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Who should screen for diabetic retinopathy in Hong Kong?

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In Hong Kong, the estimated age-standardized prevalence of type 2 diabetes mellitus for the 35-to-64 years’ age-group is around 10%.1 The incidence of diabetic retinopathy is approximately 30% in patients diagnosed with diabetes mellitus. This suggests that there are about 700,000 diabetic patients in Hong Kong, half of whom are undiagnosed. It is estimated that around 70% of diabetic patients are being regularly followed up in Hong Kong Hospital Authority (HA) facilities and 30% in the private sector. Not surprisingly, visual complications arising from sight-threatening diabetic retinopathy has caused a significant burden on social and health care systems, within both the public and private sectors.

Several multi-center randomized controlled clinical trials have demonstrated that diabetic retinopathy can be prevented or its natural course altered.2,3 The incidence of diabetes-related blindness can be reduced by early detection and treatment of retinopathy. Recommendations on screening strategies for diabetic patients by professional health care organizations, like the American Academy of Ophthalmology (AAO) and the American Diabetes Association,4,5 are well established. There is no doubt that ideally every diabetic patient should be screened by ophthalmologists who are experienced in managing diabetic retinopathy, because they are the service providers for treating this disease entity. Furthermore, a comprehensive ophthalmic examination during screening is important for detecting and quantifying the spectrum of other ophthalmic pathology, which might coexist with diabetic retinopathy. Such pathologies include cataract and glaucoma, both of which are more prevalent in diabetic patients and can be medically significant. Ophthalmologists, being medical doctors, are most appropriate to discuss the importance of diabetic control and other systemic complications of diabetes with patients during their clinic consultations, particularly if they already have diabetic retinopathy. Ophthalmologists can also reinforce the need for patient compliance with their family physician’s care plan. Liaison with physicians directly regarding clinical findings and ophthalmic management is an essential component in formulating a holistic care plan for the patient. For example, suboptimal blood pressure control may be noted during a comprehensive ophthalmic consultation, in which case the patient can be educated or referred back to their physician to optimize hypertension control.

Only when the accessibility or availability of ophthalmology services is in doubt (for reasons of geography, insufficient numbers of ophthalmologists in a given area, or financial constraints) should the screening responsibility be delegated to other accredited health care professionals. The latter could be family physicians, nurse specialists, optometrists, or accredited photograph readers.

New developments in fundus photography with digital non-mydriatic cameras have initiated new screening strategies for diabetic retinopathy. In some countries, national photo screening options such as the Ophdiat program in France6 and the English National Screening Programme for Diabetic Retinopathy in the United Kingdom7 have been set up. These help improve the reach of diabetic retinopathy screening and improve the screening accessibility in remote areas, where ophthalmology services are not readily available. Accredited personnel in the photographic reading centers can evaluate
the captured images. Implementation of such programs inevitably raise concerns about their cost effectiveness. Factors which can influence their cost effectiveness include: manpower and instrumentation costs, the incurred workload and pressure on health service due to false-positive referrals and other diabetes-related or -unrelated eye diseases being picked up during the screening. Patient compliance to the screening programs may also be a challenge. Photo screening has been found useful in increasing the number of diabetic patients that can be screened and its effectiveness is recognized by an AAO meta-analysis. According to that analysis, there was sufficient evidence from randomized clinical trials showing that single-field digital fundus photography can serve as a screening tool for diabetic retinopathy to identify patients for referral, evaluation and management by ophthalmologists.

In Hong Kong, our health care system differs from that in other countries. About 30% of diabetic patients are under the care of private physicians. Geographical accessibility to an ophthalmologist is not a problem locally. The determinant factors for regular diabetic retinopathy screening by an ophthalmologist include: the cost for comprehensive screening and the availability of ophthalmologist, which differs considerably between the public and private sectors (115 private ophthalmologists vs. 150 specialists + trainees in HA). Last but not least, patient education on the importance of regular diabetic retinopathy screening can also have a substantial influence on screening.

The affordability of an ophthalmic examination differs markedly among patients attending the private sector. Most of these diabetic patients, however, do not have diabetic retinopathy (70%) and an annual screening suffices, in which case the average daily cost is minimal. The advantages of an ophthalmologist-led screening service are obvious. If any sight-threatening retinopathy is detected, it can be treated promptly or referred to the public sector. This provides very important triaging for new cases entering the HA ophthalmology outpatient clinics and avoids unnecessary delays. The downsides of screening by a non-ophthalmologist include incomplete information or inappropriate referral, largely due to inexperience or insufficient training. Possibility of deferred treatment does exist when patients are referred to an ophthalmologist or HA eye clinic for further care. The inappropriate referrals create unnecessary pressure on the public health care system, which is already heavily overloaded.

In a public health care setting, affordability is basically not an issue to the patient. On the contrary, it is not practical for ophthalmologists to perform comprehensive ophthalmic examinations for every patient, due to the large number of patients to be seen. Thus, making new technology like digital mydriatic or non-mydriatic photography with reporting by an experienced ophthalmologist provides cost-effective diabetic retinopathy screening, especially in a public health care system. If the availability of ophthalmologists is in doubt, the photo-reading responsibility may be delegated to an accredited eye health care professional (family physician, nurse specialist, optometrist, or photograph reader). Of equal, if not more, importance, these programs should have an audit component so that false-positive and false-negative rates can be calculated. By this means the examination strategy, its sensitivity, and its cost effectiveness can be enhanced to prevent overloading the public service when a population-wide screening program is implemented. A good communication channel could facilitate up-to-date information on the patient’s ophthalmic condition and management, so that the physician can formulate a holistic care plan.

Diabetic retinopathy is only one of the complications of diabetes mellitus, other systems will also be affected. In this context, family and internal medicine physicians, and special nurses are in a good position to carry out diabetic retinopathy photographic screening, especially during comprehensive complication assessment. These programs can provide a one-stop service, to detect different systemic complications in one visit, thus improving compliance to screening and patient education. With a critical caseload, the technique of photo taking and interpretation can be enhanced through practice and audit. Ophthalmologists can be involved in different phases to provide training, support, accreditation, and quality assurance.

In Hong Kong, outside the context of a well-structured comprehensive complication screening program, the benefits of a separate consultation by a non-ophthalmologist for diabetic retinopathy screening appears doubtful and may even be detrimental to the public health care. Inexperience in the interpretation of clinical findings and absence of auditing on referrals by individual screeners may generate many inappropriate referrals, putting excessive stress on already-saturated public ophthalmology services. This would definitely undermine the quality and safety of the existing system. Patients should therefore be educated and encouraged to seek care from a medical eye doctor, who can provide timely treatment for their eye problems and understand their other systemic medical conditions. Physicians should refer their patients to ophthalmologist colleagues, who can directly treat and report back on eye conditions after regular screening. Ophthalmologists should stand in the front line to provide seamless, affordable eye screening programs to all diabetic patients. A well-planned public-private interface program can rationalize the gap between the supply and demand of ophthalmology services in the public and private health care sectors. Professional bodies like the Hong Kong Medical Association and the Hong Kong Ophthalmological Society can take an active role in this issue.

To provide the best care for our patients, communication between physicians, nurses, and ophthalmologists is of utmost importance. It is only through a multidisciplinary approach that we can expect to reduce the visual morbidity caused by diabetic retinopathy.
References


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Disc hemorrhage: what do we know?

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Abstract
This is part 2 of a review of normal tension glaucoma and will discuss a specific entity in normal tension glaucoma: disc hemorrhage. This review highlights the management issues of patients with disc hemorrhage.

Key words: Eye hemorrhage; Glaucoma; Optic disk; Retinal hemorrhage

Definition of glaucomatous disc hemorrhage
Before further evaluation of the importance of disc hemorrhage (DH) to glaucoma, it is important to define a glaucomatous DH. DH considered typical of glaucoma is usually flame or splinter shaped, often with feathered ends, and is radially oriented and perpendicular to the disc margin. DH characteristically extends from within the optic nerve head to the adjacent retina, crossing any peripapillary zone of absent or disrupted retinal pigment epithelium, but does not necessarily occupy the entire length of this typical position. The most common site of DH is the inferotemporal quadrant for both single and recurrent types.

Importantly, DH should not be considered to be related to glaucoma if the disc is swollen or otherwise abnormal from non-glaucomatous optic neuropathy such as anterior ischemic optic neuropathy. Similarly, a hemorrhage within the optic disc in the presence of diabetic retinopathy, vein occlusion, or other retinal vascular abnormality should not be mistaken as glaucomatous.

Course of disc hemorrhage and its prevalence
The prevalence of DH in the general population varies in different studies. In a retrospective study by an Australia group, the prevalence was noted to be 1.4%. The prevalence of one or more DHs increases in patients with open angle glaucoma, particularly normal tension glaucoma (NTG), to 13.8 to 28.0%. In a longitudinal study involving 1123 patients, DH was present in none of the 661 healthy eyes (0%), 6 of 1377 glaucoma-suspect eyes (0.44%), and 3 of 123 glaucomatous eyes (2.44%). The prevalence of DH in glaucomatous eyes was significantly higher than in healthy or glaucoma-suspect eyes. Despite this strong association, most DH (70%) are found in patients without definite signs of glaucoma.

Studies show that DH is more common in patients with advanced glaucoma than in patients with early glaucoma. It has been observed that the frequency of DH increased from an early stage of glaucoma to a medium/advanced stage and decreased again towards the pre-final stage of glaucoma. In eyes with absolute glaucoma, DH was not detected.

Before a florid DH occurs, optic disc characteristics—including peripapillary atrophy, superior-inferior asymmetry in the neuroretinal rim, and thin sloping of the rim—have been noted to antedate its appearance. The normal time for a DH to disappear is approximately 2 months.

Recurrent DH has been reported to occur in 12 to 73% of patients with DH. The broad variance is largely attributable to the variances in follow-up period, diagnostic parameters, and study populations in different studies. In the study by Siegner and Netland, 22% of the eyes with DH had recurrent hemorrhage at a mean interval of 21.5 months (standard deviation, 2.9 months). For patients with DH, recurrence was observed in 67% of patients with NTG, 29% of those with primary open angle glaucoma (POAG), and 54% of glaucoma suspects.
The transient appearance and recurrence of DH imposes difficulties in determining the true prevalence of this optic disc change, and limits the evaluation of predictive factors for its development.

**Associations of disc hemorrhage**

Controversies exist about the risk factors associated with glaucomatous DH. Factors observed to have significance in the incidence of DH are shown in Table 1.1,4,5,15

**Relationship with glaucoma**

The relationship of DH to NTG has been evaluated from different aspects, including the chance of having the disease, its effect on the rate of disease progression, and the benefit of managing it therapeutically with regard to disease control. There are practical clinical implications in making the distinction of impact of DH on these different factors.

DH is one of the prime risk factors involved in the pathogenesis of untreated NTG.2 This is not difficult to understand as DH is associated with localized retinal nerve fiber layer (RNFL) defects, neuroretinal rim notches, and circumscribed perimetric loss.7,16-18 A significant relationship between the location of the DH and the area of the progression of visual field loss has also been demonstrated in 44.0 to 65.4% of patients with DH.8,10

Recent studies have shown a clear association of DH not only with NTG but also with its progression.2,8-10 The cumulative probability of progression of visual field loss was noted to be significantly greater for glaucoma patients with DH than for patients without DH.4 However, whether the presence of DH signifies progression for all patients with glaucoma remains controversial. In the study by Siegner and Netland9 comparing eyes with DH and control eyes without DH, progression of visual field defects were noted to be significant in all groups of patients with POAG, NTG, and ocular hypertension (OHT). However, Rasker et al10 suggested that DH was indicative of deterioration in patients with NTG only. In the same study of patients with POAG and OHT, progression did not differ between eyes with DH and the contralateral eyes without DH.10

As the presence of DH may suggest an active disease progress, efforts have been made to delineate the association of glaucoma therapy and incidence of DH. One study has shown that glaucoma therapy may reduce the incidence rate of initial and recurrent DH in patients with high pressure glaucoma, but not in patients with NTG.14 On the other hand, in a Japanese study, the incidence of DH in NTG was reduced after trabeculectomy.19

It has been postulated that splinter hemorrhages are a result of a different pathogenic factor that causes the hemorrhage and axon damage.1 Hendrickx et al14 proposed an explanation with the concept of 2 populations with NTG (1 with DH and 1 never having had DH) as therapy appeared to have no effect on the incidence rate of DH.

The next question is whether increased incidence of DH or recurrent hemorrhage is associated with more extensive glaucomatous changes. However, the clinical significance of recurrent DH is where the controversies lie.

Ishida et al8 showed a significant progression of visual field defects in eyes that had at least 2 occurrences of DH compared with non-recurrent DH eyes. On the contrary, Siegner and Netland9 reported no differences in the rate of progression of optic disc shape or visual field defects in patients with recurrent DH and single DH. Rasker et al10 also reported no difference in the proportion of eyes progressing after single or recurrent DHs.

A more recent study by Kim and Park20 demonstrated that patients with glaucoma (mostly NTG) who had recurrent DH have a higher probability of progressive optic disc deterioration and RNFL deterioration. These authors, however, failed to show any significant differences with regard to progressive visual field deterioration between the single and recurrent DH groups. As with other studies, Kim and Park20 pointed out clearly that their study was limited by the fact that their patients received glaucoma medication in contrast to the patients in the study of Ishida et al,8 who did not. As glaucoma medications may delay the progression of visual field defects and mask the difference between the 2 groups, this may explain the failure in confirming the impact of recurrent DH on visual field deterioration.

**Conclusions**

Despite the fact that it is customary to take occurrence of DH as a sign of glaucoma and its progression, it is uncertain whether treatment will benefit these patients. A randomized clinical trial for effectiveness of treatment for DH is warranted.

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**Table 1. Factors observed to have possible association with the incidence of disc hemorrhage.**

<table>
<thead>
<tr>
<th>Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased age</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>Thinner central corneal thickness</td>
</tr>
<tr>
<td>Greater vertical cup-disc ratio</td>
</tr>
<tr>
<td>Family history of glaucoma</td>
</tr>
<tr>
<td>Smoking</td>
</tr>
<tr>
<td>Greater pattern standard deviation index on perimetry</td>
</tr>
<tr>
<td>Female sex</td>
</tr>
<tr>
<td>Increased intraocular pressure</td>
</tr>
<tr>
<td>Increased systolic blood pressure</td>
</tr>
<tr>
<td>Pseudoexfoliation</td>
</tr>
<tr>
<td>Aspirin use</td>
</tr>
</tbody>
</table>
References


Intraocular gas in vitreoretinal surgery

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Abstract

Advances in surgical techniques, instrumentation, and vitreous substitutes over the past few decades have greatly improved the anatomical and functional success of vitreoretinal surgery. Intraocular gases are the most common type of tamponade used in vitreoretinal surgery and they are indispensable for that purpose. A thorough understanding of the properties, indications, and potential complications of intraocular gases is therefore essential to optimizing the outcomes. This article reviews the properties, indications, and complications associated with commonly used intraocular gases in vitreoretinal surgery.

Key words: Fluorocarbons; Gases; Vitreous body; Vitrectomy

Introduction

Vitreous substitutes as surgical adjuncts were described as early as 1911, when Ohm injected air into the vitreous cavity to treat retinal detachment. In 1938, Rosengren further built on this concept with the technique of internal gas tamponade. Modern vitreoretinal techniques introduced by Machemer et al in the 1970s accelerated the use of vitreous substitutes for intraoperative and postoperative vitreous replacement. Advances in surgical techniques, instrumentation, and vitreous substitutes over the past few decades have greatly improved the anatomical and functional success rates of vitreoretinal surgery. The three most common types of substitutes in use today are intraocular gas, silicone oil, and perfluorocarbon liquid. This article reviews the properties, indications, and complications associated with commonly used intraocular gases in vitreoretinal surgery.

Intraocular gases and kinetics

The high surface tension between gas and fluid enables formation of an effective seal around a retinal break, thus allowing the retinal pigment epithelium (RPE) to absorb any remaining subretinal fluid to facilitate reattachment of the retina. Compared to silicone oil and perfluorocarbon liquids, gases provide the highest surface tension. Because the specific gravity of any gas is lower than that of water, the intraocular gas bubble has buoyancy that keeps the retina against the RPE, and this effect is greatest at the apex of the bubble. Buoyancy forces can be directed by careful positioning of the patient’s head so that retinal break is placed at the apex of the bubble, until such time as chorioretinal adhesions created by laser photocoagulation or cryotherapy can be established. In cases of giant retinal tear, the buoyancy force of intraocular gases may also be used to unroll the edges of a giant retinal tear. Increasingly however, this role has been supplanted by the introduction of perfluorocarbon liquids.

Four different intraocular gases are commonly used in vitreoretinal surgery: air, sulfur hexafluoride (SF₆), perfluoroethane (C₂F₆) and perfluoropropane (C₃F₈). In the vitreous cavity, these gases are colorless, odorless and inert. When injected into the vitreous cavity, air does not expand, whereas pure SF₆, C₂F₆ and C₃F₈ gases do. When gas enters the vitreous cavity, three phases can be distinguished: expansion, equilibrium and dissolution (Figure 1). The initial expansion is a result of the absorption into the bubble of nitrogen, oxygen and carbon dioxide from the surrounding tissue fluid. The most rapid rate of expansion occurs within the first 6 to 8 hours after gas injection. During the equilibrium phase, the partial pressures in the 2 compartments equilibrate as diffusion of nitrogen into the bubble is balanced by the diffusion of gas into the surrounding fluid. Finally, during dissolution, there...
is a net exit of gases as they are ultimately absorbed into the bloodstream. Absorption of intraocular gas bubbles is described reasonably accurately by first-order kinetics, which predict that a constant percentage of the volume of the intraocular gas gets absorbed over a given period of time.\(^6\)\(^8\)

Intraocular gas bubble dynamics depend on several factors, including initial gas concentration and volume, lens status and a history of prior vitrectomy.

The physical properties and gas dynamics are summarised in Table 1. A pure SF\(_6\) bubble expands to about double the volume injected within 24 to 48 hours, and exerts an effect for 1 to 2 weeks. A pure C\(_2\)F\(_6\) bubble expands to about 4 times of its original volume within 72 to 96 hours and persists in the vitreous cavity for 6 to 8 weeks. The maximum effective duration of the tamponade is approximately equal to 3 half-lives.\(^9\)

Intraocular gases can be used in office or in operative settings. Following vitrectomy for retinal detachment, most vitreoretinal surgeons use a non-expansile gas fill that allows placement of a large gas bubble to tamponade a large area of the retina. In contrast, pneumatic retinopexy involves the injection of a small, usually pure, expansile intraocular gas bubble in a non-vitrectomized eye; the objective being to provide focal tamponade over a retinal break. Intraocular gas may also be used as an adjunct in scleral buckling procedures, and are known as ‘pneumatic buckles’. Superior tears with retinal detachment without proliferative vitreoretinopathy (PVR) can be treated with air or short-acting gases such as SF\(_6\). A longer-acting gas such as C\(_2\)F\(_6\) can be used for retinal detachment with inferior tears, giant retinal tears, or more complex rhegmatogenous and tractional retinal detachment cases result in PVR, except when silicone oil is preferred.

**Techniques of fluid-air exchange and intraocular gas injection**

Following vitrectomy, intraocular gases are usually injected via the pars plana infusion line after any fluid (e.g. balanced salt solution) in the vitreous cavity is replaced by air. This fluid-air exchange may be performed by passive or active aspiration under direct visualization. With passive aspiration, a silicone tip or flute needle is used and the force of air entering the vitreous cavity through the infusion cannula causes the vitreous fluid to egress through the lumen of the aspiration needle, which is vented to the atmosphere. Fluid-air exchange with active aspiration into the vitrectomy cassette is more rapid but may result in hypotony if the aspiration of fluid is faster than the inflow of air. Subretinal fluid in eyes with a retinal detachment is usually removed during the surgery via the retinal break or a drainage retinotomy.

The introduction of perfluorocarbon liquids in vitreoretinal surgery has further enhanced surgical techniques.\(^{10}\)

Perfluorocarbon liquids have a higher specific density than water, allowing displacement of subretinal fluid anteriorly via the retinal break and flattening of the retina. Their low viscosity permits easy injection and withdrawal through instruments. Perfluorocarbon liquids are also optically clear, and tamponade using perfluorocarbon liquids can facilitate application of endolasers, especially for more posterior

**Table 1. Physical properties/dynamics of commonly used vitreoretinal surgery gases.**

<table>
<thead>
<tr>
<th>Gas</th>
<th>Molecular weight</th>
<th>Maximal expansion (hours)</th>
<th>Duration</th>
<th>Non-expansile concentration</th>
<th>Expansivity (times)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>29</td>
<td>N/A</td>
<td>5-7 days</td>
<td>N/A</td>
<td>0</td>
</tr>
<tr>
<td>SF(_6)</td>
<td>146</td>
<td>24-48</td>
<td>1-2 weeks</td>
<td>20%</td>
<td>2</td>
</tr>
<tr>
<td>C(_2)F(_6)</td>
<td>138</td>
<td>36-60</td>
<td>4-5 weeks</td>
<td>16%</td>
<td>3.3</td>
</tr>
<tr>
<td>C(_3)F(_8)</td>
<td>188</td>
<td>72-96</td>
<td>6-8 weeks</td>
<td>12%</td>
<td>4</td>
</tr>
</tbody>
</table>

Abbreviations: SF\(_6\) = sulfur hexafluoride; C\(_2\)F\(_6\) = perfluoroethane; C\(_3\)F\(_8\) = perfluoropropane; N/A = not available.
Pneumatic retinopexy in retinal detachment

Pneumatic retinopexy is primarily indicated for uncomplicated retinal detachment with retinal breaks involving the superior 8 clock hours of the fundus. The multicenter pneumatic retinopexy trial and other studies have shown that despite lower single-operation success rates (about 74%) with pneumatic retinopexy, the final surgical success rate (about 96%) is comparable with that of scleral buckling procedures.\textsuperscript{11,12} Complications of this technique include subretinal passage of gas, iatrogenic retinal breaks, progression of detachment with macular involvement, and PVR.

The technique involves the injection of intraocular gas before or after retinopexy, which creates retinal breaks with cryotherapy or laser, and maintenance of specific head postures after surgery. Preoperative eye drops or medications can be considered to lower intraocular pressure prior to pneumatic retinopexy. The desired volume of gas (usually 0.3 to 0.5 ml) is injected rapidly into the vitreous cavity in order to minimize formation of small ‘fish-egg’ bubbles (Figure 2). The intraocular pressure is monitored by digital palpation as the gas is injected into the eye. If the eye is already hypotonic after drainage of subretinal fluid, gas may be injected with a 30-gauge needle attached to a 3-ml syringe via the pars plana. If the eye is normotensive, vitreous or aqueous fluid must be removed to allow injection of more than 0.2 ml of gas, which is the maximum volume of gas that can be injected into a normotensive eye. The first method involves making a limbal anterior chamber paracentesis with a slit-knife or 30-gauge needle for aqueous drainage after gas injection. A repeat paracentesis after 5 to 10 minutes may normalize the pressure if the intraocular pressure remains elevated. The second method involves the aspiration of vitreous fluid before gas injection, using a 22-to 25-gauge needle attached to a 1- or 3-ml syringe placed via the pars plana. This method allows a larger volume of gas to be injected than the first paracentesis technique. The latter method, however, may increase the risk of retinal complications during the vitreous aspiration.\textsuperscript{13}

Intraocular gases can also be injected in association with scleral buckling procedures, especially when there is substantial residual subretinal fluid. The intraocular pressure should also be monitored for 6 hours post-injection as this is the time of maximal gas expansion.

Macular hole surgery

In the original description of macular hole repair by Kelly and Wendel,\textsuperscript{14} the surgery was a 5-step procedure: posterior vitrectomy, posterior hyaloid removal, internal limiting membrane removal, intraocular gas tamponade, and 1 week of face-down posturing postoperatively. The presence of intraocular gas provides isolation or waterproofing of the macular hole from the vitreous cavity by surface-tension at the gas-liquid interface. It may also mechanically tamponade the hole and provide a template over which a nascent bridging membrane forms. The duration of gas tamponade that is required for macular hole closure has come under debate in recent years. Recent reports have shown that hole

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Figure 2. ‘Fish egg’ bubble formation from gas injection in pneumatic retinopexy.
closure can occur as early as the first postoperative day, suggesting that prolonged gas tamponade and face-down posturing may be unnecessary. Similar macular hole closure rates have been reported in studies comparing air versus 20% SF₆, and with 20% SF₆ versus 12-16% C₃F₈. Pneumatic displacement of submacular hemorrhage

Submacular hemorrhage can result in sudden dramatic visual loss, and has many causes such as choroidal neovascularization, polypoidal choroidal vasculopathy, trauma and retinal artery macroaneurysm. The visual prognosis might be poor, especially if there is delayed presentation, a thick hemorrhage, foveal involvement, and an underlying choroidal neovascularization. Distinction should also be made between subretinal and sub-RPE hemorrhage as pneumatic displacement is generally not indicated for the latter, due to difficulty in displacing the hemorrhage. The technique of pneumatic displacement involves the injection of an expansile pure C₃F₈ gas (about 0.3 ml) via the pars plana at 3.5 mm from the limbus with a 30-gauge needle, followed by strict prone positioning for 5 to 7 days. Intravitreal tissue plasminogen activator or intravitreal anti–vascular endothelial growth factor (anti–VEGF) agents may also be injected at the same setting using expansile gas as adjuvants.

Unrolling giant retinal tear

A giant retinal tear may be unrolled using an intraocular gas bubble by placing the patient in a prone position and injecting gas via the infusion cannula, while removing fluid from the anterior vitreous cavity at the same time (upside down fluid-gas exchange). The gas bubble will expand in the vitreous cavity and push the retina against the underlying RPE, unrolling the edges of the giant retinal tear as the subretinal fluid moves to the anterior vitreous and is removed through an aspiration needle via the sclerotomies, which is in a dependent position. The patient is then returned to a supine position. Postoperatively, the patient should remain in a prone position to avoid slippage of the giant retinal tear edge. The use of gas to unroll the giant retinal tear is now mostly historical, since the availability of perfluorocarbon liquids has allowed a more convenient technique for unrolling the edges of a giant tear.

Postoperative positioning and duration of positioning

Appropriate postoperative positioning is dictated by the size of the intraocular gas bubble, the location of the retinal tear and lens status. Prone positioning in phakic patients can potentially reduce prolonged gas contact with the posterior lens surface. Pseudophakic and aphakic patients with retinal breaks in the superior periphery may avoid prolonged prone positioning because the gas bubble will provide good tamponade in the upright position.

The duration of postoperative positioning is determined by the location of the retinal breaks and the absorption rate of the intraocular gas bubble. An appropriate gas concentration is chosen to provide an adequate duration of tamponade. Superior retinal breaks without a large area of retinal detachment may be treated with air. Shorter-acting gas mixtures like 5% C₃F₈ or 20% SF₆ may be used to treat superior retinal breaks associated with retinal detachment. Inferior retinal breaks associated with retinal detachment may be treated with longer-acting 12% C₃F₈, so that the gas bubble remains large enough for at least 10 days in order to provide adequate tamponade for this particular retinal break to close. Complex retinal detachments with PVR or giant retinal tears usually require prolonged gas tamponade with 10 to 15% C₃F₈ gas mixtures.

Contraindications for intraocular gas

Postoperatively, patients with intraocular gases in situ should be advised against air travel or travelling to high altitudes, since the reduced atmospheric pressure under these conditions will lead to expansion of the intraocular gas bubble and cause considerable increase in intraocular pressure. Early manifestations include pain and decreased vision, which may be treated by prompt descent to a lower altitude. In extreme cases, the rise in intraocular pressure can result in retinal vascular occlusions and even globe explosion via surgical wounds. Experimental studies and clinical observations suggested that less than 0.6 to 1.0 ml of residual gas might be safe for air travel. It is nevertheless advisable for the patients to avoid any air travel when there is a residual intravitreal gas bubble.

Patients with intraocular gases in situ should also avoid diving. At sea level, the body is exposed to an ambient pressure of one atmosphere absolute (ATA). When diving, the absolute pressure is expressed by the formula \( \text{ATA} = \text{depth} \times \text{sea water} + 33/33 \). Hyperbaric pressures that occur during scuba diving cause the intraocular gas bubble to decrease in size according to Boyle’s law, leading to hypotony and partial globe collapse. As the eye goes from hyperbaric conditions to normal sea level, atmospheric pressure during the ascent to water surface decreases, resulting in expansion of the intraocular gas bubble and can cause a large increase in intraocular volume. Such pressure-induced changes in the volume of the gas bubble can also result in vitreous, retinal or choroidal hemorrhage. Nitrous oxide anesthesia should also be avoided in patients with intraocular gas bubbles. Since nitrous oxide in the blood is highly water-soluble, it enters the intraocular gas bubble and can lead to increased intraocular pressure whenever sclerotomies are closed. Later, as the nitrous oxide in the gas bubble returns to the bloodstream, the eye becomes hypotonous. If nitrous oxide anesthesia has been commenced during eye surgery, it should be discontinued at least 30 minutes prior to the injection of intraocular gas in order to facilitate its clearance from the bloodstream and tissues.

Complications of intraocular gases

Complications associated with the use of intraocular gas are detailed below.

Elevation of intraocular pressure

Elevation of intraocular pressure is one of the more
common complications in eyes with an intraocular gas bubble. Predisposing factors include pre-existing glaucoma, anterior synechiae, and impaired aqueous outflow at the drainage angle by hemorrhage, pigment, inflammation and neovascularization. In the majority of eyes, the elevation in intraocular pressure is transient and can be managed with topical or systemic anti-glaucoma agents. If the gas bubble expands to such an extent that the lens-iris diaphragm shifts forward and leads to angle-closure glaucoma, gas aspiration from the vitreous cavity (via the pars plana) may be indicated. Injection of viscoelastics may help in reformation of the flat anterior chamber. Aphakic eyes may be more prone to angle closure with a very large intraocular gas bubble because the iris can easily be pushed forward. This is especially likely when the patient is lying supine. Poor compliance with prone positioning may precipitate this complication. Subsequent evaluation of the anterior chamber angle of the operated eye and the fellow eye by gonioscopy can help determine whether a peripheral laser iridotomy is indicated.

Figure 3. Postoperative lens changes with intraocular gas in situ.

Cataract
Cataract may result from progressive nuclear sclerosis due to oxidative stress to the lens or trauma following vitrectomy. Prolonged contact of intraocular gas with the posterior lens surface can lead to gas-induced cataract, presenting typically as ‘lens feathering’, a manifestation of branching pattern of posterior subcapsular lens changes (Figure 3). It usually develops in the first few postoperative days in a patient who is poorly compliant to prone positioning. The posterior subcapsular feathering may be reversible by diligent prone positioning, but if the patient remains non-compliant for more than a week, permanent changes such as lens vacuolation or a diffuse posterior subcapsular cataract may develop.

Migration of intraocular gas bubble
Migration of intraocular gas bubble into the subretinal space can rarely occur as a result of pneumatic retinopexy. This ensues if the tear is larger than the bubble, or during fluid-gas exchange when there is unrelieved traction on the retina, or when the gas is injected accidentally into the subretinal space. Although the subretinal intraocular gas bubble is eventually absorbed, the retinal break may not be properly sealed by the gas bubble and thus redetachment can occur. Intraocular gas can also migrate out of the sclerotomy into the subconjunctival space if the wound integrity is not secured at the end of surgery (Figure 4). In phakic or pseudophakic patients, an intraocular gas bubble may also migrate into the anterior chamber via weakened zonules or larger posterior capsulotomy. Prolonged contact of gas with the corneal endothelium in aphakic eyes can lead to corneal decompensation. These patients should be reminded to avoid sleeping in a supine position. Gas injection in eyes with an iris claw anterior chamber intraocular lens might also cause the intraocular lens to flip around its axis and intraocular lens removal or use of silicone oil might be preferable in these cases.

Inadequate gas bubble size
Inadequate gas bubble may ensue if the surgery is completed with a smaller-than-desired intraocular gas bubble due to removal of inadequate vitreous or subretinal fluid and exchange with air. Alternatively, intraocular gas escapes through a sclerotomy during the perioperative period could lead to loss of intravitreal gas and hypotony. Inadequate gas bubble size may also be caused by premature absorption of the gas due to errors in reconstituting the gas mixture.

Other complications
Other complications include iatrogenic retinal breaks and PVR, which are important causes of surgical failure after injection of intraocular gases. Visual field defects have also been reported in eyes subjected to macular hole surgery. Prolonged contact of the intraocular gas bubble with the nerve fiber layer has been postulated to have a role in causing such defects. However, other reports have associated these visual field defects with surgical trauma or the use of certain intraoperative stains, like indocyanine green.

Conclusion
The intraocular gas bubble is one of the most useful surgical adjuncts in vitreoretinal surgery. A thorough understanding of its properties, indications and potential complications of intraocular gases is essential to optimizing the outcomes of vitreoretinal surgery.
References

Age-related macular degeneration and polypoidal choroidal vasculopathy in Asia

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Abstract
Age-related macular degeneration is the leading cause of irreversible blindness in patients aged 55 years or more in developed countries. In recent years, various epidemiological, genetic and clinical studies from Asian populations have demonstrated that age-related macular degeneration in Asians has its unique perspectives in terms of epidemiology, genetic factors, phenotypic presentations, clinical subtypes and management approach. In particular, polypoidal choroidal vasculopathy is prevalent in Asian populations compared with Caucasians. This review highlights and contrasts the clinical features and management of age-related macular degeneration and polypoidal choroidal vasculopathy in Asians.

Key words: Aged; Asian Continental Ancestry Group; Macular degeneration; Visually impaired persons

Introduction
Age-related macular degeneration (AMD) is a major cause of blindness in the elderly in Asian countries, and the number of sufferers is expected to grow significantly.1 These projected demographic shifts may be due to the urbanization of Asians, westernization of lifestyles, increasing population longevity, as well as the public’s ever-increasing disease awareness and diagnostic attentiveness. Most of our past understanding on AMD comes from studies in white and black populations. In recent years, with the increase in publications especially of epidemiological studies from Asia, we now know that Asian AMD has its own unique features in terms of epidemiology, genetics, phenotypic presentations, clinical subtypes and responses to treatment.

Epidemiology of age-related macular degeneration in Asia

Asia has mixed populations of different races and ethnicities. Not surprisingly, studies on the prevalence of AMD in Asia show wide variations. Based on increasing evidence from recent population studies, the perception that AMD is much less common in Asians than in white Caucasians is no longer tenable. The Hisayama Study in Japan2 reported that in a Japanese population aged 50 years or older, the prevalence of early AMD was 12.7% and late AMD was 0.87%; the frequency of neovascular AMD being significantly higher in men. The Singapore Malay Eye Study demonstrated the prevalence of early and late AMD in Singapore Malays aged 40 to 80 years to be 3.5% and 0.34%, respectively.3 The Shihpai Eye Study in Taiwan described an elderly Chinese population of 65 years or above with a prevalence of early AMD was 9.2% and of late AMD was 1.9%.4 In the Beijing Eye Study in China, the prevalence of early and late AMD in Chinese aged 40 years or older was reported to be low, being 1.4% and 0.2%, respectively.5 The overall impression was that the prevalence of AMD in Asians does not differ greatly from that in white Caucasians (Table 1).6

Other than race and ethnicity, there are other factors that might account for inconsistencies and disparities in prevalence between different Asian populations.6 These include: different systems for classifying AMD, the proportion of patients with dense cataracts making fundus pictures unreadable, as well as different dietary intakes,
levels of industrialization, and lifestyle factors (smoking, environmental factors such as sunlight exposure).

Two diseases that are commonly found in Asians can also affect the accuracy of an AMD diagnosis. One is central serous chorioretinopathy, which presents with pigmentary changes at the posterior pole with or without associated scattered drusen, which may masquerade as dry or early AMD. Another is polypoidal choroidal vasculopathy (PCV), which can manifest like exudative or late AMD. Future research in Asia will emphasize the incidence and risk factors of AMD and its subtypes. The target will be towards prevention of blindness with specific treatment directed to specific disease entities.

**Genetics of age-related macular degeneration in Asia**

Several research initiatives demonstrate the important role of genetics in the development of AMD. Genetic loci are strongly associated with AMD and population studies have revealed genetic heterogeneity. There are also differences in the occurrence of disease-susceptible genes and single nucleotide polymorphisms (SNPs) between white Caucasians and Asians.

The complement factor H (CFH) gene is involved in chronic inflammatory responses and drusen formation. This gene encodes a protein that regulates the complement, inflammation system, which is important for clearing out pathogens and cellular debris. SNP is a site in the genome, where a single base in the DNA often differs from person to person. A variation in SNP (rs1061147) of the CFH gene may result in a CFH protein with reduced ability to bind to C-reactive protein (CRP). Excessive levels of CRP might lead to overactivity of the complement system and chronic inflammation at the macula, resulting in cellular damage and drusen deposits. In 2005, CFH was the first strong genetic factor identified for exudative AMD. The Y402H is present in 34.9% of Caucasian populations, and is estimated to have a role in almost 60% of AMD cases at the population level. Its frequency, however, is low in the Chinese and Japanese populations, and no obvious associations with wet AMD has been noted in either of these populations.

In 2006, two other genetic factors, HTRA1, a serine protease gene (SNP rs11200638) and hypothetical LOC387715 (SNP rs10490924), were found in Hong Kong Chinese and white Caucasians with wet AMD, and they showed

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**Table 1. Prevalence of age-related macular degeneration (AMD) in Asian populations.**

<table>
<thead>
<tr>
<th>Population</th>
<th>Study (region)</th>
<th>Early AMD (%)</th>
<th>Late AMD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japanese</td>
<td>The Hisayama Study (Japan)</td>
<td>12.7</td>
<td>0.87</td>
</tr>
<tr>
<td>Chinese</td>
<td>The Beijing Eye Study (China)</td>
<td>1.4</td>
<td>0.2</td>
</tr>
<tr>
<td>Chinese</td>
<td>The Shihpai Eye Study (Taiwan)</td>
<td>9.2</td>
<td>1.9</td>
</tr>
<tr>
<td>Malay</td>
<td>The Singapore Malay Eye Study (Singapore)</td>
<td>3.50</td>
<td>0.34</td>
</tr>
<tr>
<td>Indian</td>
<td>Andhra Pradesh Eye Study (India)</td>
<td>-</td>
<td>1.90</td>
</tr>
</tbody>
</table>

**Table 2. Associations, genotype frequencies and odds ratios of susceptibility genes and single nucleotide polymorphisms (SNPs) in age-related macular degeneration (AMD) of different populations.**

<table>
<thead>
<tr>
<th>Gene</th>
<th>SNPs</th>
<th>Chinese</th>
<th>Japanese</th>
<th>Caucasian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complement factor H (CFH) on chromosome 1q31</td>
<td>Try402His polymorphism rs1061170:T&gt;C</td>
<td>No association</td>
<td>No association</td>
<td>Strong association with odds ratio of 6.32 for CC genotype</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C allele: 5.8% in cases vs 2.9% in controls (Hong Kong); 10.3% in cases vs 8.0% in controls (Beijing Chinese)</td>
<td>C allele: 4% in cases vs 4% in controls</td>
<td>C allele: 34.9% in cases vs 58.9% in controls</td>
</tr>
<tr>
<td>Promoter of high-temperature requirement A-1 (HTRA1) genes on chromosome 10q26</td>
<td>rs11200638:G&gt;A</td>
<td>Very strong association with odds ratio of 10.00 for the AA genotype (Hong Kong Chinese) 67.8% in cases vs 42.4% in controls; odds ratio was 7.90 for the AA genotype (Beijing Chinese)</td>
<td>Very strong association with odds ratio of 10.02 for the AA genotype 69% in cases vs 32% in controls</td>
<td>Strong association with odds ratio of 6.56 for AA genotype A allele: 40.3% in cases vs 25.2% in control</td>
</tr>
<tr>
<td>Hypothetical LOC387715 in the chromosome 10q26 region (upstream of HTRA1)</td>
<td>rs10490924:G&gt;T</td>
<td>Very strong association with odds ratio of 11.14 for the TT genotype (Hong Kong Chinese) T allele: 64.9% in cases vs 43.2% in controls; odds ratio was 5.45 for the TT genotype (Beijing Chinese)</td>
<td>Strong association with odds ratio of 6.20 for the TT genotype T allele: 68% in cases vs 33% in controls</td>
<td>Strong association with odds ratio of 6.09 for TT genotype T allele: 39.7% in cases vs 24.7% in control</td>
</tr>
</tbody>
</table>
a strong association with choroidal neovascularization (CNV) formation. Individuals with the risk allele of HTRA1 gene increase the production of HTRA1 protein. The latter is a member of the heat shock serine proteases which is expressed in human retina and up-regulated by cellular stress. Patients with homozygote alleles are genetically predisposed to 10- and 6-fold increased risk of wet AMD in Chinese and Caucasian populations, respectively.

The 2 major genes implicated in the development of AMD—CFH and HTRA1—are believed to govern 2 different biological mechanisms. CFH affects drusen formation in dry AMD, while HTRA1 influences the development of CNV (the hallmark of wet AMD). This may account the distinct AMD phenotypes in Asians and white Caucasian populations. Even more complex scenarios involve gene-gene and gene-environment interactions, which can affect overall disease susceptibility and non-responsiveness to treatment.16-18

### Clinical subtype of age-related macular degeneration in Asian populations

Using fluorescein angiography, exudative AMD can be classified as classic or occult CNV. The spectrum of disease associated with AMD has expanded with advancements in diagnostic technologies. Indocyanine green angiography
ICGA is able to delineate choroidal vascular abnormalities much more clearly, and new clinical entities such as PCV and retinal angiomatous proliferation (RAP) have emerged. It is well accepted that ICGA is the gold standard for the definitive diagnosis and characterization of PCV (Figure 1). Following treatment, each clinical entity is characterized by differences in clinical course, phenotypic presentation, pathogenesis and outcome (Table 3).

In a study of 155 Chinese patients with exudative AMD, 68% had CNV typical of AMD, 25% had PCV, 5% had RAP and 3% had mixed lesions. In a similar retrospective study of 104 consecutive patients with ICGA from Hong Kong, PCV accounted for 19.2% of cases. These are probably underestimations of the true prevalence, as in a study with 158 Japanese patients with exudative AMD, 55% were diagnosed to have PCV, 35% typical AMD, 5% as RAP and 5% had mixed lesions.

Highly suspicious characteristic signs of PCV that should prompt ICGA include: massive subretinal hemorrhage, hemorrhagic pigment epithelial detachments, notched pigment epithelial detachments, absence of soft drusen in either eye with exudative maculopathy, clinically visible orange-red subretinal nodules, and presentation in late middle age (persons in their 50s or 60s).

Treatment for exudative age-related macular degeneration in Asian populations

For typical neovascular AMD, if available, intravitreal anti-vascular endothelial growth factor (VEGF) monotherapy is still the preferred primary treatment. The current therapeutic standard is consecutive monthly injections of ranibizumab (Lucentis; Genentech, Inc, San Francisco, US) on a continuing, indefinite basis. This option, however, is not practical or achievable for various reasons, including treatment costs and burden. Bevacizumab (Avastin; Genentech, Inc, San Francisco, US), an anti-VEGF, is commonly used as an off-label alternative. In Asia, the choice between ranibizumab and bevacizumab depends mostly on accessibility of these treatments in the medical system, acceptance and affordability, and physician preference.

The most favorable suggested strategy is to use 3-monthly intravitreal doses (loading phase) of either anti-VEGF agent administered to maximize the initial response. This is followed by an individualized maintenance phase, during which patients should receive treatment based on their respective response as judged by visual outcomes and optical coherence tomography (OCT) findings.

Figure 2. (a) Baseline fundus photograph, (b) fluorescein angiography, and (c) indocyanine green angiography of a 59-year-old woman presenting with serosanguinous maculopathy in the right eye secondary to an active polypoidal choroidal vasculopathy. The baseline best-corrected visual acuity (BCVA) was 20/200. Photodynamic therapy and intravitreal anti-vascular endothelial growth factor with bevacizumab were performed. At 1 year after treatment, the BCVA improved to 20/30. (d) Hard exudate and hemorrhage absorbed gradually and completely resolved by 12 months' post-treatment. (e) Fluorescence angiography showed resolution of leakage and hemorrhagic pigment epithelium detachment. (f) Indocyanine green angiography also demonstrated regression of the polyps and interconnecting vessels.
Anti-VEGF and photodynamic therapy (PDT) used as dual therapy or together with corticosteroids as triple therapy may address the different pathogenic pathways of wet AMD. Such strategies could be considered for patients with persistent disease despite anti-VEGF monotherapy, the intention being to reduce the number of retreatments and/or offer longer treatment-free periods. Evidence suggested that any combination containing full fluence PDT results in functional visual acuity inferior to ranibizumab monotherapy. The negative effect is probably caused by the standard laser fluence (50 J/cm²) of PDT on the choroidal blood supply. A successful combination therapy approach involves reduced fluence of PDT, whilst the optimal energy required further investigation.

For the clinical subtype with PCV, PDT has been well accepted as an effective treatment modality. PDT has shown good results for PCV, with stable or improved vision achieved in 81 to 100% of patients at the 1-year follow-up. However, in some eyes with PCV, extensive subretinal hemorrhages are an unavoidable side-effect of PDT. Moreover, PDT appears to be less effective in PCV patients presenting late and in cases with secondary formation of fibrovascular tissue. Anti-VEGF monotherapy has been studied in PCV and demonstrated to improve visual acuity and outcomes measured by OCT, but results in only minimal or no regression of polyps as measured by ICGA. In PCV with associated exudative changes, combining PDT’s angioocclusive effect on polyps with anti-VEGF’s antipermeability effect may lead to better clinical outcomes (Figure 2). The recently completed EVEREST study, a multicenter randomized controlled trial, showed that a combination of PDT and ranibizumab therapy resulted in the highest proportion of patients with complete regression of polyps at 6 months (78% complete regression), compared to PDT monotherapy (71%) or ranibizumab monotherapy (29%). Further studies are needed to determine the long-term role of combination therapy as primary therapy for treating PCV.

Several novel investigational agents are now being evaluated. VEGF Trap-Eye (Regeneron Inc., Tarrytown, US; Bayer HealthCare AG Inc., Leverkusen, Germany), a VEGF receptor fusion protein that binds all forms of VEGF with higher affinity than ranibizumab might have a future role in the treatment of PCV. Another potential therapeutic strategy involves blockade of VEGF effects by inhibiting the tyrosine kinase cascade downstream from the VEGF receptor. These may be the future directions in enhancing the treatment success in wet AMD in order to offer maximal possible gains for our patients.

Conclusions

AMD in Asian populations reveals many differences from the western populations, especially in phenotypic manifestations and prevalence of clinical subtypes. Diversity in genetic composition and environmental interactions are among the major reasons. Accurate diagnosis of AMD subtypes is important for appropriate patient management. In Asian populations, PCV constitutes a high percentage of patients with exudative AMD, and it is known that anti-VEGF therapy alone is inadequate in achieving optimal anatomic and angiographic results. Once the diagnosis of PCV is made by ICGA, by including PDT in the therapeutic protocol, modifications may be indicated in order to improve outcomes.

References


Surgical management of ectatic corneal disorders

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Abstract

Ectatic disorders of the cornea such as keratoconus, pellucid marginal degeneration and post–refractive surgery corneal ectasia are characterized by progressive corneal thinning, irregular astigmatism and decreased visual acuity. Over the last decade, there has been a paradigm shift from penetrating keratoplasty to lamellar keratoplasty for the management of primary as well as acquired corneal ectasia. This article reviews some of the surgical approaches to the management of ectatic corneal diseases.

Key words: Corneal diseases; Keratoconus; Ophthalmologic surgical procedures

Introduction

Ectatic disorders of the cornea are characterized by progressive corneal thinning, irregular astigmatism and decreased visual acuity. They comprise primary conditions such as keratoconus, pellucid marginal degeneration (PMD) and iatrogenic corneal ectasia, all of which may occur after refractive procedures such as LASIK (laser in-situ keratomileusis) surgery.

Over the last decade there has been a paradigm shift from penetrating keratoplasty (PKP) to lamellar keratoplasty for the management of primary as well as acquired corneal ectasia. Several treatment modalities have emerged including collagen cross-linking, intrastromal implants, laser vision correction, and recent techniques in central and peripheral lamellar keratoplasty. This article reviews important surgical approaches to the management of ectatic corneal diseases.

Deep lamellar keratoplasty

PKP is the most commonly performed solid organ transplantation and has enjoyed a relatively high success rate compared to transplantation of other tissues. However, endothelial graft rejection is observed in approximately 20% of cases undergoing PKP.2 Although the results of PKP in cases of keratoconus are very good, a variable number of keratoconus patients experience one or more endothelial rejection episodes, causing graft decompensation. Deep lamellar keratoplasty (DLK) is a surgical technique that can eliminate the risk of corneal endothelial graft rejection, and has comparable optical results to PKP. DLK has been successfully used to treat various corneal pathologies that spare the corneal endothelium.3,4

Not very long ago, the concept of a ‘true’ deep anterior lamellar keratoplasty (DALK) extending down to Descemet’s membrane (DM) was proposed. Older literature does not expand on the actual depth of ‘deep’ lamellar keratoplasty. Gasset1 reported a series of keratoconus patients in the late 1970s who underwent ‘conectomy’ and received full-thickness grafts stripped of DM, transplanted into relatively deep lamellar beds. Dissection of host tissue ‘close to’ the DM and the term DALK were first introduced by Archila in 1984,4 with the use of intrastromal air injection to facilitate removal of diseased host corneal tissue. The first study on the results of DALK compared with PKP in keratoconus was reported by Sugita and Kondo in 1997.5 They showed that postoperative visual acuity was similar after DLK and PKP in cases of keratoconus. Recently DALK has gained popularity due to improvements in surgical techniques, and the availability of new surgical instruments and viscoelastics that have helped to improve surgical success and reduce surgery time.
Techniques of deep lamellar keratoplasty

The classical technique for DLK involves the removal of host tissue layer by layer until the deep stroma or the DM is bared. While stromal fibers are difficult to visualize when the amount of tissue becomes minimal, injection of irrigation fluid causes swelling of stromal fibers that can then be manipulated. The 2 techniques of DLK that have become popular in recent times are the Melles and big-bubble techniques.

Melles technique

Melles’ technique involves injection of air into the anterior chamber that creates a mirror reflex to guide surgical instruments directly into the space between DM and the posterior stroma. The difference in refractive index between air and corneal tissue creates a reflex of the surgical knife, and the distance between the instrument and reflex can be used to judge the amount of stromal tissue. The blunt end of a microsurgery knife is used to dissect the stroma down to the DM, using the reflection of the knife observed at the air-to-endothelium interface as a guide. After creation of a small DM detachment with balanced salt solution, viscodissection is performed to further extend DM detachment. After complete dissection of the DM, the overlying stroma is removed to expose the smooth surface of DM.

Modifications in Melles technique

Shimmura et al modified the Melles technique by performing anterior lamellar keratectomy prior to air injection. Senoo et al have used a sclerolimbal approach for performing DLK. The method uses trabeculectomy to detach the DM. A flap is made, as in trabeculectomy, and the region directly above the DM is reached under direct vision. DM is detached by hydrodissection and viscoelastic material is used to maintain the suprana DM space. Parmar et al used a 5-mm-long scleral incision for corneal dissection close to the level of the DM. Using this technique, a scleral pocket incision is created with a crescent knife and dissection is carried into the clear cornea. Viscoelastic is injected into the scleral pocket to facilitate separation of DM from the corneal stroma.

Funnell et al compared the outcomes and complications of DLK using Melles technique and PKP for keratoconus. There was no significant difference in the proportion of patients achieving 6/9 or better in the PKP and DLK groups.

The study found that DLK causes less astigmatism and also has the advantage of avoiding endothelial graft rejection. In another study, Watson et al compared the DLK and PKP using Melles technique in patients with keratoconus. They found that best-corrected visual acuity (BCVA), refractive results and complication rates were similar in both groups.

Big-bubble technique

Archila introduced the technique of air injection between the DM and the overlying corneal stroma. In this technique, a 26-gauge needle connected to a tuberculin syringe filled with air is inserted obliquely into the stroma up to the corneal midperiphery. Air is injected and corneal stromal trephination is done. Dissection of corneal stroma is facilitated with a spatula to separate the DM from the deeper stromal layers.

Anwar and Teichmann modified Archila’s technique by performing corneal trephination before air injection. About 60 to 80% of the corneal stroma is trephined with the help of a suction trephine. A 27-gauge needle attached to an air-filled syringe is bent at about 60° angulation 5 mm from its tip. The plunger of the air-filled syringe is depressed in order to form the big bubble between the DM and the deepest stroma. A partial thickness keratectomy is done with the help of a Beaver blade leaving a layer of corneal stroma in place. Using a sharp-tipped blade held tangentially to the cornea, a small nick is made in the corneal stroma. Dissection can be carried out in this plane with the help of a spatula and long scissors.

Since DLK does not involve replacement of the DM or endothelium, the donor quality criteria are not stringent. DM and endothelium are stripped off from the donor button which is then sutured over the host bed using 10-0 monofilament nylon sutures. The disparity between the host cut and donor button is usually between 0.25 mm and 0.5 mm, with the diameter of the graft button being larger. Some corneal surgeons prefer using the same size or an undersized donor button in patients with keratoconus (Figure 1). Several studies have reported good results with the DALK technique (Table 1).

Modifications in the technique of deep lamellar keratoplasty by air injection

Fournié et al have described a modification of Anwar’s big-bubble technique. The initial air injection is made in the
superficial corneal stroma. The aim of the first air injection is to induce corneal emphysema and facilitate superficial lamellar keratectomy. Subsequent dissection is carried out with the help of viscoelastic. Recently, Parthasarathy et al\textsuperscript{21} reported a method of using a small air bubble in the anterior chamber to help determine if a successful big bubble was achieved. The small bubble helps the surgeon assess the extent of the big bubble in cases where the cornea is opaque or when air diffusion into the peripheral cornea prevents direct visualization into the anterior chamber.

The major complication encountered during DLK is intra-operative perforation of the DM. The frequency of DM perforation during DALK depends on the surgical technique and the expertise of the surgeon and varies.\textsuperscript{15,22,23} Keratoconus patients are more prone to DM rupture than those with other diseases, either due to thinner corneas or an intrinsic property of the disease.\textsuperscript{24}

DM perforation can be micro or a macro in form. Microperforations in the peripheral cornea can be managed by careful stromal dissection and air injection at the end of the surgery. If a microperforation occurs in the central cornea, there is a risk of double anterior chamber formation in the postoperative period. Injection into the anterior chamber of a mixture of sulfur hexafluoride with air, or perfluoropropane with air can also be used to temporarily seal microperforations, or to flatten any secondary anterior chamber formed after perforation.\textsuperscript{25}

Conversion to a PKP may be required in some cases. In such a scenario, a complete dissection of the host cornea should be carried out. Use of 0.01% trypan blue dye may delineate any retained pieces of DM and facilitate dissection of the trephined host cornea.\textsuperscript{26}

A rather rare complication after DLK is corneal stromal graft rejection. This is characterized by sudden onset of decreased vision, and subepithelial infiltrates, with or without stromal edema or anterior segment activity.\textsuperscript{27} Such eyes are treated with 1% prednisolone acetate drops, gradually tapered over 4 to 6 weeks.

**Automated lamellar therapeutic keratectomy**

Microkeratome-assisted lamellar keratoplasty is another novel technique used for surgically treating keratoconus and other corneal pathologies sparing the endothelium.\textsuperscript{28,29} The major advantage of automated lamellar therapeutic keratectomy (ALTK) is that the donor cut is smooth which eliminates the risk of interface haze that can otherwise result in poor visual quality. Moreover, the dissection is easy to perform, and shortens surgical time considerably. The surgical technique offers more control in the depth of dissections and can be fairly standardized. The surgery does not require dissection up to the level of DM, therefore reducing the chances of perforation of DM.

ALTK has been primarily developed to treat cases of keratoconic corneas with a minimum corneal thickness of 380 microns.\textsuperscript{29} A 250 microns anterior corneal disc of host is excised by a microkeratome and a 350 microns thick donor corneal disc is transplanted. The donor lenticule is also harvested using a microkeratome and an artificial anterior chamber. The desired diameter of the donor lenticule is achieved by using different suction rings.

Busin et al\textsuperscript{29} evaluated the visual and refractive results of ALTK in patients with keratoconus with minimal corneal thickness of 380 microns. All patients underwent a standard ALTK surgical procedure. At the end of 1 year, best-spectacle-corrected visual acuity ≥20/40 and refractive astigmatism ≤4 diopters were achieved in majority of patients. The major complications reported in this study included irregular astigmatism (22%), high-degree astigmatism requiring secondary intervention (12%), epithelial interface ingrowth (2%) and cataract formation (2%).
‘Tuck in’ lamellar keratoplasty

‘Tuck in’ lamellar keratoplasty is a special technique of partial-thickness corneal transplantation that has been described for cases of advanced peripheral corneal thinning disorders like keratoglobus, PMD or cases with a combination of keratoconus and PMD.30,31

Surgical technique

The surgery involves the creation of partial-thickness groove of 180 to 240 µm on the host cornea using a Hessburg Barron vacuum trephine and excision of a central anterior stromal disc. Subsequently, a peripheral intrastromal pocket is created circumferentially in the corneal periphery up to a point 0.5 mm farther away from the limbus. The donor preparation involves fixing a corneoscleral donor button in an artificial chamber. An initial partial thickness incision is made up to a depth of 300 µm and superficial corneal tissue is excised leaving a central full-thickness graft with a peripheral partial-thickness flange of about 2.5 to 3 mm. The tissue is punched from the endothelial side with hand-held trephines. The DM of the donor lenticule is stripped after staining with 0.1 ml of 0.06% trypan blue. The flange of the donor lenticule is tucked into the peripheral intrastromal pocket of the host previously created, and sutured with sixteen 10-0 monofilament sutures. In the presence of inferior thinning in cases of PMD with keratoconus only, an inferior 180° peripheral intrastromal pocket is created instead of a circumferential pocket.

The central full-thickness graft provides tectonic support to the central cornea, while the thin peripheral flange tucked into the intrastromal pocket integrates into the host and provides tectonic support to the peripheral cornea. Moreover, there is no damage to the recipient’s limbal stem cells as dissection of limbal region is avoided, and subsequently this promotes healing of the epithelium at the graft-host junction (Figure 2).

Intacs

Intacs are polymethylmethacrylate segments which were designed to be surgically inserted into the deep corneal stroma to flatten the central cornea. An important advantage they offer is that the prolate shape of the cornea is preserved over the central optical zone, which is unlike laser and incisional procedures that play a role in the maintenance of contrast sensitivity and improved visual acuity outcomes. Intacs were initially approved by the US Food and Drug Administration in 1999 for correction of myopia from –1.00 to –3.00 D, with 1.00 D or less of astigmatism. However, with the advent of the excimer laser at about the same time, Intacs were not popular for refractive correction. Intacs have now been approved for use in patients with mild-to-moderate keratoconus who have a clear visual axis, upper limit of keratometry readings in the range of 55 to 57 D, and a minimum corneal thickness of 400 microns.

Intacs come in many different sizes and potentially there are many different combinations that can be used to achieve both flattening of the central cornea and reduce the astigmatism. In pure nipple cones it is best to use 2 symmetrical Intacs. If the patient is not severely myopic, lesser-size symmetrical Intacs can be used so as not to overcorrect and induce hyperopia.

The surgical procedure involves creation of corneal tunnels at about 70% of corneal depth, using 2 Sinskey hooks and a mechanical spreader. Intacs segments are implanted in the respective corneal tunnels, maintaining a space of approximately 2.0 mm between their ends. The incision site is sutured using a single 10/0 nylon stitch.32 Recently femtosecond laser has been used to create channels. Besides being quick, femtosecond results in a high degree of certainty about the depth of ring placements.

This technique may be associated with the occurrence of small epithelial defects that are evident on first postoperative

Figure 2. (a) Preoperative and (b) postoperative photographs after ‘tuck in’ lamellar keratoplasty in a case with extreme corneal ectasia after keratoplasty.
day. Deposits surrounding the ring segments are occasionally seen and may increase over time, but are not associated with effects on visual acuity. Infection most commonly occurs as a result of a loose stitch or as a gaping wound gape due to migration of the Intacs to the site of the wound.13-15

Colin et al in 200116 published the first series of 10 patients with 1-year follow-up. Intacs inserts of 0.45-mm thickness were placed in the inferior cornea and 0.25-mm thickness were inserted superiorly. Postoperative 12-month uncorrected visual acuity (UCVA) was significantly better than the preoperative UCVA. In 2003, Boxer Wachler et al17 reported the results on 74 eyes of patients with keratoconus using asymmetrical Intacs. The study concluded that asymmetric Intacs implantation can improve both uncorrected and best-spectacle-corrected visual acuity and can reduce irregular astigmatism. In 2005, Alió et al18 performed a prospective study to evaluate the effect of implanting 1 versus 2 intracorneal rings in patients with keratoconus. A single Intac was placed inferiorly in cases where the topographic pattern did not cross the 180-degree meridian, whereas 2 Intacs were placed in cases where it crossed the 180-degree meridian. At 1 year, the mean UCVA improved from 20/100 to 20/32 in the first group and from 20/400 to 20/63 in the second group.18 In 2005, Rabinowitz et al19 compared the results of femtosecond laser with that of the mechanical spreader for inserting Intacs in patients with keratoconus. Both groups showed significant reduction in average keratometry, spherical equivalent, BCVA, UCVA, surface regularity index (SRI), and surface asymmetry index. The laser group performed better in all parameters except change in SRI.

**Conclusion**

Lamellar surgeries have become popular in the management of primary as well as acquired corneal ectasia over the recent years. A more thorough understanding of these techniques should optimize outcomes in patients treated for corneal ectasia.

**References**

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