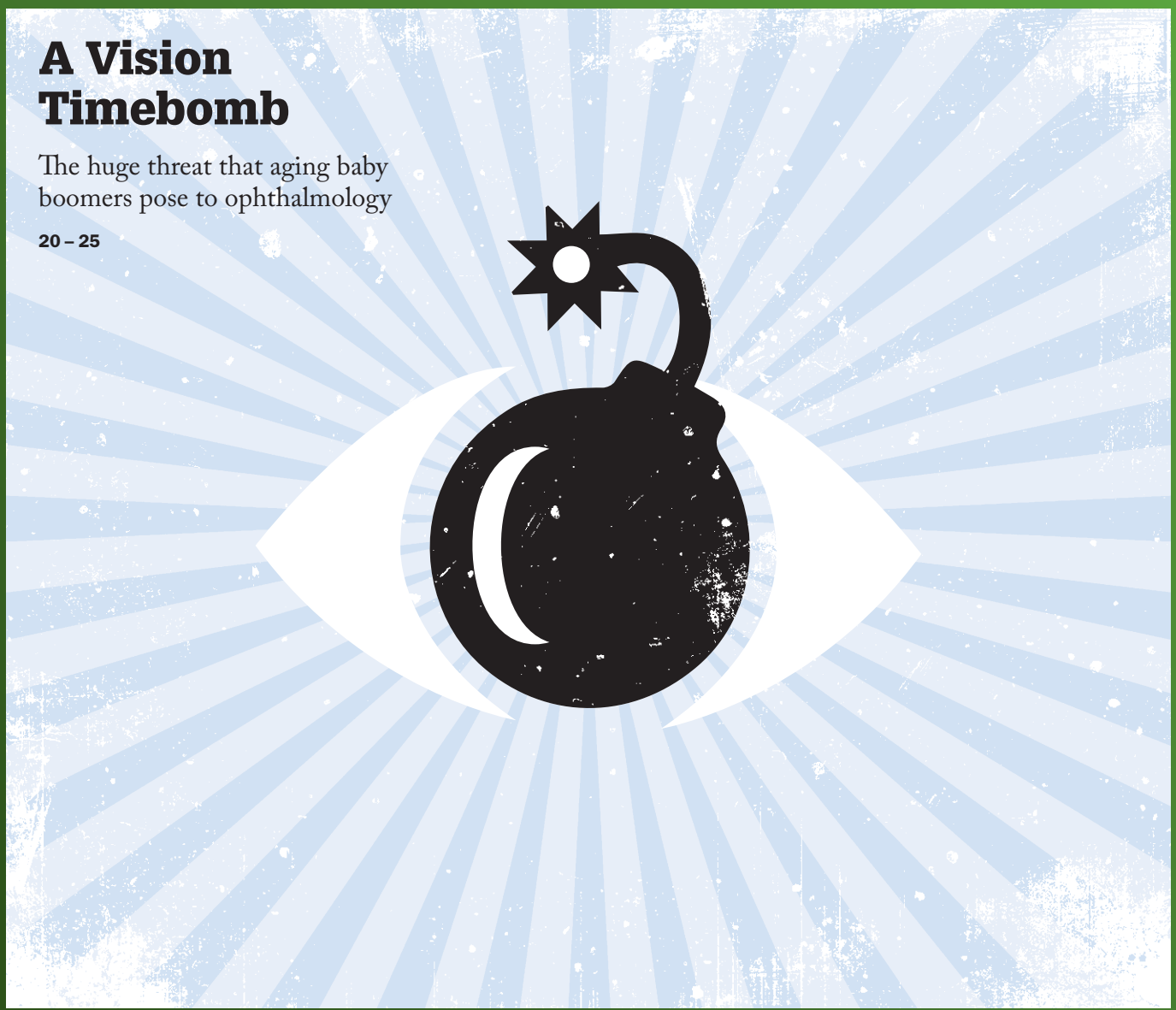
MARCH 2014 # 06

the Ophthalmologist

A Vision Timebomb

The huge threat that aging baby boomers pose to ophthalmology



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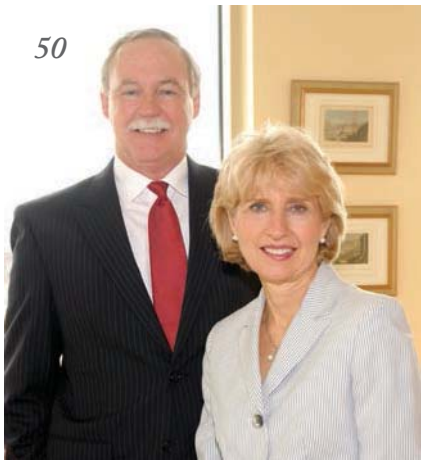

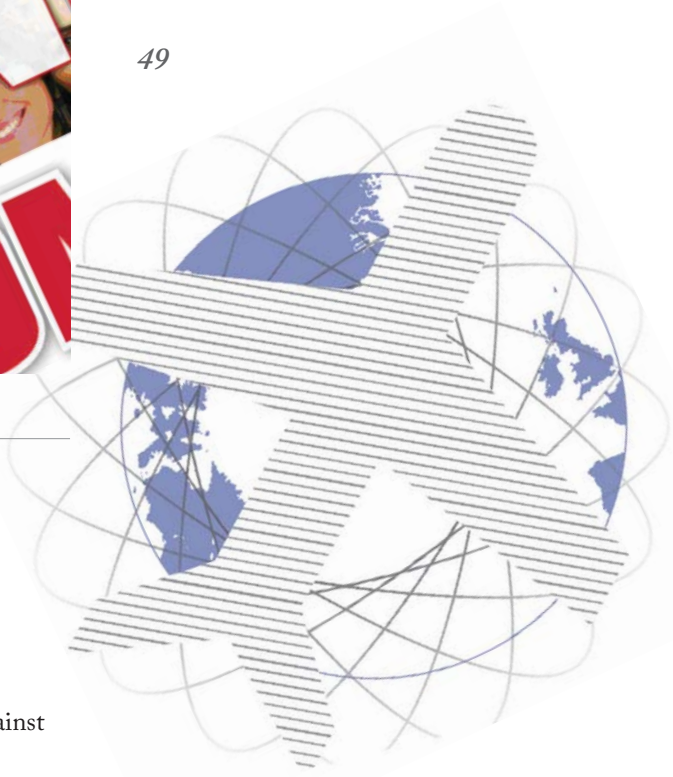

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ISSUE 06 - MARCH 2014

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Benchmarking Ophthalmology

Our cataloging of the major eye diseases is insightful, even though impact factor analysis is flawed.

In this issue we present benchmarking data for the field of glaucoma; last month, we did the same for cataract. The idea is to provide a series of reference points against which to judge performance and/or progress; today, benchmarking is being applied to everything from countries and corporations to schools and sports teams, as well as to scientific and medical sub-disciplines. It's widely used by pharmaceutical companies to identify key opinion leaders in a given field or for 'gap analyses' for a given indication, to assess if their competitors missed a trick.

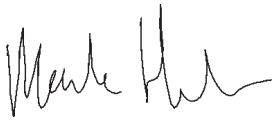
In The Ophthalmologist's benchmarking analyses, we catalogue who published what and where; and we assess what kinds of research are being performed and what impact it makes. We do so because the findings may benefit clinical research and practice. They reveal where the attention (and, probably, funding) of the field has been focused, pointing out not only what is favored but also what is underrepresented. We don't spoon-feed interpretations; instead, we present the data for you get to interpret as you see fit.

But one aspect of these analyses that troubles me is the Impact Factor (IF). Even Gene Garfield, who invented IFs isn't in favor of using them to judge the value of scientific research. They are fine for "quick and dirty" assessments of journal quality, but a few 'superstar' papers can give a journal a high IF, even if the vast majority of papers are barely cited. It's imprecise, but far better than nothing; just be aware of the limitations. Better metrics like Eigenfactors or SCImago are much more difficult to access.

As an aside, efforts to improve upon IFs led to the 'recursive Impact Factor' back in 1976 – citations from journals with high IFs attract a greater weighting than citations from low-IF journals. This was an early example of the type of algorithm, PageRank, that Google uses to rank their search results. And as any web developer will tell you, that's the most important metric to come top of these days for visibility.

Almost nobody goes into medicine for "exposure", they do it to heal the unwell. But if you're competing for research funding, it truly is the case that life is a pitch. Here's hoping that in the future, the impact and true value of your work is assessed by the best metrics possible.

Mark Hillen
Editor



Ehud Assia

Ehud Assia, once referred to as a "rock star" of ophthalmology for his role in developing CO_2 lasers for use in glaucoma surgery, is the Director of the Department of Ophthalmology at Meir Medical Center in Kfar-Saba and the Medical Director of the Ein-Tal Eye Center in Tel- Aviv, in addition to being a full Professor of Ophthalmology at the Sackler School of Medicine, Tel-Aviv University. Both he and his wife, Ayala (a pediatrician) enjoy the humanitarian mission trips they make to rural areas in countries like Nepal, China, Ethiopia, and India. Read Ehud's review of glaucoma treatment with CO_2 laser-assisted sclerectomy surgery on page 35.

Stela Vujosevic

A former Moorfields Medical Retina fellow, Stela Vujosevic is the assistant clinical professor of ophthalmology at the 800-year old University of Padova, Italy and a Medical Director of the International Microperimetry and Retina Reading Centre in Padova. Her clinical and research interests concern screening, morphological and functional instrumental diagnoses, and the laser and intravitreous treatment of degenerative chorioretinal pathologies. When not visualizing eyes, she enjoys sports activities and discovering the world through travel. On page 32, Stella looks at how the future of diabetic macular edema therapy might combine anti-VEGF injections with new laser technology.

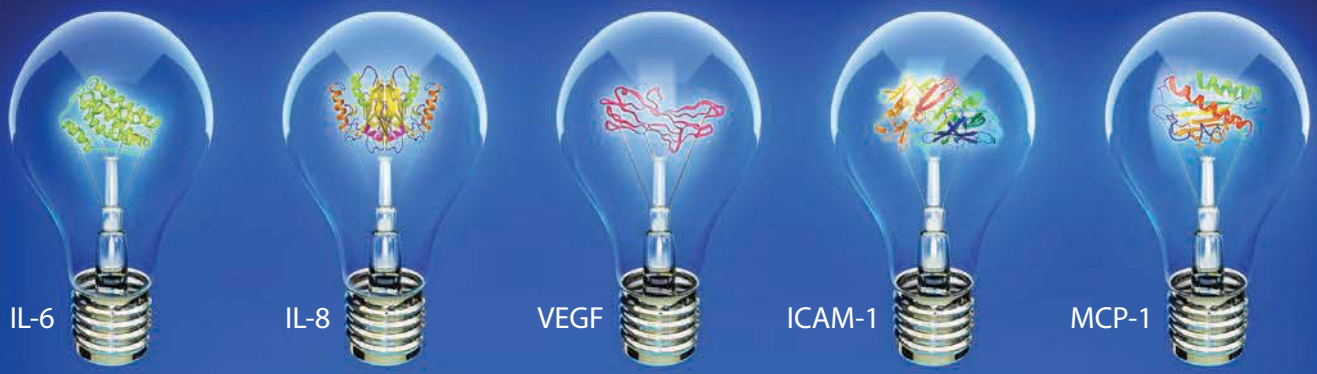
Mark Blecher

Mark Blecher is the co-director of the Cataract Service at the Wills Eye Hospital in Philadelphia, PA, USA and Assistant Clinical Professor of Ophthalmology at nearby Thomas Jefferson University. Mark can claim to have trained more cataract surgeons in the US than almost anyone else, and was recently the recipient of Wills Eye Hospital's greatest honor, the Silver Tray Award. He also operated on his own mother at her insistence and when he's not lecturing, teaching or with patients, he retreats to his farm to recharge. Mark's call to arms to find a better measurement of visual acuity than Snellen can be found on page 28.

Andrew Davies

Andy Davies is the Chief Executive Officer of Texere Publishing, publisher of The Ophthalmologist, based in Knutsford, UK. Before this, he was Group Publisher in Europe for Duluth-based Advanstar, Publishing Director at the Institution of Engineering and Technology, and has the honor of being Science magazine's first employee in Europe, where he served as Associate Director. Against this background, Andy has travelled around the world many times and attended hundreds of scientific and medical congresses. When not travelling or working, you can usually find him on an Alpine ski run. Learn his top ten tips for travel nirvana – or at least how to mitigate the pain and fatigue, on page 49.

TARGETING THE MEDIATORS OF INFLAMMATION[1]



Delivering efficacy in the clinical setting[2-5]

Ozurdex® (dexamethasone intravitreal implant) 0.7mg

These images are for illustrative purposes only and do not represent inflammatory mediator levels in the eye.

OZURDEX® (Dexamethasone 700 micrograms intravitreal implant in applicator)

Abbreviated Prescribing Information

Presentation: Intravitreal implant in applicator. One implant contains 700 micrograms of dexamethasone. Disposable injection device, containing a rod-shaped implant which is not visible. The implant is approximately 0.46 mm in diameter and 6 mm in length. **Indications:** Treatment of adult patients with macular oedema following either Branch Retinal Vein Occlusion (BRVO) or Central Retinal Vein Occlusion (CRVO). Treatment of adult patients with inflammation of the posterior segment of the eye presenting as non-infectious uveitis. **Dosage and Administration:** Please refer to the Summary of Product Characteristics before prescribing for full information. OZURDEX must be administered by a qualified ophthalmologist experienced in intravitreal injections. The recommended dose is one OZURDEX implant to be administered intravitreally to the affected eye. Administration to both eyes concurrently is not recommended. Repeat doses should be considered when a patient experiences a response to treatment followed subsequently by a loss in visual acuity and in the physician's opinion may benefit from retreatment without being exposed to significant risk. Patients who experience and retain improved vision should not be retreated. Patients who experience a deterioration in vision, which is not slowed by OZURDEX, should not be retreated. There is only very limited information on repeat dosing intervals less than 6 months. There is currently no experience of repeat administrations in posterior segment non-infectious uveitis or beyond 2 implants in Retinal Vein Occlusion. Patients should be monitored following the injection to permit early treatment if an infection or increased intraocular pressure occurs. Single-use intravitreal implant in applicator for intravitreal use only. The intravitreal injection procedure should be carried out under controlled aseptic conditions which include the use of sterile gloves, a sterile drape, and a sterile eyelid speculum (or equivalent). The patient should be instructed to self-administer broad spectrum antimicrobial drops daily for 3 days before and after each injection. Before the injection, the periocular skin, eyelid and ocular surface should be disinfected and adequate local anaesthesia should be administered. Remove the foil pouch from the carton and examine for damage. In a sterile field, open the foil pouch and gently place the applicator on a sterile tray. Carefully remove the cap from the applicator. Once the foil pouch is opened the applicator should be used immediately. Hold the applicator in one hand and pull the safety tab straight off the applicator. Do not twist or flex the tab. With the bevel of the needle up away from the sclera, advance the needle about 1 mm into the sclera then redirect toward the centre of the eye into the vitreous cavity until the silicone sleeve is against the conjunctiva. Slowly press the actuator button until an audible click is noted. Before withdrawing the applicator from the eye, make sure that the actuator button is fully pressed and has locked flush with the applicator surface. Remove the needle in the same direction as used to enter the vitreous. Immediately after injecting OZURDEX, use indirect ophthalmoscopy in the quadrant of injection to confirm successful implantation. Visualisation is possible in the large majority of cases. In cases in which the implant cannot be visualised, take a sterile cotton bud and lightly depress over the injection site to bring the implant into view. Following the intravitreal injection patients should continue to be treated with a broad spectrum antimicrobial. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Active or suspected ocular or periocular infection including most viral diseases of the cornea and conjunctiva, including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections, and fungal diseases. Advanced glaucoma which cannot be adequately controlled by medicinal products alone. Aphakic eyes with rupture of the posterior lens capsule. Eyes with Anterior Chamber Intraocular Lens (ACIOL) and rupture of the posterior lens capsule. **Warnings/Precautions:** Intravitreous injections, including OZURDEX can be associated with endophthalmitis, intraocular inflammation, increased intraocular pressure and retinal detachment. Proper aseptic injection techniques must always be used. Patients should be monitored following the injection to permit early treatment if an infection or increased intraocular pressure occurs. Monitoring may consist of a check for perfusion of the optic nerve head immediately after the injection, tonometry within 30 minutes following the injection, and biomicroscopy between two and seven days following the injection. Patients must be instructed to report any symptoms suggestive of endophthalmitis or any of the above mentioned events without delay. All patients with posterior capsule tear, e.g. those with a posterior lens, and/or those who have an iris defect (e.g. due to iridectomy) with or without a history of vitrectomy, are at risk of implant migration into the anterior chamber. Other than those patients contraindicated where OZURDEX should not be used, OZURDEX should be used with caution and only following a careful risk benefit assessment. These patients should be closely monitored for any signs of implant migration. Corticosteroids should be used cautiously in patients with a history of *ocular herpes simplex* and not be used in active *ocular herpes simplex*. The safety and efficacy of OZURDEX administered to both eyes concurrently have not been studied and is not recommended. OZURDEX is not recommended in patients with macular oedema secondary to RVO with significant retinal ischemia. OZURDEX should be used with caution in patients taking anti-coagulant or anti-platelet medicinal products. **Interactions:** No interaction studies have been performed. Systemic absorption is minimal and no interactions are anticipated. **Pregnancy:** There are no adequate data from the use of intravitreally administered dexamethasone in pregnant women. OZURDEX is not recommended during pregnancy unless the potential benefit justifies the potential risk to the foetus. **Lactation:** Dexamethasone is excreted in breast milk. No effects on the child are anticipated due to the route of administration and the resulting systemic levels. However OZURDEX is not recommended during breast feeding unless clearly necessary. **Driving/Use of Machines:** Patients may experience temporarily reduced vision after receiving OZURDEX by intravitreal injection. They should not drive or use machines until this has resolved. **Adverse Effects:** *RVO* In clinical trials the most frequently reported adverse events were increased intraocular pressure (IOP) (24.0%) and conjunctival haemorrhage (14.7%). Increased IOP with OZURDEX peaked at day 60 and returned to baseline levels by day 180. Elevations of IOP either did not require treatment or were managed with the temporary use of topical IOP-lowering medicinal products. The following adverse events were reported: Very common (≥1/10): IOP increased, conjunctival haemorrhage* Common (≥1/100 to <1/10): Ocular hypertension, vitreous detachment, cataract, subcapsular cataract, vitreous haemorrhage*, visual disturbance, vitreous opacities* (including vitreous floaters), eye pain*, photopsia*, conjunctival oedema*, anterior chamber cell*, conjunctival hyperaemia*, headache Uncommon (≥1/1,000 to <1/100): Retinal tear*, anterior chamber flare* Headache. *Uveitis* In clinical trials the most frequently reported adverse events in the study eye were conjunctival haemorrhage (30.3%), increased IOP (25.0%) and cataract (11.8%). The following adverse events were reported: Very common: Increased IOP, cataract, conjunctival haemorrhage* Common: Retinal detachment, Myodesopsia, vitreous opacities, blepharitis, sclera hyperaemia*, visual impairment, abnormal sensation in the eye*, eyelid pruritis, migraine. (*Adverse reactions considered to be related to the intravitreous injection procedure rather than the dexamethasone implant). Please refer to Summary of Product Characteristics for full information on side effects. **Basic NHS Price:** £870 (ex VAT) per pack containing 1 implant. **Marketing Authorisation number:** EU/1/10/638/001 **Marketing Authorisation Holder:** Allergan Pharmaceuticals Ireland, Castlebar Road, Westport, Co. Mayo, Ireland. **Legal Category:** POM. **Date of Preparation:** May 2013.

Adverse events should be reported. Reporting forms and information can be found at **www.mhra.gov.uk/yellowcard.** Adverse events should also be reported to Allergan Ltd. **UK_Medinfo@allergan.com** or **01628 494026.**

References: 1. Nehme A & Edelman J. Invest Ophthalmol Vis Sci. 2008;49(5):2030-2038. 2. Pommier S & Meyer F. Realites Ophthlamologuiques 2012; 195. 3. Augustin A. *et al.* Poster presented at EVER 2012, October 10-13; Nice, France. 4. Querques L. *et al.* Ophthalmol. 2013;229:21-25. 5. Rostron E. *et al.* Poster presented at North of England Ophthalmological Society (NEOS) Summer Meeting 2013, June 12; Chester, UK.

Date of Preparation: March 2014 UK/0062/2014

ALLERGAN ophthalmology

Upfront

Reporting on the innovations in medicine and surgery, the research policies and personalities that shape ophthalmology practice.

We welcome suggestions on anything that's impactful on ophthalmology; please email

mark.hillen@texerepublishing.com

See the Benefits of a Good Workout

Mice that take exercise exhibit slower retinal degeneration than those that don't. It could work for people too.

The usual reasons for going to the gym are to lose weight, keep fit, look younger and live longer; increasing your level of brain-derived neurotrophic factor (BDNF) doesn't figure. But in binding to its receptor, which is called TrkB, BDNF helps existing neurons to survive and encourages the growth and differentiation of new ones (it promotes muscle growth and repair too).

It is hard to determine where BDNF is being expressed and by how much in humans after exercise, so most studies have been performed in mice and rats. It's long been known that exercise increases BDNF levels in rat brains, particularly in the hippocampus (1). What's new today is the finding in mice that moderate aerobic exercise helps to preserve the structure and function of nerve cells in the retina after damage (2).

A group of researchers from the Atlanta VA Center for Visual and Neurocognitive Rehabilitation and Emory University demonstrated this by having mice run on a treadmill at a speed of ten meters per minute for one hour, five days a week for two weeks before exposing both exercised and inactive mice to toxic bright light (10,000 lux for four hours). This resulted in a 75 percent loss of both retinal function and the number of photoreceptor cells in the inactive mice. However, the active, exercised mice exposed to bright light had twice the retinal function and twice the number of photoreceptor cells than their inactive littermates (Figure 1).

The protective effect was mediated by BDNF. Exercise caused retinal BDNF protein levels to increase by 20 percent compared with inactive mice. Repeating the experiment, but this time administering systemic injections of a TrkB receptor antagonist to the mice, reinforced this observation. When the effects of BDNF were blocked in this way, toxic light exposure affected retinal function and photoreceptor counts equally in active and inactive mice – the protective effects of exercise were gone (Figure 1).

What does this mean for humans? Developed nations have a rapidly aging demographic, and age-related macular degeneration (AMD) is one of the leading causes of blindness in the elderly. Exercise may mitigate or delay the effects of the AMD disease process. "This is the first report of simple exercise having a direct effect on retinal health and vision," says Emory's Machelle Pardue. "This research may one day lead to tailored exercise regimens or combination therapies in treatments of blinding diseases."

Michelle Ploughman, a neuroscientist based at Memorial University of Newfoundland, Canada explained that, "These findings further our current understanding of the neuroprotective effects of aerobic exercise and the role of BDNF. People who are at risk of

macular degeneration or have early signs of the disease may be able to slow down the progression of visual impairment." *MH*

Reference

1. *N.C. Berthold et al., "Exercise primes a molecular memory for brain-derived neurotrophic factor protein induction in the rat hippocampus", Neuroscience, 133, 853-861 (2005).*
2. *E.C. Lawson et al., "Aerobic exercise protects retinal function and structure from light-induced retinal degeneration", J. Neurosci., 34, 2406-2412 (2014).*

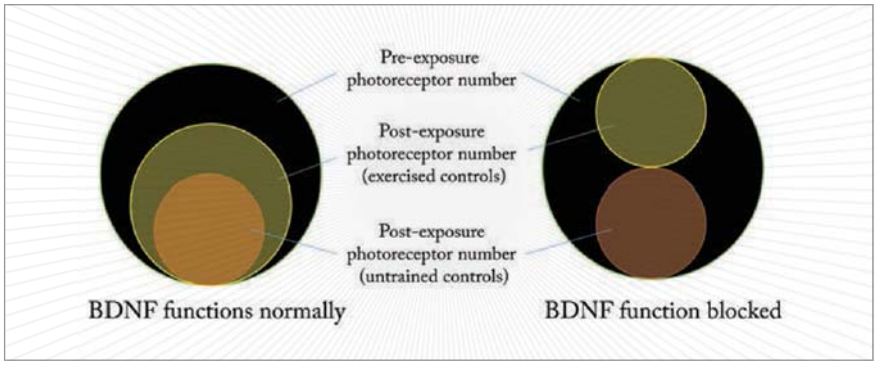


Figure 1. Representative proportion of photoreceptors before and after toxic bright light exposure. Mice that exercised were spared significant amounts of photoreceptor loss compared with non-exercised control mice. BDNF inhibition removed the protective effect of exercise.

Dua for the Price of One

The finding that the core of the trabecular meshwork is an extension of Dua's layer may have significance in understanding and treating glaucoma.

Last year, a new layer of the cornea was described by Harminder Dua and colleagues at Nottingham University, UK. Comprised of thin collagen plates, "Dua's layer" is just fifteen microns thick yet it is incredibly tough. The finding had implications for corneal surgery and the understanding of corneal diseases (1). At the time, we asked the eminent professor, "Do you think we now know the complete anatomy of the eye, or is there more to be discovered?" His reply was, "Well, as a follow-up to this paper, we will be introducing another little surprise."

We know have that "little surprise". Using electron microscopy on human donor eyes, the Nottingham team examined Dua's Layer at the extreme periphery of the cornea. There, they discovered, the collagen fibers of the layer branch out to form a meshwork. The core of the trabecular meshwork is in fact an extension of Dua's Layer (2).

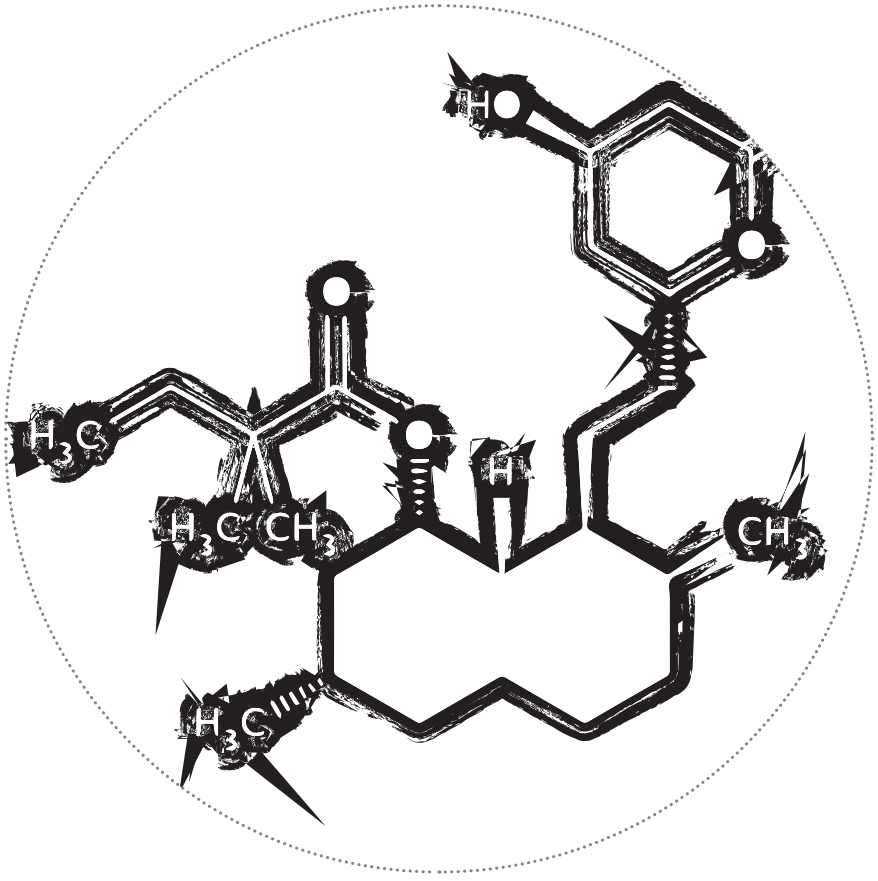
"Many surgeons who perform lamellar corneal transplant recognize this layer as an important part of the surgical anatomy of the cornea," Dua says. "This new finding resulting from a study of the microanatomy of the periphery of the layer could have significance beyond corneal surgery."

It certainly opens up a new avenue of research into glaucoma, where it may offer new clues as to why the trabecular meshwork malfunctions in this sight-robbing disease. Moorfield-based David Garway-Heath, the International Glaucoma Association Professor of Ophthalmology said of the discovery, "Trabecular meshwork dysfunction that results in impaired outflow of aqueous humor is the main cause of raised IOP in glaucoma. Knowledge of the anatomical origin and organization of the trabecular meshwork will aid our understanding of its function and may stimulate new research into modulating trabecular meshwork function which, in turn, could lead to new therapies". *MH*

References

1. *"To Galen, Mundinus and Tulp, Add Dua", The Ophthalmologist, 1, 40–41 (2013)*
2. *H. Dua et al., "The Collagen Matrix of the Human Trabecular Meshwork is an Extension of the Novel Pre-Descemet's Layer (Dua's Layer)", Br. J. Ophthalmol. (2014). Epub ahead of print. doi:10.1136/bjophthalmol-2013-304593.*

Statins Protect Elderly Against Macular Degeneration



If you're aged over 68 years, then statins significantly reduce your risk of developing AMD; it has no impact on younger age groups.

While the treatment of wet age-related macular degeneration (AMD) has been a success story over the last decade, dry AMD treatment has stalled and little progress has been made in preventing AMD from developing in the first place.

Against this background, a team of researchers from the University of California, San Francisco, and Stanford University examined the US National Health and Nutrition Examination Survey (NHANES) dataset to determine whether statin use exhibited a protective effect against AMD (1).

Why statins? Classically, they are used to reduce serum lipoprotein levels, treating dyslipidaemias like atherosclerosis. Statins have shown great benefit in reducing cardiovascular mortality and morbidity, and have prevented (or delayed) millions of heart attacks since their introduction – cardiologists half-joke that they should be offered as a condiment at fast-food restaurants (2).

Many of the risk factors that are associated with cardiovascular disease are also risk factors for AMD, including cigarette smoking, elevated serum cholesterol and hypertension. So the authors set out to determine if lipid-lowering medications exert a preventive effect in AMD development. To find out, they examined 5,604 patients aged over forty years from the NHANES dataset for the presence of AMD, statin use, comorbidities and health-related behaviors like cigarette smoking.

The mean age of patients without a history of AMD was 55 years, and with AMD was 68 years. This stratification by age provided an important insight: after adjustment for confounding factors, individuals aged 68 years or more who took statins were significantly less likely to have AMD than those who did not (odds ratio: 0.64, p=0.002). In those aged between 40 and 67 years, no significant association was found between the prevalence of AMD and statin consumption.

The authors concluded that "statin intake […] significantly lowers the odds for AMD in individuals 68 years of age or older". As dry AMD was the more common form of the disease in the study, perhaps the authors' findings may open a new therapeutic avenue for the treatment of dry AMD? *MH*

References

1. *D.T.Q. Barbosa et al., "Age-related macular degeneration and protective effect of HMG Co-A reductase inhibitors (statins): results from the National Health and Nutrition Examination Survey 2005–2008", Eye (2014). Epub ahead of print, doi: 10.1038/eye.2014.8.*
2. *E.A. Ferenczi et al., "Can a Statin Neutralize the Cardiovascular Risk of Unhealthy Dietary Choices?", Am. J. Cardiol, 106, 4, 587–592 (2010). doi: 10.1016/j.amjcard.2010.03.077.*

Aspirin not Linked to AMD

Previous studies linked aspirin use with age-related macular degeneration, but new data suggest otherwise: aspirin is innocent of all charges.

When links between age-related macular degeneration (AMD) and cardiovascular disease are discussed, the conversation is usually centered around statins; scrutiny of aspirin is less prominent. Yet, barring contraindications, almost every patient receiving treatment for cardiovascular disease gets a daily (low) dose of aspirin – it's estimated that 40,000 tons of the drug are consumed each year. Consequently, many patients with AMD also receive aspirin, begging the question of whether aspirin causes AMD.

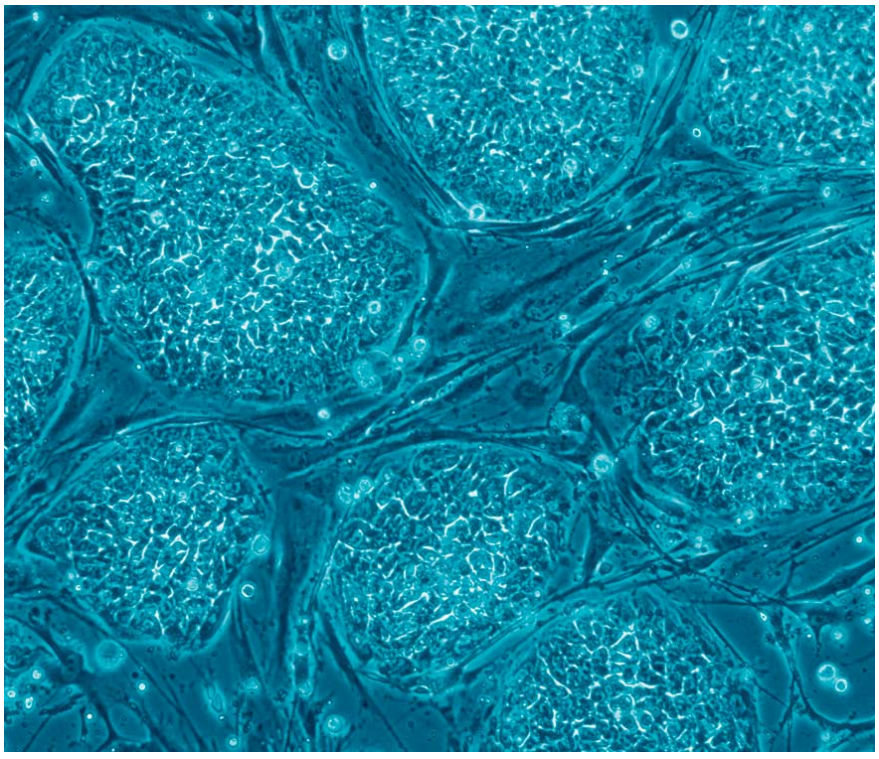
The data to date have been inconclusive. Randomized trial data suggests that aspirin protects against the development of AMD (1,2) while observational studies have suggested that aspirin use raises (3), reduces (4) or has no impact (5) on AMD progression.

Now Emily Chew has stepped in. Chew is the Deputy Director of Division of Epidemiology and Clinical Applications at the National Eye Institute in Bethesda, MD, USA, and the Chair of the Age-Related Eye Disease Study 2 (AREDS 2) study. A large multi-center randomized trial involving approximately four thousand patients, AREDS2 was designed to determine whether certain dietary supplements could help treat AMD and cataracts. Helpfully, analysis of the associated demographic data collected from the trial also generated insight into the impact of aspirin on AMD.

Chew presented the results of the investigation at the recent Angiogenesis, Exudation, and Degeneration 2014 meeting (6). It compared just over 1,900 aspirin users with matched control non-aspirin users, and examined the propensity of each group to develop AMD. No link between aspirin use and the development of AMD was found. Thus, patients receiving chronic aspirin therapy shouldn't feel unduly worried about developing AMD; the evidence suggests that they're not at increased risk. *MH*

References

1. *W.G. Christen et al., "Low-dose aspirin and medical record-confirmed age-related macular degeneration in a randomized trial of women", Ophthalmology, 116, 2386–2392 (2009).*
2. *W.G. Christen et al., "Age-related maculopathy in a randomized trial of low-dose aspirin among US physicians", Arch. Ophthalmol., 119, 1143–1149 (2001).*
3. *G. Liew et al., "The association of aspirin use with age-related macular degeneration", JAMA Intern Med., 173, 258–264 (2001).*
4. *H.L. Wilson et al., "Statin and aspirin therapy are associated with decreased rates of choroidal neovascularization among patients with age-related macular degeneration", Am. J. Ophthalmol., 137, 615–624 (2004).*
5. *R. van Leeuwen et al., "Is medication use associated with the incidence of early age-related maculopathy? Pooled findings from 3 continents", Ophthalmology, 111, 1169–1175 (2004).*
6. *E.Y. Chew, "AREDS2 Update", Oral Presentation at the Angiogenesis, Exudation, and Degeneration 2014 meeting, February 8th 2014, Miami, Florida.*



STAP! Not so fast

The new method to produce stem cells has run into difficulties in the form of image irregularities and the failure of other labs to reproduce the findings.

Last month (1), we reported on a scientific breakthrough with major consequences for stem cell-based therapies: a novel method to create pluripotent – even totipotent – stem cells. Published in two Nature papers, the method described bathing adult cells in a weak acid to produce "stimulus-triggered acquisition of pluripotency" (STAP) stem cells (2,3). The technique was notable not only because of the apparent ease of stem cell production, but also because it didn't require genetic manipulation to do so. But, two major issues with the articles are causing disquiet: problems with images and reproducibility issues.

Haruko Obokata has the image problem. She's the first author on the Nature STAP stem cell articles, and also on another stem-cell paper from 2011 (4). It's alleged that in this earlier paper a figure that apparently demonstrates the presence of one stem-cell marker was inverted and used again to demonstrate the presence of a different stem-cell marker (5). It has been suggested that in one of the Nature papers (2) a similar type of duplication has been used; images of two placentas "meant to be from different experiments look strikingly similar" (5). Furthermore, there are claims that an image of DNA separated on a gel has been manipulated, with a lane being spliced in to the image (3).

As if this wasn't bad enough, at least ten prominent stem cell researchers from other labs are having difficulties in reproducing the technique (5), contrasting starkly with last month's headlines about how simple it had become to make stem cells. Part of the issue here may be that a comprehensive protocol for the generation of STAP stem cells hasn't yet been published. But Teruhiko Wakayama, one of the senior authors of the STAP stem cell article, who was able to reproduce the technique prior to publication – now cannot (5). On the other hand, Wakayama's fellow senior author, Charles Vacanti, reports that he hasn't had any problems repeating the experiment. But rather that explain the finer details of his method, it's reported that he will let Obokata supply the protocol, "to avoid any potential for variation that could lead to confusion" (4).

Working with stem cells is challenging, and every laboratory is different, so some subtleties in the technique may have been lost in translation. For now, though, STAP stem cell therapy for ocular disease looks rather less likely than it did a month ago. *MH*

References

1. *"STAP in the name of love," The Ophthalmologist, 2, 10 (2014).*
2. *H. Obokata, et al., "Bidirectional developmental potential in reprogrammed cells with acquired pluripotency", Nature, 505, 676–680 (2014).*
3. *H. Obokata, et al., "Stimulus-triggered fate conversion of somatic cells into pluripotency", Nature, 505, 641–647 (2014).*
4. *H. Obokata, et al., "The potential of stem cells in adult tissues representative of the three germ layers", Tissue Eng Part A, 17, 607–615 (2011). doi: 10.1089/ten.TEA.2010.0385.*
5. *D Cyranoski, "Acid-bath stem-cell study under investigation", Nature News (2014). http://www.nature.com/news/acid-bath-stem-cell-study-under-investigation-1.14738#/.*

All is Not Lost

Vision training can restore some of the sight lost to glaucoma.

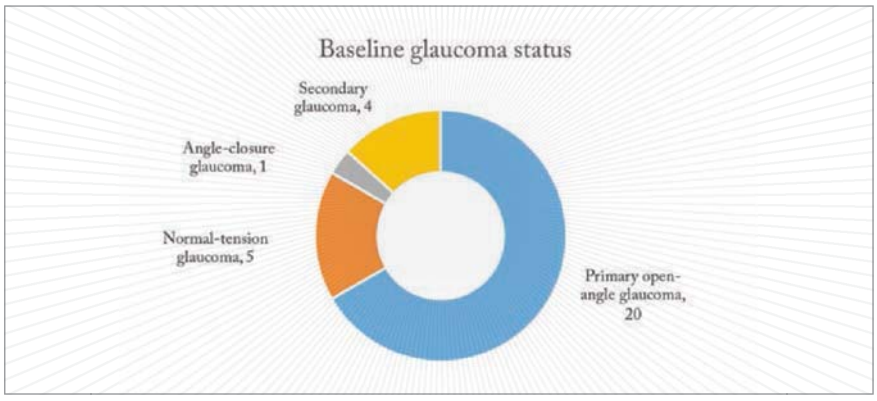


Figure 1. Baseline glaucoma type and patient number.

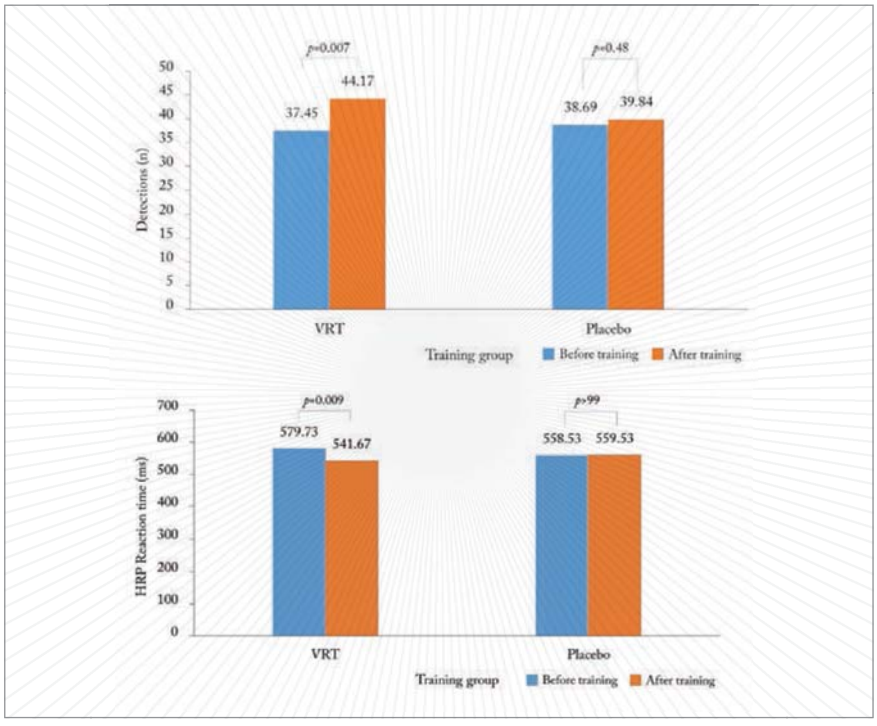


Figure 2. Before and after results for glaucoma vision restoration training (VRT) versus placebo training for (a) detection rates and (b) reaction time to on-screen stimuli.

Glaucoma is not just chronically elevated intraocular pressure levels; it's also a pernicious neurodegenerative disease. The death of retinal ganglion cells, structural changes at the optic nerve head and optic nerve lesions are all features of the disease. And it doesn't necessarily stop there: optic nerve head damage can beget further degeneration in the retina, and onwards into the brain (1).

However, vision loss in glaucoma may be reversible, according to Berhnard Sabel and Julia Gudlin, researchers at the University of Magdeburg in Germany. They performed a randomized, prospective, double-blind clinical trial of thirty patients with glaucoma, who were assigned to receive either glaucoma vision restoration training (VRT) or placebo. The baseline glaucoma status of the entire group is shown in Figure 1. Sabel and Gudlin used computer-based high-resolution perimetry (HRP) before training began, to measure the patients' natural visual field variability. An eye tracker was used during HRP to determine fixation stability.

The VRT involved a computerized luminance increment stimulus system; patients responded to visual stimuli by pressing a spacebar. Placebo VRT used a different protocol – a line segment bar was presented in one of four random orientations; patients were instructed to press a key when the bar was seen. Training was provided for a 30 minute period, twice a day, for three months.

VRT was associated with significant improvements in HRP detection rates and reaction times; placebo-training was not (Figure 2). Sabel and Gudlin also measured detection changes in the untrained eyes as a control for the experiment, and found no significant changes for either treatment group. VRT training was also associated with improvements in white-on-white and blue-on-yellow perimetry visual field tests.

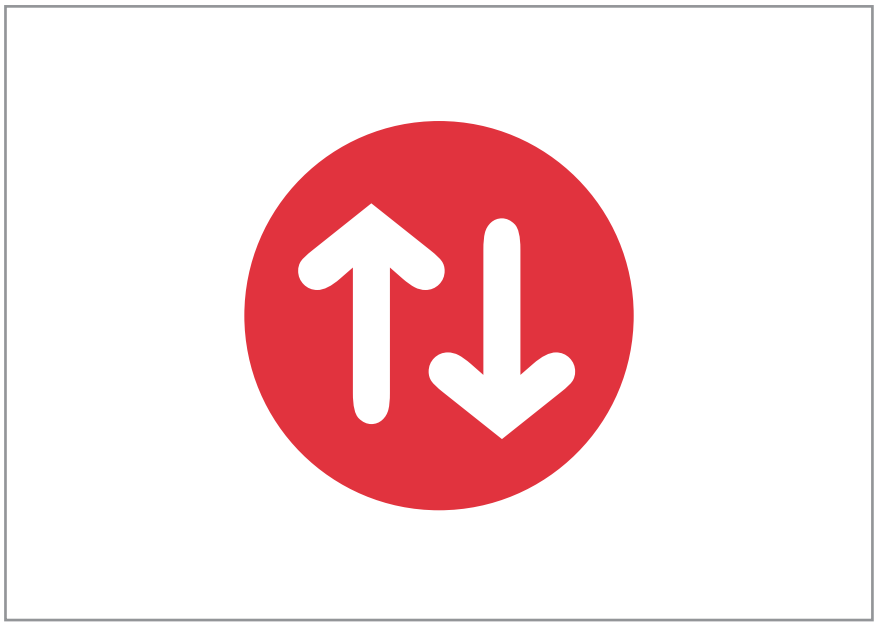
Although the patient numbers in this trial were small, and the mechanism(s) remain undetermined, it looks likely that the brain is exhibiting plasticity in its visual system in response to the VRT to make best use of the visual signal it receives. Whether these improvements are clinically significant and whether patients will comply with an hour-a-day visual training system remains to be seen, but it does show that glaucoma is not totally a story of declining vision after all. *MH*

References

1. *E.E. Chang, J.L. Goldberg, "Glaucoma 2.0: Neuroprotection, Neuroregeneration, Neuroenhancement", Ophthalmology, 119, 979–986 (2012).*
2. *B.A. Sabel, J.Gudlin, "Vision Restoration Training for Glaucoma: A Randomized Clinical Trial", JAMA Ophthalmol., (2014). Epub ahead of print, doi: 10.1001/jamaophthalmol.2013.7963.*

Big in Japan

Acucela prices its initial public offering on the Tokyo Stock Exchange at $162M.



The Seattle-based biotech Acucela is shunning Wall Street to sell 9.2 million shares of stock in an initial public offering (IPO) on the Tokyo Stock Exchange. At $17.65 per share, it should raise $162.3 million.

Although there's no precedent for Acucela's move, there are a couple of possible reasons as to why this US biotech firm has chosen to float in Tokyo. First, the founder and CEO of Acucela, Ryo Kubota, is Japanese. Second, Acucela has many ongoing collaborations with Tokyo-based Otsuka Pharmaceuticals Co. The companies suffered a setback last year when a dry eye therapy that they were co-developing, rebamipide, failed in phase III. But Acucela has a pipeline that investors are likely to believe in. It includes emixustat (ACU-4429), an oral treatment for dry AMD that's currently in phase IIb/III trials and that has already received fast-track status from the FDA; and OPA-6566, a topical glaucoma therapy that's currently in phase I. *MH*

Business in Brief

Aflibercept gets approved by NICE, STAAR's Visian ICL with CentraFLOW gets approved in Japan, and rises and falls in Allergan and Alcon's revenues.

- Bayer/ Regeneron's aflibercept has been approved by the UK's National Institute for Health and Care Excellence (NICE) as a treatment option for visual impairment due to macular edema secondary to central retinal vein occlusion. This follows the recent acceptance of the FDA to perform a standard review of aflibercept for a supplemental Biologics License Application (sBLA) for the same indication.
- STAAR Surgical announced that its Visian Implantable Collamer Lens with CentraFLOW technology has been approved by the Japanese Ministry of Health, Labor and Welfare. This follows news that STAAR's total revenue for 2013 grew by 13 percent compared with 2012's figure.
- Alcon's operating income for in 2013 fell by 16 percent to $1.2 billion, over its income in 2012, despite a rise in sales. The fall in income was ascribed to integration and restructuring costs.
- Allergan had a good fourth quarter of 2013, reporting $1.66 billion in total product net sales in that period – a 14.6 percent increase compared with the corresponding quarter in 2012.
- TRACON Pharmaceuticals and Santen Pharmaceutical have entered into an exclusive agreement for the development and global commercialization of TRACON's range of antibodies to endoglin (a endothelial cell receptor that essential to angiogenesis) in opthalmology. Santen is making a $10 million upfront payment, and will find all future global development and commercialization costs, and pay TRACON certain milestone and tiered royalty payments. *MH*

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World Travel for a Write up of Your Work

The Ophthalmologist Travel Award represents a great opportunity: the chance of a free trip to the AAO 2014 congress in Chicago – flights, accommodation, and congress registration fees, in return for a chronic DME case study.

If you're a retina specialist, you'll more likely than not to see patients with diabetic macular edema (DME) on a daily basis. Lasers and anti-VEGF therapy have transformed outcomes within a generation, but the former technology isn't appropriate for all cases, and the latter can eventually lose efficacy – or in some cases, will never work well at all. So what can be done for these patients, when their macula is thickened or has a cystoid morphology, and the usual drugs don't work?

We want to know what you do for these patients. First, the methods by which you diagnose these cases: the inflammatory markers you screen, the scale you use to measure visual acuity, the OCT images you take and what you look for. Second, how you treat the edema. How long do you persist with anti-VEGF therapy; have you tried triamcinolone? It's those sort of things we would love to hear about. We want to work out what truly is the current best practice for the assessment and treatment of DME. How? By asking ophthalmologists to submit case studies that detail how you identify and manage long-standing refractory DME.

What's in it for you? The chance to win one of five Travel Awards – we pay the winners' airfares, accommodation and delegate fees to let you to attend the AAO 2014 annual meeting in Chicago in October. There are ten second prizes of having your case study featured on The Ophthalmologist website. The closing date for this competition is March 31st, so there's not much time to ensure your great work has a chance of a great reward. *MH*

Enter online at:
theophthalmologist.com/travel-award
Sponsorship for these travel awards, including funding for travel, accommodation, and registration, is kindly provided by Alimera Sciences Limited.

Reinventing the Eyedrop: the story of Cationorm

Making an optimal eyedrop formulation has always been a major challenge; compromises had to be made. Nanodroplet emulsion technology has changed that. Here's how.

By Mark Hillen

Dry eye disease is a common disorder, that's estimated to affect between ten and thirty percent of patients aged over fifty years (1). Many treatment options exist, but almost all come in one form: topical eyedrops.

Historically, formulating those eyedrops has been a problem (2). Making an eyedrop that can deliver effective and long-lasting dry eye symptom relief to the surface of the eye has been a particular challenge. Aqueous formulations wash away quickly and cannot be used as a vehicle for lipophilic drugs. Emulsions can be; as surfactants can be used to bind together the hydrophilic with hydrophobic oil-based vehicles. However, the overall electrostatic charge of the emulsion matters. Mucins on the surface of the eye are negatively charged – so anionic emulsions will be actively repelled. By the same token, cationic emulsions are actively attracted, dramatically increasing retention time and improving the spreading of the emulsion across the eye surface.

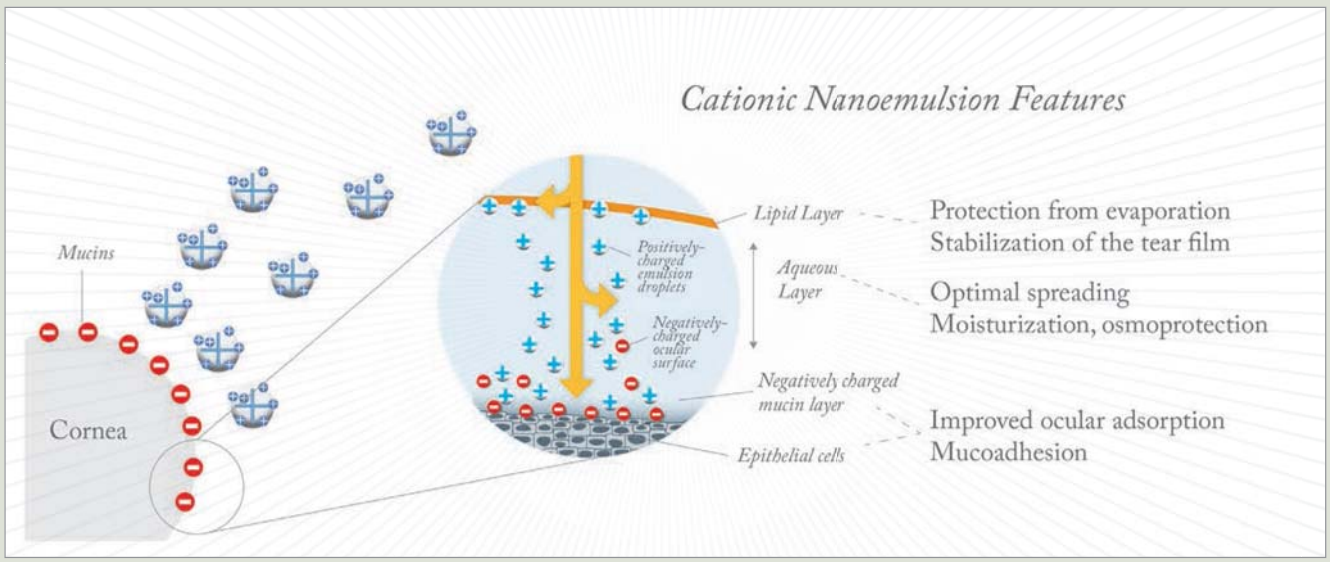
The most effective emulsion coverage requires nano-sized droplets. As the droplet size reduces, the surface area to volume ratio increases, meaning a greater total surface area of the emulsion is exposed to the ocular surface. In essence, the eye sees more of the eyedrop this way.

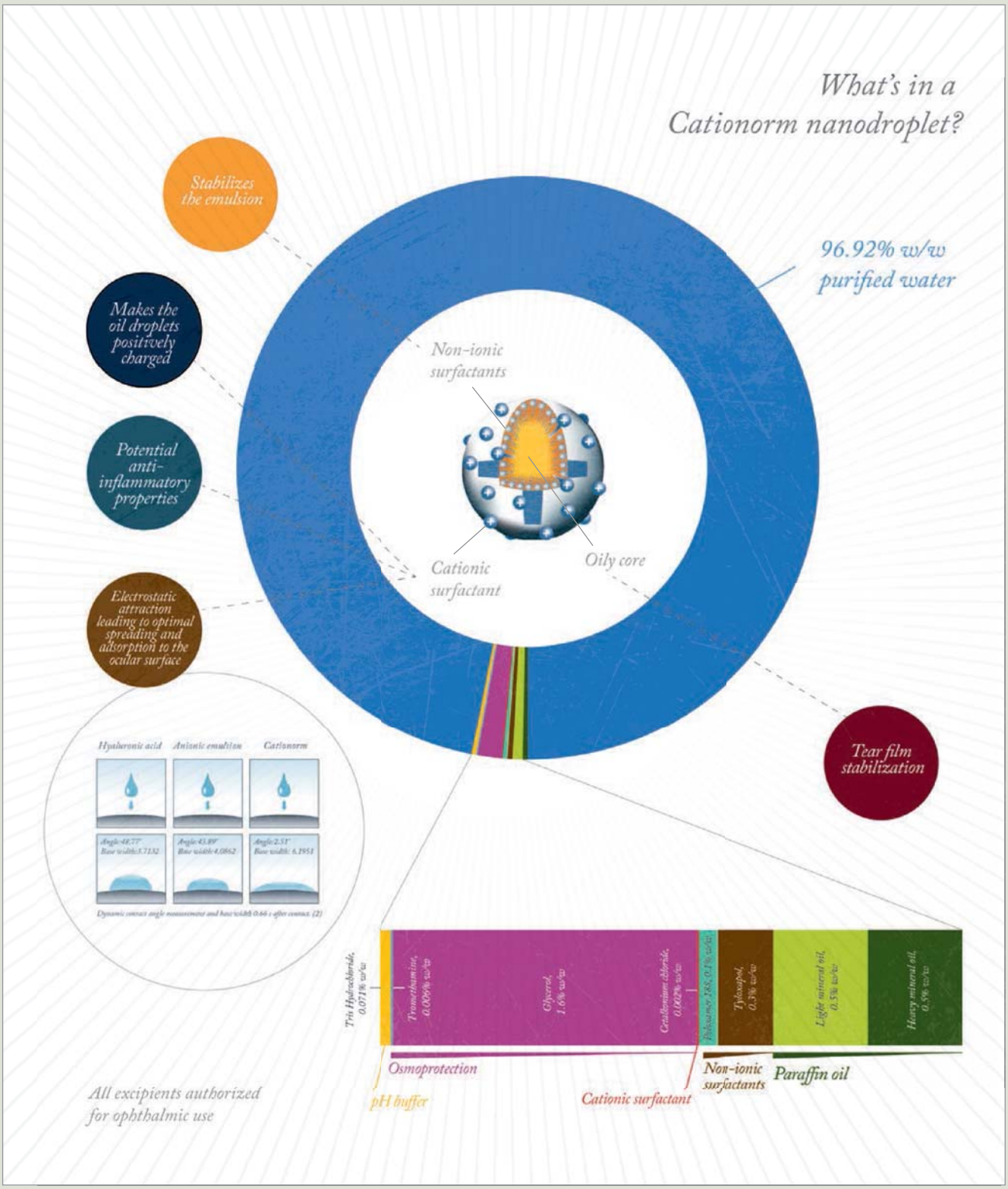
But there is a challenge in developing this technology: the list of excipients that are acceptable to use in ophthalmic eyedrop formulations is painfully short. Despite those potential setbacks, researchers from Santen's Novagli Innovation Center in Evry, France have managed to make that cationic nanodroplet vehicle: the Novasorb technology.

The vehicle alone is being used therapeutically today in Europe, and is being marketed by Santen under the name Cationorm. Notably, Cationorm has many properties that are protective of all three layers of the tear film: the oily core protects and replenishes the lipid layer and reduces evaporation; the glycerol present has an osmoprotective effect on the aqueous layer, and the eyedrops are held there for longer by electrostatic attraction.

References

1. *"The Epidemiology of Dry Eye Disease: Report of the Epidemiology Subcommittee of the International Dry Eye WorkShop (2007)", Ocul. Surf. 5,93–107 (2007).*
2. *F. Lallemand et al., "Successfully Improving Ocular Drug Delivery Using The Cationic Nanoemulsion, Novasorb", J. Drug Deliv., 2012: 604204 (2012).*




What's in a Cationorm nanodroplet?
Stabilizes the emulsion
Makes the oil droplets positively charged
Potential anti-inflammatory properties
Electrostatic attraction leading to optimal spreading and adsorption to the ocular surface
96.92% w/w purified water
Non-ionic surfactants
Cationic surfactant
Oily core
Tear film stabilization
Hyaluronic acid
Anionic emulsion
Cationorm
Angle:48.77°
Base width:5.7132
Angle:43.89°
Base width:4.0862
Angle:2.51°
Base width: 6.3951
Dynamic contact angle measurement and base width 0.66 s after contact. (2)
Tris Hydrochloride, 0.071% w/w
Tromethamine, 0.006% w/w
Glycerol, 1.6% w/w
Cetalkonium chloride, 0.002% w/w
Tyloxapol, 0.3% w/w
Light mineral oil, 0.5% w/w
Heavy mineral oil, 0.5% w/w
Osmoprotection
pH buffer
Cationic surfactant
Non-ionic surfactants
Paraffin oil
All excipients authorized for ophthalmic use

A Vision Timebomb

Although baby boomers may be in a state of denial regarding their own aging, ophthalmologists know differently. In particular, four diseases of the ageing eye comprise a demographic and economic timebomb. What will the consequences be of that bomb going off, and how might it be defused?

By Mark Hillen

At a Glance

- *Baby boomers are reaching old age*
- *They are causing a sharp spike in the number of cases of certain eye diseases*
- *Current therapeutic strategies are inadequate, especially if early signs of disease are missed*
- *The burden on ophthalmology services will be severe*
- *Strategies to address this impending disaster are urgently required*

In the year 2000, there were 69 million people aged over 80 years in the world, according to United Nations data (1). By 2050, it is estimated that this number will have grown to 379 million, a more than fivefold increase.

In Western countries, this increase is accounted for by "baby boomers", the generation born between the mid-1940s and mid-1960s – essentially the spike in births following World War II. Baby boomers constitute a demographic timebomb, one that's close to detonation: an unprecedented level of age-related disease will occur over the next three decades or so.

This article examines the impacts that aging baby boomers will have on the practice of ophthalmology.

Boomers in sickness and health

Earlier in their lives, baby boomers were, according to Wikipedia, "the wealthiest, most active, and most physically fit generation up to that time, and amongst the first to grow up genuinely expecting the world to improve with time. They were also the generation that received peak levels of income, therefore they could reap the benefits of abundant levels of food, apparel, retirement programs, and sometimes even 'midlife crisis' products."

Today, the boomers refuse to accept that they're getting old (Figure 1). The phrase "forty is the new thirty" became popular when they hit their fourth decade and their current mantra is "seventy is the new fifty". In some respects, this is absolutely true. The lives of baby boomers have been far easier than those of their forebears: for them, physical exertion became a leisure activity or an occasional chore in order to keep fit rather than a way of life, and if certain parts of the body did wear out, replacements were available. Widespread vaccination during infancy shut out the ravages of diphtheria, tetanus, whooping cough and polio, and boomers have benefited from antibiotic therapy throughout their lives, mostly avoiding infection-related morbidity and mortality.

The eye, in some respects, is a success story too. There has been a rush to refractive surgery as tens of millions each year across the world choose to have laser vision corrective surgery; clear lens exchange is a huge market, and there are a number of presbyopia-correcting interventions with sales projections that are in the stratosphere (As a rule, these are to avoid wearing spectacles, something that in baby boomers' minds is associated with old age). In most cases, the refractive outcomes in patients with premium IOLs is spectacular: a cloudy lens is removed and replaced with a clear lens that can also correct for astigmatism.

Look beyond or, more accurately, behind the lens and the situation is far less positive. Ocular diseases of senescence gradually robbed the baby boomers' parents of their sight and most of those diseases are still with us. That these conditions can't be so easily kicked down the road or cured should alarm not just baby boomers but their children and their children's children. Even with the best standard of care, the therapeutic options that work for these posterior segment diseases are not effective indefinitely. At the moment, it seems inevitable that a large proportion of baby boomers will end up with visual impairment – and the societal burden will skyrocket as their visual impairment progresses.

This article assess just how bad the situation is, and looks at the chances of medical science coming up with effective therapeutic interventions in time to avoid large-scale strife. The four eye diseases that present the biggest challenges to the baby boomer generation, namely age-related macular degeneration (AMD), diabetes-related eye disease, cataracts and glaucoma are addressed in turn.

Age-related macular degeneration

AMD is the leading cause of blindness in developed countries, and the third-leading cause in developing countries. Globally, between 20 and 25 million people are affected by AMD, and the World Health Organization (WHO) estimates that eight million people have severe blindness as a direct result of the disease (1). It is projected that the number of people with some form of AMD will double between now and 2050 (1).

Tools to treat AMD are limited. Wet AMD is addressed reasonably effectively with anti-VEGF therapy, lasers and even low-voltage x-ray therapy, but it accounts for only 10 percent of all AMD cases. Very little can be done to treat the 90 percent of patients with dry AMD, beyond a recommendation to take high doses of vitamin supplements and antioxidants (2).

Risk factors for the development of AMD have been identified, raising the possibility of avoiding the disease. Unfortunately, however, many of the factors aren't modifiable. One, advanced age, clearly comes to us all. Hereditary elements represent some of the greatest risk factors (3). Numerous gene mutations and deletions have been described (4), but the interplay of genes in building an eye is majestic in its scale and there are the complexities of gene silencing and post-transcriptional modifications to contend with, even before any protein has been made. Replacing a gene (or genes) in early life may help (or may not) but it holds little hope for our baby boomers as it seems highly unlikely that simply adding a single gene to their senescent cells in the macula will induce retinal rejuvenation or vision improvement. However, the substantial amount of research on the topic may provide promising leads for tackling the genetic susceptibility to AMD.

There are some modifiable risk factors, including smoking, hypertension, obesity, cholesterol, fat intake and oxidative stress (3) – an unfortunate cocktail of comorbidities that baby boomers

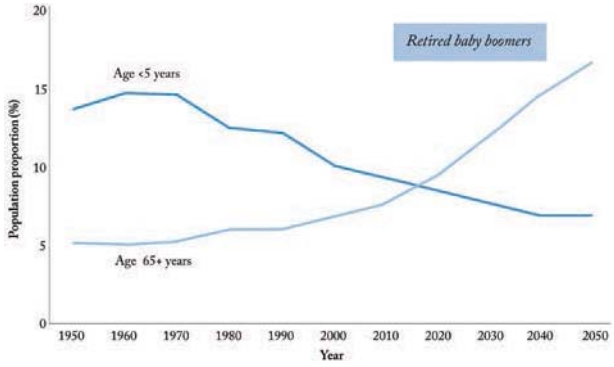


Figure 1. Young Children and Older People as a Percentage of Global Population: 1950-2050. United Nations. World Population Prospects: The 2010 Revision. Available at: http://esa.un.org/unpd/wpp.

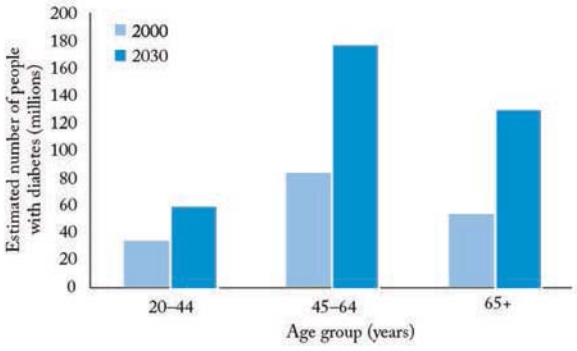


Figure 2. Estimated number of adults with diabetes by age group in the year 2000, and projections for the year 2030 (WHO data).

present with all too regularly. Interventions here, should they work, would be highly effective and cost-effective. Smoking, hypertension and obesity are massive epidemics in in their own rights, and have been targeted by other medical specialties with countless interventions and initiatives, without overwhelming success. Hypertension and cholesterol are well managed by drugs – but this has been the case for decades, and AMD levels are still inexorably rising. For the other risk factors, new approaches to addiction and dietary management would be most welcome.

The practical implications of the rise in AMD patient numbers are being felt everywhere. Retina clinics are massively oversubscribed, with specialists often working far longer than their allotted hours to get through the case loads, in part because intravitreal ranibizumab or aflibercept injections are time-consuming, and in many cases, need to be administered monthly.

Improved ways of treating wet AMD that involves fewer clinic visits are needed, whereas novel approaches for dry AMD are a desperate requirement.

Diabetes-related eye disease

The demographics of diabetes are profoundly worrying. The prevalence for all age-groups worldwide was estimated to be 2.8 percent in 2000 and is projected to reach 4.4 percent by 2030 (5). The elderly are affected disproportionately in these projections, with the hardest hit group of all being the baby boomers (see Figure 2).

Diabetes doubles a person's risk of glaucoma and it is also a major risk factor for corneal problems, cataract and macular edema (6–8). Furthermore, approximately two-thirds of people with diabetes have some form of diabetic keratopathy, which can include recurrent erosions, ulcers, corneal edema, and delays in wound healing (6–9). Of patients that do develop a keratopathy, those with diabetes are likely to experience a more severe form, respond to treatment less well, and recover more slowly (6).

Glucose is the fuel that drives all cellular respiration. It is a highly reactive aldehyde and some of the by-products of its reactions can damage cells. For short-lived cells that are routinely replaced that's okay, as they're not around long enough for significant damage to occur. But in long-lived cells like neural (and retinal) tissues and in stable protein structures like the crystallins in the lens and the cornea, it causes cumulative deterioration. Tissues exposed high levels of glucose, such as the vasculature and the pancreas also sustain damage. Indeed, the root cause of the retinal and choroidal damage in diabetes is this vascular and local tissue damage, resulting in inflammation.

The effectiveness of current therapeutic interventions is variable. Cataract and glaucoma are dealt with separately below. Diabetic keratopathies are treated in the same manner as any other keratopathy from a non-diabetic origin, with topical therapies, scraping or laser therapy, or corneal transplantation, as appropriate. The issue with the last of these interventions is that there is a shortage of corneas to transplant today: it seems highly unlikely enough will be donated for transplantation in 2030 to cope with the demand. For DME, treatment with lasers, anti-VEGF therapies, or long-acting steroid implants can be effective. Just like their use in wet AMD, anti-VEGF drugs tend to be administered monthly in order to inhibit the macular neovascularization that results in the swelling and distortion of the macula. But again, this requires monthly visits of patients to ophthalmology clinics and that is something that's not going

to be sustainable. If anti-VEGF therapy fails, the next line of treatment looks like being intravitreally-implanted steroids. The steroids act to reduce the macular swelling, and they are now available in slow-release formulations that allow therapeutic doses to be administered for as long as three years, obviating the need for monthly intravitreal anti-VEGF injections. On the other hand, the use of steroids raises risks other adverse events, primarily cataracts. These can be dealt with, but as we'll see in the next section, those that do develop cataracts will have to join the queue for treatment.

Cataract

Despite the earlier paean to the outcomes with cataract surgery, the fact remains that cataracts present a massive and worsening healthcare and societal problem. Of the 39 billion people today that are blind, almost 18 million are so because of cataracts, with the burden disproportionately affecting developing countries.

Will the burden overwhelm the capacity to cope? It's certainly a concern. Delaying the onset of cataract formation by a decade (or by otherwise avoiding the associated vision loss) could almost halve the demand for cataract surgery (10,11).

In the absence of any pharmaceutical cataract prophylactics, the possibility of adjusting risk factors has taken center stage. Age plays a role, as do genetic factors (particularly in pediatric cases), but these are essentially unmodifiable. Radiation is a better proposition. X-ray, microwave and ultraviolet (UV) light exposure – particularly UV-B radiation – have been shown to cause cataracts (12–15). UV-B exposure can be sharply reduced easily and cheaply with sunglasses, and evidence exists that wearing sunglasses from an early age protects against cataract formation. However, ask any parent how difficult it is to make children wear sunglasses for extended periods on sunny days… Smoking is a risk factor, calling attention once more to the challenges of delivering effective public health interventions; it is incredibly difficult to get smokers to kick the habit.

If lifestyle modification can't be implemented, what alternative methods are there for delaying cataract formation? For a while, it seemed that antioxidant dietary supplements might delay or prevent cataract formation, but this proved not to be the case after bigger and better evaluations. So, short of a drug that protects the crystallin in the lens from becoming opaque (or replacing the crystallin with a functional and transparent equivalent), it would appear that an awful lot of baby boomers will be lining up for cataract surgery.

Clinics must set up to cope with this influx of patients. Increasing patient throughput can help, although it is notable that femtosecond lasers procedures currently take longer than manual capsulorhexis. One likely measure is that as many delegable responsibilities as possible will be performed by support staff, leaving the ophthalmologist to perform procedures in a robot-like, production-line manner. The stark alternative is a society filling with aging, visually impaired, and therefore profoundly disabled, people; people who have a treatable condition but must wait for years and years to be seen.

Glaucoma

According to the WHO, 60.5 million people across the globe suffer from glaucoma, with 1–2 percent of the world's population developing the diseases every year (16). Of the 60.5 million with glaucoma today, 8.4 million are blind. Most common is open-angle glaucoma, which afflicts 45 million people, 10 percent of whom are blind. However, in 2020 the total is projected to hit 80 million (16), most of whom will be baby boomers.

For such a pernicious, age-related disease, the future for baby boomers with glaucoma is not as gloomy as it sounds – as long as screening picks it up (Figure 3). In the UK, according to the International Glaucoma Association, all but 5 percent of patients with an early diagnosis of glaucoma retain useful sight for the remainder of their lives. This functional vision, as opposed to blindness, is incredibly valuable: it enables people with glaucoma to continue to function independently, and not being blind has huge societal and economic benefits. For patients diagnosed with advanced-stage glaucoma it's the opposite story: blindness is staved off for a short period, but functional blindness is not far away.

Making an early diagnosis is not easy, since; in glaucoma, sight loss is slow and gradual. Most cases of primary open-angle glaucoma are symptomatic only when significant vision loss has occurred (17). The pathogenesis is complex, involving multiple concurrent processes besides raised intraocular pressure (IOP). These include retinal pigment epithelial cell death, optic nerve damage, neurodegeneration that progressses into the brain, and even damage to anterior segment structures. Some presentations of glaucoma lack even elevated IOP (17).

The ocular changes can be observed by a combination of fundoscopy and optical coherence tomography (OCT) imaging, suggesting that these procedures should be added to tonometry for routine glaucoma screening (18). That's the good news; the bad news is that the overwhelmed healthcare systems of the future may be unable to devote the time and budget required to perform glaucoma screening. Thus, what is currently a highly treatable condition (with topical eyedrops or surgical intervention) that has good outcomes if caught early enough may insidiously become more severe. It may even rob an increasing

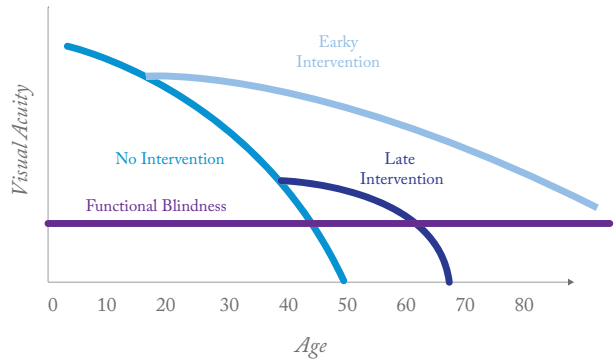


Figure 3. The impact of early therapeutic intervention in patients with glaucoma: effective vision is maintained for longer; late intervention staves off blindness for a period, and an absence of intervention leads to early blindness.

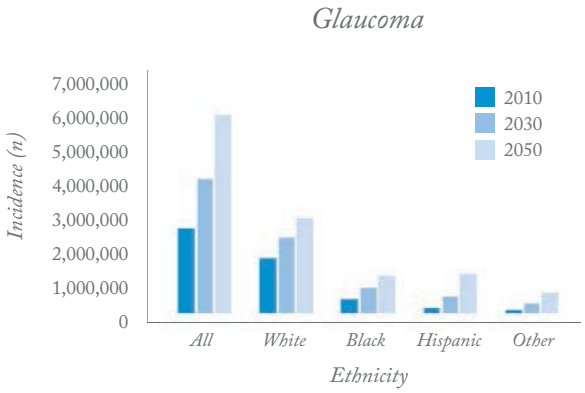


Figure 4. Estimated and projected glaucoma incidence in the USA for 2010, 2030 and 2050.

number of people of their sight for decades to come.

This disease lacks modifiable risk factors that can be attacked (19). The one possibility is that people with glaucoma are more likely to have hypertension, and blood pressure can be controlled with a variety of well-established medications. Trauma and other ocular diseases can also result in glaucoma, but these are almost impossible to mitigate against, and the remaining risk factors are genetic and ethnic (Figure 4). For the foreseeable future, the best hope for glaucoma control is early, effective screening.

Can this bomb be defused?

The sheer number of baby boomer patients is already remarkable; they have stretched the ophthalmology infrastructure to its limit. And that patient number is not yet close to peaking. At the least, a large number of boomers will receive sub-optimal treatment; at worst, the system will suffer catastrophic failure. Improving the infrastructure is absolutely essential.

Yet ophthalmologists will be in scarce supply. Currently, the numbers joining and leaving the profession are in balance, while the projected patient numbers demand a linear growth in the number. Given the many years of medical then postgraduate training that is required to create a new ophthalmologist, there seems to be no obvious solution to this part of the problem. Other areas of medicine are facing their own baby-boomer issues, suggesting that competition for physicians will be increasingly fierce.

What's certain is that the job of an ophthalmologist in ten or twenty years' time – or even in five years' time – will not look remotely like it does today. Any suggestion of inefficiency will have been removed and everything that can be delegated to support staff will have to be. Routine procedures will become even more production line-like than they are currently and face time with patients will be at a premium, something that is not conducive to best patient outcomes.

There will of course be positive developments that will help the field to cope, and perhaps even to thrive. Undoubtedly, effective new surgical interventions will be developed, and many new small-molecule drugs and biologics will be introduced. This is unarguably the most exciting and fast-paced period for both scientific progress and the development of new ophthalmology practice.

Big data will also play a role. The data-mining of entire nations' medical records may be controversial in terms of privacy, but it will help identify patients at risk of developing diseases like glaucoma, and it can automatically prompt these patients to go for a check-up. This in itself will save the sight of hundreds of thousands of baby boomers with glaucoma in the next decade.

In perhaps two decades from now it will be possible do incredible things with stems cells, including rebuilding tissues in vitro for subsequent surgical implantation, or spraying stem cells onto the retina to replace and repair diseased cells.

Retinal implants will be a mature technology in the not-too-distant future, and the daily advances being made in the meantime mean that they will soon be easier to implant and give better vision than they do today. However these are complex surgical interventions and may be destined only for the privileged few.

It is impossible to say where biomedical science will take us. Basic research continues to identify and characterize therapeutic targets, and many compounds that have the potential to

treat currently untreatable diseases like dry AMD have been identified. A slew of new drug candidate molecules for ophthalmic diseases are being screened and evaluated right now. There is definitely hope. In the meantime, there is much to do at the population level to reduce the risk of patients developing cataracts, diabetes, macular degeneration, and to be vigilant for glaucoma. Baby boomers deserve no less.

References

1. *A. Chopdar, U. Chakravarthy, D. Verma, "Age Related Macular Degeneration", BMJ, 326, 485–488 (2003).*
2. *J.S. Tan et al., "Dietary antioxidants and the long-term incidence of age-related macular degeneration: the Blue Mountain Eye Study", Ophthalmology, 115, 334–341 (2007). doi:10.1016/j.ophtha.2007.03.083.*
3. *Age-Related Eye Disease Study Research Group. "Risk factors associated with age-related macular degeneration. A case-control study in the age-related eye disease study: Age-Related Eye Disease Study Report Number 3", Ophthalmology, 107, 2224–2232 (2000).*
4. *G. Hageman, "To Cure AMD, First Define It", The Ophthalmologist, 2, 14–20 (2013).*
5. *S. Wild, "Global prevalence of diabetes: estimates for the year 2000 and projections for 2030", Diabetes Care, 27, 1047–1053 (2004). doi: 10.2337/diacare.27.5.1047.*
6. *K. Skarbez et al., "Comprehensive Review of the Effects of Diabetes on Ocular Health", Expert Rev. Ophthalmol., 5, 557–577 (2010).*
7. *National Eye Institute, "Facts about Diabetic Retinopathy", http://www.nei.nih.gov/health/diabetic/retinopathy.asp, Accessed February 26, 2014.*
8. *V.S. Jeganathan, J.J. Wang and T.Y. Wong, "Ocular associations of diabetes other than diabetic retinopathy", Diabetes Care, 31, 1905–1912 (2008). doi: 10.2337/dc08-0342.*
9. *R.O. Schultz et al. "Diabetic keratopathy", Trans. Am. Ophthal. Soc. 79, 180–199 (1981).*
10. *A. Taylor, "Cataract: relationship between nutrition and oxidation", J Am Coll Nutr., 12, 138–146 (1993).*
11. *B. Garry, T. Hugh, "Cataract blindness: challenges for the 21st century", Bull. World Health Organ. 79, 249–256 (2001). doi:10.1590/S0042-96862001000300015.*
12. *S. Wang, J.J. Wang, T.Y. Wong, "Alcohol and eye diseases", Surv. Ophthalmol., 53, 512–525 (2008). doi:10.1016/j.survophthal.2008.06.003.*
13. *J. van den Brûle, F. Degueldre, A. Galand, "Drug-induced cataracts", Rev. Med. Liege., 53, 766–769 (1998).*
14. *D.H. Sliney, "UV radiation ocular exposure dosimetry", Doc. Ophthalmol., 88, 243–54 (1995).*
15. *R.M. Lipman et al., "Cataracts induced by microwave and ionizing radiation", Surv. Ophthalmol., 33, 200–210 (1988).*
16. *A. Cook, P Foster, "Epidemiology of glaucoma: what's new?", Can. J. Ophthalmol., 47, 223–226 (2012). doi: 10.1016/j.jcjo.2012.02.003.*
17. *E.E. Chang, J.L. Goldberg, "Glaucoma 2.0: Neuroprotection, Neuroregeneration, Neuroenhancement", Ophthalmology, 119, 979–986 (2012).*
18. *T.C. Chen, "Spectral domain optical coherence tomography in glaucoma: qualitative and quantitative analysis of the optic nerve head and retinal nerve fiber layer (an AOS thesis)", Trans Am Ophthalmol Soc., 107, 254–281 (2009).*
19. *J.M. Seddon, "Genetic and environmental underpinnings to age-related ocular diseases", Invest Ophthalmol Vis Sci., 54, 28–30 (2013). doi:10.1167/iovs.13-13234.*

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Why Snellen Must Die

For the sake of our patients and our profession, we need to improve upon the nineteenth-century pictograms that are currently used for visual assessment.

By Mark Blecher

When cataract surgeons assess visual function, we almost always use Snellen charts (Figure 1). We should be ashamed of this. Why, in 2014, are we using a 19th century pictogram, with many obvious drawbacks to describe our treatment outcomes? Why don't we have a more useful real-world test of visual performance and visual function by which to judge both visual disability and our visual outcomes? In fact, we do.

Incorporating contrast sensitivity into visual assessments is one of the best methods of obtaining a comprehensive assessment of visual acuity, both before and after cataract surgery. Although not widely used in the clinic, the Early Treatment Diabetic Retinopathy Study (ETDRS) vision charts (Figure 2) are a considerable improvement on the Snellen chart. They contain the same number of letters per row (five); the letters and rows are both equally spaced out (on a logarithmic scale), and individual rows are balanced for letter difficulty, and they contain an additional advantage, namely contrast sensitivity.

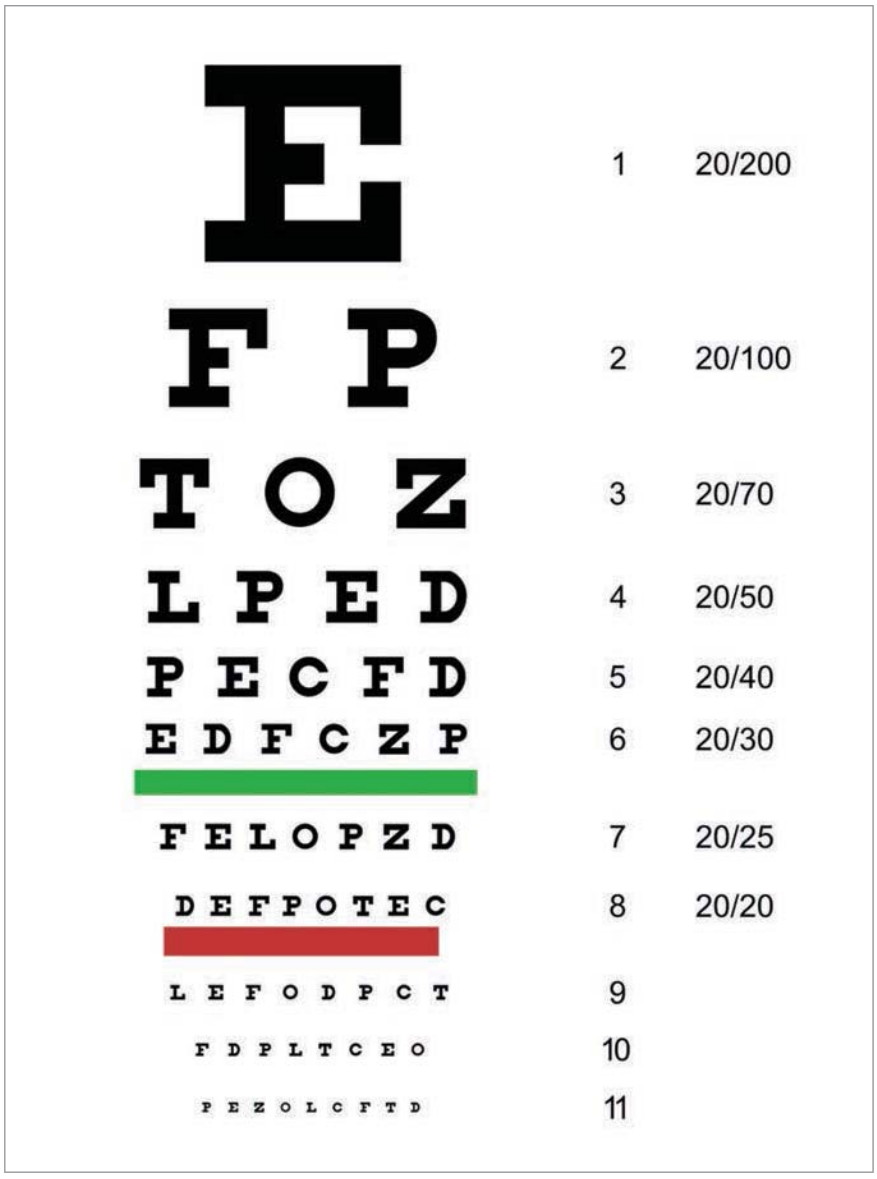

Figure 1. The ubiquitous Snellen chart that dates from 1862.

At a Glance

- *The Snellen visual acuity chart, developed in 1862, continues to be widely used*
- *Antiquity and ubiquity bear no relation to its quality*
- *Its use can prolong the wait patients have for interventions*
- *ETDRS vision charts are better, but not the ultimate solution*

The identification of contrast sensitivity problems is important. The potential causes of contrast sensitivity loss are many – ranging from corneal opacities and refractive issues to macular degeneration and neurological disease. But no matter the cause, loss of contrast sensitivity is a strong predictor of later visual acuity loss (1) and is worthy of investigation. Most visual acuity assessments (like the Snellen chart) measure the ability of patients to recognize small, high-contrast

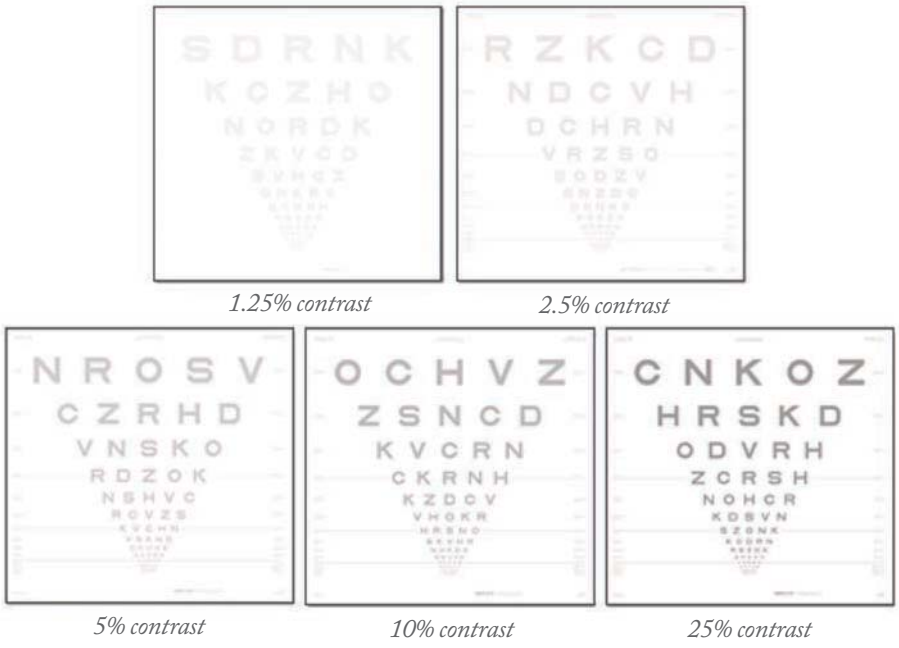

Figure 2. ETDRS charts at various contrast sensitivities.

objects (mostly black letters on a white background) under controlled, bright lighting conditions. But in the real world, it's not the size of the object that can cause problems, it's the contrast. Not seeing the last step on a flight of stairs or the kerbstone between the road and the sidewalk and falling over isn't a function of the relative sizes of the objects, it's a function of small differences in contrast between them. Many studies of the real-life function of patients have found that poor contrast sensitivity has a major impact on patient quality of life, such as that measured by the Activities of Daily Living (ADL) scale (2). So that's one great reason for considering contrast sensitivity: patient quality of life.

I have patients coming into my office with early cataracts, and they're saying, "You're telling me that I have a little bit of cataract in there. Well, can you take it out?" If I use the Snellen chart I would say "Well, physically, sure, there's nothing stopping me from taking it out. But it's not yet time, you're only 20/30." If I took it out, their post-surgical visual acuity might only show a small improvement to 20/25, prompting the question of how much visual improvement the government or the private insurance company actually bought with that procedure. Yet, I'm often told, "I'm having difficulty, please take them out". When I do the procedure, the patients come back and say, "The improvement of my visual performance is amazing", and I sit with my Snellen charts and have to say, "Well, I believe you and I'm really happy to hear this but we just don't have the ability to document it."

Clearly, we're not using the right measures. The implementation of contrast sensitivity in ETDRS isn't perfect, and the use of the Latin alphabet is inappropriate for some geographical regions – the workarounds for non-Latin alphabet-using countries like modified charts with rotated Es or broken circles are less than ideal. We can, perhaps, do even better that ETDRS.

I think that industry, and the profession as a whole, needs to decide on a better visual performance standard. So this is a call to action. Please, ophthalmologists, optometrists, researchers and visual physiologists, let's pull together and develop a standard worthy of the twenty-first century and not the nineteenth.

To drive acceptance of a new standard (and improve the lives of our patients) we need to ask the journals to mandate that all reporting of visual function tests has to be in this new standard and to reject any manuscript that solely reports Snellen acuities. It's an easily achievable target, and it's one that would benefit almost all aspects of the clinical practice of ophthalmology and optometry – and our patients.

References

1. *M.E. Schneck, "Low contrast vision function predicts subsequent acuity loss in an aged population: the SKI study", Vision Res., 44, 2317–2325 (2004). 10.1016/j.visres.2004.04.018.*
2. *B.L. Lam et al., "Longitudinal relationships among visual acuity and tasks of everyday life: the Salisbury Eye Evaluation study", Invest. Ophthalmol. Vis. Sci., 54, 193–200 (2013). doi: 10.1167/iovs.12-10542.*

How to Improve Visual Acuity Testing

The Salzburg Reading Desk is one promising approach to standardizing visual assessments for multifocal intraocular lenses.

By Florian Kretz

The last decade has seen great advances in cataract and refractive surgery; these have allowed us to set a goal, for most patients, for a visual acuity of at least 20/25 lines (0.1 logMAR).

In terms of assessing the performance of modern multifocal intraocular lenses (MIOL) we really should assess visual acuity across multiple distances – far, intermediate and near. This should be done before MIOL implantation, to determine which lens best matches the patient's needs, and after implantation, to measure the success of the intervention. Regrettably, there is no consensus in international ophthalmological practice on the best way to do this: different testing methods have been approved and are in use around the globe. The approaches vary with regard to the tested distance, letter size and distance between each of the letters. It is left up to each physician to decide what assessment method to use – and it appears to me to be a purely subjective choice.

The latest developments in MIOL optics complicate things still further. There are different near additions for refractive and diffractive optical systems, as well as their combinations, and some of the newer MIOLs are trifocal. These make intermediate and near visual acuity testing especially fraught, complicating the creation of uniform (and international) standards. The calculated focus points in acuity tests are dependent not only on the actual near addition of the MIOL but also on its how effectively the lens is positioned. There's also the patient factor to consider: their needs and habits must be at the forefront of our considerations. This means paying attention to aspects of their everyday life, such as optimizing individual working distances to achieve the maximal improvement in quality of life.

My modest proposal to achieve this is to use the Salzburg Reading Desk (SRD), an excellent method for testing near and intermediate visual acuity that was developed by Günther Grabner and Alois Dexl. Beside the typical measurements in set distances, this aperture can also measure individual distances for near and intermediate visual acuity. Rather than making patients read out single letters or numbers from a chart, the SRD uses whole sentences that patients have to read out – and the SRD evaluates the reading speed and acuity (as distance-corrected logMAR) of each patient automatically. Furthermore, luminance and contrast settings can be varied so that each patient's individual contrast sensitivity can be defined.

Grabner described the SRD thus: "This is the first system that allows for rapid, precise and unbiased comparison of different surgical techniques for the correction of presbyopia – not just with IOLs, but also interventions like corneal inlays or even scleral techniques." He also noted that, "The same holds true for the evaluation of reading ability after different anti-VEGF treatment schedules, an aspect of clinical retinal studies that has not undergone intense scrutiny to date." Dexl reinforced the point that, "each patient can use their own, subjectively convenient, reading distance and reading performance parameters", meaning that patients aren't having to strain to read a chart six metres away.

While a uniform, robust approach to measuring visual acuity still seems to be a long way off, I believe that we are headed in the right direction with technologies like the SRD. It provides a standardized platform that gives us the information we need and enables us to tailor what we do to the particular needs of each patient. Technologies like SRD help us to practice ophthalmology better by assisting us in providing a truly personalized service.

At a Glance

- *Premium, multifocal IOLs are excellent*
- *A standard test for visual acuity of IOL patients is needed*
- *The Salzburg Reading Desk is a good candidate for this role*
- *SRD provides precise visual acuity at various illumination and contrast levels*

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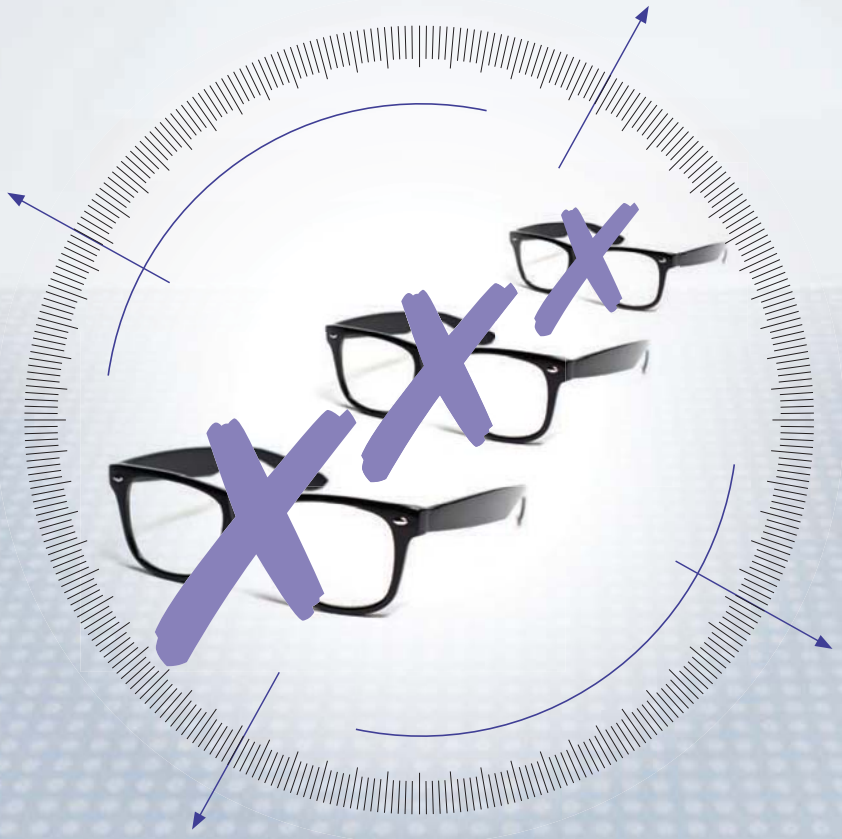

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Combining Laser and Anti-VEGF for the Treatment of DME

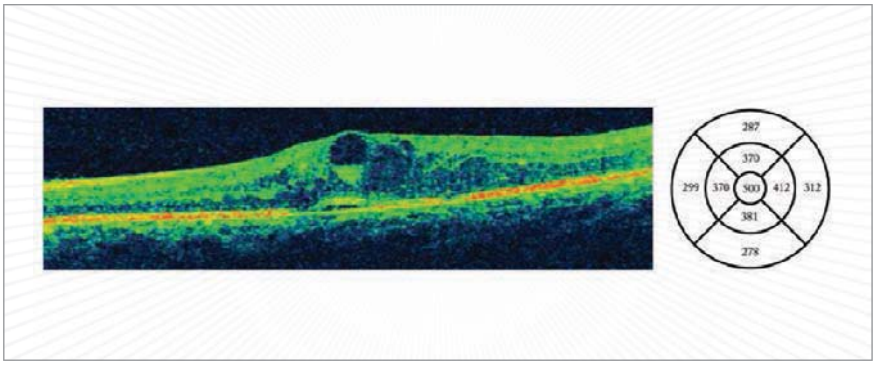


Figure 1. OCT image of cystoid diabetic macular edema with a shallow neuroretinal detachment.

Advances in understanding of the therapeutic mechanisms that underpin micropulse laser treatment suggest that protocols for treatment of diabetic macular edema should be integrated.

By Stela Vujosevic

Last year, the International Diabetes Federation estimated that 55.2 million adults in Europe – which is 8.5 percent of the population – have diabetes. Over the course of their disease, a quarter of these patients will develop diabetic macular edema (DME; Figure 1). The pathogenesis of DME is multifactorial. It includes microvascular and neuroinflammatory alterations that result in increased vascular permeability or ischemic changes.

At a Glance

- *Although pharmacotherapy for DME has been successful, frequent injections are a drawback*
- *With current micropulse laser therapy (MPLT), thermal damage to cells is no longer an issue*
- *MPLT modulates the secretion of multiple cytokines by the retinal pigment epithelium*
- *A combination of treatment modalities for DME could be most effective*

The history of DME treatment

Laser photocoagulation was essentially the first effective DME therapy. The cornerstone project for this was the Early Treatment of Diabetic Retinopathy Study (ETDRS), which began in the late 1970s. The protocols developed in the trial had, until very recently, represented the standard of care for DME. ETDRS demonstrated the efficacy of focal laser photocoagulation in reducing moderate visual loss in clinically significant DME (1). However, grid laser treatment (although considered effective against diffuse DME) induces the formation of progressively expanding scars that actually decrease vision, causing subretinal fibrosis and visual field loss (2).

The treatment protocol for DME has been revised in light of the advances in pharmacotherapy. While laser photocoagulation was effective at halting disease progression, therapies directed against vascular endothelial growth factor (VEGF) appeared to restore visual acuity. The RISE and RIDE studies demonstrated the efficacy of the anti-VEGF agent, ranibizumab. It restored upwards of 15 letters of visual acuity in a significant percentage of subjects (3), providing a viable treatment option for cases of diffuse DME. Later, the VISTA-DME and VIVID-DME trial one-year results were published that showed that the cohorts that received aflibercept achieved dramatically better results than the laser photocoagulation groups, with gains of 10 ETDRS letters or more (4).

The initial shine of anti-VEGF treatment is, however, starting to lose some of its luster. The biggest drawback is the frequency of injections required. While pro re nata (PRN) protocols are popular, patients that receive injections monthly tend to get the best results. Monthly injections are costly and many patients greatly dislike receiving them; both factors contribute to a reduction in patient compliance.

There may also be other issues. Growing evidence points to key roles played by VEGF in a healthy functioning eye (5): it may be harmful to indiscriminately prevent the function of VEGF. In addition, studies comparing anti-VEGF therapy to laser photocoagulation have not taken in to account new laser modalities, which reduce side effects and improve visual function results.

Micropulse laser therapy

When it was shown that argon macular laser photocoagulation reduced moderate vision loss by 50 percent in the ETDRS study, it was thought that burning de-bulked the diseased retina, increased intraocular oxygen tension and altered the production of vasoactive cytokines, including VEGF (6). That view has since

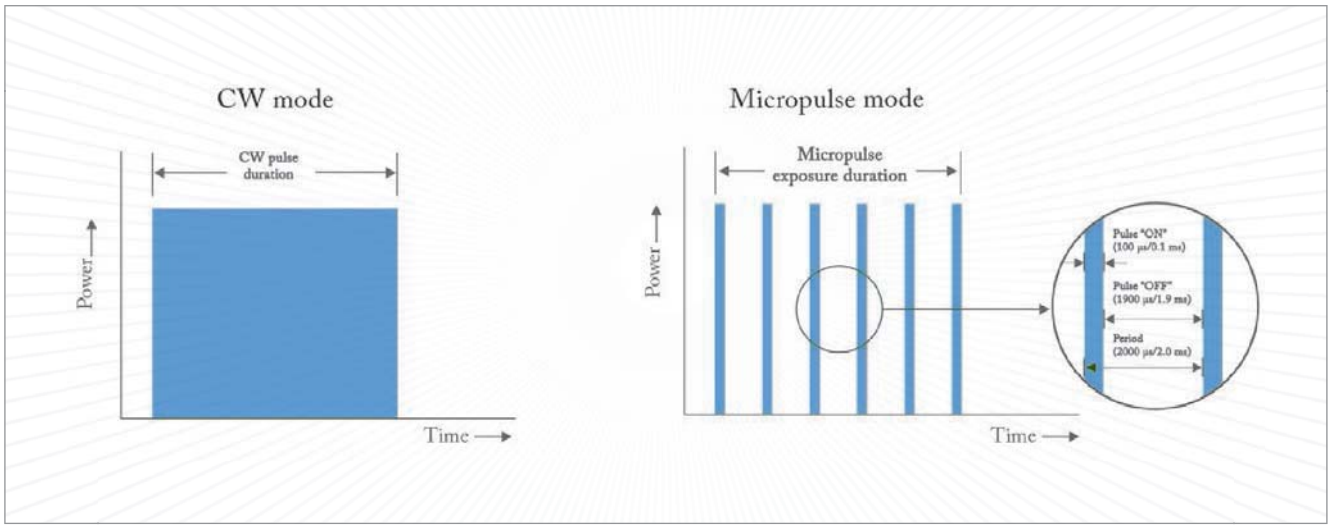


Figure 2. The long and the short of it: the two modes of the Iridex IQ 810 / IQ 577. Continuous wave (CW) mode generates a steady stream of laser energy that results in a significant thermal rise and consequent coagulation. The micropulse mode delivers the same power as the CW mode, chopped into shorter pulses, with pulse duration and frequency being adjustable by the surgeon. Shorter micropulse durations limit the time for laser-induced heat to spread to adjacent tissues, thus providing more precise confinement of energy delivered. Longer intervals between each micropulse provides additional time for tissue to cool.

Figure 3. The Iridex IQ 577 Laser System.

been revised. Modified laser treatments, such as micropulse laser therapy (MPLT; Figure 2) can avoid the retinal damage that was associated with the older laser technologies. These newer devices deliver laser energy in a more controlled manner, and are able to produce a chain of short pulses, separated by longer pauses: this allows the tissue to cool, preventing thermal buildup and the retinal damage that is associated with the heat.

The intention was to decrease negative side effects such as the destruction of retinal photoreceptors, retinal scars, choroidal neovascularization and the development of macular scotomas, and the approach represented a welcome evolution in the application of laser therapy. The first study that evaluated MPLT in patients with DME was reported in 2005; the investigators wished to establish if the new technique could avoid laser-induced retinal injury (7). The results were comparable to conventional photocoagulation in terms of visual acuity and fluorescein angiographic leakage, but without the adverse effects associated with it: the approach represented a welcome evolution in the application of laser therapy. It also instigated a revolution in our understanding of the therapeutic mechanism that underlies laser treatment for DME.

My colleagues and I recently reviewed the literature on the topic (8) and offered an explanation for the mechanism of action of sub-threshold micropulse lasers in DME, namely alterations in the retinal pigment epithelium's expression of cytokines. (The cytokines are a a family

over 100 small cell-secreted proteins that affect the behavior of other cells.)

An increase in the concentration of a variety of cytokines (including VEGF) has also been observed in the aqueous humor and the vitreous of patients with DME. Anti-VEGF treatment selectively inhibits just VEGF. Although VEGF plays an important role in both angiogenic and inflammatory pathways, selective anti-VEGF treatment is unlikely to influence other immunogenic cytokines involved in DME. On the other hand, a growing body of evidence indicates that low-intensity red and near-infrared laser promotes proliferation of multiple cell types, mainly through the activation of the mitochondrial respiratory chain and the initiation of cellular signaling.

MPLT using the IQ 810 or the IQ 577, (Figure 3, Iridex Corp, Mountain View, CA, USA) can induce favorable alterations in the expression of a large variety of potent extracellular mediators of DME, while avoiding any lethal thermal cellular damage. High-density MPLT maximizes the effective surface area and therefore the therapeutic effect. The small physiologic changes in cytokine expression resulting from MPLT may account for the slower onset and longer-lasting benefits observed following all types of laser treatment for DME. Although the slower reaction time could be considered a disadvantage of MPLT, it is compensated for by a longer-lasting effect and an excellent safety profile in comparison with other types of laser treatment. No retinal damage has been observed following MPLT with either yellow or infrared lasers, as demonstrated by color fundus photography, fundus autofluorescence (FAF) imaging, fundus fluorescein angiography (FFA) and spectral domain optical coherence tomography (SD-OCT) (10).

A combined treatment approach

In my practice, we evaluate whether or not the DME involves the center of the fovea: if it does not, we perform MPLT; if it does, we evaluate the central retinal thickness (CRT). In patients with CRT up to 400 µm, we perform MPLT. If CRT is greater than 400 µm, we first perform anti-VEGF injections and follow-up with MPLT after the edema has reduced below 400 µm. We do not see any visible scarring in our patients even after multiple retreatments, reassuring us of the safety of MPLT when performed at the lowest duty cycle.

As there is an important inflammatory element to DME, we are also investigating a role for long-term steroid therapy. Slow-release corticosteroids have shown promising results and their use may be a valid option in specific DME phenotypes.

Our understanding of both the disease processes that underlie DME and the impact of laser stimulation has dramatically improved, and we are now better able to define and evaluate treatment options. DME is a chronic disease that requires long-lasting treatment options that have minimal side-effects. To achieve this, there is still much to be investigated, such as a randomized trial of anti-VEGF combined with MPLT and a better understanding of which are the optimal cases for treatment with steroids. DME is a multifactorial disease that undoubtedly will benefit from a multi-faceted treatment approach, and time will teach us how to match protocols and disease profiles.

Stela Vujosevic is the Assistant Clinical Professor of Ophthalmology at the University of Padova, Italy.

References

1. *Early Treatment Diabetic Retinopathy Study research group, "Photocoagulation for diabetic macular edema. Early Treatment Diabetic Retinopathy Study report number 1", Arch. Ophthalmol., 103, 1796–1806 (1985).*
2. *G.G. Striph et al., "Modified grid laser photocoagulation for diabetic macular edema. The effect on the central visual field," Ophthalmology, 95, 1673–1679 (1988).*
3. *Q.D. Nguyen et al., "Ranibizumab for DME: Results from 2 phase III randomized trials: RISE and RIDE," Ophthalmology, 119, 789–801 (2012). doi: 10.1016/j.ophtha.2011.12.039.*
4. *U. Schmidt-Erfurth, "Efficacy and safety of intravitreal aflibercept in DME: results of two phase III studies (VIVIDDME and VISTA-DME)." Paper presented at: the 13th EURETINA Congress; September 27, 2013; Hamburg, Germany.*
5. *M. Saint-Geniez, P. D'Amore, "VEGF Has Physiological as Well as Pathological Functions," The Ophthalmologist, 1, 16–23 (2014).*
6. *M.A. Mainster, "Decreasing retinal photocoagulation damage: principles and techniques", Semin. Ophthalmol., 14, 200–209 (1999).*
7. *J.K. Luttrull, D.C. Musch, M.A. Mainster, "Subthreshold Diode MicroPulse Photocoagulation for the Treatment of Clinically Significant Diabetic Macular Oedema", Br. J. Ophthalmol, 89, 74–80 (2005).*
8. *S. Vujosevic et al., "Subthreshold Laser Therapy For Diabetic Macular Edema: Metabolic And Safety Issues," Curr. Med. Chem., 20, 3267–3271 (2013).*
9. *J.K. Luttrull, "Subthreshold diode MicroPulse photocoagulation for the treatment of clinically significant diabetic macular oedema," Br. J. Ophthalmol. 89, 74–80 (2005). doi: 10.1136/bjo.2004.051540.*
10. *S. Vujosevic et al., "Microperimetry and fundus autofluorescence in diabetic macular edema: subthreshold MicroPulse diode laser versus modified early treatment diabetic retinopathy study laser photocoagulation", Retina, 30, 908–916 (2010). doi: 10.1097/IAE.0b013e3181c96986.*

CLASS-y Laser Treats Glaucoma

Transforming complex, invasive and risky glaucoma surgery into a safe, elegant, and precise procedure.

By Ehud Assia

Glaucoma is the second most common cause of blindness globally. Currently, an estimated 8.4 million in the world are blinded by the disease, with a further 60 million affected by optic neuropathy (1), and these numbers will only increase. There is therefore an urgent need for improved understanding of the underlying pathology and better treatment options that this knowledge will give rise to. Thankfully, headway is being made.

Traditional treatment for glaucoma begins with topical hypotensive medications. These prevent nerve damage when used according to their prescription (2) but are much less effective for the high percentage of patients that are not fully compliant. Studies have shown that only around 46 percent of patients fulfill all of their prescriptions (3), and of those that do, less than 30 percent are instilling them correctly (4). For a disease in which the only course of treatment is to prevent ocular nerve damage, this is not good news. The traditional surgical alternatives, such as trabeculectomy and tube shunts, come into play only when the disease state is dire enough to exceed the high risks associated with surgery.

At a Glance

- *Ocular glaucoma drops, while effective, are plagued by lack of compliance*
- *Patients and clinicians are looking for an alternative to traditional, high-risk surgical options*
- *CO2 lasers are highly effective for ablation of dry tissue and are absorbed by liquid*
- *This makes CO2 laser-assisted sclerectomy surgery (CLASS) a safe and precise treatment option*

A new surgical option

In the last few years there has been a surge of surgical alternatives as clinicians and scientists search for low-risk, high-efficacy treatment options. The approach that I have helped to develop within this niche is CO_2 laser-assisted sclerectomy surgery (CLASS).

Although CO_2 lasers are well-known in the field of general surgery, especially plastic surgery, it took a laser manufacturing company, Optomedic, to bring the benefits of the CO_2 laser to my attention back in 1998. This laser is unique in that it is highly effective for dry tissue ablation while being almost completely absorbed by liquid; it is therefore not suitable for any intraocular procedure.

We hypothesized that it would be possible to ablate the dry sclera over the Schlemm's Canal and trabecular meshwork until the tissue became thin enough to allow fluid to percolate out through the tissue. The percolating fluid would absorb any additional laser energy, preventing further ablation of the tissue that may lead to penetration into the eyeball. When we studied the tissue effect of the CO_2 laser on a variety of animal and human cadaveric eyes and on living rabbits, the hypothesis was supported in these near-clinical settings: fluid percolation was achieved in all cases whereas penetration into the anterior chamber occurred in only about five percent of cases.

Our CLASS procedure was subsequently developed using IOPtiMate (IOPtima, Israel), a unique system that consists of a CO_2 laser with a wavelength of 10.6 μm (infrared), accompanied by a micro-manipulating scanner that uses an aligned HeNe laser aiming beam (red; 632 nm), and a control unit. The CLASS procedure is as follows (see Figure 1):

- A peritomy and superficial scleral flap dissection is made, which extends to the clear cornea.
- At the discretion of the physician, 0.02–0.04% Mitomycin C can be applied for 1–3 minutes after the creation of the scleral flap.
- The red aiming beam is used to identify and confine the laser ablation zone distal to the limbus.
- The laser ablation is aimed at the zone directly above Schlemm's canal and scleral tissue is removed layer by layer until fluid percolates through the tissue.
- The Laser ablation effect "automatically" stops as aqueous begins to percolate, that is, when the desired end-point is achieved.
- Once sufficient sclera has been ablated and the aqueous percolates effectively, the scleral flap is replaced and sutured.

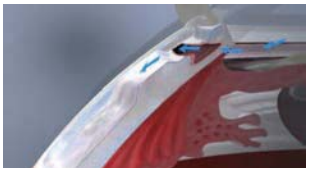
CLASS reduces elevated intraocular pressure (IOP) in patients with primary open angle glaucoma (POAG) and pseudo exfoliative glaucoma (PEXG) by thinning, but leaving intact, the sclera of the eye, thus improving drainage without penetrating the eye globe. Aqueous flow is successfully regenerated using nature's own pathways and with no need to insert any foreign drainage devices.

Figure 1. The CLASS procedure.

Step 1. Creation of the standard flap
Following standard surgical preparation and eye fixation, the conjunctiva is manually cut open and the sclera exposed. A standard scleral flap is then created above the desired percolation zone.

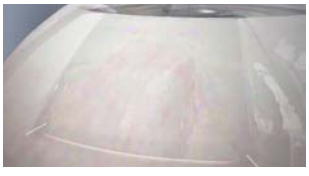
Step 2. Creation of scleral bed reservoir
A reservoir may be created using the IOPtimate laser beam to hold the fluid that percolates from the eye. This step is not mandatory and if performed a growth inhibitor or spacer may be used to hold the reservoir open.

Step 3. Tissue ablation
Utilizing the IOPtimate, the laser beam is rapidly scanned in a pre-selected ablation pattern and repeatedly ablates thin layers of sclera (between 5-30 µm), exposing and "un-roofing" Schlemm's Canal, until the desired level of percolation is achieved.



Step 4a. Fluid percolation
Once Schlemm's Canal is revealed, internal ocular fluid begins to percolate through the thinned, intact trabecular meshwork.

Step 4b. A thin layer remains intact; penetration of the eye is avoided
Upon achieving percolation, the CO_2 laser energy is absorbed by the percolating fluid, preventing further tissue ablation and inadvertent penetration into the anterior chamber.



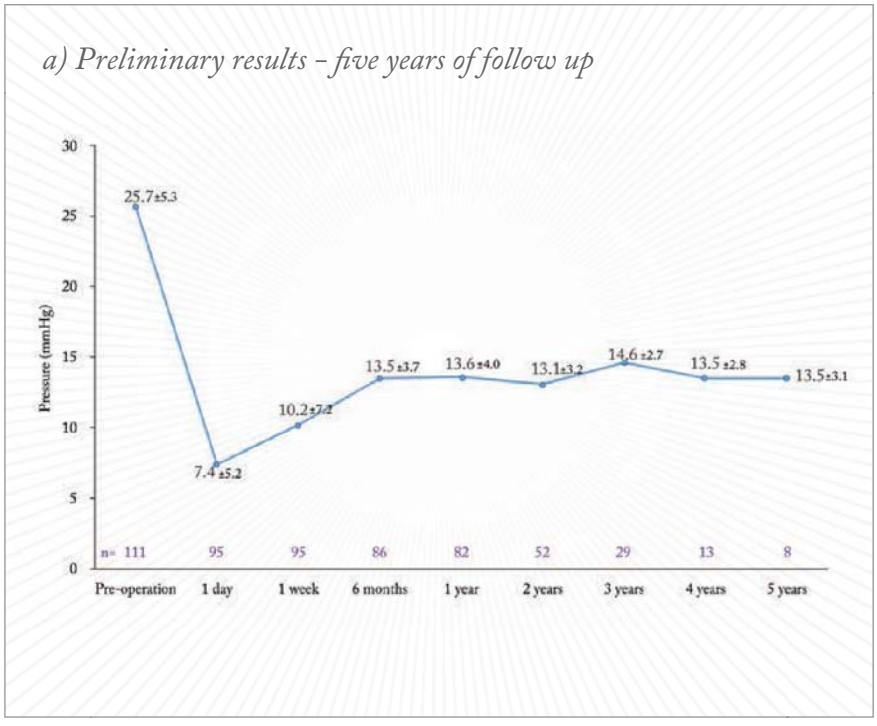
Step 5. Suturing
Once the procedure has ended, the scleral flap and conjunctiva are closed and sutured.

Results to date

In initial clinical studies performed in 2003–2004 with the CLASS procedure immediate success was seen in all cases; however, about one-half of the cases failed during follow-up, because of tissue scarring. The initial laser parameters had been set at low energy and long exposure time, essentially performing less tissue ablation and more photocoagulation. Appropriate adjustments were made to the laser parameters.

We now have data for up to five years on human eyes using the third generation of the IOPtimate system. In a prospective, multi-center study of 111 patients, the procedure was performed on 85 eyes with POAG and 26 eyes with PEXG and an average IOP of 25.7 +/- 5.3 mmHg. Mean IOP (see Figure 2a) dropped to 13.5 +/- 3.7 mmHg at six months post-operative (N=86) and remained stable through three years (N=29) and five years post-operative (N=8). The average number of hypotensive medications (Figure 2b) dropped from a mean of 2.3 +/- 1.2 at baseline to 0.3 +/- 0.7 at six months post-operative, 0.6 +/- 0.8 after three year and 0.8 + 1.0 after five years. At three years post-operative, 87.5 percent of patients achieved a reduction in IOP of 20 percent or greater, maintaining an IOP less than or equal to 18 mmHg; 59.4 percent of patients were able to maintain the IOP goals without use of any medication. Mitomycin C was used in 93 percent of procedures.

CLASS is appropriate for patients with mild to moderate POAG and PEXG, aiming to serve those patients with baseline IOP between 20 mmHg and 35 mmHg and possibly even higher. It is also suitable for combination with cataract surgery. Patients with mild to moderate glaucoma are often seen by comprehensive-care ophthalmologists rather than by glaucoma specialists, and the precision of the CLASS procedure



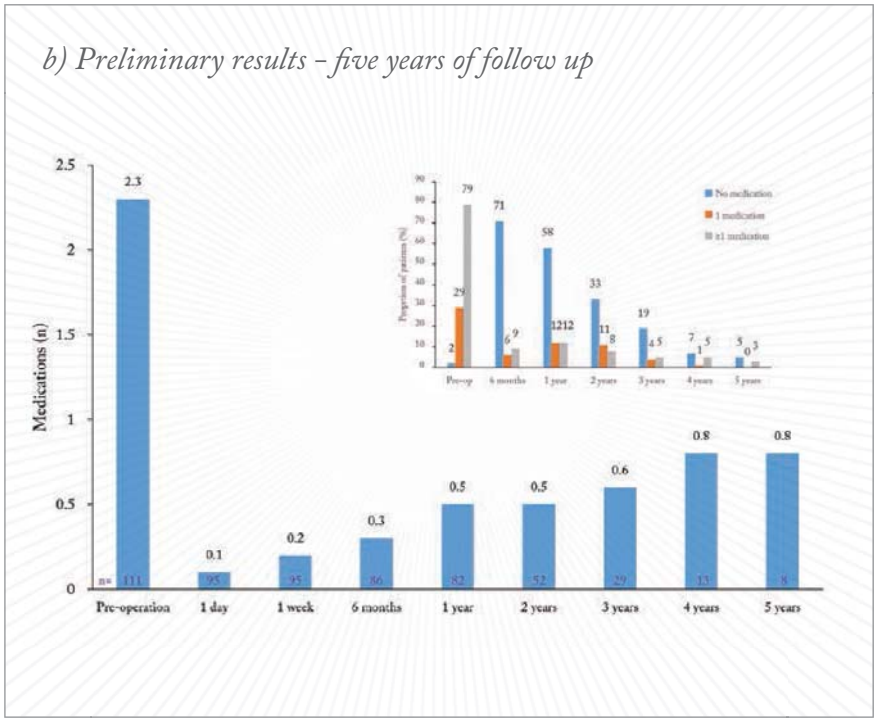


Figure 2. Five year post-CLASS procedure follow-up period data: (a) Average IOP and (b) average number of medications prescribed (inset: proportion of patients taking 0, 1 or ≥1 glaucoma medication before and after the procedure).

makes it a solution that is very accessible to all surgeons. The laser beam is precisely guided by the micro-manipulating beam, and will ablate exactly what is chosen according to the defined shape and dimensions; physicians simply have to exercise confidence in the device. Keeping the eye intact significantly reduces the risk of intra-operative and post-operative complications and the follow-up interventions commonly associated with penetrating surgical alternatives.

In multi-center clinical studies and in commercial practice, the approach is highly effective at lowering IOP, and in reducing hypotensive medication as well as resulting in lower post operative complications. CLASS has received regulatory approvals in Europe (CE), Mexico, Israel and is soon to be approved in China. So far, approximately 700 procedures have been performed worldwide.

Ehud Assia is the Director of the Department of Ophthalmology, Sapir Medical Center, Meir Hospital, Kfar Sava, Israel.

References

1. *C. Cook, P. Foster, "Epidemiology of Glaucoma: What's New?" Can. J. Ophthalmol., 47,223–226 (2012).*
2. *M.A. Kass et al., "The Ocular Hypertension Treatment Study: A Randomized Trial Determines That Topical Ocular Hypotensive Medication Delays or Prevents the Onset of Primary Open-Angle Glaucoma," Arch. Ophthalmol., 120, 701–713 (2013).*
3. *D.S. Friedman et al., "Using Pharmacy Claims Data to Study Adherence to Glaucoma Medications: Methodology and Findings of the Glaucoma Adherence and Persistency Study (GAPS)," Invest. Ophthalmol. Vis. Sci., 48, 5052–5057 (2007).*
4. *J.L. Stone et al., "An Objective Evaluation of Eyedrop Instillation in Patients with Glaucoma," Arch. Ophthalmol., 127, 732–736 (2009).*

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NextGen

Research advances
Experimental treatments
Drug/device pipelines

Benchmarking Glaucoma

What does analysis of the last five years of literature on glaucoma tell us about the priorities of the field and the major contributors to it?

By Mark Hillen

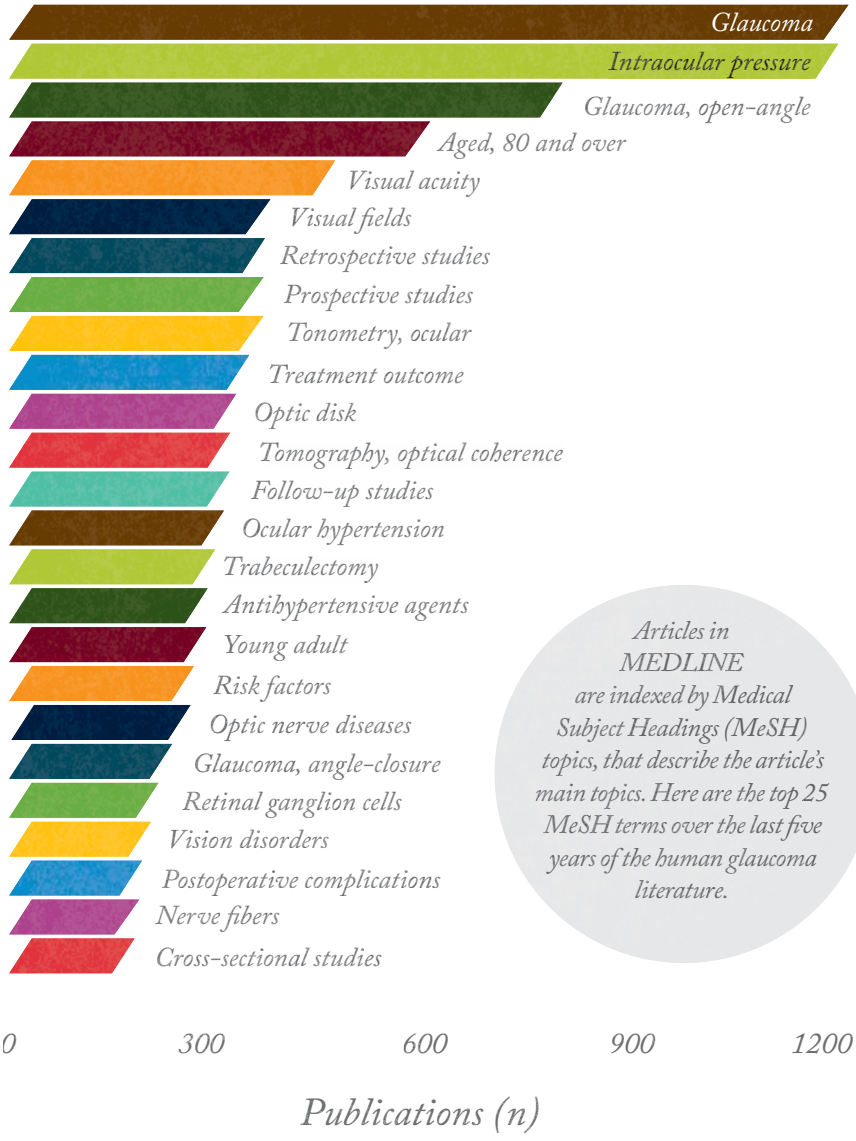
Glaucoma is second leading cause of blindness globally, after cataracts, but provides an even greater challenge: glaucoma-related blindness is permanent. This is a major driving factor for clinical research into glaucoma therapies.

To provide insight into the past and predictions for the future of the field, a series of metrics were applied to the last five years of the published literature. We asked:

- What are the major topics for the field?
- Which publications have the greatest impact?
- How is the knowledge available online?
- Who are the most prolific authors?

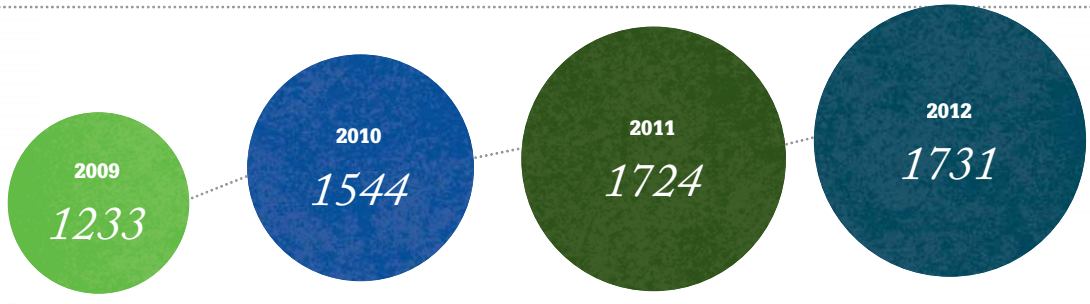
PubMed, was searched for glaucoma* with results limited to the last five years, in humans (for a clinical focus). The data were analyzed in Microsoft Excel 2013.

Most frequent topics on PubMed



Articles in MEDLINE are indexed by Medical Subject Headings (MeSH) topics, that describe the article's main topics. Here are the top 25 MeSH terms over the last five years of the human glaucoma literature.

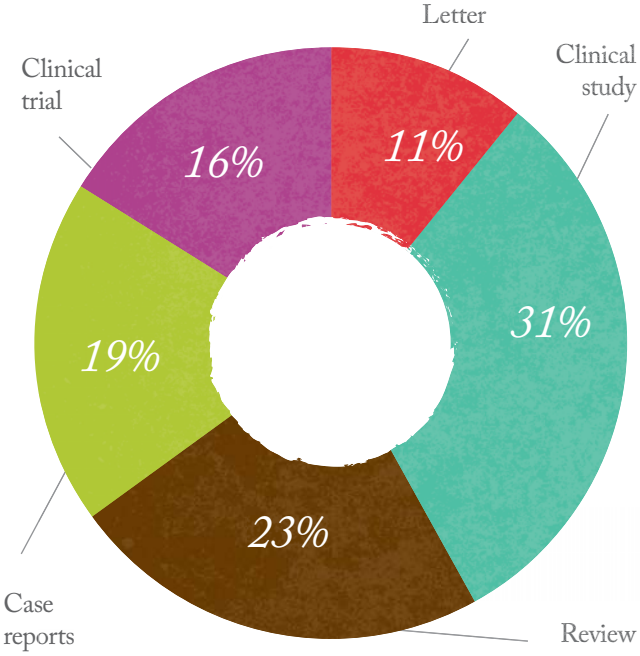
Glaucoma publications per year



Top 25 journals (by number of papers published per year)

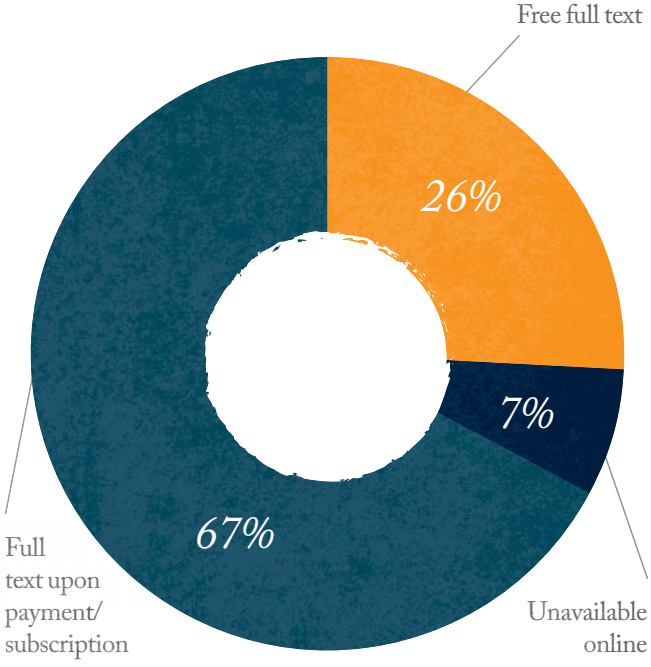
Categorization of articles

Articles are categorized according to PubMed criteria. Clinical study represents a clinical evaluation of a drug, device or technique that was not a clinical trial.

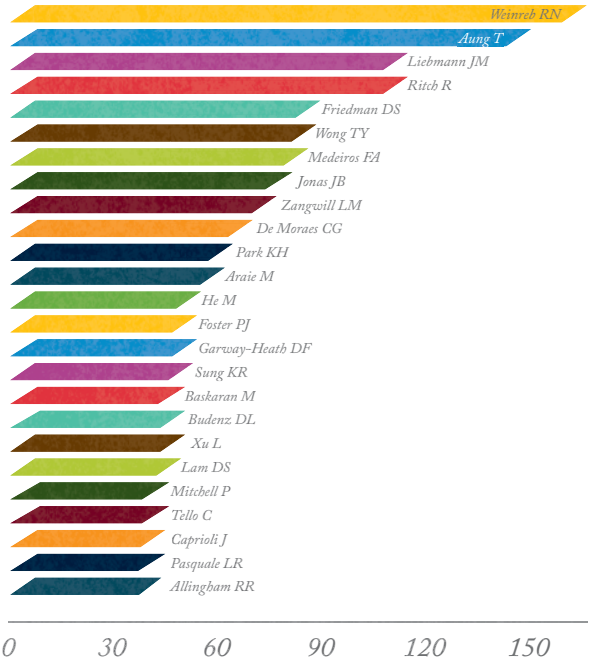


Fee or free?

Over one in every four articles are available online free of charge. However, 7 percent of these articles are not available via the web.

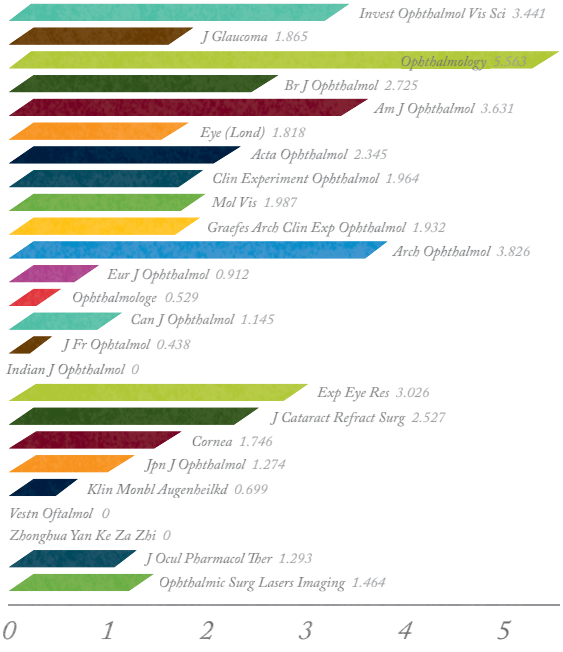


Most prolific authors in glaucoma, 2009–2013

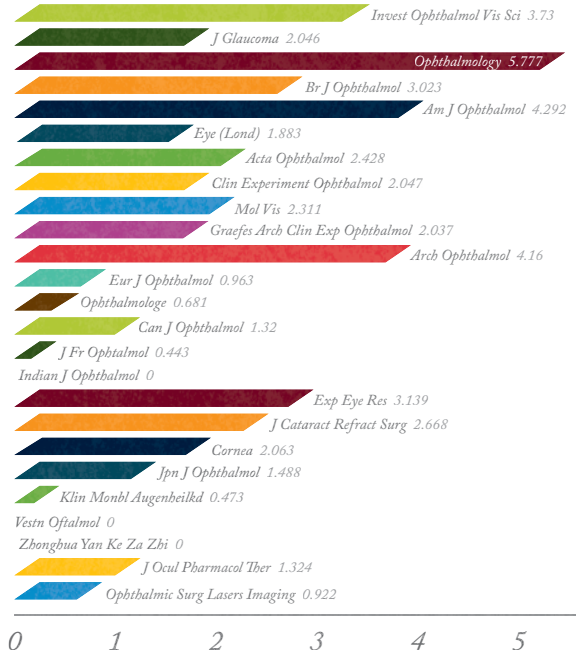


Average Impact Factor

Journal impact factors for 2013



Average impact factors for journals over the past five years



Have your say...

We are ranking the 100 most influential people in ophthalmology

Who are the clinicians and researchers with the biggest impact on our field? Which CEO has shown most integrity, leadership and creativity? And where are the role models and thought leaders that are inspiring big changes in ophthalmology?

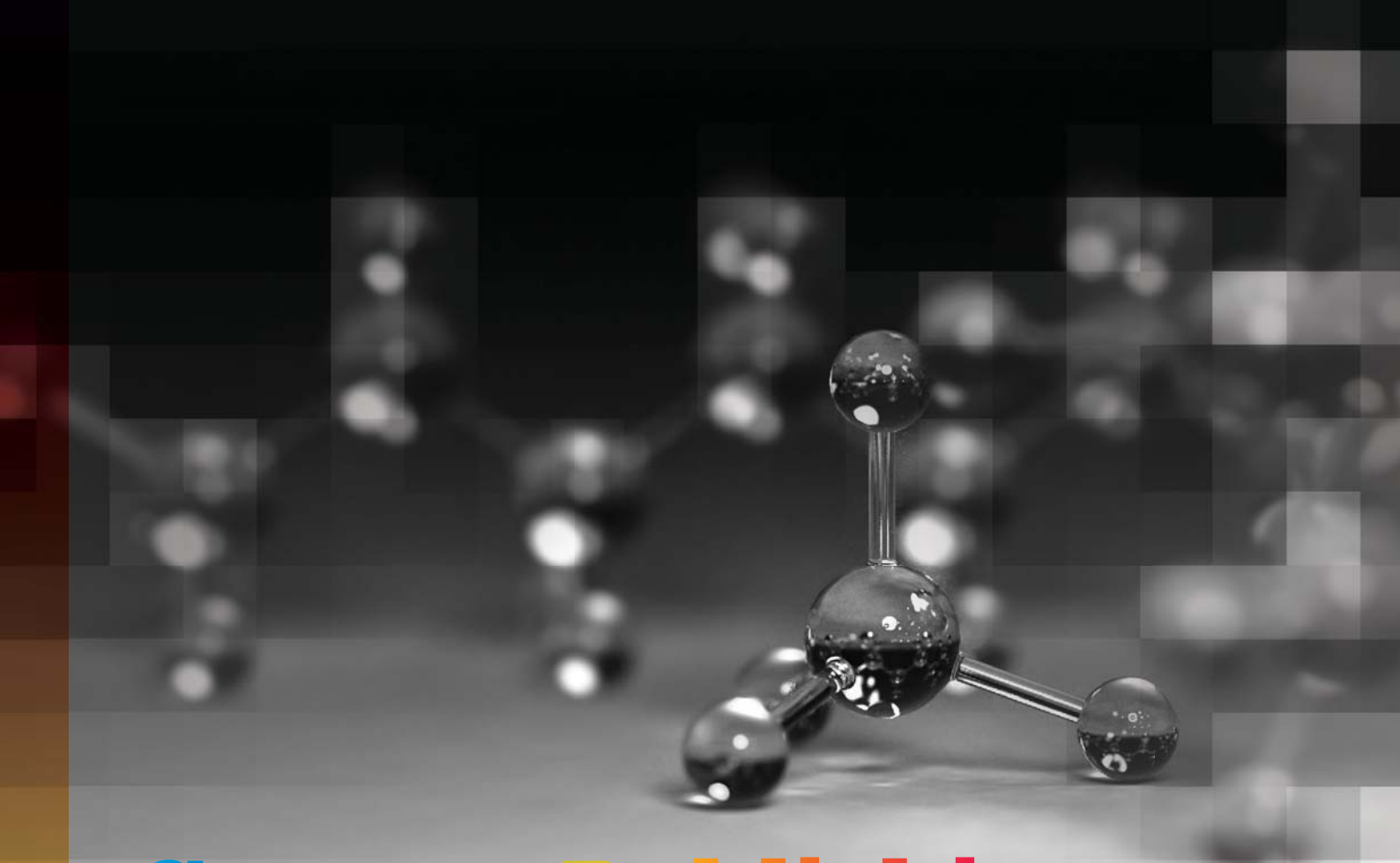
The Ophthalmologist Power List 2014 will survey the achievements of the outstanding men and women across ophthalmology. In doing so, it will celebrate their achievements and offer insight into our specialty's contribution to society as a whole. The Power List will shine a light on the physicians, scientists, engineers and business leaders who are shaping the world of ophthalmology today.

We invite you, our readers, to nominate the people that you believe are having the greatest influence. Your suggestions will be considered by our panel of judges who will select the Power List.

The Process

- Nominations for The Ophthalmologist Power List are welcome from individuals, groups or organizations
- You may nominate up to five individuals by sending an email to: info@texerepublishing.com
- The persons nominated should (a) be involved in some aspect of ophthalmology and (b) be active in their field at the time of nomination
- The deadline for nominations is 7 March 2014
- The full list of nominations will be put to the expert panel of judges
- Under the guidance of the Chair, the panel will decide on the final list of 100. The panel's decision is final and no correspondence regarding their deliberations or the final list will be entered into
- The Ophthalmologist Power List 2014 will be published in the April 2014 issue of The Ophthalmologist, in print and online

The Judges: Three ophthalmologists, one analyst and two industry executives.



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Glaucoma awareness from a global perspective

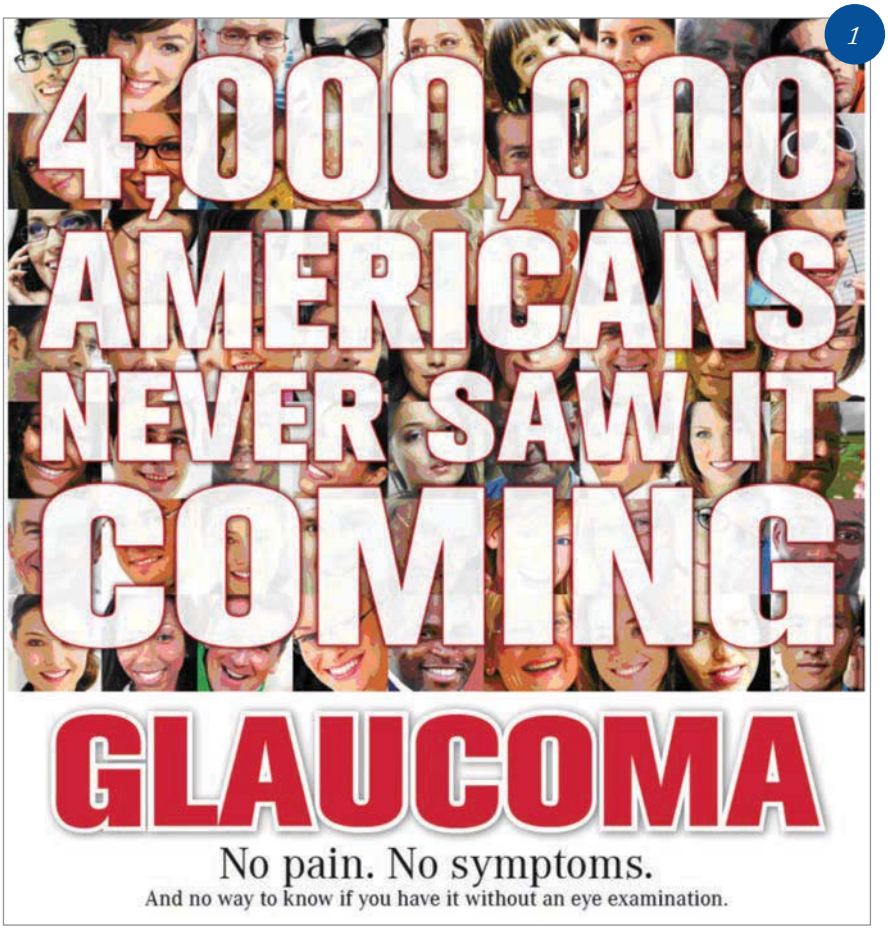
To mark World Glaucoma Week, here are some of the many creative approaches being taken to communicate awareness of the disease around the world.

With Glaucoma, timely diagnosis and intervention saves sight, while late diagnosis and treatment barely slow the inevitable progression to blindness. Public awareness campaigns are a crucial and cost-effective way to ensure that the at-risk population is screened.

There are many ways to capture the attention of the target audience, as the examples here illustrate.

Using all-caps to "shout" your message (Image 1) isn't subtle, but is effective, especially if your target audience already has some vision problems. However, more humorous approaches such as the t-shirt prints in Images 2 and 3 are potentially more memorable – assuming that they get the message across. These contrasting campaigns emanated from the USA. The Japanese contribution (Image 4) adds another twist, incorporating cartoon representations of elderly patients, in contrast to the young faces in Image 1.

Glaucoma fundraising efforts not only raise money, but can raise awareness too (Image 5), while other posters emphasize the international aspect of World Glaucoma Week (Image 6). Image 7, from Italy, revolves around a collaboration with art galleries to raise awareness, contrasting with Image 8's blunt, no-nonsense approach, developed in Guyana.



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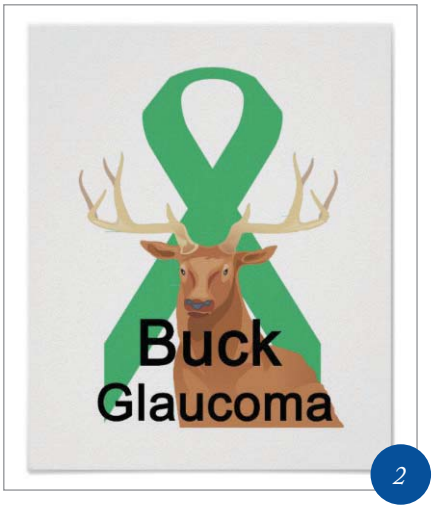


2

3

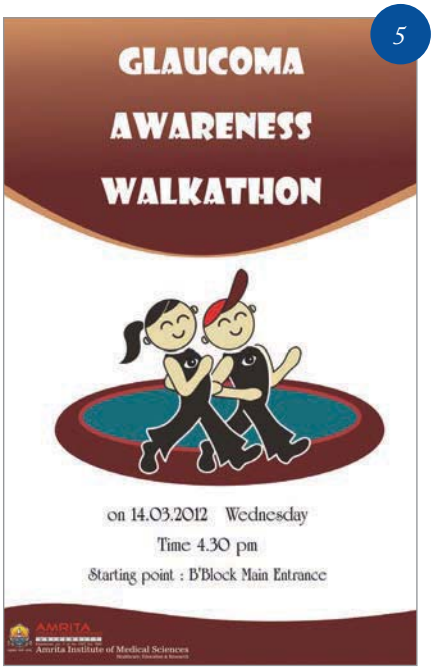
Image 9 is an infographic from the US National Eye Institute's education program, designed to be shared over social media rather than to be viewed in print or poster form. And lastly, images 10 and 11 show two contrasting but nonetheless linked styles from Indian hospitals. The former emphasizes the "free" nature of the glaucoma screening program, while the latter captures attention by linking a free car check-up to something far more important.

The creativity of these and other campaigns will surely go a long way to keeping glaucoma in check. We salute the artists and those who commissioned them.

4


World Glaucoma Week
March 10-16,2013
世界緑内障週間 市民公開講座
特別講演
大阪初開催
「緑内障を知っていますか?」
東北大学医学部 眼科 教授
中澤 徹 先生
日時
2013年3月17日(日)
15:00開演(14:00開場)-16:00終了
会場 ハービスHALL「大ホール」
定員 500名
あいさつ:一般社団法人 大阪府眼科医会会長 服部 吉幸 先生
入場無料
お申し込み方法
お預かりした個人情報は、申し込みの返信用にのみ使用いたします。
お申し込みは往復はがきに参加希望と記入し、住所、氏名、年齢、電話番号記入のうえ、下記までお送り下さい。
(返信面は両面記入不要)締め切りは2月28日(木)消印有効。
〒103-0027
東京都中央区日本橋1-2-16 Blue Mark83 501号
緑内障フレンド・ネットワーク(大阪)P 宛
会場までのアクセス
ハービスHALL
主催:緑内障フレンド・ネットワーク 後援:日本緑内障学会 一般社団法人 大阪府眼科医会 大阪府

5


GLAUCOMA
AWARENESS
WALKATHON
on 14.03.2012 Wednesday
Time 4.30 pm
Starting point : B'Block Main Entrance
AMRITA
Amrita Institute of Medical Sciences

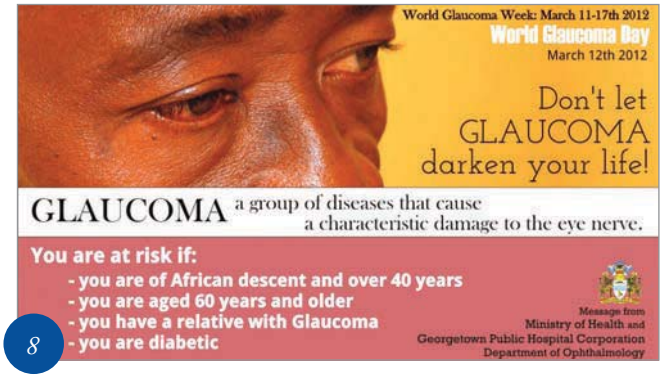
6


Semana Mundial del Glaucoma
10-16 de Marzo, 2013
10-16 de Marzo de 2013
Semana Mundial del Glaucoma
WORLD GLAUCOMA WEEK
SEMAINE MONDIALE DU GLAUCOME
Es Maravilloso ver el Mundo todos los dias
Toma de Tensión Ocular- Screening del Glaucoma.
Glaucoma en la radio (89.2 FM)
Reunión informativa sobre Glaucoma:
Aula de formación nº 4
No dejes que el Glaucoma te lo impida
Hospital de Poniente

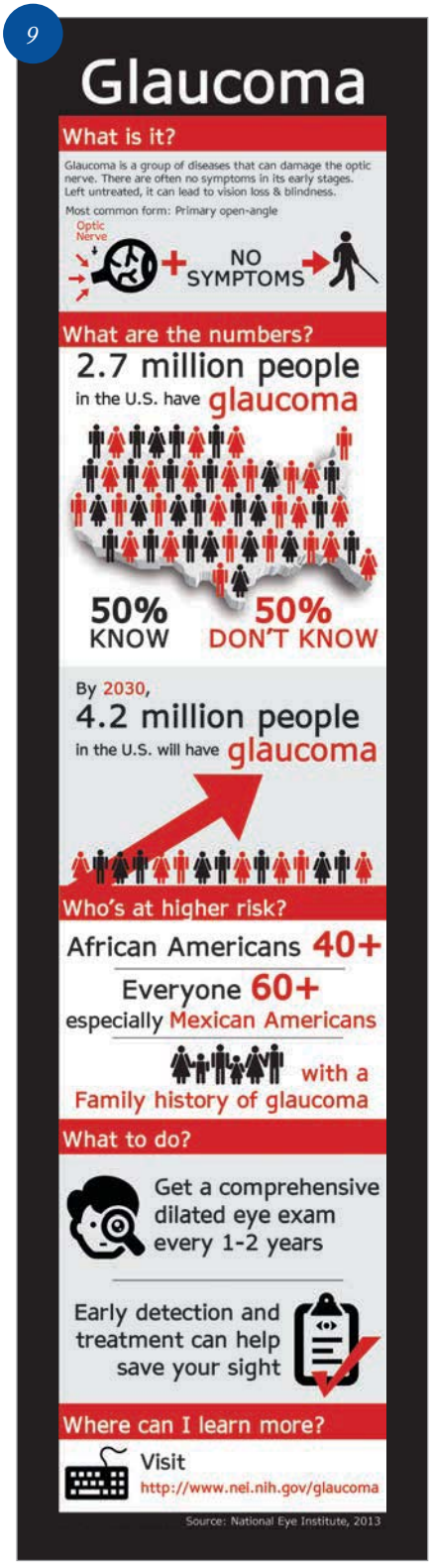
7


LA DIFFERENZA C'È
MA A VOLTE
NON SI VEDE
TI ASPETTIAMO SABATO 17 MARZO 2012
GALLERIA AUCHAN PARTECIPA
ALLA SETTIMANA MONDIALE
CONTRO IL GLAUCOMA
La riduzione avviene lentamente con una diminuzione della visione laterale.
La riduzione può riguardare anche la parte superiore del campo visivo. Dalla visione della persona con glaucoma potrebbe sparire qualcosa ma l'azione di ricostruzione del cervello potrebbe non far percepire il difetto.
Il glaucoma influenza negativamente contrasti e percezione cromatica.
È possibile perdere la porzione inferiore del campo visivo.
AIPREG ONLUS
Auchan

8


World Glaucoma Week: March 11-17th 2012
World Glaucoma Day
March 12th 2012
Don't let
GLAUCOMA
darken your life!
GLAUCOMA a group of diseases that cause a characteristic damage to the eye nerve.
You are at risk if:
- you are of African descent and over 40 years
- you are aged 60 years and older
- you have a relative with Glaucoma
- you are diabetic
Message from
Ministry of Health and
Georgetown Public Hospital Corporation
Department of Ophthalmology

9

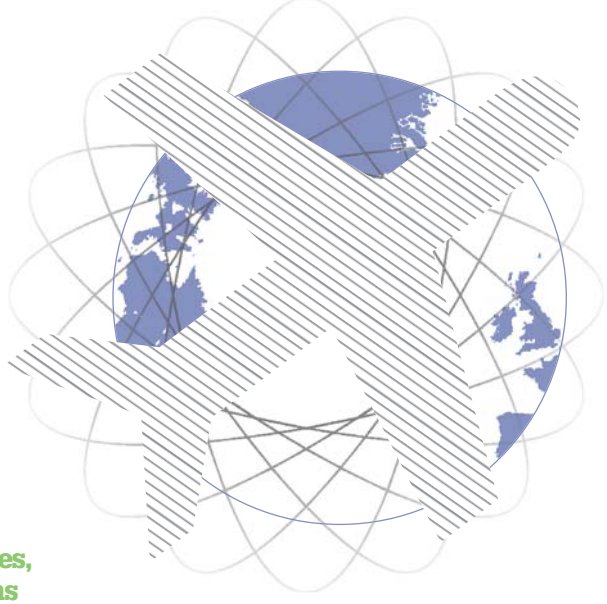

Glaucoma
What is it?
Glaucoma is a group of diseases that can damage the optic nerve. There are often no symptoms in its early stages. Left untreated, it can lead to vision loss & blindness.
Most common form: Primary open-angle
Optic Nerve
NO SYMPTOMS
What are the numbers?
2.7 million people in the U.S. have glaucoma
50% KNOW
50% DON'T KNOW
By 2030,
4.2 million people in the U.S. will have glaucoma
Who's at higher risk?
African Americans 40+
Everyone 60+
especially Mexican Americans
with a Family history of glaucoma
What to do?
Get a comprehensive dilated eye exam every 1-2 years
Early detection and treatment can help save your sight
Where can I learn more?
Visit
http://www.nei.nih.gov/glaucoma
Source: National Eye Institute, 2013


WORLD GLAUCOMA WEEK
MARCH 10-16
FREE
GLAUCOMA SCREENING PROGRAMME
the world is a wonder to see every day
so don't let glaucoma get in the way
Dates: 11- 16th March 2013
Time: 2 PM to 3 PM
Venue: Ophthalmology OPD (A block)
(Tower 1,Ground Floor)
DEPARTMENT OF OPHTHALMOLOGY
Amrita Institute of Medical Sciences
Ph:0484-400 1050/4001234
AMRITA VISHWA VIDYAPEETHAM
Amrita Institute of Medical Sciences
Speed the cure
Spread the word

10


Get a free checkup
Ignoring GLAUCOMA may cost you dearly!
NARAYANA NETHRALAYA
WORLD GLAUCOMA DAY

11



Top Tips for Travellers

Attending conferences, making presentations and sitting on committees is part and parcel of the job for leading ophthalmologists. Here are my tips to make sure you arrive fresh and look the part.

By Andrew Davies

Tip 1. Proper Packing

Start with the suit jacket. Lay it bottom-first into one half of your suitcase, leaving the upper half of the jacket hanging out of the case. Next, place a piece of tissue paper on top of the jacket. Lay your suit trousers or skirt at a 90^0 angle to the jacket with the waistband in the case and the legs or bottom of the skirt out. Place a piece of tissue between every item of clothing. and build up layers till everything is packed. Finally, fold the upper half of the first suit jacket over the pile. There are no sharp folds in your suit and the tissue paper will prevent creases from forming in your clothes.

Tip 2. Keep expensive electrical items in your hand luggage

Sadly, there have been many instances of theft from luggage in transit. As suitcases are now X-rayed at multiple points of the journey, the risk of your expensive gadgets being taken is higher than ever – and most insurance companies won't cover the loss.

Tip 3. Pack a multi-way power adapter

You're bound to be carrying more than one electrical item that needs to be recharged once in a while. Take a multi-way power adapter. This means you need access to only one electrical outlet, which can be in short supply in hotels, coffee shops and airports.

Tip 4. Don't forget plastic bags

Never go on a trip without packing plastic bags in your suitcase. Gym bunnies take note – for the smelliest of reasons. If you put any dirty washing in your suitcase, pop it in the bag, if only as an insurance measure against making your clean clothes less fresh.

Tip 5. Use TSA-approved locks

The US Transport Security Agency (TSA) is authorized to open any luggage and if their inspectors want to search yours they will, whether it's locked or not. To avoid the risk of arriving at baggage reclaim to find your suitcase cut open and wrapped in clingfilm because it as selected for a random check, use TSA-approved locks. TSA security staff have a tool that allows them to open those locks – sparing you the ignominy of carrying a vandalized suitcase for the rest of your journey.

Tip 6. Start a collection of small plastic containers

Decant your favorite toiletries into little plastic bottles. These weigh less than the large bottle you bought at the pharmacy but you still get the bulk savings. And if it's under 100 ml, you can carry it in hand luggage.

Tip 7. Avoid the specter of paper underwear

Take a change of clothes in your hand luggage in case the airline loses your luggage. Paper underwear isn't as much fun as you might imagine…

Tip 8. Let Google Translate do the talking to taxi drivers

If you don't speak the language of where you're going, spend a little time learning "please" and "thank you". It's amazing how far common courtesy will get you. Write down names and addresses of hotels and venues. For anything even slightly complex, use Google Translate to get your message across; preferably, done in advance and printed out to avoid Internet connection issues.

To ensure you don't get ripped off, email your hotel or a local contact to find out how much a taxi should cost; better still, ask the hotel or local contact to arrange a taxi pick-up at the airport – it's likely to be cheaper and will avoid queues. Of course, if it's safe and possible, use public transport if you're on a budget. It'll save you a fortune and you'll get to see more of the place.

Tip 9. If you don't ask, you don't get

Always ask for an upgrade at the airline check-in desk. Being well-dressed will help. This goes for services on the aircraft too. If Economy doesn't get newspapers, but you'd like to read one, just ask the cabin crew nicely. More often than not, they'll oblige.

Tip 10. The most important rule of all

Do not wear new shoes for a whole day, especially if if you have to do a lot of walking. Blisters hurt, and they just get worse, and worse, and worse.

Andrew Davies is CEO of Texere Publishing Limited, Knutsford, UK.

Championing the Will of Wills

Sitting down with Julia Haller, Ophthalmologist-in-Chief, and **Joseph Bilson,** Chief Executive Officer of the Wills Eye Hospital, Philadelphia, PA, USA.

What is unique about Wills Eye Hospital?

Julia Haller: Wills was the first eye hospital in the United States, the gift of a Quaker merchant called James Wills, who died in 1825 leaving his fortune to the city of Philadelphia. Part of our mission, going back to his will, is to take care of the indigent. So, while we gladly treat millionaires and people who have flown in from all over the world, our vocation is to take care of the poor and needy in our region.

Joseph Bilson: It's true, no matter where you come from, if you can get to our door, we're going to take care of you in a first-class way. I'd also say that we are uniquely busy. In addition to our main site in Center City, we have a number of ambulatory surgery centers that sit within the communities. We do close to 50,000 outpatient surgical procedures a year and top 350,000 consultations.

Does your philanthropic mission clash with the pursuit of excellence?

JH: Not at all; they're not mutually exclusive. Philanthropy is by far the major focus for us, the hospital exists to take care of the eyes of the poor. It's not easy financially…

JB: ...but we need no grants from the states or the communities—zero. Everything is paid for by our own investment, private insurance or Medicare. We have operating losses, so we do dip into some of the interest that the endowment contributes, and we do get funds donated to the hospital for the support of free care. Sometimes corporate partners donate products and supplies. It takes a lot of coordination, on our part and on the part of our supporters.

Is there a huge weight of responsibility on your shoulders?

JB: My hair was really dark when I started but it's pretty grey now and I'm trying to just keep it at this point! Actually there's a lot of energy here, and a flexibility of approach, which allows us to get a lot of things done. We helped a lot of people and that in itself is tremendously energizing. And getting the best care possible with the money that we have to spend is very satisfying.

JH: I would say it's not so much a weight of responsibility as a challenge and a privilege to help support the brilliant clinicians and scientists that we work with to eradicate blindness and visual disability.

What's your management style?

JH: I try to nurture the staff, to let them flourish. This means arranging things so that everyone can reach their full potential and take advantage of the opportunities that are open to them. That's good for us as individuals and good for us a hospital. I try to be inclusive and collegial and collaborative and show a positive example.

JB: There's a real team environment here. Everybody feels like we're part of one organization moving in one direction. And I think that's why our reputation is so high.

JH: We talk about "the Wills Eye family". It's a family-oriented, friendly place to work and we like to spend time together. Our residents know to bring a tuxedo because there are three or four black-tie events every year. We enjoy working hard and playing hard.

The hospital is a known innovator, what is exciting you right now?

JH: There's just too much to talk about. I would definitely highlight ocular oncology; we have the biggest program in the world by order of the magnitude. We treat about half of all the ocular melanomas in the US. Similarly for children, where the most common cancerous ocular tumor is retinoblastoma; four or five children are born every week in the US with a retinoblastoma and we will treat two or three of them. Another topic worthy of mention is under-served minorities, such as African-Americans with glaucoma or minorities with diabetes We have a number of projects looking at ways to provide increased access to care for them.

"Four or five children are born every week in the US with a retinoblastoma and we will treat two or three of them."

JH: I'd pick out the wellness project for students in the school system; it is a really huge project where we're trying to provide all the children in the school district with annual eye exams and get them in glasses. To contribute maximally to academic performance, we now start seeing the kids in early elementary years.

What are your views on ophthalmology right now; is at a good place?

JH: On the one hand, it couldn't be more thrilling. It's the most stimulating field of medicine, with some of the most exciting experiments and applications.

On the other hand, there are causes for tremendous concern. In the US, we're constrained in terms of available residency slots. It's a huge problem in every specialty but particularly in ophthalmology as the incidence of ocular diseases rises so sharply with age. We're very interested in working out more efficient ways of treating patients, using telemedicine for example, or employing physician's assistants – non-doctors who can help expand and extend the ability of the individual ophthalmologist to treat more patients.

For Glaucoma

Tough on IOP. Easy on Eyes.

taflotan®

15 µg/ml tafluprost

The first preservative-free prostaglandin

- Effective IOP-lowering [1]
- Low risk of hyperaemia [2]

15 µg/ml tafluprost

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The preservative-free prostaglandin.

Abbreviated Prescribing Information TAFLOTAN® (tafluprost 0.0015% eye drops, solution, single-dose container). **Presentation:** Low-density polyethylene single-dose containers packed in foil pouch. Each single-dose container has a fill volume of 0.3 ml and there are 10 containers in each foil pouch. The following pack sizes are available: 30 x 0.3 ml and 90 x 0.3 ml. One ml of eye drops contains 15 micrograms of tafluprost. **Indication:** Reduction of elevated intraocular pressure in open angle glaucoma and ocular hypertension in patients who would benefit from preservative-free eye drops or who are insufficiently responsive or intolerant or contra-indicated to first line therapy, as monotherapy or as adjunctive therapy to beta-blockers. **Dosage and Administration:** The recommended dose is one drop of TAFLOTAN® in the conjunctival sac of the affected eye(s) once daily in the evening. Not recommended in children or adolescents (under the age of 18). In renal or hepatic impairment use with caution. **Contraindications:** Hypersensitivity to tafluprost or to any of the excipients. **Precautions:** Before treatment is initiated, patients should be informed of the possibility of eyelash growth, darkening of the eyelid skin and increased iris pigmentation. Some of these changes may be permanent, and may lead to differences in appearance between the eyes when only one eye is treated. Caution is recommended when using tafluprost in aphakic patients, pseudophakic patients with torn posterior lens capsule or anterior chamber lenses, or in patients with known risk factors for cystoid macular oedema or iritis/uveitis. There is no experience in patients with severe asthma. Such patients should therefore be treated with caution. **Interactions:** Specific interaction studies with other medicinal products have not been performed with tafluprost. **Pregnancy:** Do not use in women of childbearing age/potential unless adequate contraceptive measures are in place. **Driving:** Tafluprost has no influence on the ability to drive. **Undesirable Effects:** The most frequently reported treatment-related adverse event was ocular hyperaemia. It occurred in approximately 13% of the patients treated with preserved tafluprost and 4.1% of the patients treated with preservative-free tafluprost. Other side effects include: Common (1% to 10%): eye pruritus, eye irritation, eye pain, changes in eyelashes, dry eye, eyelash discolouration, foreign body sensation in eyes, erythema of eye lid, blurred vision, increased lacrimation, blepharal pigmentation, eye discharge, reduced visual acuity, photophobia, eyelid oedema and increased iris pigmentation and headache. Uncommon (0.1% to <1%): superficial punctate keratitis (SPK), asthenopia, conjunctival oedema, blepharitis, ocular discomfort, anterior chamber flare, conjunctival follicles, allergic conjunctivitis, anterior chamber cell, conjunctival pigmentation and abnormal sensation in eye, hypertrichosis of eyelid. **Overdose:** If overdose occurs, treatment should be symptomatic. **Special Precautions for Storage:** Store in a refrigerator (2°C - 8°C). After opening the foil pouch keep the single-dose containers in the original foil pouch, do not store above 25°C, discard an opened single-dose container with any remaining solution immediately after use. **MA Holder:** Santen Oy, Niittyhaankatu 20, 33720 Tampere, Finland. **Date of Preparation:** 11/2012.

1) Taflotan lowered IOP by 6.9 - 9.7 mmHg in masked, randomized studies 1-4. 1. Uusitalo H et al. Acta Ophthalmol 2010; 88: 12-19 2. Traverso C et al. J Ocul Pharmacol Ther 2010; 26: 97-104 3. Konstas AG et al. Comparison of 24-hour efficacy with Tafluprost compared with Latanoprost in patients with primary open-single glaucoma or ocular hypertension. Abstract 5104/A2458 4. Chabi A et al. Am J Ophthalmol 2012; 153: 1187-1196 **2)** Low risk of hyperaemia among prostaglandins: SPC texts of preservative-free Taflotan.

March 2014

Santen