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Global Issues Facing the Ophthalmology Industry Discussed at APAO 2019 Plenary Sessions



by John Butcher

Ophthalmologists focused on global issues at the APAO 2019 Congress in Bangkok, Thailand, yesterday.

Issues covered included efforts to tackle the causes of blindness, myopia and misconceptions about the development of Artificial Intelligence (AI) for the ophthalmology industry.

Dr. Hugh Taylor, former president of the International Council of Ophthalmology (ICO), addressed global blindness and the progress made in tackling it over the last two and half decades.

In 1994 there were 45 million blind people worldwide, he said, with predictions that by 2020 that number would rise to 90 million.

Action by the World Health Organization (WHO) prevented that becoming a reality, with numbers significantly reduced on predictions as many people with preventable blindness were treated.

The WHO's Global Action Plan, as it was called, proved a success across the globe in both developed and developing countries, among men and women, he said.

Nevertheless, levels of visual impairment remain high and these are concerning signs, particularly in Asia, he added.

Dr. Taylor showed two maps that showed high levels of blindness across the Asia region. The main causes of blindness globally are cataracts, which accounts for about 30% and refractive errors (18%), he said, but high myopia and diabetic retinopathy are of increasing concern, particularly in China and India.

There has also been a dramatic increase in levels of glaucoma, he added, while availability of cataract surgery in China remains well behind population needs.

Statistics also show that where cataract surgery is available, the outcomes are often unsuccessful, he said, demonstrating a need for many physicians to improve their performance.

While great improvements have been made, "education and training of ophthalmologists and teams is critical," he said.

He urged leading national ophthalmologists need to become involved, provide leadership and advocate for eye care.

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DAY 1 at APAO 2019 Plenary Sessions

Page 10 On unmet needs in retinal diseases, experts continue to seek foolproof treatments.

Page 12 In discussing new frontiers in glaucoma (from bench to bedside), experts continue to seek the best strategy.

Page 18 The new ways to fight diabetic retinopathy, direct from the experts!



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"We need to think globally and nationally, but act locally," he emphasized. Dr. Ronald Kruger of the Stanley M. Truhlsen Eye Institute at the University of Nebraska Medical Center, compared levels of blindness to visual impairment and argued the case for directing resources towards treating the later surgically.

In 2015 the world population was 7.33 billion, according to statistics, with around 36 million of them blind and 217 million suffering from moderate to severe visual impairment, he told the audience.

While the magnitude of blindness increased by 17% over 25 years to 2015, the magnitude of impairment rose by 35%, he added, and levels of moderate to severe visual impairment continue to rise.

The problem was recognized by the WHO and IAPB in 2006, when they added tackling it to their Vision 2020 campaign, which had originally focused solely on eliminating preventable blindness.

Non-surgical methods for dealing with the issue are limited and costly, he said, with spectacles lasting typically two to five years, and contact lenses requiring good hygiene, education and follow ups, which is prohibitive to their use in poorer countries.

Refractive surgery, while initially costly, could in fact be a cost effective means for tackling visual impairment in the longer term, he argued, with LASIK surgery typically costing around 4,500 euros, while over 30 years contact lenses cost around 15,300 euros, prescription glasses 12,000 euros, prescription sun glasses 5,100 euros, and solutions and cases around 4,900 euros.

Laser surgery is now the most performed elective surgery in all medicine, he added, although the level of people with visual impairment having it remains in single digits percentages.

Laser eye surgery could be particularly effective in developing countries because it requires minimal follow-up, he added. Trials in Nepal, where wealthier patients subsidized treatment for poorer ones, have proved cost effective, he continued.

Resources are limited and currently targeted at areas deemed to be the most important within ophthalmology circles, he said. But more consideration should be given to diverting limited resources towards tackling visual impairment using laser surgery, he argued, as this would have a large impact on a great number of people.

Dr. Tien-Yin Wong, professor and medical director at the Singapore National Eye Centre, addressed what he called the "seven myths of artificial intelligence."

Artificial intelligence (AI) has gripped the ophthalmology industry, he told the audience, bringing concern over jobs and excitement over its possibilities in equal measure.

Despite the hype there are many misconceptions about AI and the direction it is taking, he said, the first being that we know what AI is, while the reality is that we do not. It remains a relatively fledgling and complex industry the full impact of which on ophthalmology is as yet unknown, he said.

The second myth, he continued, is that we are ready for AI. We are not yet ready, he argued, with data sets used in its development still relatively small and missing significant data. In addition, the

industry has yet to learn how to share and collaborate on AI and in ways that will validate it across countries, he added.

Myth three, he said, is that AI is just an algorithm. In reality "like any technology AI needs to be tested and validated on multiple populations in real world settings and implementation is a complex, messy and long process," he said.

Myth four is that AI is fair, quantitative and objective, he told the audience. This remains untrue while "flawed or incomplete data sets can automate bias," he said.

Myth five is that we know how to test and regulate AI, he added. Both of these are at present evolving processes, he said, with frameworks for on-the-job learning by AI algorithms and definite endpoints still unclear.

Myth six is that doctors will be redundant as a result of AI, he said. This concern has been fuelled by unhelpful comments by some ophthalmologists who have suggested there is no need to train new radiologists as AI will make the job obsolete, he said, while in reality the AI remains a long way from full development and implementation.

The final myth, he said, is that AI will prevent blindness. Similar claims were once made about computers treating cancer and they did not develop into reality, he added.

AI remains an evolving technology, he told the audience, in need to better and more data to iron out potential biases. It will be a valuable platform, he added, once frameworks are in place to regulate it properly, and will no doubt be of assistance to doctors. ☺

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September 2018

SPECTRALIS Optical Coherence Tomography (OCT): Principles and Clinical Applications

Dr. Michael M. Teusink, PhD; Rosa Diaz-Marco, MD, PhD; Dr. Marc Lepel, PhD; Dr. Tien-Yin Wong, PhD; Dr. Stephan Schulz, PhD

ABSTRACT

Optical coherence tomography (OCT) is a technique to visualize vascular perfusion in the retina and choroid without dye injection. Various commercial implementations of OCT have been introduced for use in clinical practice, each with specific strengths and weaknesses. This paper provides a comprehensive overview of the functions, strengths, and weaknesses of SPECTRALIS OCTA Module, which is part of the SPECTRALIS multimodal imaging platform. Clinical examples are shown to illustrate the design principles of the SPECTRALIS OCTA Module while highlighting its unique features and demonstrating its clinically relevant capabilities.

Key Words: Retina; Optical coherence tomography; OCT angiography; OCTA; SPECTRALIS; Heidelberg Engineering

BACKGROUND

Optical coherence tomography (OCT) is a non-invasive imaging technique that provides three-dimensional visualization of perfused vasculature of the retina and choroid. In contrast to standard structural OCT, OCTA analyzes not only the intensity of the reflected light but also the temporal changes in the reflection caused by moving particles, such as erythrocytes flowing through vessels. These changes in OCT signal are detected by repeatedly capturing OCT images at each point on the retina and allowing for the creation of an en face contrast. This technique is used to create en face OCT images of the retina and choroid, allowing for the visualization of the retinal and choroidal vasculature. To acquire reliable images, different approaches have been used by several manufacturers, making it difficult to compare results across different devices. Such variations in each device's output may result in different clinical diagnostic interpretations.

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Slicin' It with Care

Learning about Managing Anterior Surgery Complications

by Joanna Lee

The practice of surgery also comes together with hearing about others' experiences and being reminded time and again about the principles and approaches for each arising surgical complication faced.

In surgery, there are events and non-events not to be taken for granted - one must "have a high index of suspicion" according to Dr. Parthoprattim Dutta Majumder as he began his session discussing "Post Surgical Intraocular Inflammation". Even in normal cataracts surgeries, mild iritis could occur and what more with unexpected, pathological circumstances when severe fibrinous reaction or hypopyon uveitis follows an uneventful surgery. One of the tips he shared to decode the inflammation was this: If it's an acute situation, it's occurring for 6 weeks and occurs less than 12 hours of surgery, toxic anterior segment syndrome (TASS) could be considered; if it's within 12-48 hours, it could be endophthalmitis, retained lens fragments or exacerbation of uveitis. If it's more than 6 weeks, then, it could be retained lens fragments, malpositioned IOLs, delayed-onset endophthalmitis or new-onset uveitis.

Injecting some cheerful humor into the morning was Dr. Doric Wong from Singapore who rapidly but precisely shared about "Choroidal Hemorrhage and Effusion". He gave an important reminder that the reaction of the doctor operating is as important as the skills itself - in one painful looking video example, he shared a case video where the surgeon continued on despite seeing a hemorrhage while others may just panic. Patience is also a virtue in surgery, as some cases would resolve on its own. He ended with this important advice for non-retina specialists: "Please refer to your least bad-tempered retina specialist."

In what one of the chairs, Dr. Rajiv Raman described as "beautifully presented", Dr. Manoharan Shunmugam from Malaysia shared "Tips on Handling Cataract Surgery Complications". He



Panel of anterior segment surgeons on management of complications

highlighted the prevention of any diabetic complication, sharing of instrument tips, in particular sharing some guidelines the complicated cannular-associated ocular injury and how to handle external and internal eye pressures, suprachoroidals and how to address cases involving zonular weakness.

There were a few moments of gasps heard from the audience' lips when Dr. Ari Djatikusumo from Indonesia showed a few short video clips demonstrating his talk on "Posterior Capsule Rupture and Dropped Nucleus". It was understandable as intraoperative loss of the nucleus or fragments is very unfortunate. Pars plana as an approach may result in better in early postoperative outcome while again, referring to a retina colleague may help achieve better visual results in this situation.

The chairs of this session also made a special mention of Dr. Hussain Khaqan who had arrived after a 30-hour long flight journey due to a special situation to share his insights on "Post Surgical Endophthalmitis".

Speaking about "Aphakia and Dislocated IOLs", Dr. Marie Joan Loy from the Philippines brought to attention two types of IOL dislocations - the out-of-bag IOL dislocation which is considered as an early IOL dislocation or the in-the-bag IOL dislocation which is a late IOL dislocation issue. The dislocated IOLs can be retrieved using IOL forceps, perfluorocarbon liquid and extrusion cannula. The anterior chamber IOL can

cause elevation of the IOP and corneal endothelial damage. She also showed examples of ciliary sulcus placement of IOL, iris-sutured IOL, retropupillary fixation of iris claw IOL, transscleral suture fixation of IOL and transconjunctival intrascleral fixation of IOL.

The last speaker of the day, Dr. Dipak Nag covered the pros and cons of combined phaco and vitrectomy surgeries. The "phaco-vit" surgery is advantageous as it gives a better view of the retina and can clean up the anterior vitreous nicely and overcome poor fundal reflex. Some of its disadvantages include iris prolapse and post-vitrectomy refraction could be very high. 🌀



Dr. Hussain Khaqan



Dr. Doric Wong



From Trainees to Surgeons, How it's Done in Different Countries

by Khor Hui Min

Training in ophthalmology surgery is an important part of ophthalmology education, but it is also a complicated process. Different countries have different surgical training incorporated in their education curriculum.

On 6 March 2019, the first session on education in ophthalmology was organized in collaboration with the International Council of Ophthalmology (ICO). The topic was surgical training in various countries. The session was chaired by Prof. Dr. Andrzej Grzybowski, Dr. Wai-Ching Lam and Assoc. Prof. Dr. Manchima Makornwattana.

The first speaker of the day was Prof. Dr. Andrzej Grzybowski, who is a professor of ophthalmology at the University of Warmia and Mazury in Olsztyn, Poland. He gave an overview of surgical training in European countries.

"The majority of the residency programmes are 4 to 5 years. The training in France, UK, Portugal and Holland is partly surgical. In Germany, Poland, The Czech Republic, Finland, Romania, Sweden, Denmark and Poland, the training is mostly non-surgical," said Prof. Dr. Grzybowski.

He further added that formal surgical training is provided in the UK, Holland and France, but only UK and Finland have surgeon certification.

Dr. Shahzad I. Mian from the University of Michigan talked about the surgical training in the USA. He firmly believes

that surgical education should be based on competency. He also said that surgical competency for comprehensive ophthalmology is broader than cataract surgery alone.

Next Dr. Wai-Ching Lam from the University of Hong Kong and University of Toronto spoke on surgical teaching in Hong Kong and Canada.

"The Hong Kong program is somewhat similar to the Europe program, and it consists of about 6 years of training, divided into basic training of two years with procedure logbook inspections, and higher training of four years," said Dr. Lam.

He explained that in Hong Kong, there is no surgical teaching curriculum, and trainees are responsible for their own learning. Surgical teaching labs are available at the majority of training centers for practice with the use of either animal eyes or simulation models.

"In Canada, there are about 15-16 programs, with about 36 trainees per year. Trainees must pass the Objective Structured Clinical Examination (OSCE), both written and practical, before starting PGY4 training," said Dr. Lam.

Further, Prof. Dr. Charles McGhee from the University of Auckland spoke about the ophthalmic surgical training in Australia and New Zealand. He shared that the Royal Australian and New Zealand College of Ophthalmologists (RANZCO) has a structured five-year training program at well-supervised,

carefully chosen training centers. The basic training includes wetlab experience and there are regular assessments throughout the program.

Dr. Mingzhi Zhang of the Joint Shantou International Eye Center, of Shantou University and the Chinese University of Hong Kong presented on cataract surgery training in China.

"The program has been conducted in hospitals from 2004 up to now, and 2,636 health workers have been trained," revealed Dr. Zhang.

The final presentation of the session was by Dr. Avinash Pathengay from the LV Prasad Eye Institute of India. He said that 1,500 ophthalmologists become ready to practice every year, and 60% are from government medical institutions. He spoke about persistent problems and how to overcome them.

The session ended with a Q&A session. There was a comment that surgical training should be started as early as possible, at age 24 instead of 34 if possible, as it would improve their competency. Besides that, a doctor from the Philippines shared that the training program in his country was three years, and everything has to be compressed to fit that timeline, so focus and dedication is of the utmost importance.

All in all, the session was a good sharing session among surgical trainers and professors from around the world. 🌐



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Raising the Bar for Glaucoma and Retina

by Hazlin Hassan

Ahead of the APAO 2019 Congress in Bangkok, Thailand, several Ophthalmologists gathered and shared their experiences and insights on a range of tools in the fields of glaucoma and retina to boost workflow efficiencies, diagnostic performance, and patient experience at the Bangkok Marriott Marquis Queens Park, March 5. Glaucoma especially is a highlight of APAO Bangkok, where the Asia-Pacific Glaucoma Society (APGS) is running helpful APGS-MIGS wetlab courses. Efficiencies will only help in this regard.



Dr. Manchima Makornwattana, M.D. (left), prepares to speak on the FORUM Glaucoma Workplace & SITA Faster as the new testing algorithm.

AngioPlex OCT Angiography in Glaucoma

As eye care professionals, being able to thoroughly screen patients for diseases is crucial.

The AngioPlex OCT Angiography (OCTA) provides eye doctors with a comprehensive and complete tool to diagnose and treat patients suffering from progressive eye diseases such as glaucoma and diabetic retinopathy.

"The OCTA is a functional extension of the OCT machine that you already have in your clinical practice. It gives you information on the retinal and choroidal circulations without dye injections because it detects the motion contrast from flowing blood," explained Asst. Prof. Darin Sakiyalak, MD, Chief of the Glaucoma Unit, Siriraj Hospital, Thailand.

All eye doctors are familiar with the OCT (optical coherence tomography) which provides information on the structural imaging based on reflectance intensity, but the OCTA (optical coherence tomography angiography) gives you the image of the ocular vessel based on the motion contrast from the

"The OCTA is a functional extension of the OCT machine that you already have in your clinical practice. It gives you information on the retinal and choroidal circulations without dye injections because it detects the motion contrast from flowing blood."

– Asst. Prof. Darin Sakiyalak

blood flow without the dye, using the same light source from the OCT machine.

Compared to fluorescein angiography (FA), the OCTA is non-invasive, is not dye-dependent, has no fluorescein side effect or blue light toxicity, takes a shorter time to perform and provides 3D images, wider field and more functional data of vessels, she added.

It also shows both structural and

blood flow information at the same time. Looking to the future, the technology could be efficiently processed by computers to diagnose, grade, and treat diseases, she said.

FORUM Glaucoma Workplace and SITA Faster

Many documents and information are needed in glaucoma management, from fundus photography, visual field, optical coherence tomography and trend of intraocular pressure (IOP), noted Asst. Prof. Manchima Makornwattana, MD, Director, Department of Ophthalmology, Thammasat University Faculty of Medicine.

Harnessing advanced technology to make diagnosis and treatment better, the FORUM Glaucoma Workplace (FGW) (ZEISS) is a clinical software application that allows doctors to work interactively with Humphrey Field Analyzer (HFA) exam data and combines HFA exam data with CIRRUS acquisition data.

It combines structural and functional test data into a single integrated report, helping clinicians detect and manage glaucoma more efficiently. "FGW is the single diagnostic platform that gives clinicians truly unified data," she said.

The Swedish Interactive Threshold Algorithm (SITA) Faster, an individualized, self-correcting, self-directing visual field test operating system, slashes testing time by 50%, compared to SITA Standard and 30% compared to SITA Fast.

This can help clinics with long testing times, as well as lead to better therapies. "A significantly faster testing strategy may facilitate more frequent visual field testing," said Asst. Prof. Makornwattana.

This could also result in earlier detection of patients who are progressing rapidly, and the rate of progression could be determined sooner in order to tailor treatments to a patient's needs.

The SITA Faster is clinically equivalent to SITA Fast and Standard, using the same algorithm and normative data. Not only can it handle more glaucoma patients while maintaining the highest level of care for patients, it provides a more pleasant and positive diagnostic experience for them.

"Early detection is key in glaucoma management," concluded Asst. Prof. Makornwattana.

L Disease Treatment

Ultra Widefield Fundus Imaging and CLARUS 500

The CLARUS 500 retinal camera is an ultra-widefield (UWF) fundus imaging system. Its Broad Line Fundus Imaging enables the combination of ultra-wide fields of view, a full range of retinal imaging modes producing images with high contrast, resolution, and true colors, making it easier to see signs of disease in the far periphery of the retina.

It also allows for a more efficient and patient-friendly workflow, along with comfort that ensures image integrity and a satisfying patient experience.

"How important is the resolution in a picture? The importance of resolution in a picture is not just in the central macular where most of pathologies do lie but there may be a lot of peripheral diseases or lesions that we want to look at," said Dr. Jacob Cheng Yen Chuan, Consultant, Vitreo-retinal Services, Singapore National Eye Centre and Director, Retina Services, Eagle Eye Centre Singapore.

“How important is the resolution in a picture?

The importance of resolution in a picture is not just in the central macular where most of pathologies do lie but there may be a lot of peripheral diseases or lesions that we want to look at.”

– Dr. Jacob Cheng Yen Chuan

Modern Multimodal Imaging Transforms Clinical Practice

Among the many advantages of multimodal imaging (MMI) are that they allow doctors to make a diagnosis using the most non-invasive way possible. They can also guide a patient's treatment and monitor the response to it.

"We can use these multimodal imaging systems to differentiate between stable and active referable disease and even decant some stable patients in the clinic and this is really important," said Dr. Anna Tan Cheng Sim, Consultant, Medical Retina, at the Singapore National Eye Centre.

She found that MMI can also differentiate between leakage from multifocal-central serous chorioretinopathy (MF-CSCR) and type 3 neovascularization (NV), and detect secondary choroidal neovascularization (CNV) in chronic CSCR, and monitor the response to multiple complex therapy regimens.

Quiescent neovascularization can also be detected, thereby preventing vision loss. In summary, modern MMI can help to explain symptoms, help doctors to practice patient-centered medicine, make an accurate diagnosis in the most non-invasive way possible, guide treatment and monitor the response to it, she concluded. 🌟



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Experts Address Rise in Dry Eye Disease

by John Butcher

Experts addressed new methods to tackle dry eye disease on the second day of the APAO 2019 Congress in Bangkok, Thailand, yesterday.

There has been an unwillingness to tackle the condition despite its prevalence for a wide variety of reasons, said Dr. Douglas Lam, of the Hong Kong Ophthalmic Associates, including the time involved in diagnosis and re-educating patients about the causes and treatments. Frustration among some physicians may also be a factor, with improvements often slow, patients potentially demanding and many products to choose from. In addition, lack of significant financial reward, due to a limited profit margin for eye drops and an expectation of cheaper treatments among patients, may deter doctors, he added.

Despite the reluctance, the number of patients seeking treatment for dry eye disease however is rising, according to Dr. Lam. The prevalence of laser treatment, as well as heavy use of computers and smartphones, has fuelled an increase in the number of people with dry eye disease, while more are able to afford medical care and turn to physicians after finding over-the-counter eye drops ineffective, he said.

There are ways to accurately diagnose the condition in just ten to 15 minutes, according to Dr. Lam, with ocular staining and tear assessment being common ways, and methods of treatment have advanced to include lifestyle change recommendations alongside new medications.

A popular method for diagnosing dry eye disease is ocular surface staining, according to Dr. Lam, with fluorescein staining the most commonly used.

Staining allows for assessment of the blink function, observance of how the cornea is stained as well as tear break-up time (TBUT) and pattern, conjunctival staining and the status of punctum, which all help in diagnosing the condition.

Old treatments, which are sometimes still used, include tear replacement therapy, punctal occlusion and lid scrubbing, he said, while newer treatments include medications such as Ikervis (Cyclosporine A 0.1% Cationic Emulsion or CsA CE, Santen, Japan) and Diquas (diquafosol sodium, Santen, Japan).



Whatever is used, the treatment goal should be to achieve subjective improvement in the condition, restore ocular surface homeostasis, lower inflammation, reduce conjunctival infection, and maintain intact epithelium.

A typical regimen that he would recommend for treating the condition would be warm compresses, but not lid scrubs, Ikervis, Cationorm (cationic nanoemulsion, Santen, Osaka, Japan), and lifestyle changes, including less smartphone use, adequate sleep and blinking exercises.

Alongside treatment patients should receive counselling and advice, being made aware that dry eye disease is a long term condition and that certain treatments can cause discomfort, emphasized Dr. Lam. They should be asked to commit to the treatment and understand what that entails, he added, as well as agreeing to regular monitoring of their progress.

Dr. Vilavun Puangsricharn, director of the Excellence Centre for Cornea and Limbal Transplantation at King Chulalongkorn Memorial Hospital in Thailand, focused on having what she called "the right tools for the right treatment" of dry eye disease.

Definitions have changed over the years, she said, beginning with the International Dry Eye Workshop's (DEWS) definition in 2007, later revised in 2017, when the Asia Dry Eye Society (ADES) also released a definition. The common factors in both definitions are tear film instability and ocular surface damage.

Diagnosis in the first place, according to ADES, includes the finding of dry eye symptoms, plus an unstable tear film.

From there it is important to determine the film break up pattern, and whether there is any inflammation.

Tear-film oriented diagnosis then determines what type of treatment should be used, which can include warm compresses, artificial tears, diquafosol sodium and cyclosporin steroids, she added.

Dr. K.C. Yoon, of Chonnam National University Medical School, Gwangju, South Korea, suggested taking a holistic approach to the treatment of dry eye disease.

Staged management is recommended for the treatment of dry eye, he said. The first step, according to recommendations by the International Dry Eye Workshop II (DEWS II), is to educate the patient about environmental and dietary modifications that can help to treat the disease, including taking omega-3 oils, eliminating medications that might exacerbate it, using ocular lubricants, warm compresses and taking care of lid hygiene.

The second step includes using non-preserved lubricants on the eyes, topical steroids, topical secretagogues, topical immunomodulators, oral macrolide/tetracycline and punctal occlusion.

Step three involves using oral secretagogues, serum eye drops and therapeutic contact lenses such as soft bandage lenses or rigid scleral lenses.

The fourth and final step is to use topical corticosteroid for a longer duration, amniotic membrane grafts, surgical punctal occlusion, and other surgical approaches.

It is also advisable to optimize treatment according to the type of dry eye and layers of tear film affected, as recommended by the Asia Dry Eye Society (ADES), Dr. Yoon said.

If the eye was classified as having increased evaporation the treatment might be warm compresses, ointment, cationic emulsion, diquafosol sodium, rebamipide, or artificial tears, he said, while aqueous deficiency may be better treated with just diquafosol sodium and artificial tears and decreased wettability with diquafosol sodium and rebamipide.

Finally, treatment should be targeted to improve both ocular surface inflammation and tear film instability, he added.

With lifestyles fueling a rise in dry eye disease and patients better aware of it due to the Internet, demand for treatment is likely to continue rising unabated. However, diagnosis is also now relatively straightforward, according to the symposium speakers, and there are clear directions on how to treat the condition. 🌐

Tuberculous Tales

and Other Curious Cases from Asia Pacific

by Joanna Lee

The cases of uveitis and scleritis which are prevalent in the Asia-Pacific region can be traced back to its miniscule perpetrator, the *mycobacterium tuberculosis* which has wreaked havoc in this region for long. The talks featured in this session became almost as a narrative of deciphering the nemesis and managing the menace it creates along with other problems arising in the region like the prevalence of acute retinal necrosis in Japan, for instance.

Dr. Somasheila Murthy who is also one of the chairs of this session presented a thorough and engaging investigation into the uncommon but painful “Tuberculous Sclera-Uveitis: Diagnosis and Treatment”. She traced the types of tuberculous (TB) scleritis, be it anterior (the most common), posterior (rare) as well as nodular, and necrotizing nodules which may lead to scleromalacia. She also presented ways to diagnose TB scleritis along with how to manage the disease which does not respond to topical steroids alone. In fact, it may get worse with oral steroids and immunomodulators. Anti-tuberculous therapy is the recommended mainstay of treatment.

In a similar vein, Dr. Kalpana Babu's paper seemed to run with the tuberculous baton when she discussed “Tuberculous Granulomatous Anterior Uveitis Differentiation from Ocular Sarcoidosis”. In clinical, radiological and histopathological characteristics, tuberculosis and sarcoidosis look very similar. Drawing on the subtle clues presented by these two diseases, she pointed to do a Schirmer's test if the patient comes with dry eyes or *keratoconjunctivitis sicca* just to be sure. This is because about 60% of sarcoidosis patients have dry eyes. Also, doctors shouldn't miss out on detecting very small or even big granulomas in the conjunctiva as this would be indicative of sarcoidosis. Another way to diagnose would be to do a fundus analysis among other distinct clinical symptoms to look out for.

Continuing the tuberculous track was Dr. Somsiri Sukavatcharin's sharing on “Tuberculous Retinal Vasculitis: Diagnosis & Treatment”, revealing its patterns of manifestation, various etiologies and guidelines for diagnosing

intraocular tuberculosis such as using the tuberculin skin test and interferon gamma release assays (IGRA). In her summary, she said tuberculous retinal vasculitis should be ruled in endemic retinal vasculitis patients while adjacent choroiditis along vessels could be helpful in the diagnosis. Anti-VEGF is also a helpful treatment for retinal vasculitis.

The turn of narratives delved deeper as Dr. Narsing Rao took the stand to present on the complex topic of “Management of Paradoxical Reaction in Tuberculous Choroiditis”. He unpacked the unique challenge that paradoxical reactions are in the management of ocular TB from presumed diagnosis. It is also a reaction that could occur in all forms of ocular TB with exaggerated inflammatory symptoms with progressions or development of new choroiditis lesions at different sites within three months. This reaction generally responds to an increase in corticosteroid dosage with or without immunosuppressive agents.

The audience also had a look at “Ocular Tuberculosis in Acquired Immunodeficiency Syndrome” cases, presented by Dr. Jyotirmay Biswas. It was found that 12% of people newly admitted for HIV care in India also had active tuberculosis. Dr. Biswas's investigations had found a systemic association between the two diseases, bringing to awareness the various clinical presentations in HIV positive patients with TB. Ocular TB in AIDS can also occur with high CD4 cell counts, he said.

Switching the line from tuberculous situations, Professor Hiroshi Goto from Japan shared on the “Diagnosis and Treatment of Acute Retinal Necrosis”. Interestingly, approximately 15% of all acute retinal necrosis (ARN) cases are infectious uveitis in Japan where Professor Urayama first reported the case of ARN in 1971, caused by either the HSV-1, 2 or VZV virus. He then described ARN's typical clinical symptoms following diagnostic guidelines proposed by the American Uveitis Society, but not without cautioning on the differential diagnosis of acquired toxoplasmosis treated inadequately. Prof. Goto also revealed a new set of proposed



diagnostic criteria for ARN based on the parameters of early stage findings, clinical course and virological testings after test conducted by the Japanese. He also shared about using systemic anti-viral and anti-inflammatory treatment.

Dr. Sutasinee Boonsopon from Thailand discussed four case studies exemplifying the “Management Approaches to Syphilitic Uveitis”. Her case studies featured patients from different ages and backgrounds with syphilitic uveitis. Some were HIV-positive or had a history of shingles, some were homosexuals, and some were intravenous drug users who came with symptoms of blurred visions experienced in both eyes ranging from one month to a few months. They decided to use penicillin as the adjunctive treatment for the cases and with the subsequent results turning out quite well. The typical treatment for ocular syphilis consists of aqueous penicillin topped up with intramuscular benzathine penicillin injections. In one of the cases, IVT bevacizumab was used. Dr. Boonsopon termed ocular syphilis the “great masquerader” and subsequently urged those who come across uveitis patients to consider syphilis as one of the differential diagnoses.

Last but not least, the “Diagnosis and Treatment of Atypical Toxoplasmic Retinochoroiditis” presented by Dr. Wantanee Sittivarakul expounded the diagnosis and treatment of this condition along with alerts as to the atypical presentations of ocular toxoplasmosis particularly in immunocompromised patients. Laboratory tests, she shared, is often a useful and required step to confirm the diagnosis of this condition. 🌀

Seeking the Right Recipe for Foolproof Treatments



by Hazlin Hassan

Foolproof recipes to make cakes and pies that are guaranteed delicious, can sometimes elude the most experienced baker.

This also seems to be the case for some retinal diseases.

While effective treatments for retinal diseases are leading to improvement of patients' vision, many patients still have unmet medical needs, as several surgeons shared yesterday at the APAO 2019 Congress in Bangkok, Thailand.

Dr. Kazuaki Kadonosono, MD, Department of Ophthalmology and Microtechnology, Yokohama City Medical School, presented on a study to evaluate the effectiveness and safety of retinal arterial recanalization treatment for eyes with central retinal artery occlusion.

Central retinal artery occlusion (CRAO) is a disease of the eye where the flow of blood through the central retinal artery is blocked (occluded). There are several different causes of this occlusion; the most common is carotid artery atherosclerosis.

Patients typically present with sudden, dramatic onset of devastating visual loss. It is an ophthalmic emergency that requires immediate evaluation. "Cannulation with a microneedle allows us to dislodge emboli in an arterial vessel to treat retinal occlusion," he explained.

The retinal endovascular surgery is at the limit of what surgeons are able to accomplish with manual precision, he added. "There is still much to learn and improve to maximize the potential of this approach."

Dr. Yongchai Nilanont, MD, of Siriraj Stroke Center, Siriraj Hospital,



Mahidol University, Thailand, shared a presentation on "Retinal Stroke: Perspectives from Neurologist, Hematologist and Ophthalmologist". Her talk was given by a representative as she was unable to attend.

Retinal vein occlusion (RVO) is the second most common retinal vascular disease after diabetic retinopathy, affecting mainly middle age to elderly patients.

Untreated patients generally had poor visual acuity which decline further over time. This results in substantially higher medical costs and resource utilization that glaucoma or systemic hypertropia (HT) and also leads to an increased stroke risk.

It seems there aren't that many options for RVO.

"No high-quality evidence exists to support routine use of antithrombotic drugs," Dr. Nilanont said.

Anticoagulation may be considered in patients with recent onset of symptoms, and with no risk factors such as glaucoma. Long term anticoagulation may be considered for patients with persistently positive antiphospholipid antibodies.

Experience with direct oral anticoagulants such as apixaban, rivarozaban and dabigatran is lacking.

There are many current standard treatment options for acute CRAO including corticosteroids, ocular massage and carbon dioxide but none have been shown to be more effective than placebo.

Dr. Chamchan Chanchang, MD, MPH, Center of Hyperbaric Medicine, Somdech Phra Pinklao Hospital, Naval Medical Department, shared on "Hyperbaric Oxygen Therapy (HBOT)".

A retrospective study on the treatment outcome of central retinal artery with hyperbaric oxygen therapy in Somdech Phra Pinklao Hospital showed that HBOT in acute non-arteritic CRAO had a good outcome. From 41 patients, 27, or 65.9%, were improved.

The early onset group saw a better outcome of 72% than the late onset group (56.3%) but due to the small sample size, it is deemed of no statistical significance.

"Further study with more sample size needs to be continued in this Hyperbaric oxygen center," she concluded.

In summary, she noted that supplemental oxygen is essential in treating CRAO as retinal ischemic penumbra is capable of recovery within a certain timeframe, and HBOT shows good results, especially with early onset patients.

However, there are some limitations of HBOT accessibility in many areas outside Bangkok, the cost of treatment is high at 12,000-60,000 Baht per session, and protocols vary among physicians.

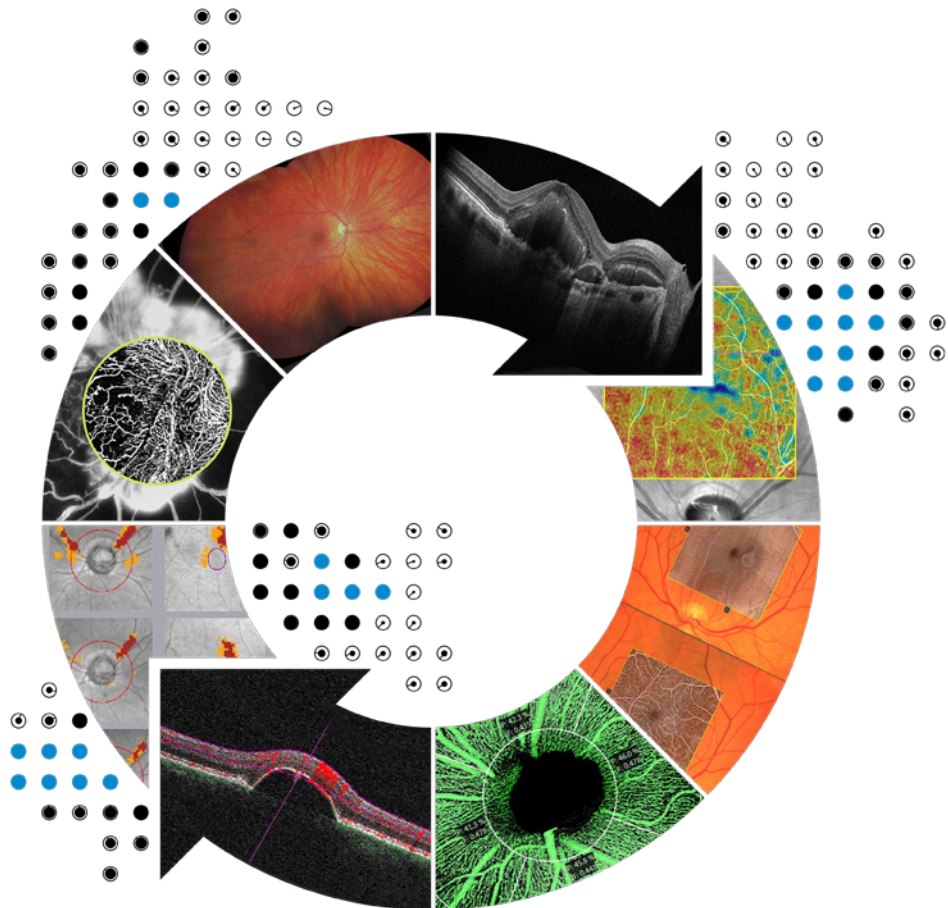
Dr. Don-Il Ham, MD, from Sungkyunkwan University, Samsung Medical Center, South Korea, told delegates that there is no proven therapy for dry age-related macular degeneration.

There are ongoing trials with stem cell therapy, to try and replace dysfunctional or dead RPE cells with cells grown from stem cells.

"Two small case series showed visual acuity improvement in over half of treated eyes," he said, adding however there were some adverse events such as endophthalmitis and cataract progression. "There is still insufficient evidence, but further research is underway," he said. 🧐

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The Perfect Recipe for

Glaucoma Treatment

by Khor Hui Min

Glaucoma can be described as a group of diseases that harm the eye's optic nerve. It can lead to loss of vision and eventual blindness. As such, early detection plays a key role in protecting and preserving vision.

In the session on 'New Frontiers in Glaucoma: From Bench to Bedside', professors and researchers talked about the 'perfect recipe' to prevent vision loss in glaucoma that combines the essential ingredients of screening, treatment and research to advance medical care in this area.

Creating a recipe for treatment

Prof. Dr. Janey Wiggs, professor of ophthalmology at Harvard Medical School, spoke on the need for Angiopoietin-1 (ANGPT1) for Schlemm's canal development in mice and humans.

"The gene TEK and ANGPT1 loss of function mutations cause glaucoma phenotypes ranging from congenital to adult onset. ANGPT1 common single-nucleotide polymorphisms (SNPs) are also significantly associated with primary open angle glaucoma (POAG) and intraocular pressure (IOP)," explained Prof. Wiggs.

SNP is a substitution of a single nucleotide that happens at a particular position in the genome. This type of variation occurs to some degree within a population.

"TEK/ANGPT signalling related to glaucoma primarily influences development and/or remodelling of Schlemm's canal, a modified lymph vessel," added Prof. Wiggs.

"Modelling of TEK-ANGPT signalling could prevent glaucoma development, especially elevation of IOP. Augmentation of ANGPT1 could

reduce IOP or protect against elevation. ANGPT1-related therapy could be most effective in individuals with ANGPT1 genetic risk factors. Thus, targeted delivery to Schlemm's canal would be beneficial."

Discovering the link to developing a great recipe

Prof. Dr. Claire Mitchell from the University of Pennsylvania talked about linking elevated IOP to inflammatory signals.

"ATP release is associated with elevated IOP and mechanical strain, which raises interleukin-1 (IL-1 β) in vivo and in vitro. P2X7R (receptor) stimulation is necessary and sufficient for IL-1 β in vivo and in vitro. This is a likely link between mechanical strain and inflammatory signals in glaucoma," said Prof. Mitchell.



Research to improve treatment formulas of the future

Furthermore, Assoc. Prof. Dr. Bo Peng presented on the origins of repopulated microglia in the brain and retina. He found that microglia rapidly repopulate the whole brain after drug withdrawal, and Nestin+ cells are the source of repopulated microglia. Also, repopulated microglia in the brain are solely derived from the proliferation of residual microglia.

In the retina and central nervous system (CNS), microglia are resident monocytes that function the same way as macrophages. They are known to react to local tissue injury or degeneration.

"The inhibition of CSF1R completely eliminates microglia in the retina, and the repopulated microglia of the retina are not derived from Nestin+ cells. The repopulated retinal microglia are primarily derived from residual microglia outside the retina," said Prof. Peng.

He found that center-emerging microglia are derived from residual microglia in the optic nerve, while periphery-emerging microglia are derived from macrophages in the ciliary body/iris.

Enhancing methods for glaucoma management

Drug delivery system (DDS) is an alternative medical treatment, and patients are receptive to methods other than eyedrops.

"Some questions that should be asked before using DDS include the duration of effect (options for different severity/stage), and the ideal location of delivery. Patient safety should also be prioritized. Therefore, long-term safety data is important," said Assoc. Prof. Dr. Tina T. Wong from the Singapore Eye Research Institute (SERI).

"In a survey of 155 board certified ophthalmologists in collaboration with the American Glaucoma Society, Duke University USA, and DUKE National University of Singapore (NUS), it was found that the shortest retreatment period acceptable is 3-4 months (49.7%) and 6-9 months (39.6%). For devices requiring minor operation procedure, one-year efficacy is preferable," she added.





Is sleep apnea a hidden ingredient in glaucoma progression?

All animals sleep. Sleep is necessary to maintain CNS physiological function, remodelling of synapses, neural plasticity, brain growth, rejuvenation of brain metabolism, and stimulation of brain function.

"In the human body, changes in cardiovascular physiology balanced by autoregulatory mechanisms help to maintain homeostasis. In obstructive sleep apnea syndrome (OSAS), this balance is upset, leading to decreased oxygenation and sympathetic activation," said Dr. Robert Ritch, founder of the Glaucoma Center at the New York Eye and Ear Infirmary.

OSAS is greatly under-diagnosed and highly treatable. It has systemic associations with hypertension, stroke, epilepsy, atrial fibrillation, impaired sympathetic tone, cerebral and coronary vascular disease, congestive heart failure, metabolic and cognitive dysfunction, endothelial dysfunction and coagulopathies, oxidative and inflammatory stress, gout, excessive daytime sleepiness, and decreased productivity and quality of life.

"POAG is more common in OSAS and vice versa, and OSAS is more common in normal tension glaucoma (NTG) than high tension glaucoma (HTG). Also, there is decreased blood flow in OSAS," explained Dr. Ritch. "The severity of OSAS is proportional to the severity of glaucomatous damage."

What's cooking in biomechanics?

Dr. Michaël J.A. Girard, Assistant Professor at Department of Biomedical Engineering, National University of Singapore, talked about new frontiers in the biomechanics of the optic nerve head (ONH). His research involved the modelling of the ocular pulse and its impact on the ONH, and the influence of connective tissue stiffness.

"The ONH is exposed to many loads. These include IOP and its fluctuations, cerebrospinal fluid pressure (CSFP) and its fluctuations, optic nerve pulling/traction during eye movements, choroidal/blood vessel swelling, and orbital fat pressure," said Dr. Girard.

Spicing things up in optic disc research

In a Blue Mountain eye study on the prevalence of disc hemorrhages (DH), it was found there was a higher prevalence in normal tension glaucoma (NTG) rather than POAG or ocular hypertension (OHT).

"In an Australian population of 3,654 persons aged 49 and above, there was a 25% prevalence in NTG (compared to 8% in POAG and 1.5% in OHT) and 13.8% prevalence in OAG (compared to 1.4% in the population)," said Dr. Ki Ho Park, from Seoul National University, South Korea.

"In a survey of 5,612 persons in Korea aged 19 and above, the prevalence was 0.42%. The associated factors were age and glaucoma. The presence of DH suggested the presence of glaucoma

with a positive predictive value of 41.4%," he added.

"In a nutshell, DH is more frequently found in NTG rather than in POAG, and it is larger and longer in NTG compared to POAG. The key DH mechanisms currently under discussion are mechanical vascular disruption and associated vascular susceptibilities. Also, there is a reasonable possibility that immunologic and/or inflammatory factors may be associated with DH."

Cooking up some medical therapy recipes

Medical science is continually evolving, incorporating the latest technological advances and breakthroughs in research to bring better and more effective treatments to patients.

According to Dr. Megumi Honjo from the University of Tokyo, the Rho kinase (ROCK) inhibitors lower the IOP via regulation of trabecular outflow resistance, affecting trabecular meshwork (TM) cells and stageman canal expander (SCE) cells.

"The ROCK inhibitor ripasudil was safe and effective in the treatment of glaucoma in Japanese patients, with a low incidence of adverse drug reaction (ADR) and reduced IOP. In glaucoma subtypes, ripasudil was especially effective in secondary open-angle glaucoma (SOAG) subjects," said Dr. Honjo.

Further investigation of aqueous humor outflow physiology may provide valuable insight into understanding glaucoma pathology and formulating new treatments. ☺

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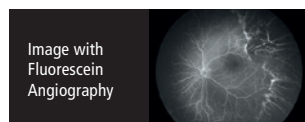


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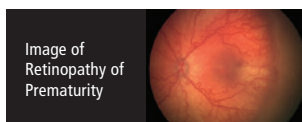


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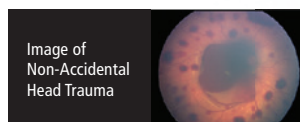


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Advancing Technology

Has Potential to Overhaul Ideas

About Ophthalmology



by John Butcher

Technology is developing fast in the ophthalmology world, bringing with it major changes as machines advance diagnosis, reduce costs and broaden the reach of eyecare.

It heralds an “exciting era,” Tien Yin Wong, professor and medical director at Singapore National Eye Centre, told a meeting on the second morning of the APAO 2019 Congress in Bangkok, Thailand, with changes driven by advances in artificial intelligence (AI) and specifically deep learning, a branch of machine learning based on learning data representations as opposed to task-specific algorithms.

There has been major progress in recent years, according to Dr. Wong, in screening using fundus photographs for diabetic retinopathy, diagnosis, screening and prognosis of age related macular degeneration (AMD) and diabetic macular edema (DME) using optical coherence tomography (OCT), glaucoma screening, real world testing and in getting regulatory approval for new technology, as a result of AI technology.

The development of Google’s deep learning system and the IDx artificial intelligence-based diagnostic system

(which was recently approved by the US Food and Drug Authority [FDA]), both of which are used for the detection of diabetic retinopathy, have led the way, he said.

Dr. Paisan Ruamviboonsuk, chief of the department of medical policy development and strategic planning at Rajavithi Hospital in Bangkok, posed the question whether AI could be used to detect DME using retinal images.

He introduced a study comparing AI results with those of experts, in which an AI deep learning system recorded high scores for sensitivity, specificity, accuracy and Cohen’s Kappa, in many cases better than the experts.

While the study had some limitations, such as sample size, it showed a definite potential to use AI to predict DME using 2D images, making eyecare more practical and accessible to patients, he said.

Dr. Sang Jun Park, of Seoul National University Bundang Hospital, South Korea, talked about the need to input good data in order for AI systems to function properly.

He outlined his own struggles that led to the development of an annotation system for photographs that could be analyzed by AI.

They began in 2015 when he began

archiving retinal fundus images. By early 2017 he had developed a significant database, he said, including 199,856 normal fundus images and 41,319 with abnormal findings.

He realized the need to clean up the data attached to each image in order to make it useable by an AI system, and this led to the development of an annotation system, labelling the quality of image, whether the eyes were abnormal or not, other findings and their regional information, diagnoses based on those findings, and their clinical significance.

“We need to consider human intelligence before artificial intelligence,” he said, in reference to the information that is fed to AI systems in order for them to learn.

Dr. Michael Chiang, a professor of Ophthalmology and Medical Informatics and Clinical Epidemiology at the Oregon Health and Science University School of Medicine, Portland, USA, spoke about the retinopathy of prematurity (ROP) and the potential for AI to be used in its diagnosis.

Plus disease in the mother is a primary indicator that a child might develop ROP, he said, but the diagnosis of Plus disease remains difficult. The general consensus among experts is that Plus disease is something experts know when they see

it, but are unable to quantify in terms of symptoms, he told the audience, which leads to a large degree of inaccuracy.

His study brought together experts and followed their diagnoses systems in order to find a way to create greater accuracy. In doing so it found there was inconsistency in the process of diagnosing between different experts, he said, with a great deal of “qualitative art” used as opposed to scientific methods.

The study then moved on to analyzing whether a machine learning approach could better diagnose Plus disease using retinal image analysis.

It found a greater degree of accuracy in the deep learning system (91%) than among the experts (eight experts, mean accuracy 82%).

Analysis of the results showed among the experts there were over-callers, who diagnosed Plus disease more aggressively, and under-callers, who tended to diagnose it less often, according to Dr. Chiang. There was consensus among experts on eyes with no abnormality and severe abnormalities, but they differed in diagnosis significantly where abnormalities were mild.

The study demonstrated the potential use of deep learning for risk modelling which children could eventually need treatment for ROP. It also showed the potential for good clinical care to be a “combination of science, technology and art,” he said.

Dr. Theodore Leng, director of clinical and transactional research at Byers Eye Institute, Stanford University School of Medicine, spoke on the ability of AI to reduce costs and broaden access to eyecare though the use of smartphones.

Smartphones are everywhere, cheap, portable, low-cost and have high quality cameras as well as built in connectivity, he said, introducing a diabetic retinopathy algorithm he was involved in developing that can be used via a phone.

The research goal was to develop a fully automated deep learning algorithm to detect diabetic retinopathy from color fundus photographs, with the ultimate aim of increasing the number of diabetics screened by five percent and increasing healthcare system efficiency by only referring patients with diabetic retinopathy to ophthalmologists.

The algorithm was developed using a dataset of more than 75,000 fundus photographs, he said, graded as having DR or not and on whether the DR was mild to severe.

The dataset was then augmented by adding other variables, such as adjusting the lighting, color and angle of photographs to accommodate different camera models and conditions.

The study concluded that an AI-based grading algorithm could be used to screen fundus photographs, and was in fact highly reliable.

Testing the algorithm on smartphones presented some additional issues, such as lighting, but also proved possible, he said, concluding that the findings could extend the reach of eyecare.

The next challenges for AI in respect to ophthalmology are non-technical, according to Dr. Wong, and include potentially evolving regulatory processes and unrealistic public expectations.

Once those are overcome only then will it have the potential to “disrupt ophthalmology,” he said. 🌐



Dr. Theodore Leng



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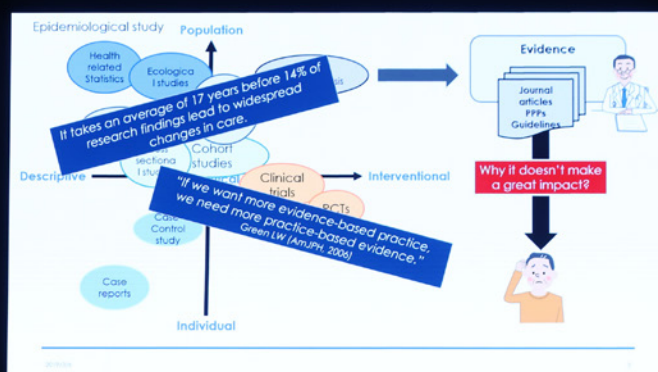
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New Ways to Fight DR,

by Hazlin Hassan

Freshly-baked from the Oven



While grandma may well know the best tried and tested recipes for a classic sponge cake or apple pie, there is always more than one way to skin a cat and a good baker is often inspired to come up with new and innovative methods.

Blindness from diabetic retinopathy (DR) continues to be a major public health issue and is often preventable.

Eminent surgeons in their field shared updates in the challenges of diagnosis and treatment of proliferative diabetic retinopathy (PDR) and maculopathy.

Among some of the exciting new developments in diabetic screening is the use of disruptive technology using AI.

In the present era of anti-VEGF therapy, new drugs and strategies in managing treatment-resistant maculopathy was also discussed.

Tien-Yin Wong, MD, PhD, Professor and Medical Director, Singapore National Eye Centre, presented this year's Jose Rizal Medal Lecture titled "War on Diabetic Retinopathy: Where are we now?"

In 2007, there were 246 million patients with diabetes worldwide. By 2030, this figure is expected to rise to 415 million.

"Gaps exist largely in populations that are not aware about diabetic retinopathy," he said.

Research suggests that more than 75% of those with diabetic retinopathy

and more than 50% of those with DR and diabetic macular edema were not even aware that they have diabetic retinopathy.

"We have not done so well in DR screening," said Dr. Wong.

In 2004, the Singapore government had recommended the establishment of a national-level DR screening program, he said, but in 2014 the program was still in development.

So far the program covers up to 200,000 patients with diabetes or 50%, in 18 primary care clinics across the city-state.

"DR is a global epidemic that needs whole country, population-wide, international strategies to tackle - we are fighting a war!"

The three ways to tackle it is to prevent diabetes, use anti-VEGF, and early screening. Also, Dr. Wong foresees that Artificial Intelligence (AI) will likely have a major impact on screening, detection and care.

However, more efforts are needed, including guidelines, to promote and develop national level DR screening programs, he concluded.

When it comes to the latest in cutting-edge ophthalmic technologies, artificial intelligence is definitely one of those on top of the list.

AI is on the cusp of transforming medicine, delivering new technologies that could empower both doctors and

their patients. Google's new AI algorithm can reportedly predict heart disease simply by scanning your retina.

"We are very excited about the idea of AI-assisted science. When we talk about Deep Learning (DL), really what we are talking about is a way to model eye dimensional data. There have been some very exciting results in recent years," said Dr. Pearse Keane, Moorfields Eye Hospital and UCL Institute of Ophthalmology, UK, on the role of clinically applicable DL in OCT for diagnosis and referral in retinal disease.

He cited the example of scientists from Google Brain looking at UK retinal fundus photographs and predicting whether the scans were from a man or a woman with a large degree of accuracy using DL.

"There may be a lot of new insights that we can get from our data using this type of modeling approach. With AI and DL, it has the potential to be transformative. However, there are also a lot of ways that it might not work. So we have to be very cautious about it and we have to require the same levels of clinical validation that we would require if this was a new drug," he said.

Dr. Taraprasad Das, Vice Chair, LV Prasad Eye Institute, Hyderabad, India, talked about "Screening Strategies and Artificial Intelligence in DR".

"In the future, it is expected that these technologies will be applied in real-world

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“Anti-VEGF injections for DME are revolutionary but up to 30% do not respond optimally.”

Dr. Andrew Chang



screening programs to improve their efficiency and affordability,” he said.

Deep neural networks offer a great advantage of screening for DR from retinal images, in improved identification of DR lesions and risk factors for diseases, with high accuracy and reliability, he added.

DL in ocular may be used in conjunction with telemedicine as a possible solution to screen, diagnose and monitor major eye diseases for patients in primary care and community setting.

This would definitely be a boon for those living in remote areas with little to no access to a healthcare provider, and where financial concerns may be a barrier.

Other speakers shared on the latest alternatives for treating DME and PDR.

Dr. Chen Youxin, Peking Union Medical College Hospital, Beijing, China, shared on the use of conbercept for the management of diabetic macular edema (DME) and proliferative diabetic retinopathy (PDR). Conbercept is a new anti-VEGF fusion protein drug.

The SAILING study, conducted to assess the safety and efficacy of intravitreal injection of conbercept on visual acuity and anatomic outcomes in patients with DME, had demonstrated the efficacy and safety of conbercept for the treatment of DME, he noted.

“Conbercept can regress NVD rapidly in PDR patients, meanwhile

administration of conbercept before pars plana vitrectomy (PPV) can also bring additional benefits for PDR patients,” he said.

Dr. Andrew Chang, PhD, Sydney Retina Clinic, Sydney Eye Hospital, Sydney University, Australia, presented on the management of refractory DME.

“Anti-VEGF injections for DME are revolutionary but up to 30% do not respond optimally,” he pointed out.

A study on treatment-resistant DME, the “Aflibercept Switch Study”, explained Dr. Chang, sought to evaluate the visual and anatomical outcomes following switching therapy from bevacizumab to aflibercept in patients with persistent DME.

Five intravitreal aflibercept injections were given every 4 weeks until week 16, with assessments conducted at every four weeks and every six months.

Findings from the study include that a switch to aflibercept may offer vision and anatomic improvements for patients with bevacizumab-resistant DME.

Vision improved by 3.7 letters at 48 weeks; injections were well-tolerated and there was an improvement in diabetic retinopathy scores.

There you have it, some of the latest concoctions cooked up by eminent researchers and scientists in the ophthalmology field. Here’s to more of these well-prepared and well-seasoned recipes in the near future. 🍷

One Drop,
Once Daily¹

Break the
Vicious cycle²
is the ultimate aim
to manage DED.



Ikervis® is indicated for the treatment of severe keratitis in adult patients with dry eye disease, which has not improved despite treatment with tear substitutes.^{1,2}

**IKERVIS eye drops, emulsion
(Cyclosporin 1 mg/mL)**

Reference : 1. Full prescribing information of Ikervis_Sep2015 2. TFOS DEWS II Management and Therapy Report. L. Jones et al. The Ocular Surface;15(2017): 575-628.

PRODUCT DESCRIPTION Eye drops, emulsion. Milky white emulsion. One mL of emulsion contains 1 mg of cyclosporin. **INDICATIONS** Treatment of severe keratitis in adult patients with dry eye disease, which has not improved despite treatment with tear substitutes. **POSLOGY AND METHOD OF ADMINISTRATION** IKERVIS treatment must be initiated by an ophthalmologist or a healthcare professional qualified in ophthalmology. **Essentialy Adults** The recommended dose is one drop of IKERVIS once daily to be applied to the affected eye(s) at bedtime. Response to treatment should be reassessed at least every 6 months. If a dose is missed, treatment should be continued on the next day as normal. Patients should be advised not to instill more than one drop in the affected eye(s). **Elderly patients** The elderly population has been studied in clinical studies. No dose adjustment is required. **Patients with renal or hepatic impairment** The effect of IKERVIS has not been studied in patients with hepatic or renal impairment. However, no special considerations are needed in these populations. **Paediatric population** There is no relevant use of IKERVIS in children and adolescents aged below 18 in the treatment of severe keratitis in adult patients with dry eye disease, which has not improved despite treatment with tear substitutes. **Method of administration** Ocular use. Precautions to be taken before administering the medicinal product Patients should be instructed to first wash their hands. Prior to administration, the single-dose container should be gently shaken. For single use only. Each single-dose container is sufficient to treat both eyes. Any unused emulsion should be discarded immediately. Patients should be instructed to use nasolacrimal occlusion and to close the eyelids for 2 minutes after instillation, to reduce the systemic absorption. This may result in a decrease in systemic undesirable effects and an increase in local activity. If more than one topical ophthalmic medicinal product is being used, the medicinal products must be administered at least 15 minutes apart. IKERVIS should be administered last. **CONTRAINDICATIONS** Hypersensitivity to the active substance or to any of the excipients. Active or suspected ocular or peri-ocular infection. **SPECIAL WARNINGS AND PRECAUTIONS FOR USE** IKERVIS has not been studied in patients with a history of ocular herpes and should therefore be used with caution in such patients. **Contact lenses** Patients wearing contact lenses have not been studied. Careful monitoring of patients with severe keratitis is recommended. Contact lenses should be removed before instillation of the eye drops at bedtime and may be reinserted at wake-up time. **Concomitant therapy** There is limited experience with IKERVIS in the treatment of patients with glaucoma. Caution should be exercised when treating these patients concomitantly with IKERVIS, especially with beta-blockers which are known to decrease tear secretion. **Effects on the immune system** Medicinal products, which affect the immune system, including cyclosporin, may affect host defences against infections and malignancies. Co-administration of IKERVIS with eye drops containing corticosteroids could potentiate the effects of IKERVIS on the immune system. **Excipient** IKERVIS contains cetalkonium chloride which may cause eye irritation. **INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION** No interaction studies have been performed with IKERVIS. **Combination with other medicinal products that affect the immune system** Co-administration of IKERVIS with eye drops containing corticosteroids could potentiate the effects of cyclosporin on the immune system. **FERTILITY, PREGNANCY AND LACTATION** **Women of childbearing potential/contraception in females** IKERVIS is not recommended in women of childbearing potential not using effective contraception. **Pregnancy** There is no data from the use of IKERVIS in pregnant women. Studies in animals have shown reproductive toxicity following systemic administration of cyclosporin at exposure considered sufficiently in excess of the maximum human exposure indicating little relevance to the clinical use of IKERVIS. IKERVIS is not recommended during pregnancy unless the potential benefit to the mother outweighs the potential risk to the foetus. **Breast-feeding** Following oral administration, cyclosporin is excreted in breast milk. There is insufficient information on the effects of cyclosporin in newborns/infants. However, at therapeutic doses of cyclosporin in eye drops, it is unlikely that sufficient amounts would be present in breast milk. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from IKERVIS therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. **Fertility** There is no data on the effects of IKERVIS on human fertility. No impairment of fertility has been reported in animals receiving intravenous cyclosporin. **EFFECTS ON ABILITY TO DRIVE AND USE MACHINES** IKERVIS has moderate influence on the ability to drive and use machines. This medicinal product may induce temporary blurred vision or other visual disturbances which may affect the ability to drive or use machines. Patients should be advised not to drive or use machines until their vision has cleared. **UNDESIRABLE EFFECTS** **Summary of the safety profile** In four clinical studies including 532 patients who received IKERVIS and 398 who received a IKERVIS vehicle (control), IKERVIS was administered at least once a day in both eyes, for up to one year. The most common adverse reactions were eye pain (19%), eye irritation (17.8%), lacrimation (6.2%), ocular hyperaemia (5.5%) and eyelid erythema (1.7%) which were usually transitory and occurred during instillation. The majority of adverse reactions reported in clinical studies with the use of IKERVIS were ocular, and mild to moderate in severity. **List of adverse reactions** The following adverse reactions listed below were observed in clinical studies. They are ranked according to system organ class and classified according to the following convention: very common (>1/10), common (>1/100 to <1/10), uncommon (>1/1000 to <1/100), rare (>1/10,000 to <1/1000), very rare (<1/10,000), or not known (cannot be estimated from the available data). **Infections and infestations** : Uncommon such as Keratitis bacterial, herpes zoster ophthalmic. **Eye disorders** : Common such as Erythema of eyelid, lacrimation increased, ocular hyperaemia, vision blurred, eyelid oedema, conjunctival hyperaemia, eye irritation, eye pain. Uncommon such as Conjunctival oedema, lacrimal disorder, eye discharge, eye pruritus, conjunctival irritation, conjunctivitis, foreign body sensation in eyes, deposit eye, keratitis, blepharitis, corneal decompensation, chalazion, corneal infiltrates, corneal scar, eyelid pruritus, indolent. **General disorders and administration site conditions** : Very common such as Instillation site pain. Common such as Instillation site irritation, instillation site erythema, instillation site lacrimation. Uncommon such as Instillation site reaction, instillation site discomfort, instillation site pruritus, instillation site foreign body sensation. **Description of selected adverse reactions** Instillation site pain was a frequently reported local adverse reaction associated with the use of IKERVIS during clinical trials. It is likely to be attributable to cyclosporin. One case of severe epithelial erosion of the cornea identified as corneal decompensation by the investigator resolved without sequelae was reported. Patients receiving immunosuppressive therapies, including cyclosporin, are at increased risk of infections. Both generalised and localised infections can occur. Pre-existing infections may also be aggravated. Cases of infections have been reported uncommonly in association with the use of IKERVIS. **OVERDOSE AND TREATMENT** A typical overdose is not likely to occur after ocular administration. If overdose with IKERVIS occurs, treatment should be symptomatic and supportive. **PHARMACODYNAMICS/PHARMACOKINETICS** 1. Pharmacodynamic properties **Pharmacotherapeutic group** : Ophthalmologicals, other ophthalmologicals, ATC code: S01XA18. **Mechanism of action and pharmacodynamic effects** Cyclosporin (also known as cyclosporin A) is a cyclic polypeptide immunomodulator with immunosuppressant properties. It has been shown to prolong survival of allogeneic transplants in animals and significantly improved graft survival in all types of solid organ transplantation in man. Cyclosporin has also been shown to have an anti-inflammatory effect. Studies in animals suggest that cyclosporin inhibits the development of cell-mediated reactions. Cyclosporin has been shown to inhibit the production and/or release of pro-inflammatory cytokines, including interleukin 2 (IL-2) or T-cell growth factor (TCGF). It is also known to up-regulate the release of anti-inflammatory cytokines. Cyclosporin appears to block the resting lymphocytes in the G0 or G1 phase of the cell cycle. All available evidence suggests that cyclosporin acts specifically and reversibly on lymphocytes and does not depress haematopoiesis or has any effect on the function of phagocytic cells. In patients with dry eye disease, a condition that may be considered to have an inflammatory immunological mechanism, following ocular administration, cyclosporin is passively absorbed into T-lymphocyte infiltrates in the cornea and conjunctiva and inactivates calcineurin phosphatase. Cyclosporin-induced inactivation of calcineurin inhibits the dephosphorylation of the transcription factor NF-AT and prevents NF-AT translocation into the nucleus, thus blocking the release of pro-inflammatory cytokines such as IL-2. 2. Pharmacokinetic properties **Formal pharmacokinetic studies** have not been conducted in humans with IKERVIS. Blood concentrations of IKERVIS were measured using a specific high-pressure liquid chromatography-mass spectrometry assay. In 374 patients from the two efficacy studies, plasma concentrations of cyclosporin were measured before administration and after 6 months (SICCANOV study and SANSIKA study) and 12 months of treatment (SANSIKA study) After 6 months of ocular instillation of IKERVIS once per day, 327 patients had values below the lower limit of detection (0.050 ng/mL) and 35 patients were below the lower limit of quantification (0.100 ng/mL). Measurable values not exceeding 0.206 ng/mL were measured in eight patients, values considered to be negligible. Three patients had values above the upper limit of quantification (5 ng/mL) however they were already taking oral cyclosporin at a stable dose, which was allowed by the studies' protocol. After 12 months of treatment, values were below the lower limit of detection for 56 patients and below the lower limit of quantification in 19 patients. Seven patients had measurable values from 0.105 to 1.27 ng/mL, all considered to be negligible values. Two patients had values above the upper limit of quantification, however they were also on oral cyclosporin at a stable dose since their inclusion in the study. **STORAGE** **CONDITION** Do not store above 30°C. Protect from light. Do not freeze. After opening of the aluminium pouches, the single-dose containers should be kept in the pouches in order to protect from light and avoid evaporation. Any opened individual single-dose container with any remaining emulsion should be discarded immediately after use. **DOSAGE FORM AND PACKAGE AVAILABLE** IKERVIS is supplied in 0.3 mL single-dose, low-density polyethylene (LDPE) containers presented in a sealed laminate aluminium pouch. One pouch contains five single-dose containers. Pack sizes: 30 and 90 single-dose containers. Not all pack sizes may be marketed. **MANUFACTURED BY**: EXCELVISION 27, rue de la Lombardie, 07100 Annonay, France. **UNDER LICENSE OF**: SANTEN OY Tampere, Finland **IMPORTED BY**: SANTEN (THAILAND) CO., LTD. Bangkok, Thailand. **DATE OF REVISION OF PACKAGE INSERT** September 2015

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FOR MEDICAL AND HEALTHCARE PROFESSIONALS ONLY

A New Paradigm of Cataract Refractive Surgery

by Joanna Lee

A lunch symposium yesterday marked the unveiling of the latest tools that Alcon is bringing to Thailand as well as the Asia-Pacific region, which means cataract surgery could only get better. On hand to share the discoveries that would be undergirded by their testing and experiences were Dr. John Chang from Hong Kong and Dr. Dandapani Ramamurthy from India who moderated the session.

In an era where hydrophobic acrylate intraocular lenses (IOL) dominate the market, especially in Europe, the question is always, "which is the best?". Professor Gerd Auffarth from the Department of Ophthalmology, Ruprecht-Karls-University of Heidelberg, Germany took this question to task as he demonstrated how the Clareon (Alcon, USA) intraocular lens performs through a material laboratory analysis.



Speakers at the Alcon symposium presented new tools on cataract refractive surgery.

It is similar to the Acrysof's material with slightly more water content – the idea behind the innovation to make the material more pristine and pure. When Professor Auffarth tested the lens, the Clareon was shown to be glistening-free. Not only that, laboratory analysis results which revealed the Clareon to have a wider angle with better intraocular performance in terms of capsular bag performance. Apart from these advantages, the Clareon has also shown promising results in preventing posterior capsule opacification (PCO), comparable, and if not, better than Acrysof IOLs (Alcon, USA). It also showed the lowest level of glare and the least risk for



Dr. David Lubeck discussed tips, tricks and interesting cases in intraoperative aberrometry at the Alcon symposium yesterday.

positive dysphotopsia.

He also touched on the breakthrough instrument that delivers the IOL. The Clareon® AutonoMe is the first ever automated delivery system that is preloaded and disposable, helping to make cataract surgery safer and more precise.

Taking the discussion further, Dr. John Chang, director of the Guy Hugh Chan Refractive Surgery Centre of Hong Kong Sanatorium & Hospital candidly shared how he was impressed with the new PanOptix (Alcon, USA) lens and why he favors this diffractive lens.

He said once the diffraction is above order +2, +3 or above, there has been "wasted energy" which he believes contributes to glares before proceeding to explain using a graph how the lens' profile works. By this, he was able to compare the PanOptix lens in the lab to show the order and profile of diffraction.

With a constructive interference that actually augments the light, this gain of energy provides more than 88% of useful light energy (thereby reducing the wasted light energy by 12%), which significantly diminishes the glare, Dr. Chang said, explaining the technicalities behind the diffraction orders. The tests ultimately showed the PanOptix as having a continuous range of focus with minimal halo (1.14) with a strong vision of 40-60 cm. More importantly, another study they conducted showed high patient satisfaction while using the PanOptix along with better visual acuity - some with 20/15 and 20/20 results after three weeks.

In the larger scheme of things, digital imaging and planning in cataract refractive surgery has never been better than with the Verion machine (Alcon, USA). For this segment, the prolific Dr. Dandapani Ramamurthy of The Eye Institute India in Coimbatore,

India, shared how the Verion eliminates opportunities for errors while increasing efficiency. First, it helps acquire a high resolution image for positional reference. Then, at the planning stage, the Verion helps determine the basic IOL power to be implanted, where to make the incisions, determines the capsulorhexis (CCC), centration of the IOL, the toric IOL orientation and astigmatic keratotomy.

"Subsequently, it also acts as a guide for your execution at the operating table," Dr. Dandapani explained. Verion can determine the K1 and K2, WTW and limbus position, pupil position and corneal reflex position. He also shared how it is a multifaceted technology while the microscope integrated display (MID) is compatible with various microscopic brands. It is also helps correct astigmatism besides providing multiple modalities and at the same time, it assists in precise laser arcuate keratotomy. In short, the Verion is the "glue that binds preoperative planning with intraoperative execution" as succinctly summarized by Dr. Dandapani.

Complementing and giving an insightful round up to all the presentations beforehand was Dr. David Lubeck's session on intraoperative aberrometry. The Director of Cataract, Corneal, and Advanced Anterior Segment Surgery at Arbor Centers for Eyecare in Chicago, Illinois, USA, shared enthusiastically about the ORA (Optiwave Refractive Analysis) machine, similar to the Verion which helps to optimize refractive outcomes, presenting seven cases comparing the Barrett against the ORA with results favorable towards the ORA. Positioning doctors as surgical marksmen, Dr. Lubeck encouraged doctors to utilize all the technologies available. Precision, safety and accuracy, after all, are the ultimate goals. ☺

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Change in Cutter Technology - Making a Difference

Macular Surgery with 3D Visualization

Digital Era of Vitreoretinal Surgery and Latest Technology

SPEAKER

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Srinivas JOSHI, MD
India

ZHANG Chun, MD
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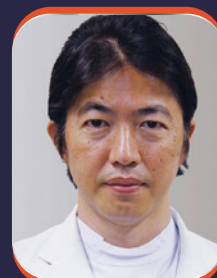
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