) and foveal retinal thickness (FRT) were taken, if present.

Results In all cases an acceptable level of concordance was achieved. One case proved more problematic than the others and results were more varied. For OHRB, SRF, PED, cyst, MRT and FRT the measurements by individual graders were consistent in 4 out of 5 cases. One case showed wider-ranging measurements with the range for OHRB varying by 0.25mm (mean thickness 0.22mm).

Conclusion The present study shows an acceptable level of concordance for OCT grading across NetwORC UK. In difficult cases, the complexity of AMD grading explained the lack of total concordance when an abnormal thickening of the OHRB is present. The most problematic case had an area of moderate hyperreflectivity anterior to the OHRB which caused difficulty and highlighted a specific area for further training and a protocol amendment. The exercise was useful in highlighting both individual and overall training needs which are currently being addressed in each of the RCs. The concordance study is being extended to include a larger dataset.

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Treatment of myopic neovascularization with ranibizumab

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Purpose To determine the safety and efficacy of ranibizumab, as a treatment of choroidal neovascularization associated with pathological myopia

Methods A retrospective, non-comparative study of 14 patients treated with injections of intravitreal Ranibizumab. Four patients had been treated before with photodynamic therapy and had not improved visual acuity, whereas the patients treated with ranibizumab improved visual acuity. After a complete ophtalmologic examination, fluorescein angiography (FAG) and optical coherence tomography (OCT) intraocular injection was practised, retreatment was decided according to the subjective impression of the patient, visual acuity, presence or absence of metamorphopsia, biomicroscopy of posterior pole and characteristics of OCT. The patients were included after a minimal follow-up of 6 months.

Results We analysed 17 eyes of 14 patients. The average age of patients was 56 years. The spherical equivalent average was 13.6 diopters. The initial and final average visual acuity was 0,29 and 0,57 respectively. All neovascular membranes were classified as classical and localized sub or yuxtafoveal. Visual acuity improved or remained stable in all eyes. In all cases retinal thickness and macular edema observed in OCT decreased. There were no systemic or ocular complications,one patient responded with macular haemorrhage and decrease in visual acuity after four injections of ranibizumab.

Conclusion The short-term results of this small study suggest that Ranibizumab may be a good therapeutic option in the treatment of myopic neovascularisation. It improves visual acuity and anatomy, even in patients that don´t respond to photodynamic therapy.

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Evidence for association of HTRA1 promoter polymorphism in Polish patients with age-related macular degeneration

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Purpose Age-related macular degeneration (AMD) is a leading cause of visual impairment in developed countries, particularly in the Caucasian population above 65 years. It is a complex disorder with both genetic and environmental factors playing a role. Variants of HTRA serine peptidase 1 gene (HTRA1), particularly a single nucleotide polymorphism (SNP) in its 5' regulatory region –512G>A (rs11200638), is among those most strongly associated with AMD susceptibility but so far its frequency has not been analyzed in the Polish population. The purpose of this study was to investigate the association of rs11200638 with AMD in Polish patients.

Methods AMD patients (n=140) and age-matched controls (n=162) were enrolled in the study. Total genomic DNA was isolated from blood and rs11200638 was genotyped in both groups by restriction fragment length polymorphism (PCR-RFLP) analysis using MspI endonuclease and direct sequencing. PCR primers were designed based on the reference sequence of the gene (AF157623). Allele and genotype frequencies were compared between the groups by Chi square test and odds ratio (OR) with 95% confidence intervals (95% CI) were calculated to estimate risk.

Results Frequencies of the GG, GA and AA genotypes were 52%, 33% and 15% in control subjects and 28%, 15% and 57% in AMD patients, respectively. The AA genotype was significantly more prevalent in patients with AMD than among control subjects (OR= 7.7, 95%CI: 4.4-13.2, Chi square 53.6, P<10-6).

Conclusion In the present study, polymorphic variant of HTRA1 gene (rs11200638) showed strong association with AMD, verifying its significant role as a disease susceptibility gene also in Polish patients.

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Effects of photodynamic therapy on subfoveal blood flow in neovascular age-related macular degeneration patients

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Purpose To assess the short-term changes in choroidal blood flow after photodynamic therapy (PDT) in patients with neovascular age-related macular degeneration (AMD).

Methods Fourteen patients with exudative AMD were included after complete ophthalmologic examination, fluorescein and indocyanine green angiography and optical coherence tomography. Subfoveal choroidal blood flow was assessed using laser Doppler flowmetry (LDF) in both treated (n=14) and nontreated controlateral (n=8) eyes, 1 h and 1 week after PDT. Ocular perfusion pressure was calculated.

Results The detection sensitivity of the LDF measurements at 2-min intervals before PDT in treated eyes was 7.4% for volume, 6.3% for velocity, and 10.4% for choroidal blood flow. Initial mean visual acuity was 0.68±0.3 logMar. Macular thickness at baseline as measured by OCT3 was at median [interquartile range], 326.5 mm[188–367]. One hour and 7 days after PDT, a significant increase in velocity (15.8% and 24.4%, respectively) and a significant decrease in volume (11% and 17.9%, respectively) were noted in treated eyes. Choroidal blood flow and ocular perfusion pressure remained similar during follow-up. No significant change in flow parameters was reported in untreated eyes.

Conclusion The LDF technique provides feasible and reliable measurements of blood flow parameters before and after PDT in a selective population of patients with exudative AMD. The prognostic value of these early blood flow parameter changes also needs to be assessed.

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Neovascular AMD; Effect of intravitreal ranibizumab on the retinal arteries

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Purpose To study the effect of intravitreal injection of ranibizumab on the retinal arteries' diameter in patients with neovascular age-related macular degeneration

Methods Five patients with new-onset neovascular age-related macular degeneration were evaluated. All patients had three monthly administrated intravitreal injections of ranibizumab. The diameter of the retinal arteries was measured in vivo with a Retinal Vessel Analyzer (RVA). The measurements were performed before the first intravitreal injection and at days 7 and 30 after the first, the second and the third injection. Blood pressure was also monitored at the same time-points.

Results No significant change on the retinal arterial diameter was observed after the first injection and 7 days after the second injection when compared to baseline; mean decrease in retinal arterial diameter was 1.64% and 3.5% respectively. A significant vasoconstriction of the retinal arteries was observed thereafter. Thirty days following the second and third injection, there was a mean decrease of 12.4% and 17.8% respectively on the retinal arterial diameter compared to baseline values ($p < 0.05$). There was no significant change in mean arterial systolic or diastolic blood pressure during the period of follow-up.

Conclusion These results suggest that intravitreal ranibizumab induces retinal vasoconstriction in patients with neovascular age-related macular degeneration following the second injection. Further studies with larger sample sizes are needed to confirm these results as well as its potential adverse effects in the retinal circulation in patients with age-related macular degeneration and with other retinal vascular diseases.

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Choroidal neovascularization management in uveitic patients – our experience

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Purpose Choroidal neovascularization (CNV) is well documented complication of posteroir uveitis which can lead to severe visual loss. There are varying management options for this condition. We present our experience in managing CNV in uveitic patients.

Methods Retrospective study of uveitic patients with CNV treated in our hospital during last eight years. Data collected were: gender and age of patient, type of uveitis, CNV localization, visual acuity at the time of diagnosis, visual acuity at the last follow-up visit, management of condition.

Results 38 patients with posterior uveitis developed CNV in one or both eyes (12 males, 26 females). Average age at the time of diagnosis was 41,7 years. Management of CNV depended on clinical presentation. Treatment options that were used: laser photocoagulation, photodynamic therapy, corticosteroids, vitreoretinal procedure and anti-VEGF therapy. Different treatment options were combined in some patients. Some patients were only observed. Follow-up period ranged from one to eight years. Visual acuity improved in 19 eyes and remained stable in 9 eyes.

Conclusion The results of varying management options for CNV in uveitic patients are limited. Individual approach in the management decision is necessary because of various clinical presentations. Additional clinical trials are needed to define an optimal approach.

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To investigate the association between visual acuity and visual function questionnaire in patients having ranibizumab treatment

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Purpose The investigation of the responsiveness of the National Eye Institute (NEI) 25-item Visual Function Questionnaire (VFQ-25) to changes in visual acuity (VA) in patients having Ranibizumab treatment for neovascular age-related macular degeneration (ARMD).

Methods A total of 60 consecutive cases awaiting intravitreal ranibizumab injection for neovascular ARMD were recruited. The main outcome measures were interviewer administered NEI VFQ-25 composite score and Snellen VA represented as a logMAR equivalent, both before treatment and after their third Ranibizumab injection. VFQ-25 composite scores and VA were compared between pre- and post-treatment and also analysed for correlation between VA and NEI VFQ-25.

Results There was no statistically significant difference between pre- and post-treament VA, with a mean difference of 0.04 (95% CI 0.06, 0.15). There was an improvement in the VFQ-25 composite score with treatment of 7.5 that was statistically significant (95% CI 3.83, 11.67). The association between pre-treatment VA and VFQ-25 composite score was not statistically significant(Pearson correlation=0.14, p=0.37). The association between post treatment VA and composite VFQ-25 score shows a weak but statistically significant correlation (Pearson correlation=0.36, p=0.013). The association between the change in VA and the change in VFQ-25 composite score was not statistically significant (Pearson correlation=0.034, p=0.82).

Conclusion The VFQ-25 composite score does not show a close correlation with logMAR VA either pre- or post-Ranibizumab injection. However, these composite scores show a significant improvement with Ranibizumab injection.

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Clinical features of serous pigment epithelial detachment using optical coherence tomography

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Purpose To analyse clinical features of serous pigment epithelial detachment (PED) using optical coherence tomography (OCT).

Methods Retrospective analysis was performed for 38 eyes of 34 patients with serous PED one-fifth disc diameter or greater in size. Each patient was studied clinical examination with color photography, FAG and OCT. Cross-sectional retinal images(the height, location and sectional area)through the center of the fovea were obtained from all eyes by OCT. They were statistically analyzed and correlated with best corrected visual acuity. To avoid cases associated with AMD, upper age limit was not 55 year. Patients with evidence of any other retinal or choroidal disease, including extensive drusen, were also eliminated.

Results At initial examination, visual acuity was 20/25 or better in 23 eye, the Amsler grid was positive in 18 eyes, there were no drusen in 34 eyes and only minimal drusen in 4 eyes. The final visual acuity was 20/25 or better in 24 eyes, In 22 eyes of them, visual acuity was 20/50 or better. There was statistically correlation between final visual acuity and amount of subretinal fluid. The size, location of PED was not important factors affection visual acuity.Idiopathic CNV and subretinal hemorrhage can occur with this disease. This patient was treated with photocoagulation treatment.

Conclusion The prognosis in Serous PED of eyes is excellent, because development of vascular complication was in only one case. Also OCT is potentially useful as a new, noninvasive diagnostic technique for quantitative examination by objectively monitoring the degree of serous PED.

■ 637

Effect of paclitaxel labeled cationic liposomes (EndoTAG1) and succinyl-paclitaxel labeled cationic liposomes (EndoTAG SPA) in laser-induced choroidal neovascularisation (L-CNV) of mice

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Purpose Cationic liposomes bind specifically to activated endothelial cells. In this study we used paclitaxel (Taxol) and succinyl-paclitaxel labeled cationic liposomes to reduce CNV in laser-induced choroidal neovascularization (L-CNV) of C57BL/6J mice.

Methods Mice underwent ARGON-Laser coagulations on day 0. Injection of different liposome formulations tagged with paclitaxel or succinyl-paclitaxel via tail vein was performed on day 1,3,5,7 and 9. As control paclitaxel, succinyl-paclitaxel, cationic liposomes or trehalosebuffer alone were injected at the same time points. Animals were perfused with fluorescein dextrane and enucleated at day10. Choroido-sclera flat mounts were prepared for quantification of the CNV. Quantification of CNV was carried out by measuring the area of fluorescein dextrane positive vessels.

Results There is a significant reduction of CNV area by EndoTAG1 and EndoTAG SPA compared to trehalose control group. The reduction of CNV area caused by paclitaxel, succinyl-paclitaxel and cationic liposomes is not significantly different either to EndoTAG1, EndoTAG SPA or trehalose buffer group. However, there was a trend of EndoTAG1 and EndoTAG SPA being superior either to paclitaxel, succinyl-paclitaxel or cationic liposome alone.

Conclusion Cationic liposomes can be used to carry paclitaxel or succinyl-paclitaxel to activated endothelial cells and reduce the groth of CNV membranes. In general, cationic liposomes could be used as a universal vector to transport different kinds of drugs specifically to activated endothelial cells.

■ 638

Subcutaneous nadroparin calcium in the treatment of retinal vein occlusion

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Purpose To date, no systemic intervention has been demonstrated to favorably affect the natural history of retinal vein occlusion (RVO). The purpose of this study was to evaluate the efficacy of nadroparin calcium in the treatment of RVO.

Methods 13 patients with acute RVO (i.d. within a week of onset) were treated with subcutaneous injections of nadroparin calcium for 2 months. The same dose used for the treatment of deep venous thrombosis (200UI/kg/die) was given. Best corrected visual acuity (BCVA) in the affected eye was measured at baseline and after 3 months. In addition, macular thickness was measured by Stratus OCT (Carl Zeiss Meditec, USA) at baseline and after 3 months.

Results Mean visual acuity was 0.39±0.33 at baseline and 0.70±0.32 after 3 months; differences were statistically significant (P=0.024). Macular thickness was measured in 8 patients; mean thickness was 510±239 µm at baseline and 331±190 µm after 3 months; differences were not statistically significant (P=0.12). After 3 months, fluorescein angiography disclosed no signs of retinal ischemia in all cases.

Conclusion This preliminary study suggest that subcutaneous nadroparin calcium may be effective in the treatment of RVO. Larger long-term studies are warranted to confirm this results.

■ 639

Case of ischemic retinopathy induced by chemotherapy with paclitaxel and carboplatin

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Purpose To report a case of ischemic retinopathy induced by chemotherapy for non-small cell lung cancer (NSCLC).

Methods Case report. A 59-year-old man was diagnosed with NSCLC, and began treatment with both paclitaxel and carboplatin on June 1, 2007. Thereafter, he consulted our department for a fundus examination due to diabetes mellitus.

Results Corrected visual acuity was 3/20 in both eyes. In spite of good control of blood glucose, shown by an HbA1c level of 5.8%, large numbers of soft exudates and retinal hemorrhages were observed in both eyes. Although no microaneurysm was found, non-perfusion areas were revealed in the nasal retina by fluorescein angiography. We performed laser photocoagulation for the non-perfusion areas in the retina of the left eye, however, retinopathy gradually progressed. We suspected a side effect from the chemotherapy and consulted with the attending physician. After changing the anticancer drugs, the soft exudates and retinal hemorrhages decreased and promptly disappeared. In January 2008, a vitreous hemorrhage was found in the left eye. Fluorescein angiography showed no neovascularization in the retinas of both eyes, however, the non-perfusion areas were increased in the left. Following additional laser photocoagulation, the vitreous hemorrhage disappeared.

Conclusion It is important to remember that anticancer drugs can induce severe retinopathy. Patients should be followed even after retinopathy is improved for possible recurrence.

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Treatment of patients with central retinal vein occlusion by anticoagulation

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Purpose For patients with central retinal vein occlusion (CRVO) no effective causal therapy has been described to date. The aim of our study was to assess the safety and efficacy of anticoagulation with warfarin in patients with CRVO.

Methods Retrospective interventional study evaluated 93 patients with CRVO treated with warfarin for one year between 2002 and 2007. Patients were divided into two subgroups according to the initial best corrected visual acuity (BCVA) measured by Early Treatment Diabetic Retinopathy Study (ETDRS) charts. Group A included patients with BCVA 20/200 or worse (logMAR ≥ 1,0), group B with 20/40 or better (logMAR ≤ 0,3). Main outcome was BCVA, the frequency of unfavourable final BCVA (20/200 or worse) was evaluated and the results were compared with published results of the natural course of CRVO (Quinlann et al, Am J Ophthalmol. 1990).

Results The part of patients with unfavourable final BCVA (20/200 and worse) was significantly smaller in patients treated with warfarin compared to untreated patients (21,6 %; versus 49,5 %). The significant effect of anticoagulation to final BCVA was found in patients with non-ischemic CRVO and initial VA 20/200 or worse (37,5 % versus 88,2 %). In patients with initial VA 20/40 and better as well as in patients with ischemic CRVO no significant effect of anticoagulation was found. Relevant is the reduction of neovascular glaucoma in patients with ischemic CRVO. No adverse events (severe bleeding)were observed.

Conclusion Anticoagulation seems to be an effective method affecting the causality of CRVO and reduces the frequency of unfavourable final BCVA in patients with initial BCVA 20/200 or worse. Further randomized and controlled studies are required to confirm the observed effect.

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Fast accurate measurement of macular pigment with a novel technique for setting flicker thresholds

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Purpose To evaluate a new clinical method for estimating Macular Pigment Optical Density (MPOD) in large populations.

Methods The principle of heterochromatic flicker photometry is used. For a series of green-blue ratios, the modulation is slowly reduced from 60Hz (at 6 Hz/sec). Observers press a button when they detect flicker of a green-blue (530-465nm) temporally modulated target. Repeatability was tested on 11 subjects. Measurements (n=5) were repeated after an interval of at least three days. Healthy subjects (n=22, 22-64 years) were tested with the new method and compared with an established spectral fundus reflectance technique. MPOD spatial profiles (n = 7) were obtained with the new method. MPOD data were collected from 5581 subjects (2435 females and 3146 males) measured in 48 optometric practices in the US.

Results The new method has good repeatability (r =0.96, ~12%). The data compare well with retinal reflectometry (r =0.85, p<0.001). The spatial profiles are described by a decaying exponential function (r = 0.99), consistent with previous reports. The mean MPOD of the large data set was 0.33 ± 0.187 which is similar to previous studies.

Conclusion The task is relatively easy for naïve and elderly observers. The instrument can be readily operated by non-professional staff under clinical conditions. A further advantage is that there is a real-time graphical output indicating satisfactory progress. The instrument provides fast, reliable, accurate MPOD data. It is ideal for large-scale epidemiological study of the macular pigment and also for every-day use in ophthalmic clinics and offices.

Commercial interest

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The relationship between macular pigment optical density and ApoE genotype

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Purpose To investigate the relationship between macular pigment optical density (MPOD) and ApoE genotype in healthy subjects with and without a family history of age-related maculopathy (ARM).

Methods We recruited 336 subjects for this study. Demographic and health details were recorded. MPOD was measured by customised heterochromatic flicker photometry using the Macular Densitometer. Genotype data was downloaded from HapMap for the CEU population. Genotyping was performed using SNaPshot assays on an ABI 3100 genetic analyser.

Results 4 subjects did not meet our analysis criteria and were excluded. Genotype data were available on 94.3% of our sample. 62.6% of subjects had the ε3ε3 genotype (non-risk); 25.2% had at least 1 ε4 (protective) allele; 12.7% had at least 1 ε2 (risk) allele. Only 1 subject had the ε2ε2 genotype; this subject had a family history of ARM. Of the 8 subjects with the ε4ε4 genotype, only 2 had a family history of ARM. There was no significant difference in the remaining genotype distribution between subjects with and without a family history of ARM. We divided our sample into 3 genotype groups: Group 1: ε2ε2 or ε2ε3 (n=38); Group 2: ε3ε3 (n=194); Group 3: ε2ε4, ε3ε4 or ε4ε4 (n=78). There was a statistically significant difference in peak MPOD between these groups: Group 3 had the highest mean MPOD; Group 1 had the lowest (p=0.002). This significant association remained after controlling for age, sex, BMI, family history of ARM, smoking, alcohol intake, dietary and serum lutein and zeaxanthin.

Conclusion The presence of the Apo ε4 allele appears to be associated with higher MPOD values in healthy subjects. The importance of this finding rests on the fact that the Apo ε4 allele is protective against ARM.

Commercial interest

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Changes in macular pigment optical density and serum concentrations of lutein and zeaxanthin, in response to weight loss

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Purpose Studies investigating the relationship between macular pigment optical density (MPOD) and percentage body fat have consistently shown an inverse relationship between these variables. This study was designed to investigate changes in MPOD, and serum concentrations of lutein (L) and zeaxanthin (Z), in response to a weight loss.

Methods We plan to recruit 100 subjects into this 12 month, multi-visit, randomized-controlled study. Adiposity was assessed by dual energy x-ray absorbtiometry (DEXA), MPOD was measured using customised heterochromatic flicker photometry (cHFP). Dietary and exercise intervention was provided to subjects enrolled into the intervention group of this study. Inclusion criteria were: age 18-60 years; body mass index > 28; absence of any ocular pathology; lack of a family history of age-related maculopathy.

Results To date, 93 subjects have been recruited. 22% of existing intervention subjects have lost ≥ 7 kgs in weight. A further 27% have lost up to 3.5 kgs in weight, and are maintaining this trend. Of note, preliminary statistical analysis of 11 subjects based on their 6 month data, indicate a positive, but statistically insignificant, relationship between MPOD and percentage body fat lost.

Conclusion Preliminary results indicate a positive relationship between MPOD and weight loss. We await completion of this study and analysis of final results to allow us to comment further on this interesting relationship.

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Macular pigment and its contribution to spatial vision

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Purpose The optical properties and distribution of macular pigment (MP) are such that it may theoretically contribute to visual performance by attenuating the effects of chromatic aberration and light scatter. We assess whether MP optical density (MPOD) influences spatial vision by means of selective short wavelength light absorption prior to photoreceptor light capture.

Methods 51 young (mean=29+/-6 years) healthy subjects were recruited. The spatial profile of MPOD was assessed by customised heterochromatic flicker photometry. Visual performance was assessed by psychophysical tests including recognition acuity (VA), mesopic and photopic contrast sensitivity. Each subject completed a visual performance questionnaire, generating a performance index of the subjects' perception of their functional vision.

Results Mean peak MPOD was 0.39+/-0.14. Pearson's correlation coefficient showed a statistically significant positive relationship between VA and MPOD at 0.25deg and 0.5deg retinal eccentricity (r=0.345 p=0.013; r=0.317 p=0.024 respectively); the questionnaire derived VA index (VAI) also correlated strongly with MPOD at 0.25deg (r=0.281 p=0.046). Photopic and mesopic contrast thresholds exhibited an inverse and statistically significant correlation with central MPOD (mesopic contrast threshold @ 5.7 cycles/deg and MPOD at 0.25deg: r=-0.394 p=0.004; photopic contrast threshold @ 5.7 cycles/deg and MPOD at 0.25deg: r=-0.313 p=0.027).

Conclusion Our results support the hypothesis that retinal image quality is optimised, and visual performance across the full contrast range is more refined, with higher levels of MP. The findings are limited by the observational nature of this study. However, further interventional studies are warranted.

Commercial interest

▪ 645
Quantifying the abnormal macular pigment distribution in macular telangiectasia type 2

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Purpose Recently, increased central confocal blue reflectance was reported to be a characteristic finding in patients with Macular Telangiectasia type 2. This was thought to be due to an altered distribution of macular pigment, namely depleted in the centre of the macula with a remaining peripheral ring at 6 degrees eccentricity. The goal of this study was to objectify the substance of which this ring is constituted unambiguously.

Methods We used the objective technique of fundus reflectometry, that enables to quantify absolute values of macular pigment optical density (MPOD), without the need of a reference point.

Results Measurements showed very low MPOD values at 2 and 4 degrees foveal eccentricity in all subjects. In the majority of eyes measured, MPOD values were clearly augmented at 6 degrees eccentricity with respect to measurements at other ecentricities.

Conclusion Macular pigment was depleted at 2 and 4 degrees foveal eccentricity. The aforementioned ring at 6 degrees foveal eccentricity proved indeed to be macular pigment. Further, the data showed a significantly more pronounced depletion at temporal compared to nasal eccentricity.

▪ 646
Relationship between macular pigment and straylight on the retina

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Purpose Macular pigment (MP) filters short-wave light, counteracting the deleterious effects on foveolar resolution of scattering in the ocular media. Large individual differences in MP might also be expected to lead to variations in disability glare and reduce contrast in the retinal image. This study was performed to relate variations in foveal MP density levels to light scattering in the eye

Methods Measurements were obtained from 138 healthy subjects aged 52 ± 22.3. The optical density of the MP was estimated at the fovea using the Metropsis Test (Cambridge Research System), which is based on the apparent motion photometry method and employs a CRT monitor for stimulus presentation. Scattered light on the retina was measured using the C-Quant straylight meter (Oculus AG, Germany) according to the psychophysical compensation comparison method. Values are expressed as logs (of the straylight parameter) for which higher values indicate more scattered light and more sensitivity to glare.

Results Mean foveal MP optical density was 0.28 density units (SD 0.16; range 0.0 to 0.74). Mean straylight value was 1.10 log units (SD 0.24; range 0.73 to 1.68). With the regression analysis of linear model, we found a significant correlation (Pearson's correlation = -0.25; p-value < 0.01) between foveal MP and light scattering in the eye at the 99% confidence level. Straylight was significantly higher for subjects with lower foveal MP level.

Conclusion Inter-subject differences in foveal MP density levels showed correlation with light scattering in healthy non-cataractous eyes.

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Macular pigment and its correlation with colour vision and SWAP perimetry

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Purpose To investigate the effects of macular pigment optical density (MPOD) oncolour vision and colour modulated visual fields using short-wavelengthautomated perimetry (SWAP).

Methods Macular pigment (MP) spatial profile was measured using customisedheterochromatic flicker photometry (cHFP) on 51 normal subjects. Colourvision was assessed using the Oculus anomaloscope [Moreland equation(AME)] and Farnsworth-Munsell 100-Hue (FM) with optimum confusion axes. A custom designed program on the Humphrey automated perimeter, was used to determine SWAP thresholds at the fovea, and at each degree of retinal eccentricity for the central five degrees. A 440nm Goldmann V stimulus presented on a 100cd/m2 bleaching background was used to isolate the short wave sensitive pathway.

Results While inter-relationships were evident between AME, FM and SWAP, only one colour vision measure (on FM) correlated with MPOD (r=.302,p= 0.03). At similar degrees of eccentricity, SWAP was inversely andstatistically significantly correlated with MPOD (e.g. 1-degree retinaleccentricity: r = -0.198, p = 0.047; 3 degrees retinal eccentricity r =-0.290, p = 0.03).

Conclusion Colour vision, even using sensitive tests targeting blue-yellow andblue-green confusion is surprisingly independent of MPOD, while SWAP sensitivity is reduced with increased MPOD. We hypothesize that this is due to long-term adaptation of the retinal blue-yellow pathway to prevailing MPOD in normal subjects, this adaptation being upset by short-term chromatic adaptation in SWAP.

Commercial interest

▪ 648
Neuronal plasticity and macular edema

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Purpose The aim of this study is to analyze the retinal structure of the macula of patients having recovered from ME due to perfused retinal vein occlusion(RVO) and compare it to histology of experimental RVO in rats.

Methods In 26 patients with perfused RVO having recovered from ME, averaged high resolution OCT cross scans were acquired. The aspect of retinal layering was analyzed and compared to that of fellow eyes. In parallel, the retinal structure of rats subjected to transient RVO was analyzed by immunohistochemistry and electron microscopy.

Results All eyes had a normal macular profile. In 7 out of 14 eyes with normal visual function, disorganization of the layers presumably corresponding to the outer plexiform layer(OPL) was detected associated with variable thinning of the outer and inner nuclear layer (ONL, INL). Loss of central vision occurred was present only when disruption of the OS reflectance was apparent. In rats, a similar profile of OPL dizorganisation and ONL and INL thinning was observed. Electron microscopy objectivated synaptic migration into the ONL.

Conclusion Neuroglial plasticity is challenged during macular edema. Remodeling of retinal layers may be detected by OCT even when visual acuity is normal. Post-RVO ME neuroglial remodeling initially affects the OPL. Loss of cone OS is a crucial milestone during the course of ME, being the first event leading to irreversible visual loss. The fact that OPL damage precede cone OS loss may suggest that deafferentation participates to cone OS loss.

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Photodynamic therapy without verteporfin for central serous chorioretinopathy

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Purpose To report the use of photodynamic therapy without verteporfin as treatment for patients with focal retinal pigment epithelial leaks secondary to central serous chorioretinopathy (CSC).

Methods Four symptomatic patients with CSC without clinical improvement in a period of time up to three months were included. Photodynamic therapy without verteporfin was applied without any other treatment.

Results Neurosensory detachment and fluorescein leakage resolved in all patients within two months. Visual acuity improved in all of them and none lost vision or suffered any treatment-related complications.

Conclusion The treatment of CSC with photodynamic therapy without verteporfin may result in resolution of persistent neurosensory detathment and fluorescein leakage. Although this case series is limited in follow-up and number of patients, the encouraging results, lack of complications and cheap procedure suggest that further investigation is warranted.

Commercial interest

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Photodynamic therapy with verteporfin combined with intravitreal injection of bevacizumab for central serous chorioretinopathy: a case series

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Purpose To discuss the effect and outcome of a combined photodynamic therapy and intravitreal injection of Bevacizumab in treating central serous chorioretinopathy (CSC).

Methods 4 Patients with chronic central serous chorioretinopathy (CSC) were treated with intravitreal injection of 1,25 mg Bevacizumab administered within 24 hours after standard PDT laser treatment (83 sec., 689nm) with Verteporfin. (5,7ml Verteporfin over 10 min. intravenously). Before, 3, and 6 month after treatment visual acuity, OCT examinations (retinal thickness) and fluorescein angiography were performed.

Results Mean visual acuity increased from baseline 20/50, to 20/25 after 3 month. Subretinal fluid almost resolved completely after treatment. OCT- and FLA- findings are presented in our patients. OCT 1, 3 and 6 month after combination therapy showed a reduced retinal thickness compared to baseline. 1 patient had full recovered vision after 6 month.

Conclusion Photodynamic therapy combined with injection of intravitreal Bevacizumab was very effective in our patients. Current literature depicts medical treatment, focal laser, SRT and PDT as treatment options for CSC. To our knowledge this is the first report of a combination therapy in CSC. The treatment was well tolerated and we did not see any complications. The patients presented with ongoing recovered vision during follow up. Further experience is necessary to evaluate the treatment option of PDT and Avastin® combination therapy especially in chronic central serous chorioretinopathy (CSC).

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Dynamic phototherapy as a treatment of central serous chorioretinopathy

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Purpose To analyse the angiographic and tomographic results both the visual acuity of a group of patients presenting a serous central chorioretinopathy (which is acute or chronic) treated by dynamic phototherapy. This treatment has been guided by the data of the ICG angiography.

Methods This is a retrospective-prospective nonrandomized study bearing on 31 eyes of 27 patients including 8 acute forms and 23 chronic forms. One or more spots were managed according to the standard protocol of the DMLA and delivered on the zones of choroidal hyperpermeability highlighted by the ICG angiography. The criteria of success are founded on functional signs, visual acuity, sensitivity to contrasts, and persistence of a point of leakage in angiofluorographic control at 3 months and on study of serous retinal detachment in OCT.

Results An increase of the visual acuity (3,58 +/- 3,22 lines ($p<0,0001$)) has been observed whatever the form of treated CSCR. 90,32% patients presented a reapplication of serous retinal detachment within a period of 7,28 weeks +/- 3,93. No tear of the retinal pigmentary epithelium or choroidal neovascularization were observed. 12,9% patients presented recurrence within a period of 28 weeks +/- 16,24, only chronic CSCR were concerned. At 8 +/- 4,2 months, visual acuity of patients (except patients with recurrence) remained unchanged (0,356 +/-0,4 LogMAR or 20/50-20/40).

Conclusion Although the number of patients included in this study is limited, dynamic phototherapy seems to be currently an effective and sure treatment of CRSC. A randomized study on a great series is desirable to confirm these results.

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EphB4 is expressed in preretinal neovascularization in a mouse model of oxygen-induced retinopathy

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Purpose EphrinB2 is predominantly expressed in arteries, while its ligand EphB4 is predominantly expressed in veins. Activation of ephrinB2 and EphB4 by receptor dimers have been shown to enhance neovascularization, whereas inhibition of EphB4 reduced neovascularization both in vitro and in vivo in a mouse model of oxygen-induced retinopathy (OIR). These data suggest a role of the ephrinB2-EphB4 system in retinal neovascularization. We looked for expression of these membrane-bound factors in a mouse model of OIR.

Methods Heterogenic EphB4lacZ+/- mice were examined in a well-established mouse model of oxygen-induced retinopathy. Mice were kept in 75% oxygen for postnatal days P7-P12. Returned to room air, they underwent a relative hypoxia and developed a proliferative retinopathy within the next 5-7 days. Eyes were enucleated on P17-P19 during the peak of vascular proliferation, stained for LacZ, and embedded in paraffin. Sections were investigated for LacZ staining.

Results Sections show a strong expression of EphB4 in preretinal neovascularization both in small and larger vessels. EphB4 is also mildly expressed in vessels in the inner plexiform layer and in the ganglion cell layer.

Conclusion The expression pattern suggests a role of EphB4 in preretinal neovascularization in a mouse model of OIR. Further studies of the intracellular localisation of EphB4 are needed to add to understanding the role of the ephrin system in OIR.

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Indocyanine green-induced toxicity to retinal neurones in cultures is enhanced by light

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Purpose To deduce whether light influences the effect of indocyanine green (ICG) in primary rat retinal cultures.

Methods 5-day-old primary rat retinal cultures were exposed to concentrations of ICG (0.01%, 0.05% and 0.1%) that are used clinically for 2 minutes. Some cultures were then additionally exposed to 3000lux of white light for 10 min. Twenty four hours later cell viability was assessed with the MTT assay. In addition, cultures were stained for the presence of GABA neurones, reactive oxygen species (ROS) using 2,7'-dihydroethidium (DHE) and DNA breakdown (TUNEL procedure) to indicate apoptosis.

Results 0.1% ICG was found to significantly reduce cell viability and the number of GABA-immunoreactive neurones in primary rat retinal cultures. Lower concentrations of ICG also had an effect on these parameters suggesting dose-dependence. 0.1% ICG also significantly increased the appearance of ROS and numbers of TUNEL positive cells in cultures. The effects caused by ICG were potentiated by light.

Conclusion Evidence is provided to suggest that the toxic effect of ICG to retinal neurones in culture is exacerbated by light. The relevance of these studies is self evident in relation to vitreoretinal surgery where use of a normally safe concentration of ICG may be rendered toxic because of the used light.

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Morphological features of abnormal fundus autofluorescence (FAF) using Spectral Domain OCT

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Purpose To evaluate morphological features of hyper and hypo autofluorescence areas using Spectral Domain OCT technology.

Methods 16 patients (10 male , 6 females) with first diagnosis of age related maculopathy and dry AMD have been enrolled.Visual acuity test (Snellen chart) and Amsler' grid test have been performed. Patients underwent to fundus autofluorescence (FAF) study (cSLO HRA 2 Laser source 488 nm , Barrier filter 500 nm, Heidelberg , Germany) and Specral Domain OCT evaluation (SD OCT OTI , Canada). The FAF abnormalities have been compared to OCT images using gray scale and colour inversion system. Abnormalities in outer limiting membrane (OLM) profile , photoreceptor inner-outer segment junction and RPE layer have been recorded for each patient.

Results OCT did not show any morphological changes in areas of hyperautofluorescence . In cases of hypoautofluorescence , main OCT changes were : abnormal profile of the OLM with continuous gaps , disruption of the IS/OS junction with focal breaks and granular destructuration of the RPE layer .No alterations inside neurosensory retina or modifications of retinal thickness and volume have been recorded.

Conclusion Abnormal FAF is mainly derived from RPE lipofuscin . Excessive accumulation of lipofuscin has been associated with degeneration of RPE cells and photoreceptors. SD-OCT is able to show retinal morphological changes associated to abnormal FAF improving our knowledge in pathophisiologic pathways.

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Maculopathy associated with angioid streaks

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Purpose To present choroidal neovascularization and macular atrophy without neovascularization associated with angioid streaks by means of two case reports.

Methods Two middle aged man (42 an 46 years old) with angioid streaks were evaluated. The first pacient showed choroidal neovascularization and subretinal fibrosis, which was treated with intravitreal ranibizumab. The second case had macular atrophy in one eye in association with subretinal fibrosis in the contralateral eye.

Results A single dose of intravitreal ranibizumab improved the structural features of exudative maculopathy. Functional improvement (visual acuity) was less important because of subretinal fibrosis. Atrophic maculopathy was not susceptible to treatment.

Conclusion Angioid streaks diagnosis is usually late. It must be suspect in middle aged pacients with choroidal neovascularization and their visual prognosis depends on early treatment. Macular atrophy associated to angioid streaks is very uncommon.

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Retinopathy in intravenous coaxil drug dependents

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Purpose To study the clinical manifestation, course and the outcome, as well as treatment variants and it's efficacy in retinopathy followed by intravenous coaxil (tianeptinum) injection.

Methods 23 heroine dependent males (age range 19-36) were examined. 16 patients had lowering of the visual acuity (VA) from 5 to 20% within 3-8 days before they applied to our clinic. In 7 patients a significant lowering of VA was attended by retinal neoangiogenesis; 4 of them appeared with hemophthalm and iris rubeosis. Increased intraocular pressure in 3 patients was a result of neovascular glaucoma. All patients had concomitant hepatitis B or C virus infection of different activity, one with neovascular glaucoma was HIV-infected.

Results The mechanism of origin, clinical course and outcome of retinopathy induced by intravenous coaxil injection is similar to those described in "talc retinopathy", which occurs after intravenous injection of solution made of crushed and dissolved in water talc-containing tablets. The difference is in more significant retinal damage. The disease affects both eyes. In the acute stage of retinopathy it may manifest in vascular emboli of retina and choroid, confirmed by FAG. Ophthalmoscopic examination reveals large areas of ischemia and accumulation of crystals mostly in the central retina, hemorrhages are a result of arterial and venous thrombosis followed by neovascularization of the optic nerve head and the retina, as well as hemophthalm and neovascular glaucoma. Two cases of retinopathy progressed untill blindness.

Conclusion Development of the retinopathy depends on the cumulative dose in the amount of 4,500 tablets. Medical and laser treatment is unsuccessful. Thus, prognosis of retinopathy in intravenous coaxil users is unfavorable.

▪ 657
Retinal thickness and age - optical coherence tomography study

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Purpose To test the hypothesis is retinal thickness of the temporal disc margine - just independent of age.

Methods 60 eyes in 60 healthy volunteers were included in this study. Three OCT (STRATUS - Zeiss) scans were performed, aligned vertically and placed at the temporal edge of the optic disc. Retinal Thickness (RT) and retinal nerve fiber layer thickness (RNFLT) were calculated, with variance and correlated with age.

Results Both of paramethers tested - RT and RNFLT decrease with age. The mean nerve fibre layer thickness was 112 (SD=21) - in correlation with increasing age, and the mean retinal thickness (MRT) was 237 (SD=24) - not in correlation with age increase . The mean coefficients of variation were 8,3% for RNFLT and 3,9%for total RT.

Conclusion OCT testing is of high reproducibility for total retinal thickness and in nerve fibre layer thickness messurements. Both of paramethers decrease with age, but decrease of RNLFT, only, significantly correlates with increasing age. This put optic disc parameters (when a reference plane) in three dimensional tomography, for possible reassesment - adjusting to age.

▪ 658
Visual loss following scoliosis surgery. A case report

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Purpose We report a case of a 15-year-old boy who experienced visual loss in the left eye during the immediate perioperative period after scoliosis surgery. We observed a cherry-red-spot in the macula and a slightly swollen optic disc a day after spinal surgery and a disc pallor, hypopigmentation of the peripapillary choroid and constriction of the peripapillary vessels a week later. Risk factors of visual loss during non-ocular surgery are assumed to be a long lasting surgery, hypotension, anaemia, excessive hydratation, systemic hypertension, direct external pressure of the eye. In young, otherwise healthy patients, the pathogenesis of this complication is likely to be the same, but further possible explanations of the pathogenesis should be considered.

Methods We conducted a complete vascular workout included perimetry, colour Doppler imaging, nail-fold-capillary microscopy, analysis of circulating endothelin-1.

Results The results are very indicative for primary vascular dysregulation responding to various stimuli (cold, psychological stress,adrenalin) and showed pathological peripheral vasoconstriction. In this case, we postulate hypersympathicotonus occurred during scoliosis surgery and provoked massive vasospasm of the ophthalmic artery, followed by occlusion of the central retinal artery and short posterior ciliary arteries.

Conclusion Heavy blood loss or sympathomimetic medication are known risk factors for complications in the eye during spinal surgery. Mechanic irritation of the perispinal region could induce hypersympathicotonus and provoke peripheral vasospasm. Analysis of vascular dysregulation factors in young healthy patients holds the potential to increase our knowledge of the pathomechanism for visual loss after uncomplicated non-ocular surgery.

▪ 659
Malignancies after Tacrolimus therapy in the management of ocular inflammatory disease

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Purpose The appearance of "de novo" tumors in adults receiving immunosuppressive treatment with tacrolimus in ocular inflammatory disorders has not been elucidated.

Methods All 180 patients who received Tacrolimus as a steroid sparing agent for the management of high risk PKP, uveitis, scleritis or corneal stem cell allograft were studied. Tacrolimus treatment schedule, monitoring and duration of treatment was noted.

Results During the last 8 years a total of 11 patients who had received Tacrolimus for their immunosuppresion developed a malignancy. Three patients developed cancer of prostate, bladder (1), bronchogenic carcinoma – squammous cell carcinoma (SCC) (1), cancer skin - (SCC) (1), breast cancer(2), recurrence of NHL (1) and recurrence of breast cancer (1) and large intestinal tumour (1). The primary diagnosis for the commencement of Tacrolimus included high-risk PKP (8), Scleritis (1), Panuveitis (1) and Wegeners Granulomatosis (1). The rate of increase of bladder cancer was 149.26 followed by NHL 82.33 and recurrent breast carcinoma 30.7. The rest of tumours had a rate of increase in the range of 10 - 20 fold. The average dose of Tacrolimus was 1954.37 mg SD +/- 2197 mg. Female/male ratio was 2:1. The mean age of patients was 73 years SD +/- 10.4 years. The mean follow-up time of tumour patients on treatment was 45 months with SD +/- 26 months and the mean duration of follow-up after diagnosis was 23 SD +/- 19 months. None of the eleven patients had any additional predisposing factors or were on any other carcinogenic agents which could affect their mortality by the cancer identified.

Conclusion Long term immunosuppressive management of patients requires regular oncologic screening.

▪ 660
Non-surgical treatments to periocular basal cell carcinomas. Imiquimod versus photodynamic therapy

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Purpose To study the efficacy of non-surgical treatment in patients with nodular basal cell carcinoma (BCC) placed around the eyes that have been treated with imiquimod 5% (IMQ) on the skin versus those that have received photodynamic therapy (PDT). To analyze clinical development, pathological remissions, aesthetic results and tolerance to the treatment .

Methods Five patients with clinical and pathological diagnostic as nodular BCC were divided into two groups for therapeutic intervention: three of them received treatment with IMQ and the other two patients were treated with PTD after the application on the skin of metilaminolevulinate (MAL), a photosensitiser substance.

Results The tolerance to the treatment was better in the group treated with PTD. Clinical and pathological remissions were obtained in treated patients. One of them, who received PTD, presented residual tumour at the end of the treatment, but the biopsy showed granuloma without histologically BCC component.

Conclusion The effectiveness of BCC treated with IMQ 5% on the skin (five times a week for six weeks) is similar to the effectiveness of surgical treatment. Non- invasive treatment is better tolerated than surgical treatment in this kind of tumour. Moreover, the aesthetic and functional results are better than the surgical ones.

▪ 661
Apocrine hidradenocarcinoma in eyelid with corneal invasion

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Purpose Apocrine hidradenocarcinoma has been named with different terms as apocrine carcinoma, malignant clear cell hidradenoma, nodular hidradenocarcinoma, eccrine acrospiroma, and some others. This wide terminology, together with the rarity of the tumour and variability of the cells that compose it, make it difficult to diagnose.

Methods Description of a case.

Results 81 years-old female, with a history of pterygium, subject to enucleation of the eye globe after a preoperative diagnosis of squamous cell carcinoma affecting ocular adnexa, this tumor infiltrated bulbar conjunctiva and cornea.

Conclusion Malignant tumours of sweat glands are rare. Among these, hidradenocarcinoma has been described in multiple cutaneous locations and exceptionally in the eye. The frequency is not easy to determine because the terminology that has been used makes difficult to compare the data. In the eye, it may originate from glands of the eyelid or from lacrimal gland. The immunohistochemical study is not important for diagnosis. The neoplastic cells express low molecular weight cytokeratins, and cytokeratin 19. EMA and CEA are expressed in the luminal edge of glandular structures. It is an aggressive tumour, which can widely metastasize and can be cause of death.

▪ 662
Clinical presentation of reactive lymphoid hyperplasia (RLH) on the ocular surface – report of 6 cases

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Purpose Reactive lymphoid hyperplasia (RLH), also called inflammatory pseudotumor, benign lymphoma or pseudolymphoma, is a benign and reversible enlargement of lymphoid tissue probably as a reaction to antigen hyperstimulation. RLH consists of dense sheets of small mature lymphocytes with the formation of primary and secondary follicles reminiscent of normal lymph node architecture. In this study we wanted to evaluate the clinical presentation of RLH on the ocular surface.

Methods We reviewed 6 patients (3 males, 3 females) with RLH of the ocular surface. The mean age at the time of diagnosis was 28 yrs (range: 8 to 77 yrs). Paraffin sections were stained with H&E and PAS and further evaluated using immunohistochemistry.

Results In 2 patients, RLH was confined to the caruncle. One patient presented with a large cyst-like lesion, another one with a conjunctival nodule near the medial canthus, and in the oldest patient the RLH manifested itself as a pemphigoid-like conjunctival lesion in the lower fornix. A 26-years old female patient with a Non-Hodgkin-Lymphoma of the left conjunctiva developed conjunctival RLH one month later in the lower fornix of the fellow eye. Follow-up (1-11 yrs) was uneventful in all patients.

Conclusion In our case series, RLH presented as a singular lesion with varying clinical morphology. Obviously, it has to be carefully distinguished from lymphoma and should be considered in the differential diagnosis even of cyst-like lesions and at unusual sites such as the caruncle.

▪ 663
Lymphoma of the conjunctiva

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Purpose Description of the treatment and follow-up of conjunctival lymphomas

Methods Retrospective reportage of 16 patients with a conjunctival lymphoma seen at the department of Ophthalmology of Leiden University.

Results In the last 20 years, 15 patients with a local conjunctival lymphoma and one patient with generalized lymphoma of the skin with a conjunctival lymphoma were treated. Histologically all 16 patients showed to have an extranodal marginal zone B-cell lymphoma (MALT-lymphoma). Mean age of the patients at presentation was 64.8 years (37.2-84.5 years). In two patients there was a bilateral lymphoma. Thirteen patients were treated with external irradiation (30 Gray in 15 sessions), one patient with cryotherapy and one patient with CHOP chemotherapy. After a mean follow-up time of 6 years, all patients are still alive, without recurrence.

Conclusion The new international classification of conjunctival lymphoma shows the great differences in survival of conjunctival lymphoma patients. Here we illustrate that patients with the favorable marginal zone B-cell lymphoma have a very good prognosis. When treated with external irradiation, there is an extremely low rate of recurrence

▪ 664
Imaging features of orbital and ocular adnexal lymphomas

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Purpose Lymphoma is the most frequent primary orbital tumour in adults. Imaging diagnosis is a useful tool but is not specific.

Methods A non comparative retrospective review of clinical and imaging characteristics between 1996 and 2006 was conducted in our department. Included patients consisted of orbital or lacrymal gland lymphoma with Magnetic Resonance Imaging (MRI) and/or Computed Tomography (CT) imaging.

Results Ten patients were assessed. CT-scan and MRI-scan showed a well-circumscribed homogenous lesion moulding at adjacent tissues. Lack of calcifications and lack of bone destruction were observed in all cases. Most lesions were localized in the anterior extraconal orbit. Doppler showed an hypoechogenic hypervascularised lesion.

Conclusion Imaging of orbital lymphomas was not specific but some characteristics were highly evocative. Imaging cannot differentiate lymphoma from some metastasis or non specific inflammation. However, imaging can in most cases differentiate lymphoma from primary tumours.

▪ 665
International review of orbital diffuse large B cell lymphoma

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Purpose Compare findings of orbital diffuse large B cell lymphomas (ODLBCL) from 4 international centres.

Methods 38 ODLBCL cases (14 Manchester (MA), 10 Adelaide (AD), 9 Houston (HO), 5 (Hyderabad (HY) were retrieved from Ophthalmology records of each centre. Clinical, radiological and pathological findings, and treatment and outcome were reviewed.

Results Median age was 69 (7-89). M:F ratio was 1.6:1, however, 7/10 AD patients were women. 24(63%) patients had an extraconal mass, which also involved lacrimal gland or apex in 2 and 3 cases respectively. Extension to bone or sinus was observed in 12(31%) cases. Proptosis (47%) and periocular swelling (39%) were common presenting findings. Interestingly 8/14 MA patients complained of visual acuity loss, which was not relevant in other centres. A positive B-cell marker (CD20 or CD79a) was confirmed in these cases. Other positive markers were CD30 (30%), CD10 (23%) and BCL2 (8%). Evidence of transformation from other lymphoma type was seen in 6 cases. Almost 50% presented at stage II, 26% stage IV and 21% stage I, however, in MA at least 44% were at stage IV followed by stage II (33%). More than 80% of patients had chemotherapy but 1/2 of them also had a combination with radiotherapy at least. After an average 28 month follow up, 19(50%) patients were reported to be alive, 5 died and 14 lost follow up. All HO patients were alive at the end of the study.

Conclusion ODLBCL is an aggressive tumour. Most cases presented initially as an extraconal mass. Treatment varied slightly across centres. Although most MA cases presented at a more advanced stage, the MA survival rate was in keeping with the overall figures.

▪ 666
Isolated optic nerve involvement in chronic lymphocytic leukaemia

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Purpose We present a case of isolated optic nerve involvement by B-cell small lymphocytic lymphoma/chronic lymphocytic lymphoma (SLL/CLL).

Methods A 57 year old woman with CLL stage 1 developed right-sided visual loss progressing to blindness. There was optic disc swelling and secondary central retinal vein occlusion (CRVO). Imaging revealed a thickened right optic nerve. A clinical diagnosis of optic nerve sheath meningioma was made. Biopsies were taken from optic nerve sheath and abnormal-looking optic nerve tissue.

Results Histopathology revealed infiltration of optic nerve by small B-cell lymphoma, with CD5, CD20 and CD23 positive, cyclin D1 negative, neoplastic B-cells, with kappa light chain restriction. Molecular genetic analysis with heavy chain primers confirmed a dominant band of PCR products, consistent with monoclonal B-cell expansion. This lymphoma phenotype was consistent with that of the previously diagnosed stage 1 CLL. Optic nerve sheath dura was uninvolved, with reactive meningeal hyperplasia only.

Conclusion Although primary intraocular lymphoma and optic nerve lymphoma are present in up to 20% of cases of primary central nervous system lymphoma, isolated optic nerve lymphoma is rare. We believe this case is only the sixth reported where optic nerve biopsy was diagnostic. Other authors have noted the lack of dural involvement by lymphoma in this condition. We wish to add that in addition to potential diagnostic failure if optic nerve sheath alone is biopsied, the presence of reactive meningeal hyperplasia might lead to an erroneous diagnosis of optic nerve sheath meningioma on an inadequate biopsy specimen. Also, it is possible for accurate diagnosis to be achieved without sacrificing the optic nerve, although visual loss may not be avoided.

▪ 667
Spectrum of conjunctival tumors in an ocular oncology unit: review of 314 cases

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Purpose To report the frequency and spectrum of conjuctival tumors in an Ocular Oncology Unit from 1992 to 2008.

Methods Retrospective noninterventional case series. Review of clinical charts of patients with the diagnosis of conjunctival tumor diagnosed at the Ocular Oncology Unit of the University Hospital of Valladolid from 1992 to june 2008. Demographic information and tumor features were introduced in Microsoft Access database. Results were analyzed with SPSS (version 15.0).

Results Among a total of 314 cases, the mean patient age at diagnosis was 49 years, 43.3% were females and 56.7% males. Regarding the diagnosis, 149 cases (47.6%) were melanocytic, 124 (39.6%) epithelial, 30 (9.6%) soft tissues and 10 cases (3.2%) lymphoid origin. The majority of tumors were benign (63.9%) followed by the precancerous lesions (28.1%). Most of melanocytic lesions were benign (87.9%) and most epithelial were precancerous (64.5%).

Conclusion Most frequent conjunctival tumors were melanocytic origin (the majority benign) and epithelial (the majority precancerous). Melanocytic, epithelial and lymphoyd tumors accounted for 90% of cases. These results are similar to others series previously published.

▪ 668
Iodine -125 episcleral brachytherapy for uveal melanoma : 133 cases

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Purpose To assess the results of I125 Episcleral Brachytherapy (EB) in uveal melanoma: tumor control, visual acuity, eye preservation and survival

Methods Prospective and consecutive study of patients with the diagnosis of uveal melanoma at the ocular oncology unit in the Valladolid University Hospital treated with EB between september 1997 and june 2008. Ocular examination, extraocular and systemic extension data have been registered in a database at the time of the diagnosis and during the follow up.

Results Among a total of 310 patients diagnosed between September 1997 and June 2008, 133 were treated with EB with a mean age of 58.6 years. Mean follow up was 45.4 months. The onset was symptomatic in 78.2% and 66.9% were nodular and 30.1% mushroom shape. Regarding the size 80.5% were medium, 7.5 % small and 12% large. The median tumor height were 5.7 mm and median basal diameter 12 mm. The median dose to tumor apex delivered 89.6 Gy. After 4.9 year of follow up tumor were controlled in 99% with a 57.9% reduction in the mean height; only two patients showed recurrence; 64.1.% maintain visual acuity > 0.1 and 33.3% > 0.5 with . Only 7 patients underwent enucleation due to complications and there are 1 death related to melanoma up to date.

Conclusion I125 Episcleral Brachytherapy is effective regarding tumour control, allowing preservation of the eye and useful visual function for the majority of patients with uveal melanoma.

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Case of choroidal melanoma with massive extraocular extension through sclera

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Purpose To report a case of choroidal melanoma with massive extraocular extension through the sclera.

Methods A 64-year-old woman presented visual impairment in the right eye with a few months duration. On her first visit, her corrected visual acuity was 10/20 OD. Ocular examination revealed a raised choroidal mass behind the lens and serous retinal detachment in the lower retina. The choridal mass showed a mushroom shaped solid lesion on ultrasonography. The diagnosis of peripheral choroidal melanoma was confirmed by further examinations with the computed tomography, magnetic resonance imaging, and brain perfusion scintigraphy.

Results Because no systemic metastasis was found, we proposed her enucleation. However, she refused the enucleation and wished to be followed without any treatment. Seven months later, the tumor showed extraocular extension, and invasion of the subconjunctiva through the sclera. Finally, her right eyeball was enucleated. Histopathologically, the tumor was determined as mixed cell malignant melanoma of the choroid. The eyeball was congested with tumor cells and the tumor showed massive extraocular extension through the sclera to the orbit. The intraocular tumor presented marked necrotic lesions that indicate rapid growth of the tumor.

Conclusion Choroidal melanoma extends rapidly, and resulted in extraocular extension through the sclera.

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Imaging techniques in the dosimetry of episcleral brachytherapy

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Purpose To compare the doses calculated from the measurements of the tumour obtained by different imaging techniques.

Methods It is a retrospective study of 50 enucleated eyes corresponding to 50 patients with diagnosis of choroidal melanoma. For every case, there was recorded information about height of the tumour obtained by means of studies of pathological anatomy both in the macroscopic and in the microscopic preparation, and the obtained with the available imaging techniques for this measurement: magnetic nuclear resonance RNM, computerized tomography CT and B ultrasound US. Dose distribution was calculated in the tumour apex by means of the brachytherapy treatments planning system Bebig for three applicators type COMS of three and all slots filled for a duration of treatment of 1 hour, and was analyzed later by a spreadsheet Excel and the statistical application SPSS.

Results Apex dose differences (%)
Comparison with the macroscopic preparation

Applicator size	10 mm	16 mm	22 mm
CT	16,5	14,8	13,4
MNR	3,6	4,9	5,5
US	6,0	7,3	5,0

Conclusion Obtained results can be influenced partly by the size of the studied tumours, in the main of big size, and for the small muestral size in someone of the imaging techniques. They show the importance of the election of the imaging technique to obtain the information for dosimetry. Particularly relevant they are the obtained ones in the comparison with the CT due to the difficulty for this technology of distinguishing between the tumour and the detachment of retina associated.Acknowledgments:
This work has been financed partly by a grant of the Junta de Castilla y León (Order SAN/1829/2007 of November 13, BOCYL of November 15, 2007)

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Electronic vs paper based clinical pathway for episcleral brachytherapy. Preliminary results

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Purpose To evaluate the clinical pathway for electronic episcleral brachytherapy and their comparison with the paper-based format.

Methods Patients: Patients diagnosed with choroidal melanoma or angioma treated with episcleral brachytherapy in our hospital since the entry into operation of the clinical pathway. The electronic clinical pathway was developed with an database Access. To quantify the following variances regarding the clinical pathway, in two formats are examined: The number of variances, number of patients with variances, variances related to patient-related professionals, related to the hospital, not attributable to any of the above, correctable and not correctable. Data treatment: chi-square test to determine the differences between the variations of the two formats clinical pathway is employed. The data were analyzed using a spreadsheet Excel and SPSS statistical application.

Results There were no significant differences between the completion of both formats clinical pathway.

Conclusion The computerisation benefit the continuity of the records of patients, allows easy access to information and provides a tool to monitor and evaluate the provision of care. It is described that help the decision-making in the individualized treatment and allows the work in ways that are not possible in paper-based environments. Acknowledgments:This work has been financed partly by a grant of the Junta de Castilla y León (Order SAN/1829/2007 of November 13, BOCYL of November 15, 2007)

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Lack of association of the Toll-like receptor 4 gene polymorphisms Asp299Gly in Italian patients with Fuchs uveitis

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Purpose Fuchs uveitis is a chronic low grade intraocular inflammation of unknown etiology that is usually painless and characterized by the presence of persistent infiltrating cells in the anterior chamber and vitreous. One commonly occurring Single Nucleotide Polymorphism (SNP) in the human TLR4 gene (Asp299Gly) has been shown to be associated with increased risk of Gram-negative bacteremia in sepsis patients and with susceptibility to inflammatory bowel disease and autoimmune disease.

Methods 75 Italian patients with Fuchs heterochromic cyclitis and 210 healthy age and sex matched blood donors were genotyped for the Toll-like receptor 4 gene polymorphisms Asp299Gly gene by molecular methods.

Results The distribution of allele and genotype frequencies of the Toll-like receptor 4 gene polymorphisms Asp299Gly did not differ significantly between the patients with Fuchs heterochromic cyclitis and the healthy controls.

Conclusion Our data suggest that the Toll-like receptor 4 gene polymorphisms Asp299Gly in Italian patients with Fuchs uveitis is not associated with susceptibility of Fuchs uveitis Italian patients.

▪ 673 / 6426
Presentation of orbital aspergillosis

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Purpose To describe the presentation, diagnostic difficulties and treatment in three rare cases of aspergillosis of the (peri)orbita.

Methods Retrospective reportage of three patient histories.

Results The first patient, known with leukemia, presented with total vision loss and ophthalmoplegia. Clinical suspicion was raised for a sinus cavernosis and apex syndrome, but could not be revealed by imaging at first, but only later in the disease progression. The patient was treated with chemotherapy and Amfotericine, but died few weeks later.A second patient presented with complaints with bilateral decrease of visual acuity and sinusitis. No process could be revealed in the cavernous sinus, but bilateraly in the ethmoids. An endonasal ethmoidectomy was done, and oral steroids were given, with good result. A third patient was referred with diplopia since four days. CT-scan together with MRI made the suspicion of fungal disease with found after tumor excision of the sphenoid MRI showed at first desctruction of the sella floor, without intraorbital infection but forced duction invasion toh orbit. The patient was treated with amphotericin and itraconazole with vanishment of the infection in one month.

Conclusion These three cases with aspergillosis infection show that a combination of MRI and CT may be necessary to locate the infection but clinical suspicion and symptoms may be present before imaging can reveal them.

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Management of ocular disease in epidermolysis bullosa variant: Laryngo-onycho-cutaneous (LOC) syndrome

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Purpose To assess the long term outcomes of ocular surface reconstruction and immunomodulation in Laryngo-onycho-cutaneous (LOC) syndrome

Methods Prospective, interventional, case series

Results Four children with LOC were treated by multiple operations involving excision of ocular granulation tissue and amniotic membrane graft reconstruction. The clinical course was monitored for an average period of 4.7 years +/- 2 SD (range 3 to 7 years). In all patients, surgical intervention was successful in the medium term with regression of granulation tissue, visual improvement and symptomatic relief from ocular discomfort. Granulation tissue recurred in 8 months (3.7 SD). One patient received Thalidomide trial which stabilized systemic manifestations but had limited effect on ocular disease progression. Immunomodulation with Infliximab infusions stabilized ocular disease in all patients. All patients had stabilisation or slight improvement in vision.

Conclusion Ocular disease in LOC syndrome can be successfully managed with repeated amniotic membrane grafts and immunomodulation. The treatment is effective in maintaining the ocular surface integrity and managing the symptoms of ocular inflammation, although long term visual outcomes remain disappointing.

▪ 675
In vivo confocal microscopy of keratic precipitates in anterior uveitis related to Herpesviridae

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Purpose To study the pattern of keratic precipitates (KPs) in anterior uveitis due to Herpesviridae using in vivo confocal microscopy

Methods KPs of 17 consecutive patients (average age: 54+/-8 years), addressed for anterior uveitis related to either Herpes simplex virus (HSV), Varicella-zoster virus (VZV) or cytomegalovirus (CMV), were examined using the HRT II Rostock Cornea module, between May 2006 and June 2007. The diagnosis of HSV, VZV or CMV infection was based on PCR or specific antibodies production within the aqueous humor, or on clinical history for uveitis that rapidly followed herpes zoster ophthalmicus. At the time of in vivo confocal microscopy, the uveitis was in an acute period (recent increase of inflammation).

Results The HRT II Rostock Cornea provided reproducible images of KPs, with both a heap-shaped pattern and stars which were characterized by branches in weak number and of modest size. HRT imaging of the fellow eye was normal in all cases (control eyes).

Conclusion Herpesviridae are a classic cause of unilateral and hypertonic uveitis. If the clinical pattern is often very suggestive, certain cases may be difficult to differentiate from other causes of uveitis, notably Fuch's heterochromic cyclitis. The reproducible pattern of KPs in viral uveitis using in vivo confocal microscopy should be helpful to differentiate from non-herpetic etiologies.

▪ 676
Retrospective study of 40 cases of sarcoid uveitis

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Purpose The aim of this study was to describe the clinical characteristics,the evolution and prognosis of sarcoid uveitis and to assess the best diagnostic procedure for the disease.

Methods All patients with sarcoid uveitis have been seen in Caen University hospital over the last ten years. Inclusion criteria were a positive biopsy showing noncaseating granuloma or patients with a high presumption of sarcoidosis (at least 2 abnormalities amongst the main systemic diagnostic investigations).

Results Biopsy was positive for 27 patients. Thoracic CT-scan,negative tuberculin skin test, serum angiotensin converting enzyme, bronchoalveolar lavage and gallium scanning suggested the diagnosis in all other cases. Forty patients were included. There were 25 women (62%). The mean age was 43 years. The mean follow-up duration was 55 months. Uveitis was bilateral in 29 cases. Anterior segment manifestations occured in 83% of cases,associated with a posterior segment involvement in 66% of cases. We reported a high frequency of cystoid macular oedema (CMO)(37%)and optic disc swelling(35%). The lung was the most common organ involved over the uveitis evolution period and CT-scan was a superior imaging modality compared to chest X-rays. Corticosteroids were the mainstay of treatment. Visual prognosis was good: mean final visual acuity was 15/20. CMO played a decisive role in poor visual outcome ($p<0,05$). Ocular complications were early cataract(7),epiretinal membrane(4),chronic glaucoma(3),retinal neovascularisation(1) and retinal detachment(1).

Conclusion There is a high incidence of posterior involvement in sarcoid uveitis. CMO is frequent and correlated with a worse final visual acuity. Pulmonary involvement occurs in more than 90% of cases, therefore CT-scan must always be performed.

▪ 677
Human papillomavirus DNA in pterygia

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Purpose To examine pterygium and normal conjunctiva tissue for the presence of human papillomavirus (HPV) and to determine the genotypes of HPV.

Methods METHODS: The study involved 89 patients undergoing surgical procedures at the I Department of Ophthalmology, Medical University of Lublin, Poland.Patients were divided into 2 groups: group I with pterygium (n = 58; 51 primary, 7 recurrences) and group II with with normal conjunctiva (n=31). The material was collected during elective surgical procedures. Specimens were tested for the presence of HPV genome using polymerase chain reaction (PCR). Once the presence of HPV DNA was confirmed, 28 HPV genotypes were determined using reverse hybridisation.

Results In group I, HPV DNA was identified in 16 patients (27.6%) whereas in group II - in 3 cases (9.7%). Moreover, there was a statistically significant difference in the presence of HPV genome in pterygium patients compared to those with no clinical lesions of the conjunctiva (p=0.041). HPV type 16 was most frequently observed in 56% of HPV positive cases of pterygium. In 19% of cases, HPV 16 and HPV 6 co-infections were found while in 13% - HPV 18 and HPV 6 co-infections were detected. Amongst 7 cases of recurrent pterygium, HPV 16 was detected in 2 cases. In group II, all 3 patients with HPV showed HPV 18.

Conclusion In Poland, no studies concerning the presence of HPV in ocular lesions have been carried out. The group examined in our study is one of the largest populations of patients with pterygium studied for the presence of the HPV genome worldwide. Our findings show that HPV is likely to play a synergistic role in the multi-stage process of the development of pterygium, although it is not necessary to induce this condition.

▪ 678
Cytokine profile in intermediate uveitis

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Purpose Intermediate uveitis (IU) represents a chronic type of uveitis of unknown cause with the vitreous as the major site of the inflammation. The associated diseases include mostly multiple sclerosis (MS) and sarcoidosis, the majority of cases is idiopathic. The aim of this prospective study was to elucidate intraocular and serum cytokine profiles of patients with IU and relate the laboratory results to clinical features.

Methods Aqueous humor (AqH) and serum samples were collected from 39 IU patients in various stages of uveitis activity and from 10 controls with cataract and no uveitis during cataract surgery. The concentration of inflammatory mediators was measured by multiplex immunoassay and included interleukin (IL) 8, 1β, 6, 10, 12p70, TNFα, CCL5/RANTES, CCL3/MIP-1alpha, CCL4/MIP1-beta, CCL2/MCP1.

Results Serum samples of patients and controls were not distinct; however intraocular samples of IU patients had higher levels of interleukin-6 (IL 6), interleukin-8 (IL 8) and MCP 1 than non-uveitis controls (for all P=<0.05). Intraocular IL6 and IL8 levels exceeded that of serum in 22/39 (56%; P= 0.001) and 29/39 (74%; P= < 0.001) respectively. Active intraocular inflammation and the presence of CME were associated with higher levels of IL 6 and IL 8 than intraocular samples from patients with quiescent uveitis (P=<0.05) and those not affected by CME (P=<0.05). No significant associations were found for other measures cytokines.

Conclusion IL 6 and IL 8 are two most abundant cytokines in intraocular environment of patients with IU and their levels were associated with IU activity and the presence of CME. The findings of normal serum levels of proinflammatory cytokines in patients do not support the presence of associated systemic inflammation.

▪ 679
Can tumor necrosis factor inhibitors induce scleritis ?

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Purpose Tumor necrosis factor alpha is a pro-inflammatory cytokine which plays an important role in the physiology of many inflammatory diseases. There are three tumor necrosis factor inhibitors : etanercept, infliximab, adalimumab. Etanercept's most consistent side effect is injection-site reaction. Inflammatory eye disease has also been one of the rare adverse events associated with etanercept.

Methods We report two cases of female patients who presented a scleritis , while they were treated for rheumatoid arthritis by etanercept 35 mg twice a week.

Results These two patients presented a first episode of unilateral anterior nodular scleritis after respectively 16 and 12 months of etanercept. Their rheumatoid disease was in remission. The non steroidal anti-inflammatory agents and steroids were not much effective on the scleritis symptoms. After having stopped the etanercept, the scleritis decreased. A review of the literature pertaining to inflammatory eye disease associated with the use of etanercept was performed. Multiples drugs have been associated with ocular inflammation : in scleritis (biphosphonates, topiramate) and in uveitis (rifabutine, sulfonamides, metipranolol eyedrops,...). These cases suggest that etanercept is one of them.

Conclusion The possibility of a iatrogenic cause must be envisaged in case of non efficacity of usual treatment (non steroidal anti-inflammatory agents, steroids, immunosuppressive therapies). The question of a specific ophthalmological follow-up of such patients is also addressed.

▪ 680
Topical use of Nerve Growth Factor on ocular flora and cytology in dogs eye surface

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Purpose To investigate if topical Nerve Growth Factor (NGF) affects the ocular flora and to study corneal conjunctival cytology in dogs with different eye surface disease.

Methods The present study has been conducted on 9 dogs (18 eyes) affected by different ocular surface disease. The dogs were various ages (from 2 to 10 years old) and different sexes (5 males - 4 females). 6 dogs were affected by dry eye, 1 had a superficial keratitis and 2 dogs had a cornea ulcer. All dogs underwent the following examinations: cornea evaluation by slit lamp, fluorescent staining, Schirmer tear test I (STT I), corneal and conjunctival cytology. All samples made with ocular swabs were placed in a sterile blood agar. 6 dogs showed no bacteria, 3 dogs displayed Staphylococcus spp. Cytology pointed out many inflammatory cells. The dogs were topically treated with purified murine NGF diluted in paraffin oil (200 microg/ml) for 4 weeks (50 microg every 12 h).

Results The result revealed that all swabs were sterile, while the cytology analysis showed a significant reduction in the number of corneal inflammatory cells. This latter observation is related to a decrease of the corneal inflammatory reduction.

Conclusion This report demonstrated that NGF exerts an antibacterial and anti inflammatory activity that confirmed and extended previous evidences on NGF research. Moreover, our results suggest a potential therapeutic use of NGF in dogs with different ocular inflammatory surface. However, further clinical studies need to be done to assess the consistency of this clinic approach.

▪ 681

One year analysis of the cost of uveitis treatment in France: a retrospective chart review

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Purpose To determine current treatment strategies and evaluate one year consumption of health care resources for patients with uveitis in France.

Methods Review of consecutive patients (N = 100) from 4 French referral centers with 12 months follow-up after the first visit. Data abstracted from the patient charts included basic demographic data, characterizing clinical parameters, and all disease- or treatment-related resource consumption. Direct health care costs were estimated using publicly available standard unit costs. Indirect costs were based on standard sick leave for each type of inpatient admission or outpatient intervention and a gender-specific cost of employment.

Results 82% of patients were below age 60 (retirement age). Diseases were: posterior uveitis (36%), panuveitis (33%), chronic anterior (24%) and intermediate (7%). Patients received drug treatments (91%), triamcinolone or dexamethasone injections (8%), and laser treatment (2%). Mean direct costs per patient were €3403. Inpatient stays accounted for the largest proportion, with a mean cost of €2889 per year. For patients below 60 years with an admission or intervention, the estimated average productivity loss was €1750, leading to a mean indirect cost of €830 per patient. The estimated total minimum annual costs per patient were €4230.

Conclusion Annual treatment costs in this sample were driven by frequent, extended inpatient stays. This may be due to the more severely diseased patients treated by these specialized centers. In the current sample, most patients were of working age, suggesting a substantial amount of indirect costs arising from sick leave.

Commercial interest

▪ 682

Genetic analysis of pseudomonas aeruginosa isolates from patients with post-operative endophthalmitis

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Purpose To establish clonal relationship between strains of Pseudomonas aeruginosa isolated from 24 patients with postoperative endophthalmitis following cataract surgery

Methods All the patients with postoperative endophthalmitis were operated at the same operation theatre in the same hospital in Tiruchirapalli, Tamil Nadu, India. All the cases occurred within a time period of one month. Polymerase chain reaction (PCR) with enterobacterial repetitive intergenic consensus (ERIC) primers (ERIC-PCR) was used to establish clonal relationship between the different isolates.

Results ERIC-PCR disclosed 4 different patterns. Seventeen isolates showed an identical pattern, whereas 2 other strains were closely correlated with the former 17. Two other isolates, with identical ERIC-PCR pattern, were genetically similar, but to a lesser extent, to the first group. The remaining 3 isolates showed identical ERIC-PCR pattern, but they were less correlated with the other strains.

Conclusion The results of this study indicate that the outbreak of postoperative P. aeruginosa endophthalmitis presented here was caused predominantly by isolates with identical or very similar genetic patterns, thus suggesting a common source of infection in most cases. ERIC-PCR appears to be an inexpensive, fast, reproducible, and discriminatory DNA typing tool for effective epidemiological surveillance of outbreaks of P. aeruginosa eye infections.

▪ 683

The corneal endothelium in an endotoxin-induced uveitis model: Correlation between in vivo confocal microscopy and immunohistochemistry

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Purpose To analyze the involvement of the corneal endothelium in uveitis in order to better understand the formation mechanisms and the keratic precipitate composition. In vivo confocal microscopy images were correlated with ex vivo immunostaining of corneal endothelium from rat eyes with endotoxin-induced uveitis (EIU).

Methods EIU was induced in Lewis rats by lipopolysaccharide (LPS) injection. Slit-lamp examination and in vivo confocal microscopy were performed 6, 24, 48, 72 and 96 h after the LPS injection. Immunohistochemistry on corneal endothelium, using antibodies to ICAM-1, phalloidin, CD68 (anti-macrophage), MA967 (anti-granulocyte), alpha beta-TCR (anti-lymphocyte) was performed on flat-mount corneas and was analyzed using a 3D laser confocal microscope.

Results In vivo confocal microscopy showed numerous hyper-reflective round dots on the corneal endothelium, in the anterior chamber and in the anterior stroma corresponding to inflammatory cells until 96 h, peaking at 24 h. On immunostaining, corneal endothelial cells in rats with EIU overexpressed ICAM-1. Compared to controls, CD68, MA 967 and alpha beta-TCR expression was observed in corneas in rats with EIU.

Conclusion The correlation between in vivo confocal microscopy and ex vivo immunostaining helped to better understand in vivo confocal microscopy images. The two new techniques applied here were very effective and complementary in evaluating the corneal endothelium involvement in EIU. Based on these findings, in vivo confocal microscopy in clinical practice could be very helpful to better analyze keratic precipitates and corneal modifications in patients with uveitis.

▪ 684

Patient demographic data for phase 2/3 clinical trials of a novel calcineurin inhibitor, lx 211, for the treatment of non-infectious uveitis

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Purpose LX211 is the oral formulation of a novel calcineurin inhibitor (CNi) possessing four-fold greater potency, an altered metabolic and pharmakokinetic profile, and potentially improved safety compared to the prototypical CNi, cyclosporine A.

Methods Three global, prospective, double-masked, parallel-group, dose-ranging, placebo-controlled, randomized multicenter studies comprise the LUMINATE Program, which is currently in progress. Study LX211-01-UV evaluates 210 patients with active predominantly posterior manifestations. Study LX211-03-UV evaluates 100 patients with active predominantly anterior manifestations. Study LX211-02-UV evaluates 220 patients whose disease is controlled and will evaluate the role of LX211 in sparing systemic corticosteroid.

Results The studies are ongoing. Pooled masked data from the studies to date indicate that in Study LX211-01 (N=81) the distribution of patient anatomic diagnoses is : panuveitis (48.1%), intermediate uveitis (29.6%), anterior + intermediate uveitis (8.6%) and posterior uveitis (13.6%). The mean age is 42 years with a F/M of 2. Study LX211-02 (N=101) has a similar distribution of anatomic diagnosis. The mean age of subject ins LX211-02 is 43.4 years with a F/M of 2. Study LX211-03 was similar to Studies LX211-01 and LX211-02 with respect to the proportion of female (68.6%) to male (31.4%) subjects.

Conclusion The LUMINATE Program are the first randomized placebo-controlled trials for a corticosteroid-sparing immunomodulatory agent in various anatomic forms of sight-threatening non-infectious uveitis.

Commercial interest

▪ 685

Clinical and microbiological features of acute bacterial conjunctivitis at the primary eye care unit in a hospital of central Italy

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Purpose Aim of this study is to identify bacteria causing conjunctivitis in a central Italian area and to analyze their chemosusceptibility.

Methods From 2005 to 2006, 91 conjunctival swabs were collected from acute conjunctivitis cases who were examined in the primary eye care unit at the "S. Maria alle Scotte" Hospital in Siena. All swabs collected were screened for common bacteria and fungi. Susceptibility tests were performed on isolates.

Results Isolated bacteria were Staphylococcus aureus, Streptococcus pneumoniae and Haemophilus influenzae for an amount of 86.2%. Overall, 100% of strains were susceptible to chloramphenicol and 96.6% to quinolones. Conversely, 20.7% of isolates were tetracycline-resistant and, even if all Gram negative isolates were susceptible to gentamicin, more frequently isolated pneumococci are constitutively resistant.

Conclusion Acute "red eye" is one of the commonest reasons for consultation with primary eye care physicians; in the majority of cases an acute bacterial conjunctivitis is diagnosed, the pathogens most frequently responsible are Streptococcus pneumoniae, Haemophilus influenzae and Staphylococcus aureus. Guidelines on the management of conjunctivitis recommend antibiotic routine use where bacterial infection is suspected. This study provides a support in rational choice of empiric therapy with distinct regional preferences in the topical agent to be used.

▪ 686

Changes on optic nerve with sarcoidosis patients

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Purpose Sarcoidosis is a rare autoimmune disorder. Since in 20% of the cases optical manifestations represent the first sign of a systemic disease and that 75% of sarcoidosis patients are under the age of 40, we considered it appropriate to perceive the manifestations of sarcoidosis on the optic nerve and to notice the consequences for the vision.

Methods The examination was being carried out on 32 patients who had come for an ophthalmological check-up in the Eye Clinic of the Clinical Centre of Montenegro for the first time, and who had been made sarcoidosis diagnosis. With the patients showing the obvious signs of neurosarcoidosis with the spreading over the optic nerve, additional diagnostic examinations were being carried out: FA, ICG, NMR, EEG, VEP, lumbar punction, as well as endocrinological examinations. The patients were being monitored during the following year, with monthly control check-ups.

Results Optical manifestations within the framework of the basic disease were found with 17 patients, whilst optical symptomatology was the first sign of the disease with 4 patients. The changes on the optic nerve were noticed in various forms and they appeared either as the initial manifestation of sarcoidosis or at any time during the duration of the disease.

Conclusion The changes found on the optic nerve within the framework of sarcoidosis were numerous and variable. PNO edema, papillitis, granuloma PNO, retrobulbar neuritis, are only part of clinical manifestations which appear upon the optic nerve being affected by sarcoidosis.

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EVER 2008

ABSTRACTS

October 1-4, 2008
Portoroz, Slovenia

All authors of abstracts are listed alphabetically.

Three digit numbers refer to posters.
Four digit numbers refer to oral presentations.
The digit numbers marked in bold indicate a first author abstract.