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Contents

Editorial

- **Editorial** 2
  Dr Ian YH WONG

Medical Bulletin

- **Updates on Treatment Options for Keratoconus** 4
  Dr Alex LK NG & Dr Arthur CK CHENG CME
- **MCHK CME Programme Self-assessment Questions** 7
- **Current Trends in the Management of Thyroid Eye Disease** 9
  Dr Emmy Yuen-mei LI
- **Minimally Invasive Glaucoma Surgery** 16
  Dr Jonathan CHAN & Dr Jasper WONG
- **Demyelinating and inflammatory optic neuropathies: an overview** 24
  Dr Jonathan Chun-ho HO & Dr Andy Chi-on CHENG
- **Latest Measures in Controlling Myopia Progression in Children** 28
  Dr Patrick Kai-wah WU

Life Style

- **Walking With the Poor Communities** 33
  Dr Nim-chung CHAN

Dermatological Quiz

- **Dermatological Quiz** 40
  Dr Chi-keung KWAN

Medical Diary of March 38

Calendar of Events 39

Disclaimer

The Cover Shot

This ***Euphrates Poplar***, or desert poplar, was taken at the 'Strange-tree forest' in the Ejina County of the Inner Mongolia Autonomous Region of China, which is located in the Gobi Desert near the border neighbouring Mongolia.

The desert poplar has leaves of variable sizes and shapes, ranging from spindle shape, heart shape, and sometimes resembling that of a maple leave. This plant is usually found in the deserts in Inner Mongolia and parts of the United States only. Its colour is usually green most time of the year, but turns golden-yellow for a few weeks around October during the 'Poplar Festival'.

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Editorial

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Editor

Dr Ian YH WONG

In the last two decades, the medical world has witnessed dramatic advancements in ophthalmology. From imaging advancements to new therapeutic agents and strategies, many eye diseases which were not amenable to treatment can now be treated, or at least, enable us to have a better understanding of the underlying pathophysiology. In this issue of the Hong Kong Medical Diary, we have gathered experts in the various subspecialty areas within ophthalmology, to summarise various important disease entities for our readers.

One of the major advancements in recent years has been the development of minimally invasive glaucoma surgery (MIGS), which has been a popular and promising new treatment in the management of glaucoma. This was made possible by the advancements in the manufacturing technology such that these micro devices could be made with precision. In this issue, Dr Jonathan Chan and Dr Jasper Wong have provided a comprehensive account of this new development.

Another important advancement is the use of collagen cross-linking in the treatment of corneal diseases. This technology enhances cross-linking bonding formation between corneal stromal collagen fibrils and increases the overall strength and stability of the cornea. It has been implemented in the treatment of corneal conditions such as keratoconus. Dr Alex Ng and Dr Arthur Cheng have together written a very in-depth review of this new technique, and how it has transformed the management of keratoconus in recent years.

With the advancement in laboratory diagnosis, discovery of novel serum antibodies was made possible. Following the discovery of the serum antibodies against water channel protein aquaporin-4 (AQP4) in patients with neuromyelitis optica (NMO) in 2005, NMO has now proven itself to be a separate disease entity with distinct clinical features. In this issue, Dr Jonathan Ho and Dr Andy Cheng have together written a comprehensive review of NMO, along with a few other neuro-ophthalmological conditions.

Another major development in recent years is the use of atropine in the control of myopia progression. Since the early 1960s atropine was found to be able to retard the progression of myopia in both animal and human studies. However, the use of the standard dosage of 1% inevitably produces pupil dilation, thus resulting in photophobia and inability to accommodate. This prevents the practical use of atropine and thus popularity is low. Only until recently the use of atropine in retarding myopia progression has been revisited. This was largely due to the findings in the ATOM1 and ATOM2 studies in Singapore, which found that the use of 0.01% atropine was well tolerated without the noticeable side effects but at the same time able to achieve a significantly lower rate of progression in the same period when compared to other higher concentrations such as 0.1% and 0.5%. This re-ignited the enthusiasm of the scientific world in the search of the holy grail in preventing myopia progression. In this issue, Dr Patrick Wu has reviewed and summarised the latest measures in this regard.

Dr Emmy Li has given a very detailed account of the latest updates on the management of thyroid eye disease. The clinical features and grading system are revisited, and the measures to control the disease discussed. This enables non-ophthalmologists to grasp the fundamentals in the management of the ocular manifestation of this important systemic condition.

Last but not least, in the Life Style section, Dr Nim-chung Chan has shared with us his legendary days spent in Afghanistan before the Taliban came to power, where he helped to train the local ophthalmologists, and to serve the poor and needy. He also shares his experience in Myanmar where he and his wife have helped to setup local medical facilities in mountain villages. In his story, one can feel the courage humanitarians possess, and also the greater love that inspires enemies to become friends. His experience has been most unique in many ways, especially in that it reminds us that we should be grateful for what we already have and should not take things for granted. More importantly, it shows us the simplest way how a doctor should serve his or her patients. This could be distorted at times in the sophisticated world where we live in.

Once again, I would like to thank all the authors of this issue for their contributions. I am sure both ophthalmologists and non-ophthalmologists would enjoy reading them, and would find it informative.

Updates on Treatment Options for Keratoconus

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This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded 1 CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 31 March 2018.

Introduction

Keratoconus is a bilateral, non-inflammatory, ectatic disorder of the cornea characterised by progressive corneal thinning and bulging, resulting in a protruded, cone-shaped cornea. It usually manifests between the first to the third decade of life, and causes irregular astigmatism that could not be corrected by spectacles, severely affecting the patient's quality of vision. Keratoconus is a multi-factoria[1] disease. Common causative factors include genetics, chromosomal disorders (e.g. Down syndrome), atopy, connective tissue disorder (e.g. Marfan syndrome) and frequent eye rubbing.[1] The diagnosis of keratoconus is mainly based on corneal tomographies and pachymetry. With recent advancements in imaging techniques such as corneal tomographies with Scheimpflug imaging systems or swept-source optical coherent tomographies, more accurate diagnosis and detection of earlier stages of the disease is now possible.[2]

For many years, treatment options for keratoconus were limited. The role of spectacles or contact lenses is to improve the vision by means of correcting the associated refractive errors. However, they do not alter the disease process nor correct the underlying problem. Traditional spectacles approach often fails because of its inability to correct irregular astigmatisms, and patients often have very asymmetric refractive errors between both eyes. Specialty contact lenses like rigid gas-permeable hard contact lenses or scleral contact lenses can correct irregular astigmatism but they may be uncomfortable to wear. Surgical approaches such as corneal stromal ring implantations can also improve the corneal irregularity, but the disease would still progress due to the cornea's in-born weakened biomechanical properties. In advanced keratoconus when the above options have failed, corneal transplantation is required.

Treatment options for keratoconus have a dramatic change in the last decade after the emergence of corneal collagen cross-linking (CXL). CXL is a technique that enhances cross-linking bonding formation between corneal stroma collagen fibrils and increases the overall strength and stability of the cornea. CXL alone or in-combination with other surgical techniques has dramatically changed our approach to keratoconus in recent years. Now, there are two treatment goals: to stop the disease progression, and to improve the vision.[3,4]

The aim of this article is to briefly discuss how we use CXL to stop disease progression, and how to improve vision with modalities including contact lenses, intra-corneal ring segments implantation, photorefractive keratectomy, corneal transplantation and intra-ocular lens implantations.

Corneal Collagen Cross-linking (CXL)

Corneal collagen cross-linking is a photochemical reaction that occurs when riboflavin (vitamin B2) are activated by ultra-violet A in the presence of oxygen. It increases the bonding formation between collagen fibrils in the corneal stroma and thus increases the overall mechanical strength of the cornea. In keratoconic eyes, the corneal biomechanical strength is reduced, and cross-linking can restore it. Applying CXL in the treatment of keratoconus was first reported in 2003 in Europe. Since then, a number of studies with long follow up durations have consistently reported that CXL is able to halt the keratoconus progression, both in paediatric and adult populations, and has an excellent safety profile.[5,6] In other words, CXL can stiffen the cornea to prevent it from further coning and thinning. Apart from this, most studies also report an improvement in visual acuity and corneal topographic parameters. In 2016, it received the FDA's approval for treating keratoconus.[7] Nowadays, CXL is indicated for most keratoconic eyes to stop the disease progression, unless it is diagnosed at a very advanced stage where the patient may need a transplant straight away, or at an advanced age where there is no longer disease progression (as the cornea naturally stiffens with increasing age). Recent advances in CXL include how to improve the surgical technique, aiming for a shorter treatment duration, or ways to preserve the corneal epithelium intra-operatively.[8]

Contact lenses

As mentioned in the introduction, apart from stopping disease progression with CXL, the other main treatment aim is to improve visual function. Using contact lenses is the usual first line for this purpose. In keratoconus, patients have irregular astigmatism where the anterior corneal surface is non-uniform due to progressive coning and steepening. Conventional spectacles or soft contact lenses are designed to only correct a uniformly oval – shaped cornea (meaning regular astigmatism) and could not correct irregular astigmatism. Instead,

they need rigid gas-permeable (RGP) 'hard contact lenses' to improve vision. They can usually improve the visual quality significantly in the earlier stages of disease. Some recent newer contact lens designs (such as hybrid lenses or mini-scleral lenses) can also improve the comfort level when wearing them. However, in moderate to advanced stages, the cornea may be too irregular, making lens fitting impossible. In these cases, other surgical interventions will be needed to reduce the irregularity of the cornea, so that contact lenses would become feasible again.[9]

Topography-guided phototherapeutic keratectomy (tPTK)

Phototherapeutic keratectomy (PTK) is a type of laser refractive surgery where an excimer laser is used to ablate corneal stromal tissue directly. Before the era of CXL, any form of laser vision correction is contraindicated in keratoconus, because ablation of corneal stromal tissue in the already weakened-cornea (keratoconus eyes are biomechanically weaker than normal eyes), it will accelerate further disease progression. Fortunately, because now we can increase the corneal biomechanical strength with CXL, tPTK can be combined with CXL to safely treat keratoconus. Together, the procedure can improve the regularity of the anterior corneal surface, as well as stopping the disease progression from the CXL effect.[10] The main aim of PTK, with the help of topography-guidance, is to reduce the irregularity of the corneal surface, making it easier for contact lens fitting or even spectacles correction. The amount of the refractive error can also be reduced. Large case series have proven the safety and efficacy of this technique. (Fig. 1 (left) shows the pre-operative irregular corneal surface from a Pentacam scan (Scheimpflug tomography), and the right shows it has become much more regular after receiving combined tPTK with CXL. Best-corrected visual acuity also improved from 20/100 to 20/20) Main limitations of the procedure include its dependence on the pre-operative corneal thickness which limits the amount of corneal stromal tissue available for laser ablation (the more advanced disease stage, the thinner is the cornea), and the availability of the excimer laser platform.

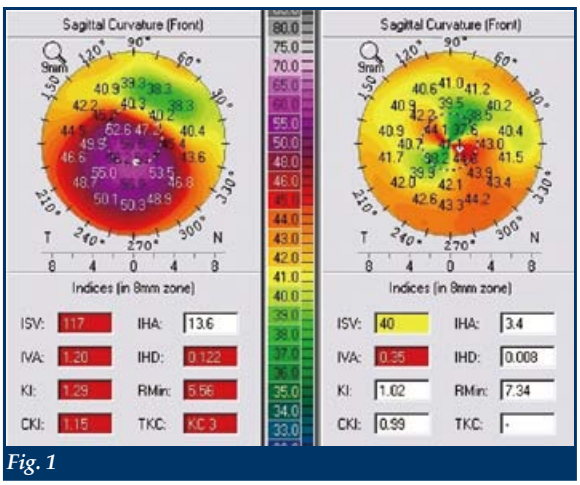

Fig. 1

Intra-corneal Ring Segments Implantation

Apart from using excimer lasers to modify the corneal shape, implanting intra-corneal ring segments (ICRS) into the corneal stroma can also improve the shape and refractive power of the cornea. These ring-like implants are synthetic materials of various sizes and thicknesses. They are inserted into a corneal stromal tunnel, created either mechanically or with a femtosecond laser machine. The sizing, placement location and number of implants required depend on the topographic maps of the cornea, with the aim of flattening and regularising the corneal shape. Studies have reported that ICRS implantation is a safe, predictable and reversible option for keratoconus, and patients with reduced best-corrected visual acuity pre-operatively would most likely benefit from the procedure.[11] It can also be performed at the same stage with CXL, or sequential to CXL. Fig. 2 shows the slit lamp photo of an eye implanted with an ICRS.

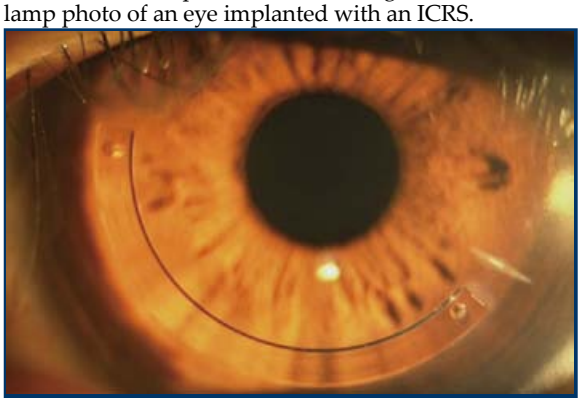
Fig. 2

Corneal Transplantation

In advanced stages when the above options have failed, or when corneal scarring has developed, corneal transplantation would be indicated. By replacing the diseased cornea with a new full-thickness cornea (penetrating keratoplasty, PK), vision can be restored. Long term problems of corneal transplantation include risk of rejection, steroid-induced glaucoma (long term steroid is required to prevent rejection), graft failure and significant astigmatism. Previous studies have reported an average graft span of 18 years using regression models.[12] In recent years, lamellar transplantation where surgeons only replace the diseased layer(s) of cornea, has gained popularity with good results. In keratoconus, the innermost layer (endothelial layer) is often unaffected. Thus, we could replace only the diseased anterior layers (corneal stroma) with deep anterior lamellar keratoplasty (DALK). Because the patient's own corneal endothelium is now preserved, the rejection rate is much reduced, so is the need of using long-term steroids. Studies have proven a lower rejection rate and longer graft survival using DALK when compared with PK.[13,14] However, intra-operative challenges in DALK remain, where sometimes the surgeon needs to convert back to PK intra-operatively. Nevertheless, with the increasing use of CXL in stopping keratoconus disease progression, it is predicted that less keratoconus patients will require corneal transplant in future. Fig. 3 shows a patient who has received corneal transplant.

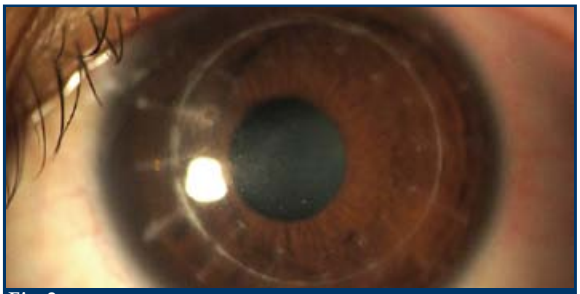

Fig. 3

Lens-based surgery

For most of the treatment options discussed above, the keratoconus disease progression could be halted, and the amount of refractive error including irregular astigmatism could be reduced. Nevertheless, residual refractive error often remains. Implanting intraocular lenses (IOL), either during cataract surgery (in the older age-groups) or as phakic IOL (preserving patient's own crystalline lens and inserting another IOL on top), can further reduce the refractive errors, especially for myopia or hyperopia. However, IOLs should only be used when the corneal condition has already stabilised. Furthermore, irregular astigmatism could not be corrected with IOLs, and has to be managed with other options discussed above.

Summary

In summary, a variety of treatment options are available for keratoconus. The treatment decision would depend on lots of factors, in particular, the patient's condition, life style and expectation, and the availability of the expertise and equipment. Using cross-linking to stop disease progression has dramatically changed our management algorithm, as well as the patient's prognosis in the long-term.

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MCHK CME Programme Self-assessment Questions

Please read the article entitled "Updates on Treatment Options for Keratoconus" by Dr Alex LK NG and Dr Arthur CK CHENG and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 31 March 2018 Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-10: Please answer T (true) or F (false)

1. **The following are all causative factors for keratoconus?**
   A. Genetics B. Ageing C. Chromosomal disorders D. Connective Tissue disorders
2. **Keratoconus is a significant risk factor for glaucoma, leading to blindness in keratoconus patients.**
3. **Corneal collagen cross-linking is the only treatment option that can halt keratoconus disease progression.**
4. **Use of rigid gas-permeable contact lenses should be considered as first-line treatment for keratoconus patients with irregular astigmatism not corrected by spectacles.**
5. **Corneal transplantation is most suitable for keratoconus patients with late stage disease?**
6. **Eye rubbing can cause keratoconus to deteriorate.**
7. **Early keratoconus can have no apparent signs on clinical / slit lamp examination.**
8. **Corneal collagen cross-linking should be considered in all keratoconus patients with evidence of disease progression.**
9. **Corneal refractive surgery alone (e.g. LASIK) can be safely performed in patients with early stage keratoconus.**
10. **Some forms of corneal refractive surgery, when combined with corneal collagen cross-linking, can be safely performed in patients with early stage keratoconus.**

ANSWER SHEET FOR MARCH 2018

Please return the completed answer sheet to the Federation Secretariat on or before 31 March 2018 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Updates on Treatment Options for Keratoconus

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1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

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Answers to February 2018 Issue

Primary Cleft Lip and Palate Repair

1. F 2. T 3. F 4. T 5. T 6. T 7. T 8. F 9. T 10. F

LUCENTIS®: STATE-OF-THE-ART PREFILLED SYRINGE[1-3]

4 EASY STEPS[1]

1 RELEASE

Release the syringe from its pack

- Use aseptic technique throughout the procedure
- The prefilled syringe is for single use only
- Do not use if any part of the packaging is damaged or if the solution is discolored, cloudy, or contains particles

2 SNAP

Snap off the protective syringe cap

- Do not twist – the cap must be snapped off

3 ATTACH

Attach the injection needle of your choice

- Attach a 30G x 1/2 inch sterile injection needle
- Do not wipe the needle at any time

4 SET

Set the dose

Align the edge below the dome of the stopper with the **dose mark**

- The rubber stopper is non-retractable to prevent air from being drawn into the syringe
- 0.05 mL equals 0.5 mg of ranibizumab

EASY TO HANDLE to potentially minimize ocular risk[1,2]

- Non-retractable stopper[2]
- Advanced siliconization process[1,2]
- Easy to hold[2]

EASY TO USE with fewer preparation steps[1]

EASY TO SAVE TIME in your daily practice[3]

* *versus* the LUCENTIS® vial, 91% out of the 98 physicians surveyed (from 6 countries). The physicians had experience of ≥10 LUCENTIS® PFS injections.

Easy to offer the benefits of LUCENTIS® to your nAMD, DME, BRVO, CRVO, and CNV patients[1-3]

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Note: Before prescribing, consult full prescribing information. **Presentation: Vial:** Ranibizumab. Each vial contains 2.3 mg of ranibizumab in 0.23 mL solution. **Pre-filled syringe:** Ranibizumab. Each pre-filled syringe contains 1.65 mg of ranibizumab in 0.165 mL solution. The extractable volume of one pre-filled syringe is 0.1 ml. This provides a usable amount to deliver a single dose of 0.05 ml containing 0.5 mg ranibizumab. **Indications:** •Treatment of neovascular (wet) age-related macular degeneration (AMD). •Treatment of visual impairment due to diabetic macular oedema (DME). •Treatment of visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO). •Treatment of visual impairment due to choroidal neovascularisation (CNV). **Dosage and administration:** •The recommended dose is 0.5 mg (0.05 mL) given as a single intravitreal injection. The interval between two doses injected into the same eye should be at least four weeks. •Treatment is initiated with one injection per month until maximum visual acuity is achieved and/or there are no signs of disease activity. •Thereafter, monitoring and treatment intervals should be determined by the physician and should be based on disease activity as assessed by visual acuity and/or anatomic parameters. •Monitoring for disease activity may include clinical examination, functional testing or imaging techniques (e.g. optical coherence tomography or fluorescein angiography). In patients with wet AMD, DME and RVO, initially, three or more consecutive, monthly injections may be needed. The treatment of visual impairment due to CNV should be determined individually per patient based on disease activity. Some patients may only need one injection during the first 12 months; others may need more frequent treatment, including a monthly injection. For CNV secondary to pathologic myopia (PM), many patients may only need one or two injections during the first year. **•treat-and-extend regimen:** While applying the treat-and-extend regimen, the treatment interval should be extended by no more than two weeks at a time for wet AMD and extended by up to one month at a time for DME. For RVO, treatment intervals may also be gradually extended, however there are insufficient data to conclude on the length of these intervals. If disease activity recurs, the treatment interval should be shortened accordingly. **•Lucentis and laser photocoagulation in DME or in branch RVO:** Lucentis has been used concomitantly with laser photocoagulation in clinical studies. When given on the same day, Lucentis should be administered at least 30 minutes after laser photocoagulation. Lucentis can be administered in patients who have received previous laser photocoagulation. •Lucentis must be administered by a qualified ophthalmologist using aseptic techniques. Broad-spectrum topical microbicide and anesthetic should be administered prior to the injection. •Not recommended in children and adolescents. **Contraindications:** Hypersensitivity to ranibizumab or to any of the excipients, patients with active or suspected ocular or periocular infections, patients with active intraocular inflammation. **Warnings and precautions:** •Intravitreal injections have been associated with endophthalmitis, intraocular inflammation, rhegmatogenous retinal detachment, retinal tear and iatrogenic traumatic cataract. Therefore proper aseptic injection techniques must be used. Patients should be monitored during the week following the injection to permit early treatment if an infection occurs. •Transient increases in intraocular pressure (IOP) have been seen within 60 minutes of injection of Lucentis. Sustained IOP increases have also been reported. Intraocular pressure and the perfusion of the optic nerve head must be monitored and managed appropriately. Patients should be informed of the symptoms of these potential adverse reactions and instructed to inform their physician if they develop signs such as eye pain or increased discomfort, worsening eye redness, blurred or decreased vision, an increased number of small particles in their vision, or increased sensitivity to light. •There is a potential risk of arterial thromboembolic events following intravitreal use of VEGF inhibitors. A low incidence rate of arterial thromboembolic events was observed in the Lucentis clinical trials in patients with AMD, DME, RVO and CNV and there were no major differences between the groups treated with ranibizumab compared to control. Patients with known risk factors for stroke, including history of prior stroke or transient ischemic attack should be carefully evaluated by their physicians as to whether Lucentis treatment is appropriate and the benefit outweighs the potential risk. •Available data do not suggest an increased risk of systemic adverse events with bilateral treatment. •As with all therapeutic proteins, there is a potential for immunogenicity with Lucentis. •Lucentis has not been studied in patients with active systemic infections or in patients with concurrent eye conditions such as retinal detachment or macular hole. •There are insufficient data to conclude on the effect of Lucentis in patients with RVO presenting irreversible ischaemic visual function loss. •Should not be used during pregnancy unless the expected benefit outweighs the potential risk to the fetus. For women who wish to become pregnant and have been treated with ranibizumab, it is recommended to wait at least 3 months after the last dose of ranibizumab before conceiving a child; use of effective contraception is recommended for women of child-bearing potential; breast-feeding is not recommended. •Following treatment patients may develop transient visual disturbances that may interfere with their ability to drive or use machines. Patients should not drive or use machines as long as these symptoms persist. •Risk factors associated with the development of a retinal pigment epithelial tear after anti-VEGF therapy for wet AMD and potentially also other forms of CNV, include a large and/or high pigment epithelial retinal detachment. When initiating Lucentis therapy, caution should be used in patients with these risk factors for retinal pigment epithelial tears. **Interactions:** No formal interaction studies have been performed. **Adverse drug reactions: •Very common (≥10%):** vitritis, vitreous detachment, retinal hemorrhage, visual disturbance, eye pain, vitreous floaters, conjunctival hemorrhage, eye irritation, foreign body sensation in eyes, lacrimation increased, blepharitis, dry eye, ocular hyperemia, eye pruritus, intraocular pressure increased, nasopharyngitis, headache, arthralgia. **•Common (1 to 10%):** hypersensitivity, retinal degeneration, retinal disorder, retinal detachment, retinal tear, detachment of the retinal pigment epithelium, retinal pigment epithelium tear, visual acuity reduced, vitreous hemorrhage, vitreous disorder, uveitis, iritis, iridocyclitis, cataract, cataract subcapsular, posterior capsule opacification, punctuate keratitis, corneal abrasion, anterior chamber flare, vision blurred, injection site hemorrhage, eye hemorrhage, conjunctivitis, conjunctivitis allergic, eye discharge, photopsia, photophobia, ocular discomfort, eyelid edema, eyelid pain, conjunctival hyperemia, urinary tract infection*, anemia, anxiety, cough, nausea, allergic reactions (rash, pruritus, urticaria, erythema). **•Uncommon (0.1 to 1%):** blindness, endophthalmitis, hypopyon, hyphema, keratopathy, iris adhesions, corneal deposits, corneal edema, corneal striae, injection site pain, injection site irritation, abnormal sensation in eye, eyelid irritation. **•Serious adverse events** related to intravitreal injections include endophthalmitis, blindness, rhegmatogenous retinal detachment, retinal tear and iatrogenic traumatic cataract. **observed only in the DME population* A meta-analysis of pooled safety data from completed, randomized, double masked global studies showed a higher incidence rate of non-serious, non-ocular wound infection/inflammation in DME patients treated with ranibizumab 0.5 mg (1.85/100 patient years) compared to control (0.27/100 patient years). The relationship to ranibizumab remains unknown. **Packs:** 1 vial or 1 pre-filled syringe per pack. Not all packs are marketed. **Legal classification:** P1S1S3.
Ref: EMA Dec 2016 • CDS07665 (TGA)

1. Lucentis Product Information (Hong Kong) **2.** Michaud JE, *et al.* Ranibizumab pre-filled syringe approved in the European Union: innovation to improve dose accuracy, reduce potential infection risk, and offer more efficient treatment administration. Poster presented at the Association for Research in Vision and Ophthalmology (ARVO 2014). **3.** Souied E, *et al.* Ranibizumab pre-filled syringe versus single-use vial: syringe-preparation time in real-world clinical practice. Poster 256 presented at ESASO 2014 Istanbul, Turkey.

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Current Trends in the Management of Thyroid Eye Disease

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Introduction

Thyroid eye disease (TED) is also known as Graves' ophthalmopathy/orbitopathy, thyroid-associated ophthalmopathy/orbitopathy or thyrotoxic/endocrine exophthalmos. It is the most important extrathyroidal manifestation of autoimmune thyroid diseases including Graves' disease and Hashimoto thyroiditis. It was estimated that up to 50% of patients with autoimmune thyroid diseases develop TED, and of these, as many as 10–20% develop severe inflammation, orbital congestion, impaired ocular motility or dysthyroid optic neuropathy (DON).

Orbital inflammation in TED is due to shared antigens and cross-reactivity of orbital and thyroid tissues, circulating thyroid antibodies stimulate proteins of the extraocular muscles and orbital fat, resulting in lymphocytic infiltration, proliferation of fibroblasts and production of glycosaminoglycans. The expansion of fibroadipose tissue and the infiltration of extraocular muscles lead to orbital congestion and exophthalmos, impaired ocular motility, diplopia, and rarely, sight threatening compressive optic neuropathy. These changes progress during the active phase of disease, typically lasting 6–18 months and followed by a stable plateau of inactive disease. The plot of the natural history of the orbital disease over time is called the Rundle's curve. A steeper slope in the active phase means a more acute onset and likely more serious sequelae (Fig. 1).

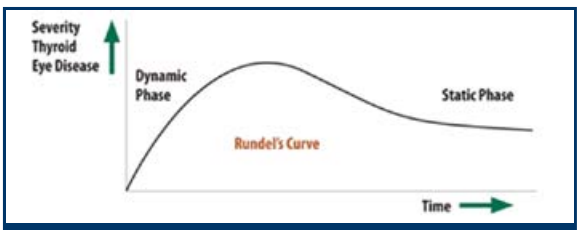

Fig. 1. Rundle's curve describes the natural history of TED. Progressive active phase lasts for up to 18 months before settling in the stable inactive phase

TED tends to have a bimodal presentation during the fourth or sixth decade of life. The female-to-male ratio is about 9:1 for all forms of clinical TED and drops to 3:1 for the severe form. About 20% of patients have concurrent ocular and dysthyroid features at presentation, around 23% of patients present before the diagnosis of thyroid dysfunction, and 57% develop ocular features after being treated for thyroid dysfunction. Risk factors for the development of TED include the male gender, older age (>50 years) at onset, smoking, use of radioactive iodine (RAI), and post-ablative hypothyroidism. Compared with nonsmokers, smokers have more severe TED, a higher rate of recurrence, are more likely to show progression or occurrence of TED after radioactive iodine, and are less responsive to immunosuppressants or orbital radiotherapy. Statin use was shown to have a 40% decreased hazard for TED but it may increase the risk of liver derangement in patients receiving intravenous steroids for active TED.

Clinical Features of Thyroid Eye Disease

Typical signs of TED in Caucasians include eyelid retraction, lid lag, proptosis, restrictive myopathy, and optic nerve dysfunction. In Asians, extraocular features including lid puffiness, lid retraction (Fig. 2a), lid lag, lagophthalmos, proptosis, restrictive strabismus, and acquired lower lid epiblepharon are observed. Intraocular features include conjunctival injection, particularly around the insertion of the rectus muscle, superior limbic keratitis, exposure keratopathy (Fig. 2b), chemosis, raised intraocular pressure, optic disc swelling, retinal venous congestion, and choroidal folds are the signs to be looked for. Lid retraction is the most common sign in TED. The normal upper lid rests at 1-2 mm below the superior limbus (corneoscleral junction), and the lower lid rests at the inferior limbus. Other causes of lid retraction include facial paralysis, myasthenia gravis, myotonic dystrophy, Marcu-Gunn jaw winking, metabolic disease (uraemia, cirrhosis), dorsal midbrain syndrome, Parkinson's disease, contralateral ptosis, and aberrant third nerve regeneration. These conditions are however not associated with lid lag. Patients with TED have axial non-pulsatile proptosis/exophthalmos secondary to orbital venous congestion, enlargement of the extraocular muscles and enhanced adipogenesis. Exophthalmos can be clinically quantified using various types of exophthalmometers (e.g. Hertel) or radiologically with axial orbital scans (Fig. 3). Diplopia or double vision in TED is related to restrictive myopathy rather than muscle paralysis. The inferior rectus is most commonly involved, followed by the medial, superior, and lateral rectus. Movement is therefore usually worst in elevation or abduction.

Vision loss in TED can be caused by optic nerve dysfunction (DON), exposure keratopathy, uncontrolled intraocular pressure, and globe subluxation. Asian patients often have a delayed and atypical presentation

of TED compared with Caucasians. With a darker complexion, thicker skin and conjunctival tissues and possibly a higher pain threshold, clinical examinations often underestimate the deeper orbital involvements. More Asian patients with DON are 'cold-presenters' with minimal signs of active inflammation. DON is thought to be a result of optic nerve compression by the enlarged extra-ocular muscles (EOM) at the orbital apex. Postulated mechanisms of DON include inflammation, ischaemia or mechanical stretching. Signs of DON include impaired vision, colour vision and/or visual field, presence of afferent papillary defects and optic disc swelling. Asian patients with shallow orbits and patients with existing diabetes are at higher risk of developing DON. Advanced radiological imaging available nowadays may help to identify 'subclinical', localised inflammation and allow prompt medical treatment to reduce the development of DON and progressive deformity requiring subsequent rehabilitative surgery.

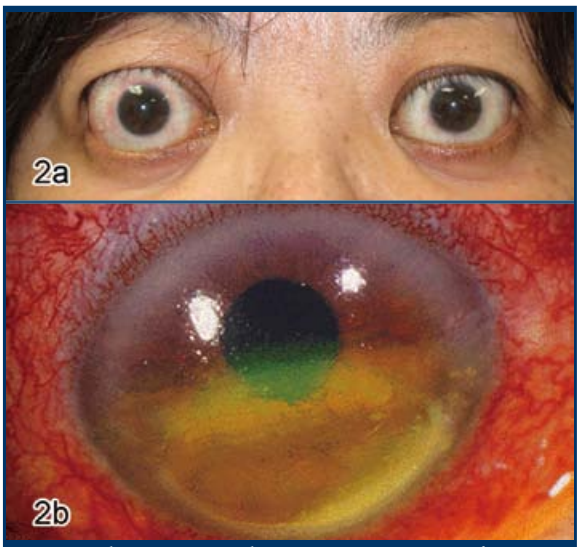

Fig. 2a. Lid retraction and proptosis are common features in patients with TED
Fig. 2b. Corneal breakdown from exposure keratopathy resulting from incomplete eyelid closure

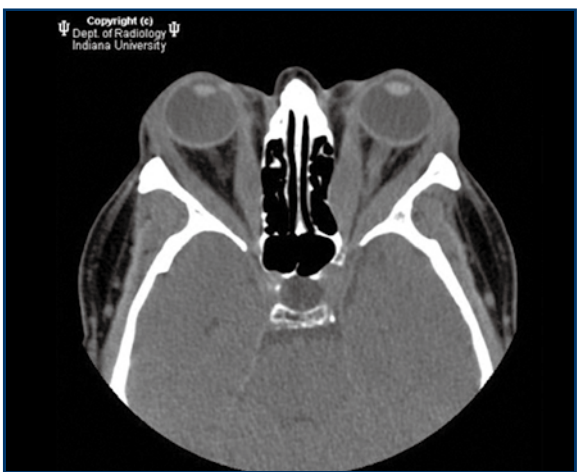

Fig. 3. Axial CT scan showing enlarged muscle belly with significant proptosis in TED

Grading and Investigation of Thyroid Eye Disease

TED is graded by its disease activity (extent of inflammation) and disease severity (degree of deformities). The Clinical Activity Score (CAS) is used to measure the degree of inflammation. One point is given for the presence of each of the parameters assessed, including spontaneous orbital pain, gaze evoked orbital pain, eyelid swelling, eyelid erythema, conjunctival redness, chemosis and inflammation of the caruncle. The sum of all points defines clinical activity: active orbitopathy if the score is above 3/7 at the first examination or above 4/10 in successive examinations. The NOSPECS Grading is a traditional assessment on disease severity which describes the combination of deformities (N = Normal, O = Only sign, S = Soft tissue involvement, P = Proptosis, E = Extraocular Motility, C = Corneal exposure, S = Sight-threatening). The European Group On Graves' Orbitopathy (EUGOGO) has proposed a standard protocol to assess the severity of TED and offer image atlases (http://www.eugogo.eu/) for assessors to take reference. According to the EUGOGO Classification, mild disease has minimal eyelid swelling, lid retraction or proptosis with little or no extraocular muscle dysfunction, with a minor impact on daily life. Moderate disease implies inflammatory features interfering with the ability to function, possible ocular motility dysfunction with diplopia, lid retraction greater than 2mm and variable proptosis. At this grade, the disease has sufficient impact on daily life to justify the risks of immunosuppressants in cases of active disease, or surgical intervention in inactive cases. Severe disease refers to sight-threatening conditions such as DON or corneal ulceration from exposure keratopathy, which oftennecessitates some form of surgical intervention. The VISA system is recently proposed by the International Thyroid Eye Disease Society (ITEDS) (http://www.thyroideyedisease.org/) which tries to combine the assessment of disease activity and severity into one. The system assesses 4 severity parameters: V (vision), I (inflammation/congestion), S (strabismus/motility restriction) and A (appearance/exposure). Each feature is considered and graded independently to give a global severity grade with a maximum score of 20.

Diagnosis of TED is still largely clinical, based on a history of autoimmune thyroid disease and compatible examination findings. All patients should have appropriate endocrinological evaluation with thyroid function test for serum sensitive thyrotropin, free thyroxine and triiodothyronine levels. Thyroid-related antibodies, specifically thyrotropin receptor antibodies, may be evaluated in patients without a clear history of thyroid disorder. Other ancillary ocular evaluations include visual field (automated perimetry), colour vision assessment (Ishihara pseudoisochromatic plates), Hess chart (for extraocular movement), and most importantly a field of binocular single vision for patients with diplopia. Differential diagnoses of TED include other orbital disorders such as idiopathic orbital inflammation (pseudotumour), orbital or preseptal cellulitis, carotid-cavernous fistula and orbital tumour. Orbital imaging revealing proptosis with EOM enlargement and expansion of the fatty compartment can help to differentiate TED from these conditions. Rarely, a tissue

biopsy is required in patients with euthyroid TED and atypical clinical features to confirm the diagnosis.

Management of Thyroid Eye Disease

Measures for All Patients with Thyroid Eye Diseases

Restore Euthyroidism
Management of patients with TED includes restoring and stabilising thyroid function. Patients with uncontrolled thyroid dysfunctions are more likely to experience severe disease. Constant monitoring (every 4–6 weeks) of thyroid function is particularly important during the early stages of treatment. Evidences suggest that radioactive iodine (RAI) worsens the active ocular disease in 15% of cases within the 6 months after the treatment. Patients who are smokers, with unstable thyroid function and high levels of thyroid-stimulating immunoglobulin are at risk. RAI should be avoided in patients with active TED (clinical activity score ≥3/10). Standard dose oral prednisolone prophylaxis (0.4-0.5 mg/kg for 3 months) should be prescribed in patients with mild to moderate TED and a high risk of progression, whereas a lower dose (0.2- 0.3 mg/kg for 4-6 weeks) is preferred for patients with mild TED or without preexisting TED but with risk factors.

Conservative Measures
Patients should be advised to adopt general measures such as the use of artificial tears, sunglasses, and sleep with the head of the bed slightly elevated. Nocturnal ointment is of great benefit for incomplete eyelid closure to protect the cornea.

Smoking Cessation
Smoking is the most important modifiable risk factor in patients with TED and the risk is proportional to the daily cigarette intake. Smokers with TED are more likely to develop a severe condition and have poor response to immunosuppressant therapies. It was demonstrated that smoking, even past smoking, is an independent risk factor associated with impaired response to intravenous corticosteroids in patients with TED. Never smokers with active moderate-to-severe TED, who were treated with cumulative doses of 4.5 g intravenous methylprednisolone within 3 months, responded better than both active smokers and past smokers.

Measures for Patients with Mild Thyroid Eye Diseases

Local measures are the mainstay therapy for patients with mild TED that generally have a self-limiting process. Studies investigating the natural history of TED in untreated patients show that the disease improved in 50% of the patients, remained stable in about 35%, and worsened in approximately 15%. A recent study showed that a 6-months course of oral selenium (100 μg twice daily) significantly improved the quality of life, reduced ocular involvements, and prevented progression in patients with mild TED. The use of oral corticosteroids is usually not recommended in patients with mild TED. Botulinum toxin injection may be considered to reduce upper lid retraction. It is a valuable therapeutic option in active disease where definitive surgery is contraindicated.

Measures for Patients with Moderate to Severe Thyroid Eye Diseases

In these patients, the eye involvement has sufficient impact on daily life to justify the risks of immunosuppressant treatment (if active) or surgical intervention (if inactive).

Immunosuppressive Medical Treatment and Orbital Radiotherapy
Only patients with active disease will respond to immunosuppressive treatments. These treatments have no benefit for patients in the quiescent phase in whom disease manifestations are the consequence of fibrotic changes in the orbital tissues. Among the available options for immunosuppression, corticosteroids continue to be the first-line treatment of moderate-to-severe active TED. They can be administered orally, intravenously, and locally via injection into the orbital soft tissues directly. The overall response rate was 82% and 53.4% for intravenous (IV) and oral steroids respectively according to a review. Pulses of IV steroids were also associated with fewer side effects, shorter treatment courses, and a lower relapse risk compared with oral administration. Oral corticosteroids might be considered when IV infusions are not logistically possible or if the patient prefers the oral route. Oral corticosteroids might be prescribed in some moderate to severe cases when the determination of activity is uncertain. A trial of therapy using a three-day course of oral prednisolone (50 mg) can determine whether clinical features show improvement, and guide subsequent IV corticosteroids or radiotherapy. A commonly used regimen for IV corticosteroids is 500 mg methylprednisolone weekly for 6 weeks followed by 250 mg weekly for another 6 weeks, giving a cumulative dose of 4.5 g. This weekly protocol of 4.5 g IV methylprednisolone cumulative dose is not only safer but is also more effective than a daily protocol (500 mg daily for 3 consecutive days per week for 2 weeks, followed by 250 mg daily for 3 consecutive days per week for another 2 weeks, and by tapering oral prednisone). If there is no clinical response, treatment with corticosteroids may be discontinued after the first 6 weeks. Prolongation of treatment after 12 weeks in patients who are responsive to corticosteroids should be related to disease severity and its impact on the quality of life, providing that the cumulative dose does not exceed 8 g and consecutive day-dosing should be avoided. Liver function tests, detection of hepatitis viral markers, and autoantibodies have to be performed prior to the administration of IV treatment. Patients with recent hepatitis, liver dysfunction, severe cardiovascular morbidity, or severe hypertension must be excluded. Liver enzymes, glucose levels, and blood pressure should be monitored monthly during treatment.

In patients who are not responsive to corticosteroids, other treatments may be attempted. Orbital radiotherapy is a useful adjuvant for patients with steroid-dependent, intolerant or resistant inflammatory orbitopathy, recent-onset progressive myopathy, and in some cases of DON. It consists of fractionated external beam irradiation of 20G in 10 sessions over 2 weeks. Orbital radiotherapy is supposed to work through its nonspecific anti-inflammatory effects and the high radiosensitivity of lymphocytes infiltrating the orbital space and, hence


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reduces the secretion of proinflammatory cytokines from activated lymphocytes. Orbital radiotherapy may not show benefits for several days to weeks, but its effects last longer. Compared with oral corticosteroid therapy, orbital radiotherapy has a comparable effect for moderate to severe orbitopathy and a better long-term effect on motility restriction. Combined IV pulse steroid plus orbital radiotherapy is more effective than IV pulse steroid alone. The risk of DON was reduced in the combined orbital radiotherapy and steroid group than in the steroid-only group. Orbital radiotherapy is most useful when administered during the course of IV pulse steroid yet should be avoided in young patients (age <30 years) or those with diabetic retinopathy. Complications of orbital radiotherapy include dry eyes, cataract, radiation retinopathy, optic neuropathy, and an increased long-term risk of malignancy.

It was observed that some patients seem to have an active phase which lasts longer than usual. They have recurrence of inflammation soon after withdrawal of corticosteroid treatment. These patients can go for a trial of methotrexate (MTX), which has been shown to be effective as sole treatment in patients who fail corticosteroids or become steroid-dependent, weekly dose varied from 5 to 20 mg. Mycophenolate mofetil (MMF) is an immune modulatory drug which demonstrates superior response, in terms of reduction of CAS, improvement in diplopia and proptosis and less disease reactivation, compared to corticosteroids. Alternatively, patients who are nonresponsive to corticosteroids may be treated with a combination therapy of cyclosporin A (5 mg/kg/day in 2 doses plus oral prednisolone), azathioprine, or specific monoclonal antibody agents. In preliminary clinical trials, rituximab significantly reduced the inflammatory activity and severity in patients with TED. However, two recent randomised trials on the efficacy of rituximab in moderate to severe TED reported conflicting results. There are some evidences in short series reports on the efficacy of other immune modulators such as tocilizumab, adalimumab, or etanercept. Other promising treatments such as the production of TSH-R antagonists, either as monoclonal TSH-R-blocking antibodies or as small-molecule-ligand antagonists of TSH-R, are being developed.

Surgical Treatment

Elective surgery is only recommended at least 6 to 9 months after stabilisation of endocrine and TED status. Available procedures include orbital decompression for disfiguring proptosis; strabismus surgery for diplopia; eyelid recession for eyelid retraction causing lagophthalmos, exposure keratitis, and disfigurement; and blepharoplasty for excessive soft tissue prominence of the eyelids. In planning surgery, orbital decompression must be first addressed because of its influence on ocular motility and lid width, followed by strabismus surgery and, finally, eyelid surgery.

Many different techniques and approaches have been described for orbital decompression surgery, including 1-, 2-, and 3-wall(s) decompression and/or orbital fat removal depending on the degree of proptosis. Different combinations of medial, inferior, and lateral wall decompression have been used as areas of bone removal. New-onset diplopia is the most common complication of orbital decompression, with the highest rates of 38%–60% reported with inferomedial decompression, possibly as a result of inferomedial shift of the globe after removing the inferomedial strut. Balanced orbital decompression reduces the incidence of postoperative diplopia by producing a more equivalent displacement of the medial and lateral soft tissues into the surrounding space. Newer techniques such as deep lateral wall orbital decompression or modified endoscopic medial orbital fat decompression seem to carry a lower risk of ocular motility problems while offering a significant proptosis reduction.

Strabismus surgery in TED is challenging due to the fibrotic muscles and surrounding soft tissues. The goal of strabismus surgery in patients with TED is to restore binocular single vision at the primary gaze. Residual double vision may persist in peripheral gaze. The basic concept of most operations is to recess the fibrotic muscles in order to correct ocular ductions. Muscle resections should be avoided since any restriction is likely to be aggravated if a muscle is shortened. Most vertical deviations can be corrected by single inferior rectus recessions due to high-dose effect. Dose effects for medial rectus recessions are lower and bilateral medial rectus muscle is often required to treat horizontal strabismus. Different techniques have been proposed to improve the outcomes including an intraoperative relaxed muscle positioning technique, the use of adjustable sutures, operating under monitored anaesthetic care or local anaesthesia, and simultaneous recession of the tenon capsule. Detachment of the lower lid retractor is also recommended to minimise postoperative lower lid retraction or inferior scleral show.

Lid retraction of both upper and lower eyelids is probably the most common feature of TED. Surgery is recommended for significant upper lid retraction of >1 mm, asymmetry of palpebral apertures, or presence of lateral flare. Surgery for upper lid retraction is divided into the anterior approach through an eyelid crease incision where the levator aponeurosis and Müller's muscle are disinserted from the tarsus until an appropriate height of the eyelid is achieved and a posterior approach through the conjunctiva and Müller's muscle. In most cases, the use of implants is not necessary. In lower lid retraction corrections, the conjunctiva and lower lid retractors are detached from the edge of the tarsus through a posterior approach and a spacer (auricular cartilage, hard palate mucosa, expanded polyethylene microplates, autogenous tarsus transplants, porcine acellular dermal matrix, donor sclera, or pericardium) is placed between the retractors and tarsus to achieve lower eyelid lengthening.

Upper and/or lower eyelid blepharoplasty is sometimes needed as the last step in the functional and cosmetic rehabilitation of TED patients.

Measures for Patients with Sight-Threatening TED

Patients with sight-threatening TED due to DON must be treated urgently. High-dose intravenous corticosteroids are recommended as the first-line treatment for DON (500 mg to 1 g on 3 consecutive days; if necessary, repeated the following week). If the response is insufficient after 1-2 weeks, or the dose/duration of steroid treatment induces significant side

effects, surgical orbital decompression (deep medial orbital wall decompression including posterior ethmoidal cells near the orbital apex) should be carried out promptly. Immediate surgical decompression as first-line therapy has not resulted in a better outcome than the use of IV steroids followed by decompression in patients with no response.

Depending on the severity of the proptosis, cases of corneal exposure keratopathy could be treated with aggressive topical lubrication, moisture chamber, botulinum toxin, levator recession surgery, tarsorrhaphy, or orbital decompression. Intravenous steroids should be administered prior to surgery if the disease is still active.

Conclusion

TED is the most important extrathyroidal manifestation of autoimmune thyroid diseases. It is the most common cause of lid retraction and proptosis in adults. Morbidity arises from restrictive strabismus causing diplopia and a spectrum of orbital soft tissue changes. Vision loss in TED can be caused by optic nerve dysfunction and corneal breakdown. Different grading systems have been proposed to gauge disease activity and severity, guiding the subsequent approach to treatment. Early stabilisation of thyroid function and smoking cessation are the key measures in the management of TED. Although most TED patients can be managed conservatively, patients with active or severe disease warrant specialist evaluation and timely treatment with intravenous steroid, orbital radiotherapy, and/or surgical decompression. Staged rehabilitative surgeries can be offered to correct the functional deficits and aesthetic deformities when there is evidence of disease quiescence for more than 6 months.

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Community Doctor Consultation Program for Gastroesophageal Reflux Disease (GERD)

GERD has become more prevalent in Hong Kong.[1] GERD symptoms not only impair patient's quality of life, its nocturnal symptoms also deteriorate sleep quality and productivity at work.[2] Despite its severity, study demonstrated that current routine clinical care helps most patients remain stable or improve over a 5-year period.[3]

In order to support proper diagnosis and disease management for suspected GERD patients, you are cordially invited to join the Community Doctor Consultation Program for GERD.

Recruitment Target:

Private practice doctors actively managing GERD patients and willing to offer free initial consultation to potential patients.

Program Detail:

1. **Potential GERD patients can register through program hotline or website, and will be randomly assigned to one participating medical practitioner based on their selected district.**
2. **Participating medical practitioners will provide free initial consultation for enrolled potential GERD patients (for medication and diagnostic test if needed, the cost can be charged to patients according to the practitioner's decision.)**
3. **GERD education materials will be provided to participating medical practitioners.**

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Minimally Invasive Glaucoma Surgery

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Introduction

Glaucoma is increasingly becoming a major cause of blindness around the world, mainly because there is currently no treatments which can reverse the optic nerve damage (glaucomatous optic neuropathy) which defines it. Despite numerous research on neuroprotective agents, intraocular pressure (IOP, measured in millimetres of mercury or mmHg) reduction remains the only proven method to prevent or decelerate progression (2017 Guideline from the National Institute for Health and Care Excellence, UK)[1]. Although topical glaucoma medications are normally the first line treatment in most patients, glaucoma surgery remains the most potent method for achieving a target IOP level. For many decades after the introduction of the guarded filtration surgery by Cairns[2], trabeculectomy has remained largely unchanged as the most commonly performed glaucoma procedure for patients requiring surgical intervention for lowering their IOP, except for the use of intra-operative antifibrotic agents (like mitomycin C) since the 1980's to try to decrease postoperative scarring of the drainage site and improve the surgical success rate[3,4]. In most clinical settings, this is usually after multiple medical treatments have been tried and failed, either due to inadequate IOP lowering or because of intolerable side effects from medical treatment. Even though tube-shunts have become more popular, especially in the United States, since the Tube Versus Trabeculectomy (TVT) Study[5], it should be noted that even there, trabeculectomy with mitomycin C is still the most frequently performed incisional surgery for glaucoma[6]. However, both trabeculectomy and tube-shunt surgery involve creation of large surgical sites that cover at least one quadrant of the scleral surface, which affects both the recovery time, as well as preclude possible further glaucoma surgery at the operated site. The 5-year result from the TVT Study showed that both procedures were associated with significant early (>20% for tube, >35% for trabeculectomy) and late (both >35%) complications of varying severities[7]. Though both procedures were able to achieve a mean IOP below 15 mmHg over 5 years, there are patients with milder degree of glaucoma, or of more advanced age, who do not need their IOP to be so aggressively lowered, especially if recovery can be hastened and complication rates lowered. Minimally invasive glaucoma surgery (MIGS), or micro-invasive glaucoma surgery as it was initially coined[8], has become an increasingly popular method for lowering the IOP or reducing the medications requirement for these patients in the past 10 years[9,10]. As MIGS is not a single procedure but a group of widely varying procedures using different IOP lowering approaches, we will take a brief look at the various types currently available in Hong Kong, or will soon be available.

Definition

It is generally accepted that MIGS are associated with:

1) Minimal surgical trauma (no scleral dissection or extensive conjunctival manipulation)
2) Rapid postoperative recovery
3) Low rates of serious complications
4) Less IOP reduction compared to trabeculectomy or tube-shunts

However, even with these accepted generalities, there are areas of disagreements among glaucoma specialists. For example, when the EX-PRESS Glaucoma Filtration Device (Alcon) was introduced almost 20 years ago, it was initially used without the need to incise the sclera (sclerectomy) unlike standard trabeculectomy, and so could be considered as a form of MIGS. The current usage of this device however, involves sclerectomy to create a scleral flap to cover the back plate of the implant, thus transforming it more into a modified trabeculectomy rather than a MIGS procedure. Also, some would not even consider any procedure involving conjunctival incision or manipulation as MIGS. For this review, we will adopt a more inclusive approach although this is not meant to be an exhaustive list of every procedure currently available.

Classification

The widely different types of MIGS available can be divided into which pathway is being utilised for aqueous outflow from the anterior chamber of the eye. Currently, these are mainly of 3 types; Schlemm's canal, suprachoroidal space, and subconjunctival space.

Schlemm's canal

Most of the normal aqueous humour outflow passes through the trabecular meshwork (TM), which forms the inner wall of the Schlemm's canal, then into the episcleral veins via the collecting channels connected to this canal. In primary open angle glaucoma (POAG) or ocular hypertension (OHT), this trabecular outflow is impaired due to increased resistance at the TM, limiting the flow of aqueous into the Schlemm's canal. Some MIGS seek to bypass or remove the TM in order to

facilitate and re-establish this outflow to the Schlemm's canal (and hence to the episcleral veins).

1) Goniotomy / Ab interno trabeculotomy

Goniotomy and trabeculotomy involve incising the TM so that aqueous can directly access the Schlemm's canal. It has traditionally been used for congenital glaucoma in children with high success rates in most reports. Its success rate when performed in a similar fashion in adults is much lower[11,12]. The following procedures aim to ablate or remove an entire strip of TM rather than just incising it, thus allowing a more persistent access to the Schlemm's canal.

I. Trabectome (NeoMedix, CA, USA)

This instrument received FDA approval in 2004 for the treatment of adult and juvenile open angle glaucoma. A disposable, single-use, 19.5-gauge hand-piece with an insulated footplate containing high-frequency electrocauterisation, irrigation and aspiration functions (Fig. 1.) is inserted into the anterior chamber through a small (usually temporal) clear corneal incision. The end plate is inserted through the TM opposite to the corneal wound, and thermal ablation of the TM is performed for 60 to 120 degrees under gonioscopic viewing. Complications are few and mild, and include transient IOP spike in the first day after the procedure and mild hyphema. The main advantage is that the conjunctiva remains undisturbed, allowing for future trabeculectomy or tube-shunt surgery if required. In a recent meta-analysis in POAG, at 12 months after Trabectome procedure, the mean IOP reduction, mean IOP, mean reduction of medications and mean number of medications used were 25-34%, 14.8-16.8 mmHg, 0.40-0.57 and 2.1-2.4, respectively[13]. However, none of the studies included in the analysis are randomised controlled trials (RCT) as none yet exists despite the Trabectome being commercially available for over 10 years.

Fig. 1.

II. Kahook Dual Blade (New World Medical, CA, USA)

This simple single-use device (Fig. 2.) was developed much later than the Trabectome although it uses the same principle of introducing the instrument through a clear corneal incision opposite to the surgical site, and removing the TM there to allow direct access of aqueous into the Schlemm's canal and its collecting channels (Fig. 3.). After its initial in vitro evaluation in human cadaver eyes[14] which noted that the dual blade produces less collateral damage during goniotomy than cauterisation using the Trabectome, it was introduced into the market. Due to its recent introduction, there is only one large case series reporting on its short term (6 months) results[15]. This prospective, interventional, non-randomised study examined the use of the dual blade goniotomy when combined with cataract extraction (phacoemulsification) in patients with various types of glaucoma, although the majority (70%) were POAG. No significant complications were encountered and the most common (39.4%) adverse event was the not-unexpected intraoperative blood reflux from the collector channels after removal of the TM, which resolved spontaneously in all cases. At 6 months, compared to baseline, there was significant reduction of both IOP and glaucoma medications use, with a mean reduction of IOP and medication use of 4.6 mmHg (26% drop) and 0.7, respectively. The mean IOP and mean number of glaucoma medications used at 6 months postoperatively were 12.8 mmHg and 0.9 respectively, compared to the baseline of 17.4 mmHg and 1.6 respectively. It would be interesting to have a direct comparison of this simple instrument with the more elaborate Trabectome in future in vivo studies to evaluate their respective effectiveness and safety profile.

Fig. 2.

Fig. 3.

2)iStent (Glaukos, CA, USA)

This micro-implant (G1 model, 1 x 0.3 mm in size and 60 micrograms in weight; Fig. 4.) received FDA approval in 2012, being the first MIGS device to do so. Unlike goniotomy (or ab interno trabeculotomy), no ablation or cutting of the TM is involved. Instead, a tiny nonferromagnetic titanium shunt (with a 120-micron lumen) is inserted thru the TM using its own specially designed preloaded injector, with one opening situated within the Schlemm's canal, and the other opening outside and communicating with the anterior chamber. Like goniotomy, the procedure is performed under gonioscopic viewing (Fig. 5.) with access provided by a clear corneal incision opposite to the surgical site,

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*OAB: Overactive Bladder + LUTS: Lower Urinary Tract Symptoms
α_1-blockers are often considered the first line drug treatment of male LUTS[3]

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Abbreviated prescribing information of Harnal OCAS® 0.4 mg Tablets
Version: 002 PI version: Sep 2013. **Composition:** Tamsulosin HCl **Indication:** Lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH). **Dosage:** 1 tab daily, can be taken independently of food. **Administration:** Swallow whole, do not chew/crunch. **Contraindications:** Hypersensitivity to tamsulosin hydrochloride or to any of the excipients. **Special warnings and special precaution for use:** As with other α1-adrenoceptor antagonists, a reduction in blood pressure can occur in individual cases during treatment with Harnal OCAS® 0.4 mg Tablets, as a result of which, rarely, syncope can occur. At the first signs of orthostatic hypotension (dizziness, weakness), the patient should sit or lie down until the symptoms have disappeared. Before therapy with Harnal OCAS® 0.4 mg Tablets is initiated, the patient should be examined in order to exclude the presence of other conditions, which can cause the same symptoms as benign prostatic hyperplasia. Digital rectal examination and, when necessary, determination of prostate specific antigen (PSA) should be performed before treatment and at regular intervals afterwards. Treatment of patients with a history of orthostatic hypotension should be approached with caution. The treatment of patients with severe renal impairment (creatinine clearance of <10 ml/min) should be approached with caution, as these patients have not been studied. The treatment of patients with severe hepatic dysfunction should be approached with caution. The 'Intraoperative Floppy Iris Syndrome' (IFIS, a variant of small pupil syndrome) has been observed during cataract and glaucoma surgery in some patients on or previously treated with tamsulosin hydrochloride. IFIS may increase the risk of eye complications during and after the operation. Discontinuing tamsulosin hydrochloride 1-2 weeks prior to cataract or glaucoma surgery is anecdotally considered helpful, but the benefit of treatment discontinuation has not been established. IFIS has also been reported in patients who had discontinued tamsulosin for a longer period prior to the surgery. The initiation of therapy with tamsulosin hydrochloride in patients for whom cataract or glaucoma surgery is scheduled is not recommended. During pre-operative assessment, surgeons and ophthalmic teams should consider whether patients scheduled for cataract or glaucoma surgery are being or have been treated with tamsulosin in order to ensure that appropriate measures will be in place to manage the IFIS during surgery. Tamsulosin hydrochloride should not be given in combination with strong inhibitors of CYP3A4 in patients with poor metaboliser CYP2D6 phenotype. Tamsulosin hydrochloride should be used with caution in combination with strong and moderate inhibitors of CYP3A4. Cases of allergic reaction to tamsulosin in patients with a past history of sulfonamide allergy have been reported. If a patient reports a previously experienced sulfa allergy, caution is warranted when administrating tamsulosin hydrochloride. **Undesirable effects:** *Common (>1%, <10%), Uncommon (>0.1%, <1%), Rare (>0.01%, <0.1%), Very rare (<0.01%). Cardiac disorder: Uncommon:* Palpitations. *Gastrointestinal disorders: Uncommon:* Constipation, diarrhoea, nausea, vomiting. *General disorders and administration site conditions: Uncommon:* Asthenia. *Nervous systems disorders: Common:* Dizziness (1.3%). *Uncommon:* Headache. *Rare: Syncope. Reproductive system and breast disorders: Common:* Ejaculation disorders. *Very rare:* Priapism. *Respiratory, thoracic and mediastinal disorders: Uncommon:* Rhinitis. *Skin and subcutaneous tissue disorders: Uncommon:* Rash, pruritus, urticaria. *Rare:* Angioedema. *Vascular disorders: Uncommon:* Orthostatic hypotension. ***Post-marketing experience:*** The following events have also been reported during the post-marketing period. These events are reported voluntarily from a population of uncertain size, therefore it is not possible to reliably estimate their frequency: visual disorders (e.g. blurred vision, visual impairment), dermatitis exfoliative, erythema multiforme and epistaxis. During cataract and glaucoma surgery a small pupil situation, known as Intraoperative Floppy Iris Syndrome (IFIS), has been reported. **Full prescribing information is available upon request.**

Abbreviated prescribing information of Betmiga® prolonged-release tablets
Version: 003 PI version: Apr 2016. **Composition:** Mirabegron **Indication:** Symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome. **Dosage:** Adult including elderly 50 mg once daily with or without food. **Administration:** Swallow whole with liquids. Do not chew/divide/crush. **Contraindications:** Mirabegron is contraindicated in patients with - Hypersensitivity to the active substance or to any of the excipients. - Severe uncontrolled hypertension defined as systolic blood pressure ≥ 180 mm Hg and/or diastolic blood pressure ≥ 110 mm Hg. **Special warnings and precautions for use:** Renal impairment: Betmiga has not been studied in patients with end stage renal disease (GFR < 15 mL/min/1.73 m2 or patients requiring haemodialysis) and, therefore, it is not recommended for use in this patient population. Data are limited in patients with severe renal impairment (GFR 15 to 29 mL/min/1.73 m2); based on a pharmacokinetic study a dose reduction to 25 mg is recommended in this population. Betmiga is not recommended for use in patients with severe renal impairment (GFR 15 to 29 mL/min/1.73 m2) concomitantly receiving strong CYP3A inhibitors. Hepatic impairment: Betmiga has not been studied in patients with severe hepatic impairment (Child-Pugh Class C) and, therefore, it is not recommended for use in this patient population. Betmiga is not recommended for use in patients with moderate hepatic impairment (Child-Pugh B) concomitantly receiving strong CYP3A inhibitors. Hypertension: Mirabegron can increase blood pressure. Blood pressure should be measured at baseline and periodically during treatment with Betmiga, especially in hypertensive patients. Data are limited in patients with stage 2 hypertension (systolic blood pressure ≥ 160 mm Hg or diastolic blood pressure ≥ 100 mm Hg). Patients with congenital or acquired QT prolongation: Betmiga, at therapeutic doses, has not demonstrated clinically relevant QT prolongation in clinical studies. However, since patients with a known history of QT prolongation or patients who are taking medicinal products known to prolong the QT interval were not included in these studies, the effects of mirabegron in these patients is unknown. Caution should be exercised when administering mirabegron in these patients. Patients with bladder outlet obstruction and patients taking antimuscarinics medications for OAB: Urinary retention in patients with bladder outlet obstruction (BOO) and in patients taking antimuscarinic medications for the treatment of OAB has been reported in postmarketing experience in patients taking mirabegron. A controlled clinical safety study in patients with BOO did not demonstrate increased urinary retention in patients treated with Betmiga; however, Betmiga should be administered with caution to patients with clinically significant BOO. Betmiga should also be administered with caution to patients taking antimuscarinic medications for the treatment of OAB. **Undesirable effects:** Summary of the safety profile: The safety of Betmiga was evaluated in 8,433 patients with OAB, of which 5,648 received at least one dose of mirabegron in the phase 2/3 clinical program, and 622 patients received Betmiga for at least 1 year (365 days). In the three 12-week phase 3 double blind, placebo controlled studies, 88% of the patients completed treatment with Betmiga, and 4% of the patients discontinued due to adverse events. Most adverse reactions were mild to moderate in severity. The most common adverse reactions reported for patients treated with Betmiga 50 mg during the three 12-week phase 3 double blind, placebo controlled studies are tachycardia and urinary tract infections. The frequency of tachycardia was 1.2% in patients receiving Betmiga 50 mg. Tachycardia led to discontinuation in 0.1% patients receiving Betmiga 50 mg. The frequency of urinary tract infections was 2.9% in patients receiving Betmiga 50 mg. Urinary tract infections led to discontinuation in none of the patients receiving Betmiga 50 mg. Serious adverse reactions included atrial fibrillation (0.2%). Adverse reactions observed during the 1-year (long term) active controlled (muscarinic antagonist) study were similar in type and severity to those observed in the three 12-week phase 3 double blind, placebo controlled studies. List of adverse reactions: The table below reflects the adverse reactions observed with mirabegron in the three 12-week phase 3 double blind, placebo controlled studies. The frequency of adverse reactions is defined as follows: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. Infections and infestations: Common: Urinary tract infection. Uncommon: Vaginal infection, Cystitis. Psychiatric disorders: Not known (cannot be estimated from the available data): Insomnia*. Eye disorders: Rare: Eyelid oedema. Cardiac disorders: Common: Tachycardia. Uncommon: Palpitation, Atrial fibrillation. Vascular disorders: Very rare: Hypertensive crisis*. Gastrointestinal disorders: Common: Nausea*, Constipation*, Diarrhoea*. Uncommon: Dyspepsia, Gastritis. Rare: Lip oedema. Skin and subcutaneous tissue disorders: Uncommon: Urticaria, Rash, Rash macular, Rash popular, Pruritus. Rare: Leukocytoclastic vasculitis, Purpura, Angioedema*. Musculoskeletal and connective tissue disorders: Uncommon: Joint swelling. Reproductive system and breast disorders: Uncommon: Vulvovaginal pruritus. Investigations: Uncommon: Blood pressure increased, GGT increased, AST increased, ALT increased. Renal and urinary disorders: Rare: Urinary retention*. Nervous system disorders: Common: Headache*, Dizziness*. *observed during post-marketing experience. **Full prescribing information is available upon request.**

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usually the main wound for phacoemulsification when performed together with cataract surgery, which is often the case. The second generation iStent (G2 or iStent inject) is even smaller (0.36 x 0.23 mm), making it the smallest approved medical implant for use in humans. In a multi-centre randomised control trial comparing phacoemulsification alone (control group) versus phacoemulsification with iStent in 240 eyes, the 12-month success rate, defined primarily as an unmedicated IOP of 21 mmHg or lower, or secondarily as an unmedicated IOP reduction of 20% or more, was significantly higher for subjects who received the iStent implant than those who did not, being 72% versus 50% for primary success and 66% versus 48% for secondary success[16]. At 24 months, primary and secondary success in the iStent group were 61% and 53%, compared to 50% and 44% for the control group[17]. In this study, there was no significant differences in adverse events between the two groups of subjects. More than one iStent can also be used in the same procedure to achieve a greater IOP reduction. A multi-centre prospective case series examining the use of 2 iStents (G2 model, Fig. 6.) as a solo procedure (not combined with cataract surgery) for 99 subjects with open angle glaucoma, reported 66% of subjects achieving an unmedicated IOP of 18 mmHg or less and 72% having an unmedicated IOP reduction of 20% or more, at 12 months after surgery. The mean IOP at 12 months postoperatively dropped from a mean baseline of 26.3 mmHg to 15.7 mmHg, with 71.7% of subjects being able to reduce their treatment requirement by 2 or more medications. In another prospective, randomised study comparing one, two or three iStents as a solo procedure in 119 subjects with POAG[18], at 18 months after surgery, the mean unmedicated IOP was 15.9 mmHg among the one-stent subjects, 14.1 mmHg in the two-stent subjects, and 12.2 mmHg for the three-stent subjects, while glaucoma medications were required in 7 one-stent subjects, 4 two-stent subjects, and 3 three-stent subjects. Due to the higher effectiveness of inserting more than one implant, Glaukos (CA, USA) now supplies the second generation iStent (G2, or *iStent inject*) preloaded with 2 devices.

Fig. 4.

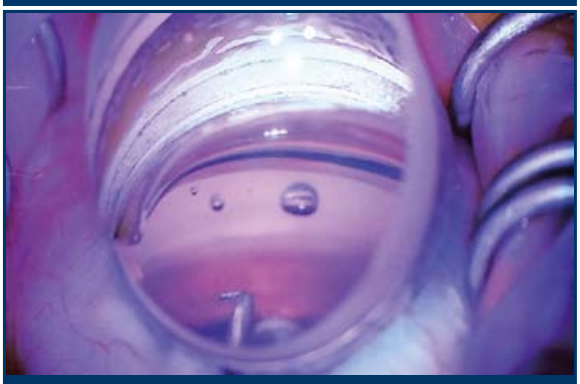

Fig. 5.

Fig. 6.

3) Hydrus (Ivantis, CA, USA)

Compared to the first and second generation iStents, the Hydrus Microstent is noticeably larger, being 8 mm in length (covering 3 clock hours of the TM), and designed to act as an intracanalicular scaffold that dilates the Schlemm's canal nine times its cross-sectional area. Made of flexible nitinol, an elastic nickel-titanium alloy, the curved device is designed to conform to the arc of the Schlemm's canal (Fig. 7.), with the non-intracanalicular end bypassing the TM and communicating with the anterior chamber directly. Similar to the iStent, it requires a clear corneal incision of 1-1.5 mm width (if not performed as combined procedure with phacoemulsification) opposite to the quadrant of insertion (usually nasal or inferior). As with any procedure involving an ab interno approach to the TM, good gonioscopic visualisation is a prerequisite (Fig. 8.) to successful placement (Fig. 9.). Unlike the iStent, it is still currently undergoing phase IV clinical trial in the USA. In the HYDRUS II Study, a randomised control study comparing combined Hydrus and phacoemulsification with phacoemulsification alone for 100 eyes with open angle glaucoma and cataract, at 24 months after surgery, in the eyes which received the Hydrus, 80% were able to achieve at least 20% IOP reduction and the mean unmedicated IOP was 16.9 mmHg; while for those who did not receive the Hydrus, only 46% were able to achieve at least 20% IOP reduction and the mean unmedicated IOP was 19.2 mmHg[19]. Almost 73% in the Hydrus group did not require glaucoma medication at 24 months, compared to around 38% in the non-combined surgery group.

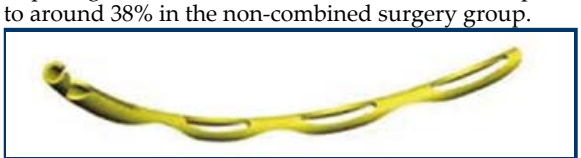

Fig. 7.

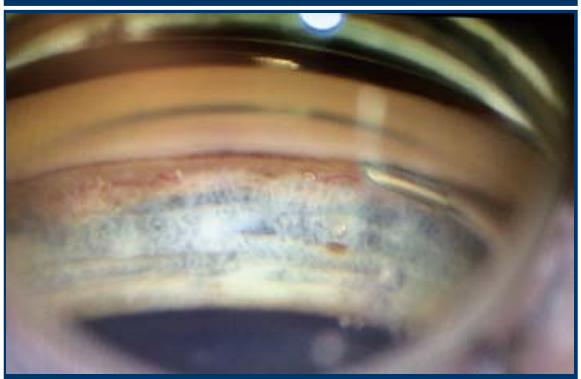

Fig. 8.

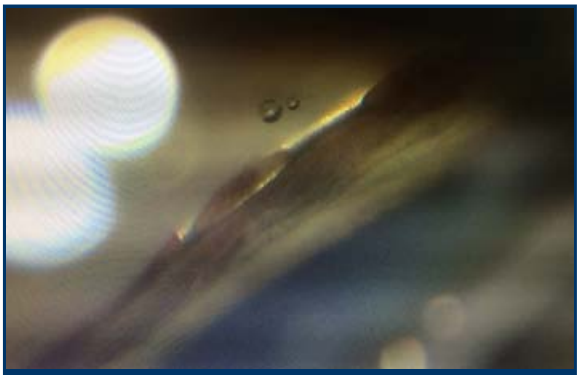

Fig. 9.

Suprachoroidal space

Some aqueous leaves the anterior chamber into the suprachoroidal space normally, termed as uveoscleral outflow. Glaucoma mediations which are prostaglandin analogues lower IOP by increasing this outflow, and some MIGS use a miniature shunt to direct even greater flow into the suprachoroidal space to try to reduce the IOP further.

1) CyPass Micro-Stent (Alcon, TX, USA)

The CyPass implant is a small stent inserted into the suprachoroidal space via an ab interno approach (Fig. 10.). The stent is made of polyamide material with a length of 6.35mm. There are openings along its whole length to allow aqueous to drain into the suprachoroidal space (Fig. 11.). A 1.5mm clear cornea insertion is made and the stent is implanted with a manual inserter and a guidewire to the suprachoroidal space. In a multi-centre randomised trial[20], 505 patients with open angle glaucoma and cataract were randomised to phacoemulsifcation only or phacoemulsifcation with Cypass implantation. With a pre-operative IOP of 24.5mmHg & 24.4mmHg, the IOP was reduced by 5.4 mmHg in the phacoemulsification group and 7.4 mmHg in the Cypass group, respectively. In the Cypass group, 85% did not require medications at the end of second year and the mean number of medications was reduced by 67%. In another study[21] involving 55 phakic or pseudophakic eyes, stand-alone Cypass implantation procedures were performed. After 12 months, the mean IOP decreased from 24.5mmHg to 16.4mmHg while the number of medications reduced from 2.2 on average to 1.4. Adverse events such as implant obstruction, transient hyphema or IOP spike was uncommon in both studies.

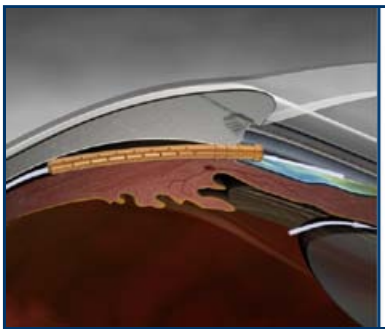

Fig. 10.

Fig. 11.

Subconjunctival space

Similar to trabeculectomy and tube-shunt in concept, this method seeks to create a new pathway for aqueous outflow from the anterior chamber of the eye into the subconjunctival space, but without the associated tissue trauma.

1) XEN (Allergan, CA, USA)

XEN gel stents aim to create a subconjunctival filtration bleb via an ab interno approach in eyes without pre-existing conjunctival scar. It is 6 mm in length and composed of porcine gelatin crosslinked with glutaraldehyde. It could be done with a cataract surgery or as a stand-alone procedure. The stent is implanted into the subconjunctival space via a small corneal incision, creating a fistula connecting the anterior chamber (Fig. 12.). An anti-metabolite such as mitomycin C (MMC) is usually injected subconjunctivally 20 minutes before the procedure to prevent bleb failure due to conjunctival scarring. A recently published prospective study involving 30 eyes with open angle glaucoma and cataract showed that the mean IOP reduction was 6.2 mmHg at 12 months, from preoperatively 21.2 mmHg to 15.0 mmHg, a 29.3% reduction. So far there are only limited clinical data and trials are still ongoing. Long-term studies are necessary to prove the efficacy as well as safety of XEN gel stents.

Fig. 12.

2) InnFocus Microshunt (Santen, Osaka, Japan)

In contrast to the XEN gel stents, the InnFocus Microshunt creates a subconjunctival filtration bleb via ab externo approach. The 8.5-mm long shunt (Fig. 13.) is made of a non-reactive, non-erodible polystyrene called SIBS. It is inserted ab externo into the anterior chamber via a 3-mm needle track after limited peritomy and subconjunctival mitomycin C application (Fig. 14.). The fin in the middle of the shunt would be sealing the scleral tract and anchoring the shunt within the sclera. According to a recent case series[23] of 79 eyes implanted with the device, 80% achieved IOP of 14 mmHg or less from a mean baseline of 24.8 mmHg at 4 years. Mean number of glaucoma medications needed also reduced from 2.3 at baseline, to 0.9, with 62% of patients taking no glaucoma medications. Very little clinical data are currently available for the device. Further clinical trials are needed to establish its efficacy and safety profile.

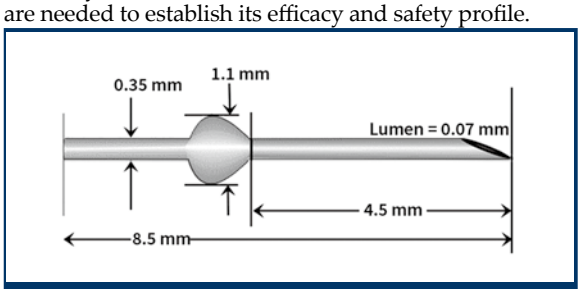

Fig. 13.

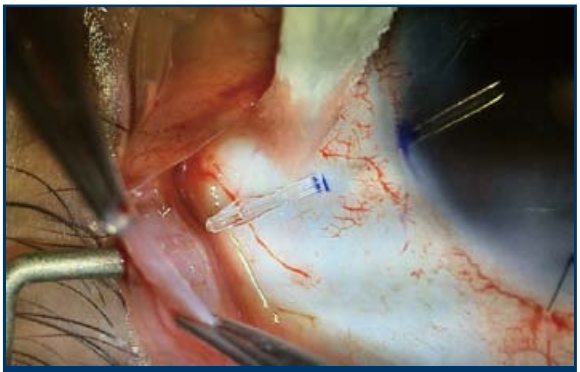

Fig. 14.

Conclusion

The current popularity and variety of MIGS probably stem from a previously unmet need for surgical interventions which have a much better safety profile than the current standard of trabeculectomy and tube-shunts, as well as offering faster recovery and, in most cases, minimal or no conjunctival manipulation (thus maximising potential future sites for more aggressive procedures as needed). One trade off of MIGS has generally been the lower IOP reduction and increased cost compared to trabeculectomy and tube-shunts, which necessitate careful selection of suitable patients. Not all patients require aggressive IOP reduction (for example, less than 12 mmHg) or to be completely off all medications, especially if it will entail the possibility of serious complications. Many will tolerate using 1-2 glaucoma eye drops (or one fixed combination eye drop) postoperatively, if required, to achieve their target IOP. If cost is not an issue, then MIGS can allow for greater flexibility when planning for surgical intervention, especially in those with borderline suboptimal IOP control or treatment compliance issue, where the risks of standard surgical procedures like trabeculectomy may outweigh the possible benefits.

Acknowledgement

The colour intra-operative photos were taken during the author's (JC) 4-week clinical attachment in June 2017 with Ike Ahmed in Toronto, Canada. Dr Ahmed is one of the pioneers and leading experts of MIGS.

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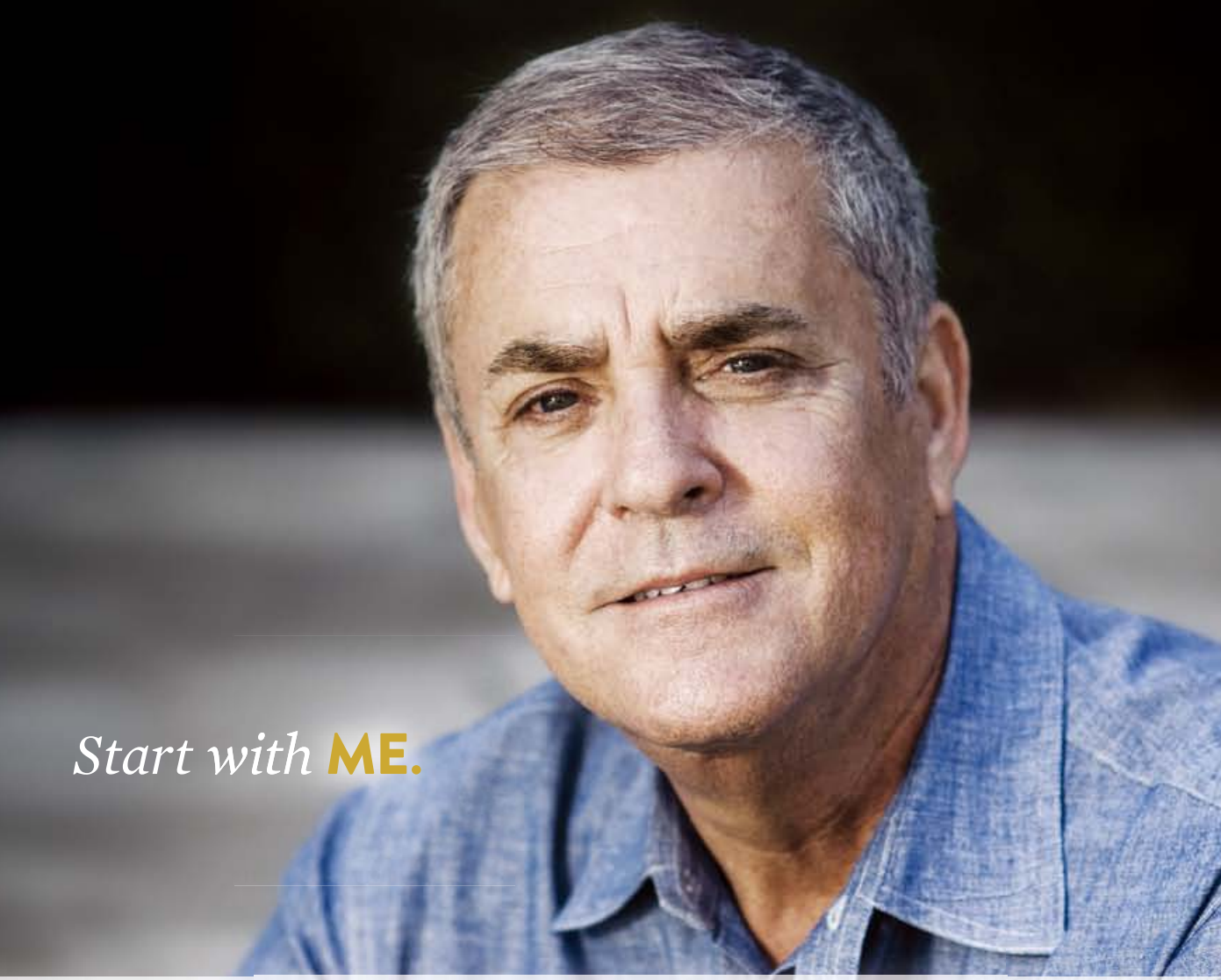

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Demyelinating and inflammatory optic neuropathies: an overview

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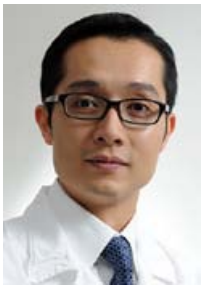

Dr Jonathan Chun-ho HO Dr Andy Chi-on CHENG

Introduction

Optic neuritis (ON) is one of the leading causes of visual loss in the young to middle age populations worldwide, with the triad of visual loss, periocular pain and dyschromatopsia[1]. Chinese patients, following an episode of ON, are found to have a lower conversion rate to multiple sclerosis (MS), compared to Caucasian populations. However, ON might well be the initial manifestation of neuromyelitis optica spectrum disorder (NMOSD), carrying a worse visual prognosis. Optic perineuritis (OPN) is a form of idiopathic orbital inflammatory disease (IOID) targeting the optic nerve sheath and its surrounding tissue, representing a key differential diagnosis of ON[2]. In this article, we will review our current understanding of these three disease entities, delineate features crucial for their differentiation in terms of presentation, investigation findings, treatment and prognosis.

Idiopathic demyelinating optic neuritis (IDON) / Multiple sclerosis-associated optic neuritis (MS-ON)

The common age of presentation is 20 – 45 years, and its incidence to be three times higher in women. The classic pattern is subacute loss of vision progressing over a span of hours to 10 days, with a spectrum of severities ranging from mild acuity loss to no light perception and normally reaching its nadir within 2 weeks. Any form of visual field defect is possible in IDON / MS-ON, although the 15-year follow-up report from the Optic Neuritis Treatment Trial (ONTT) reported diffuse and central field losses to be more commonly detected at the initial visit, and partial arcuate, paracentral and arcuate losses in subsequent follow-ups[3]. Complete or near-complete recovery of visual acuity and field loss is usually seen - any progressive worsening of vision lasting over 2 weeks, or a lack of recovery beyond 8th week since symptom onset should prompt investigations for an alternative diagnosis. Dyschromatopsia occurs early on in the course of IDON / MS-ON and is often out of proportion to the degree of visual acuity deficit. Periocular pain and retro-orbital pain occur in more than 90% of cases in a predominantly Caucasian population.[4] On the other hand, pain is less commonly a presenting feature in optic neuritis in the Chinese population, as low as to be about 28% in our local study[24]. It can precede or coincide with the onset of visual impairment, aggravated by eye movement but usually non-severe, and often resolves within days. A swollen optic nerve head is seen in 1/3 of cases.

In IDON, magnetic resonance imaging (MRI) with gadolinium typically demonstrates contrast enhancement of the affected optic nerve[5]. (Fig. 1) MRI brain with gadolinium may reveal the characteristic spatial and temporal dissemination of lesions as set forth by the 2010 McDonald MRI criteria[6]. The presence of demyelinating white matter lesions in brain MRI scans, ≥3 mm in diameter, ovoid in shape, located in periventricular white matter radiating toward the ventricular spaces has been identified as the single most predictive factor for conversion to clinically definite MS. In the ONTT, 25% of patients with no MRI lesions at presentation still went on to develop MS, 50% of those with 1 or more MRI lesions developed MS within 5 years[7] and 72% within 15 years. Optical coherence tomography (OCT) may be employed to visualise the retinal nerve fibre layer (RNFL), the thickness of which increases in the initial period of optic nerve swelling but subsequently decreases secondary to axonal loss. Such thinning is often less severe than in NMOSD-ON eyes[8]. Lumbar puncture might demonstrate raised cerebrospinal fluid oligoclonal bands alongside mild pleocytosis.

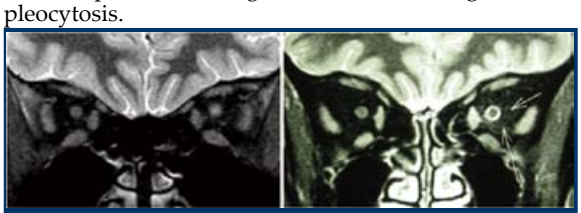

Fig. 1. MRI (coronal short TI inversion recovery images) of the orbit in patients with left optic neuritis showing hyperintensity of the optic nerve (left), left optic perineuritis showing perineural hyperintensity around the left optic nerve (donut sign) with dirty fat sign depicted with arrows (right) [24]

The clinical course of IDON is often favourable: spontaneous improvement in visual function is observed in more than 80% patients within 1 month[9] even in the absence of treatment, followed by stabilisation or sustained improvement up to 1 year. Acute management usually employs high-dose intravenous corticosteroids followed by an oral taper, which is shown to accelerate initial visual recovery. ONTT protocol is also recommended for typical ON patients in the presence of 3 or more MRI signal abnormalities, or patients requiring prompt resolution of visual deficits, including monocular patients, bilateral disease involvement, employment demands and patient preference[10]. Regarding long-term management, a number of disease-modifying agents, available in injections or oral medications, are available nowadays

to delay subsequent relapses and conversion to MS including β-interferons, glatiramer acetate, fingolimod, teriflunomide, dimethyl fumarate, natalizumab and alemtuzumab[11].

Inflammatory optic neuropathy

Neuromyelitis optica spectrum disorder

NMOSD is an autoimmune inflammatory disorder of the central nervous system characterised by recurrent attacks of optic neuritis and transverse myelitis, features also found in MS. NMO has been considered a variant of MS, until in 2005 the discovery of serum antibodies against the water channel protein aquaporin-4 (AQP4) in NMO patients[12].

While MS displays a prominent geographical distribution and prevails in the white population, NMO appears to have a more worldwide occurrence, with 20-50% of NMO patients quoted to be of non-white ethnicity in UK and US studies. The age of onset of symptoms is on average 10 years older than MS patients at initial presentation. Also, UK studies have reported over one-fifth of Caucasian NMO patients to have an age of onset over 60 years[13]. A very late age of onset may thus be in favour of a diagnosis of NMO. 50% of NMO patients initially present with isolated ON, among which 20% have bilateral involvement[14]. Isolated simultaneous bilateral optic neuritis, in particular, is a classical feature of NMO-ON. Importantly, NMO-ON causes more rapid, profound and persistent visual loss. During an acute attack 80% of NMO-ON sufferers experience a visual acuity of less than 20/200, compared to 36% in MS-ON. If inadequately treated, approximately 60% of NMO-ON patients experience unilateral or bilateral blindness at a median of 7.7 years following disease onset, in contrast to only 4% in MS-ON patients at 15-year follow up[15-16]. The optic nerve head can be of normal appearance. Altitudinal field deficits, if present, corroborate a diagnosis of NMO-ON[17], although this can also occur in non-arteritic anterior ischaemic optic neuropathy. Relapses are much more common and severe than in IDON.

IgG-antibody to AQP4 is a sensitive and highly specific serum marker of NMO, and cell-based assays being the most reliable[18]. However, not all NMOSD patients have positive testing at presentation, thus we currently rely on the International Panel for NMO Diagnosis guidelines in 2015 to establish a clinical diagnosis[19]. It is stratified according to the AQP4-IgG status, and certain clinical and radiological criteria have to be fulfilled. Another IgG-antibody implicated in NMOSD is against myelin oligodendrocyte glycoprotein (MOG). Once thought to be a mild and usually monophasic variant, a retrospective review of 50 MOG antibody-positive cases revealed a multiphasic course in 80%, with severe visual impairment or functional blindness in 36% in long-term follow-up. 70% of eyes developed functional blindness in one or both eyes during at least one ON attack. Coexisting autoimmune disorders are more often seen in AQP4-IgG positive NMOSD (1/3), compared to MOG-IgG positive NMOSD (9%)[20].

MRI typically shows optic nerve enhancement, which is more extensive, affecting posterior portions and/or optic chiasm. MRI of the spinal cord might demonstrate longitudinally extensive transverse myelitis affecting ≥3 contiguous vertebral segments, with central/gray matter involvement and the presence of T1 hypointense acute lesion[21]. OCT of RNFL exhibits more marked peripapillary RNFL loss than in MS-ON, and a more widespread atrophy involving the superior and inferior quadrants[8, 22]. In terms of CSF findings, NMOSD patients often have pleocytosis and may contain neutrophils and eosinophils, in contrast to the presence of lymphocytes and macrophages in MS patients. Oligoclonal bands, present in up to 95% of patients with MS, are only detected in 10-25% of patients with NMO.

Acute attacks should be treated with high-dose intravenous methylprednisolone for 3-5 consecutive days. For patients in whom symptoms are severe or refractory to steroid, plasmapheresis is a recommended adjunct. Once the diagnosis of NMO-ON is established, attack prevention should be taken in the form of long-term systemic immunosuppression via agents such as azathioprine, mycophenolate mofetil, rituximab, and oral glucocorticoids. There is no consensus on the optimal duration of immunosuppressive treatment, but the prevailing practice is for AQP4 seropositive patients to receive immunosuppression for a minimum of 5 years[23]. In general terms, delayed initiation and premature withdrawal of treatment is associated with poor outcome and recurrence.

Optic perineuritis

OPN is a form of idiopathic orbital inflammatory disorder affecting the optic nerve dural sheath and is distinct from demyelinating optic neuritis[24]. While most cases are isolated and idiopathic, OPN occasionally occurs as a manifestation of a specific infectious or inflammatory disorder, such as Wegener's granulomatosis, giant cell arteritis, Crohn's disease, acute phase of secondary syphilis and neurosyphilis.

OPN tends to occur in older patient (age > 50) and progressive loss of acuity and/ or visual field loss (peripheral or arcuate) might last for weeks. Associated orbital sign such as diplopia, subtle ptosis and chemosis, might be present. There can be pain with eye movement and examination might reveal a swollen (50-70%)[24,25] or a normal-appearing optic disc.

MRI findings of OPN can be grouped anatomically into perineural, intraneural and orbital[25]. There is a characteristic pattern of enhancement in the optic nerve sheath, namely tram track and donut signs on axial and coronal cuts respectively. Streaky enhancement of extra-ocular muscles, sclera or orbital fat (dirty fat sign), and intraneural enhancement due to inflammation of pial septa, may be present. (Fig. 1 and 2)

Intravenous methylprednisolone can be considered as initial treatment to cover for both ON and OPN, especially if neuroimaging is not readily available. However, if the diagnosis of OPN is certain, a high dose of oral systemic steroid has proven to be effective also. Early initiation of high-dose oral prednisolone and prolonged treatment for OPN often lead to an excellent prognosis. It is essential to prevent irreversible visual

loss and recurrent attacks; delay in initiating therapy or premature withdrawal of corticosteroids can lead to poor visual outcomes.

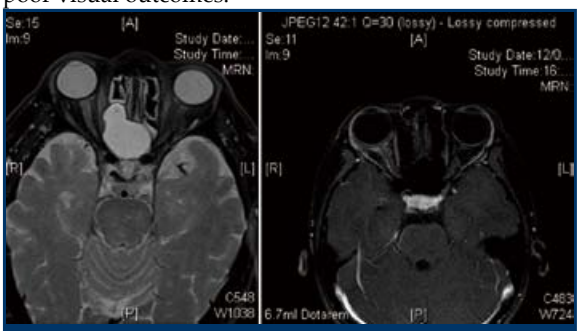

Fig. 2. MRI (coronal short TI inversion recovery images) of the orbit in a patient with right optic perineuritis demonstrating the tram track sign (right).

Conclusion

MS-ON, NMO-ON and OPN have disparate pathogeneses and treatment responses. An accurate diagnosis among the three is paramount, as misdiagnosis and maltreatment may end up with poor ophthalmological and neurological outcome.

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香港中文大學 醫學院 矯形外科及創傷學系

Master of Science in

Musculoskeletal Medicine Rehabilitation and Geriatric Orthopaedics

骨關節醫學、康復及老年醫學理學碩士

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Latest Measures in Controlling Myopia Progression in Children

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Introduction and Definitions

Myopia (near- or short-sightedness) is the most common eye disorder in humans[1]. It is a refractive state where light rays from distant objects focus in front of, rather than on the retina. It can be secondary to excessive elongation of the eyeball, or less commonly, abnormally high refractive power of the cornea or lens. Most babies are hyperopic (long-sighted) at birth. This hyperopia gradually decreases in the first two years of life by changes in the cornea, lens and axial length. After that, the cornea and lens stabilise but myopia can continue to progress as the eyeball elongates over the next two decades[2,3]. In numeral terms, the severity of myopia is measured in dioptres (D). Simple myopia normally refers to those with myopia from 0.00 to 6.00 D, and myopia >6.00 D is often regarded as high myopia[1]. In Hong Kong, 1 D (or 1.00 D) is habitually spoken as '100 degrees' (and so on) by the general public.

Epidemiology & Possible morbidities

Besides inconvenience and socio-economic costs to the individuals, myopia can be associated with many blinding eye conditions, including retinal detachment, macula degenerations (Fig. 1), premature cataract and glaucoma[4-9]. The prevalence of myopia is much higher in Asian countries compared to the West[10]. In Hong Kong, the myopia prevalence is 17.0% in children <7 years, which increases to 37.5% in 8-year-olds and 53.1% in children above 11 years[5]. Even more worrying, increasingly earlier onset is also observed. The prevalence of myopia in preschool children has escalated significantly from 2.3% to 6.3% over a ten-year period[11]. Myopia control has become a major health issue in many developed countries[12].

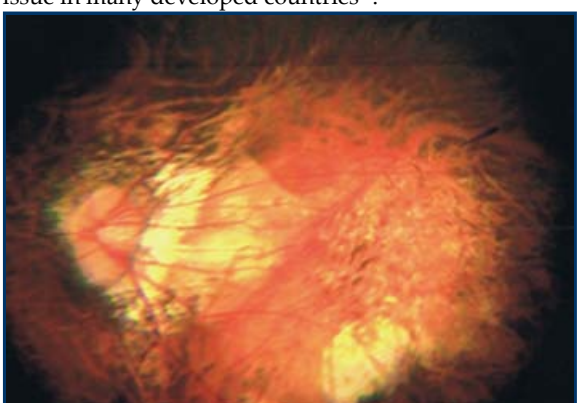

Fig. 1. Macula degeneration associated with high myopia

Risk factors

Genetics plays a major role in a child's refractive error status, as shown in studies relating to myopic status of parents[13-15], siblings or twin studies[16,17]. However, no single chromosomal locus has been associated with myopia development[18]. Environmental factors are also important, as shown in myopia association with education levels, years of schooling and school results[19]. Although near work has long been suspected a risk factor, few studies have found a strong correlation with either the onset or progression of myopia[13-15]. Increasing evidence suggests that the intensity of near work, i.e. sustained reading at closer distance (<30 cm) with few breaks, may be more important than the total hours[19,20].

On the other hand, increasing outdoors time can decrease the likelihood of becoming myopic[14,21,22]. Studies suggested that 2-3 hours a day outdoors, outside of school hours, would provide considerable protection[23,24]. The postulated mechanisms include relations to light intensity, dopamine release and vitamin D[25]. Paradoxically, outdoors time, though beneficial to delaying the onset, does not slow down progression in established myopia[23].

Interventions to retard myopia progression

Many interventions aiming at retarding myopia progression have been proposed. In the latest meta-analysis involving 30 randomised controlled studies (RCTs)[26], proven methods are not many. They are grouped under: (1) Pharmacological, or (2) Optical.

Pharmacological Agents

Atropine eye drops

Atropine is a non-selective muscarinic antagonist. Its efficacy for retarding myopia development was supported by human[27-29] and animal studies involving tree shrew, monkeys and chicks[30-32]. Blockage of accommodation by paralysing the ciliary muscles has long been thought to be the mechanism of atropine. Yet unlike the mammalian eye, the avian (chick) eye contains striated intra-ocular muscles only and has no muscarinic receptors; it indicates that the anti-myopic effect is via nicotinic pathway rather than accommodative mechanism[32-34]. Probably, atropine

functions via neurochemical cascade at M1 or M4 receptors in the retina; or atropine has a direct effect on scleral fibroblasts by inhibiting glycosaminoglycans synthesis via a non-muscarinic mechanism[35].

As early as the 1960s, use of atropine to retard myopia progression has been shown to be effective in humans[35]. Yet the conventional use of 1% atropine (Fig. 2) unavoidably results in photophobia and blurred near vision, making its widespread usage not popular.

Fig. 2. Atropine eye drops

The 'Atropine for the Treatment of Myopia' studies (ATOM 1 &2) by the Singapore group were randomised, double-masked, placebo-controlled trials involving 400 children[36]. ATOM 1 showed that 1% atropine eye drops instilled nightly in one eye over a 2-year period reduces myopia progression significantly by 77% (0.28 D with atropine versus 1.2 D in the control) and reduces the axial length elongation (0.39 mm in controls versus no growth in atropine group). The topical atropine was well tolerated without systemic side effects. Multifocal electroretinogram testing showed no significant effect on retinal function[37]. The pupil reactivity and accommodation paralysis were quickly reversible upon cessation of treatment[38,39]. Thus, the clinical safety and efficacy of atropine 1% is established.

At the ATOM 2 study, a slightly dose-dependent response to atropine was observed. The myopia progression of -0.49, -0.38 and -0.30 D in the atropine 0.01, 0.1 and 0.5% groups respectively at 24 months were shown[40], but these differences were not significant. However, when atropine was stopped for 12 months after 24 months of treatment (phase 2 of ATOM2), a rebound increase in myopia progression was observed in children originally treated with higher concentrations of atropine, whereas those receiving the 0.01% concentration showed minimal change[41]. This resulted in significantly lower myopia progression in the 0.01% group (-0.72D) at 36 months, compared with that in the 0.1% (-1.04D) and 0.5% (-1.15D) groups. The 0.01% group also caused less pupil dilatation (thus minimal photophobia) and no significant loss of accommodation or near visual acuity (thus no need for progressive lenses).

In the final phase (phase 3), spanning the fourth and fifth years of ATOM2 study, children who continued to progress (>0.5D/year) during the washout phase were treated with atropine 0.01%[42]. Over 5 years, atropine 0.01% eye drops were effective in slowing myopia progression by 50% compared with controls. It was concluded that atropine 0.01% has the best therapeutic index, with clinically insignificant visual side effects but remains as effective as higher doses[35].

Separately, Taiwanese cohort studies using atropine 0.025-0.05% also proved its efficacy in slowing myopia[43]. And an USA study similarly found that atropine 0.01% significantly reduced myopic progression with minimal side effects in a mostly white population[44].

Furthermore, atropine has been studied as a tool to prevent myopia onset. A retrospective cohort study conducted in Taiwan[45] over a period of 12 months on pre-myopic (<+1.0 D hyperopia) showed that 0.025% atropine can prevent myopia onset (myopic shift was -0.14D/yr c.f. -0.58 D/yr) ($P<0.0001$), and the percentage of children with onset of myopia was reduced from 54% to 21% ($P=0.016$).

Pirenzepine Ophthalmic Gel

In contrast to atropine (a non-selective anti-muscarinic agent), pirenzepine blocks M1 receptors only, which are less concentrated in the iris and ciliary body. It does not dilate the pupil or reduce accommodation as much as atropine. Topical pirenzepine 2% eye gel used twice daily in two RCTs showed approximately 40% reduction in myopia progression with a corresponding reduction in axial elongation after 12 months[46,47]. However, further trials and registration of this drug were not continued, and pirenzepine gel is no longer available.

Optical methods

Bifocals & Progressive Spectacles

These glasses allow children to clearly see far objects through the top portion of the lens while the bottom portion contains the reading power.

Animal and human studies suggest that increased retinal defocus and high accommodative lag are associated with myopia progression[48]. Bifocals or progressives were postulated to provide clear vision over a range of viewing distances to reduce retinal defocus, and slow myopia progression. However, RCTs showed no significant slowing of myopia with bifocals[49,50], or only have a small but significant benefit in retarding myopia progression in children with near point esophoria only.

On the other hand, RCTs on the use of progressive additive lenses suggested either no effect on myopia retardation or a minor but significant effect in the first year only[51,52]. It is concluded that bifocals or progressive lenses to correct myopic children have little effect (-0.50D at most) on myopia retardation, and this effect is probably too modest to warrant a change from the use of single vision lenses to bifocals or progressive lenses[51].

Contact Lenses

RCTs showed that ordinary soft contact lenses and rigid gas permeable (RGP) lenses were not effective in

retarding myopia progression[53,54]. In the CLAMP study, the difference in myopia progression was probably attributable to less corneal curvature steepening only[55].

Orthokeratology (also known as OK, ortho-K and corneal reshaping) is a type of RGP contact lens to be worn at bedtime and removed upon wakening. It temporarily reshapes (flattens) the central cornea and provides a clear vision during the day without any glasses or contact lenses. It gives convenience to children especially for activities like sports. OK lenses correct central refractive error while leaving peripheral myopic blur, which may act a putative cue to slow myopia progression[56].

Orthokeratology has shown to slow axial length growth compared to single vision RGP lenses, single vision soft contact lenses, and single vision spectacles[56-58]. The first RCT on orthokeratology myopia control demonstrated significantly slower mean axial elongation in children wearing OK lenses (0.36+/-0.24 mm) than wearing single vision spectacles (0.63+/-0.26mm) over a 2-year period[58]. As shown in a recent meta-analysis of seven eligible studies, myopic progression was reduced by approximately 45% after 2 years[56]. However, no well-controlled, long-term study demonstrating sustained myopia control effect is available, and numerous potentially blinding complications including microbial keratitis (Fig. 3) related to orthokeratology have been reported[59,60,61]. The risks associated with OK lenses must be carefully weighed against possible benefits, and parents should be adequately counselled before decision for use in their children[62].

Fig. 3. Microbial keratitis secondary to ortho-K wear

Peripheral retinal defocus spectacles or contact lenses

Like OK lenses creating peripheral myopic blur, spectacle lenses that decreased relative peripheral hyperopia were found to reduce myopia progression in children significantly in a study[63], while little consistent influence was shown in others[64-66]. The rate of myopia progression was reduced by approximately 30% in eyes wearing contact lenses designed to reduce hyperopic defocus compared with single-vision spectacles[67]. It was also shown that daily wearing of a "defocus incorporated soft contact" lens (a bifocal soft contact lens with concentric rings design) retards myopia progression by 25% compared with single vision lenses[68]. However, longer term results are still awaited for these newer designs.

Under-correction/part-time wear of spectacles

The objectives of undercorrection were to achieve myopic defocus, and to reduce the accommodative stress in near-point environments. However, prospective clinical trials suggest that undercorrection of myopia in humans either increases or has no effects on myopia progression[69,70].

Concerning the pattern of wear, preliminary data on 43 patients suggest that there is no effect on the progression of myopia with either of: full-time wear, myopes who switched from distance to full-time wear, distance wearers or non-wearers[71]. Larger randomised controlled studies are warranted.

Conclusion

Myopia is highly prevalent in Hong Kong, and the incidence is on the rise. Both genetic and environmental factors are involved. Atropine 0.01% produces clinically significant 50% reduction in myopia progression while having no significant visual side effects, thus appears to have a good risk-benefit ratio. Higher concentrations atropine may have a role in some children (e.g. fast progressors). The potential additive beneficial effect of combining atropine with other therapies (e.g. orthokeratology, peripheral defocus lenses) will need further evaluation.

Orthokeratology also appears to slow axial elongation by approximately 40%, but potential cornea-related complications need serious consideration. Peripheral defocusing lenses (contact lenses or spectacles) may have a role in slowing myopia progression.

The epidemic of myopia is related to its increasingly early onset, together with rapid rates of progression. Ideally, myopic control involves delaying its onset and retarding its progression. Increased outdoor time can reduce the onset of myopia. Low dose atropine eye drops may also have a role in its prevention.

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Jointly organised by

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Objectives:

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Date	Topics	Speakers
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10 May	Basic Statistics for Evaluation of QoL Measures	Dr. Daniel FONG Associate Professor, School of Nursing The University of Hong Kong
17 May	Linguistic and Psychometric Evaluation of QoL Measures	Dr. Daniel FONG Associate Professor, School of Nursing The University of Hong Kong
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31 May	Using QoL in Health Evaluation	Dr. Carlos WONG Assistant Professor (Research), Department of Family Medicine and Primary Care The University of Hong Kong
7 Jun	Assessing QoL in Cancer Patients	Dr. Winnie SO Associate Professor, The Nethersole School of Nursing The Chinese University of Hong Kong

Dates : 3, 10, 17, 24, 31 May 2018 & 7 June, 2018 (Every Thursday)
Time : 7:00 pm – 8:30 pm
Venue : Lecture Hall, 4/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong
Language Media : Cantonese (Supplemented with English)
Course Fee : HK$750 (6 sessions)
Certificate : Awarded to participants with a minimum attendance of 70%
Enquiry : The Secretariat of The Federation of Medical Societies of Hong Kong
Tel: 2527 8898 Fax: 2865 0345 Email: info@fmshk.org

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Walking With the Poor Communities

Dr Nim-chung CHAN

MBBS(HK), FRCS (Glasgow), FCS(HK), FRCOphth, FHKAM(Ophthalmology), FCOphthHK
Private Practicing Ophthalmologist

Dr Nim-chung CHAN

"Good morning! You are still alive?" That was how we sometimes jokingly greeted each other with the local friends in Afghanistan after heavy aerial bombing or rocketing through the nights. I was living and working in Kabul, capital of Afghanistan, with my wife from 1993 to 1999. I was the Medical Director of the NOOR Eye Institute, and my wife was working in the Physiotherapy School of Kabul. She is an occupational therapist specialised in children with disabilities. Both of these specialties of ophthalmology and rehabilitation, which are usually slow to develop in poor countries, were started by the organisation that we worked with, the International Assistance Mission, in the 60s and 80s respectively.

Those years were life-changing for us. In the first 3 years 4 factions of the Mujahideen (freedom fighters) were fighting each other in Kabul. Then the extremist Taliban entered the city in 1996. In fact the war has never stopped till now. The book and the term "The Great Game" well describes and explains the history, social-economic and political turmoil of Afghanistan. The Soviets, Britishs, Americans, and neighbouring countries were all interested. The central high mountain range forms a natural barrier between the former Soviet Union and the former British India. Central Asia is rich in oil. Afghanistan has some natural gas and semi-precious stones. Only recently lithium worths US$1 to 3 trillion has been found in the country! In addition, the majority Pashtun tribe was divided by the Afghan-Pakistani border set by the British. They demanded a Pashtunistan country of their own, which never happened. And the Taliban, formed mainly by the Pashtuns, gradually rose after the Soviets left. All these contributed to the longstanding unrest of Afghanistan. To date, the largest population of refugees comes from Syria, and the second is still Afghanistan.

We learned the language Dari, lived amidst the heavy fightings, struggled together with the Afghans. Almost all of our local colleagues, citizens and even officials of the Islamic government are friendly and helpful to us. Surprisingly our medical training and facilities continued to develop during the worst time. I managed to start their professional diploma examination for ophthalmologists. They are still continuing with that now.

Looking back, there are many things I could not have learned if I were to live in Hong Kong only. I notice that there is a broad spectrum of the attitudes and behaviours of aid workers and also donors in relief and development work. But to me it was a humbling experience. Too easily we point our fingers at the wrong-doers and government leaders. But in fact we are all part of the world exploiting and discriminating others. Not that the victims are more holy, but often through the striving of the poor people, they demonstrate the bright side of humanity. They are more humble, thankful, resilient, generous, flexible, often joyful with a good sense of humour, stronger in faith, dignity, people relationship and hospitality. I do have a lot to learn from them.

For the past 11 years (2005-2016) I was the Chief Executive of the CEDAR Fund, and now I am a board member, while I am still practising ophthalmology on a part-time basis. CEDAR Fund is a Christian NGO established in HK in 1991. The focus is overseas projects in more than 10 countries in Asia, Africa, and China. There are more than 60 projects. We partner with local organisations and churches which live among the communities. This is more efficient in terms of our resources, and more appropriate in their culture and context. There are 3 levels of engagement in poverty alleviation: relief, development, and justice. However each one needs a deeper reflection of its meaning and implementation.

1. Relief. When a disaster happens and news reports are everywhere, people are moved and ready to donate a lot of material resources. There are good and bad effects. But more commonly, people and organisations will forget these victim communities rather quickly. And also there is uneven distribution of assistance to them. Communities slightly away from the disaster centre do not get the help they need. Life is more difficult for them. CEDAR Fund is familiar with these situations and we often locate such needs through our local partners. And we continue to support them for many years if needed. Another 2 important components in our projects are disaster risk reduction and resilience. These involve a lot of education, creative measures, advocacy, and community development. Many government institutions are not able to reach deeply into communities and families for such purposes.

2. Development. We prefer to use the term transformational development. If development only means economic growth and better living conditions, it does not necessarily promise a better society. We need to be very careful not to impose the value system of wealthy societies. There are many corrupted or unhealthy practices that the world does

not agree. It is possible to lift the communities out of poverty, but it's very easy to damage human relationship by setting the goals and values wrong. We pay a lot of respect to the locals, and it's always a participatory approach. And we have to be intentionally inclusive, especially for the voices and roles of women, children, the disabled, and the marginalised.

3. Justice. "Don't give them fish. Teach them how to fish," is not a simple solution to poverty alleviation. Skilled and non-skilled labour are both suffering from social injustice, power game, and unfair distribution of resources resulting in poverty. Advocacy on justice issues may be for the poor communities, with them, or by them. After years of efforts systems and social values could be improved. But it seems like a never ending struggle. The root cause is not only an unjust system. It is from the human hearts. For thousands of years human beings are asking the same philosophical questions. Each generation seems to be making similar mistakes, then again reflecting on radical and spiritual reasons. Before any significant improvement lasts long, people return to the terrible exploitation and fighting against each other. Worse still, people are using different definitions of justice, and insist on their own. In my humble opinion, a higher level of justice is the one of a Christ-like humility, forgiveness and love. It seems opposite to our familiar ways of power wrestling in achieving our goals. But again and again I have seen life transforming stories not coming from the powerful people, but from the insignificant grassroots who dedicated their lives. I like the term "the power of the powerless" from Václav Havel. It is also very biblical, and subversive.

One of our amazing stories happens in Myanmar. The country is now in the spotlight since Aung San Suu Kyi came to power. Before that the military was in control and there was a long history of internal conflicts with many ethnic army groups. CEDAR Fund has a long presence in the country. One of our close partners is the Fullmoon Children Home. The founder Mr. U Ba Hla gave up his opportunities as a professor or politician. He was a well-known lawyer, but decided that he would take care of the orphans resulted from the mountain wars. He promised God that he would not reject any child who came for help in front of his door. And so the number of children increased from about 20 to more than 300 at this stage. He is old now, but still strong enough to visit the communities in the mountains. His daughter Ni Sat is now leading the ministry. This family dedicated their lives to serve the children.

Aung San Suu Kyi is very impressed by the children. She has been longing for peace and unity in her country, but it's so difficult with the baggage of bitter history. However she can see the love and care among the children from all different ethnic groups. They are united by their Christian faith, even though a lot of healing and forgiveness is not yet completed in their hearts. This is possible because the founder of this children home has gone through his own tough stories. He was blamed and put in prison. He was despised. His elder daughter and son-in-law were murdered by an army group. Yet he stands firm in love and forgiveness.

Now the first few batches of children have grown up and finished their studies. In 2012 I was among the first few outsiders who went up to a mountain village in Mon State. It used to be a battlefield and even now the government officials and army dare not go up there. We were protected by gunmen. In that visit we were planning for a resettlement project for war refugees who were living in the forests. CEDAR Fund raised some money from HK, and we built some simple houses, farms, a water system, a primary school, a small clinic, and later solar energy and bridges. Although this was mainly a Christian initiative, the Buddhist monks in the village also got the same benefits. Here we respected each other as friends. They even sent their congratulations on our Christmas day! Apart from the hardware setups, more importantly there were a lot of stories telling and healing of their past years of difficulties and pain, and reconciliation.

The Peace Leader of this village area was the first official I met at the mountain. He protected us on the way. In fact he was an army leader but then he decided he should put down his weapons. Later some of the graduates from our children home decided to go up to serve in this village as nurses and teachers. And to my surprise, some of their parents were actually killed by this same army group under the now Peace Leader! They are able to forgive their enemy, and come back to serve the people! One night the Peace Leader asked U Ba Hla, "I don't know where I'll go when I die. I have killed so many people." U Ba Hla comforted and blessed him, "Do what is right for now. God will judge in His kindness."

This resettlement project is still going on and expanding. Other areas are very interested in what we are doing, the truth and reconciliation, which the government is not able to replicate. We have started similar projects in other states in Myanmar.

Restorative justice is different from retributive justice. The aim is to restore relationship among the 3 parties: the offender, the victim, and the community. Similarly the approach of conflict transformation is better than conflict resolution in that it seeks to transform the causal factors of conflict into positive motivation towards real peace, reaching into deeper levels of humanity.

The present world is experiencing a unique era of tension. But creative tension could become a driving force for reflections and innovations. A new order and paradigm shift has begun. And I am excited to explore new areas of integration of spirituality and social issues.

300+ children

All our children go to schools


Bullet in orbit


Fullmoon Children Home, a big compound

I walked with our children to school


Mine explosion injury to eyes and face


New housing in resettlement village, with solar panels


NOOR Eye Institute with sandbags cover


Primary school in resettlement village


Teaching Afghan lady ophthalmologist on retinal detachment repair operation

Truth & Reconciliation Conference 2015, Myanmar

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1. AcrySof® IQ PanOptix™ IOL Directions for Use. 2. PanOptix™ Diffractive Optical Design. Alcon internal technical report: TDOC-0018723. Effective date 19 Dec 2014. 3. Charness N, Dijkstra K, Jastrzembski T, et al. Monitor viewing distance for younger and older workers. Proceedings of the Human Factors and Ergonomics Society 52nd Annual Meeting, 2008. http://www.academia.edu/477435/Monitor_Viewing_Distance_for_Younger_and_Older_Workers. Accessed April 9, 2015. 4. Average of American OSHA, Canadian OSHA and American Optometric Association Recommendations for Computer Monitor Distances.

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Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
				★HKMA Hong Kong East Community Network and Centre for Health Protection of the Department of Health - Antibiotic Stewardship Programme in Primary Care ★HKMA-Kowloon East Community Network - Management of Degenerative Joint Diseases - Local Perspectives for Primary Physicians **1**	**2**	**3**
4	**5**	★HKMA Yau Tsim Mong Community Network and Centre for Health Protection of the Department of Health - Antibiotic Stewardship Programme in Primary Care ★HKMA Tai Po Community Network - Avanafil - A New Generation of PDE5 Inhibitors ★FMSHK Officers' Meeting ★HKMA Council Meeting **6**	★HKMA Central, Western & Southern Community Network - An Update on AF Management and Screening **7**	★HKMA-HKS&H CME Programme 2017-2018 –"Update in Medical Practice" Topic: Management of Ischaemic Heart Disease ★HKMA-New Territories West Community Network - How to Optimize Diabetic Treatment in Elderly Patients **8**	**9**	★Refresher Course for Health Care Providers 2017/2018 **10**
11	**12**	★HKMA-Kowloon West Community Network - Diagnosis and Management of Attention Deficit Hyperactivity Disorder (ADHD) in Children **13**	★HKMA-Central, Western & Southern Community Network - Update in the Management of Idiopathic Pulmonary Fibrosis ★MPS Workshop – Mastering Professional Interactions ★Hong Kong Neurosurgical Society Monthly Academic Meeting –To be confirmed **14**	★HKMA Hong Kong East Community Network - Prescription of Insulin Therapy in a Primary Clinic ★HKMA Kowloon East Community Network - Update on Long-Term Management of Postmenopausal Osteoporosis **15**	★HKMA Kowloon City Community Network and Primary Care Office of the Department of Health - Assessment and Management of Older Adults' Cognitive Impairment in Primary Care Setting **16**	**17**
18	**19**	★HKMA-Tai Po Community Network - Updates in Mild Cognitive Impairment and Dementia Assessment for Busy Clinicians **20**	★MPS Workshop – Mastering Your Risk **21**	★MPS Workshop – Achieving Safer and Reliable Practice ★FMSHK Executive Committee Meeting **22**	★HKMA Shatin Doctors Network - Diagnosis and Management of Attention Deficit Hyperactivity Disorder (ADHD) in Children ★HKMA Yau Tsim Mong Community Network - Benefits of SGLT2 Inhibitors in Asians **23**	★MPS Workshop – Achieving Safer and Reliable Practice **24**
★HKMA Football Day **25**	**26**	★HKMA-Kowloon West Community Network - Hypertension 2018 **27**	**28**	**29**	**30**	**31**

Date / Time	Function	Enquiry / Remarks
1 THU 1:00 PM	**HKMA Hong Kong East Community Network and Centre for Health Protection of the Department of Health - Antibiotic Stewardship Programme in Primary Care** Organiser: HKMA Hong Kong East Community Network; DH-Centre for Health Protection; Chairman: Dr. LEUNG Kwan Kui, Terence; Speaker: Dr. LAM Tin Keung, Edman; Venue: HKMA Wanchai Premises, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, HK	Ms. Candice TONG Tel: 2527 8285 1 CME Point
1:00 PM	**HKMA-Kowloon East Community Network - Management of Degenerative Joint Diseases - Local Perspectives for Primary Physicians** Organiser: HKMA Kowloon East Community Network; Chairman: Dr. AU Ka Kui, Gary; Speaker: Dr. Ho Hon Shuen; Venue: Lei Garden Restaurant, Shop No. L5-8, apm, Kwun Tong, No. 418 Kwun Tong Road, Kowloon	Mr. Ian YAU Tel: 2527 8285 1 CME Point
6 TUE 1:00 PM	**HKMA Yau Tsim Mong Community Network and Centre for Health Protection of the Department of Health - Antibiotic Stewardship Programme in Primary Care** Organiser: HKMAYau Tsim Mong Community Network; DH-Centre for Health Protection; Chairman: Dr. HO Fung; Speaker: Dr. LAM Tin Keung, Edman; Venue: Crystal Ballroom, 2/F, The Cityview Hong Kong, 23 Waterloo Road, Kowloon	Ms. Candice TONG Tel: 2527 8285 1 CME Point
1:45 PM	**HKMA Tai Po Community Network - Avanafil - A New Generation of PDE5 Inhibitors** Organiser: HKMA Tai Po Community Network; Chairman: Dr. CHOW Chun Kwan, John; Speaker: Dr. CHAN Lung Wai; Venue: Chiuchow Garden Restaurant, Shop 001-003, 1/F, Uptown Plaza, No. 9 Nam Wan Road, Tai Po	Ms. Candice TONG Tel: 2527 8285 1 CME Point
8:00 PM	**FMSHK Officers' Meeting** Organiser: The Federation of Medical Societies of Hong Kong; Venue: Gallop, 2/F, Hong Kong Jockey Club Club House, Shan Kwong Road, Happy Valley, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
9:00 PM	**HKMA Council Meeting** Organiser: The Hong Kong Medical Association; Chairman: Dr. CHOI Kin; Venue: HKMA Wanchai Premises, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, HK	Ms. Christine WONG Tel: 2527 8285
7 WED 1:00 PM	**HKMA Central, Western & Southern Community Network - An Update on AF Management and Screening** Organiser: HKMA Central, Western & Southern Community Network; HK College of Cardiology; Chairman: Dr. YIK Ping Yin; Speaker: Dr. CHAN Pak Hei, Michael; Venue: Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central	Mr. Ian YAU Tel: 2527 8285 1 CME Point
8 THU 1:00 PM	**HKMA-HKS&H CME Programme 2017-2018 –"Update in Medical Practice"** **Topic: Management of Ischaemic Heart Disease** Organiser: The Hong Kong Medical Association & Hong Kong Sanatorium & Hospital; Speaker: Dr. Raymond H.W.CHAN; Venue: Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central	HKMA CME Dept. Tel: 2527 8285 1 CME Point
1:00 PM	**HKMA-New Territories West Community Network - How to Optimize Diabetic Treatment in Elderly Patients** Organiser: HKMA-New Territories West Community Network; Chairman: Dr. CHEUNG Kwok Wai, Alvin; Speaker: Dr. Tong Chun Yip, Peter; Venue: Pak Loh Chiu Chow Restaurant, Shop A316, 3/F, Yoho Mall II, 8 Long Yat Road, Yuen Long	Mr. Ian YAU Tel: 2527 8285 1 CME Point
10 SAT 2:15 PM	**Refresher Course for Health Care Providers 2017/2018** Organiser: Hong Kong Medical Association; HK College of Family Physicians; HA-Our Lady of Maryknoll Hospital; Speaker: Dr. IP Fong Cheng, Francis; Venue: Training Room II, 1/F, OPD Block, Our Lady of Maryknoll Hospital, 118 Shatin Pass Road, Wong Tai Sin	Ms. Clara TSANG Tel: 2354 2440 2 CME Point
13 TUE 1:00 PM	**HKMA-Kowloon West Community Network - Diagnosis and Management of Attention Deficit Hyperactivity Disorder (ADHD) in Children** Organiser: HKMA-Kowloon West Community Network; Chairman: Dr. TONG Kai Sing; Speaker: Dr. Wong Juen Sing, Mark; Venue: Fulum Palace, Shop C, G/F, 85 Broadway Street, Mei Foo Shun Chuen, Mei Foo	Mr. Ian YAU Tel: 2527 8285 1 CME Point
14 WED 1:00 PM	**HKMA-Central, Western & Southern Community Network - Update in the Management of Idiopathic Pulmonary Fibrosis** Organiser: HKMA-Central, Western & Southern Community Network; Chairman: Dr. YIK Ping Yin; Speaker: Dr. Wan Chi Kin, Raymond; Venue: HKMA Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central	HKMA CME Dept. Tel: 2527 8285 2.5 CME Point
6:30 PM	**MPS Workshop – Mastering Professional Interactions** Organiser: The Hong Kong Medical Association & Medical Protection Society; Chairman: Dr. CHOI Kin; Speaker: Dr. Lee Wai Hung, Danny; Venue: Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central	Mr. Ian YAU Tel: 2527 8285 1 CME Point
7:30 PM	**Hong Kong Neurosurgical Society Monthly Academic Meeting –To be confirmed** Organiser: Hong Kong Neurosurgical Society; Chairman: Dr CHIU Hok Ming; Speaker: Dr NG Chat Fong; Venue: Seminar Room, G/F, Block A, Queen Elizabeth Hospital	1.5 points College of Surgeons of Hong Kong Dr. LEE Wing Yan, Michael Tel: 2595 6456 Fax. No.: 2965 4061
15 THU 1:00 PM	**HKMA Hong Kong East Community Network - Prescription of Insulin Therapy in a Primary Clinic** Organiser: HKMA Hong Kong East Community Network; Chairman: Dr. WONG Chun Por; Speaker: Dr. TSO Wai Kwan, Annette; Venue: HKMA Wanchai Premises, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, HK	Ms. Candice TONG Tel: 2527 8285 1 CME Point
1:00 PM	**HKMA Kowloon East Community Network - Update on Long-Term Management of Postmenopausal Osteoporosis** Organiser: HKMA Kowloon East Community Network; Chairman: Dr. AU Ka Kui, Gary; Speaker: Dr. Tsang Wai Yin, Kevin; Venue: V Cuisine, 6/F, Holiday Inn Express Hong Kong Kowloon East, 3 Tong Tak Street, Tseung Kwan O	Mr. Ian YAU Tel: 2527 8285 1 CME Point
16 FRI 1:00 PM	**HKMA Kowloon City Community Network and Primary Care Office of the Department of Health - Assessment and Management of Older Adults' Cognitive Impairment in Primary Care Setting** Organiser: HKMA Kowloon City Community Network; DH-Primary Care Office; Chairman: Dr. CHIN Chu Wah; Speaker: Dr. LUK Kam Hung; Venue: President's Room, Spotlight Recreation Club, 4/F, Screen World, Whampoa Garden, Hung Hom	Ms. Candice TONG Tel: 2527 8285 1 CME Point

Date / Time	Function	Enquiry / Remarks
20 TUE 1:00 PM	**HKMA-Tai Po Community Network - Updates in Mild Cognitive Impairment and Dementia Assessment for Busy Clinicians** Organiser: HKMA-Tai Po Community Network; Chairman: Dr. CHOW Chun Kwan, John; Speaker: Prof. Adrian WONG; Venue: Chiu Chow Garden Restaurant, Shop 001-003, 1/F, Uptown Plaza, No. 9 Nam Wan Road, Tai Po	Ms. Candice TONG Tel: 2527 8285 1 CME Point
21 WED 6:30 PM	**MPS Workshop – Mastering Your Risk** Organiser: The Hong Kong Medical Association & Medical Protection Society; Chairman: Dr. CHOI Kin; Speaker: Dr. Lee Wai Hung, Danny; Venue: Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central	HKMA CME Dept. Tel: 2527 8285 2.5 CME Point
22 THU 6:30 PM	**MPS Workshop – Achieving Safer and Reliable Practice** Organiser: The Hong Kong Medical Association & Medical Protection Society; Chairman: Dr. CHOI Kin; Speaker: Dr. Cheng Ngai Shing, Justin; Venue: Crystal Ballroom, 2/F, The Cityview Hong Kong, 23 Waterloo Road, Kowloon	HKMA CME Dept. Tel: 2527 8285 2.5 CME Point
8:00 PM	**FMSHK Executive Committee Meeting** Organiser: The Federation of Medical Societies of Hong Kong; Venue: Council Chamber, 4/F, Duke of Windor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
23 FRI 1:00 PM	**HKMA Shatin Doctors Network - Diagnosis and Management of Attention Deficit Hyperactivity Disorder (ADHD) in Children** Organiser: HKMA Shatin Doctors Network; Chairman: Dr. MAK Wing Kin; Speaker: Dr. LEE Ming Chung, Marshall; Venue: Royal Park Chinese Restaurant, Level 1, Royal Park Hotel, 8 Pak Hok Ting Street, Shatin	Ms. Candice TONG Tel: 2527 8285 1 CME Point
1:00 PM	**HKMA Yau Tsim Mong Community Network - Benefits of SGLT2 Inhibitors in Asians** Organiser: HKMA Yau Tsim Mong Community Network; Chairman: Dr. CHENG Kai Chi, Thomas; Speaker: Dr. TONG Chun Yip, Peter; Venue: Crystal Ballroom, 2/F, The Cityview Hong Kong, 23 Waterloo Road, Kowloon	Ms. Candice TONG Tel: 2527 8285 1 CME Point
24 SAT 2:30 PM	**MPS Workshop – Achieving Safer and Reliable Practice** Organiser: The Hong Kong Medical Association & Medical Protection Society; Chairman: Dr. CHOI Kin; Speaker: Dr. Cheng Ngai Shing, Justin; Venue: Harbour Plaza Resort City, Tin Shui Wai	HKMA CME Dept. Tel: 2527 8285 2.5 CME Point
25 SUN 12:00 PM	**HKMA Football Day** Organiser: The Hong Kong Medical Association; Chairman: Dr. CHAN Chi Wing, Timmy; Dr. CHAN Hau Ngai, Kingsley; Venue: Stanley Ho Sports Centre	Miss Kayin LEE/ Miss Sinn TANG Tel: 2527 8285
27 TUE 1:00 PM	**HKMA-Kowloon West Community Network - Hypertension 2018** Organiser: HKMA-Kowloon West Community Network; Chairman: Dr. TONG Kai Sing; Speaker: Dr. Wong Wing Kwong, Raymond; Venue: Fulum Palace, Shop C, G/F, 85 Broadway Street, Mei Foo Sun Chuen, Mei Foo	Mr. Ian YAU Tel: 2527 8285 1 CME Point

Dermatological Quiz

Dr Chi-keung KWAN

MBBS(HK), MRCP(UK), Dip Derm(Glasgow), PDipID (HK), MFM (Monash) FHKCP, FHKAM(Medicine)

Specialist in Dermatology & Venereology

Dr Chi-keung KWAN

Fig. 1: bilateral lower limbs of the patient

Fig. 2: close-up of patient's right shin

This 24-year-old man complained of general skin itchiness since childhood which was precipitated in winter and low humidity. His father and elderly brother have a similar problem. Physical examination revealed nothing abnormal except dryness of the skin especially on the limbs (Fig. 1). A closer look of the lower limbs revealed some "brown" and "scales" appearance on the extensor aspect of the shins (Fig. 2). He also had some eczema over the waist and keratosis pilaris over the upper arms.

Questions

1. What is the diagnosis of the skin lesion?
2. What is the underlying pathology?
3. How do you manage this gentleman?

(See P.41 for answers)

Answers to Dermatological Quiz

Answer:

1. Ichthyosis Vulgaris
   The diagnosis is ichthyosis vulgaris and can often be reached from its characteristic clinical features. Ichthyosis is from the Greek word meaning fish and vulgaris means common. Ichthyosis vulgaris often called as "fish scale disease" or "fish skin disease". Dry (xerotic) and scaly skin on the extensor surface of the limbs and central face is the characteristic sign. It is associated with keratosis pilaris and atopic dermatitis.

2. Ichthyosis vulgaris results from mutation in the gene encoding the functional protein filaggrin and causes a decrease in the production of filaggrin. Filaggrin is an effective skin barrier to retaining skin moisture in the stratum corneum. Thereby, ichythosis vulgaris cannot maintain the skin moisture and increases the trans-epidermal water loss. It is autosomal dominant. However, if mutation happens in one gene of the paired chromosome, it results in a milder form whereas if mutation occurs in both genes, it results in moderate to severe xerosis.

3. There is no definite treatment for ichthyosis vulgaris. The management is mainly conservative. The aim is to reduce the dryness, scaling and thickening of the skin. Frequently applying skin emollient to maintain skin moisture is the key measure. Sometimes occlusive methods after applying the moisturiser can enhance skin hydration. The cream or lotion containing salicylic acid, glycolic acid, lactic acid and urea may be used to exfoliate the scaling or thick skin. Oral retinoid can be tried in severe cases.

Dr Chi-keung KWAN
MBBS(HK), MRCP(UK), Dip Derm(Glasgow), PDipID (HK), MFM (Monash) FHKCP, FHKAM(Medicine)
Specialist in Dermatology and Venereology

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- High Ocular Penetration [3]
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[Composition]

Cravit ophthalmic solution is a pale to light yellow, clear sterile aqueous solution. Each mL contains 5 mg of levofloxacin. Its pH is 6.2-6.8 and its osmotic pressure ratio is 1.0-1.1.

[Indications]

<Indicated bacteria>

Susceptible strains of Staphylococcus sp., Streptococcus sp., Streptococcus pneumoniae, Enterococcus sp., Micrococcus sp., Moraxella sp., Corynebacterium sp., Klebsiella sp., Enterobacter sp., Serratia sp., Proteus sp., Morganella morganii, Haemophilus influenza, Haemophilus aegyptius [Koch-Weeks bacillus], Pseudomonas sp., Pseudomonas aeruginosa, Stenotrophomonas (Xanthomonas) maltophilia, Acinetobacter sp., and Propionibacterium acnes.

<Indications>

Blepharitis, dacryocystitis, hordeolum, conjunctivitis, tarsadenitis, keratitis (including corneal ulcer), and aseptic treatment during a perioperative period for ocular surgery.

[Dosage and Administration]

Usually, instill 1 drop a time 3 times daily. The dosage may be adjusted according to the patient's symptoms.

[Contraindications]

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Reference:

1. Masahiko Usui. Clinical Evaluation of Levofloxacin Ophthalmic Solution – A Multicenter Phase III Double-masked Clinical Trial. J. Eye. 1997, 14(4): 641-648.
2. Masahiko Usui. Clinical Evaluation of Levofloxacin Ophthalmic Solution – A Multicenter Phase III Open Label Trial. J. Eye. 1997, 14(7): 1113-1118
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