Kerala Journal Of Ophthalmology
VOL. XXVI, ISSUE 3, SEPTEMBER 2014

The Kerala Journal of Ophthalmology is the official scientific publication of the Kerala Society of Ophthalmic Surgeons and 4 issues are published every year.

It welcomes original articles, interesting case reports, update articles, book reviews, journal abstracts and research papers in Ophthalmology. Original articles are accepted on condition that they have not been published in any other journal.

Cover Photo
Spectralis OCT and Fundus Autofluorescence image of congenital toxoplasmosis scar with colobomatous change and secondary choroidal neovascularisation at the nasal edge of the coloboma

Courtesy
Department of Retina & Vitreous
Chaithanya Eye Hospital
Trivandrum

Subscription Rate
Annual : Rs. 600 (4 issues)
Single Copy : Rs. 150

Subscription should be sent by demand draft in favour of Kerala Journal of Ophthalmology payable at Ernakulam addressed to the Editor, KJO

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Dear Friends,

It feels great bringing out yet another edition of KJO. This time we have Mike Denton, a pioneer who has worked with Retinitis Pigmentosa families in Kerala, dedicating a series of articles on genetic disorders. We also have Dr. Rajiv Raman and Dr. Tarun Sharma, doyens in research in the field of retina, contributing an article on optic pit. I take this opportunity to thank each and everyone who has contributed to this edition of KJO despite his/her busy schedule.

Publishing a scientific paper is no easy task. It is the culmination of months of careful systematic investigation and data acquisition. Appreciation of our work by our peer scientific community is indeed a great honour and publication of our work is a recognition of the scientific content and quality of research. However, this great honour also entails an immense responsibility for the author to ensure the authenticity of the work, novelty of the scientific approach, accuracy of statistical information, and even minor details as the appropriateness of references.

Hence there are certain important things that I feel one should embark, before beginning to work on a paper. Well, the first question the author should ask himself is, “does our study truly reflect the reality?” It is not enough if the authors alone are convinced about it, but it should also accurately reflect statistically in it. So it is essential that we devise a “Statistical Plan” beforehand and not just do some jugglery in the end to make things look statistically significant. Any statistical test can give a false result, but the chance is acceptably small. Even though a very large number of tests will appear to give more data, we should also understand that with more tests, there are more opportunities for errors to creep in and be accumulated in the results. Many of our dissertations today clearly indicate this desperation of data mining from erroneous data to get statistically significant results.

Genuine research is like a studious student doing his lessons daily and not just before exams. Research is serious responsibility and one should try to maintain quality. Quality research may involve significant financing and manpower and it is high time that hospitals and institutes take it up seriously and channelize their resources for high quality research. Doing routine work can make a difference to your patients but the impact of good research can change the outlook of entire mankind.

Jai KSOS

Dr Ashok Nataraj
Editor, KJO
Basic Eye Care Delivery in Kerala-An Appraisal

The State of Kerala has made rapid strides on the Health front after Independence thanks to the development of Medical Education and the Health awareness of an enlightened public. With levels of literacy at a high level, the general public is receptive to new informations on the preventive and curative aspects of health and willing to translate these concepts into practice. This has been the pillar on which we could build an edifice. Today the Health Professionals of our State have received acclaim world over and are part of advanced medical systems in countries like U.K., U.S.A, and others.

Evolution of Eye care facilities runs parallel to these advances. Institutionalized facilities that were limited to Medical colleges, District Hospitals and only a few private hospitals in urban areas, gradually extended to smaller towns and now we can see them permeating to the villages and remote areas.

The Eye care activities received a fillip with the launching of the National Programme for Control of Blindness (NPCB) in 1976 with the avowed objective of mitigating Blindness by emphasizing the Right to Eyesight of all citizens. It is a 100% Centrally sponsored Programme aimed at reducing blindness to 0.3% by 2020. The main causes of blindness were identified as Cataract (62.6%), Refractive errors (19.7%), Glaucoma (5.8%), Posterior segment disorders (4.7%) and Corneal blindness (0.9%). Systematic strategies were outlined for control of blindness by co-ordinating governmental and non governmental initiatives. The backlog of blindness was sought to be reduced by identifying and treating the blind. The eye care facilities in every district were to be strengthened. Development of Human resources and steps to improve the quality of service delivery by upgrading infrastructure facilities received utmost attention. Particular care was taken to rope in the participation of Voluntary Organisations in Eye care activities. Liberal Grants were provided for these organizations for strengthening or expansion of Eye care units in rural and tribal areas. Eye Banks and Mobile Eye units in government or Voluntary sector were financially supported. All these measures yielded good results as can be seen by the reported number of Cataract surgery alone in 2013-'14 at 1,25,000.

From the late '70s Screening Eye Camps have become a regular feature. These camps reach out to the remotest areas of the state to provide eye care to the poor and needy. At the least, they help to identify the cataract cases which can be operated upon at the base hospital. In this context the co-operation of the general public in organizing and conducting these camps is worth mentioning. Similarly School screening camps have helped in no small measure to reduce the incidence of childhood blindness from Refractive errors, Squint, Amblyopia and Congenital diseases to a considerable extent.

What Does the Future Portend?
While speciality eye services like Retina, Glaucoma, Cornea and Refractive procedures are provided in urban areas, Basic Eye Care in a rural setup tends to get neglected. This could be seen reflected in the higher concentration of Ophthalmologists – the large majority of the 1700 odd of them- in the cities while smaller numbers only are seen in the peripheral areas. This, indeed, is a cause for concern to us and should be taken up at Government level. A package of incentives like better equipped Eye departments, opportunities for higher studies and training, better emoluments and physical facilities may yield positive results. A counterpoint could be that Kerala is a large metropolis and Ophthalmic service is available within only a few kilometers from such areas. Perhaps this is only a stage in development. With passage of time, say in another 20 years, things will improve and we will see Basic Eye care delivery better in those under-served areas.

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Optic Pit Maculopathy: A Review of Literature and Suggested Treatment Algorithm

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Introduction

Optic disc pits (ODP) are congenital excavations of optic nerve head, usually seen in association with other abnormalities of the optic nerve and peripapillary retina. These pits are caused due to faulty closure of embryonic fissure that extends along the inferior aspect of the globe which also results in diversity of other cavitatory disc lesions.

Furthermore, histopathological examinations demonstrate similarities between ODP, morning glory syndrome and typical coloboma; suggesting these cavitatory disc anomalies probably represent a spectrum of disease. In each case dysplastic retina is herniated posteriorly through a defect in lamina cribrosa and/or juxtapapillary area, ranging from a focal defect in ODP to a circumpapillary defect as seen in morning glory anomalies. On the other side, ocular and systemic associations with each anomaly often differ, which suggests that each anomaly is better considered as a distinct disease entity; probably molecular genetics in the future may help us answer this intriguing question.

ODP was described for the first time by Weith in 1882 in a 62-year-old woman. They occur in 1 in <10,000 eyes, although there is considerable variance among studies and are bilateral in 10 to 15% of cases, approximately two third of patients with ODP develop serous macular detachment. These may occur during childhood or later in life but most common between age group of 20 and 40.

ODP are usually located in temporal side of the disc in 70% of cases and 20% are situated centrally; the remaining found inferiorly, superiorly, and nasally. Central ODP behave differently from temporal pits. They are full thickness defects in lamina cribrosa centre with no serous retinal detachment or herniation of neural tissue and they do not develop maculopathy. Moreover, majority of disc with central ODPs are found to have glaucoma with gaucomatous neuroretinal thinning, RNFL loss and corresponding field defects.

ODP are reported to have presented with other ocular and systemic associations in few isolated case reports. Co-existence of keratoconus, papilledema, and disc coloboma are reported in the literature. Acquired ODP in myopia has been reported and the eyes with ODP are more myopic, have significant larger axial length, larger optic discs than highly myopic eyes without pits. Mechanical expansion of papillary region was thought to be primary cause of ODP in these cases.

Although spontaneous resolution of maculopathy has been reported, most eyes with ODP associated with macular detachment have poor visual prognosis if left for its natural course. Cystic retinal degeneration, macular hole formation and retinal pigment epithelial atrophy often limits visual recovery in these cases. However, there are reports that ODP associated maculopathy remains stable for a long time, Jonathan et al reported six patients with pit maculopathy having vision > 20/200 observed on presentation and remained unchanged at an average follow-up of 19.5 months.

Pathomechanism of maculopathy

Role of Vitreous traction:

In many case series, maculopathy was treated successfully by standard vitrectomy with or without ILM peeling claiming equal surgical outcomes. The role of laser in cases undergoing vitrectomy is less, suggesting PVD induction with vitrectomy is essential step to flatten the macula. These clinical based evidences stress the importance of transverse and antero-posterior traction exertion by vitreous as main pathogenic event.

Vitreous fluid is speculated source of fluid implicated in ODP maculopathy. John et al studied optic pit architecture using scanning laser microscope and serial histopathological sections. They found holes in the diaphanous membrane overlying the disc at the edge of the pit and believe that...
these membranous defects provide access for passage of vitreous fluid into adjacent neurosensory retina.

Brown et al.20 conducted experimentation on collie dogs injecting Indian ink into vitreous cavity and observing it in subretinal space. Intracranial migration of silicon oil,21 subretinal migration of gas bubble22 from vitreous cavity suggests indirect evidence of connection between vitreous cavity and subretinal space and vitreous as a source of fluid. Successful attempt to endoaspirate the subretinal fluid at the optic disc site intraoperatively in many cases16,23,24 also suggests the communication between subretinal fluid and the pit.

On the contrary, many critical reviews of optical coherence tomography (OCT) images in the ODP failed to show any vitreous traction causing tenting of the macula or traction over the disc.16,25,26,27 Development of maculopathy in young children long before the development of partial PVD and traction also remains unanswered28 if the vitreous theory holds true.

Role of Cerebrospinal Fluid (CSF): Irvine29 and Gass30 suggested CSF may leak from the optic nerve arachnoid space into ODP and eventually into intra and subretinal space. However, intrathecal injection of dye failed to demonstrate any connection in experimental animals.20 However in a recent analytical study by Nieraj et al.31 the author postulated the role of translaminar pressure in causation of ODP maculopathy. The dynamic translaminar (intraocular - intracranial) pressure gradient fluctuates throughout the day and sometime becomes large enough to drive the CSF into pit and by repeated small aliquots of fluid driven into retinal stroma causes progressive schisis like retinal edema. Fluid ejected from the pit sac in a given eye could be liquid vitreous, CSF, or even a mixture of the two fluids.

Clinical presentation: Optic pits are usually incidental findings on fundus examination and remain asymptomatic unless complicated by macular lesions such as edema, schisis or serous detachment. A patient with macular involvement generally presents with visual acuity of worse than 20/70 in the affected eye, and 80 percent of these eyes lose visual acuity to 20/200 or worse.14 It has been suggested that these patients have a greater propensity to develop normal/high tension glaucoma,33-38 although the arcuate visual field defects may be caused by the optic pit itself rather than by glaucomatous damage.

Morphology of the optic pit: Congenital pits of the optic nerve head vary in size, shape, depth and location. They appear as small, hypopigmented, greyish, oval or round excavated depressions in the optic nerve head. They are usually about 500 μm in size and may be bilateral in 10 to 15 percent of cases. Optic pits are most commonly located on the temporal side of the optic disc, but they may be situated centrally or anywhere along the margin of the optic disc.8

Macular changes: Optic pits along the rim of the optic disc are most likely to lead to serous detachments of the retina, with associated full-thickness or laminar retinal holes, retinal pigment epithelium mottling and general cystic changes. The retinal detachments are usually confined between the superior and inferior vascular arcades and are contiguous with the optic disc, sometimes through a visible isthmus of subretinal fluid. The elevated retina contains cystic cavities in the outer plexiform layer. The symptomatic maculopathy is most commonly seen at age around 30 years; probably the age related vitreous changes may have a role.

Optical coherence tomography: OCT of an optic pit usually shows a schisis like separation between the inner and outer retina and a larger retinal detachment.

Visual field testing: Optic pits may be associated with visual field changes, which can be due to one or both of the following mechanisms.36

- An optic pit, especially if large, may displace nerve fibers to produce an arcuate scotoma or may lead to an enlarged blind spot.
- Associated serous macular detachment may manifest as metamorphopsia or blurred vision, and visual fields may demonstrate central scotoma. However, unlike degenerative or reticular retinoschisis, there is no absolute scotoma in optic pit maculopathy.

Fluorescein angiography: Fluorescein angiography is usually unremarkable in cases of optic pit.37 There is no dye accumulation in the area of the serous detachment, although there may be late hyperfluorescence of the optic pit. It has been suggested that vitreopapillary traction in this area may cause leakage from optic disc blood vessels.8, 18, 38

Electrophysiological testing: An electroretinogram (ERG) may show poorly defined and low-amplitude waveforms, consistent with schisis and serous detachment. Preoperative evaluation of macular function is important for predicting the likelihood of central vision recovery after successful macular reattachment but cannot be used alone as prognostic
Patients with a poor ERG response are less likely to experience visual acuity improvement even after anatomical reattachment.

**Structural alterations in Optic pit maculopathy based OCT:**

Bilaminar model: Lincoff et al in pre-OCT era proposed a bilaminar structure in which retinal elevation that communicates with ODP is frequently a schisis like separation of intraretinal layers of retina and separation of outer layers of retina is secondary phenomenon that starts in macula. Separate case series by Rutledge et al, Krivoy et al and Akito Hirakata et al have supported this bilaminar model using OCT.

**Fluid movement:** The recent studies showed wide variation and different architecture of maculopathy contradicting bilaminar model. Immamura et al in his series of 17 patients, characterised the architecture using high resolution OCT concluding that the fluid from pit can go directly to the subretinal internal limiting membrane space, ganglion cell layer, inner nuclear layer, outer nuclear layer or subretinal space.

Similar recent study including 32 eyes, author opine that collection of fluid in ORL is the first step in optic pit maculopathy and explained the possible movements of fluid. Fluid from outer retinal layers could follow bidirectional seepage either into subretinal space or through inner retinal layers into subretinal space or just into inner retinal layers with no involvement of subretinal space.

Gaurav sangli et al opine that intraretinal fluid may split any of the inner and outer retinal layers suggesting bilaminar structure proposed by lincoff may not be appropriate. An outer layer hole could be demonstrated in 73% of cases with schisis and OLD (outer layer detachment) suggesting origin of SRF could be an extension of fluid from schisis like cavities into subretinal space.

**Disc in Optic pit is crowded; should present with Glaucoma and not maculopathy?**

Anton et al studied the planimetry in 23 patients with optic pit and compared with age matched controls and found optic pit patients have generally bigger areas in their optic nerve heads compared to normals of their age group. Also they have thicker RNFL thus making the glaucoma susceptibility akin to normal population.

**Management:**

Patients with asymptomatic optic pits need regular monitoring for the onset of any macular involvement. The management of optic pits with associated macular involvement is not well defined; various treatment modalities have been tried with variable success. Less-invasive treatments like laser photocoagulation should be tried initially, followed by a combination of vitrectomy, complete posterior vitreous detachment (PVD) induction and internal gas tamponade if symptoms persist.

When the optic pit is asymptomatic, the patient should be advised about the importance of regular comprehensive eye exams, including dilated retinal evaluations and threshold visual fields. Patients should be educated about the use of home visual acuity assessment and Amsler grid testing to monitor for the onset of maculopathy. They should be made aware of the signs and symptoms (e.g., blurred vision and metamorphopsia) of macular complications.

**Laser photocoagulation**

This is used to produce one or several rows of laser burns between the area of the serous retinal detachment and the optic disc. The objective is to achieve a very light white laser burn with little collateral damage to the nerve fiber layer. This presumably creates a wall of scar tissue to block the passage of fluid from the optic pit to the inner retinal schisis cavity and subretinal space (although the scarring may also involve peripapillary retinal tissue). While studies have reported successful resolution of the serous detachment in eyes that have been treated with photocoagulation, this does not always translate into improved final visual outcome.

Laser treatment alone had very poor results in previous studies that led to use of lasers as additional procedure to improve the post-op outcomes before or after standard vitrectomy. Most authors used Argon blue green laser, green 532nm, red or infrared lasers and none of them noted any significant field defects except enlarged blind spot in few.

Lincoff theorized that primary communication with ODP is inner layers of retina. However laser energy primarily absorbed by RPE and choroid may account for overall low success rate. OCT imaging has clarified that laser photocoagulation alone is typically ineffective because it fails to produce a barrier to intraretinal fluid migration.

**Pneumatic displacement with or without vitrectomy**

The principle of surgery is to place a large air gas bubble in the vitreous cavity that will dry and compress the retinal layers in the juxta papillary area and facilitates displacement of OLD. Lincoff et al studied C3F8 gas tamponade in 3 of his patients. 2/3 had reappearance of OLD which was
confirmed by OCT at 1 month and 5th year; 3rd case had no improvement from the beginning. Author opines that the effect is temporary because the reservoir created by gas displacement flattens and closes with time while from disc pit remains constant.

Justice et al\textsuperscript{23} reported case of vitrectomy and endodrainage of intraretinal fluid causing flattening of schisis which maintained well during post-operative period without tamponade and face down position. Similar studies have shown ineffectiveness of tamponade to flatten the elevation in cases which had already developed PVD.\textsuperscript{48} In contrast, gas tamponade successfully flattened macula which had previous vitrectomy with non-resolving macular elevation.\textsuperscript{49}

Alute Hirakata\textsuperscript{17} observed persistent subretinal fluid in patients who had undergone vitrectomy with tamponade for long time post-operatively. Eventually the fluid resolved long after disappearance of gas tamponade doubting its actual role and suggested not to contemplate additional surgical procedure too early for macular attachment. Hideo et al\textsuperscript{50} used 0.3\% SF\textsubscript{6} in his 8 Japanese patients. Four out of eight cases had complete resolution and none of them had recurrence but remaining 4 were managed subsequently with vitrectomy and ILM peeling. He observed that eye may require upto 1 year to reattach. He recommends that the patients should be treated initially with intravitreal gas.

**Vitrectomy with adjuncts**

Vitreous traction is believed possibly to induce a small tear in diaphanous tissue overlying disc, additionally vitreous traction on peripapillary retina and/or macula is thought of having the potential to facilitate accumulation of fluid in the macula.

This assumption was clinically proved in large case series where vitrectomy with Posterior vitreous detachment resulted in resolution of maculopathy in majority of cases.\textsuperscript{17,18,43}

Supporting above theory, Bonnet\textsuperscript{18} found no clinical evidence of PVD in all 25 cases and 2 of the 4 untreated eyes that exhibited spontaneous retinal reattachment later developed PVD.

Pars plana vitrectomy with tamponading without laser or ILM peeling resulted in complete resolution in 10/11 cases but it took long time for visual recovery implying vitrectomy has major role than short living tamponade in flattening the macula.\textsuperscript{17} Recently, the trend towards vitrectomy with additional procedures is gaining wide acceptance in managing pits with good outcomes. Importance of ILM peeling as an additional step to eliminate tangential traction for good surgical success has been suggested by few case series.\textsuperscript{16,51,52}

Wisdom of peeling ILM over extremely thin retina ending in full thickness macular hole has been questioned by few and have argued that vitrectomy along with tamponade alone had shown good results. Shukla et al\textsuperscript{16} had 4 cases of full thickness macular hole out of 7 which had vitrectomy with ILM peeling, among which 3 holes closed completely during post-operative period. The author observed that the final visual acuity appeared unaffected by the macular hole in entire group (mean BCVA 20/30 and 20/25 respectively) in eyes with or without macular hole. On other side, macular hole which developed postvitrectomy was successfully treated with revision surgery involving ILM peeling and tamponade.\textsuperscript{17}

**Additional procedures**

In a case report by Richard et al,\textsuperscript{15} partial thickness fenestrations were made over schitic retina adjacent and temporal to pit which created alternate outflow path for SRF. He suggested that the redirection of flow seems to offer a rationale alternative to block passage of fluid through tamponade or laser irrespective of the origin of SRF.

Makoto inoue et al\textsuperscript{53} noted glial tissue over optic disc intraoperatively and that the glial tissue might have developed after continuous vitreous traction attached to the ODP. Mechanical separation of the posterior hyaloid may relieve anteroposterior forces on the peripapillary retina, over that removal of condensed vitreous and glial tissue may remove additional traction on the retina around or within the pit. However, Gregory et al\textsuperscript{25} observed two of the three cases where vitreous was separated but fibrous tissue was not peeled from the pit; OCT imaging showed complete resolution of the retinal detachment at the most recent follow-up visit.

Endodrainage of SRF has been tried intraoperatively resulting in flattening of macular elevation which was later stabilised with\textsuperscript{16} or without tamponade.\textsuperscript{23} The endodrainage is not an essential step when combining laser and tamponade and its effectiveness for long term is not known. Drainage retinotomies\textsuperscript{54} temporal to macula without post-op complications have also been reported previously.

**Conclusion**

Maculopathy caused by optic pits has an overall poor prognosis, and long-term studies involving large groups of these patients are lacking. Given that the exact pathophysiology is still a matter of debate, management
Case studies

Case 1: A 25-year-old male came for routine check-up. VA was OU 6/6. Examination showed disc with pit but no maculopathy (Fig 1a&1b).

Highlights:
1. Despite large pit there was no macular changes
2. Maculopathy is unrelated to size of pit

Case 2: A 37-year-old male presented with sudden loss of vision in the left eye since 3 months (Fig-2a&2b). VA was 6/36, N36. He gives past h/o laser treatment in OS. He was advised Pneumatic displacement.

After intravit C3F8 injection, post operatively (Fig-2c) the fluid reduced but the Vision was 6/36, N18.

Highlights:
5. Nearly 1/4th of the eyes with macular involvement have outer lamellar hole
6. Progressive reduction of vision despite laser and OCT progression are indications of other interventions.
7. There may be slight or no improvement in Vision after pneumatic displacement. However, in this case there was an improvement of near vision.

Case 3: A 19-year-old male presented with sudden loss of vision in the right eye since 3 months. VA was 6/36, N12 (Fig 3a). He underwent laser to the margins of pit. After 2 months he was symptomatically better, VA improved to 6/12, N8 (Fig3b).

Highlights:
8. Treatment of laser alone is effective in selected group of patients.
9. Though there may be improvement in Vision and OCT characteristics, still OCT changes of maculopathy may persist.

**Case 4:** A 31-year-old male presented with sudden loss of vision in the left eye since 1 months (Fig 4a). VA was 2/60, <N36. He underwent Vit + ILM peeling + Glial tissue removal + endoaspirate + EL(diode) + C3F8. Post operatively (Fig 4b) after 2 months vision improved to 3/60, N36.

**Highlights:**
- Fibrous traction over the disc pit requires vitreoretinal intervention.
- Poor vision and large NSD are indications of vitreoretinal surgery.
- There is a high risk of postoperative macularhole formation especially if there is presence of inner layer schisis.

**Fig 4a:** Pre-operative OCT images showing traction at the disc (Right image) and Elevated retina with thinned inner & outer layers (left image).

**Fig 4b:** Post-operative OCT images showing Relief of traction at the disc(right image) and Full thickness macular hole at fovea (left image).

**Suggested treatment algorithm for optic pit maculopathy:**

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Optic pit maculopathy

Vn better than 6/60
- Vision stable for last 6 months
  - Observation
- No/Min NSD: Laser alone or laser with Pneumatic displacement

Vn less than 6/60
- Vision stable for last 6 months
  - Observation: If changes of chronicity Laser alone or with Pneumatic displacement
  - Vitrectomy with/without ILM peel and Gas inj
- H/o recent loss of Vn
  - High NSD: Pneumatic displacement/Vit with/without ILM peel laser
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References


Amniotic Membrane Transplantation

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Introduction
Amniotic membrane (AM) is the innermost layer of the fetal membranes. It has a stromal matrix, a thick collagen layer, and an overlying basement membrane with a single layer of epithelium. In the field of ophthalmology, amniotic membrane transplantation was initially used in the 1940s for conjunctival defects. De Roëtth reported the first use of amniotic membrane in ophthalmology for symblepharon correction and Sorsby used amniotic membrane as a biological bandage in the treatment of caustic burns to the eye. In 1995, Kim and Tseng reintroduced the use of amniotic membrane in an experimental model of chemical injury. Since then, amniotic membrane transplantation (AMT) has been used in the treatment of several ocular surface diseases, such as cicatricial keratoconjunctivitis (Stevens–Johnson syndrome [SJS], ocular cicatricial pemphigoid [OCP], and ocular burn), corneal epithelial defect, recurrent pterygium, and symblepharon.

Anatomy
The amnion of the human placenta varies in thickness from 0.02 mm to 0.5 mm in thickness. It contains no blood vessels and has no direct blood supply. Bourne described the amnion as consisting of five layers from within outward: (a) epithelium; (b) basement membrane; (c) compact layer; (d) fibroblast layer; and (e) spongy layer. The epithelial layer consists of a single layer of amniotic membrane epithelium. These cells are polygonal in shape and vary from columnar over the placenta to cuboidal or flat away from the placenta. The basement membrane is a thin layer composed of reticular fibers. It is closely adherent to the amniotic epithelium from which multiple processes interdigitate into it. The compact layer is a dense layer almost totally devoid of cells and consists mainly of a complex reticular network. The fibroblastic layer is the thickest layer of the amnion and consists of fibroblasts embedded in a loose network of reticulum. The outermost spongy layer forms the interface between the amnion and chorion and consists of wavy bundles of reticulum bathed in mucin.

Method of preparation
Human placentas are obtained from consenting mothers who undergo cesarean sections and are negative for hepatitis B and C, syphilis, and human immunodeficiency virus. These tests are mandatory and are carried out in the third trimester of pregnancy, as close to the date of cesarean section as possible. All the above tests, especially HIV, are repeated six months after delivery and the tissue used for surgery only if all tests, on both occasions, are negative or non-reactive.

Processing and preparation of the membrane is carried out under sterile conditions. Under a lamellar flow hood, the placenta is first washed free of blood clots with sterile saline. The inner amniotic membrane is separated from the rest of the chorion by blunt dissection (through the potential spaces between these two tissues), and rinsed in sterile saline (2 litres). Samples are taken for microbiology to assess sterility. An antibiotic cocktail to cover Gram-negative and Gram-positive bacteria and fungi is used in washing and storage solutions. In the method popularized by Tsuboto’s group wherein the membrane is cut into pieces measuring 10 cm × 10 cm and rinsed sequentially for five minutes in each of 0.5M dimethyl sulfoxide (DMSO) (4%w/v in 0.01M phosphate buffered saline PBS), 1.0M DMSO (8%w/v in 0.01M PBS), and 1.5M DMSO (12% w/v in 0.01M PBS). The second method was popularized by Kim and Tseng. The membranes are washed with phosphate-buffered saline containing 50 mg/ml penicillin, 50 mg/ml streptomycin, 100 mg/ml neomycin, and 2.5 mg/ml amphotericin. The amniotic membrane is flattened onto a sterilized nitrocellulose filter paper with the epithelial side up. The paper with the adherent membrane is then cut into pieces 3 × 3 and 4 × 4 cm. The HAM is then stored in 50% Dulbecco’s modified Eagle’s medium and 50% glycerol at -80°C. The membrane is defrosted immediately before use by warming the container to room temperature for 10 minutes, and rinsed three times in saline. Recently storage of amniotic membrane in sterile vials containing RPMI media at -80°C has been reported.
The tissue is stored frozen at -80°C. In UK it is released for use only after the second serological screening test, carried out six months after delivery. Tissue has been stored and used for up to 2 years post-delivery. Due to the risk of infection with HIV and hepatitis C, tissue transplantation laws in different countries require different protocols for preservation, testing, and storage. Several workers have used fresh membrane for clinical use. There may be some theoretical advantages of fresh membranes over preserved membranes. But the risk of HIV infection can be there despite seronegativity, due to the window period between infection and sero-conversion.

Properties of amniotic membrane

The amniotic membrane is a thin, semitransparent tissue from the inner part of the placenta. The amniotic membrane has a thick basement membrane and an avascular stromal matrix. The basement membrane facilitates migration of epithelial cells, reinforces adhesion of basal epithelial cells, and promotes epithelial differentiation. The basement membrane also plays a role in preventing epithelial apoptosis. Collectively, these are the possible actions by which the amniotic membrane permits rapid epithelialization. Amniotic membrane is also found to have anti-inflammatory and antiscarring effects. It reduces, cicatricial and angiogenic reactions, and seems to be immunologically inert.

Amniotic membrane has unique properties including antiadhesive effects, antibacterial effects, wound protection, pain reduction, and epithelialisation effects. Its antiadhesion property can be striking enough to cause severe symblepharon lysis completely. Amniotic membrane is composed mainly of a thick collagen layer and overlying basement membrane components including laminin and type IV collagen. The probable mechanism of this effect is contact of the unhealthy ocular surface with normal substrates; contact with healthy tissue induces an arrest in tissue proliferation. In addition, the amniotic membrane transplant may also function as an anatomical barrier to fibrous tissue proliferation.

The membrane, especially the epithelium, also produces various growth factors including basic fibroblast growth factor, hepatocyte growth factor, and transforming growth factor. Studies on human amniotic membrane preserved at -80°C for 1 month revealed the presence of EGF, TGFβ, KGF, HGF, bFGF, TGF-β1, and -β2 by RTPCR for the mRNA and by ELISA for the protein products. TGF-β3 and growth factor receptors KGFR and HGFR were also detected by RT-PCR. A higher level of various growth factors were found in amniotic membrane with epithelium than without epithelium indicating an epithelial origin for these growth factors. The epithelium of the amniotic membrane has been found to survive for up to 70 days after preservation. The growth factors may modulate the differentiation and proliferation of conjunctival and corneal cells. Its unique characteristics make the amniotic membrane a suitable material for treating subconjunctival fibrosis. It has been shown that amniotic membrane induces a downregulation of transforming growth factor signalling responsible for fibroblastic activation in wound healing. It causes reduced expression of TGFβ1, β-2, and β-3 isoforms in addition to reduced expression of TGF-Receptor II. This had the subsequent effect of preventing fibroblast activation into myofibroblasts. Tse ng et al maintain that this mechanism is primarily responsible for the anti-scarring properties of amniotic membrane. Similar results were found by Lee et al. when human conjunctival fibroblasts and pterygial fibroblasts were cultivated on the matrix side of amniotic membrane. In a study in rabbits, Choi and Tseng demonstrated that corneal epithelial cells induce differentiation of keratocytes into myofibroblasts and this effect could be prevented by placing amniotic membrane as a “barrier” between the epithelial sheet and corneal stroma/ keratocytes, both in vivo and in vitro.

The stromal matrix of the amniotic membrane excludes inflammatory cells, contains various forms of protease inhibitors and prevents myofibroblast differentiation of normal human corneal and limbal fibroblasts. Amniotic membrane was found to reduce inflammatory cell infiltration and loss of keratocytes and thereby reduced corneal haze in rabbit eyes undergoing excimer lasers. Hao et al identified the presence of mRNA for cytokines IL-1RA (receptor antagonist) and IL-10 in both amniotic epithelial and mesenchymal cells. These cytokines are potent inhibitors of inflammation. Shimmura et al showed trapping of inflammatory cells in the matrix of amniotic membrane. They also showed apoptosis of trapped inflammatory cells and suggested that this might explain some of the anti-inflammatory effects of amniotic membrane.

Hao et al, using the reverse transcriptase polymerase chain reaction, demonstrated messages for several anti-angiogenic chemicals like thrombospondin-1 and endostatin expressed by both amniotic epithelial and mesenchymal cells. In addition mRNA expression of all four tissue inhibitors of metalloproteases (TIMP-1, -2, -3 and -4) was demonstrated and these proteases are known to have a potent antiangiogenic effect. They suggest that these findings may explain the anti-angiogenic properties of amniotic membrane. In addition they suggest that the
anti-inflammatory properties of amniotic membranes further dampen the stimulus to angiogenesis.

Another unique characteristic of amniotic membrane is its lack of immunogenicity; the tissue does not express the usual major histocompatibility antigens—for example, HLA-A, B, or DR28. As a result, amniotic membrane does not induce immunological rejection after its transplantation. Antibacterial effects of both amnion and chorion have been demonstrated against a wide range of bacteria, including Hemolytic streptococcus group A, Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa29.

The amniotic membrane may promote nerve regeneration by maintaining nerve growth factor (NGF) signalling. The amniotic membrane contains a large amount of NGF, and preferentially maintains the NGF signalling system for human limbal epithelial cells in culture thereby causing healing of neurotrophic ulcers23.

Surgical methods
Amniotic membrane transplantation (AMT) is generally performed with peribulbar anaesthesia using 2% lidocaine. Bed for amniotic membrane is prepared by conjunctival peritomy and superficial keratectomy leaving the adherent epithelia intact30. Symblepharon release and fornix reconstruction is done in case of cicatricial ocular surface diseases. Amniotic membrane is peeled from the nitrocellulose paper and the membrane of the measured size is sutured to the corneal or conjunctival surface with the epithelial side up with interrupted 10-0 monofilament nylon radial sutures. The epithelial side of the amniotic membrane is determined by identifying the opposite side to which the chorion was attached. The orientation of the amniotic membrane is confirmed by touching a surgical sponge to the amniotic membrane—the “stickier” side being the stromal side and the less sticky side the basement membrane side31. Bandage contact lens is applied. In case of TLD, after the amniotic membrane and limbal transplantation, lateral tarsorrhaphy can be performed in the most severe cases to prevent desiccation30.

Postoperatively, topical antibiotic and steroid eyedrops are started with artificial tear supplements. On subsequent follow-ups, steroid medication is tapered, and the patient is continued on artificial tears. Bandage contact lens is removed after one month when all the sutures are removed32.

Patch or overlay Technique: One layer of AM is placed over the entire cornea and limbus. When used as a “patch” amniotic membrane will eventually fall off or is removed.

When used as a patch, epithelialization is expected to occur beneath the membrane, with the membrane acting as a bandage.

Sandwich technique: the graft and patch techniques are combined33. Sutureless amniotic membrane transplantation has been performed using fibrin glue in various conditions like partial LSCD34, corneal ulcers or perforations35,36, scleral melt37, conjunctivochalasis 38,39 and pterygium40. When sutures are used to secure the membrane to rabbit41 or human33 corneas, epithelialization may occur both over and under AM. It has been shown that in contrast to suturing, epithelial growth takes place only over AM when fibrin glue is used for central epithelial defects in rabbit corneas41. In the procedure using fibrin glue, the amniotic membrane is placed on the denuded ocular surface with the stromal side facing down. Half of the amniotic membrane is flipped to disclose the denuded surface. Both components of the fibrin glue are applied to this surface and the membrane is then flipped back. After waiting for five to 10 seconds, a muscle hook is used to spread the fibrin glue under AM. The same procedure is then applied to the other half of the membrane. The excessive membrane and fibrin gel are trimmed off to flush with the surrounding corneal, limbal, and conjunctival edges. The standard method of applying fibrin glue for fixing amniotic membrane has certain limitations. The membrane will bulge forward if it is not pressed into the glue clot within seconds and this is difficult to achieve because of the properties of the membrane. The short drying period of the glue does not allow sufficient time for a precise manipulation.
of the membrane, especially when used in the management of deep and uneven corneal ulceration. So another method is proposed by Uhlig et al. The corneal ulcer is cleaned and the components of fibrin glue are applied separately. Amniotic membranes are rotated through the fibrinogen component and subsequently into the site of the ulceration where thrombin is already applied. An overlay membrane is sutured additionally on top. They report that this application technique prevents development of foam and leads to a thin fibrin film, which minimizes any irregularities of the fixed membranes and creates extra time to adjust the membranes’ position.

Amniotic membrane may be used either to cover the cornea partially or completely, or to cover the bulbar and fornical conjunctiva or for total ocular surface cover.

Partial or subtotal corneal cover: The membrane may be used to partially cover the cornea when a small non-healing area is covered by a membrane of appropriate size and held in place with a few sutures. It is usually trimmed manually to a size and shape to fit the defect. Subtotal corneal cover is usually required in bullous keratopathy or when it is used as a graft in association with auto or allo-limbal transplant. Complete corneal cover: In large corneal epithelial defects or in association with limbal transplant operations, it may be necessary to suture the membrane 360° around the limbus to peritomized conjunctiva. It may act either as a patch or a graft depending on the state of the underlying corneal stroma once the fibrovascular membrane has been removed.

Bulbar and fornical or palpebral cover: In lid surgery and conjunctival surgery, especially after release of symblepharon or excision of pterygium, the membrane may be used as a patch or graft to cover areas of denuded sclera or episclera. In such situations it is usually applied as a graft. In fornix reconstruction, fornix-deepening sutures may need to be placed and tied on the skin surface over bolsters.

Total ocular surface cover: In severe ocular surface burns when extensive areas of the corneal and conjunctival epithelium have been destroyed, the membrane can be used to cover the entire ocular surface. A large patch of membrane is placed over the lids and with a blunt instrument such as a squint hook, the membrane is tucked into the fornices so that a double layer is formed, one covering the palpebral surface and one covering the bulbar surface and cornea. Fornix-deepening sutures are placed and tied on the skin over bolsters, superiorly, inferiorly, medially, and temporally. Excess membrane is then trimmed at the lid margin and the edge tacked to the lid margins.

The orientation of the membrane can be epithelial side up or epithelial side down or combined approach. When required as a substrate for migrating cells, that is, when used as a graft, the membrane has to be sewn in place with the basement membrane or epithelial side up. When the membrane is supplied, spread on a filter paper, the epithelial side is usually up, with the stromal side applied to the surface of the paper. The membrane is used with the epithelial side against the ocular surface when it is used as a biological bandage, primarily to contain the inflammatory reaction while epithelialisation is occurring beneath the membrane. The stromal side of the membrane traps inflammatory cells and induces apoptosis reducing inflammation. In the combined approach two membranes can be used, one epithelial side up and the other down. The inner membrane applied to the ocular surface is sutured with the epithelial side up, to act as a graft. The other, usually larger membrane is sutured on top of the first, with the stromal side up. The second membrane acts as a protective bandage for the first membrane and the cells growing on it. Dua et al modified this by overlapping the edges of the second membrane with the recessed and peritomized conjunctiva. The conjunctival edge is then tacked on to the membrane. This ensures that any centripetally migrating epithelium from the conjunctiva will grow on the second membrane and not on the corneal/first membrane surface (as can happen when the second membrane is not used). When only one membrane is used as a graft, the advancing conjunctival epithelium has to be sequentially scraped away until the corneal or amniotic graft surface is covered by limbus derived epithelial cells.

Multiple Layers: Multiple layers of amniotic membrane, stacked one on top of the other, can be used to fill in an area of corneal melt or thinning. The final layer is slightly larger...
as corneal epithelium covering only the superficial surface of the AM. This is the most common integration pattern.

Intrastromal Integration: The term intrastromal integration is used for cases in which AM stroma is surrounded by corneal stroma, without any contact with the corneal epithelium. This is observed only after multilayered AMT, the technique indicated for deep stromal lesions.

Superficial Localization (Disintegration): Superficial localization means lack of real integration; that is, the AM is attached to the corneal surface, but is not covered by any corneal tissue.

Although the integration process depends on many factors, the classification of integration patterns after AMT may be useful in understanding the fate of AM on (or in) the cornea in the context of different diseases, and may aid in choosing the most appropriate technique of AMT and (where necessary) the proper timing of PK after AMT.

The application technique of AMT seems to have a great impact on the morphology of AM integration. The surgical technique depends on the type and severity of ocular surface disease. In general, authors state that a patch disappears most often during the first 1 or 2 weeks after AMT without remnants, so it is preferred for central corneal lesions, especially shallow stromal defects, due to optical reasons. For peripheral lesions, graft AMT might be preferred. If layers of corneal epithelium grow between AM layers, they may help to integrate the AM into the cornea and to guarantee some degree of stabilization, especially in the presence of very deep ulcers or even descemetoceles. Using the sandwich technique, the patch is typically lost early after AMT (similar to single patch), but all layers of grafts may be integrated into the corneal stroma and stay there for many months, potentially reducing vision. Connon et al showed that amniotic membrane, once transplanted into the corneal stroma, can remain intact within the eye for many months postoperatively without being broken down or dissolved by the host tissue. They showed that its continued presence within the eye does not result in inflammation, rejection, or a loss of transparency and therefore, amniotic membrane is highly suitable for the surgical reconstruction of the corneal stroma.

Kruse et al found out using vital staining that no viable AM epithelial cells remain after cryopreservation. Resch et al found by TEM, that AM epithelial cells which are present in cryopreserved amniotic membrane, showed intracellular signs of degeneration. After transplanting fresh AM
immediately after preparation (without cryopreservation), a longer survival of the AM epithelium could be expected, but proliferation of AM epithelium does not seem to occur. Anderson et al. found calcification of the cornea in 12.8% of cases after graft AMT, but never after patch.

After amniotic membrane transplantation in limbal deficiency, successful ocular surface reconstruction is defined on the basis of corneal epithelialization, decrease in corneal neovascularization, and improvement in visual acuity. Corneal epithelialisation is based on 3 criteria: a clear appearance without epithelial defect on slit-lamp examination, the absence of abnormally high fluorescein permeability, and the absence of conjunctiva-derived goblet cells on impression cytology. If all 3 criteria are fulfilled, that is an indication that the epithelium is of corneal origin and that surgery has been successful.

Indications for amniotic membrane transplantation

Chemical injury

Several surgical techniques have been proposed for ocular surface reconstruction in chemical burn with limbal dysfunction. Simple excision of fibrous tissue and conventional keratoplasty are not sufficient to avoid recurrence of the fibrovascular pannus in severe cases. Success rates of ocular surface reconstruction with limbal allograft or autograft transplantation were reported to range from 70% to 90% during a follow-up of 2 years. However, a decrease in these rates to 50% was reported after a follow-up of 5 years, probably as a result of limbal graft failure caused by persistent perilimbal stromal inflammation. Amniotic membrane transplantation has been found to successfully reconstruct the ocular surface epithelia in eyes with chemical and thermal burns. Amniotic membrane seems to function as substrate, promoting proper epithelialization while suppressing excessive fibrosis. Repeat amniotic membrane transplantation may have to be performed in patients with chemical injuries. When there is severe conjunctival involvement, amniotic membrane transplantation with limbal autograft transplantation, appears to be effective. It is believed that amniotic membrane restores a noninflamed perilimbal stromal environment to support the transplanted limbal epithelial stem cells, which seems to increase the success of subsequent corneal surface reconstruction.

Acute stage

Ophthalmic interventions during the acute stage of chemical and thermal injury and acute Stevens-Johnson syndrome have traditionally been supportive in nature, like aggressive lubrication, prophylactic topical antibiotics, and lysis of adhesions. But these are not effective to improve the poor ophthalmic prognosis associated with this condition. Amniotic membrane has been used as a temporary patch graft in acute phase of chemical and thermal injury and acute Stevens-Johnson syndrome. Amniotic membrane transplantation is reported to enhance epithelialization, reduce inflammation, reduce scarring, improve visual acuity, and prevent the occurrence of conjunctivalization in such cases. In the majority of patients, the entire ocular surface, that is, the cornea, the bulbar and palpebral conjunctiva, and the eyelid margins, needs to be covered with amniotic membrane. During the procedure, the eyelids are retracted with a lid speculum and a sheet of cryopreserved amniotic membrane is placed on the ocular surface with the basement membrane side facing away from the corneal surface and secured to the corneal surface with sutures. A variable number of additional 10-0 nylon sutures are placed more posteriorly to the limbus to further secure the amniotic membrane to the bulbar conjunctival surface. A large-diameter bandage contact lens is then applied to the eye. Then lid speculum is removed. A second sheet of cryopreserved amniotic membrane is placed on the eyelid, again with the basement membrane side facing away from the corneal surface and secured to the corneal surface with sutures. A variable number of additional 10-0 nylon sutures are placed more posteriorly to the limbus to further secure the amniotic membrane to the bulbar conjunctival surface. A large-diameter bandage contact lens is then applied to the eye. Then lid speculum is removed. A second sheet of cryopreserved amniotic membrane is placed on the eyelid, again with the basement membrane side facing away from the corneal surface. One end of the sheet of amniotic membrane is sutured to the eyelid skin, close to the eyelid margin. A muscle hook is then used to push the amniotic membrane into the fornix. Two double-armed 5-0 or 6-0 prolene sutures are then passed through the amniotic membrane, passed through the eyelid, and then secured over the skin with a bolster. The same procedure has to be performed for both upper and lower eyelids. Amniotic membrane coverage of the ocular surface in its entirety coupled with the use of intensive short-term topical corticosteroids during the acute phase of SJS and TEN is associated with the preservation of good visual acuity and an intact ocular surface. Partial amniotic membrane coverage of the ocular surface may not serve to minimize the cicatrizing ocular sequelae of SJS and TEN as effectively as complete coverage.
In a study evaluating the efficacy of AMT for treating moderate to severe ocular burns in the acute stage, Meller et al. showed that AMT can be considered an early, if not immediate, surgical procedure to promote epithelialisation and suppress inflammation so that scarring-induced sequelae can be prevented in the chronic stage. Amniotic membrane transplantation rapidly restores the ocular surface, especially in mild to moderate (grades II and III) chemical or thermal burns. In severe (grade IV) burns, AMT alone reduces limbal stromal inflammation, restores the conjunctival surface, and prevents symblepharon formation, but cannot prevent the development of limbal stem cell deficiency. The latter requires additional stem cell transplantation to restore the corneal surface integrity.

Persistent inflammation with leukocyte infiltration, a key characteristic of acute burns, is known to prevent epithelialization and contribute to the melting process in the acute stage and to formation of granuloma and scar in the chronic stage, also leads to limbal stem cell deficiency in humans and failure of autologous limbal conjunctival transplantation in rabbits. Without effective measures to suppress inflammation in the acute stage, the remaining population of the epithelial stem cells declines, paving a difficult way to recovery. Furthermore, leukocyte infiltration comes in two waves in burns, the first within 12 to 24 hours and the second starting at day 7; the first wave is crucial for the recruitment of the second. Thus AMT performed at the early stage may help suppress the gradual recruitment of more inflammatory infiltration, and collectively may shorten the duration and extent of inflammation further. The action of AM to suppress acute inflammation alone may not explain its entire efficacy because various medical therapies to suppress acute inflammation had limited success. Early epithelial replacement has been regarded as essential in the management of ocular burns. AMT is an effective surgical measure to promote epithelialization and to restore normal epithelial phenotype by expanding the remaining epithelial stem cells. For epithelialization to take place on its basement membrane side, the basement membrane of AM may be substituted for the damaged basement membrane of the normal conjunctiva. One other important action of AM is to help preserve and expand the slow-cycling property of the epithelial progenitor cells. Scarring in the lid margin causing cicatricial entropion and inward turning of lashes, and symblepharon, which obliterates the formation of tear meniscus and interferes with eyelid blinking, generate a vicious cycle leading to more ocular surface failure in the chronic stage and present difficulties for subsequent ocular surface reconstruction. Amniotic membrane prevent scarring directly and indirectly by reducing inflammation. Low incidence of symblepharon formation is noted when AMT is performed in the acute stage, a finding also noted by Sorsby and colleagues.

**Limbal stem cell deficiency**

Dysfunction of the stem cells of the corneal epithelium is identified by the presence in the central cornea of goblet cells derived from the conjunctiva (“conjunctivalization”), persistent epithelial defects or completely keratinized epithelium accompanied by an absence of palisades of Vogt. Partial limbal deficiency [PLD], can be treated with AMT alone. Total limbal deficiency [TLD] requires AMT and conjunctival and limbal stem cell transplantation. This results in complete epithelialisation and reduced inflammation and vascularization of the ocular surface. Amniotic membrane transplantation expands remaining limbal stem cells and corneal transient amplifying cells during the treatment of partial limbal deficiency. However, this specific action is not effective when there are no stem cells, and then limbal stem cells needs to be transplanted. Amniotic membrane has been safely used to inhibit neovascularization before limbal stem cell transplantation. It is believed that the amniotic membrane restores a noninflamed perilimbal stromal environment to support the transplanted limbal epithelial stem cells, which seems to increase the success of subsequent corneal surface reconstruction. AM transplantation using fibrin glue appears to be a safe and effective method of restoring a stable corneal epithelium for cases with partial LSCD.

Santos et al. showed that conjunctival limbal grafts associated with AMT are useful for restoring corneal epithelium phenotype in eyes with total limbal stem cell deficiency. However, the cumulative survival declined substantially over a 2-year period. Dry eye was found to be the most important prognostic parameter.

**Pterygium**

Shimazaki et al. reported that the combination of an amniotic membrane transplant to inhibit subconjunctival fibrosis, and a limbal autograft to restore limbal function is an effective surgical procedure for treating patients with...
Ang et al\textsuperscript{14} studied the efficacy of autologous cultivated tissue at the limbal region. Conjunctival autograft health may be demonstrated by early graft vascularization and perfusion; however, there is a delay in graft vascularization after AMT that may be related to the antiangiogenic effects of the membrane. In a study by KUÇÜK ERDÖNMEZ et al\textsuperscript{52}, in contrast with the early vascularization of the conjunctival autografts, there was no vascularisation in the AMT group, and the grafts remained avascular, showing hypofluorescence during ICGA one month after surgery. Except for the underlying vascular network of the episcleral bed, the grafts showed no hyperfluorescence or isofluorescence as a sign of reperfusion, as is seen in conjunctival autografts. This study results seems to support the barrier phenomenon suggested by Tananuvat and Martin \textsuperscript{53} in AMT, which could be demonstrated as a lack of vascularization from host tissue at the limbal region.

Ang et al\textsuperscript{14} studied the efficacy of autologous cultivated conjunctival epithelial sheet in the management of pterygium. Conjunctival biopsy was done from the eye with pterygium 2 weeks prior to surgery and exvivo expansion of these conjunctival epithelial cells was done over amniotic membrane. They reported that transplantation of autologous cultivated conjunctival epithelial sheet facilitated early postoperative epithelialization and recovery, and may aid in preventing serious complications associated with simple denuded HAM transplantation, such as scleral necrosis and secondary infection.

**Persistent epithelial defect**

Treatment of persistent epithelial defects consists of correction of the underlying cause and tissue lubrication. In cases refractory to medical treatment several options can be considered, including AMT. Lee and Tseng\textsuperscript{4} used amniotic membrane to treat persistent epithelial defects. AMT is useful in patients with persistent epithelial defects, although most cases require further surgery for visual and ocular surface rehabilitation\textsuperscript{5}.

**Severe corneal and scleral ulcers**

Azuara-Blanco et al\textsuperscript{5}, in a study of eyes with severe ulceration and impending perforation found that AMT failed to stabilise the cornea, and additional urgent tectonic procedure had to be undertaken, but they had used AMT as a patch and not as a graft. In case of graft, as proposed by Lee and Tseng\textsuperscript{4}, epithelialisation occurs over the membrane, which is incorporated into the corneal tissue. This alternative might be more helpful to build up the corneal thickness and to provide a healthy substrate in cases of severe ulceration and impending or recent perforation.

In a study by Hanada et al\textsuperscript{50}, amniotic membrane transplantation was done for severe corneal ulcers with perforation or descemetocele and scleral ulcers. In the surgical method they have described, first, the bottom of the ulcer is debrided, and poorly attached epithelium at the edge of the ulcer is removed as bluntly as possible. After the ulcer surface is treated and healthy corneal or scleral stroma is exposed, the first segment of amniotic membrane is transplanted as filling material in the stromal layer (amniotic membrane filling). The amniotic membrane is cut into small pieces and stuffed into the ulcer. In the scleral ulcer cases, the ulcer is filled with autotenon’s capsule tissue. The second amniotic membrane is transplanted as a basement membrane (amniotic membrane graft) with epithelial side up and the third amniotic membrane is transplanted as a cover (amniotic membrane patch). The amniotic membrane patch is placed on the entire wound and corneal limbus with epithelial side up to protect the area of re-epithelialization. They used multilayered amniotic membrane transplantation to achieve the following goals. Amniotic membrane filling provides a substitute for collagens, the amniotic membrane graft provides basement membrane for proper epithelialization, and the amniotic membrane patch protects the wound. In their study eight out of 11 eyes (72.7%) were successfully treated by this method with a mean epithelialization period of 16.5 ± 8.0 days.

**Neurotrophic ulcers**

Interruption of the corneally derived sensory afferent nerve anywhere along its course of V1 may result in a disease state termed neurotrophic keratopathy, which is characterised by corneal anaesthesia and epithelial breakdowns leading to persistent and progressive neurotrophic ulcers. Common causes of neurotrophic keratopathy include herpetic infection (simplex or zoster), alkali burn, diabetes mellitus, tumours affecting the trigeminal ganglion or sensory routes, radiation, and anterior segment surgeries. Chen et al\textsuperscript{23} did a study of amniotic membrane transplantation in severe neurotrophic ulcers. Amniotic membrane was fitted to fill up the ulcer and cover the defect by trimming off the excess edges. More than one layer of amniotic membrane was used if the ulcer was deep, and in those instances the bottom layers were left unsutured and only the top layer was sutured. Depending on the aqueous tear status and the eyelid blinking function, a bandage contact lens, amniotic membrane as a temporary patch, or temporary tarsorrhaphy was added. Amniotic membrane was used...
corneal epithelial defect. Yoshita et al. found that AM has corneal epithelium are important for treating persistent hydration of epithelium, and less external friction to fragile Baum proposed that sufficient oxygen supply, enough filtration surgery especially in trabeculectomies performed may occur as an early or late complication of glaucoma Leakage of aqueous humor from conjunctival filtering blebs Glaucoma mediated microtrauma, resembling therapeutic soft contact lens (TSCL) and tarsorrhaphy as speculated by Baum. Baum proposed that sufficient oxygen supply, enough hydration of epithelium, and less external friction to fragile corneal epithelium are important for treating persistent corneal epithelial defect. Yoshita et al. found that AM has a higher water content and a higher Dk than TSCL which helps explain why AM is also effective in treating persistent defects.

Glaucoma
Leakage of aqueous humor from conjunctival filtering blebs may occur as an early or late complication of glaucoma filtration surgery especially in trabeculectomies performed with 5 Fluorouracil or mitomycin c. Bleb leaks have been repaired successfully with bleb function maintained with amniotic membrane graft. The leaking area is covered by amniotic membrane graft without excision of the leaking bleb. This technique has several advantages. The membrane can be measured accurately to cover the cystic, leaking area, thereby eliminating the risk of developing a too small or tight flap. And because of the antimicrobial properties, amniotic membrane graft seems to have fewer risks of postoperative infection. Amniotic membrane graft enhances the healing of the bleb leaks while maintaining the bleb function, because of its strong epithelialisation effect. But in a study conducted by Budenz et al. where amniotic membrane transplant was compared with conjunctival advancement in patients with leaking glaucoma filtering blebs, they found that after an average follow-up of 19 months, there were seven failures in the amniotic membrane transplant group out of 15 eyes and there were no failures in conjunctival advancement group. The cumulative survival rate for amniotic membrane was 46% at 2 years whereas it was 100% for conjunctival advancement. This suggests that this material may not be a suitable substitute for conjunctiva in the repair of leaking filtering blebs.

Permanent repair of an extruding glaucoma drainage device (GDD) may be difficult to achieve in eyes with extensive conjunctival scarring from ocular surface disease or previous surgery such as scleral buckling. Donor sclera may melt if inadequately covered with conjunctiva, yet adequate mobilization may be hampered by the above factors. Failure to repair an exposed GDD may necessitate removal or risk endophthalmitis. Rai et al suggested that AMT may be used satisfactorily to cover donor sclera in eyes with an extruding GDD. Where extensive scarring or conjunctival shortening hampers closure, AMT acts as a scaffold for regrowth of conjunctival epithelium and after a period of time appears indistinguishable from other conjunctiva that has undergone surgery.

Symblepharon
The cause of cicatricial diseases includes Stevens-Johnson syndrome, chemical burn, chronic cicatricial conjunctivitis of unknown cause, multirecurrent pterygium, mucous membrane pemphigoid, pseudopemphigoid, multiple previous surgeries for lid tumours etc. Several reports showed that fornix reconstruction could be accomplished by AMT with or without intraoperative MMC. Keirkhah et al. studied surgical strategies for fornix reconstruction based on symblepharon severity. For grade I symblepharon where the residual and recessed conjunctiva was sufficient to cover the entire palpebral surface, and for grade II symblepharon where the residual and recessed conjunctiva was sufficient to cover the tarsal surface but not the entire palpebral surface, cicatrix lysis and AMT alone was successful. For grades III and IV symblepharons where the residual and recessed conjunctiva was not sufficient to cover the tarsal surface, the procedures of cicatrix lysis, AMT, and anchoring sutures were not as effective, but overall success increased to 100% if included with either oral mucosal graft or conjunctival autograft to the tarsus.

Bullous keratopathy
Amniotic membrane transplantation to the corneal surface has been reported as effective in reducing the formation of epithelial bullae and associated ocular discomfort in patients with painful aphakic bullous keratopathy and pseudophakic bullous keratopathy. Patients with intolerable pain preoperatively become pain-free postoperatively. However, regression of epithelial bullae and recurrence of pain and discomfort can occur depending on the use of different modifications of the AMT technique (inlay or overlay) or different side of AMT coming above. Recurrence of symptoms can also occur after dissolution of the AMT. The AMT is performed as inlay (or graft) or overlay (or patch) technique in most cases with bullous keratopathy. Graft allows the migrating epithelial cells to grow over the membrane, whereas the patch acts a biological contact lens protecting the healing surface beneath and as a barrier
to the chemical mediators in the tear film and reducing inflammation.

Various suturing techniques have been described for amniotic membrane in bullous keratopathy like suturing into peripheral cornea, suturing beneath conjunctival peritomy and a modified technique by Espana and associates where amniotic membrane is sutured into lamellar pockets. The modified technique may be more advantageous by providing a new basal membrane more resistant to bullae formation but it is recommended to leave the limbus out, so that re-epithelialization must be over and not under the AMT. This is in contrast to direct suturing of AM on the cornea, which may allow some epithelialization to take place under AM if the suturing method does not ensure tight approximation. Altiparmak et al reported a modification of Espana’s technique by creating more regular contours of the stromal pockets, using a corneal trephine and cutting the AM with a punch trephine to fit into this pocket. This is theoretically more advantageous by ensuring that epithelialization will take place on the top of AM.

Infectious keratitis

Amniotic membrane transplantation has been used successfully in infectious keratitis. Studies have shown that human AM transplantation promotes rapid epithelialization and reduces stromal inflammation and ulceration in herpes simplex virus (HSV)-1 keratitis. When used with antifungal agents as adjunctive treatment, AM transplantation can enhance epithelialization and prevent corneal perforation in acute fungal keratitis.

Kim et al did a study of amniotic membrane transplantation in infectious keratitis with causative organisms including Staphylococcus species, Pseudomonas species, Acanthamoeba species, fungus, and herpesvirus. Sufficient antibacterial, antifungal, or antiviral agents were applied to eradicate causative organisms before permanent or temporary amniotic membrane transplantation, or a combination of the two in few patients. The amniotic membrane was soaked in antinfective agents before transplantation in all cases. The corneal surface was healed successfully and recurrences of microbial infection were not noted in any case. Visual acuity was improved in cases that were nonscarring or after additional penetrating keratoplasty.

Gicquel et al did a study on patients with severe bacterial keratitis and reported immediate pain relief and epithelial healing that they attributed to early AM transplantation combined with topical corticosteroids. 12 patients with severe microscopically-proven BK were treated with immediate maximal topical antibiotics followed by AMT at 48 hours (single-layer epithelial side-down or multilayer epithelial side-up), plus topical steroid treatment at 72 hours. The organisms causing the keratitis included Pseudomonas aeruginosa, Klebsiella pneumoniae, Moraxella catarrhalis, Staphylococcus aureus, Staphylococcus epidermidis, and Streptococcus pneumoniae.

In an experimental study of staphylococcus aureus keratitis in rats by Barequet et al, the group treated with antibiotic drops and amniotic membrane transplantation was found to have the best clinical results compared to the groups treated with antibiotic drops alone and amniotic membrane transplantation alone. They reported that AM transplantation is a useful adjunctive treatment after bacterial keratitis. The transplanted AM improved the healing process, resulting in decreased corneal haze and less neovascularization.

Miscellaneous indications

Amniotic membrane has been used to cover bare sclera in oral mucous membrane grafting for total limbal stem cell deficiency and also to cover the mucous membrane graft. Ocular motility defects and diplopia are well recognized problems after operations to treat retinal detachment. The fat adherence syndrome plays a significant role in causing restriction. Conventional extraocular muscle surgery has shown only limited success. Yamada et al described an alternative treatment, the transplantation of amniotic membrane onto the extraocular muscle, to prevent regrowth of restrictive scar tissue. Here the therapeutic effects of amniotic membrane like suppression of recurrent subconjunctival fibrosis and lysis of symblepharon was utilised.

After resection of neoplasms like conjunctival melanoma, amniotic membrane can be used to replace the large conjunctival defect avoiding the need for extensive repair with a conjunctival or oral mucous membrane graft.

Ligneous conjunctivitis, a rare form of membranous conjunctivitis particularly resistant to treatment, is characterized by woodlike indurated membranes on the upper and lower tarsal conjunctiva. Barabino et al reported that amniotic membrane transplantation in ligneous conjunctivitis provides a favorable outcome.

In the treatment of large conjunctival defects that may follow strabismus surgery, Mocan and Azar reported the use of AMT. Conjunctival dehiscence is a potential complication of strabismus surgery. It can lead to exposure
of sclera and the recessed muscle. Previous surgeries of the conjunctiva make tissue manipulation difficult and increase the probability of conjunctival rips or uncontrolled tears. In the treatment of large conjunctival defects that may follow strabismus surgery, AMT may be an alternative to conservative management or primary conjunctival closure.

Conjunctivochalasis (cch), defined as a redundant, loose bulbar conjunctiva interposed between the globe and the eyelid, tends to affect both eyes of older populations. CCh is a common cause of ocular surface irritation and its clinical significance is often overlooked. No treatment is needed if patients with CCh remain asymptomatic. For symptomatic cases, medical therapies are directed to suppressing ocular surface inflammation, and when they fail, surgical removal of the redundant conjunctiva becomes necessary. Surgical technique usually includes excision of the bulbar conjunctiva or suture fixation of the conjunctiva to the sclera. Amniotic membrane transplantation (AMT) has been shown to be successful in reconstructing the conjunctival surface after removal of CCh. Previously, focal inflammation of host conjunctiva, scar formation, and suture-induced granuloma were noted in some cases, after AMT using sutures for CCh. Using fibrin glue, similar incidence of focal inflammation of host conjunctiva is noted only adjacent to the border of AM in the fornix.

Amniotic membrane can be used to reconstruct the ocular surface after excision of the invading granulation material typical of LOGIC syndrome (laryngeal and ocular granulation tissue in children from the Indian subcontinent). Moore et al reported a case where after 24 operations to treat the ocular complications induced by LOGIC syndrome, amniotic membrane transplantation was the first effective treatment. In the early follow up period (2-3 months), there was complete cessation of the proliferation of granulation tissue and reepithelialization of the corneal surface. Longer follow up (10 months) demonstrated limited recurrence, which required retreatment.

Complications and drawbacks
Despite the widespread use of amniotic membrane in ocular surgery, very few complications have been reported. The complications which are reported are suture granuloma and persistent inflammation, and these are not specific to the membrane. Gabler and Lohmann reported hypopyon after repeated amniotic membrane transplantation in a case of neurotrophic ulceration who developed a hypopyon 2 days after the second and again after the third amniotic membrane transplant. On both occasions it responded to topical steroids. The authors suggest that use of membrane from different donors (when required repeatedly) may help minimize the risk since it is likely to be an immune reaction. Accumulation of blood (hematoma formation) under the membrane in the immediate postoperative period or during suture removal has been reported.

Failure to achieve the intended effect with amniotic membrane is perhaps the most significant drawback. Another one important drawback is the loss of membrane, either by degradation or by cheese wiring of the sutures, in the immediate postoperative period. Another less significant undesirable effect is the residual subepithelial membrane that persists in some cases. According to Dua et al this is more likely to happen if the membrane used is from the relatively thicker portion of the amnion, near the umbilical cord. When this occurs in the visual axis, it can affect the visual acuity. Then there is the potential danger of spread of virus and bacteria. As membrane from a single donor can be used in several patients, a single donor can cause infection to multiple recipients. Adequate donor screening to cover the window period, proper handling, processing, and storage, and frequent microbiological tests on used and stored membranes should minimize this risk.

Recently, temporary amniotic membrane patching has successfully been used for acute chemical burns of corneas, a devastating and emergency condition in ocular surface management. In the acute phase of ocular burns, intraocular pressure (IOP) may increase significantly and should be monitored carefully. However, once amniotic membrane is patched onto the eye, measurement of IOP through the amniotic membrane becomes difficult using conventional methods, such as Goldmann applanation tonometer. The accuracy of IOP measurement by the Tono-
Pen XL over a single layer of amniotic membrane patching was demonstrated using rabbit eyes78. IOP by Noncontact Tonometer (NCT) was found to be reliable through a combination of a single-layer AM/TSCL(therapeutic soft contact lens) on normal human eyes. However, IOP measured by NCT over a combination of a double-layer AM/TSCL was inaccurate and tended to be an underestimation79.

**Modifications**

Cryopreserved AM requires some processing and the storage of cryopreserved AM requires space-consuming freezers. Furthermore, there is no reliable method of sterilizing the cryopreserved AM. To resolve these problems, a hyperdry AM was developed by Kitagawa et al80 that is processed using far-infrared rays and microwaves, then is sterilized by y-ray irradiation; it is capable of being stored at room temperature.

PROKERA is a device, in which a cryopreserved amniotic membrane is clipped into a dual polymethyl methacrylate ring set that acts like a symblepharon ring81. The conformer fits snugly over the cornea and under the eyelids. PROKERA is stored at -80 °C before use. After thawing at room temperature for five to 10 minutes, PROKERA is rinsed with physiological saline before insertion with the aid of an eye speculum and topical anaesthetic. PROKERA is found to affect visual functions in normal human eyes. Both distant and near visual acuities but not color vision deteriorated after insertion. Significant annoying symptoms were also noted after insertion of PROKERA, presumably owing to the contact of rigid polymethyl methacrylate skirt with the eye like a symblepharon ring. Such discomfort was not noticeable in eyes with neurotrophic conditions, and was markedly reduced by a softer skirt made of polycarbonate material. However, it is conceivable that a softer skirt may present some disadvantages, especially in cases that may benefit from a symblepharon ring.

Although some of the activity of amniotic membrane can be attributed to a mechanical effect of the basement membrane, the biologic role of amniotic epithelium is increasingly recognized. Parmar et al82 assessed the effect of tissue-cultured human amniotic epithelial cells (AECs) in restoring the ocular surface, transplanted using a collagen shield seeded with AECs supported by a soft contact lens. AECs were isolated from serologically screened donor human placenta, seeded onto collagen corneal shields, and incubated in tissue culture medium for 7 days. These collagen shields were placed over the persistent epithelial defect (PED) and supported by an overlying soft contact lens. The collagen shields dissolved by 72 hours, and the contact lenses were removed after this time. This cycle was repeated every week until healing of PED was achieved.

**Conclusion**

Amniotic membrane is a useful tool in many ocular surface diseases. But the success of the procedure differs in different patients. The efficacy of the procedure depends on a lot of factors like the severity of the ocular surface disorder, the technique used (patch or graft), the orientation of the membrane (epithelial or stromal side up), the suturing technique, inter and intra donor variations in the membrane and the depletion or alterations in its constituents subsequent to processing and storage. The exact mechanism of action of the membrane causing healing of the various surface disorders is still not clear and there is plenty of scope for future research. The risk of infection and the unpredictable results after the amniotic membrane transplantation has led to the search for a more standard synthetic membrane using collagen or polymer matrices impregnated with putative beneficial ingredients, such as growth factors and antimicrobials.

**References**


Genetic Counseling in Retinitis Pigmentosa

Dr. M. J. Denton Ph.D

About 50% of cases of RP belong to one of the three basic mendelian genetic types, establishing the family tree is an essential component of the clinical interview and work up of any new RP case. And the same applies to all the allied inherited retinal disorders. Determining the particular inheritance pattern of a patient's RP is an essential step in providing genetic counseling to the patient and his family so that they can be informed of the genetic risks associated with the particular genetic subtype in their family.

In the case of autosomal dominant(ad) RP a typical family tree is often obtained on interviewing the proband. However a typical pedigree may not be obtained because some affected individuals [ie carrying the RP gene] do not exhibit the RP phenotype either because of incomplete penetrance, or because of very late onset. The variable expression of many adRP genes makes diagnosing the disease from family tree analysis somewhat difficult.

Sibs of a proband: In adRP in which one of the parents has the disease (genotype G G*) the risk to sibs (brothers and sisters) of the affected is 50%. In other words each sib has a 50% chance of inheriting the mutant RP gene [G*] from the affected parent.

Children of a proband: Each child of a patient affected with adRP (ie having the genotype GG*) has a 50% chance of inheriting the disease gene and RP.

Note: Because of the variable expression of many adRP mutations the development of the disease may not follow the same course as in the case of the proband.

In the case of autosomal recessive(ar) RP the disease is only manifest in an individual when both copies of a particular autosomal RP gene are mutated or defective, ie when the patient has the genotype G*G* If an individual carries one defective RP gene (and the other is normal or wild type, G) the individual does not exhibit RP but is a carrier of the disease gene (genotype GG*). Each parent of the proband carries a single copy of the mutant RP gene and a single copy of the ‘wild type’ RP gene (GG*). Both parents are termed obligate heterozygotes.

Sibs of a proband: Each sib has a one in four chance (25%) of receiving two copies of the mutated RP gene (one copy from each of his parents and having the disease genotype GG*, and hence of developing the disease; a one in two chance (50%) chance of inheriting one defective gene and one good gene and being an asymptomatic carrier having genotype GG*, a one in four chance (25%) of receiving two wild type genes (one from each parent) and being unaffected and NOT a carrier having genotype GG.

Children of a proband: All children of an affected who has married a non affected are obligate carriers having genotype GG*. The sibs of obligate carriers (such as the proband’s parents i.e., his maternal or paternal uncles and aunts) have a 50% chance of also being obligate carriers (GG*).

In the case of arRP the counselor should point out that the chance of either the proband or his sibs having a child with RP is greatly increased by marrying a close relative. For estimates of risk involved in such marriages the proband should be referred to a genetic specialist. Where the proband is intending to marry an unrelated individual then the risk of having an affected child is greatly reduced.

In X-linked recessive(XL) RP the disease affects males who inherit a defective RP gene G* on their X chromosome they inherit from their mothers. Affected males pass on the defective X chromosomal gene, G*, to their daughters all of whom are obligate carriers. Female carriers have one copy of the good gene, G, on one of their X chromosomes and a copy of the defective gene G* on their other X chromosome (ie. genotype G G*). They are unaffected because the wild type RP gene, G, provides sufficient healthy gene product to ensure normal function . Any women in an established X linked RP pedigree who has an affected son is an obligate carrier having the bad gene, G*, on one of her X
chromosomes.

Sibs of proband: If there is a family history which implies that the mother is a carrier [genotype, GG*] then all female sibs of the proband have a 50% chance of inheriting the bad gene from their mother. Each brother of the proband has a 50% chance of being affected.

Children of affected: The daughters of affected males are all obligate carriers as each receives her fathers X chromosome and one of her mother’s two X chromosomes. There is no male to male transmission as a son does not inherit his father’s X chromosome carrying the bad gene G*. Sons of affected fathers are generally unaffected unless their mother is a carrier.

As well as risk estimates knowing the genetic subtype can provide useful prognostic information for the family. For example the chances of preservation of good visual acuity (central vision) beyond 60 are greater in adRP compared with arRP and XLRP

Molecular diagnosis: Carrier detection and prenatal testing: The next logical stage in the work up of a new RP case, after having established the genetic subtype, is to identify the RP gene responsible for the disease by genetic screening using DNA analytical techniques. There are many benefits to knowing the actual mutation.

In the case of arRP and XLRP while risk of carrier status may be assessed from knowledge of the family history only by testing at risk individuals for the actual mutation itself can the actual carrier status of those at risk be definitively determined. For example in families with XLRP DNA can reveal the actual genetic status of at risk females i.e., sisters of boys with XLRP and the sisters of women with an affected son. As XLRP is a severe form of the disease this information may be vital for female relatives intending to marry or planning to start a family. In the case of adRP although non carriers are non affected, because of incomplete penetrance and variable onset of the disease, the only safe way to establish carrier status is by detecting the actual RP mutation.

A married couple at risk of conceiving an affected child with RP may request prenatal diagnosis. Female carriers of an XLRP mutation may wish to abort an affected fetus as many cases of XLRP are relatively severe. The early onset forms of arRP and LCA are also very severe leading to blindness from infancy or birth and many couples at risk of conceiving a child afflicted with such severe retinal diseases may also request prenatal diagnosis. In the case of adRP which tends to be less severe than arRP or LCA there may be less demand for prenatal diagnosis.

Carrier detection may be important in regions of the world such as south Asia where consanguineous marriages are common and where relatives of an affected with arRP may wish to marry another closely related family member.

There are other benefits from DNA testing detection. Knowing the underlying mutation can establish definitely the diagnosis before clinical symptoms have become apparent. This can be important in the case of childhood dystrophies where the clinical prognosis may differ greatly depending on the gene implicated. DNA diagnosis can also be important in confirming the diagnosis and determining the genetic subtype of isolated cases.

Moreover although heterogeneity and variability of expression is one of the hallmarks of RP knowing the mutation does have a certain predictive value. In the case of RHO mutations it is well established that certain mutations tend to be more severe than others. For example as mentioned above the P23H causes a relatively mild and late onset form of RP. It is also widely considered that XLRP and arRP tend to be more severe than adRP.

Finally as Daiger et al (2007) point out “in the not to distant future knowing the gene responsible will be important as increasingly gene specific therapies become available .. and knowing the gene responsible will be important in the enrollment of patients into clinical trials.”

There are two major problems which must be overcome if the RP gene mutation responsible for the disease is to be detected in the majority of RP cases presenting at the retinal clinic.

One problem is that only approximately 50% of all RP cases are caused by mutations in known genes. However as mentioned above some authors expect that in about 10 years time most of the mutations causing RP and allied retinal disorders such as LCA may have been identified at least for north American and European populations. This will allow the widespread application of genetic testing of RP sufferers at least in western countries. A second problem is the great complexity of the genetics of RP and of the allied retinal disorders. Moreover in the case of many RP genes, RHO and RPGR for example, a great number of different mutations have been identified. Clearly identifying the mutation in every RP patient that presents for counseling at an ophthalmic clinic is a huge technological challenge.
and this is bound to grow as more RP genes and mutations are identified.

However this challenge is lessened to some extent by the finding that mutations in only a small number of RP genes are responsible for nearly one half of all RP cases. Remarkably already mutations in only 9 known RP genes are responsible for nearly one half of all RP cases. Indeed mutations in only 2 genes RHO and RPGR are responsible for more than 10 % of all cases of RP and 17 % of non syndromal RP. Because of the high prevalence of RHO and RPGR mutations in RP, mutational analysis of these two gene has considerable diagnostic relevance. The fact that relatively few RP genes cause a significant proportion of RP greatly lessens the complexity and burden of providing a useful DNA diagnostic service.

Moreover developing technologies including large throughput direct sequencing machines and the development of microarrays is making possible the detection of an ever increasing inventory of RP mutations. The fact that perhaps only a relatively small number of genes will be found to be responsible for most cases of RP in conjunction with the rapid technological advances in mutation detection, raises the prospect of providing eventually and perhaps within 10 years for US and European populations a molecular diagnostic service for most families with RP. Indeed Daiger et al (2007) speculate that “high – throughput sequencing methods will make genetic testing of all genetic diseases affordable and efficient, at least in the developed world, within 10 years.”

### Autosomal Recessive

<table>
<thead>
<tr>
<th>RP Gene</th>
<th>Percentages of cases</th>
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<tr>
<td>RP1</td>
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<tr>
<td>RHO</td>
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<tr>
<td>RDS</td>
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<tr>
<td>RP2</td>
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</tr>
<tr>
<td>Total</td>
<td>17.49</td>
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</tbody>
</table>

**TABLE**

RP GENES AVAILABLE FOR TESTING IN THE US AND THE PERCENTAGE OF ALL RP CASES (NON SYNDROMIC AND SYNDROMIC) CAUSED BY EACH GENE
Note
1. The RPGR gene has proved difficult to screen for mutations because of the high purine content and unusual structure of exon ORF15 (Shu et al 2006). However there is great clinical utility in screening this gene. The clinical utility lies in the value of RPGR mutation identification for (i) carrier testing, (ii) prenatal diagnosis and (iii) clarifying the mode of inheritance for genetic counselling. A significant proportion (29%) of males with early onset and severe RP with no family history were found in one study to have RPGR mutations, so that this test will clarify the mode of inheritance in this subgroup of patients (Shu et al 2006).
2. Chip technology - Microarrays: A major challenge for the future is to develop techniques that provide a means of rapid detection of RP mutations for carrier detection [in families with recessive disease and X ] and for early diagnosis of individuals in adRP pedigrees. Zernant et al (2005) used arrayed primer extension (APEX)technology to design a genotyping microarray for early-onset, severe retinal degenerations [early onset RP and Leber congenital amaurosis] that includes all of the >300 disease-associated variants currently described in eight genes already known to cause this class of retinal degenerations. The resultant array allows simultaneous detection of all known disease-associated alleles in any patient with early-onset RP.Other workers are aiming at similar arrays for later onset arRP (Nawajes et al 2005). Ultimately it may be possible to detect thousands of RP mutations routinely applying various chip technologies. From Pagon and Daiger (2005). Percentages from Daiger et al (2007: Table 3) and assuming that 20% of cases of RP are adRP, 13 % are arRP [not including early onset recessive RP which is usually diagnosed as LCA] and 8% XLRP (Daiger et al, 2007).

Reference
Correlation Between Serum Level of Homocysteine, Folate and Vitamin B12 in Elderly Patients with Primary Open-Angle Glaucoma

Dr. Rani Menon MS, DO, FRCS, Dr. Sobha Ramesh MS, DNB

Abstract
Elevated level of homocysteine (Hcy), a derived amino acid, is an independent risk factor for vascular diseases. The metabolism of Hcy requires enzymes with vitamin B12, and folic acid as coenzymes. High level of Hcy was suspected in glaucoma mainly pseudoexfoliative glaucoma.

Aim: The aim of this case-control study is to find out the level of serum Hcy, vitamin B12 and folic acid in elderly male and female (65-80 years) patients with primary open-angle glaucoma and their correlation.

Methods: Forty four patients with glaucoma (25 men of age 71 ± 4 and 19 women of age 72 ± 4) and 10 age matched controls (5 men of age 72 ± 6 and 5 women of age 69 ± 5) were included in this study. Levels of serum Hcy, vitamin B12 and folic acid were measured using enzyme immunoassay. The levels were statistically analyzed for their correlation.

Results: A higher mean value, statistically non-significant, for Hcy was observed in male glaucoma patients with that of control subjects. No significant difference could be observed between the level of folate and B12 in glaucoma patients with that of control. Hcy level in male and female patients were 21.7 ± 11.4 and 14.1 ± 4.6 μmol/l, respectively. However, 36 % (9/25) of male and 31.5 % (6/19) of female patients showed significantly higher level of Hcy. The levels were 33.5 ± 12.1 and 25.0 ± 5.8 μmol/l for male and female patients, respectively glaucoma group. Significant negative correlation found between the level of Hcy to both B12 (p < 0.02), and folic acid (p< 0.02) in male patients. In female patients, the negative correlation between Hcy and B12 (p<0.01) was significant, whereas between Hcy and folate was non-significant.

Conclusion: The results of this study concluded that higher level of Hcy was found mainly in elderly men with glaucoma than that of the age matched control. The negative correlation between Hcy and folic acid suggests the necessity of supplementing folate to prevent further ocular vasculopathy.

Introduction
Nutrition is an important determinant of health in persons over the age of 65 and is often under diagnosed. Though there are no uniformly accepted definitions for malnutrition in the elderly people, specific vitamin deficiencies have been well described as reliable indicator. Homocysteine (Hcy) is a derived amino acid formed in trace amount during the metabolism of the essential amino acid, methionine and is found to be cytotoxic when present at elevated levels. Genetically, autosomal recessive inherited defects in the metabolism of Hcy are the most important primary determinants for its elevation. The metabolism of Hcy requires enzymes with vitamins such as vitamin B12 (B12), pyridoxine and folic acid as coenzymes. There is an inverse relationship observed between elevation of Hcy with the levels of B12 as well as folate. A direct dose-response association between hyperhomocysteinemia with vascular disease has been reported. Risk is mainly due to the inhibition of the endothelial synthesis of nitric oxide (NO) by asymmetric dimethylarginine which is increased by elevated Hcy. Hence, chronic elevation of plasma Hcy impairs endothelium dependent NO mediated vasodilatation. Treatment with folate and B12 reduces Hcy levels in subjects with or without any defect in the enzymes involved in its metabolism. Willems et al. reported that supplementation with these vitamins can improve vascular function in hyperhomocysteinemic patients with evident coronary artery disease.

Glaucoma is one of the prominent causes of blindness. Intraocular pressure (IOP) is assumed to be the most significant risk factor in glaucoma. However, recent evidences indicate that vascular risk factors may also play a role. Apoptosis of retinal ganglion cell has been observed
either due to impaired blood supply to the head of optic nerve or direct toxic action of various cytotoxic agents including Hcy.\(^{11,12}\) Previous prospective studies reported significant high level of Hcy in patients with pseudoexfoliative glaucoma (PEXG).\(^{13-16}\) However, it was unaltered among the other glaucoma patients.\(^ {13-16}\) The mean serum folic acid level was found to be significantly low in subjects with PEXG.\(^ {13-16}\) The increased risk of vascular disease among patients with PEXG glaucoma can be explained by the impaired endothelium dependent vasodilatation by the elevated Hcy.\(^ {17}\) Although the positive correlation between the level of Hcy and PEXG glaucoma has been reported, its prevalence in Indian patients with glaucoma or its correlation with the level of folate and B12 has not yet been established. Further, a gender based study in glaucoma patients is required to rule out the prevalence of hyperhomocysteinemia. The outcome of the study may be beneficial to treat the hyperhomocysteinemia in order to prevent further damage to retinal ganglion cell in glaucoma patients. Since, B12, and folate are among the most common dietary factors to influence Hcy, this study is also aimed to determine the influence of folate and B12 on Hcy levels in elderly male and female patients with primary open-angle glaucoma.

**Materials and Methods**

**Inclusion criteria**

Forty four patients (25 men, age 71 ± 4 years and women, age 72 ± 4 years) with glaucoma and 10 age matched subjects (5 men, age 72 ± 6 years and 5 women, age 69 ± 5 years) as control, were randomly selected for this study. All patients underwent complete ophthalmic evaluation including visual acuity, slit lamp examination, gonioscopy, tonometry, fundoscopy and visual field examination. POAG was defined by the presence of an open angle on gonoscopy, IOP more than 22 mm of hg measured with applanation tonometer, typical glaucomatous cupping and visual field defect in at least one eye on standard automated permentantly (HFA 24-2). Fasting blood samples were collected from patients diagnosed with or with out primary open-angle glaucoma as a part of the routine laboratory investigations and further for the examination of serum levels of folate, B12 and Hcy. Informed consent was obtained from the subjects and the study was conducted according to the guidelines/ethics prescribed by Indian Council for medical Research for the experimental studies in human subjects.

**Exclusion criteria**

Patients with history of inflammatory diseases (ocular inflammation, autoimmune disease), cardiomyopathy, coronary artery disease, cerebrovascular disease, peripheral vascular diseases, retinal occlusive disease, vasculitis, renal or hepatic dysfunction, peptic ulcer, malabsorption or maldigestion, psychiatric illness, dementia, chronic alcohol abuse or tobacco consumption were excluded from the study. Patients with vitamin supplements, or known familial history of vascular diseases or inborn errors of metabolism were also excluded from the study. Age matched controls were selected from the subjects who visited the clinic for their vision check-up.

**Determination of homocysteine, folate and vitamin B12**

Blood samples were collected from all the subjects after an overnight fasting (8-10 hrs). Levels of serum Hcy were measured using immunoassay, and those of serum B12 and folic acid were measured using competitive chemiluminescent enzyme immunoassay by the referral laboratory.

**Statistical analysis**

Significant difference between the age, level of Hcy, folate and B12 in patients with the glaucoma and control were done using two-tailed student t test, whereas the correlation between the level of Hcy, folate and B12 in patients was done by Pearson correlation analysis using GraphPad InStat software package (GraphPad Software Inc., San Diego, CA, USA). P value less than 0.05 was considered as statistically significant.

**Results**

Level of Hcy in patients with glaucoma is depicted in figure 1. A gender wise difference in the mean value of Hcy in elderly patients with that of control could be observed in this study (Table 1). The mean value of Hcy (21.7 \( \mu \text{mol/l} \)) was elevated in the elderly men with glaucoma when compared to that of the reference value (13.3 \( \mu \text{mol/l} \)). However, these values did not show any statistically significant difference. In female patients, the Hcy level was 14.1 \( \mu \text{mol/l} \), which was again found to be non-significant with respect to the control

**Figure 1. Level of homocysteine (Hcy) and folate in control and patients with glaucoma. Values are mean ± SD, (n = 10 in control and n = 44 in glaucoma patients). P > 0.05 (Student t test) non-significantly different from each other**
(15.25 ± 3.0 μmol/l). Elevated Hcy with decreased folate and B12 found in the men age group 70-75, whereas in women a similar observation was seen in the 75-80 age group (Table 2).

Level of folate and B12 in both groups is depicted in figure 1 and 2. No statistically significant difference could be observed between these values with that of the control group.

Correlation analysis in elderly male patients indicates a negative correlation between the level of Hcy to that of folate and B12 which was found to be significant (p < 0.02) (Table 3). Similarly, correlation between the levels of Hcy to that of B12 in female patients was also found to be significant (p < 0.01). However, no such statistically significant correlation could be observed between the Hcy level and folate in the female patients.

**Discussion**

An elevation of mean Hcy level could be observed in the men with glaucoma than that of the control group. However, the values are consistently overlapping and hence a statistically insignificant difference obtained between them. On the other hand, Hcy level in female glaucoma patients did not show any such alteration. These findings are in agreement with the previous report that no significant elevation of Hcy could be found in open angle glaucoma patients when compared with the age matched control.16

Some of the vitamin deficiencies, particularly B12, B6, and folate, are associated with cognitive impairment.8,18,19 and may affect the perception of vision. B12 deficiency is expected to be higher in elder Indians owing to the strict vegetarian diet and prevalence of Helicobacter pylori infection. The atrophic gastritis may also be implicated in the impaired B12 adsorption in the elderly population.20 Since, B12 has direct role as coenzyme in the conversion of Hcy to methionine, B12 analysis has also been included in this study. In this study, level of B12 did not differ among the control and glaucoma patients. However, the level of B12 was found to be decreased with an increase in Hcy in both

---

### Table 1. Levels of homocysteine (Hcy), folate and vitamin B12 in control and elder patients with glaucoma

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 10)</th>
<th>Patient with glaucoma (n = 44)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male (n = 5)</td>
<td>Female (n = 5)</td>
</tr>
<tr>
<td></td>
<td>Male (n = 25)</td>
<td>Female (n = 19)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>72 ± 6</td>
<td>69 ± 5</td>
</tr>
<tr>
<td></td>
<td>71 ± 4</td>
<td>72 ± 4</td>
</tr>
<tr>
<td><strong>Hcy (μmol/l)</strong></td>
<td>13.3 ± 1.8</td>
<td>15.25 ± 3.0</td>
</tr>
<tr>
<td></td>
<td>21.7 ± 11.4</td>
<td>14.1 ± 4.6</td>
</tr>
<tr>
<td><strong>Folate (ng/ml)</strong></td>
<td>7.5 ± 2.5</td>
<td>4.9 ± 1.2</td>
</tr>
<tr>
<td></td>
<td>11.0 ± 7.7</td>
<td>12.6 ± 8.9</td>
</tr>
<tr>
<td><strong>Vitamin B12 (pg/ml)</strong></td>
<td>382.6 ± 183.1</td>
<td>370.4 ± 239.4</td>
</tr>
<tr>
<td></td>
<td>616.5 ± 559.2</td>
<td>706.4 ± 565.3</td>
</tr>
</tbody>
</table>

Values are mean ± SD, p > 0.05 (Student t test) non significantly differ from control group

### Table 2. Levels of homocysteine (Hcy), folate and vitamin B12 in glaucoma patients with respect to age

<table>
<thead>
<tr>
<th>Age</th>
<th>Hcy (μmol/l)</th>
<th>Folate (ng/ml)</th>
<th>B12 (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male glaucoma (n = 25)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-70 (n = 8)</td>
<td>22.4 ± 14.6</td>
<td>12.6 ± 7.9</td>
<td>428.1 ± 299.0</td>
</tr>
<tr>
<td>70-75 (n = 10)</td>
<td>24.9 ± 11.4</td>
<td>7.1 ± 4.6</td>
<td>393.8 ± 177.1</td>
</tr>
<tr>
<td>75-80 (n = 7)</td>
<td>16.4 ± 5.0</td>
<td>14.8 ± 9.4</td>
<td>1150.0 ± 798.2</td>
</tr>
<tr>
<td><strong>Female glaucoma (n = 19)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-70 (n = 6)</td>
<td>12.8 ± 6.1</td>
<td>12.2 ± 9.3</td>
<td>801.8 ± 677.0</td>
</tr>
<tr>
<td>70-75 (n = 7)</td>
<td>13.9 ± 5.8</td>
<td>15.3 ± 10.1</td>
<td>971.8 ± 619.4</td>
</tr>
<tr>
<td>75-80 (n = 6)</td>
<td>14.9 ± 2.9</td>
<td>11.3 ± 7.4</td>
<td>416.3 ± 114.4</td>
</tr>
</tbody>
</table>

Values are mean ± SD, p > 0.05 (Student t test) non significantly different from each other as well as from the control group

### Table 3. Pairwise correlation analysis in old aged control and patients with glaucoma

<table>
<thead>
<tr>
<th>Pairwise correlation</th>
<th>Male glaucoma</th>
<th>Female glaucoma</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hcy with Folate</td>
<td>-0.45***</td>
<td>-0.39 NS</td>
<td>-0.70*</td>
</tr>
<tr>
<td>Hcy with B12</td>
<td>-0.44**</td>
<td>-0.56*</td>
<td>0.28NS</td>
</tr>
</tbody>
</table>

*P < 0.01, **P < 0.02 considered significant and NS P > 0.05 not significant
genders. In the elderly female patients, the decline of B12 with respect to HCY was statistically significant. Cumurcu et al.\textsuperscript{16} and Turgut et al.\textsuperscript{21} have reported the levels of B12 does not statistically differ in patients with PEXG or open-angle glaucoma. The normal B12 level observed in this study also supports one of the previous reports by Shoba et al.\textsuperscript{22} that no deficiency of B12 is seen in elderly Indians. Since, a negative correlation could be observed between the B12 and HCY in male patients in this study, the mechanism of hyperhomocysteinemia can be explained with the lowered B12 level.

The low folate level is a strong determinant of hyperhomocysteinemia in elderly age group\textsuperscript{23}. Decreased serum folic acid level was also found in PEXG group.\textsuperscript{21} However, no statistically significant difference in serum folate levels was reported in patients with other types of glaucoma. Results of this study also support that no significant decrease of folic acid was observed in both male and female patients. However, significant negative correlation found between the levels of HCY to folate acid in male patients. Therefore, the exhibited elevated HCY in this study could be further ascribed to the declined level of folic acid. This observation is supported by the findings of Cumurcu et al.\textsuperscript{16} in PEXG patients that, serum levels of HCY in male patients in this study, the mechanism of hyperhomocysteinemia can be explained with the lowered B12 level.

A high level of serum HCY is observed in disorders of HCY metabolism, vitamin deficiencies, systemic arterial hypertension, chronic renal insufficiency, or in malignant neoplasms. Additionally, habitual smoking and coffee intake, some medications, alcohol consumption, and physical activity may also affect HCY levels.\textsuperscript{24,25} In this study, the patient’s exclusion criteria could eliminate all these possible variants. Further, oral and dental issues, esophageal motility, and atrophic gastritis may also affect nutritional status. Some of the previous reports revealed that for some seniors, it may be difficult to meet daily micronutrient requirements with the reduced caloric intake.\textsuperscript{26,27,28} Therefore, a rapid weight loss as a result of malnutrition has been observed. It is unclear that alterations in normal physiological changes such as taste and smell are associated with aging might be contributed to decreased food intake.\textsuperscript{20,29} Other gastrointestinal changes occuring with age may also affect the oral intake of calories. Appetite after an overnight fast is often lower in the elderly. In this study, all the subjects were with no loss of body wt which was evidenced from the body weight at the time of their first consultation as well as during the subsequent follow-up (data not included). Nevertheless, results of this study could not make a correlation between hyperhomocysteinemia and the incidence of open-angle glaucoma.

The internationally accepted treatment for hyperhomocysteinemia involves the use of folic acid, B12, under fasting conditions and pyridoxine after meals. Sato et al.\textsuperscript{30} reported the effect of folate and B12 in Japanese patients with hyperhomocysteinemia. Folic acid and B12 alone was shown to reduce HCY levels by 22 and 11%, respectively. But both can act synergistically to cause a reduction of 38.5% in the HCY levels. Further, pyridoxine does not add to the effect of folate and B12 in the fasting state. Amongst Indians, a dietary deficiency of the HCY lowering B vitamins is often present. Urban men were significantly more likely to have hyperhomocysteinemia than rural men.\textsuperscript{31} Study conducted in middle aged men concluded that 67% of the men had low vitamin B12 concentration and 58% had hyperhomocysteinemia.\textsuperscript{32} In general, high mean HCY value (varying from 19.5 to 23.2 μmols/l) is observed in eldest Indian population.\textsuperscript{31,32} This study failed to take the dietary habit of the subjects and the size of the aged control group population was too small to suggest a normal biological reference value.

An elevation of HCY level may cause changes in the microvasculature in the optic nerve head and impair optic nerve blood flow and ocular vasculopathy via a vasoconstrictive effect, endothelial injury, smooth muscle proliferation, platelet activation, thrombogenesis, and apoptotic cell death in retinal ganglion cells.\textsuperscript{33,34} Therefore, aged subjects with elevated HCY should be encouraged to include high folate food items in their diet. Dietary folic acid (0.5–5 mg/day) supplementation found to reduce the basal HCY levels by 25%.\textsuperscript{17} However, a general recommendation for supplementing folate, B12 and other nutritional vitamins in elder subjects is outside the scope of this study. A multi-centric population based longitudinal study is further warranted for the establishment of relation between HCY.
with glaucoma in our population.

Conclusion
The results of this study suggest that supplementation of folate and B12 is required in elder male patients with glaucoma to lower the Hcy level. Furthermore, this study may suggests the necessity of measuring the serum levels of Hcy, B12 and folate periodically in elderly subjects with glaucoma that may help to prevent further optic vasculopathy.

Conflict of interest: none to declare

Acknowledgement
The valuable help of Dr Ajith TA., Professor of Biochemistry, Amala Institute of Medical Sciences, Amala Nagar, Thrissur, Kerala, India during the preparation of this article is gratefully acknowledged.

References


A Study on External Dacryocystorhinostomy (DCR) with Silicone Intubation at A Tertiary Eye Care Centre

Dr Ann J K DO.DNB, Dr Ani Sreedhar MS

Abstract

Purpose: To evaluate the functional outcome and complications associated with external DCR surgery with silicone intubation.

Materials and methods: A retrospective study of 10 patients from a time period of August 2009 to June 2013 was undertaken. Minimum follow up period was three months. A detailed history of presenting complaint and previous lacrimal surgeries were recorded. Preoperative syringing and probing were done to locate the site of obstruction. Patients were allocated into two groups depending on the site of obstruction based on probing. External DCR with silicone intubation was performed in all the patients. Patients were followed up on day 1, day 14, at 3 months and 6 months. Postoperative success was determined by lacrimal patency to irrigation and subjective resolution of epiphora. Any complications associated with silicone intubation were also noted.

Results: Ten patients were included in the study. Age ranged from 30 to 78 years. Five patients had a history of previous lacrimal surgeries. Nine out of ten patients had improvement of the conditions. One patient had no improvement. No complications associated with silicone intubation were recorded in these patients.

Conclusion: External DCR with silicone intubation is safe and effective surgery in patients whom we expect less favourable outcome. The complications associated with silicone intubation are negligible. There is no statistically significant difference in outcome between pre sac and post sac obstruction.

Aim of the study

To evaluate the efficacy and complications of external DCR with silicone intubation in patients with nasolacrimal obstruction.

Materials and methods

It was a retrospective study of 10 patients. Study period was from Aug 2009 to June 2013. Patients with a review period of minimum 3 months were included in the study. Age and sex of the patient, history of presenting complaints, history of any acute attack of dacryo cystitis, history of previous surgical procedures like dacryocystectomy (DCT), DCR or lacrimal abscess drainage were noted. Patients were examined carefully for lid margin disease, punctal or lid malposition or laxity. Co-existing sinus or nasal pathology was excluded. Patients were investigated to rule out any bleeding/clotting disorders.

Patients included were who underwent external DCR with intubation for either epiphora or discharge or both. All patients had obstruction of nasolacrimal system during syringing. Level of obstruction was determined by preoperative probing. All patients with soft stop during probing were grouped as presac obstruction and patients with hard stop as post sac obstruction. In case of pre sac obstruction, patients with distal canalicular block only, i.e. > 8mm patency during probing, were taken up for surgery. All procedures were done under local anesthesia using similar technique by either one of the authors.

A bicanalicular silicone intubation with external DCR was done. Patients were put on antibiotic eye drops, nasal decongestant drops and systemic anti-inflammatory drugs post operatively. Patients were followed up next day after surgery, at 2 weeks and at the end of 3 months. Syringing was done on next day and also during follow up visits. Suture removal was done at the end of 2 weeks and silicone tube removal was done at 3 months.

The procedure was considered as successful when there is resolution of tearing and discharge, and also by lacrimal patency to irrigation. If there is no improvement with persistent watering both indoors and outdoors were
considered as failure. Any tube related complications like slitting of the punctum or canaliculus or granuloma formation were also looked for during follow up visits. Data analysis was done by Fisher exact test.

Results
Total number of cases was 10. Females were 9 and male 1 (Fig 1). Age ranged from 30 to 78 years, mean (51.5). Minimum duration of follow up was 3 months; maximum 46 months (mean 12.4).

Four patients had a history of prior DCR surgery and one patient had a history of DCT. One patient had undergone lacrimal abscess drainage.

Based on probing 6 (60%) patients had pre sac obstruction (soft stop) and 4 (40%) had post sac obstruction (hard stop). (Fig 2)

Patients were assessed at the time of tube removal (3 months) and at the end of 6 months. All of our 6 patients with pre sac obstruction had a successful outcome with complete resolution of epiphora and free syringing at 3 months. Among post sac obstruction, out of 4, one patient reported persistent watering after tube removal, which was considered as a failure. (Table 1)

Outcome of surgery
We also recorded the result of the surgery at the end of 6 months. We had only 7 patients who have completed the 6 months follow up i.e. 5 patients from the pre sac obstruction group and 2 from the post sac group. In pre sac group 4 out of 5 patients had no complaints, but 1 patient complained of occasional watering outdoors. In post sac group, one patient had no improvement. (Table 1)

Comparison of cases with a history of previous surgeries was also done. We had six patients with previous surgical procedures.

Comparison of cases with and without a history of previous surgery
We had 6 patients with a history of previous surgery and at 3 months. 5 were in success group and 1 was in failure group. We had only 7 patients with 6 months follow up of which out of 3 patients with a history of previous surgery 2 were success and one failure. And all 4 patients with no history of previous surgery were in success group. (Table 2)

<table>
<thead>
<tr>
<th>Level of obstruction</th>
<th>At 3 months</th>
<th>At 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of patients</td>
<td>Success</td>
</tr>
<tr>
<td>Pre sac</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Post sac</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 1

<table>
<thead>
<tr>
<th>History of previous surgery</th>
<th>At 3 months</th>
<th>At 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of patients</td>
<td>Success</td>
</tr>
<tr>
<td>YES</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>NO</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 2
Figure 3 shows the graphical representation of our results. Regarding complications associated with silicone tube intubation, none of our patients had problems related to intubation.

**Discussion**

Obstructive epiphora due to blockage of distal part of nasolacrimal apparatus is major indication of external DCR. The success rate of DCR without stenting varies between 75% to 90% according to various studies. Common causes of failed DCR are a) stenosis of the common canalicular opening in the sac b) closure of sac mucosa anastomosis by fibrous tissue c) incorrect position of anastomosis. The cause of common canalicular obstruction is due to the collection of fibrin and other inflammatory debris around the opening causing early fibrosis and subsequent closure of this tiny opening. The remedy to prevent closure is to use a stent in lacrimal passages which may be silicone tube; fine rubber catheters; fine polythene tubes; polyamide suture material. Another explanation why epiphora was resolved is that a bicanalicular silicone intubation can control punctal position by supporting it, and thus appose both upper and lower puncta during the closure phase of blinking, and thus enhance lacrimal pump function. Some suggest that the silicone intubation causes the canalicular lumen to narrow, thereby increasing the capillarity which enhances lacrimal tear drainage.

We performed external DCR with silicone intubation in our 10 patients in whom we expect poor outcome such as distal canalicular obstruction, atrophic sac, and history of acute attack, cases of repeat surgeries such as DCR and DCT where chances of fibrosis are more. In our study there was a female predominance (90%). We compared the outcome to find out whether there is any difference in pre sac and post sac obstruction group. On comparing the outcome we found that all our presac obstruction group patients improved after surgery- success rate was 100% at 3 months post operatively. One patient with postsac obstruction was still complaining of discharge from the eye. The surgical course was uneventful in that patient. She had undergone DCR surgery earlier. Probing after tube removal showed hardstop. We presume that this patient had bony regrowth. One patient from each group turned up with occasional watering outdoors when they are exposed to hot weather and wind. Syringing was free in both of them. So we consider a possibility of reflex tearing due to dry eye in these patients. These patients were grouped under success group. Both of them reported their condition is much better than before. The differences in outcome between two groups were not statistically significant. (p= 0.286)

In a study done by Y M Delaney et al and Nam Ju Kimset al 8 females are found more affected. In their 50 patients, subjective resolution of epiphora was reported in 91% in post sac and 67% in pre sac obstruction at 3.6 months follow up in the study done by Y M Delaney et al. There was a statistically significant association between a pre sac obstruction and postoperative recurrence in epiphora. This is not in accordance with our study. But they found a decline in success rate at 3 years down the line.

In their study of 40 patients of repeat DCR with silicone tube intubation by Imtiyaz A Lone et al at SKIMS medical college, Srinagar, they found that 38 patients revealed absence of symptoms at 12-18 months follow up. In the same study 20% patients had common canalicular block.

Another comparison was the difference in outcome between patients with and without history of prior surgery. At 3 months and 6 months the patients with a history of prior surgical procedure did less well than (83.3% and 66.5% respectively) other group (100%).The difference was not statistically significant. (p=0.273). The chance of fibrosis and the occlusion of the lumen is more in repeat surgeries. That may be the reason for less number of successes.
Regarding the complications of silicone tube intubation, none of our patient had problems. We removed the tube at the end of 3 months in all of them. Limitations of our study are less number of patients and short follow up period.

Conclusion
External DCR with silicone intubation is safe and effective surgery in patients whom we expect less favourable outcome. The complications associated with silicone intubation are negligible. There is no statistically significant difference in outcome between presac and post sac obstruction. No significant difference in the outcome between patients with and without a history of previous surgery. There is a tendency for the symptoms to recur after tube removal. We recommend a longer follow up with more number of patients to evaluate its long time results.

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Ultrasound Biomicroscopic Evaluation of Changes in Anterior Segment Morphology After Nd:YAG Laser Iridotomy in Primary Angle Closure Glaucoma

Dr. Smrithy Sadanandan MS, Dr. K.V. Raju MS, Dr. Bindu S. MS, Dr. Kala K. Madhavan MS

ABSTRACT

Purpose: To prospectively quantify changes in anterior segment morphology after laser iridotomy using ultrasound biomicroscopy (UBM) in angle closure glaucoma.

Study Design: Prospective interventional study

Methods: Patients presenting as Primary Angle Closure, Primary Angle Closure Glaucoma & Primary Angle Closure Suspect (PAC, PACG & PACS) were examined with UBM having probe frequency of 35 MHz to measure anterior segment parameters including ACD, TIA, AOD500, TCPD, ID1 & ID3. Sequential measurements of the same were taken 2 weeks post Nd:YAG laser iridotomy and changes noted.

Results: 42 eyes of 22 patients were examined. There was a statistically significant increase in ACD, TIA, AOD500, TCPD in all the subgroups. Iris thickness was seen to decrease post LPI, though not found to be clinically significant.

Conclusion: Anterior segment dimensions can be significantly influenced by laser peripheral iridotomy in primary angle closure, offering significant protection against acute angle closure and UBM unlike gonioscopy, is a viable tool for documentation and quantification of angle morphology.

Aim

- To assess the anterior segment morphology of the PACS, PAC and PACG using UBM
- To further quantify the changes in anterior segment morphology of these patients post Nd:YAG laser iridotomy using UBM.

Materials & Methods

The study design was a prospective interventional study. Patients presenting with PAC (occludable drainage angle and features of trabecular obstruction, such as peripheral anterior synechiae (PAS), iris whorling, glaukomflecken, excessive pigment deposition on the trabeculum, and/ or raised IOP) or PACG (PAC together with signs of glaucomatous optic neuropathy) or PACS (suspects with normal IOP) at our tertiary referral centre were included in the study. Exclusion criteria included:

1. Presence of other PAS-associated disorders like iris neovascularization
3. Presence of secondary angle closure glaucoma due to lens abnormalities, retinal surgeries or other cause
4. Use of any pupillary diameter altering drugs

The diagnosis was based on clinical history & examination, slit-lamp biomicroscopy, visual field testing and indirect gonioscopic examination.

Gonioscopy was done with a Goldmann 2 mirror lens. The gonioscopic criteria taken for an occludable angle were:

1. The trabecular meshwork invisible in 270° or more of the entire angle in the primary position of gaze without manipulation or
2. The angular width was less than 20 degrees by the Shaffer grading.

After initial assessment of angle closure patient, the anterior chamber parameters were measured using the Sonomed VuMax-1 UBM, which is a high frequency ultrasonic B-Scan with a water-bath probe, with transducer of center frequency 35 MHz, made of gold-coated polyvinylidene fluoride (PVDF). The theoretical axial resolution of the 35 MHz transducer is 0.0219 mm and lateral resolution is 0.42 mm in tissue. The scan depth is 15 mm.

After surface anesthesia with 4% xylocaine, a plastic eyecup containing physiologic saline was applied to the eyeball between the eyelids. The scanning was performed by placing the probe at the limbus and ciliary body region, always perpendicular to the surface of the eyeball, and profile images of the limbic area in the superior, inferior, nasal and temporal meridians of the angle were obtained per eye with the patient in a supine position. An image centered on the pupil was also captured. The UBM examination was done in the undilated state under dim light illumination, the
conditions being uniform for the whole examination. The various parameters listed below were measured by a single observer to rule out interobserver variability. The various parameters measured include

**Anterior chamber depth (ACD)** indicates the distance between the endothelium and the anterior surface of the lens along the visual axis.

**Angle opening distance (AOD500)** corresponds to the distance between the trabecular meshwork and the iris at 500 μm anterior to the scleral spur.

**Trabecular iris angle (TIA)** is defined as an angle formed with the apex at the iris recess and the arms passing through the point on the meshwork 500 μm from the scleral spur and the point on the iris perpendicularly opposite.

**Trabecular ciliary process distance (TCPD)** indicates the distance between the trabecular meshwork and the ciliary process at 500 μm anterior to the scleral spur.

**Iris thickness (ID1)** - thickness measured at same line as TCPD; ID3- max iris thickness near pupillary margin.

The LPI was performed using a Nd:YAG laser, set at variable energy levels between 2 and 6 mJ (5–10 shots). All patients received the same preinterventional regimen that consisted of pilocarpine QID before the intervention and continued use of antiglaucoma medications if on any. Using an Abraham lens, one opening was performed selecting, if possible, a crypt in the peripheral superotemporal or superonasal iris. After the intervention, patients were given systemic azetazolamide 250mg BD for 2 days, along with topical Dexamethasone QID which is later tapered.

The same patient was then reassessed 2 weeks following Nd:YAG laser iridotomy with indirect gonioscopy and UBM for changes in anterior segment parameters, along visual acuity and IOP reassessment. The measurements were tabulated and compared using students paired T test.

**Results**

As per inclusion criteria, 42 eyes of 22 subjects diagnosed as either PACS, PAC or PACG were evaluated. Of which 16(38%) were PACS, 18(43%) were PAC and 8(19%) were diagnosed as PACG. The age of presentation varied from 46 to 70 years with a mean age of 56.05 ±6.98 years. The maximum frequency was seen in the age group of 46-50 years.

The mean anterior chamber depth (ACD) pre-laser iridotomy was 1.855±0.242mm and post laser iridotomy was 1.950±0.252mm.(p=0.000) The mean change in ACD in each group is as follows.

<table>
<thead>
<tr>
<th></th>
<th>ACDprePI</th>
<th>ACDpostPI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACS</td>
<td>1.912±0.257</td>
<td>2.000±0.260</td>
<td>0.000</td>
</tr>
<tr>
<td>PAC</td>
<td>1.727±0.189</td>
<td>1.812±0.191</td>
<td>0.000</td>
</tr>
<tr>
<td>PACG</td>
<td>2.031±0.178</td>
<td>2.153±0.187</td>
<td>0.018</td>
</tr>
</tbody>
</table>

The TIA, mean value pre-laser iridotomy was 8.006±1.838º & post iridotomy was 15.964±2.941º(p=0.00). The mean change in each group is as follows.

<table>
<thead>
<tr>
<th></th>
<th>TIAprePI</th>
<th>TIApostPI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACS</td>
<td>8.781±1.663</td>
<td>16.093±1.359</td>
<td>0.00</td>
</tr>
<tr>
<td>PAC</td>
<td>7.388±1.655</td>
<td>16.055±4.165</td>
<td>0.00</td>
</tr>
<tr>
<td>PACG</td>
<td>7.843±0.855</td>
<td>15.500±2.065</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Angle opening distance at 500μm(AOD500) increased from a mean value of 0.075±0.016mm to 0.144±0.020mm

The net mean value of AOD500 for each sub group is as follows.

<table>
<thead>
<tr>
<th></th>
<th>AOD500prePI</th>
<th>AOD500post-PI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACS</td>
<td>0.081±0.013</td>
<td>0.150±0.014</td>
<td>0.00</td>
</tr>
<tr>
<td>PAC</td>
<td>0.071±0.019</td>
<td>0.138±0.024</td>
<td>0.00</td>
</tr>
<tr>
<td>PACG</td>
<td>0.070±0.007</td>
<td>0.145±0.018</td>
<td>0.00</td>
</tr>
</tbody>
</table>

The Trabecular ciliary process distance(TCPD), showed a statistically significant mean increase from a figure of 0.681±0.060mm to 0.737±0.058mm.

There was a mean increase in TCPD by 0.054mm in PACS, 0.058mm in PAC & 0.056mm in PACG groups.

There was a mean increase in TCPD by 0.054mm in PACS, 0.058mm in PAC & 0.056mm in PACG groups.

<table>
<thead>
<tr>
<th></th>
<th>TCPDpre</th>
<th>TCPDpost</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACS</td>
<td>0.693±0.055</td>
<td>0.747±0.054</td>
<td>0.00</td>
</tr>
<tr>
<td>PAC</td>
<td>0.667±0.568</td>
<td>0.725±0.577</td>
<td>0.00</td>
</tr>
<tr>
<td>PACG</td>
<td>0.689±0.763</td>
<td>0.745±0.071</td>
<td>0.00</td>
</tr>
</tbody>
</table>

The iris thickness(ID1) is measured along the same line as TCPD; ID3- max iris thickness near pupillary margin.

The average values computed for each group include

<table>
<thead>
<tr>
<th></th>
<th>ID1pre PI</th>
<th>ID1post PI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACS</td>
<td>0.396±0.028</td>
<td>0.393±0.029</td>
<td>0.28</td>
</tr>
<tr>
<td>PAC</td>
<td>0.395±0.025</td>
<td>0.385±0.024</td>
<td>0.00</td>
</tr>
<tr>
<td>PACG</td>
<td>0.424±0.053</td>
<td>0.414±0.049</td>
<td>0.01</td>
</tr>
</tbody>
</table>
The values reached statistical significance only in PAC & PACG group.

The mean ID3 the maximum iris thickness measured near the pupillary margin pre-laser iridotomy was 0.564±0.052mm & post iridotomy was 0.559±0.051mm.

The mean ID3 values for each group is as follows

<table>
<thead>
<tr>
<th>Group</th>
<th>ID3pre PI</th>
<th>ID3post PI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACS</td>
<td>0.556±0.035</td>
<td>0.554±0.035</td>
<td>0.155</td>
</tr>
<tr>
<td>PAC</td>
<td>0.559±0.058</td>
<td>0.552±0.059</td>
<td>0.000</td>
</tr>
<tr>
<td>PACG</td>
<td>0.591±0.060</td>
<td>0.585±0.057</td>
<td>0.012</td>
</tr>
</tbody>
</table>

The values reached statistical significance only in PAC & PACG group.

Discussion

Laser peripheral iridotomy and if indicated laser iridoplasty is the mainstay of treatment of angle closure by influencing the aqueous humour dynamics and reducing the pressure gradient between the anterior and posterior part of the AC, with the iris falling back, causing apparent widening of the angle with lowering of the intraocular pressure. Visualization of the anterior chamber is therefore important in narrow and occludable angles, which is routinely done by gonioscopy. UBM provides a more objective assessment of iridocorneal angle. It enables clinicians to quantitatively assess the iris curvature and degree of angle opening, since it images a cross-section of angle structures similar to that of a low power microscope section. One can determine the state of closure of the entire angle, even when it cannot be visualized by gonioscopy.1,2

In this study 42 eyes of 22 subjects were examined pre and post laser iridotomy. Out of the 42 eyes 16(38%) were PACS, 18(43%) were PAC and 8(19%) were PACG. Of the 18 PACEyes, 16 patients presented with features of acute attack like nausea, vomiting, periorbital pain, coloured haloes with blurred vision, raised intraocular pressure with evidence of corneal edema, mid-dilated pupil and shallow anterior chamber. The other two eyes had peripheral anterior synchiaue but with no evidence of glaucomatous damage to optic nerve. The other eye of these subjects were included as PACS, if satisfying the diagnostic criteria. Two eyes were excluded due to the presence of neovascular glaucoma in one eye & due to loss of follow up in the other eye. Out of the 8 PACG eyes, 3 eyes presented with acute attack. The mean age of presentation was 56.05±6.98years, the range varied from 46-70years.

The mean anterior chamber depth (ACD) pre-laser iridotomy was 1.855±0.242mm and post laser iridotomy was 1.950±0.252mm with an average increase of depth by 0.095mm. The ACD increased by 0.088mm in PACS, 0.085mm in PAC & 0.12mm in PACG.

Gazzard et al5 in his prospective study on Asian population in PACS eyes did not find significant increase in ACD after laser iridotomy (2.41±0.28mm vs. 2.42±0.30mm). Similar finding was obtained by Caronia et al6 in his study.

In study on Indian population by T Dada et al9, described a statistically significant increase in ACD in PAC(2.19mm to 2.30mm), as against PACG where the increase was not statistically significant (1.79mm to 1.82mm). Savita et al10 also in her study on PACS & PAC obtained a significant increase in ACD from 1.24±0.25mm to 1.44±0.21mm. The significant increase in ACD in PACG eyes in our study population can be explained on the basis of significant PAS being present in only 2 eyes & 4 eyes suspected to be having combined mechanism glaucoma.

The mean Trabecular iris angle (TIA), which is the angle formed with the apex at the iris recess, pre-laser iridotomy was 8.006±1.838º & post iridotomy was 15.964±2.941º with a mean increase of 7.958±3.774º. There was an average increase of angle by 7.312º in PACS, 8.667º in PAC and 7.657º in PACG. In all the groups the superior angle was found to be the narrowest and inferior the widest angle which opened correspondingly after laser iridotomy.

Giorgi et al6,7 in his study found a mean anterior chamber angle of 11.72º in acute PACG & 19.87º in chronic PACG in comparison to normal patients with 31.29º. Caronia et al8 study on Caucasian population demonstrated similar figures to the present study with angle opening from 8.3±1.3º to 18.6±2.8º. Kyung-Chul et al9 displayed an increase in mean TIA from 11.92±3.40º to 27.31±5.23º post LPI. After LPI, the mean superior TIA increased significantly from 6.46±6.68º to 12.1±8.1º, and mean inferior TIA increased from 7.5±6.7º to 12.9±8.5º in study on Indian population by T Dada et al8 which were comparable to the present study.

The Angle Opening Distance at 500μ (AOD500), is a measure of the angle opening at the level of the anterior Schwalbe’s line in the present study, increased from a mean value of 0.075±0.016mm to 0.144±0.020mm which was statistically significant. Significant change in AOD500 was obtained in each sub groups well, with it increasing by a value of 0.069mm in PACS, 0.067mm in PAC and 0.075mm in PACG. The individual increase in each examined quadrant was also statistically significant in each group.
The values for mean AOD500 obtained for acute PACG was 0.13±0.09mm & chronic PACG was 0.21±0.10mm in the study done by Giorgio et al.7 which were slightly higher than those obtained in the present study. In the prospective study by Mansouri et al10, the mean superior AOD increased from 0.060±0.07 to 0.107±0.07 mm (P=0.09), and the mean inferior AOD increased from 0.100±0.10mm to 0.152±0.08 mm after LPI in light conditions(P=0.148). Maraffa et al11 described an increase of AOD500 from 0.109±0.07mm to 0.183±0.09mm.

Kyung-Chul et al described an increase in AOD500 to 187.15±13.30mm from mean of 69.46±25.39mm in PAC, 89.58±25.39mm in PACG.Kaushik et al12 in a study including 55 angle closure patients, found a mean increase of AOD500 in the LPI quadrant from 0.112±0.08mm to 0.170±0.08mm i.e. an increase of 71.2%.

The Trabecular Ciliary Process Distance(TCPD) is a parameter of primary importance since it indicates the gap available for the iris between the trabecular meshwork and the ciliary process. In the study population, TCPD showed a statistically significant increase from a figure of 0.681±0.060mm to 0.737±0.058mm which can be speculated as due to the anteriorly displaced ciliary process moving backwards to relieve the occludable angle. The TCPD in each group showed statistically significant improvement post iridotomy. There was a mean increase in TCPD by 0.054mm in PACS, 0.058mm in PAC & 0.056mm in PACG groups.

The Liwan eye study13 found a mean increase in TCPD by 0.024mm post LPI. Dada et al9 though found no significant change in the trabecular ciliary process distance (0.751±0.22 to 0.785±0.23 mm, P=0.12) in the total study population, in PAC the TCPD increased from 0.748±0.19mm to 0.837±0.19mm which was statistically significant.

The mean Iris thickness(ID1), measured along the same line as TCPD pre-laser iridotomy, was 0.401±0.034mm & mean value post laser iridotomy was 0.394±0.033mm.(p<0.05) The change was found to be statistically significant. The mean Iris thickness(ID3), which is the maximum thickness at pupillary margin, pre-LPI was 0.564±0.052mm & post iridotomy was 0.559±0.051mm(p=0.00) i.e there was a decrease by 0.005mm which was found to be statistically significant.

Kyung et al3 described a decrease in iris thickness both ID1 & ID3 from a 545.38±108.68μm to 505.38±104.61μm and 620.77±108.28μm to 569.23±89.58μm respectively.(p=0.2). Dada et al9 described a decrease in the ID1 from 0.473±0.08mm to 0.486±0.11mm in PAC(p=0.42) & from 0.492±0.12mm to 0.484±0.096mm(p= 0.195) in PACG.

Most of the studies do not quote a significant difference in iris thickness post LPI. Though small but statistically significant flattening and thinning of the iris was observed in the study population post LPI, it doesn’t seem to have a clinical significance, because individual values for each quadrant in different subgroups did not all reach statistical significance.

The present study highlights that LPI is effective in opening up the angle recess and deepening the anterior chamber in primary angle closure glaucoma when there is only an appositional closure of the angle and also when synechial closure is not extensive.

**Conclusion**

This study shows that anterior segment dimensions can be significantly influenced by laser peripheral iridotomy in primary angle closure, offering significant protection against acute angle closure and UBM unlike gonioscopy, is a viable tool for documentation and quantification of angle morphology.

**Reference**

6. Giorgio Marchini, Andrea Pagliaruso, Andrea


Retinal Pigment Epithelial Tears (Rips) in the ERA of Anti Vegf - When and Why?

Dr Sreelekha S. MS, DNB, DO, FRCS, Dr Manoj Soman DNB, FICO, FRCS, Dr. Unni Nair MS, FRCS, Dr. Ruminder Kaur

Abstract

Aim
To evaluate the clinical profile, etiopathogenesis, morphological characteristics, evolution and prognosis of RPE tears (rips) in eyes with age-related macular degeneration (AMD) treated with anti VEGF therapy.

Materials and Methods
This was a retrospective analysis of 95 eyes with retinal pigment epithelial detachments (PED) due to various etiologies that presented between January 2012 and January 2013 which received anti VEGF therapy with a minimum follow up of 6 months. PEDs were characterized based on spectral domain OCT and angiographic findings. Prior treatments, nature of the lesion, time to tear, and pre-injection and final visual acuities were all studied. Eyes with rip were compared to those without and an evaluation of predictive factors was done. Management and outcome of these eyes were also analyzed.

Results
Among 95 eyes studied, 11 cases (11.58 %) of RPE rips were noted during follow up. RPE rips were more common in PEDs with internal reflectivity (82 %) than in PED’s without (18 %). Rips following anti VEGF were more likely to occur with PEDs >1000 μm diameter and > 400 μm height compared to eyes with no rip which had smaller PEDs. Rips frequently occur at the fovea (71.43 %) than elsewhere. All these eyes continued to receive anti VEGF therapy and showed an improvement in visual acuity from baseline. The mean post-treatment visual acuity was 6/36, compared to the pre-treatment vision of 1/60.

Conclusion
Retinal pigment epithelial tears are infrequent complications in eyes with PED undergoing anti VEGF treatment. Eyes with large and tense vascular PEDs are at greatest risk. In spite of the predilection for the fovea, continued treatment with Anti VEGF resulted in improved visual outcome.

Aim of Study
Tears of the retinal pigment epithelium (RPE) are a recognized complication that occur in patients with retinal pigment epithelial detachment (PED) associated with neovascular age-related macular degeneration (wet AMD) and related conditions such as polypoidal choroidal vasculopathy (PCV) and retinal angiomatous proliferation (RAP). While rips following PDT has been reported in literature, rips following anti VEGF therapy, though reported, have not been studied in detail. As anti VEGF therapy is the mainstay in the treatment of wet AMD including PCV, the study of RPE rips is more relevant in this present scenario. This retrospective study is aimed at evaluating the clinical profile, etiopathogenesis, morphological characteristics, evolution and prognosis of RPE tears in eyes with AMD treated with anti VEGF therapy.

Materials and Methods
This was a retrospective analysis of 95 eyes with retinal pigment epithelial detachments due to various etiologies that presented between January 2012 and January 2013 which received anti VEGF therapy with a minimum follow up of 6 months. The clinical course of these 95 patients were analyzed based on data collected from case files to study the incidence of new RPE tears during a mean follow up period of 53.11 ± SD 15.55 weeks (range 26 to 78 weeks) while receiving repeated anti-VEGF therapy. There were 52 (54.7 %) males and 43 (45.3 %) females. The mean age was 67.68 ± SD 8.88 years (range 40-86 years). Of the total, 20 eyes received ranibizumab, 54 eyes received bevacizumab and 21 eyes received combined therapy with PDT. PEDs were associated with occult choroidal neovascularization in 53.68% (51/95), polypoidal choroidal vasculopathy in 36.84% (35/95) and retinal angiomatous proliferation in 9.5 % (9/95) of the eyes. During the follow up period, RPE tears developed in 11 eyes. Among the RPE eyes 9 eyes received bevacizumab, 1 eye received ranibizumab and 1 eye received combination therapy with bevacizumab and PDT. The eyes were evaluated at baseline using spectral domain OCT.
OCT, digital fundus fluorescein angiography (FFA) and Indocyanine Green angiography (ICGA) of HRA Spectralis to confirm the presence of PED and neovascularization (Fig 1). Prior treatments, nature of the lesion, time to tear, and pre-injection and final visual acuities (Snellen and logMAR) were all studied. PEDs were characterized based on their internal reflectivity (serous, fibrovascular, haemorrhagic and drusenoid), largest basal diameter (μm) and maximum height (μm). Eyes with RIP were compared to those without and an evaluation of predictive factors was done. Management and outcome of these eyes were also analyzed.

Treatment of the PED was recommended in the presence of sub-retinal or intra-retinal fluid and deterioration of best-corrected visual acuity (BCVA). Intravitreal anti-VEGF therapy was given in accordance with PRONTO schedule with either 0.5mg/0.05ml ranibizumab or 1.25mg/0.05ml bevacizumab. The initial treatment consisted of 3 monthly injections in all patients. The patients were followed up 2 weeks after each injection. After completion of 3 injections, follow-up examinations were scheduled at 6 weekly intervals, or less frequently if no new visual symptoms developed or visual acuity remained stable. The BCVA, fundus evaluation by slitlamp biomicroscopy, FFA/ICG angiography, and OCT were done to assess the morphological and functional changes after treatment. Retreatment was recommended if there was decrease in visual acuity in association with new or increased sub-retinal or intra-retinal fluid. Presence of PED alone was not an indication for retreatment. Patients who responded poorly to anti VEGF therapy received combination therapy with PDT. None of the patients developed any intra operative complications or post operative adverse drug events.

The difference in morphological features of PEDs such as internal reflectivity, largest basal diameter and maximum height in eyes with and without rips were compared. The time at which the RPE tear developed following anti-VEGF therapy and influence on final visual outcome were analyzed. Adjacent RPE abnormalities (thinning, irregularity, and absence), inner segment-outer segment (IS-OS) loss and scarring were also noted.

**Statistical Methods:** Independent t-test was used for assessing the statistical significance between the groups of non-rip eyes and rip eyes for their PED diameter and height. Paired t-test was used to assess the statistical significance of pre-rip and post rip final visual acuity among the 11 rip eyes.

**Results**

Among 95 eyes studied, 11 cases (11.58%) of retinal pigment epithelial tears (RPE rips) were noted during follow up. Of these, 7 eyes (63.63%) were due to PCV and 4 eyes (36.36%) were due to typical late AMD. The development of RPE tear following anti-VEGF therapy were observed within 8 days to 12 weeks after the intra vitreal injection (mean 26.82 days SD± 25.51 days). In our case series, 7/11 eyes (63.63%) developed rip within 2 weeks of the very first injection of Bevacizumab. We could pick up this abruptness of RPE rip due to our scheduled first follow up at 2 weeks after every injection. The mean number of injections received before the occurrence of RIP was 1.45. The median time interval between the injection and RIP was 2 weeks.

![Time to rip Days](Figure 2: Time to rip in days among eyes with rip)
RPE rips were more common in PED’s with internal reflectivity (9/11, 82%) than in PED’S without (2/11, 18%). Among the RIP eyes, there were 7 fibrovascular, 2 hemorrhagic and 2 serous PEDs. Sub-retinal fluid was present in all 11 cases and intra-retinal fluid in 3 eyes. The rip was located at the base of the PED in all cases. The average basal diameter of PED in non-rip eyes was 1636.29 μm (±SD 908.10 μm) and in rip eyes was 3547.63 μm (±SD 1047.2 μm). The difference in average basal diameter between the two groups was highly significant (p=0.0001). Average height of PED in non-rip eyes was 238.6 μm (±SD 108.12 μm) and in rip eyes was 629.55 μm (±SD 92.65 μm). (Fig 4). The difference in the average height between the two groups was also found to be highly significant (p=0.0001). All the RIP eyes had PEDs >1000 μm in diameter and > 400 μm in height whereas most of the eyes without rip had smaller PED’s. 2 patients (2/11, 18%) who had a spontaneous rip in one eye developed rip in the fellow eye following anti VEGF. 1 patient who underwent combination therapy developed RIP after PDT. All RIP eyes continued to receive anti VEGF therapy as scheduled. 1 eye which had un-resolving vitreous hemorrhage underwent vitrectomy and 1 eye received pneumatic displacement along with anti VEGF therapy.

Vision improved in 9/11 eyes (82 %), stabilized in 1 eye (9.09 %) and decreased in 1 eye (9.09 %). Among the RIPs, 8 (72.72 %) were foveal rips and 3(27.27 %) were extrafoveal. The mean final visual acuity among the foveal rips was 6/60 and among the extra foveal rips was 6/12. Even though there was a drop in vision noticed at the time of RPE tear in those cases of foveal rips, the final visual acuity was still better than pre-treatment vision. The mean post-treatment visual acuity was 6/36, which showed a significant improvement from the mean pre-treatment vision of 1/60 (p=0.005). The final visual acuity also improved in both the cases where vitrectomy and pneumatic displacement was done, with the former having extra foveal rip and the latter a foveal rip. None of the patients developed any intraoperative complications or other post operative ocular complications or systemic side effects infrequently reported with anti VEGF therapy.

![Figure 3: OCT images of Case No: 8 prior to rip (1a), after occurrence of rip (2a) and following resolution and scarring (3a)](image)

![Figure 4: Distribution of PED diameter(μm) and height(μm) among Rip and Non-rip eyes](image)
Discussion

Retinal pigment epithelial tears are documented as a complication that can occur in the natural history of evolution of neovascular age-related macular degeneration with associated retinal pigment epithelial detachment or following treatment with laser, photodynamic therapy (PDT) or intravitreal anti vascular endothelial growth factor (anti VEGF) treatment. Incidence of RPE tear in eyes with exudative AMD is reported between 2% to 6% where as it is 12% to 25% in those with a preexisting PED. The generally poor visual outcome in RPE tears occurring spontaneously or following laser photocoagulation or photodynamic therapy (PDT) were attributed to massive subretinal bleeding, disciform scarring or atrophy in the RPE-free area, and development of rip was considered an end stage phenomenon where no treatment was possible. But with the advent of Anti VEGF, the scenario has changed for the better. Inspite of the occurrence of rip, consolidation of the neovascular process and significant improvement in visual acuity from baseline were observed in majority of these eyes.

The incidence of RPE tears during anti-VEGF therapy in eyes with PED has been reported in about 12–17% of treated eyes. Similar to that reported for the natural history of untreated PED. In our study rips occurred in 11.58%. The relatively quick occurrence of RPE tears within 2 weeks of initiation of anti VEGF therapy needs speculation. The mechanisms postulated are the rapid reduction in fluid with collapse of huge PED in response to anti AEGF therapy, mechanical contraction of tissue due to shrinkage of CNVM or from a loss of RPE integrity. The most commonly reported tractional event following anti VEGF therapy is RPE tear. It has been reported that the rate of rip following anti-VEGF therapy was higher than that observed in elderly patients not receiving therapy (10%). In a multicenter study of 1,280 eyes receiving intravitreal bevacizumab, 16.8% of eyes with vascularized PEDs developed RPE tear with vertical height being the only significant risk factor in a multivariate analysis. In another study involving 60 eyes, no difference were noticed between the agents used (Ranibizumab, Bevacizumab and Pegaptanib), with the basal diameter and vertical height significantly increasing the risk. Chan et al have suggested that the exclusion of patients with preexisting RPE detachments in the pivotal pegaptanib and ranibizumab trials may explain the very low occurrence of RPE tears in these trials. Our study also brings out the fact that rips were more common in PED eyes. As discussed by various authors, we also found >1000 μm diameter and >400 μm height of the PED as a significant risk factor for RIP in these eyes. Chan et al have also reported a PED height of >400 μm as a significant risk factor for RPE tears.

The visual outcome in rip eyes was generally good in our study. Improvement in vision occurred in 82% of eyes. Foveal location of rip was common (72.72%) and a major limiting factor for the poorer visual prognosis in this group. Varying frequency of foveal involvement from 23% to 75% has been quoted in literature. This highlights the unpredictability of the location of rips which will ultimately depend on the initial location of the PED and the subsequent direction of tractional vectors in relation to the fovea. A gradual decrease in vision with increasing RPE contraction has also been reported. A major limitation of our study is the relatively small sample size and further prospective studies in larger series with longer duration of follow up is recommended to arrive at a definitive conclusion regarding the outcome of retinal pigment epithelial tears in eyes with PED undergoing anti VEGF treatment.

Conclusion

Retinal pigment epithelial tears are infrequent complications in eyes with PED undergoing treatment with anti VEGF agents and occur usually 2 weeks after intravitreal injection. The dimensions and content of the PEDs are helpful in predicting this risk and eyes with large and tense PEDs and those with internal reflectivity (vasularity) are at greatest risk. The relatively rapid onset of this complication with therapy, the need for continuation of therapy despite the occurrence of rip and the possible adverse effects on long term visual outcome must be taken into consideration in eyes at risk and explained to the patient beforehand. If one eye had already developed a spontaneous rip, then the risk of developing rip in the fellow eye is increased with therapy. In spite of the predilection for the fovea, continued treatment with Anti VEGF resulted in improvement or stabilization of vision.

References

5. Chan CK, Meyer CH, Gross JG, Abraham P, Nuthi AS,


Abstract

Compare the effectiveness of Phototherapeutic keratectomy (PTK) in treatment of corneal dystrophies and superficial corneal scars with recurrent corneal erosions: visual outcomes, recurrence rate and safety profile.

Methods

PTK was performed in 73 eyes of 64 patients. Data regarding the demography, indications for PTK, ablation depth, optical zone, keratometry, BCL removal, symptomatic relief, pre- and postoperative best spectacle-corrected visual acuity (BSCVA), spherical equivalent changes, recurrence and complications were analyzed. The indications for PTK in our study were classified into two categories – group A: eyes with corneal dystrophies and corneal scars (n=41) and group B (n=32) with recurrent corneal erosions.

Results

The average age of the patients was 32.25 years (±16.4). The mean follow up period was 3.875 months (±10.01 months). The ablation depth in Group A ranged from 100 μ to 15 μ and in group B 5μ to 10 μ Post operatively, there were no significant complications. All eyes were epithelized within 7 days (average 4 days) While the overall BSCVA in the patients improved from 1.78 (LogMAR) to 0.18 in group A as compared to group B in which BSCVA improved from 1.19 logMAR to 0 The most common indication in group A was superficial stromal corneal dystrophy (n=32) and the most common indication in group B was post traumatic/corneal erosions (n=30). Ninety-six percent (n=62) of all patients had alleviation of symptoms. Recurrence of symptoms was seen in 1 eye with recurrent corneal erosions which required retreatment.

Conclusion

PTK is a safe and effective procedure. This study outcome suggests that PTK improves BSCVA. PTK appears to improve ocular surface health. Furthermore, PTK can be recommended to most patients with corneal dystrophies as a treatment modality prior to other more invasive procedure (viz. penetrating keratoplasty).

Keywords

phototherapeutic keratectomy, PTK, corneal scars, keratoplasty, corneal dystrophy, recurrent corneal erosions

Introduction

Corneal diseases such as scars, degenerations, dystrophies, bullous keratopathy, and band-shaped keratopathy (BSK) are important causes of corneal blindness; anterior stromal disease being superficial can be treated using various minimally invasive surgical procedures like lamellar keratoplasty (LKP) or superficial keratectomy or by excimer lasers, that is, phototherapeutic keratectomy (PTK). Phototherapeutic keratectomy (PTK) is an important excimer laser based surgical tool for the treatment of numerous anterior corneal disorders. PTK can be considered to be a bridge between medical and surgical management of corneal diseases. Apart from macular,1 granular2, lattice3 and map dot fingerprint4 dystrophies; other indications for which PTK has been reported to be an effective treatment include recurrent corneal erosion syndrome5–7 stromal scar tissue such as post surgical scars and Salzmann nodular degeneration.

Aim

We evaluate in this study the effectiveness of PTK in treatment of variable pathologies with anterior corneal lesions.

Materials and Methods

All cases of corneal disease which had undergone PTK from January 2010 to December 2012 at the Excimer Lasik Centre were retrospectively reviewed. The details of the cases were retrieved from the medical records. A thorough preoperative clinical evaluation was performed for all patients. This included detailed history, refraction, Slit lamp examination, Corneal Topography, ultrasonic Pachymetry, schirmer’s test, intraocular pressure measurement and posterior segment evaluation.

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Email: aneetajabbar@yahoo.com
Photo Therapeutic Keratectomy (PTK) was performed in 73 eyes of 64 patients. The PTK Corneal ablations were performed under topical anesthesia. A 6 to 6.5 mm treatment zone was used. Allegreto WaveLight Excimer Laser was used in all cases, and included a 193-nm UVC beam.

Central corneal epithelium was removed using 20% Alcohol applied for 20 seconds. The corneal deposits were thoroughly scraped using a scraper. The surface was smoothened of the underlying irregularities by doing PTK.

A thin layer of sodium hyaluronate, 0.1%, was then applied with a lightly moistened surgical sponge and PTK resumed. One surgeon (AJ) performed all surgeries. At the end of the procedure, Moxifloxacin 0.5% or Ofloxacin 0.3% eye drops were instilled. A bandage contact lens was placed in the eye and immediate slit lamp examination was conducted. Patients were then put on Fluorometholone, 0.1% for one month in a tapering dose and antibiotic eye drops for one week.

Patients were followed up at approximately 1 week, 1 month, 3 months, 6 months, and at 1-year intervals thereafter. During each visit, ophthalmologic examinations were performed.

Data regarding the demography, indications for PTK, ablation depth, optical zone, keratometry, BCL removal, symptomatic relief, pre-and postoperative best spectacle-corrected visual acuity (BSCVA), spherical equivalent changes, recurrence and complications were analyzed. The indications for PTK in our study were classified into two categories – group A: eyes with corneal dystrophies and corneal scars (n=41) and group B (n=32) with recurrent corneal erosions.

### Ablation depth

The ablation depth in Group A ranged from 100 μ to 15 μ and in group B 5μ to 10 μ.

Table 1 – Indications of PTK

<table>
<thead>
<tr>
<th>Indication</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granular Dystrophy</td>
<td>11</td>
<td>15.06%</td>
</tr>
<tr>
<td>Macular Dystrophy</td>
<td>15</td>
<td>20.6%</td>
</tr>
<tr>
<td>Band Shaped Keratopathy</td>
<td>6</td>
<td>8.2%</td>
</tr>
<tr>
<td>Lattice Dystrophy</td>
<td>1</td>
<td>1.3%</td>
</tr>
<tr>
<td>Post traumatic scars</td>
<td>10</td>
<td>13.6%</td>
</tr>
<tr>
<td>RCE ( Idiopathic)</td>
<td>21</td>
<td>28.76%</td>
</tr>
<tr>
<td>RCE ( post traumatic)</td>
<td>7</td>
<td>9.58%</td>
</tr>
<tr>
<td>RCE ( Dystrophic)</td>
<td>2</td>
<td>2.73%</td>
</tr>
</tbody>
</table>

Abbreviation: RCE Recurrent Corneal Erosion

Post operatively, there were no significant complications. All eyes were epithelized within 7 days (average 4 days).

While the overall BSCVA in the patients improved from 1.78 (LogMAR) to 0.18 in group A as compared to group B in which BSCVA improved from 1.19 logMAR) to 0.

Ninety-six percent (n=62) of all patients had alleviation of symptoms. Recurrence of symptoms was seen in 1 eye with recurrent corneal erosions which required retreatment.

### Discussion

PTK has been used as an effective therapeutic tool in the management of corneal pathologies for over two decades now. It has several advantages such as precise control of the depth of ablation, fast postoperative recovery, ease of use, creation of a smooth base for corneal re-epithelialization, and the ability to repeat treatment if required. PTK is best suited for disorder in the anterior 10%–20% of the corneal stroma.

In our study, patients were classified depending on the indication, and formed 2 groups; group A had patients with corneal dystrophies and group B included recurrent corneal erosions; because PTK in corneal dystrophies benefit from both visual clarity as well as treat the associated recurrent corneal erosions, while other superficial corneal pathologies in group B benefit mainly from the visual disturbance as well as symptomatic relief.

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**Table 1 – Indications of PTK**

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</tr>
</tbody>
</table>

Abbreviation: RCE Recurrent Corneal Erosion
There is one large series Indian study. Sharma et al\textsuperscript{9} stated that in their study, bullous keratopathy accounted for 52.7\% of the patients and a mere 0.15\% of the patients had corneal dystrophies. In the study by Sharma et al, patients were divided into two groups: those with bullous keratopathy and those with other corneal pathologies.

The mean improvement of BSCVA seen was 20/222 (0.09) to 20/86 (0.23) in the corneal pathology group and 20/384 (0.05) to 20/202 (0.09) in the bullous keratopathy group. In our study, the overall BSCVA in the patients improved from 1.78 (LogMAR) to 0.18 in group A as compared to group B in which BSCVA improved from 1.19 logMAR) to 0.

In Group A, comprising of patients with corneal dystrophies, the improvement of BSCVA was in accordance with other similar studies by Hafner et al\textsuperscript{1} and Wagoner and Badr.\textsuperscript{10} Hafner and co-authors reported temporary improvement in BSCVA in patients with macular dystrophy for limited time period in which 90\% of cases had dystrophy recurrence and 60\% did penetrating keratoplasty in a later date. This was probably due to diffuse corneal haze and the opacities persisting in the deeper layers of the cornea after PTK.\textsuperscript{1} This explains the importance of having PTK in superficial corneal dystrophy to have the best visual results.\textsuperscript{10}

In the PTK literature for recurrent corneal erosions, the reported rate of success, regarding alleviation of symptoms and prevention of recurrence ranges between 74\% and 100\%.\textsuperscript{11} In our study Ninety-six percent of all patients had alleviation of symptoms. Recurrence of symptoms was seen in 1 eye with recurrent corneal erosions which required retreatment.

Our case series, had post traumatic recurrent corneal erosions (RCE) 21 eyes with idiopathic recurrent corneal erosion patients and two eyes with Map dot fingerprint dystrophy, who were treated with PTK. The mean follow up period for the RCE patients was 19.14 months (±8.78, range: 12–36 months) and of these patients one eye needed a repeat procedure at 3 months after the first procedure respectively.

Furthermore, Barlya et al studied the efficiency of PTK for RCE. The mean follow up period was 17.4 months. They reported the recurrence rate of RCE to be 36\%4 which is higher than our results All recurrences in the current study were in the first year after the procedure similar to the other studies in which most recurrences were noted in the first year. In a recent review of recurrent corneal erosion syndrome, PTK was found to be the most effective treatment modality.\textsuperscript{11}

This is partly explained by the observed histological findings that PTK increases the density of hemidesmosomes in the cornea.\textsuperscript{12}

In our study, corneal haze was rare and the significant induced hyperopia was limited for cases with deeper PTK ablation. In our series, there was no significant change in the spherical equivalent post-PTK in the recurrent erosion patients secondary for the superficial stromal ablation (10 microns).

PTK is a safe and minimally invasive procedure for the treatment of superficial opacities and helps to gain a moderate increase of visual acuity. Patients with stromal corneal dystrophies also benefit from improved vision as demonstrated in our study.

Treatment in these cases when performed for reduced visual acuity is largely successful by clearing central corneal opacification and deposits. Mild transient superficial stromal haze developed in some (55\%) eyes in this series, but visual improvement and rehabilitation was rapid in the majority of cases.

A repeat PTK procedure can be performed for recurrence of dystrophies which is usually central and superficial may help maintain good visual acuity for a longer period of time. This reduces the strain on the supply of corneal buttons, especially in developing countries.

Also a prior PTK procedure does not compromise the outcome of subsequent penetrating keratoplasty. Refractive changes following PTK are variable. Induced hyperopia does occur when deeper ablation is performed. A “hyperopic shift” was seen only in the 33\% patients in the current study. A possible explanation for this could be a large ablation zone, the use of masking fluid, and the centration of the laser aperture over the mid periphery and not the apex of the cornea. A myopic shift was seen in 17\% of subjects in this study possibly as a result from central steepening of the cornea with more peripheral ablations or due to central island formation. This can be confirmed by topographic studies. Unfortunately due to the retrospective study we could not assess this aspect on topography. Some of the other factors that may affect the refractive results include epithelial remodeling, associated nuclear sclerosis, or the inaccuracy of preoperative refraction due to corneal scarring.

Conclusion
To conclude, our study shows that PTK is a safe, simple
and effective procedure that helps achieve symptom alleviation, increase visual acuity, and delays the need for penetrating keratoplasty, and PTK has minimal side effects and complications.

References
A New Technique of Sutureless SF IOL

Dr. Veerappan Saravanan MS

Introduction
Intraocular lens (IOL) implantation to correct aphakia offers a better visual rehabilitation in comparison to aphakic spectacles or contact lenses. In the absence of adequate capsular support, anterior chamber IOLs, iris fixated IOLs and scleral fixated intraocular lens (SFIOL) may be considered. Anterior chamber IOLs are associated with complications such as glaucoma, hyphaema, uveitis, cystoid macula oedema, and corneal decompensation. SFIOL is an accepted alternative, but has its own associated limitations. SFIOL has been used in both adults and children with success, either as a single procedure or combined with penetrating keratoplasty and other vitreoretinal procedures. There are many variations of the technique and a range of complications of varying frequencies, which include suture and knot erosions, lens tilt, dislocation or decentration, infection, glaucoma, cystoid macular oedema, corneal decompensation, retinal detachment, and suprachoroidal haemorrhage. Complications are common, and suture degradation is an important long-term complication, particularly in young patients.[1]

To avoid the suture related intraoperative and postoperative problems, Gabor and authors introduced a new technique wherein they developed a sutureless technique for sulcus fixation of a posterior chamber IOL using permanent incarceration of the haptics in a scleral tunnel parallel to the limbus. This method combines the control of a closed-eye system with the postoperative axial stability of the posterior chamber IOL while avoiding suture related problems.[2]

In his technique, Gabor et al used cannulas to create a limbus-parallel tunnel at approximately 50% scleral thickness, starting from the ciliary sulcus sclerotomies and ending with externalization of the cannula after 2 or 3 mm. A standard three-piece foldable IOL with a haptic design fitting to the diameter of the ciliary sulcus was implanted with an injector, and the trailing haptic was fixated in the corneal incision. The leading haptic was then grasped at its tip with an end-gripping 25-gauge forceps, pulled through the sclerotome, and left externalized. With the same forceps, the haptic was then introduced into the intrascleral tunnel. The same maneuvers were performed with the trailing haptic. The ends of the haptics were left in the tunnels to prevent foreign body sensation and erosion of the conjunctiva and to reduce the risk of inflammation. The sclerotomies were checked for leakage. If necessary, they were sutured.[3]

We describe a much simpler technique which is a modification of the above mentioned Gabor’s technique. It also avoids the use of a specialized forceps for the haptic insertion. Any 25 gauge micro vitreoretinal forceps with a firm grip (e.g. Alcon Grishaber max grip or serrated forceps) can be used.

A linear cut (2mm approx.) is made adjacent and perpendicular to the limbus in the upper right (supero temporal quadrant in right eye, superonasal quadrant in left eye) (Fig 1). This cut is deep enough to cut through the conjunctiva and approximately 50% of scleral thickness. Using a 1 mm to 1.5mm keratome blade, a limbus parallel 3mm scleral pocket is fashioned starting from the groove incision downwards along the limbus (Fig 2 to 4). This step is then repeated in the lower left quadrant (inferonasal in right eye and inferotemporal in left eye) diometrically opposite to the first scleral pocket (Fig 5 to 7). A 24gauge needle or 25G trocar used for MIVS (MicroVitreoRetinal Surgery) is used to make two sclerotomies at 1.5 mm from limbus within the groove on either side(Fig 8 to 9).An anterior chamber maintainer is used to maintain the IOP throughout the surgery.

Main incision
A clear corneal tunnel incision is made in superior quadrant for injecting the foldable 3 piece IOL (Fig 10). A good anterior vitrectomy is done. The IOL is then injected into the anterior chamber.

Haptic externalisation
As the IOL is being injected, a 25G micro vitreos retinal forceps is introduced into the globe through the lower left sclerotomy and the tip of leading prolene haptic is held inside the eye and externalized(Fig 11 to 12). The trailing
haptic is then held with the MVR forceps introduced through the upper right sclerotomy using a handshake technique and externalized (Fig 13). Care should be taken to hold the haptics at the very tip to avoid kinking or fracture of the haptic. In case of IOL flip during the process of insertion, the haptics will face in the wrong direction. Holding both the haptics with McPherson forceps and rotating them like a bicycle pedal can correct this.

**Tucking the haptics**

The tip of the haptic is held with a McPherson forceps and tucked into the already fashioned limbus parallel scleral pockets (Fig 14 to 15). If the IOL is not centered well in the pupillary axis, the haptics can be pulled out or pushed in to the scleral pocket on either side to center the IOL (Fig 16).
There was a significant improvement in visual acuity from Uncorrected pre operatively 1.63 Log MAR to post operative best corrected of 0.21Log MAR.

**Intra-operative complications**
1. Haptic bending (can be straightened with Mcpherson’s forceps before tucking the haptic).
2. Haptic breaking needs removal and re-doing the procedure if adequate length of haptic is not available for tucking and stabilizing the IOL
3. Scleral pockets not exactly 180 degree apart may result in decentration of the IOL
4. Leaking sclerotomies may require an absorbable scleral suture
5. Hyphema

**Post operative complication**

**Early (within one month):**
Mild corneal edema and vitreous hemorrhage which resolved without any intervention are the most frequent early complications.

**Late (after one month):**
Raised IOP and cystoid macular edema were the most frequent complications.

Almost all the complications were managed mostly conservatively. No case had clinically significant scleral or conjunctival changes in the pocket area were haptics were tucked. None of the case had clinically significant IOL decentration or dislocation in the study period.

**Conclusion**
As this technique avoids the risk of long term suture degradation and IOL dislocation associated with sutured Scleral fixated IOLs, this may be a safe and simple procedure in cases where conventional in the bag IOL implantation was not possible and it can be done in pediatric age group also.

**References**
Pearls in Performing A Good Biometry

Dr. Sony George MS

Cataract surgery has advanced in a rocket pace in the recent past making it a kind of refractive surgery, aimed at an unaided restoration of the perfect range of vision of 6/6 N6 with perfect intermediate vision too. The surgical techniques have also advanced with femtosecond laser cataract surgery gaining popularity, and premium IOLs- multifocal, multifocal toric, trifocal and accommodative IOLs being the in thing.

It is in this pretext that a precise biometry and a perfect IOL power calculation becomes a very essential prerequisite for a perfect cataract surgery. There is no space for a residual error in the premium cataract surgery scenario.

What is Biometry?
Biometry is a precise technique, fine tuned over time, to calculate the exact power of the Intraocular Lens to be implanted in the capsular bag after cataract removal, so as to give the patient an emmetropic correction for far vision and if possible near and intermediate too.

Major factors affecting IOL power calculation
The major factors which determine the IOL power calculation are mainly the following
1. Axial length measurement of the eye
2. Corneal curvature measurement ie : keratometry
3. Estimation of the anterior chamber depth (ACD)
4. Personalisation of A Constants/Surgeons factor(SF)
5. Prediction of Effective Lens Position (ELP)

Although ELP is not taken into consideration in the older formulae, in the fourth generation formulae like the Holladay 2 it is an important determinant of the IOL power.

Keratometry
Accurate assessment of the corneal curvature is of utmost importance in many ways
1. To plan the incision site for the cataract procedure. An incision placed on the steep meridian can negate or reduce preexistent corneal astigmatism .
2. To aid in the IOL power calculation as inputs into the various formulae used
3. In calculations for Toric IOLs using online calculators as inputs, in eyes with significant preexistent corneal astigmatism

Each dioptre of error in keratometry can give rise to a 0.9 D error in the IOL power prediction.

Keratometry can be done in 4 ways
1. Manual Keratometry : This technique uses a manual B&L model keratometer. Mires projected onto the corneal surface are mechanically aligned to get the horizontal(K1) and vertical(K2) K readings. The central 3 mm of the cornea is measured. An experienced technician can obtain fairly accurate readings with this equipment. The equipment is quite economical. Regular calibration aids is increasing accuracy.
2. Automated keratometry : This mode uses the Autorefractokeratometers(ARK) for measuring K values. Most of the commercially available models yield reasonably accurate values. It is upto the technician to take repeated measurements and delete bizarre readings so as to obtain accuracy. Regular calibration is a must with this tool too.
3. Automated keratometry of the IOL Master/ Lenstar: As opposed to the manual keratometer these measure the central 2.5 mm of the cornea. About 60 data points are measured with each attempt and an averaging is done which makes it quite accurate.
4. Topographic Keratometry : In centres where a topographic facility is available, topobased K values will aid accuracy

Axial length measurement
The two major modalities of axial length assessment are
1. Ultrasound Biometry- A Scan : This is a time tested and still relevant modality. One could do a contact method or an Immersion method which is much more accurate.
2. Optical Biometry : This is a relatively new modality. It
uses Partial Coherence Interferometry or Polarimetry\cite{1,2} for measuring axial length. It is much more precise than the ultrasound. Although more precise, this method has the disadvantage of not being able to assess the axial length in white mature cataracts and thick posterior subcapsular cataracts.

**Ultrasound biometry**

A transducer probe emitting ultrasonic waves of 10 MHz is used. The waves travel from the anterior corneal surface to the vitreo-retinal interface and back, which is picked up by the probe and the axial length is interpolated from the time taken for the travel. The axial length is measured in mm from the anterior cornea to the Internal Limiting Membrane (ILM).

The procedure claims an accuracy of +/- 0.1 mm, in experienced hands and a relatively emmetropic eye.

**A Scan Ultrasound machine with immersion technique compatibility**

**Contact Method**

Here the transducer probe, after anaesthetizing the cornea, is placed in direct contact to the anterior corneal surface centrally at the pupillary area in a perpendicular fashion. A number of readings are taken in a manual or auto mode. The readings with improper spikes are deleted and an averaging is done.

Due to the possibility of inadvertent pressure on the cornea, an indentation of upto 0.3 mm is possible in this method which can cause an error of 1.0 to 1.5 Dioptre in the IOL calculation. Hence this technique is getting obsolete in most of the Ophthalmic Centres world wide.

**Immersion Technique**

This is a much more accurate technique. Here a waterbath is placed on the cornea using a sclera shell (eg. Praeger Shell). The hard tip transducer is applied to the shell. The rest of the procedure is similar to the contact method.

If done properly, immersion technique gives very accurate and reproducible results in all types of cataracts. The technique does not require any expensive add ons except the Praeger shell, which now is supplied by most manufacturers of A Scan equipment. The procedure has a very short learning curve.

To those of us who still use the contact method, it is highly recommended to shift to immersion as soon as possible for very obvious reasons.

**Prager sclera shell used for immersion ultrasound**

**A Scan**

**Optical biometry**

This method utilizes Partial Coherence Interferometry for axial length measurement. The IOL Master from Carl Zeiss is an example. The IOL Master utilizes a modified Michaels Interferometer and uses coaxial infrared rays of 780 nm wavelength and a coherence length of 130 nm.

It is a non contact, no anaesthesia procedure and is very fast. It measures the axial length from the anterior cornea to the Retinal Pigment Epithelium (RPE).

The equipment claims an accuracy of 0.01 to 0.02 mm, which is almost 5 times that of the ultrasound.

Unlike ultrasound, it is not much affected by the extremes of axial length i.e: too long or too short, which makes it more useful in ammetropic patients.

The technique is also not much affected by the state of accommodation and pupil size.

The settings are also easily adjustable for aphakia, pseudophakia and silicon oil filled eyes.

One major advantage is that it is an all in all procedures for
biometry ie, keratometry, axial length and AC Depth are all measured in one go. There is no need for entering values from outside to the equipment. This eliminates errors in IOL power calculations due to clerical data entry errors.

The IOL Master- Optical Biometry

ACD Measurement

This is a standard modality now in most advanced A Scan machines as well as the Optical Biometry devices. The ACD can be calculated from the corneal epithelium or the endothelium.

The IOL master typically measures ACD from the corneal epithelium. It is possible in phakic eyes only. It is a slit based, measurement from the anterior corneal vertex to the anterior lens vertex. It has an accuracy of +/- 0.1 mm. The ACD is needed in the 4th generation formulae to predict the effective lens position (ELP).

How to perform a good biometry?

Always pre-assess the eye to be scanned prior to the procedure. It is always better to treat or stabilize any ocular surface disease or dry eye prior to the procedure. Liberal use of lubricants is beneficial to get proper keratometric readings.

Keratometry

Always do the keratometry prior to any procedure which involves corneal contact ie, applanation tonometry, contact biometry etc. It is also advisable to avoid use of anaesthetic drops, stains like fluorescein etc since these can alter the corneal surface characteristics.

Manual keratometry

Make sure that the equipment has been calibrated. Position the patient and the eye comfortably and properly on the keratometer. Ask the patient to blink so as to wet the ocular surface. Project the mires onto the cornea and focus the mires so as to make it crisp and clear. Align the mires in the horizontal and vertical meridia using the turning knobs on either sides. Ensure perfect superimposition of the plus and minus symbols.

In case the mires are not parallel, turn the tube in a circular fashion till they becomes parallel and then align and superimpose. Take multiple readings from each eye. After excluding bizarre reading take an average.

Automated keratometry - ARK/ IOL Master/Lenstar

Calibrate the machine. Ensure proper wetting of the cornea by blinking or use lubricants. Instruct the patient to look at the fixation light or target depending on the machine. Take multiple readings and delete bizarre ones. Take an average of all the acceptable readings.

Topographic K readings

Wherever possible try and get Topographic K Readings

It is always advisable to use more than one method of keratometry, to reduce chances of errors. Whenever there is a suspicion of error please repeat the procedure and take multiple readings. If there is a difference of more than 1 D in the average K between the eyes, it is better to repeat, if possible by a second technician or surgeon.

Anterior chamber depth

This can be done using the newer generation ultrasound based machines and the optical equipment like the IOL Master. In the IOL Master go to the ACD measurement mode, which gives you a slit beam. Use the joystick to focus the light spot crisp on the anterior lens surface. Click the button once focused. Delete bizarre readings and take the average.

Axial length measurement

If you are planning a Non Contact Biometry, like the IOL Master, always do that first, before an Ultrasonic Biometry since it involves contact to the corneal surface by the waterbath/sclera shell/ fluid. This may affect the keratometric/ axial length reading acquisitions.

Immersion biometry – ultrasonic

Calibrate your equipment at least once at the beginning of the day. Carefully enter the keratometric values to the equipment, to avoid clerical errors. Make the patient lie down comfortably. Anaesthetise the cornea with proparacaine/lignocaine eye drops. Place the Praeger shell on the eyeball and fill it up with saline. Take multiple readings and delete the ones with improper spikes. In a good measurement there should be 5 spikes of equal and full heights, the cornea, the anterior lens spike, the posterior lens spike, the retina, the sclera. Posterior to the sclera, the orbital spikes should be gradually attenuating.

Any measurement with irregular or incomplete spikes should be discarded or deleted. Always try to measure the contralateral eye also, wherever possible. Repeat measurements by a second person if there is a difference of more than 0.5 mm in axial length between the eyes unless there is a preexistent evidence for anisometropia.
Ascan picture showing an acceptable recording. Note that the corneal, lens, retinal and sclera spikes are full and of equal heights.

**Optical Biometry**

Always make sure that the eye is moist, by blinking or use of artificial tears. Position the patient on the machine and align the device to get a proper focus. Ask the patient to look straight into focusing target.

Use the joystick to get a good focus and press the click button to acquire the readings. Follow the instructions given by the machine eg. Ask the patient to blink etc.

Delete all bizarre readings. Take the average as the axial length. Like in ultrasound always measure both eyes and repeat if there is more than 0.5 mm difference in AL.

**Choosing the right formula for IOL calculation**

Perhaps this is one area where a lot of prudence is required in obtaining target emmetropia. The common formulae in use presently are:

- **Empirical**: SRK II
- **Geometric Optical**: SRK-T, Hoffer Q, Haigis and Holladay SRK II

This formula can still be used and gives relatively good results in normal axial lengths. However in longer and shorter eyes the results are erratic. The following normogram can be used in these circumstances.

<table>
<thead>
<tr>
<th>Axial length</th>
<th>Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-22 mm</td>
<td>1 D to the calculated IOL power</td>
</tr>
<tr>
<td>20-21 mm</td>
<td>Add 2 D</td>
</tr>
<tr>
<td>&lt; 20 mm</td>
<td>Add 3 D</td>
</tr>
<tr>
<td>&gt; 24.5 mm</td>
<td>Minus 0.5 D</td>
</tr>
</tbody>
</table>

**SRK-T**

This formula is the most widely used presently. It gives relatively accurate IOL calculations in normal to moderately long eyes ie 22.5 mm to 28.0 mm. In longer eyes over 28 mm the results become less accurate with an underestimation of the IOL power.

**Holladay 1**

This formula can be used in normal to long eyes of axial lengths of 22.5 to 32 mm. The calculations are relatively more accurate in axial lengths of more than 28 mm when compared to the SRK-T.

**Hoffer Q**

This is useful in short eyes, normal and slightly long eyes of axial lengths 20.0 D to 26.0 D.

**Haigis**

This formula can be used over a wide range of axial lengths with the use of optimized A constants:

- A0, a1, a2 optimised a constants
- Extreme short to short eyes: 17mm to 19 mm
- Long eyes: 28mm to 34 mm

**Holladay 2 IOL Consultant**

Relatively most accurate in all ranges of axial lengths of 17 mm to 34 mm.

**Personalising A constants**

Select 15 or more patients with each IOL being used.

Take the preop (wherever possible) and post op refraction readings.

Calculate the ideal IOL power based on the residua refractive error. Calculate the error in IOL power if any. Take an average of the errors in IOL powers and make suitable adjustments to the A constant provided by the manufacturers to arrive at your personalized A constant.

**Example**:

If you are getting an average error in IOL power of -0.25 with an IOL of A constant 118.0, then your personalized A constant would be 118.25.

If you are using an Optical equipment like the IOL Master, then your pre and post op data for 15 patients each of all the IOLs can be fed directly to the machine and the software will...
Mean absolute prediction errors with various formulae

<table>
<thead>
<tr>
<th>AL in mm</th>
<th>SRK-T</th>
<th>Haigis</th>
<th>Holladay 1</th>
<th>Holladay 2</th>
<th>Hoffer Q</th>
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<tr>
<td>20-21.99</td>
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<td>0.25-0.5</td>
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<td>24.5-25.99</td>
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<td>0.25</td>
<td>0.25-0.5</td>
<td>0.25-0.5</td>
</tr>
<tr>
<td>28-30.0</td>
<td>0.25-0.5</td>
<td>0.25</td>
<td>0.25</td>
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</tr>
<tr>
<td>Minus power IOLs</td>
<td>0.5-1.0</td>
<td>0.25</td>
<td>0.25-0.5</td>
<td>0.25</td>
<td>not recommended</td>
</tr>
</tbody>
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automatically personalize your A constant.

ULIB
This site http://www.augenklinik.uni-wuerzburg.de/eulib.com allows you to download personalized A constants for most of the IOLs. This is provided and updated by a user group of IOL Master. This data can be fed to your IOL Master.

Biometry in post refractive surgical cases
This topic itself is exhaustive and beyond the scope of this article. However, we shall briefly discuss this issue. The main problem here is the error possible in the keratometric value determination since the corneal curvature and thickness have been modified by the refractive surgical procedure.

If you have the preop and post op refraction readings, keratometric and topographic data then the History method can be used to calculate the K reading to be fed into the Biometry.

\[
\text{Kact} = \frac{\text{Kpre} + \text{Rx pre} - \text{Rx act}}{1-0.012 \text{Rx pre}} - \frac{1-0.012 \text{Rx act}}{1-0.012 \text{Rx act}}
\]

Kact : needed actual corneal power
Kpre : corneal power before refractive surgery
Rxact : actual refraction
Rxpre: refraction before refractive surgery

Contact lens method
Here an over refraction is done after placing a hard contact lens

\[
\text{Kact} = \frac{\text{Pcl} + \text{Pzcl} + \text{Rx with} - \text{Rx without}}{1-0.012 \text{Rx with}} - \frac{1-0.012 \text{Rx without}}{1-0.012 \text{Rx without}}
\]

Rx with: Refraction with Contact Lens
Rx without: Refraction without Contact Lens
Pcl: Power of hard Contact lens
Pzcl: Power of the back surface (base curve) of the hard contact lens

The newer formulae like the Shammas can be used which has provisions for entering the pre refractive and post refractive surgical data directly into the formula.

One can also use the Arranberrys double K method for the calculations. Normograms are provided whereby depending on the axial length and the refractive correction, done values are available to be added or reduced from the IOL power obtained. The normograms are available individually for various formulae.

The ascrs website ( ASCRS POST KERATOREFRACTIVE ONLINE CALCULATOR) or the site www.doctor-hill.com can be helpful. The Holladay 2 IOL consultant will also be of help in these situations.

Common contributing factors for poor refractive outcomes after Lens surgery
1. Use of outdated formulae/non optimized IOL constants
2. Incorrect measurement of axial length
3. Incorrect Keratometry values
4. Mistakes in entry of data into the IOL calculation programme
5. Incorrect labeling or packaging by the manufacturer
6. Mistakes in providing the correct IOL at the time of surgery eg: mix up IOL with another patient

Golden rules for a perfect IOL power calculation
1. Have well trained and experienced technicians attentive to the minutest details in performing keratometry and biometry
2. Calibrate all equipment for keratometry and biometry periodically
3. Measure both eyes always wherever possible.
4. Repeat or double check the measurements whenever in doubt and whenever possible especially when there is a difference of more than 0.2 mm in the same eye or more than 0.3 mm between the eyes unless explained by reasons like preexistent anisometropia.
5. Always use 3rd generation formulae or 4th generation formulae
6. Double check all manual entries like keratometry and axial length.
7. Use special formulae or special methods for calculating...
the corneal power to be fed in post refractive surgical cases.
8. Have a proper IOL calculation report in the OR and make a final verification prior to IOL implant.

References
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Therapeutic Challenge: Retina

Dr Mahesh Gopalakrishnan. MS DNB FRCSEd

Case
A 42 year old gentleman presented with scotoma and defective vision of left eye for last 6 months. No subjective improvement was noted by him over the period. Best Corrected Visual acuity was Right Eye (OD) 6/6 N6 and Left Eye (OS) 6/18 N10. Serial Optical Coherence Tomography (OCT) was done and shows serous macular detachment which is not resolving over last 4 months. Fundus Autofluorescence shows hyper auto fluorescent area in the central macula. Diagnosis - Non resolving Central Serous Chorioretinopathy (CSCR). Patient was not on any steroids in any form. He was a non smoker non alcoholic, Type a personality. Fundus photo, Fundus Fluorescein Angiography (FFA) (Early, mid and late) and Indocyanine Green Angiography (ICG) (Early and late) are given below.

Questions
1. How long will you wait in a case of fresh CSCR?
2. In this case what is the preferred method of treatment?
3. What is the role of different types of Photo Dynamic Therapy (PDT) - Half dose, quarter dose, reduced fluence, full fluence in CSCR
4. In your opinion is there any role of anti Vascular endothelial Growth Factor (VEGF) drugs in CSCR with foveal leak

Dr. Mahesh P Shanmugam
Sankara Eye Hospitals. Bangalore

This 42 year old gentleman has persistent chronic central serous retinopathy necessitating treatment.

1. In a fresh CSCR, I ask the patient come back a month later after baseline OCT. If there are no quantified signs of resolution on OCT of the extent of the neurosensory detachment, I would suggest treatment. If there is evidence of improvement assessed by decrease in area of neurosensory detachment on OCT, I would watch.

2. Preferred modality of treatment in this case would be photodynamic therapy considering the multiple leaks that appear juxta foveal. There are no other modifiable risk factors such as steroid therapy, systemic illness suggestive of hypercortisolism etc. Persistence of chronic CSC, being the indication for treatment in this gentleman.

3. Full dose PDT is best avoided, particularly in Indian population (increased Retinal Pigment Epithelium (RPE) pigmentation) to minimize risk of RPE atrophy. Half dose or half fluence can be considered and a recent head to head comparison has found half dose to resolve the SRF faster with lesser number of recurrences when compared to half fluence. Decreasing the fluence further may be ineffective or deleterious.

4. I have not had favorable results by treating CSC with anti-VEGF - this of course is my personal experience of
less than a handful of cases and should not be given much consideration.

Dr Nitin Shetty
Manipal Hospital, Bangalore
1. Generally 1-2 months. Photoreceptor damage has been reported by the 4th month - hence the need to treat much before that.

2. Would prefer a Low fluence PDT in this case

3. PDT has been found to be quite effective for CSC - thought to work by reducing the choroidal hyper permeability and by tightening the blood retinal barrier at the RPE. Low dose and low fluence PDT have both been found to be effective - has a possible advantage of causing less PDT related complications like acute vision loss and increased RPE alterations.

4. Don’t think there is a role for Anti VEGF in treatment of CSC

Dr Rajesh Puthusseri
Al Salama Hospitals, Perinthalmanna
1. Detachment of macula for more than 3 months can result in photoreceptor atrophy. Since the fluid takes around another 1 month to disappear after laser I do the laser at 2 months. Indications for an earlier treatment are the job related requirements or poor visual outcome to observation in the other eye. Recurrent cases also receive earlier treatment.

2. Here the leakage is just inside the edge of foveal avascular zone. Thermal laser cannot be done since it can result in a foveal scar. Low fluence or low dose PDT can be tried. PDT is currently the recommended treatment modality for CSCR since it addresses the underlying pathology of choroidal hyper permeability. Since PDT is expensive, for our patients it may be reserved for chronic CSCR with diffuse retinal pigmentary changes or non resolving acute CSCR with leakage involving the fovea

3. Full fluence PDT may cause persistent choroidal ischemia in the treated area, RPE changes, CNVM and damage to the adjacent normal choroid. Half fluence has less chance for these complications. The rationale behind half dose PDT is also the same. Half dose PDT has been reported to be more effective than 1/3 rd dose PDT.

4. VEGF levels have not been demonstrated to be elevated in the aqueous in CSCR. It is hypothesized that there is localized secretion of VEGF secondary to hypoxia in choroid and RPE, which may respond to anti-VEGF injections. Current evidence does not support the use of anti VEGF injections for CSCR.

Dr Chirag Bhatt
Susrut Eye Hospital, Calcutta
Through this non resolving CSCR case you have raised very important questions:

1) In a case of fresh CSCR with good vision in other eye, we would like to wait for at least 3 to 4 months as natural history shows it resolves spontaneously and 80-90% patients return to 20/25 or better vision.

2) In this case as it has been already 4 months and still it has not resolved, it should be treated. FFA and ICG reveals leakage within Foveal Avascular Zone (FAZ) so thermal laser should not be used instead half fluence PDT should be the preferred treatment.
3) PDT is believed to hasten both fluid resorption and visual recovery. Multiple authors have used PDT as a first-line therapy for acute focal leaks from CSCR with reported success. Most papers describe resolution of subretinal fluid within 1 month of treatment.

Lai et al described the use of half dose verteporfin in the treatment of CSCR. They proposed 3 mg/m² of verteporfin infused over 8 minutes, followed 2 minutes later with ICG guided PDT. Of the eyes treated, 85% showed complete resolution of the neurosensory retinal detachment and/or pigment epithelial detachment by 1 month after treatment. Reibaldi et al evaluated the treatment efficacy of standard-fluence PDT versus low-fluence PDT using microperimetry. The study found improvement of macular sensitivity following treatment along with greater efficacy in treatment overall using low-fluence PDT.

Another option is ICG mediated photothrombosis is a technique using a low-intensity laser combined with ICG dye infusion to treat focal areas of hyperpermeability in the choroid. Like PDT, it addresses treatment to the level of the choroidal vasculature. An 810-nm laser is applied after infusion of ICG dye. Without prior ICG dye, investigators have also used the 810-nm laser as transpupillary thermotherapy (TTT) with moderate anecdotal success.

4) Intravitreal bevacizumab (Avastin) has been used to successfully treat the rare complication of choroidal neovascularization following CSCR. There are reports of Anti-VEGF agents such as bevacizumab and ranibizumab being used to treat the neurosensory detachment of CSCR in the absence of choroidal neovascularization. Bae et al conducted a prospective randomized study comparing intravitreal ranibizumab to low-fluence photodynamic therapy in chronic CSCR. At 6 months, they concluded that the anatomic outcomes with ranibizumab injections were “not promising” compared with low-fluence photodynamic therapy. Semeraro et al compared intravitreal bevacizumab to low-fluence photodynamic therapy for treatment of chronic CSCR. The series was limited to 22 patients total and no statistical significant difference could be identified. At present we believe there is not concrete evidence to treat neurosensory detachment in CSCR without Choroidal Neovascular Membrane (CNVM) with intra vitreal AntiVEGF.

In this patient, the best treatment option would be PDT, either half fluence PDT (25 J/cm²; 300mW) or half dose PDT (3m/m²) with standard fluence. Both the safety enhanced Half and half fluence PDT have shown similar safety and efficacy with respect to SRF resolution and visual improvement. In our experience, half fluence PDT has around 90% success in chronic CSCR cases. We base it on FFA and try to keep the treatment spot size to the minimum (Always < 4500microns) to prevent collateral photoreceptor damage.

Standard fluence PDT works well, but has the risk of vision loss due to RPE atrophy, foveal thinning, and choroidal ischaemia. There are anecdotal reports of Avastin use in CSCR. However, the current evidence does not recommend its use in Chronic CSCR. In a recent comparative study of PDT versus Avastin in CSCR, though the visual outcome was maintained in both groups, only 25% in avastin group had SRF resolution compared to 75% in PDT group, at final follow up.

If this patient cannot afford PDT, then graded sub threshold TTT (Transpupillary thermotherapy) with 50% reduction of the threshold power, is a good and safe option with around history of the disease, that 75% cases of fresh CSCR takes 4-6 months for resolution. I would wait for a minimum of 4 months in a case of acute CSCR before intervention, with serial OCT follow -ups in 2 months. If SRF shows signs of reduction on OCT, then conservative approach is sufficient. If patient is one eyed or his profession requires early visual rehabilitation, then plan an early FFA and LASER. Focal laser to the RPE leak points only hastens the recovery and does not prevent recurrence or changes the final visual outcome.

Dr George Manayath
Aravind Eye Hospitals, Coimbatore
As mentioned, this is a clear-cut case of chronic CSCR of 6 months duration and sub foveal ink-blot leak. This patient requires intervention. As we know from the natural
80% success, comparable to the PDT results, but requiring marginally higher treatment sittings (1-3 sittings). This is a cost-effective option in Indian scenario.

**Conclusion**

For Non resolving central Serous Chorioretinopathy with foveal leak photodynamic Therapy using verteporfin appears to be a promising treatment. It addresses the actual pathology of CSCR i.e. choroidal hyper permeability. Enhanced depth imaging of choroid of CSCR patients have demonstrated that there is increase in choroidal thickness in affected as well as other eye of patients with CSCR. Thermal laser just closes the leak but will not prevent the recurrence of CSCR. But PDT reduces choroidal hyper permeability and choroidal thickness. This helps to prevent further recurrences also. The exact dosage of PDT, whether half dose or quarter dose or full fluence or reduced fluence is beneficial is still under investigation. Generalized feeling is that half or reduced dose with reduced fluence will help in the preservation of retinal pigment epithelium function and reducing the adverse events.

**References:**

Introduction

Ocular trauma is a common ophthalmic emergency. The Birmingham Eye Trauma, Terminology System (BETTS) classifies mechanical eye injuries broadly into open and closed globe injuries because these have different pathophysiological and therapeutic ramifications. It is important for the ophthalmologist to differentiate closed globe from open globe injuries as latter may leave the eye with an open wound which can lead rapidly to sight-threatening complications. Therefore prompt recognition of open globe injuries are essential because they need immediate surgical repair to maintain the integrity of the globe and to maximize visual restoration. In the case reported here the history and the initial clinical picture misled us before we clinched the diagnosis!

Case Report

A 74 year old male after having been gored by his bull the day before was brought to casualty with complaints of loss of vision, redness and pain in his right eye. He had a visual acuity of Perception of Light (PL) with accurate projection in the right eye and 6/60 N24 NIG in the fellow eye which was due to immature senile cortical cataract. Slit Lamp examination of the affected eye showed a patch of dense subconjunctival haemorrhage in the temporal quadrant. Cornea appeared little hazy, and details of iris or the pupil could not be made out due to near total hyphaema. Obviously there was no view of the fundus in this eye. Intraocular tension digitally appeared normal and when recorded was 14 mm Hg in both the eyes.

A provisional diagnosis of closed globe injury was made and patient was subjected to Ultra Sound B Scan to assess the posterior segment as there was no ophthlmoscopic view of the fundus due to hyphaema. B Scan showed normal globe integrity with dense vitreous haemorrhage. However the shadow of the lens was missing. This prompted us to get back to the patient to know if the patient had undergone cataract surgery. The patient gave history of having undergone cataract surgery 2 years back. He was not sure if a lens was implanted in his eye. When asked he also said that he had no useful vision in that eye after cataract surgery. CT orbit showed absence of lens and there was no evidence of globe rupture. (fig 1)

Fig: 1 Showing normal globe contour and absent lens on the right side

The picture now seemed like a closed globe injury in an aphakic eye.

When the patient was examined next day in slit lamp, to our surprise an Intra Ocular Lens (IOL) was well visible in the temporal quadrant over the area where a subconjunctival haemorrhage was seen the previous day (fig 2). The blood on the surface of the IOL had moved to the margins of the optic making it visible. So it was now clear that we were dealing with a Pseudophakic eye with the IOL extruded subconjunctivally. After a careful examination no suspicious area of scleral rupture was noted even after paying special attention to the areas that are likely to give way like superior limbus (cataract surgery incision) and insertion of recti muscles. So we decided to explore. On the previous day all odds were against it being an Open Globe injury because the conjunctiva, cornea and sclera appeared intact, IOL was not seen and the IOP was also normal.

Patient was subjected to exploration and explantation of the dislocated IOL. Through a conjunctival incision adjoining where the optic of IOL was visible the IOL was pulled out (fig 3 a & b). Surprisingly one of the haptics of the IOL was missing and there was no evidence of sclera having...
given way there. We further explored the superior limbus to inspect the cataract surgery scar. The missing haptic was seen lying superior to cataract incision scar. The area of cataract incision was taken a closer look. It was a sclera-corneal tunnel incision. The wound looked well apposed. No uveal pigments or blood was seen overlying the cataract wound. When an area overlying the wound was clasped with forceps and pulled up the wound gaped easily (fig 4). The blunt trauma had caused the cataract wound to give way resulting in expelling the broken IOL in parts to a subconjunctival location. The globe integrity was restored by securing the gaped wound and reforming the Anterior Chamber (AC). What looked like a closed globe injury (Type A Grade D Pupil A Zone III) finally turned out to be an open globe injury (Type A Grade D Pupil A Zone II) based on BETTS Classification.

This is to highlight that Open globe injury can mimic as Closed globe injury and arriving at the right diagnosis and delivering timely but the right intervention is needed to save the eye.

Now the patient is under follow up. We are planning to implant a secondary IOL if feasible at a later date under guarded visual prognosis after evaluating the posterior segment.

Discussion:
Biedner et al first reported a case of subconjunctival dislocation of an IOL implant and termed it pseudophacocoele. The implant was a Binkhorst iris clip lens fixed after uncomplicated intracapsular cataract surgery. Subsequently, Bene and Kranias and Sandramouli et al reported dislocation of PC IOL into the subconjunctival space following blunt trauma.

Pseudophacocoele is diagnosed when an IOL is seen in a subconjunctival location after a pseudophakic eye has sustained a blunt trauma of significant magnitude for the sclera to rupture and extrude the lens. The most common site of rupture in an eye without a history of previous intraocular surgery is under the rectus muscles where the eyewall is the thinnest. The diagnosis of a ruptured globe can be difficult with the periocular and ocular swelling, and since the rupture often occurs under the rectus muscles, the wound may be occult. In eyes with a previous surgical incision, the rupture usually occurs at the previous incision, even many years later as in this case. Modern well-constructed, small, self-sealing cataract incisions may, however, have little tendency to rupture even following severe blunt injury compared to their conventional counterparts.

In this case reported here, at the time of presentation neither was the subconjunctivally dislocated IOL visible nor was there any signs of sclera having given away like a rupture and related hypotony. Moreover B scan and CT scan showed normal globe integrity. So high index of clinical suspicion is required to diagnose open globe injury in misleading situations like these. Therefore patients with a history of significant ocular and periocular blunt trauma should be considered open globe until proven otherwise. Prompt recognition and ophthalmologic intervention are
essential to maximizing functional outcome.

References


Fig 4: rupture site identified as the previous cataract incision site
Paediatric Fungal Endophthalmitis

Dr. Seema K.M. DO, DNB, Dr. Ashok Nataraj MS

Introduction

Infectious endophthalmitis is a rare but devastating condition resulting from exogenous or endogenous spread of pathogens into the eye. Reports of paediatric endophthalmitis are rare in the literature. A diagnosis of endophthalmitis is not often suspected in otherwise healthy paediatric patients with no prior eye surgery or trauma. Poor communication in paediatric patients and denial of trauma for fear may lead to delay in diagnosis. We report a case of a fourteen year old healthy boy who presented to us with severe fibrinous iridocyclitis in the Right Eye (RE) following viral keratoconjunctivitis, without any history of trauma or systemic disease and finally turned out to be fungal endophthalmitis.

Case Report

A fourteen year old healthy boy presented to us with pain, redness and foreign body sensation in the RE of 3 weeks duration and loss of vision in the RE since last 4-5 days. His complaints had started as redness and foreign body sensation with discharge in Both Eyes 3 weeks back and was diagnosed locally to be viral keratoconjunctivitis. He was started on topical antibiotic – steroid combination and lubricant eye drops. At around the same time his parents also developed viral conjunctivitis which subsided with treatment in around ten days time. His left eye became symptom free in around 2 weeks time but pain and redness increased in his RE. He also developed loss of vision in the RE since last 4-5 days when they panicked and he was referred. The boy denied any history of trauma even on repeated probing. There was no history suggestive of any previous iridocyclitis, viral keratitis or previous ocular surgeries. There was no history of any systemic illness and he was immunized till date.

General and systemic examinations were normal. Visual acuity in his RE was perception of light with accurate projection and visual acuity in his Left Eye (LE) was 6/6. Anterior segment examination of the RE showed conjunctival and circumcorneal congestion, minimal corneal stromal edema and grade 2 anterior chamber cells. An exudative membrane adherent to iris and obscuring the pupillary area and most of the iris could be seen. There was no view of the lens or the posterior segment. Examination of the left eye was normal. Intraocular pressures in the RE and LE were 20 and 14mm of Hg respectively. Posterior segment of the RE was evaluated using Bscan ultrasonography which turned out to be normal.

He was admitted with a provisional diagnosis of RE fibrinous iridocyclitis with suspected infective / inflammatory etiology and started on systemic moxifloxacin, systemic betamethasone and fortified cefazolin, vigamox and 1% atropine eye drops. Blood routine showed leucocytosis (total count 14,600). Differential count Polymorphs-67%, Leucocytes-25%, Eosinophils-1%, Monocytes-7%. ESR 55mm/1st hour. Retroviral antibody tested negative. Blood culture was also negative.

On the following day as the condition was more or less the same he was taken up for an aqueous tap and anterior chamber wash with vigamox and voriconazole. The membrane was found to be tough and leathery and adherent to the iris and lens. Viscodissection was done and the membrane peeled off. Underlying lens was found to be cataractous and exudates were pouring out from the undersurface of the iris. The exudates and membrane were plated on chocolate agar.

On the following day, there were fresh exudates in the pupillary area and in the anterior chamber wash with total cataract. Considering infective etiology systemic steroid was stopped. A repeat B scan was taken the next day which showed doubtful vitreous echoes in high gain (100db). Meanwhile, the culture report of the Anterior Chamber (AC) exudate turned out to be negative and the clinical condition seemed to be worsening with no definite etiologic diagnosis. Hence the child was again taken up for an aqueous tap for Polymerase Chain Reactor (PCR). Vitreous aspiration was also done in the same sitting along with intravitreal injections
of vancomycin, ceftazidime and voriconazole. The vitreous sample was sent for gram stain, KOH wet mount, AFB stain and for culture.

The reports were available the following day and KOH wet mount was positive for fungal filaments. Systemic ketoconazole and topical natamycin and voriconazole drops were added to the treatment regime. B scan repeated on the following day showed an increase in the vitreous echoes. Vitreous aspirate culture turned out to be negative, but the PCR report was positive for panfungal genome. In view of the increasing vitreous echoes and the positive PCR report the child was immediately taken up for pars-planu lensectomy, vitrectomy, endolaser, silicone oil injection along with intravitreal injection of voriconazole. Endoexudates adherent to the pars plana and vitreous exudates were cleared as far as possible. [fig 2] View of the posterior segment improved considerably by the second postop day. Some mobile residual exudates started retracting well. A repeat intravitreal injection of voriconazole was given on the fourth postoperative day. Following this he slowly improved considerably, the exudates in the pupillary area retracted well, the residual posterior segment exudates also cleared and he was discharged on the tenth postoperative day on systemic and topical antifungals.

Systemic ketoconazole was continued until day 15 and topical antifungals were continued for 6 weeks along with topical nepafenac eye drop. The ocular condition progressively improved, the exudates retracted fully. Topical steroid 0.1% flurometholone eye drop was added after 6 weeks. He is currently on follow up with us. Cornea developed band shaped keratopathy [fig 3] by 2 months for which EDTA chelation was attempted with partial clearing. At the end of 3 months, his Best Corrected Visual Acuity (BCVA) in the RE with +7.0DS/ +2.0 DC at 180deg is 6/24. Posterior segment examination is normal, but the IOP recorded is persistently low. Hence oil removal is being debated.

Discussion

Endophthalmitis is a form of panuveitis which presents with reduced vision, progressive vitritis and hypopyon, as well as red eye, pain and lid swelling. Exogenous endophthalmitis is more commonly encountered and can occur following surgery, trauma, corneal ulcer or periocular infection that invades an adjacent ocular wall. Endogenous endophthalmitis occurs through hematogenous spread of micro-organisms that cross the blood-retinal barrier. Risk factors for endogenous endophthalmitis include the presence of systemic or local infections, relative states of immunosuppression or procedures that increase the risk of blood-borne infections.

Children account for only 0.1 percent of all cases of endogenous endophthalmitis.1 Post-traumatic endophthalmitis in children is rare; in reviewing one large series of patients, only 2-8% of post-traumatic endophthalmitis occurred in children of 18 years or younger.2

In both adult and pediatric series of posttraumatic endophthalmitis from around the world, Staphylococcus and Streptococcus species (sp.) are the most frequent
pathogens. Pseudomonas aeruginosa and Bacillus cereus also are frequently identified but their prevalence varies with geographic location. In two recent studies from Saudi Arabia and India, fungi made up 3.8% and 7.3% of post-traumatic endophthalmitis respectively. Gupta et al noted filamentous fungi especially Aspergillus sp. and Fusarium sp. were usually isolated.

In our patient, initial suspicion for infectious endophthalmitis was low, given the lack of history of trauma, hypopyon, lid swelling or significant ocular pain. The patient was otherwise healthy with no other risk factors for endophthalmitis. The boy denied any history of trauma and there was no wound of entry visible. Additionally, our patient’s history of viral keratoconjunctivitis and the initial normal B scan along with initial negative microbiology contributed to our thought process that he had a noninfectious, inflammatory condition. We still lack a clear source for his infection but suspect an episode of some unnoticed trivial eye trauma which must have led to some small self sealed wound. In a study by Vasumathy et al on post traumatic endophthalmitis, wound of entry was visible in 83.5% eyes, 74.1% of which were self-sealed wounds.

Infectious endophthalmitis should be considered in the differential diagnosis of paediatric patients presenting with panuveitis, even in the absence of reported trauma or other risk factors. This may be particularly important when evaluation has not otherwise determined the etiology of the uveitis. Early diagnostic vitrectomy should be considered.

PCR is a highly sensitive and specific test that allows rapid and accurate diagnosis of paediatric fungal endophthalmitis. PCR gives a much more sensitive and more rapid result than Gram stain and culture technique with comparable high specificity. Thus, we recommend the use of conventional methods as culture and stained smears as they are useful if positive, inexpensive, and available in all laboratories along with PCR assay, which must be added to the protocol of management in difficult cases of paediatric endophthalmitis.

References
Abstract

Frontal mucoceles present first to ophthalmologists as the symptomatology includes visual complaints like diplopia, diminution of vision, visual field defect, ptosis, orbital swelling, retro-orbital pain, displacement of eye-globe and proptosis. Our extensive multimedia search revealed only three such cases of frontal mucocele presenting with a forehead mass in the literature.

This article presents an unusual case of frontal mucocele in a 60-year-old female who presented with painless slowly progressive subcutaneous swelling over the forehead of 3-year duration. The discussion of the case and the related literature is reviewed.

Key Words
Frontal Mucocele, orbital extension, eccentric proptosis, bony erosion of sinus wall, subcutaneous mass.

Introduction

Mucoceles are benign cystic lesions and expand slowly. It occurs when a sinus ostium or a compartment of a septated sinus undergoes chronic or intermittent obstruction, causing the sinus cavity to become filled with mucus and to become airless. The etiology includes congenital anomalies, allergy, infection, inflammatory, trauma, polyp, surgical intervention in the nose and neoplasm. Sinuses frequently affected are frontal, maxillary, anterior ethmoidal and rarely the posterior ethmoidal and sphenoidal.

Frontal sinus mucoceles alone account for about 65% of the mucoceles, Frontal mucoceles could be either exclusively frontal or fronto-ethmoidal. Mucoceles are usually observed in the fourth to sixth decade of life. No gender preference has been observed. Only two cases of giant frontal mucoceles have been reported in the western literature so far.

Case Report

A 65 year old female patient presented to our department with the complaints of facial pain right sided for last 1 month, diminution of vision Right Eye (RE) for last 2 years and large mass over same eye for last 3 years. The pain had been confined to right half of the face close to RE, dull aching in nature, persistent throughout the day, with occasional tingling sensation which relieved temporarily with oral analgesics. The diminution of vision was gradual and progressive for last 2 years. No other ocular symptoms could be associated. She was neither a diabetic nor hypertensive. Mass over the RE over last 3 years had been slow in onset and gradually progressive to the present size. The mass had been painless throughout except for generalized facial pain for the last one month, probably due to the size effect. A year after the onset of the mass, the vision had been gradually deteriorating. There was no variation in the size of the mass on exertion or any aggravating or relieving factors.

On Inspection: A mass roughly measuring 8x7x6cms arising from the right fore-head, adjoining superior orbital margins and extending forwards and downwards. The forward protrusion was by about 6cms. The eye-ball is eccentric in its position and buried under the mass to be almost unnoticed. The skin over the swelling is glossy with a pigmented patch of 2mm and a visible vein. There was no visible pulsation over the swelling or variation in size with posture/valsalva manouvre. The lids displaced from their normal position with pseudo-ptosis. The anterior segment structures were barely visible.

On Palpation: The surface of the mass was uniformly smooth, firm in consistency, immobile, non-tender, non-fluctuent, transluscent, non-trans-illuminant, non-reducible, non-compressible, non-retropulsive and did not yield to finger insinuation all around. However, there was a prominent dilated vein, a solitary pigmented patch over the skin of the swelling and loss of eye-brows over lateral half. A serrated bony defect was palpable along the superior orbital margins.

Ocular examination (RE) revealed the following: On primary gaze, the position of the eye had been eccentric
and looked almost buried under the mass. Marked pseudoptosis due to the size-effect was seen. The vertical inter-palpebral aperture was markedly reduced. It was possible for the anterior segment to be examined only after voluntarily elevating the upper-lid. The eye ball was directed downwards and infero-nasally. The upper & lower fornices were obliterated. The conjunctiva showed mild hyperemia with no visible chemosis, tortuous veins or Antero-Venous (AV) fistulas. The cornea was hazy with prominent arcus senilis. Corneal sensations were intact. Fluorescien staining was negative. Anterior chamber was optically clear with normal depth. Iris color and pattern was normal. Pupils were very sluggish with no RAPD. Lens showed immature cataract (NS-III). Fundus examination did not yield due to the lens changes and inadequate pupillary dilatation. Visual acuity fell to perception of light with inadequate projection of light.

Ocular examination of Left Eye (LE) revealed only immature cataract (NS-II), with a visual acuity of 4/60 with pin-hole improvement to 6/24 and a normal fundus. The anatomy of the LE orbit was normal on examination.

Investigations
X-ray (plain), AP view revealed a soft tissue density shadow in the region of the right frontal sinus and overlying right orbit. Lateral view- revealed thinning and elevation of the anterior wall of the right frontal sinus with absence of its lower portion. The nasal septum had been midline. Opacifacation of the left frontal sinus also noted.

CT –plain axial and coronal views revealed, a soft tissue density mass of size 8-7-6cms size extending inferiorly causing impression over the globe with considerable proptosis. There was expansion of the right frontal sinus with partial destruction and thinning of the inferior and lateral wall of the sinus. Anterior wall of the sinus showed remodeling / scalloping of the bone with no evidence destruction of the bone or extension into brain parenchyma. No discontinuity of the ethamoidal margin noted. Nasal septum appeared midline with both turbinates normal. A diagnosis of a large expansile right frontal sinus soft tissue density mass suggestive of a frontal mucocele was made.

High resolution sonogram of orbit and mass revealed, a large complex cystic mass of size 72-50mm in the right orbital region. Mass appeared to push the right orbit downwards. Mass showed fine internal echoes. Lens showed opacities. Posterior chamber and vitreous appeared normal. Left orbit appears normal. A diagnosis of a large cystic mass right frontal region pushing the right orbit downwards most probably a frontal mucocele (CT-correlated) was made.

Discussion
The differential diagnoses for unilateral proptosis include dysthyroid eye disease, retrobulbar orbital tumour, inflammatory pseudo tumour, sinus tumour, metastatic lesion and mucoceles of the paranasal sinuses. As to mucoceles, frontal mucoceles are a common cause of long standing unilateral proptosis.

Although mucoceles occur secondary to varied causes, in our case the exact cause could not be identified even after detailed history and ENT examination. The possible pathogeneses could be continuous or intermittent obstruction of the sinus ostium followed by gradual distension, thinning and erosion of the bony wall of the sinus due to progressive accumulation of mucoid material.

The proximity to orbit and the least resistance offered by virtue of its thinness in superior aspect causes the frontal mucocele to encroach the orbit commonly as compared to intracranial extension. Thus rarely these lesions could present as a forehead swelling. Our extensive multimedia article search through internet revealed only three cases of frontal mucocele presenting as forehead swelling so far. Of all the above published articles, ours is probably the ever documented largest frontal mucocele presenting as a forehead swelling.

The symptomatology in mucoceles may be attributed to pressure against the globe and mechanical interference with its motility. The proptosis due to frontal mucoceles is usually eccentric (non-axial), with the globe being displaced away from the site of the mucocele. The visual acuity may be affected by direct compression of the optic nerve in the orbit, a vascular or inflammatory process involving the optic nerve, refractive errors induced by the indentation on the globe, exposure keratopathy or secondary glaucoma. In our patient the fall in visual acuity to PL may be attributed to compressive effect on the optic nerve as suggested clinically by poor pupillary response.

CT is the most preferred mode of imaging for paranasal sinus pathology as it delineates the extent of the lesion and its relations to other surrounding structures, extent of bone destruction and differentiates the high attenuated regions of mucus from the low attenuated regions of surrounding mucosa. MRI is useful in complicated cases like infection and intracranial extension.

Orbital ultrasonography is another useful imaging tool as
it helps to determine whether the lesion is a cystic or a solid mass. In our case HRSG was done as the posterior segment could not be examined clinically and its role was only complimentary.

The definitive treatment of mucoceles is primarily surgical. The aim of surgical management is to re-establish adequate drainage of the sinus without producing cosmetic or functional deformity. Surgical treatment could be accomplished with a craniotomy with craniofacial surgery or a minimally invasive endoscopic procedure. Endoscopic surgery has increased the safety and efficacy of intranasal marsupialization for the treatment of mucoceles in all paranasal sinuses. Endoscopic sinus surgery combined with transcranial surgery is advisable in cases of giant frontal mucocele. The cyst lining may be removed and the sinus obliterated with soft tissue like abdominal fat. The bony defect during surgery may be reconstructed with the help of autologous cranial bone graft, Methyl-methacrylate and porous polyethylene.

Conclusion
Frontal mucoceles may present with varied ophthalmic features. However being benign, curable and with low recurrence rates overall prognosis is good. An early surgical intervention has a favourable outcome on vision. Appropriate clinical and radiological evaluation is necessary to diagnose frontal mucoceles. As the prognosis for visual function depends on the duration, it is important that clinicians consider mucoceles as an easily remediable cause of visual loss.

References
6. Tan CSH, Yong VKY, Yip LW, Amrith S. An unusual presentation of a giant frontal sinus mucocele manifesting with a subcutaneous forehead.
Ocular Manifestations of AIDS

Dr. Kala K Madhavan MS, Dr. K.V. Raju MS, DO

Acquired Immunodeficiency Syndrome (AIDS)
The etiological agent of AIDS is the Human Immunodeficiency Virus (HIV), belonging to the Human Retrovirus family, and subfamily of Lentiviruses. The CD4+ T cell counts is the best indicator of the state of the immunological status of HIV infected patient. The normal CD4 + T lymphocyte count is 500 -1600 cells/mm³.

Ocular Manifestations Of HIV/AIDS
Ocular manifestations of HIV/AIDS are primarily due to the opportunistic infections and neoplasias that accompany the syndrome. The HIV virus has been found in the tear film and other ocular structures such as the cornea, vitreous and chorioretinal tissue. The ocular manifestations involve the adnexae and anterior and posterior segments of the eye and also present with orbital and neuro-ophtalmic manifestations. Anterior segment involvement results in tumours and external infections while posterior segment involvement results in HIV-retinopathy and a number of opportunistic infections of the retina and the choroid. Early detection of the ocular manifestations of HIV/AIDS is important because these ocular manifestations may be the primary presentation of the systemic infection.

Adnexal Manifestations
1. Keratoconjunctivitis sicca (KCS): Symptoms are foreignbody sensation, photophobia and decreased visual acuity.
2. Blepharitis and Blepharoconjunctivitis: Due to reduced ability to control the normal flora that the eye is exposed to.
3. Herpes Zoster Ophthalmicus (HZO): Painful vesiculobullous dermatitis which results from a reactivation of Varicella-Zoster virus infection. HZO usually begins as pain over the first division of the trigeminal nerve and is followed by erythematous macules which progress within days into papules and vesicles and later pustules which rupture and crust. When the nasociliary branch is involved, a vesicle may appear on the tip or side of the nose- Hutchinson’s sign. Corneal involvement is in the form of epithelial keratitis.
4. Kaposi sarcoma (KS): Caused by Kaposi Sarcoma associated Herpes virus. It presents as a painless vascular tumour. KS on eyelids presents as red or purple lesions, while in the conjunctiva, it appears as persistent subconjunctival hemorrhage or raised purplish red marks.
6. Conjunctival Microvasculopathy: Micorvascular changes in conjunctiva include capillary dilatation, irregular vessel caliber and microaneurysms.

Anterior Segment Manifestations
1. Infectious Keratitis: This may be caused by viral, bacterial, fungal or protozoal cause. The most common cause of infectious keratitis in HIV positive individuals are Varicella zoster and Herpes simplex viruses. Varicella zoster keratitis is usually associated with HZO and it’s complications include subepithelial infiltrates, stromal keratitis, disciform keratitis, uveitis and secondary glaucoma. Complications of Herpes simplex keratitis include dendritic and geographic epithelial keratitis, stromal keratitis and iridocyclitis. Fungal keratitis are mainly caused by Candida, Fusarium and Aspergillus species.
2. Iridocyclitis: Uveitis is a manifestation of several chronic infections commonly seen in HIV infected people.
persons and also due to medications commonly prescribed for such patients. It presents as one of the earlier signs of tuberculosis, syphilis, histoplasmosis, coccidomycosis and toxoplasmosis. Medications like rifabutin and zidovudine can also cause iridocyclitis. Uveitis in HIV positive individuals is most commonly due to posterior segment disease, most common of which is CMV retinitis.

Orbital Manifestations
Orbital manifestations of HIV infection include orbital cellulitis and orbital lymphoma. Causative organisms include Aspergillus, Propionibacterium acnes, Staphylococcus aureus, Pseudomonas aeruginosa, Trypanosoma pallidum, Rhizopus arrhizus, Toxoplasma gondii and Pneumocystis carinii.

Neuro-Ophthalmic Manifestations
Neuro-ophthalmic manifestations include optic nerve disease (edema, inflammation and atrophy), papilledema due to raised intracranial pressure, retrolubular neuritis, cortical blindness, pupillary defects, cranial nerve palsies, ocular motility disorders and visual field defects. Most of these conditions are caused by infective lesions of the CNS.

Iatrogenic/ Post Treatment Manifestations
Immune Recovery Uveitis (IRU): This condition is defined as “new inflammation in an eye with controlled CMV retinitis or other opportunistic infection, not attributable to an alternative cause, following substantial recovery of immunity.” It is most frequent if patients with CMV retinitis who receive HAART. Manifestations of IRU include cataract, vitritis, macular edema, optic disc edema and epiretinal membrane.

Steven Johnson Syndrome: SJS is an immune complex mediated hypersensitivity disorder. It is a syndrome that affects skin and mucous membranes and in patients with HIV/AIDS and is drug induced or viral in etiology.

Posterior Segment Manifestations
Posterior segment manifestations are seen in up to 50 percent patients with HIV/AIDS. These disorders are broadly categorized into disorders associated with non infectious causes and those associated with infectious causes. Majority of these diseases are seen in severely immunocompromised individuals with CD4+ T cell counts of less than or equal to 100 cells/mm3. Most common posterior segment manifestations of HIV/AIDS are retinal microvascularopathy and CMV Retinitis.

Manifestations Not Due To Opportunistic Infections
HIV Microangiopathy: This is found in 70% of patients with HIV/AIDS. It is also referred to HIV retinopathy, HIV related ocular microangiopathic syndrome or retinal microvasculopathy. It is a non infectious microvascular disorder characterized by cotton wool spots, microaneurysms, retinal hemorrhages, Roth spots, telangiectatic vascular changes and areas of capillary non perfusions. HIV retinopathy is a late manifestation of AIDS and is seen in less than 50 percent of patients with CD4+ T cell count of less than 50 cells/mm3.

i. Cotton wool spots (CWS): Most common ocular microangiopathic manifestations of HIV. HIV retinopathy resembles diabetic and hypertensive retinopathy, but lacks the hard exudates found in these disorders.

ii. Retinal Hemorrhages: These appear as flame shaped hemorrhages when they affect the nerve fibre layer and as dot and blot hemorrhages when they affect deeper layers of retina.

iii. Telangiectatic Vascular Changes: These are characterised by irregular dilatation, microaneurysms and vessel failure.

Manifestations Due To Opportunistic Infections

1. Cytomegalovirus Retinitis (CMV Retinitis): CMV is the most common viral opportunistic infection in HIV/AIDS. CMV is found in up to 40% individuals with advanced HIV. The most common presentation of CMV in the body is CMV Retinitis, with infections of gastrointestinal tract, lungs and the nervous system reported less frequently. Generally, clinical manifestations of CMV disease are delayed until the CD4+ T cell count drops below 100 cells/mm3. Increased risk of occurrence of CMV disease with CD4+ T cells counts less than 50/mm3.

There are 3 clinical forms of CMV retinitis:

a. Classical form or Pizza pie retinopathy or Cottage cheese with ketchup, characterised by confluent retinal necrosis with hemorrhage, mainly in the posterior retina. Over several weeks, untreated lesions progress to full thickness necrosis with resultant retinal gliosis and pigment epithelial atrophy.

b. Indolent form is recognized as granular lesion in the peripheral retina with little or no hemorrhage.

c. Frosted branch angiitis.

Fifteen percent of active CMV retinitis are asymptomatic. Routine screening with dilated indirect ophthalmoscopy is recommended at 3 month interval in patients with CD4+ cell count less than 50/mm3. CMV retinitis may result in serous or rheumatogenous retinal detachment. After the introduction of HAART, there has been a significant decline
in the incidence of CMV retinitis and alteration in its clinical course. Treatment of CMV disease includes anti retroviral therapy continued indefinitely, and specific anti CMV medication continued until the immune status improves to a CD4+ T cell count of more than 100/mm³. Currently available anti CMV agents include Ganciclovir and its prodrug Valganciclovir, Foscarnet, Cidofovir, Fomiviren, Ganciclovir implant and oral Valganciclovir.²

2. Toxoplasma Retinochoroiditis: Toxoplasma retinochoroiditis presents as multifocal retinochoroiditis with less frequent vitritis than in immunocompetent individuals. Toxoplasma retinitis in immunocompromised individuals is often bilateral, multifocal and not associated with chorioretinal scars and retinal hemorrhage.⁸

3. Ocular Tuberculosis: The most common ocular manifestation is granulomatous uveitis, which is usually accompanied by choroiditis. It presents as multifocal choroidal tubercles with discrete yellow lesions mainly at the posterior pole, associated with exudative retinal detachment and vitritis.

4. Fungal Retinitis: Most common organism causing fungal retinitis is Candida, while Histoplasmosis and Aspergillus infection more often affect choroid. Candida retinitis is characterised by fluffy white mound of retinal infiltrates which may enlarge to involve the vitreous also.

5. Bacterial Retinitis: Ocular syphilis is the most common intraocular bacterial infection. It presents as necrotic retina infiltrated with multiple histiocytes. Other posterior segment manifestation of syphilis are retinal perivasculitis, intraretinal hemorrhage, papillitis and panuveitis.

6. Cryptococcus Chorioretinitis: Causative agent is Cryptococcus neoformans. Pápilledema is common due to increased Intra Cranial Pressure (ICP) from cryptococcal meningitis.

7. Pneumocystis Choroiditis: Pneumocystis carinii is the causative agent and choroiditis is the most common ocular manifestation. Clinical lesions are slowly progressive, multiple yellowish, well demarcated choroidal lesions in the posterior pole referred to as frothy, vacuolar, eosinophilic choroidal infiltrates which contain cystic and crescentic organism.

8. Acute Retinal Necrosis (ARN): It is a progressive necrotic herpetic viral retinitis. Varicella zoster virus is the most common causative organism, while Herpes simplex virus and CMV also are known to cause this manifestation. ARN is common in healthy persons and AIDS patients with only mild immune dysfunction and elevated CD4 counts. It causes severe bilateral visual loss. ARN is characterised by peripheral retinal whitening that progresses to necrosis within several days.⁹

9. Progressive Outer Retinal Necrosis (PORN): This is also a form of necrotizing herpetic retinitis. Unlike ARN, Herpes simplex virus type I is the major etiological agent. PORN is most often bilateral, and is characterised by severe visual loss occurring within weeks. It is characterised by retinal lesions which are multiple punctate white spots that coalesce. In contrast to ARN, severe immune compromise and previous herpetic infection is necessary for presentation of PORN. Risk factors are low CD4+ cell count and recurrent recent or current cutaneous, cerebral or visceral VZV or HSV infection.¹⁰

Reference


A 48 year old gentleman gave history of injury to left side of face with a wooden stick few days back. On examination there was discharge of pus on pressing lower lid. All ocular movements were restricted in left eye with marked restriction of elevation.

CT ORBIT and PNS was initially reported as fracture floor of left orbit with trapped inferior rectus muscle in fracture fragments, fracture medial wall of left orbit with hemosinus in left maxillary sinus and left ethmoid air cells. But what did we miss?
Closer examination of CT films showed orbital foreign body.

Orbital foreign body was removed through conjunctival route. Orbital floor fracture exploration and repair was done. Postoperatively ocular movements improved, but there was limitation of elevation in left eye which may be due to residual fibrosis of inferior rectus.
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11 year old male, Gradual, painless protrusion of left eye from 1.5 years of age onwards

What is the Diagnosis and Syndrome associated with this condition?

Send your answers to: drashok.eye@gmail.com

The answer for the question in the last issue is
Choroidal Osteoma with Secondary Choroidal Neovascular Membrane (CNVM).

Treatment: Observe if Asymptomatic; Intravitreal Anti-VEGF / Photo Dynamic Therapy if CNVM is active.

Winner: Dr. Lathika Rajesh, Amala Institute of Medical Sciences Thrissur.
Acute intraoperative rock-hard eye syndrome and its management.
Oliver C F Lau, Jessica M Montfort, Benjamin W C Sim, Chris H L Lim, Tony S C Chen, Claire W Ruan, Ashish Agar, Ian C Francis


This study evaluated the use of parsplana needle aspiration of retrolenticular fluid in immediate management of acute intraoperative rock-hard eye syndrome (AIRES). It was a retrospective case series study over 18 months during which 6 cases (1.45%) of AIRES occurred in 413 phacoemulsification surgeries. All patients with AIRES had acute intraoperative shallowing of anterior chamber with marked rise in intraocular pressure (IOP) during phacoemulsification as evidenced by rock-hard consistency of eye on corneal and scleral instrumental palpation in the absence of signs of suprachoroidal hemorrhage or effusion. Preoperative and post operative (day 1, 1 week, 1 month) datas of posterior segment status, IOP and corrected visual acuity were evaluated.

Each case of AIRES was managed intraoperatively with emergent parsplana needle aspiration of retrolenticular fluid with 23 G needle and 3 ml syringe which was introduced 3 mm from surgical limbus transconjunctivally, trans sclerally using direct visualisation of needle position in vitreous. Retrolenticular fluid between posterior capsule and anterior hyaloid membrane was aspirated until reduction in tense convexity of cornea and normalization of anterior chamber depth were achieved after which needle was rapidly withdrawn.

In all six cases of AIRES, parsplana needle aspiration of 0.1-0.3 ml of retrolenticular fluid was successful in achieving immediate palpable softening of globe and deepening of anterior chamber. All 6 cases were females with mean age of 81±6 years. On Locs II grading, 2 eyes had grade 2, 3 eyes had grade 3 and one eye had grade 4 nuclear cataract. At one month, IOP was normal in 5 out of 6 cases and the remaining case developed steroid induced glaucoma after treatment for temporal arteritis. Mean visual acuity showed a significant improvement after CXL, from 1.925±0.173 before surgery to 1.75±0.296 at 1 month after surgery (P = 0.010), but deteriorated to 1.81±0.23 at 3 months. Symptomatic relief after CXL was at a maximum at 1 month, with a worsening trend at 3 months. Eighteen patients showed a reduction in corneal haze 1 month after CXL. The effect was maintained in 9 of 12 patients at 3 months. The mean central corneal thickness decreased significantly from 846.46±88.741 to 781.0±98.788 μm at 1 month (P<0.01) after CXL, but increased to 805.08±136.06 μm at 3 months. Immunofluorescence microscopy revealed anterior stromal compaction in 7 of 12 patients (58.3%) in group A and in 5 of 12 patients (41.6%) in group B. Staining of keratocyte nuclei with 4',6-diamidino-2-phenylindole dihydrochloride revealed a relative uniform distribution throughout the stroma suggesting that epithelium has regrown in all cases after CXL.

The study concluded that parsplana needle aspiration is a safe, rapid, efficient, inexpensive and relatively non-invasive method of restoring surgical environment in AIRES.

Role of Corneal Collagen Cross-Linking in Pseudophakic Bullous Keratopathy
Ritu Arora, Aditi Manudhane, Ravindra Kumar Saran, Jawaharlal Goyal, Gaurav Goyal, Deepa Gupta

Ophthalmology. 2013; 120(12): 2413-8

This study aimed at evaluating the clinical and histopathological changes induced by Corneal Collagen Cross-Linking (CXL) in Pseudophakic Bullous Keratopathy (PBK). It was a randomized, prospective study. 24 patients with corneal edema, resulting from PBK of more than 4 months duration, and awaiting keratoplasty, were enrolled to undergo CXL followed by penetrating keratoplasty (PKP). They were allocated randomly into two groups of 12 patients each, of which group A underwent PKP at one month after CXL ,and group B underwent PKP at 3 months after CXL ,and corneal buttons were subjected to histopathological and immunofluorescence evaluation. The primary outcome of the study were based on visual acuity, ocular discomfort (tearing, redness, pain), corneal haze, central corneal thickness and histopathological and immunofluorescence evaluation.

Mean visual acuity showed a significant improvement after CXL, from 1.925±0.173 before surgery to 1.75±0.296 at 1 month after surgery (P = 0.010), but deteriorated to 1.81±0.23 at 3 months. Symptomatic relief after CXL was at a maximum at 1 month, with a worsening trend at 3 months. Eighteen patients showed a reduction in corneal haze 1 month after CXL. The effect was maintained in 9 of 12 patients at 3 months. The mean central corneal thickness decreased significantly from 846.46±88.741 to 781.0±98.788 μm at 1 month (P<0.01) after CXL, but increased to 805.08±136.06 μm at 3 months. Immunofluorescence microscopy revealed anterior stromal compaction in 7 of 12 patients (58.3%) in group A and in 5 of 12 patients (41.6%) in group B. Staining of keratocyte nuclei with 4',6-diamidino-2-phenylindole dihydrochloride revealed a relative uniform distribution throughout the stroma suggesting that epithelium has regrown in all cases after CXL.
CXL is a new treatment used to increase the biomechanical strength of corneal tissue by increasing the diameter of collagen fibres and linking them in close association with each other. CXL aims to create chemical bonds inside the corneal stroma by means of a highly localized photopolymerisation while minimizing exposure to surrounding structures of the eye.

Collagen cross-linking causes symptomatic relief and a decrease in central corneal thickness and anterior stromal compaction in PBK. However, the effect decreases with time and depends on disease severity. The authors concluded that corneal CXL may be advocated as a new tool for temporary reduction in corneal edema in patients with bullous keratopathy awaiting keratoplasty, as it was found to improve corneal transparency, corneal thickness and ocular pain after surgery.

**Topical Rebapamide Treatment for Superior Limbic Keratoconjunctivitis In Patients With Thyroid eye Disease**

Yasuhiro Takahashi, Akihiro Ichinose, Hirohiko Kakizaki


Aim of the study is to evaluate efficacy of topical Rebapamide for Superior Limbic Keratoconjunctivitis (SLK) in patients with thyroid eye disease. This was a retrospective observation study that included 33 eyes from 20 thyroid eye disease patients with SLK who received topical 2% Rebapamide 4 times per day.

Patients were evaluated before and 4 weeks after the treatment by Rose Bengal staining, fluorescent staining, Schirmer test, Tear Film Break up time, Hertels ophthalmometry and Margin reflex 1,2.

At 4 weeks, 28 eyes out of 33 patients showed complete disappearance of SLK (84.8%). The remaining 5 eyes (15.2%) had significant improvement but residual punctate staining. These 5 eyes had proptosis of more than 17.7 mm with upper or lower lid retraction. Severity of Rose Bengal staining and fluorescent staining improved significantly after treatment (p value< 0.001) and Tear Film Break up time also increased post therapeutically (p value= 0.009).

Rebapamide is a Quinolone derivative that increases production of mucin like substances in cornea and conjunctiva, suppresses expression of cytokines, attenuates TNF-α, promotes wound healing, increases tear film stability and ameliorates corneal and conjunctival epithelial damage. This study concluded that Rebapamide may be considered as a safe first line drug for SLK in thyroid eye disease which is caused by local mucin deficiency and inflammation between upper lid and superior corneal limbus.
In the modern era there has been a great revolution in the field of cataract surgery. This book is a very useful guide to interested surgeons to sharpen their technical skills in the field of microincision surgery. This book has an impressive collection of chapters divided in four sections to cover all aspects of MICS beautifully. It deals with coaxial and biaxial MICS, phacodynamics and surgical techniques. Special techniques like microphakonit by Prof Amar Agarwal and TriMICS by Dr Jerona Jean-Philippe Bovet are included. MICS techniques in special circumstances like pediatric cataract, hard cataract etc are dealt with. The common complications and their management is discussed in great detail. The history of MICS is beautifully narrated. Special feature is their line-up of famous international contributors who have shared their experiences regarding pearls and strategies of MICS techniques.

It will definitely be a useful armamentarium for interested cataract surgeons. This book goes from basic concepts described many years ago until recent applications in MICS like the very new FemtoMICS.

Clinical comments are included throughout the book to emphasize common clinical problems, disease processes or abnormalities that have a basis in anatomy or physiology. The textbook is fully referenced and information gathered from historical and current literature is well documented. This book will be very useful for students for building a good foundation in ophthalmology and for practicing ophthalmologists to update their knowledge.
Dear Editor,

It is with great interest that I read the case report titled “Tilted Disc Syndrome” in the last issue of KJO. This entity is often under diagnosed as a cause of serous macular detachment (SMD) and can have a variety of ramifications. Fluorescein angiography may show window defects on the border of the staphyloma, due to atrophy of the choriocapillaris. Other macular complications may include polypoidal choroidal vasculopathy, classic choroidal neovascularization, focal serous retinal detachment or atrophy of the retinal pigment epithelium alone. Management of these complications are quite obscure and debatable. Many treatments from laser to intravitreal Anti-VEGF has been tried with varying results. The focal hyperfluorescence noted along the the inferior disc margin may even represent an occult optic nerve head pit causing SMD with a different pathophysiology altogether. I congratulate the authors for this report and creating an awareness regarding this condition.

References

Dr V S Prakash
Comtrust Hospital, Calicut

Authors Reply
I thank Dr V S Prakash for taking interest in our case report and writing about it. It is quite true that it is often missed in our daily practice and awareness regarding this entity is essential for diagnosis. From our literature survey we found that no treatment is effective in managing the serous macular detachment in this entity. As pointed the assumption of an ONH pit on the distorted inferior disc margin was another factor that made us go ahead with focal laser.

Dr Ashok Nataraj, Dr Remya M P
Little Flower Hospital, Angamaly

Dear Editor,

I must appreciate Dr Reesha for presenting a very challenging case of posterior uveitis in the “Diagnostic and therapeutic challenges” section (June 2014)

Acute retinal necrosis (ARN) is defined by American Uveitis Society by its clinical characteristics and disease course, not by the causative agent or immune status of the patient.

Diagnostic criteria include
1. One or more discrete foci of peripheral retinal necrosis
2. Circumferential spread
3. Occlusive arteriolar retinopathy
4. Prominent vitreous or anterior chamber reaction
5. Rapid disease progression in the absence of specific therapy

Though uncommon, there are reports of non necrotising Varizella related retinopathies and vasculitis, transient retinal arteriolaritis, bird shot like choroiditis and purely occlusive retinal vasculopathy.

Differential diagnosis of infectious retinitis include Toxoplasma, Viruses (mainly VZV, HSV, CMV ) and
Syphilis. As Dr Prakash V S has rightly pointed out, absence of severe vitreous reaction, presence of discrete retinal lesions which lack the typical circumferential spread and presence of haemorrhages especially at the posterior pole are not commonly seen in typical ARN. However cases of various atypical forms of non necrotising retinopathies are increasingly being reported. The occlusive vasculopathy seen in the picture is typical of ARN. In an immuno compromised patient the fundus picture would have been more suggestive of non fulminant type of CMV retinitis (lack of vitreous reaction and presence of haemorrhages). Toxoplasmosis can have varied clinical presentations but occlusive vasculopathy is not common. Since VZV retinitis hardly ever causes CRAO, I am sure Dr Reesha would have ruled out alternative causes of CRAO like a cardiac source of embolism. Presence of severe associated anterior uveitis is uncommon in auto immune systemic diseases.

Based on the PCR report we would have treated the patient on similar lines. However when the clinical picture is typical of ARN it will be prudent to start oral antiviral along with oral steroids initially itself pending more definitive investigations into the etiology. This case also illustrates the importance of PCR of ocular fluids which helped clinch the diagnosis. Prompt antiviral therapy has shown to reduce the incidence of bilateral ARN. It is very important to follow up the patient in the first 6 months to detect the presence of any retinal breaks though the incidence of RD is maximum within 3-4 weeks. As far as further management is concerned we would have treated the patient with PRP to prevent painful blind eye.

Reference

Dr. Sandhya N
Giridhar Eye Institute, Kochi

Author’s reply
I thank Dr. Sandhya for reading this article in detail with deep interest and for critically analyzing it. She very well discussed the various possibilities in this patient who presented with an acute retinal necrosis with some atypical features. As she mentioned we could have started the antiviral treatment in the first visit itself without waiting for the PCR report. As she assumed, we had ruled out cardiac causes of central retinal artery occlusion in this patient. Even though we advised panretinal photocoagulation, he was not ready to undergo laser treatment.

Dr. Reesha K.R.
Little Flower Hospital, Angamaly
Dear Editor,
The efforts of the editorial team to bring out a quarterly journal encompassing the varied aspects of Ophthalmology are to be appreciated.

The article ‘Surgically Induced Astigmatism (SIA) and Visual Outcome after 2.8mm Incision Phacoemulsification in Patients with Cataract’ is of immense importance in this era of ‘refractive surgery’. Cataract surgery is no longer a procedure to restore vision alone, as more and more patients demand freedom from spectacles or at least a reduced dependence on spectacles. A ‘CCTI’ (clear cornea temporal incision) is slowly becoming routine as it provides greater comfort to the surgeon, better surgical field exposure, easier for the patient to fixate with few exceptions (eg: steep vertical meridian).

The size of the incision has also aroused a lot of debate; but as mentioned by the authors a 2.8mm incision is optimal as the change in WTR astigmatism from baseline was not statistically significant. The authors have emphasized the role of corneal topography which helps determine corneal astigmatism. The SIA is not being taken into consideration routinely and this aspect needs a lot of rethinking on the part of the phaco-surgeon.

Calculating SIA, which depends upon numerous factors like size, site, wound configuration, pre-existing astigmatism, laterality of the eye and the patient’s age will enhance the post-operative refractive outcome.

Therefore as highlighted by the authors, corneal topography should be made mandatory in the pre-operative evaluation of the potential cataract patient.

Dr. Lilan Bhat
Sr.Consultant, Cornea Services, LFH, Angamaly.

Authors reply
We thank Dr Lilan Bhat for the interest shown on the subject of our article titled ‘Surgically induced astigmatism (SIA) and visual outcome after 2.8mm incision phacoemulsification in patients with cataract’. We appreciate that she has reiterated on the important aspects of the study.

We conducted this study on SIA at our institution because of the high demands of the patients for perfect visual outcome after cataract surgery.

We recommend all Phaco-surgeons to use corneal topography to find out the preoperative and postoperative astigmatism and to use this data to calculate the surgically induced astigmatism. Soft ware like SIA CALCULATOR 3.1 are available on the internet free of cost( www.insighteyeclinic.in/ SIA-calculator.php (Insight Eye clinic, New Delhi, India)

We are at present conducting a study on the role of incision site in reducing the SIA depending on the degree of pre-existing astigmatism.

Dr Devi Sujith, Dr Amita Verghese, Dr Verghese Joseph
Eye Microsurgery and Laser CentreTiruvalla
Dear Editor,

The June edition of KJO had an excellent collection of articles. I would like to make a special mention of the article “Glautrak- a surgical procedure which can save vision in end stage glaucoma” by Dr Anil B Das.

Management of Refractory glaucoma is a problem faced by all glaucoma surgeons. The procedure described is just a modification of the standard trabeculectomy and not difficult for an experienced glaucoma surgeon to perform. The dissection of long posterior scleral flap may be time consuming. The limbal based flap with its tight sutures may help to prevent hypotony. I understand that a suture passed through the scleral bed acts as an implant, inhibiting fibrosis and facilitating drainage posteriorly. Further details like the number and type of cases done so far along with the results and complications need to be published before the technique can be adopted by others. Let me congratulate Dr Anil for this innovative technique and hope to see the details of his cases published soon.

Dr Girija K
Senior Consultant, Glaucoma services
Little Flower Hospital, Angamaly
girijarafeeq@gmail.com

Authors reply

Dear Dr. Girija, Allow me to thank you first for the interest you have taken to go through the procedure and for your kind words. What was given for publication was not an exhaustive study but rather a mention of the procedure.

The study period extended from 1-7-2006 to 30-7-2012. Performed in 73 problematic eyes which included cases of absolute, neovascular, traumatic, uveitic - glaucomas, failed trabs ICE syndromes etc.

The follow up period extended from 9 months to 5 years.

12 cases of absolute glaucoma, 15 cases of neovascular glaucoma, 17 cases of uveitic glaucoma, one case of aniridia with aphakia and vitreous loss, 3 cases of ICE syndrome and 25 cases of failed trabs.

61 cases (84 %) required no further treatment.

As the procedure was new and not standardized problems encountered were tackled on a case to case basis.

In the case of aniridia there was a 100% failure . It was a case of aphakia with vitreous loss and corneal decompensation. We did Glautrak and IOP was controlled initially. But after a week it started rising. We could make out the vitreous in the wound through the hazy cornea. Vitrectomy was suggested but the patient was not willing as the eye was practically blind.
Another cause for failure was presence of secondary aqueous (inflammatory and hemorrhagic secretion from the uveal tissue produced due to surgical trauma and high vascular perfusion due to steep fall in IOP by post op excessive drainage) blocking the drainage track.

<table>
<thead>
<tr>
<th>Type of cases</th>
<th>Success %</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 cases of absolute glaucoma</td>
<td>11 cases (91%)</td>
</tr>
<tr>
<td>15 cases of neovascular glaucoma</td>
<td>10 cases (66%)</td>
</tr>
<tr>
<td>17 cases of uveitic glaucoma</td>
<td>15 cases (88%)</td>
</tr>
<tr>
<td>1 aniridia with aphakia and vitreous loss</td>
<td>0 cases (0%)</td>
</tr>
<tr>
<td>3 cases of ICE syndrome</td>
<td>2 cases (66%)</td>
</tr>
<tr>
<td>25 cases of failed trabs</td>
<td>23 cases (92%)</td>
</tr>
</tbody>
</table>

This problem was particularly acute in neovascular glaucoma and uveitic glaucoma. Best way to tackle it was to use steroids - topical, oral and subconjunctival liberally. If still not controlled then we can open up the track through the scleral tunnel using a iris repositor or similar instrument after the AC reaction has stabilized.

A third common problem especially in young patients with profuse subconjunctival tissue was excessive scarring and subsequent mechanical pressure over the scleral flap obstructing it. Here it is safer to suture the flap slightly loose and give sub conjunctival steroids near the bleb post op daily till the hyper vascularity around the bleb subsides. If not corrected it may lead to scarring and may necessitate a resurgery.

If you need any assistance I will be glad to help with whatever limited experience I have had in the procedure.

**Dr. Anil. B. Das**
Vasan Eye Care
Kochi
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