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"No duty is more urgent than that of returning thanks".

James Allen

Respected Seniors & Dear Friends,

At the outset I would like to take this opportunity to thank all the members of Delhi Ophthalmological Society for giving me the opportunity to serve the society as its Secretary. It is a big responsibility and I will try my best to live up to the expectations of the members.

I am very pleased and excited to begin the tenure with the help of talented and hard working executive members who are willing to help me at every stage. With the active support of my colleagues and guidance and blessings of the seniors, we are hopeful of taking the society to greater heights. An extremely successful Annual DOS Conference 2013 and excellent work of the previous executive has set a very high standard for our Society. We have to move further up the ladder and for this the current executive has to make huge efforts.

It is a matter of pride for us that DOS Times is amongst the most popular ophthalmic magazines in India. It is with great pleasure that I introduce myself as the new editor-inchief of DOS Times magazine.

Every new project that is undertaken has its own challenges. If you don't expect to have issues then you're being extremely naive. But I believe to work on something that is sincerely of value to you as well as others, surround yourself with the best people and never give up. The fact that the work of an educational magazine is aimed at the long range betterment of ophthalmologists across the world is part of what makes me and my team so passionate about what we do.

The goal of DOS Times will be to provide highly pertinent and practical information to ophthalmologists in an accessible format. All the articles will undergo an editing process so that the tone of the articles meshes with our goal of a user friendly publication. However we will strive to preserve the author's accuracy and voice. The function of education is to teach one to think intensively and to think critically. I hope we are able to achieve this goal of true education that is the advancement of knowledge and the dissemination of truth.

For the next two years we will be having "Theme" based issues of DOS Times. This is an effort towards having a focused approach of imparting information regarding various subspecialties of ophthalmology. Change is not for good or bad, but to break the monotony so as to bring about some freshness in the minds of the people. We sincerely hope that our endeavours will be appreciated.

Sincerely Yours

Rajesh Arika

Rajesh Sinha Secretary, Delhi Ophthalmological Society





The World Health Organization estimates that there are 4.8 million people with bilateral and 22 million people with unilateral corneal blindness globally. India has a huge burden of blind & visually disabled persons (approx. 10 million, 1/3rd of world's total blind population), and out of this nearly two million persons have corneal blindness. According to WHO calculations this number could double by the year 2020 unless immediate interventions are made.

Patients with corneal blindness can be visually rehabilitated through transplantation of damaged corneas with healthy donor corneal tissues. India needs 2 lakh donor eyes per year to take care of corneal blinds in our country. Although there

are over 700 registered eye banks in India, these collect only 25,000 donor eyes per year. There is an urgent need to improve efficiency of eye banking system in India.

Penetrating keratoplasty (PK) has high success rates compared to other tissue & organ transplantation, and is the most frequently performed corneal replacement procedure. Despite the success, immunological endothelial rejection occurs in upto 20% eyes undergoing PK.

The past decade has witnessed a resurgence of lamellar corneal transplant procedures that aim to selectively replace diseased layers of the cornea. Anterior lamellar keratoplasty (ALK) replaces stromal tissue leaving behind Descemet membrane (DM) and healthy host endothelium. Posterior lamellar keratoplasty or endothelial keratoplasty (PLK / EK) replaces DM with healthy donor tissue. Major advantage of ALK over PK, being lack of endothelial rejection. Prolonged steroid therapy is not necessary thereby avoiding complications such as cataract & glaucoma. Surgery is performed with closed globe, thereby minimizing risk of expulsive haemorrhage. Donor corneas with poor endothelial cell counts can be used for ALK, thereby improving tissue utilization from eye banks. Deep anterior lamellar keratoplasty (DALK) using big bubble technique to separate DM from stroma, allows complete removal of stroma & is associated with faster visual recovery. Numerous studies comparing DALK & PK have found comparable visual outcome, with improved graft survival following DALK. ALK procedures have been recommended as preferred choice of transplant surgery for corneal diseases with healthy endothelium.

EK has the advantage of absence of surface incision or sutures, & small incision. This results in smoother surface topography, faster visual recovery, and greater tectonic stability. Suture related complications can be avoided, which is very important in our scenario wherein this is one of the major cause for graft failure following PK. (suture related infections, or induced immunological rejection episodes). The risk of immunological rejection has also been found to be lower with EK procedures compared to PK. Donor corneas with evidence of prior refractive surgery, pterygium, superficial corneal opacity etc, but having good endothelial cell counts can be used for EK surgery. (usually rejected for PK)

In USA, in 2012 out of total of 68,681 corneal transplant surgeries, 36716 were PK, 1855 were ALK, and 24277 were EK procedures. In India, PK still accounts for over 85% of corneal transplant surgery. There is a need to train more corneal surgeons in India with these newer lamellar surgical procedures. Taking into account the advantages compared to PK, both ALK and EK surgery would help improve graft survival, provide better visual outcome, and improve tissue utilization. Eye banks across India, should focus at improving tissue retrieval, standardize tissue evaluation, and equitable tissue distribution.

Thanks

Dr Rajesh Fogla DNB, FRCS (Edin), MMed (Ophth) **Apollo Hospitals**, *Hyderabad*

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President Column



I wish to extend my best wishes and greetings to all members of DOS.

Delhi Ophthalmological Society is the largest state society of the country with representation from all across the country and abroad. I would consider it as truly a national capital society. Therefore we all have huge commitment to fulfill the demands and desires of our society members. I believe on delivering goods with ethical values and working as per the constitutional norms of the society, we all should respect the laid down rules and byelaws of the society. My team will work on further improving academic and social relationship through various conferences, meetings and publications of DOS. We are committed to strengthen bond with national society (AIOS) and all other state societies.

I would like to invite and encourage our members to be

actively involved with all the activities of the society, interact with each other through our website. All members should update their particulars and postal address so that secretariat can maintain the proper member information.

DOS provides various accesses to member's namely online DOS website with all routine activities, monthly DOS Times and quarterly DOS Journal. We should publish articles and write ups in these DOS publications. All members should be aware of opportunity to avail DOS Travel fellowship for National and International Conferences, I would request every member to go through the guidelines and improve their DCRS points.

This year, we have successfully introduced for the first time a guest case presentation in the monthly meetings by a member from institution / practice other than the Institution who are allotted the meetings. This will give opportunity to members who have good cases and willing to present.

Throughout this calendar year we are going to work in a manner which will give DOS a definite improvement in its activities in the field of academics, social works and more importantly, charitable work. Members who are doing good charitable work should inform DOS secretariat so that information can be circulated to all.

I would invite all members of the society to be with this executive so that we do better and better.

Thanks

Prof. Jeewan S. Titiyal President, DOS

Corneal Collagen Cross-Linking



A. J. Kanellopoulos

Collagen cross-linking of the cornea (C3R) is a new curative approach to increase the mechanical stability of cornea in corneal ectasias such as keratoconus or post LASIK ectasia. The last few years have seen a rapid growth in interest in this treatment protocol worldwide and C3R is now seeing wider acceptance with more and more cornea and refractive surgeons been incorporating this into their practice. This EXPERTS' CORNER on C3R is about the discussion of **Dr. Himanshu Shekhar** with C3R experts **Dr. Anastasios John Kanellopoulos**, **Dr. Paolo Vinciguerra**, **Dr. Ritu Arora**, **Dr. Rohit Shetty**, **Dr. Namrata Sharma**, and it brings to you the interactive deliberations on CXL related issues and practice pearls from the panel of experts with wide experience on C3R and its related issues.

Dr. Anastasios John Kanellopoulos (AJK): MD, is the *Clinical Professor of Ophthalmology*, NYU Medical School, New York, NY, U.S.A. and *Medical Director*, Laservision gr. Institute, Athens, Greece.

Dr. Paolo Vinciguerra (PV): MD, is working in the *Department of Ophthalmology*, Istituto Clinico Humanitas, Rozzano, MI, Italy

Dr. Ritu Arora (RA): MD, *Professor of Ophthalmology,* at Guru Nanak Eye Centre, Maharaja Ranjit Singh Marg, New Delhi

Dr. Rohit Shetty (RS): DNB , FRCS, *Vice Chairman, Cornea & Refractive Surgeon* working at Narayana Nethralaya Rajaji Nagar, Bangalore, India.

Dr. Namrata Sharma (NS): MD, is *Professor of Ophthalmology in Cornea, Cataract & Refractive Surgery Services* at Dr. Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India

Dr. Himanshu Shekhar (HS): MD, is Senior Resident in Cornea, Lens & Refractive Surgery Services, Dr. Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India.

HS: What is corneal collagen cross linking and how does it act?

AJK: Corneal collagen cross linking has been a time proven technique in which a photochemical reaction propagated by the coexistence of riboflavin (vitamin B2) and ultraviolet light (wavelength around 370 nm) are present in the corneal stroma creating a stiffening effect on the natural human corneal collagen. This has been found specifically effective in diseases which relate to corneal collagen softening such as primary keratoconus which is an inherited trait disease and in post refractive surgery ectasia which is a rare complication of LASIK mainly but also PRK.

PV: The Corneal cross linking increases the binding between corneal stromal fibers. There has also been observation of an increased size of fiber section and a reduced space between fibers. The result is a strengthening of the biomechanical properties of cornea that has been evaluated also in peer reviewed papers.

RA: Collagen cross linking (CXL) involves the application of UVA light to corneas treated with riboflavin (photosensitizing substance). The interaction results in the release of oxygen radicals which induce the photopolymerization of stromal fibres of cornea. The resultant cross linkage stiffens the cornea, thereby stabilizing its shape and halting the progression of ectatic disorder like keratoconus.

RS: Collagen cross linking is a minimally invasive procedure used for the treatment of progressive ectatic disorders like keratoconus, Pellucid marginal degeneration or post surgical ectasia. The procedure involves the use of riboflavin (vitamin B12) topically along with UV- A light (370nm) which in the prescribed energy and duration acts as a photosensitizer causes crosslinking



P. Vinciguerra



Ritu Arora



Rohit Shetty



Namrata Sharma

between collagen fibrils in the stroma, thereby increasing the corneal strength and reducing the chance of progression of ectasia.

NS: Corneal collagen cross-linking is a minimally invasive technique that improves corneal stability through the use of photosensitizing agent, riboflavin, and ultraviolet A (UVA) light to induce formation of intrafibrillar and interfibrillar covalent bonds. The standard method involves the removal of corneal epithelium followed by saturation of the corneal stroma using 0.1% isosmolar riboflavin solution in 20% dextran and exposure to UVA light at 3mW/cm².

HS: What in your opinion are the criteria for selecting patients for cross-linking in keratoconus? Do you think it should be done in all the diagnosed cases of keratoconus in which it is permissible?

AJK: My European practice is in Greece which is a southern European country and keratoconus is rampant. We estimate that 1 out of 50 young male people in Greece between ages of 18 and 22 have some clinical signs of keratoconus present on regular Placido disc topography or Scheimpflug derived topography such as Pentacam and the data are compelling that keratoconus progresses in most of these patients under the age of 35 years. So, if we convert the question "what are the criteria for selecting patients of keratoconus for cross linking"- Any keratoconus case that's under the age of 30 years in my opinion should be considered for stabilization as further propogation of ectasia may make it more difficult to halt and may make visual rehabilitation more difficult as well. Patients between 30-35 years should be followed closely every six months interval for any signs of progression and patients between 35-40 years every 1 year. Even patients after 40 years old sometimes can downgrade into ectasia but I think this is very rare and follow up every 2-3 years is reasonable. So, any younger patient with any signs of progression or even patients under 30 years and that at first clinical evaluation shows significant irregularity between 2 eyes, signs of thinning and inferior cornea is steepening are definite indications for treatment for stabilization with high fluence collagen crosslinking.

PV: My suggestion is to Cross link all patient in pediatric age as soon as possible to prevent the rapid progression of the disease. The progression in this age is very rapid. In all other cases I look at progression. It is a false concept that keratoconus progresses only in young patients. We have observed it in patients 72 yrs old also!!

I perform corneal topographies and tomographies at fixed interval from first examination that is between 3 and 6 monthly in age between 18 and 29 depending on the keratoconus grading, 6 monthly between 30 and 40 and 12 monthly over 40. Nobody can observe progression only by looking at simple topographic images. We should select differential maps and look at even mild changes. The best maps are instantaneous curvature maps and pachymetry maps. I also recommend to have careful look at elevation maps, particulary posterior elevation is the first sign of progression.

RA: When I started doing cross linking for keratoconus, I was very specific in my approach and would only select progressive keratoconus cases. Progression being defined as increase in maximum K by 1 D and /or increase in refractive error myopia/astigmatism by 1.0 D. Over the last 5 years, I have realized that CXL is reasonably safe and waiting for progression may make one lose on the corneal thickness and BCVA. Therefore, I am relatively more aggressive in my approach on CXL in young patients i.e upto the age of 25 years and advise CXL at earliest when keratoconus is diagnosed. Beyond this age I wait for progression over next 6 to 12 months. Also in a study done at our centre and to be published in Cornea, we found that long term effect of CXL in terms of arresting the progression of keratoconus and improvement of refractive and topographic indices was statistically more significant when the procedure is performed for grade 1,2 keratoconus over grade 3 keratoconus. I thus recommend this procedure essentially for all cases of keratoconus especially if the patient is less than 25 years, keeping all the necessary pre requisites in mind.

RS: There are various selection criteria for selecting patients for corneal collagen cross linking; most important being that the disease should be progressive. Other important points to keep in mind are the age of the patient; younger patients (<25 years) are more likely to be progressive, ocular allergy is also associated with higher risk of progression especially with a history of eye rubbing, family history of keratoconus, and thin pachy < 425 microns. These cases need to be crosslinked without too much of delay due to the higher risk of progression in them.

The prerequisite for doing a corneal collagen crosslinking is to have a progressive ectasia, and can be done in all cases which show significant progression on topography.

NS: Collagen Cross linking should be done in cases where the keratoconus progresses. There are various criteria for evidence of progression of keratoconus. We generally do collagen cross linking in cases where there is an increase in maximum keratometry by one diopter over a period of one year. In cases of children who have had acute hydrops in one eye, I would do cross linking in the fellow eye.

HS: Do you follow a specific cut off with regards to age of the patient?

AJK: I think this was answered in previous question.

PV: No, only progression is my driving guide.

RA: As I said before I am more aggressive in patients between 10-25 years, fellow eyes of patients of keratoconus who had PK/DALK done few years back-here I have done CXL even when the patients are in there thirties with earliest signs of topographic keratoconus and vision drop to 6/9.

RS: Ideally any patient who is showing progression can be planned for collagen crosslinking. Even children can undergo this procedure as it is minimally invasive and needs limited cooperation. We have cross linked patients in the age range of 10 -35 years depending on these basic criteria.

NS: I am more aggressive in children and in those

patients who are less than 25 years of age. I would perhaps not do it for those cases who are more than 40 years of age as it is unlikely to progress in older age group.

HS: What are the indications other than keratoconus for which you consider performing collagen cross linking?

AJK: We have introduced since 2007, the combination of prophylactic collagen cross linking in high risk LASIK, meaning patients who are under 30 years old, have myopia treated over 6D, have significant myopic astigmatism which be define as astigmatism of >1.5D, have severe asymmetry between astigmatism of one eye and fellow eye i.e., more than 1D astigmatism between two eyes. So, in those cases we would prophylactically perform collagen cross linking in the primary LASIK procedure.

PV: RK, post refractive surgery ectasia, pellucid marginal degeneration, terrien marginal degeneration are main indications. In all cases when I need to perform PTK in thin corneas, I always combine PTK and CXL. Before removing graft sutures when a good post-operative astigmatism has been reached, CXL can be done to reduce the risk of the increasing the post suture removal astigmatism.

RA: I have performed CXL procedure for decompensated corneas awaiting keratoplasty for symptomatic relief the effect though is only temporary and wears off by 3-4 months. It might be worthwhile to try this procedure in early cases of corneal oedema also. I have not used it in infectious keratitis, though some recent reports show good results.

RS: Collagen cross linking has been found to be effective in stopping the progression of ectasia other than keratoconus such as Pellucid marginal degeneration or post refractive surgery ectasia. We have found the procedure to be effective in both these conditions both as a stand alone procedure and as an adjuvant procedure to Intrastromal rings or topoguided PRK.

Recently there has been a lot of interest in the use of CXL for treating nonresponsive microbial keratitis. The protocol followed is the Dresden protocol (30 minutes of riboflavin soak time and 30 minutes of UV A at 3 mW/cm² total energy 5.4J) as it has been found that a prolonged UV exposure is required for desired effect. We have tried this in a few cases of nonresponsive keratitis of both bacterial and fungal etiology and found dramatic results in a couple of cases.

NS: Other than keratoconus we have used cross linking in cases of pellucid marginal degeneration and post refractive surgery ectasia. We did a study in cases of sympomatic pseudophakic bullous keratopathy in 50 eyes where collagen cross linking was done. Collagen cross linking decreases the central corneal thickness in these cases as measured by both ultrasonic pachymetry and anterior segment optical coherence tomography. However, this was temporary for only one month. The visual acuity also improved for the same duration. At the end of 6 months there was no benefit of collagen cross linking. This study will be published in the journal Cornea.

We also did a randomized controlled trial in cases of fungal keratitis where in one group we gave medical therapy consisting of Natamycin 5% along with cross linking on the first day of presentation and in the second group we gave medical therapy alone consisting of Natamycin 5%. We did not find any difference in cases which were treated additionally with collagen cross linking in terms of time to healing, decrease in size of the infiltrate, size of the scar and visual acuity. We believe that cross linking has no role in mycotic keratitis based on these findings.

HS: What is the technique that you follow for performing the procedure?

AJK: In primary keratoconus and post refractive surgery ectasia, we have described a procedure which is the Athens protocol and is the combination of topography guided normalization of the corneal surface. This is done transepithelially following a 50 micron PTK removal of epithelium and upto 40- 50 microns stromal removal.

The aim of this intervention is to normalize the irregular cornea produced by keratoconus. We use the Wave light platform which offers both the Placido disc and Scheimpflug derived topographic image and after that we perform high fluence collagen cross linking 6 m W/cm² for 15 minutes. This procedure we have published for many years with multiple articles and is called the Athens protocol. Now in LASIK Xtra which is the prophylactic intervention for routine LASIK cases, we at the end of LASIK procedure soak the cornea with 0.1% riboflavin for 60 sec just the underlying treated stroma trying to avoid any riboflavin to come in contact with folded flap. After that the residual riboflavin is rinsed, the flap placed in position and the interface rinsed thoroughly, the flap respositioned as if the procedure will be terminated, following that with hydration with BSS. The eye is exposed to very high fluence collagen cross linking 30 mW/cm² for 80 seconds. We use the Avedro device for this technique and then place the bandage contact lens for lubrication.

PV: Soaking time of never less than 25 min is mandatory. I use a suction ring (Vinciguerra Ring Janach Italy) that maintain the solution over the cornea in a more repeatable way. I use an Iroc laser with 10mw for 9 min. A beam optimizer is used to reach the same depth in the center and in the periphery.

RA: I perform CXL after epithelial debridement. After putting topical paracaine, we measure corneal thickness centrally and at cone apex ultrasonically. Central 8 mm epithelium is removed after soaking it locally with 20% ethyl alcohol. Ultrasonic pachymetery is repeated. If thickness is less than 400 microns, cornea is treated with distill water for few minutes till corneal thickness improves to 400 microns. 0.1% Riboflavin drops (0.1% riboflavin-5-phosphate in 10 ml dextran-T-500 20% solution) are applied every 3 minutes for half hour and we make sure that it has penetrated into anterior chamber. We use UV-A ray source from Vega with 8mm aperture and has 2 diodes for UV generation in six cycles of 5 minutes each, making sure that application is exactly central 8 mm and well focused. Needless to say that UV delivery system is calibrated using an ultraviolet A meter at a working distance of 10-12 cm before the start of the procedure and it ensures delivery of 3mW/cm² of UV rays with surface irradiance of 5.4J/cm². At the end of procedure BCL is inserted and patient is prescribed oral analgesics and topical antibiotic drops, diluted steroids and lubricants.

RS: We have used both the traditional collagen cross linking (CXL) according to the Dresden protocol which entails a 30 minute soak time with riboflavin 0.1% after scraping the corneal epithelium, followed by a UVA exposure for 30 minutes at 3mW/Cm², with total energy being 5.4J. We have also had experience with the accelerated cross linking system from Avedro Inc. which shortens the crosslinking time drastically by an increase in the power to 30 mW/cm² and a decrease in the UV time to 4 minutes, total energy 7.2 J. The newer accelerated cross linking gives a flexibility to the surgeon to tailor the procedure to the patient's eye. The modification is not restricted only to the soak time and UV A power and exposure time. Another significant advancement has been in the riboflavin formulations used; since we have experience with the Avedro system, I am highlighting the drops available from the company (No financial Interest)

- Vibex- used for accelerated crosslinking (formulation similar to that used in standard cross linking (epithelium off).
- 0.1% riboflavin, 20% dextran, isotonic
- *Paracel* used for transepithelial crosslinking (epithelium on)
- 0.25% riboflavin, HPMC, BAK, EDTA, TRIS
- Vibex rapid- 0.1% riboflavin, saline , HPMC, (NO dextran) No dehydration of cornea, faster diffusion
- Vibex xtra- used in LASIK Xtra which combines LASIK with a flash crosslinking to reduce the risk of ectasia post procedure.
- 0.25% riboflavin, saline.

NS: All procedures are performed under topical anesthesia with 0.5% proparacaine hydrochloride administered twice 15 minutes before the procedure. A lid speculum is inserted, followed by removal of the central corneal epithelium (7-mm diameter) using a blunt spatula. Commercially available isotonic riboflavin (0.1% riboflavin with 20% dextran; Medio-Cross, Italy) eye drops are administered every 5 minutes for half an hour. The UV device (UV-X, IROC, Zurich, Switzerland) is used to deliver UVA light of 365 nm wavelength and 3mW/cm² irradiance via a 9-mm aperture, at a distance of 5 cm from the apex of the cornea, for 30 minutes. After irradiation, the eye is rinsed with a sterile saline solution, one drop of moxifloxacin hydrochloride (0.5%; Vigamox, Alcon Laboratories, Fort Worth, TX) is applied, and a bandage soft contact lens (PureVision; Bausch & Lomb, Rochester, NY) is inserted and retained for 4 days.

HS: What has been your experience with the transepithelial technique?

AJK: We have shown our results with transepithelial crosslinking. They appear to be promising although all the biometric markers that we evaluated with collagen cross

linking such as tensile strength of cornea, OCT findings with hyperreflectivity and epithelial changes appeared to be less with transepithelial technique. We currently use for transepithelial technique a product – which is an abrasive 0.1% riboflavin solution followed with VibeX Xtra, which is a riboflavin solution to penetrate the weakened epithelium and then very high fluence collagen cross linking 30 mW/cm² for 3 minutes.

PV: I found the demarcation line was more superficial (60 micron). I have modified the technique for pts > 40yrs old. I perform very thin epithelial scratches in cornea to open pores for riboflavin. In this way 200 micron depth can be reached.

RA: I have used only in few cases but am not happy with the results. Here riboflavin used is 0.1% Riboflavin with tris hydroxymethyl aminomethane+EDTA to facilitate the penetration of riboflavin. It has advantage of being useful when corneal thickness is less than 400 microns and has no complications related to epithelial debridement.

RS: The trans epithelial CXL using the standard 0.1% riboflavin with dextran is not as effective in crosslinking the cornea as the CXL after scraping the epithelium as we have discussed in our article published in the Journal of refractive surgery-' In vivo imaging of riboflavin penetration during collagen cross-linking with hand-held spectral domain optical coherence tomography. J Refract Surg. 2012 Nov;28(11):776-80'.

Newer riboflavin formulations with BAK, TRIS and HPMC improve the penetration of the riboflavin drops through intact epithelium. It is useful to use this procedure in cases with corneas with thin pachymetry not fit for regular CXL. We have had very encouraging short term results with this new technique of transepithelial CXL. The protocol used at our hospital for transepithelial CXL is - 10 minute soak time with Paracel transepithelial riboflavin drops (Avedro Inc), followed by 2 minutes 40 seconds of UV A exposure at 45mW/cm². The 6 month results have been stable but we are awaiting the long term results for the efficacy of the procedure.

NS: We have done transepithelial collagen cross linking in a couple of cases only and have limited experience with the transepithelial technique.

HS: Have you used the hypo-osmolar riboflavin in your cases? Do you think it has a place in clinical practice?

AJK: We have used the hypoosmolar riboflavin very early on but we found it not to be effective. In our clinical and laboratory work, we found out that hypoosmolar does cause corneal thickening but this is to the expense of the riboflavin concentration bioavailable within the cornea to undergo collagen crosslinking because one has to consider that the cornea swells from absorption of aqueous and that aqueous dilutes the concentration of riboflavin. So, in my opinion hypoosmolar riboflavin solution should be 0.2% rather than 0.1% because its effective dilution in the cornea becomes much lower and thus achieves less corneal crosslinking. We have seen this in many clinical cases in the past that we have treated with hypoosmolar riboflavin in order to swell the cornea and be able to treat the thinner corneas with collagen cross linking have proven to progress into further ectasia. So our recommendation would be to use regular riboflavin solution but with lesser time exposure. If one is using the standard Dresden protocol which is 3mW/cm² for 30 minutes, they can use it for 25 minutes or 20 minutes. We with the higher fluence protocol that we introduced used in corneas that are thinner than 400 microns 6mW /cm² instead of 15 minutes 12 minutes and in the corneas that are thinner than 350 microns instead of 12 minutes 10 minutes and we found out to be safe and effective.

PV: No I have not used it.

RA: I have used hypoosmolar riboflavin for crosslinking when minimal corneal thickness is less than 420-430 microns at the beginning of surgery to swell up the cornea. On the contrary have found Distilled water working better to increase the corneal thickness above 400 microns. I don't think hypoosmolar riboflavin has much role in clinical practice.

RS: Yes, rarely for borderline thin corneas hypo osmolar riboflavin can be used and has been found to be effective and safe. The newer formulation of transepithelial riboflavin is also a hypo-osmolar concentration and plays the dual role of better penetration and increased safety during UV light exposure.

NS: Yes we use it in cases with thinner corneas. However I believe it is pseudo thickening which occurs in these cases. I don't think it works a well as the isoosmolar riboflavin.

HS: In the postoperative period, when do you prescribe topical steroid and for how long?

AJK: For the standard cross linking without LASIK we prescribe topical steroid for just a week. In the Athens protocol patients, we describe topical steroid for 4 t/ d for a month and then 2 t/ d for another 1 month.

PV: Twice a day only for 10 days. I feel steroids works against the basic principle of CXL.

RA: We prescribe topical diluted steroids from day one only every 6 hourly and continue for 4 -6 weeks depending upon the corneal haze. TBCL is usually removed on 3rd or 4th day with the healing of epithelial defect.

RS: We start topical steroids in the immediate post operative period and continue for 3 weeks in routine cases, with close monitoring of intraocular pressure at each visit.

NS: We start topical diluted steroids in gid doses, that too after the bandage contact lenses in removed and complete epithelisation has occurred. We subsequently taper it in the next 4 weeks.

HS: In your clinical experience what has been the outcome on the basis of which its efficacy can be defined?

AJK: The efficacy of CXL in my opinion can be described in several ways. There are several biological markers such as hyper reflectivity within the cornea with high resolution ASOCT which establishes the efficacy, the depth and its distribution. Also the fact that cross linking changes the epithelial behavior, we have published on this already as

well. It appears that ecatsia cases that have been effectively cross linked, change their epithelial thickness profile more to normal and I will add this reference to your convenience. Other biological markers of cross linking have been recently a very positive adjunct in hyperopic LASIK. We have found that hyperopic LASIK Xtra offers long term stability in hyperopia which is known to invariably regress after the first year. We have described that this is probably intrinsic biomechanical effect of hyperopic LASIK which appears to be stabilized in conjunction with collagen crosslinking and we find this a great clinical reinforcement of the effect of collagen cross linking in these cases.

PV: Depth of demarcation line and topographic/ tomographic stabilities of parameters.

RA: We define efficacy based on maintainence of UCVA,BCVA, refractive error, reduction in spherical error, contact lens fitting and tolerance, periodic topographic indices in the form of central K, sim K values, apical K and regaining of corneal thickness by one year. Reduction in eleration in anterior float has also been seen in some cases.

RS: The best measure of efficacy of collagen cross linking is a stable keratometry on topography, although this may take 3 to 6 months to happen. It is necessary to repeat topographies at routine interval to look for the stability or progression.

NS: We define efficacy based on the stability of topography mainly considering the values of central K, Sim K and apical K as well as ultrasonic pachymetry.

HS: What are the possible complications and side effects of cross-linking?

AJK: There have been multiple complications, we have published in a book chapter before. Obviously with any corneal procedure, corneal infection is the first most feared complication. Other collagen related complications may be corneal scarring from delayed epithelial healing as well as white spots in the cornea which may possibly represent over cross linking or even immune response to cross linking.

We also have seen complications such as corneal melt in some cases. I think one would better read a book chapter on this issue. Nevertheles, the complications we have found to effect less than 3% of the patients and we have an experience of treating almost 5000 patients treated primarily with collagen cross linking or in conjuncture with LASIK.

PV: Most frequent complications is deep stromal opacities. We have published a paper in JCRS, where we observed that during soaking time, esp. with dextran solution corneas become too thin and unsafe to treat. Since we do have moved to isotonic solutions without dextrane, we have not observed the deep stromal opacities.

RA: We have had 5 cases of sterile infiltrates which had typical pattern and responded well to frequent topical full strength steroids. Word of caution to rule out infectious aetiology before starting steroids. There was one case of infectious keratitis and two cases of sterile corneal melts needing PK. On retrospective analysis of cases of sterile coeneal infiltrates and melts we found that they had coexisting VKC or allergic conjunctivitis. Therefore now when we perform CXL with these coexisting conditions, we control them with topical steroids before proceeding with CXL.

Central corneal haze after CXL is common but is temporary and usually disappears by 4-6 weeks.

RS: Cross linking is a relatively safe procedure with rare side effects. The possible side effects can be secondary microbial keratitis which can heal with corneal scarring, sterile infiltrates and corneal melt or iridocyclitis which is treated as in any other case.

NS: We have had 4 cases of sterile infiltrates and one case of microbial keratitis due to Pseudomonas keratitis. The latter case along with the review of literature was published in the Journal of Cataract & Refractive Surgery. Ever since this infection we defer topical corticosteroids until the bandage contact lens is removed and complete epithelisation occurs.

HS: Do you have any experience with the accelerated CXL system? How do you rate its efficacy in comparison to conventional CXL?

AJK: We introduced high fluence CXL since 2005. We have in all biological markers studied shown that it appears to be as safe and as effective as the standard CXL. We currently use the Avedro device with fluences that can reach upto 45mW/cm². I described previously the fact that we used 6 mW/cm² for 15 minutes used for the Athens protocol applied to keratoconus and post LASIK ectasia. We used 30 mW/cm² for 80 seconds for LASIK Xtra. We also used 45mW/ cm² for 3 min for enhancement of astigmatic keratomy using femtosecond laser and we all have these published soon in the peer reviewed literature.

PV: We feel it is too early to compare it to conventional CSL.

RA: No, I have not used accerlated CXL system. Various accerlated CXL systems available deliver increased intensity of UV-A rays for shorter time. They may deliver 5mW/cm² for 18 minutes or 18mW/cm² for 5 minutes or 30 mW/cm² for 3 minutes, while with LASIK XTRA or PRK XTRA it is 45mw/cm² for one minute. The ribolflavin is dynamized by UV-A rays generated by special equipment: this second step lasts shorter time, during which the riboflavin penetrates the corneal surface by a few microns and induces the lamellae to move closer together. The same total amount of UVA light energy (5.4 J/cm²) is delivered, with these high irradiance devices.

RS: We have been using the accelerated CXL system from Avedro Inc. for over a year now, and have found extremely promising. The 1 year results have shown all cases to be stable on topography and no safety issues like increased endothelial cell loss or stromal haze. It seems to be as efficacious as the conventional CXL in the limited numbers evaluated.

NS: As of now we have no experience with the system. We have recently acquired the system and would be starting the cases soon on this system.

HS: Do you advocate combination of Excimer laser treatment with CXL?

AJK: As we described above with significant comparative studies we have shown compelling evidence that combining topography guided ablation and we have only found out that Wavelight Alcon platform to be applicable for this with higher fluence CXL to be superior to any other application of CXL in cornea including the use of intracorneal ring segments.

PV: We should be very careful in it. Frequently corneas shows a flattening because of the CXL that makes the combination very unpredictable.

RA: Topography guided Excimer laser treatment and CXL is being advocated in Athen's protocol. Here laser is given to the apex of the cone and ablation of 40-50 microns is done in a similar fashion as PRK and additional peripheral hyperopic laser is applied .The procedure is combined with CXL with the aim to take care of refractive aspects. Here

Higher fluence CXL is performed for 10' with 10mW/ cm² of UV energy is delivered.

There are several technical limitations to combining UVA with excimer laser therapy. If laser is used first there is danger that it may leave the cornea thinner than 400 microns making CXL treatment unsafe for the endothelium. If crosslinking is used first an interval of 6 months may be needed between two treatments to stabilize the cornea before applying laser, also ablation rate for the crosslinked cornea may not be same. The limitations of the combined treatment restrict its use to corneas that are still relatively thick. Topography guided laser treatment and not the standard laser treatment is to be performed.

RS: In selected cases of early to moderate keratoconus, combining a limited excimer ablation meant to regularize the cornea, has been found to have extremely good results. It is termed topography guided Photorefractive keratectomy (TPRK). The important point is to remember that it is NOT a refractive correction and is only a limited ablation for possibly improving the quality of vision. It is essential to have a minimum pachymetry of 500 microns before planning this procedure to avoid worsening the pre-existing ectasia. The collagen crosslinking procedure is usually done simultaneously with the topoguided PRK to ensure the stability of the cornea.

NS: We do not advocate excimer laser treatment with CXL. The use of collagen cross linking makes the outcomes of excimer laser surgery in these cases very unpredictable. We do not have normograms right now to treat refractive errors in cross linked corneas. It is too much to extrapolate data on normal corneas to cross linked corneas.

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Corneal Triple Procedure



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Keratoplasty when combined with cataract surgery and intraocular lens implantation is classically known as triple procedure.

Since the time of first successful corneal transplantation in 1906 by Edward Zirm, corneal transplantation has been considered one of the most successful organ transplantations¹.

Indications for corneal grafting have changed over the last few decades. Modern day cataract surgery with intraocular lens implantation has led to pseudophakic bullous keratopathy being the most common indication for corneal grafting, followed by regrafts, corneal scars, dystrophies and keratoconus².

Success of corneal transplants depends on various factors. The indication for transplant may dictate the success rate. Keratoconus, small nonvascularised central scars, lattice dystrophy, macular corneal dystrophy are the ones with higher success rate. Regrafts, vascularised corneal scars and herpetic eye disease have less chances of long term success.

In patients with corneal pathology coexisting with cataract, triple procedure is an effective method to restore visual acuity.

Combined procedures vs only corneal grafting

Indications for a combined surgery are those patients who have corneal disease along with cataract. Many studies have compared the success rates of combined surgery vs sequential procedures and found the results to be comparable³. If improvement in visual acuity can be achieved by corneal grafting alone or only by cataract surgery with IOL implantation, then combined surgery is avoided and the simpler route is preferred. Sometimes the corneal opacity may be too dense and amount of lenticular opacity may not be clinically evident, here the decision to do a combined procedure may be taken intraoperatively. Likewise, during cataract surgery if the corneal opacity is deemed to be causing significant visual loss, penetrating keratoplasty may be done along with the cataract surgery (subject to tissue availability).

The corneal surgeon is often called upon to make this judgement- ie need for penetrating keratoplasty (PK) along with cataract surgery vs cataract surgery alone. For example, nonprogressive corneal opacities such as corneal scars after healed keratitis may benefit after cataract surgery alone. A corneal surgeon will have to make the judgement based on clinical appaearance, potential acuity measurement, specular microscopy and pachymetry. Endothelial dystrophies with cell counts < 1000/mm², corneal thickness > 600 microns need a triple procedure.

Advantages of triple procedure over two stage procedure are many, which includes-



Figure 1: Triple Procedure



Figure 2: Triple Procedure



Figure 3: Specular microscopy 6 months post triple procedure showing good endothelail cell count

- Earlier visual rehabilitation
- Reduces cost of second surgery
- Reduces damage to donor corneal endothelium (the donor endothelium is affected when cataract surgery is done after corneal grafting.)

One of the major draw backs of triple procedure is IOL power calculation may be inaccurate. The longer operating time in a triple procedure may lead to the devastating complication of expulsive hemorrhage especially in patients who in their anxiety may move, cough or squeeze the eyelids during the open sky procedure. Lid block is extremely important along with a good blepharostat or lid speculum to avoid pressure of the eyelids on the globe.

A triple procedure may be one of the following

- Penetrating keratoplasty (PK) with extracapsular cataract surgery (ECCE) and intraocular lens implantation (IOL)
- Phacoemulsification + IOL followed by PK
- PK with IOL exchange
- PK with secondary IOL implantation

PK + ECCE + PCIOL With the popularization of extra capsular cataract surgery and refinements in the surgical techniques, it was combined with penetrating keratoplasty. The posterior capsule is a protective barrier between the anterior and posterior segments of the eye and allows implantation of a posterior chamber intraocular lens. The posterior chamber IOL causes less damage to endothelium of the graft as compared to an anterior chamber or iris supported lens.

PK + phacoemulsification If visibility permits, phacoemulsification may be done before corneal grafting. Phacoemulsification before penetrating keratoplasty reduces chances of intraoperative complications as seen with ECCE and ICCE. Advantages of phacoemulsification before PK are.

- Anterior chamber is well maintained throughout procedure
- Less chances of iris prolapse
- Iris -lens diaphragm movement is reduced
- Capsulorrhexis is controlled with less chances of extension
- Chance of posterior capsular rupture is less
- Cortex removal , IOL implantation is easier
- Chances of vitreous loss is less
- Chances of expulsive choroidal haemorrhage are reduced

Role of viscoelastics

Viscoelastic devices help to protect the corneal endothelium, expand the capsular bag, form the anterior chamber and perform a safer procedure. Before advent of viscoelastics, IOL implantation had to be abandoned many times due to positive pressure on the posterior capsule.

Indications for triple procedure²

- Corneal opacities with significant cataract
- Fuchs endothelial dystrophy significant corneal edema or endothelial cell count <1000/mm² and corneal thickness >600 microns
- Adherent leucoma with significant cataract



Figure 4: The new triple Descemet's Stripping Endothelial keratoplasty (DSEK)+ phacoemulsification

- Keratoconus with cataract
- HSV keratitis with cataract

Contraindications for triple procedure

Contraindications are the same as those for corneal grafting alone. Ocular cictricial pemphigoid, Stevens Johnson syndrome are poor candidates for PK and so also for PK with cataract surgery. Uncontrolled glaucoma, proliferative diabetic retinopathy and recurrent uveitis are poor candidates for triple procedures.

Investigations

Dense corneal opacity with no view of anterior chamber may require to be investigated by ultrasonic biomicroscopy (UBM). A 50 mhz or a 35 mhz probe may be used. Peripheral synechaie, presence or absence of crystalline lens and intactness of the posterior capsule, location of IOL can all be adequately visualized. Surgical planning is done based on all these findings.

Visually evoked potential (VEP) also helps to determine optic nerve function and the visual potential post operatively. Low amplitude and or increased latency, if seen will indicate poor prognosis for recovery of good visual acuity post operatively.

Ultrasound of posterior segment by B Scan is also necessary when fundus evaluation is not possible due to media opacity.

Surgical technique

IOL Power calculation

Once a decision has been made to perform a triple procedure, intraocular lens power has to be calculated.

Every surgeon has to evaluate the results of his or her corneal grafts by measuring the keratometric values of their corneal grafts using standardized suturing techniques and use that average K to calculate the IOL power. This, however, may not be entirely accurate. Several studies have emphasized the importance of using personalized constants in a given formula⁴. Theoretical formulas such as Hoffers which are based on axial length may be useful to calculate the intraocular lens power⁵.

Anesthesia

Once the decision has been made to perform the triple procedure, the IOL power is calculated and the appropriate IOL is ordered. The procedure may be performed under general or local anesthesia. Generally local anesthesia with proper lid block and softening of the globe with a Honan's balloon or a "pinkie" ball is done. Combination of bupivaciane and lidocaine anesthesia with hyaluronidase is used.

Preoperative dilation of the pupil is also necessary in case of the triple procedure. It is done as in a routine cataract surgery with tropicamide and phenylephrine.

After cleaning and draping the eye, the speculum is placed to retract the lids. Choosing the right speculum is of importance. The speculum should avoid putting pressure on the globe and has to retract the lids adequately. Many of our Asian and Indian eyes are deep set. Lid sutures and superior and inferior rectus sutures may have to be employed in some cases where adequate exposure of the surgical field is not obtained. Again the importance of lid block cannot be overemphasized.

Some studies have advocated core vitrectomy or aspiration of vitreous before starting the procedure in order to decrease positive pressure intraoperatively⁶. There appeared to be no posterior segment complications after vitreous aspiration in these studies.

Use of Fleiringa's ring- some surgeons use it routinely. Use is advocated in paediatric eyes, vitrectomised eyes, high myopes, eyes where vitrectomy is anticipated (ie aphakes). The ring is secured in place with 6-0 silk sutures.

Steps of Surgery

Peritomy is not required in cases of central grafts. In cases where eccentric trephination is required (mostly in peripheral perforations, large therapeutic grafts), peritomy is done in localized areas. Removal of epithelium of the recipient bed is done in cases where it is loose or thick and hypertrophied. This aids in preventing slippage of the trephine and ensures proper placement of sutures.

Selection of trephine – central corneal grafts usually have a donor size upto 8.25 mm (8 mm -8.5 mm) and recipient bed size of 7.75 mm (7.5 mm – 8.0 mm). The donor is

usually punched endothelial side up on a teflon block with a modified Iowa punch. Barron's vacuum trephine is also used routinely to give a good donor button. When whole globes are used and cut from epithelial side, the graft-host disparity need not be 0.5 mm. Disparity may be only 0.25 mm. However a certain disparity is maintained between donor and recipient due to tissue compression which occurs due to sutures and the contour of the grafts is maintained. This avoids undue flattening of the graft curvature. Some surgeons also use artificial anterior chamber to cut the donor corneoscleral rim from the epithelial side. The Hanna trephine is used to cut a central corneal button. Advantage of this technique is that the donor and recipient are cut from the epithelail side. There is no tissue mismatch and avoids a "bevel" cut of the donor. Marks for suture placement can be put both on donor and recipient and they can be perfectly aligned.

The donor button is preferably prepared before recipient trephination to ensure its availability as soon as the globe is opened. The button is place epithelial side down on ateflon block and a few drops of Mckarey – Kaufman medium or Optisol (which ever medium the donor was stored in) is put on the button and it is kept covered.

Host bed trephination is done with either disposable hand held trephines or Hessburg Barron's vacuum trephines. The centre of the host bed is marked by taking a 6mm caliper and measuring from limbus to centre at 3, 6, 9 and 12 o'clock position. An inked 8, 12 or 16 incision radial keratotomy marker is used to mark the host bed for suture placement. Paracentesis is made at the limbus between suture marks preferably at 10 o'clock position and viscoelastic is injected into the anterior chamber to protect the intraocular structures from getting cut by the trephine blade. The paracentesis is also used later in the procedure to reform the anterior chamber and avoid entering the anterior chamber from the graft host junction, which can lead to stripping of the donor Descemet's membrane.

Host bed trephination is only made partially with Hessburg Barron suction trephine or hand held trephine. The anterior chamber is entered with a Beaver blade or no. 11 blade or diamond knife. The edge of the incision is held with a toothed forceps and right and left corneal transplant micro scissors are used to complete the host cornea removal. It is important not to damage the intraocular structures during host cornea removal. The remanants the host Descemet's membrane is trimmed.

Cataract Surgery- anterior capsulotomy is preferably achieved by doing a capsulorrhexis. Radial tears may occur due to positive vitreous pressure. If this occurs, it is best to complete the capsulotomy by cutting the capsule with scissors. Hydrodissection of the crystalline lens can be done and the nucleus is dialed out with sinsky hook. "pressure – counter pressure method" is best avoided as zonular dialysis and removal of the capsular bag may occur. Earlier even cryoprobe was used to remove the nucleus.

The lens cortex is then removed by irrigation and aspiration. Manual or automated removal can be done. It is important to use less fluid as the excess fluid obscures the surgeon's view and causes may reflexes. Gentle positive pressure on the posterior capsule (PC) is needed to strip the cortex from the capsular fornices.

A 6.5 mm optic PMMA lens is the preferred choice in the open sky technique. When phacoemulsification has been performed, a foldable lens can be placed in the capsular bag. Viscoelastic is used to distend the capsular bag. If rhexis could not be perfomed, then lens is placed in the sulcus. In case of a PC rent or inadvertent removal of the bag, scleral fixation of IOL may be required. Gentle pressure on the PC is required to prevent the IOL from being pushed out by the positive vitreous pressure. Sometimes, due to intense positive pressure, placement of the IOL may not be possible. In such cases, we have place the donor button, secured it with 4 cardinal sutures and a few more sutures in the inferior quadrant, thus having a closed system to insert the lens. However, in such circumstances, accurate placement of the IOL may be difficult due to poor visibility due to donor corneal edema and some endothelial damage may also occur.

Posterior capsular rupture- small PC rents which are central may still permit PC IOL implantation. Significant PC tear with vitreous loss will need automated anterior vitrectomy. It is very important to keep automated vitrectomy instrumentation ready in all open sky procedures. Open looped Anterior chamber lenses, iris fixation IOLs can also be used if adequate iris support is present. In cases where iris support is inadequate, scleral fixation of IOL may be required.

Donor button is then removed from the teflon block with a Patton's spatula, placed over the recipient bed, anchored with 4 cardinal sutures. The remaining sutures are either 16 interrupted or 8 interrupted with a running continuous suture or double running sutures, according to the surgeon's preference. The suture are tied in 3-2-1 or 2-1-1 fashion and the knots are buried in the peripheral host cornea. The chamber can be deepened with viscoelastics through the paracentesis in the initial stages and later the viscoelastic can be replaced by balanced salt solution.

Sutures may be replaced intraoperatively, if they are too tight or too loose with the aid of an intra-operative keratoscope or even seeing the reflection of the disposable trephine on the surface of the donor. The continuous sutures can likewise be titrated.

After checking the wound for water tight seal, the surgery is completed.

Few pearls

- Preop evaluation needs to be thorough
- Need for AC IOL or scleral fixated lens has to be anticipated. If SFIOL is anticipated, then scleral flaps which cover the prolene suture knots (for the SF lens) may be made ahead of trephination of the host bed
- Good lid block to avoid squeezing of the eyelids in case of local anesthesia
- Choosing a lid speculum which does not put pressure on the globe
- Viscoelastic devices such as viscoat or healon protect the donor endothelium during suturing.
- Preparation of donor button prior to recipient bed trephination to ensure availability of tissue and to be able to close quickly in case of positive pressure
- Keeping vitrectomy instruments ready

Newer triple procedures

Lamellar corneal surgeries have now nearly replaced penetrating keratoplasty⁷. Deep anterior lamellar keratoplasty is done when the pathology is in the anterior stroma and the endothelium is healthy. Posterior lamellar surgery is now the preferred practice in Fuch's dystrophy, pseudophakic bullous keratopathy and in many cases of aphakic bullous keratopathy.

Lamellar surgery can be accompanied by cataract surgery in the same sitting. For Fuch's dystrophy, where visibility through the diseased cornea is good, phacoemulsification with foldable lens implantation can be done followed by insertion of the donor endothelium – a DSEK button (endothelium + a thin layer of stroma) or descemet's membrance endothelial keratoplasty (DMEK) (only Descemet's membrane)⁸.

Small incision cataract surgery (SICS) followed by DSEK or by DMEK can also be performed if the cataract is too advanced to remove by phacoemulsification or if visibility is an issue.

Rehabilitation is rapid after the new triple procedures as the anterior surface of the cornea which is the major refracting surface of the eye, is not distorted by sutures.

Post operative management

The post operative regimen is as for a routine PK. However, post operative inflammation may be slightly more after triple

procedure as opposed to PK alone or cataract surgery alone. Management of corneal epithelium, dry eye, postoperative suture management is the same as for a keratoplasty alone.

Clinical results of triple procedure

Many studies have evaluated the results of triple procedures in terms of visual acuity (uncorrected and best corrected), graft clarity and long term graft survival⁹. Upto 10 years follow up have also shown clear grafts in upto 95% of cases with good visual acuity of 6/18 or more in upto 70% of cases.

The study by Jonas et al⁹ found the most important factors influencingvisual outcome after central penetrating allogenic keratoplasty combined with IOL surgery were preoperative visual acuity, graft size, and reason for keratoplasty. Other factors such as age, sex, diabetes mellitus, and preoperative refractive error do not substantially influence postoperative visual outcome.

Another retrospective study by Sridhar et al¹⁰ of 104 cases of triple procedures found that 72% of the grafts remained clear (1.6- 79 months) with 40% maintaining visual acuity > 6/12.

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Acute Corneal Hydrops



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A cute corneal hydrops (CH) is the development of marked corneal edema due to a tear in Descemet membrane (DM) followed by acute leakage of aqueous into stroma and epithelium¹. The first report of CH in Keratoconus (KC) was probably reported by Plaut (1900) as a sudden opacity at the apex of the cornea due to a rupture of DM². Most of the cases are reported in cases of KC. It can also occurs in other corneal ectasias such as pellucid marginal degeneration (PMD), keratoglobus, Terrien's marginal degeneration (TMD), LASIK-associated keratectasia, keratectasia after radial keratotomy (RK), after deep anterior lamellar keratoplasty (DALK) and penetrating keratoplasty (PK) for KC¹.

Epidemiology

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The overall incidence of CH in corneal ectasias is around 3.15% over 10-year period¹. CH occurs in approximately 2.4% - 3% of eyes with KC^{1,3}, 6% to 11.5% in cases of PMD¹ and 11% in cases of keratoglobus¹ (Table 1). Most of the cases occur in 2nd to 3rd decade. Males are 2 to 3 times more affected than females. Bilateral cases are rare¹. No racial predisposition has been reported so far.

Aetiopathogenesis

The various risk factors which are associated with increased risk of CH include; earlier age at onset, eye rubbing, vernal keratoconjunctivitis, atopy, Down's syndrome. Among all eye rubbing appears to be the most important risk factor^{1,4}. Tearing and rolling of the edges of a torn DM with subsequent seeping of aqueous into stroma leads to corneal edema. This leads to separation of the collagen lamellae and formation of large fluid-filled intrastromal clefts. This theory is supported by recent studies employing ultrasound biomicroscopy (UBM)⁵. Over a period of time ranging from 5 to 36 week, the adjacent endothelium grows over the defect with subsequent resolution of stromal edema¹.

Complications

Complications are rare but can occur. These are infection, perforation, intrastromal clefts, and corneal neovascularization¹.

Clinical features

The presenting symptoms of acute CH are; markedly reduced visual acuity, intense photophobia, and pain. Often there may be a preceding history of vigorous eye rubbing or coughing preceding the onset¹.

Slit-lamp examination usually reveals marked stromal edema (Figure 1), epithelial microcystic edema, intrastromal cyst/clefts and conjunctival hyperemia. The location and area of corneal involvement varies. Corneal edema can be graded into three groups based on the extent⁵;

- Grade 1- within a circle of 3 mm diameter
- Grade 2 between circles of 3 mm and 5 mm diameters
- Grade 3 larger than a circle of 5 mm diameter

Table 1: Clinical entities in which hydrops can occur ¹	
Clinical entity	Prevalence
Keratoconus (KC)	2.4% - 3%
Pellucid marginal degeneration (PMD)	6% - 11.5%
Keratoglobus	~11%
Terrien's marginal degeneration (TMD)	Rare
LASIK-associated keratectasia	Rare
Keratectasia after radial keratotomy	Rare
DALK graft for KC	Rare
Penetrating keratoplasty graft for KC	Rare



Figure 1: A case of acute corneal hydrops in advanced keratoconus showing marked corneal edema.



Figure 2: Anterior segment optical coherence tomography in a case of acute corneal hydrops showing corneal edema and presence of a large intrastromal fluid filled cleft.

Time for resolution of edema and subsequent final best corrected visual acuity (BCVA) achieved are inversely related to the area of involvement.

Investigations

Diagnosis is based on history and slit-lamp findings. Investigations helps to determine the size/extent of edema and DM tear, formulating the treatment plan, monitoring the response to treatment and identifying any complication. These investigative modalities are; ultrasound biomicroscopy (UBM), anterior segment optical coherence tomography (ASOCT) (Figure-2)^{6,7}. The number (single or multiple), site, size, and communication of the intrastromal cysts/clefts could be discerned. ASOCT reveals epithelial edema, stromal edema, intrastromal fluid clefts, and DM detachments and helps in diagnosis and in monitoring the response to treatment by recording serial corneal thickness.

Management

Treatment of CH can be divided into two broad categories; conservative treatment or surgical intervention^{1,3,4} (Table 2). Surgical approach includes intracameral injection of air/gas and other modalities that are helpful in special situations such as; compressive sutures along with gas injection, penetrating keratoplasty (PK), Cyanoacrylate tissue adhesive with bandaged contact lens (BCL) and amniotic membrane transplantation (AMT) with cauterization^{1,8,9,10}.

Conservative approach

Medical therapy aims at providing symptomatic relief till spontaneous resolution occurs. The final best corrected visual acuity (BCVA) is found to be as good as cases in which intracameral gas/air is used. It includes topical lubricants, antibiotics (prevent secondary infection), cycloplegics (to

Table-2 Advantages and limitations of different treatment approaches for Hydrops							
Treatment approach	Advantage	Limitations					
Medical management	No surgery and associated risks	Prolonged visual recovery Increased chances of complications such as; corneal neovascularisation, fistula, perforation, infection					
Intracameral Air	Early visual recovery Relatively less chance of IOP rise	Repeated injections required Risk of surgery such as infection					
Intracameral SF6	Early visual recovery	Repeated injections required (<air) Increased IOP Risk of surgery such as infection</air) 					
Intracameral c3f8	Early visual recovery Nil or few repeat injection	More chances of raised IOP Risk of surgery such as infection					
ASOCT guided Intrastromal fluid drainage with air tamponade	Useful in cases with large/multiple fluid pockets Early visual recover Nil repeat injection	Long-term results not available Risk of surgery such as infection					

reduce pain and photophobia), hypertonic saline eye drops (help draw fluid), anti-glaucoma medications (to lessen the hydrodynamic force on the posterior cornea), and topical steroids or nonsteroidal anti-inflammatory drugs (NSAIDs) [for easing inflammation and pain]^{1,3}. The final BCVA is found to be as good as with surgical intervention. Sometimes a BCL may be indicated to provide pain relief until the edema subsides or patient is comfortable¹.

Intracameral air/ gas injection

Intracameral air/gas injection shortens the period of persistence of corneal edema in acute hydrops. Various agents used so far includes air⁵, 20% sulfur hexafluoride (SF6)⁸ and 14% perflouropropane (C3F8)³. The fundamental difference between these agents lies in their duration of action. Air stays for a shorter time hence repeated injections are required. SF6 is long acting compared to air (around 2 weeks) however repeat injections may still be required. C3F8 is the longest acting among all and usually repeat injections are not required.

Mechanism of action

As long as the patients keep a supine position, air prevents aqueous penetration into the stroma by its tamponade effect. Secondly it may also unroll the ends of the rolled up DM. Air may bring the margins of ruptured DM closer together, facilitating faster wound healing of corneal endothelial cells over the exposed stroma with deposition of the new DM.

Surgical technique

The technique of injecting air or gas may differ among different surgeons. The commonly followed procedure includes; preoperative pupillary constriction by topical application of 2% pilocarpine nitrate eye drops at 15-20 minute intervals 1 hour before surgery to avoid intraoperative injury to the lens; anterior chamber (AC) paracentesis under aseptic conditions with a 26/27 -gauge needle or alternately a limbal paracentesis; aspiration of 0.1 ml of aqueous humor; injection of gas (14% nonexpansile concentration of C3F8, 20% nonexpansile concentration of SF6, sterile air) enough to fill two thirds of the AC^{1,3,4}. An alternate technique involves inserting a second empty tuberculin syringe with a 26/27-gauge needle without plunger in an oblique fashion into the AC from a different site so that aqueous contents gets pushed out through the second syringe when gas in the first tuberculin syringe is injected into the anterior chamber¹. The later technique may allow smooth unrolling of the curled DM. A surgical peripheral iridectomy (PI) can be performed before injecting air/gas to avoid pupillary block¹. A subconjunctival injection of gentamicin 20 mg in 0.5 ml can be given at the end of the procedure¹. Postoperatively, patient is advised to remain in supine position for 2 weeks. Topical antibiotics, hypertonic saline and steroids are given. Antiglaucoma treatment may have to be given to avoid any rise of intraocular pressure (IOP). In case of persistence of edema, repeat injections can be given¹.

Complications

The various compilations of intracameral air injection include- elevation of IOP, infection, endothelial damage and intrastromal migration. Elevated IOP depends upon the amount of air/gas injected and reported incidence ranges from 0 to 23.8%¹. Eyes showed no elevation of IOP and pupillary block if an appropriate volume of air is injected¹. C3F8 persists in the AC for a longer period compared to SF6 hence the chance of developing secondary glaucoma is expected to be higher. Another concern with C3F8 gas is endothelial toxicity¹, but the use of nonexpansile concentration of C3F8 in a recent study did not found any significant effect on endothelium¹¹. Microbial keratitis is known to occur after gas injection¹, hence strict asepsis should be maintained. Intra-operative fish egging of the C3F8 gas bubble can lead to intrastromal migration of the gas, which may prevent the closure of the intrastromal cleft and may impede the resolution of acute hydrops¹².

Intracameral air/gas injection is highly successful in cases of CH in KC but same is not true for PMD or keratoglobus. In cases of PMD the gas tamponade is not that effective due to the peripheral and inferior location of the tear. In eyes with keratoglobus, the large extent of the DM tear accounts for the poor outcome¹.

Other procedures

Compressive sutures along with gas injection have been tried in several cases with wide separation of the DM edges and multiple stromal clefts^{1,9}. PKP is required rarely in cases of persistent edema, perforation, large DM tear, large intrastromal cyst and corneal neovascularisation^{1,4}. Cyanoacrylate tissue adhesive with BCL can be done in cases of small perforation with fistula formation¹. AMT with cauterization has been tried in persistent hydrops in mentally retarded patients as a quick and effective treatment with good results¹⁰.

For extensive corneal edema and presence of multiple stromal fluid pockets we have standardized a new technique called "Intrastromal fluid drainage with air tamponade: an ASOCT guided technique¹⁵. In this technique multiple corneal stromal venting incisions are given depending upon the location of fluid pockets as determined from preoperative ASOCT to drain out the collected fluids along with anterior chamber air tamponade. Our technique not only reduces the duration of morbidity but also avoids the potential complications associated with repeated gas injection.



Figure 3: A case of resolved corneal hydrops.

Outcome

Hydrops leaves a residual scar and causes flattening of the cone (Figure3). Some improvement in VA after healing of hydrops in KC occurs as in most of the cases the cone does not involve the central area¹. Corneal flattening may also improve the contact lens fitting¹. However in most of the cases once the CH resolves other procedures such as DALK or a PKP is carried out for visual rehabilitation.

To conclude, CH occurs not only in KC but also in other ectatic disorders. Mild improvement in vision can occur but it still adversely affects the prognosis since subsequent keratoplasty is required in most of the cases. Although intracameral gas injection does not affect the final visual outcome it reduces the duration of morbidity and also the risk of complications such as corneal neovascularisation that may jeopardize the subsequent graft. Newer treatment modalities such as tissue adhesive, AMG, and compressive sutures may further widen the available options for corneal surgeons but further studies are required to validate these techniques.

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Congratulations

Heartfelt Congratulations from DOS fraternity to **Dr. Namrata Sharma**, Professor of Ophthalmology, Dr. R.P. Centre for Ophthalmic Sciences, AIIMS, New Delhi who is the recipient of "American Academy of Ophthalmology Senior Achievement Award for the year 2013" in recognition for her outstanding contribution in research, teaching and publications in the field of Ophthalmology.

Dr. Reena Sethi was awarded the prestigious ISRS Gold Medal, in recognition of her contribution to her teaching advanced techniques in Phaco and active particiption in Community Ophthalmology.

Cornea

Therapeutic Keratoplasty



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Corneal ulcers are the major cause of unilateral blindness especially in developing countries. Management of corneal ulcers is primarily medical and based on microbiological reports of corneal scrapings. However, not all cases respond to medical therapy. In cases refractory to medical management and perforated corneal ulcers, the main management is surgical.

Therapeutic Keratoplasty is a term used for the procedure which is used either to remove an infection or inflammatory process in cornea or to give tectonic support to the eye.

Indications of therapeutic Keratoplasty

Primary indications for Therapeutic Keratoplasty are:

- Non resolving microbial keratitis after maximum medical therapy,
- Perforated corneal ulcers
- Descemetocele formation,
- Scleral involvement adjacent to limbus

It is also done in patients in whom the microbiology has not revealed any organism and patient is not responding to the broad spectrum antibiotics.

Preoperative evaluation

A detailed pre operative evaluation is done to rule out any adnexal diseases (lid margin diseases). Size of the epithelial defect, infiltrate and its relation to limbus should be carefully documented. Extent of thinning or perforation, if any, should be documented. Status of lens (phakic, pseudophakic, aphakic) should be noted. Fundus, if visible, should be evaluated or a B Scan should be ordered to rule out any posterior segment involvement. Intraocular pressure should be evaluated and a preoperative intravenous mannitol 5ml/kg body weight should be given preferably in all cases unless it is contraindicated for medical reasons.

The general systemic condition of the patient should also be evaluated.

Donor cornea

Donor cornea selection is very crucial for favourable outcome of the procedure and also to prevent iatrogenic spread of infections. The donor blood sample should be investigated for HIV and HBs Ag. Cause of death of the donor and any associated sepsis should be noted. The donor cornea should be evaluated thoroughly, noting specifically, the size of the epithelial defects, stromal edema, infiltrates, scars, stress lines, if any. Specular microscopy should be done on all tissues. Preferably, good-quality donor tissue should be used in cases of therapeutic keratoplasty. Postoperatively, the healthy donor endothelium maintains a clear graft despite the associated inflammation and elevated intraocular pressure. Use of healthy donor tissue with an intact epithelium also minimizes the risk of graft re-infection. Our criteria for donor tissue quality are not as stringent as for optical keratoplasty. This situation is due to paucity of good-quality donor tissue in developing countries such as ours, as well as the emergency situation under which this surgery is often performed. Donor cornea with fair quality may be used in case of emergency, to attain tectonic stability. After the integrity of the globe is preserved and ocular inflammation has subsided, a smallerdiameter optical keratoplasty may be performed later for visual rehabilitation.

Anaesthesia

In small grafts up to 10 mm diameter, local anaesthesia can be given if the patient cooperates. Careful peribulbar block with a mixture of 1% lidocaine and 0.50% Bupivacaine is



Figure 1: Steps of therapeutic keratoplasty

(a): Assessing the size of reciepient bed with callipers, (b): Side port preparation, (c): Partial trephination of the recipient bed,
 (d): Excision of diseased cornea with corneal scissors, (e): Gently peeling the exudates from the iris surface, (f): Peripheral iridotomies (2 or 3 are made), (g): Placing the donor button, (b): First four cardinal sutures, (i): After 16 sutures

given to achieve akinesia and analgesia. Good preoperative hypotony is desirable, however use of excessive massage and application of pinky ball should be avoided in cases where there is a suspected thinning or perforation.

In perforated corneal ulcers and in cases with extreme thinning it is advisable to apply tissue adhesive before proceeding with the block to avoid any expulsion of intraocular contents during anaesthesia.

General anaesthesia is preferred in cases where there is pre-existing corneal perforation or when the surgical time may be prolonged, as in large grafts, and in young children or very old frail elderly patients who might not cooperate with local anaesthesia.

Surgical procedure: The surgical procedure includes the following steps¹. (Figure 1)

Exposure: Self retaining speculum is used to get adequate exposure of the eye. In cases of excessive thinning of cornea or frank perforation, the placement of the speculum should be gentle so as to avoid expulsion of contents of the eye.

Extent of the ulceration should be clearly delineated and a careful peritomy is done to rule out any scleral involvement when suspected.

Fleringa ring (18 to 20mm) is used to avoid any possible distortion or collapse of the globe during surgery. It is useful especially in aphakia, in eyes with high myopia, pediatric age groups and situations where anterior vitrectomy may be needed during the surgical procedure. The ring is sutured to the episclera with 6-0 silk taking care to provide equal traction in all the four quadrants

Recipient bed preparation: The primary goal of therapeutic keratoplasty is to excise all the infected tissue. The size of



Figure 2: Eccentric Grafts [(a): Fungal infection of phacoemulsification tunnel incision, (b): Patch graft, (c): advanced Mooren's Ulcer, (d): Crescentric graft)

the recipient bed should be measured with callipers. It is essential to remove all the infected tissue with a 1mm of healthy rim all around. Simple disposable hand held trephines are used most often for this purpose. To check the appropriateness of the recipient bed the trephine is placed over the cornea and the epithelium is indented and globe is examined in all directions to look for the clear margins in all directions.

- **Perforated corneas:** Recipient bed preparation is aided by the use of tissue adhesive, cyanoacrylate glue, to seal the perforation. The pressure applied should be minimal so as to avoid any expulsion of intraocular contents. In such cases suction trephines like Hessberg Baron trephines are useful.
- **Eccentric grafts:** Peripheral or eccentric grafts in the form of patch graft, banana shaped graft or crescent grafts may be needed in cases where the pathology involves the peripheral cornea such as corneoscleral tunnel infection, extreme cases of peripheral ulcerative keratitis. These could be done with small sized trephines or could be shaped with free hand dissection. (Figure 2)

Corneal scraping may be repeated on table preoperatively. It is very important especially in those cases where the etiological diagnosis could not be made earlier, as it will aid in the postoperative management

Entry into anterior chamber: It is achieved using a MVR blade. Entry should be very gentle in cases of perforated corneas. Side portentry is also used to sweep the incarcerated iris from the site of perforation with a cyclodialysis spatula.

The recipient bed is trephined up to 80% depth with the trephine and anterior chamber entry is made with the help of 11 number surgical blade or MVR blade. The recipient bed is then excised using Castroviejo's right and left corneal scissors. Left over posterior ledge may be trimmed with vannas scissors, however, leaving a larger posterior ledge may be useful in large grafts to prevent wound leak.

In cases of presence of vitreous in the site of perforation, proper anterior vitrectomy should be done to avoid any postoperative vitreous in anterior chamber.

The excised corneal specimen should be divided into two parts and sent for microbiological and histopathological examination. **Clearing the anterior chamber of exudates:** Irrigation of the anterior chamber is done to remove exudative material from the eye. Membranes over the iris should be carefully peeled off. Intracameral antibiotics or antifungals may be used if needed.

Two or three large peripheral iridotomies are done to avoid postoperative pupillary block. Trauma to the lens should be avoided as much as possible. Careful vitrectomy should be done if any vitreous loss is suspected. Vitreous tap with intravitreal antibiotics injection is done in cases of suspected endophthalmitis.

Donor cornea preparation: The donor cornea preparation in therapeutic keratoplasty is done after the preparation of the recipient bed to achieve the correct size of the graft. The size of the graft is taken generally 0.5 mm more than the recipient to improve cooptation and decrease the risk of glaucoma. In larger graft, it may be up to 1mm more than the host bed.

The donor tissue is placed on the Teflon block and centred under the microscope and is punched using a corneal punch. In cases of sclerokeratoplasty and large grafts occasionally free hand cutting of the tissue may be required.

Suturing of donor cornea to the host tissue: Suturing techniques in inflamed, infected eyes should always be interrupted. Full thickness sutures should be avoided to prevent entry of infection into the anterior chamber. The sutures should be taken approximately at 75% depth. Longer bites should be taken to achieve proper wound closure. The sutures should be in moderate tension so as to avoid cheese wiring of the tissue. Interrupted sutures also allow early suture removal in case of excessive sectoral inflammation, vascularisation or suture infiltration. In case of small grafts, 16 sutures are taken and in large grafts, 24 sutures are taken.

Additional procedures: Vitreous biopsy is taken and intravitreal antibiotics (Vancomycin 1mg/0.1 ml, Ceftazidime 2.5 mg/0.1 ml) are given in cases of suspected endophthalmitis.

Predisposing conditions like lid abnormalities, dry eyes should be addressed and if required tarsorrhaphy can be performed after keratoplasty.

Post operative management: The most important points to look for on the first postoperative day are signs of any residual infection, evidence of any wound leak, thickness of the graft, status of the corneal epithelium, depth of the anterior chamber, intraocular pressure, degree of inflammation, presence of synechiae and pupillary block.

Complications of therapeutic Keratoplasty^{2,3}**:** Retro bulbar haemorrhage, globe perforation may occur during anaesthesia. Scleral perforation may occur while suturing the fleringa ring. Incomplete or eccentric trephination

can occur. Damage to the iris can occur specially while trephining the perforated cornea. Supra choroidal haemorrhage and expulsive haemorrhage are the most devastating complications which can occur if there is increased vitreous pressure after removing the recipient cornea.

Early postoperative complications: Wound leak, endophthalmitis, infectious keratitis (residual or new infection), suture related complications (suture infiltrate, loose suture etc), filamentary keratitis, iritis, anterior synechiae formation and glaucoma are the common complications noted in early postoperative period.

Late postoperative complications include cataract, glaucoma, graft failure secondary to rejection, infection, endothelial decompensation, and graft ectasia and phthisis bulbi.

Postoperative management of therapeutic Keratoplasty: The postoperative management of a therapeutic Keratoplasty is as challenging as the surgery itself. Basic principles¹ in guiding the management are:

- Eradicate all remnants of infection and prevent reinfection: Therapeutic Keratoplasty often provides surgical excision of all the infection but in cases where there is a reasonable doubt, the antimicrobials should be continued till the epithelium heals. Duration of treatment depends on severity of infectious organism. In general, fungal and acanthamoeba infections require very long postoperative treatment.
- Promote reepithelialization of cornea and wound healing: Prolonged over treatment of cornea with fortified medications, antimicrobials should be avoided when treating for any epitheliopathy. In such situations non preserved drugs are useful.
- Control inflammation with corticosteroids: Concomitant use of steroids along with antibiotics is justified in cases of bacterial keratitis. In herpetic keratitis, steroids can be given without risk as long as patient is managed with topical or oral antiviral therapy. There is a controversy as to timing of steroids in acanthamoeba and fungal corneal ulcers. We, at our institute, wait for 2 weeks before starting steroids in fungal keratitis. When there is even a faint doubt regarding the presence of any residual infection steroids should be with held.
- Management of intraocular pressure: Raised intraocular pressure is an important complication postoperatively because of associated inflammation (iritis, trabeculitis, anterior synechiae) and should be managed aggressively with intravenous mannitol and / or oral acetazolamide.

Corneal debulking procedures: In this initially lamellar dissection is done at the level of posterior stroma using lamellar dissectors such as cresent knife. It is useful in cases of perforated corneal ulcers where iris is adhered to cornea. After the initial lamellar separation anterior chamber is entered and the remaining part of the cornea is removed. This technique described by Vajpayee et al is useful to protect the iris⁴.

Lamellar keratoplasty for corneal ulcers: This technique is advised when the ulcers are not too deep and has been shown to be useful in some acanthamoeba and fungal ulcers. However care must be taken in case selection.

Post operative regimen

Bacterial keratitis

- Antibiotic with most sensitivity given hourly and topically
- Combination therapy or a broad spectrum antibiotic is used when antibiotic sensitivity is unknown
- Topical corticosteroids—every 1–2 hours initially if sensitivity of antibacterial is known
- Cycloplegics
- Antiglaucoma medication, if intraocular pressure is elevated

Fungal keratitis

- Topical antifungals—every hour initially
- Systemic antifungals—oral Ketoconazole 200 mg two times daily initially
- Topical nonsteroidal anti-inflammatory drugs initially
- Corticosteroids—started after 2 weeks once possibility of reinfection and residual infection is ruled out
- Cycloplegics

Acanthamoeba keratitis

- Topical amoebicidal drugs—every 1–2 hours
- Topical corticosteroids given judiciously
- Cycloplegics

No organism in corneal scraping

Based on microbiologic and histopathology report of Corneal button, an appropriate antimicrobial may be used

Visual prognosis after therapeutic Keratoplasty: The final visual prognosis for therapeutic keratoplasty depends on the infecting organism and its susceptibility to treatment. Bacterial keratitis generally has a better visual prognosis than fungal and acanthamoeba keratitis⁵.

The severity of inflammation at the time of surgery also holds an impact on graft survival.

Size of the graft also has an impact on graft survival; grafts more than 9.5 mm in diameter have a significantly decreased chance of graft survival.

Therapeutic keratoplasty is generally an emergency and a high-risk procedure that challenges the surgical and medical skills of the corneal surgeon. It requires meticulous attention to detail and careful postoperative monitoring. Therapeutic keratoplasty play a definitive role in the treatment of microbial keratitis refractory to medical therapy. Advances in microsurgical technique and antimicrobial therapy, with the availability of new and more effective antibiotics, and better control of inflammation have resulted in an improved prognosis for therapeutic keratoplasty, in turn, leading to improved visual outcomes.

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Approach to a Case of Infectious Keratitis



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nfectious keratitis is one of the leading causes of blindness in the world. As in most cases, prompt and proper diagnosis with appropriate therapy can lead to good functional outcomes. It is imperative for every ophthalmologist to be aware how to approach and manage a case of corneal ulcer. Though there are many non infectious causes for keratitis, this article would focus exclusively on the work up and management of various causes of infectious keratitis.

Work up of a case of corneal ulcer

A good history taking and thorough clinical examination is the first and foremost important step in a case of corneal ulcer (Table 1). Details must be ascertained with regard to the mode of onset, inciting event, laterality, duration and nature of symptoms. Trauma with vegetative matter, use of topical steroids purchased over the counter for redness of eyes, long duration of symptoms points towards a likely diagnosis of fungal keratitis. History of any long standing systemic illness like stroke, road traffic accident (RTA) which could predispose the patient to corneal exposure with secondary infection should be ascertained. A detailed treatment history with the type of medications used and their frequency needs to be noted. Also important is to check whether the patient had been compliant to the prescribed treatment.

Clinical examination

Much of the diagnosis of a case of corneal ulcer is dependent on a very good and methodical clinical examination (Table 2). Visual acuity (with projection of rays) is crucial as it helps to prognosticate a case. Next ocular adnexa needs to be examined for the presence of any lid margin abnormalities like entropion / ectropion / trichiasis / lagophthalmos. Chronic dacryocystitis should be ruled out by looking for any regurgitation form the lacrimal sac. On slit lamp biomicroscopy, the size and location of epithelial defect, infiltrates, corneal thinning, descemetocele, perforation needs to be noted. It is imperative to draw a good topography of clinical findings (wherever the facility of clinical photography is not available) for record. The presence of superficial and deep vascularisation with the

Table 1 Clinical History and the markers for diagnosis							
History of Pointer							
Trauma with vegetative matter	Fungal keratitis						
Contact lens use	Acanthamoeba, pseudomonas, fungal, Bacterial keratitis						
RTA/stroke/Patient on ventilator	Keratitis secondary to corneal exposure						
Diabetes, HIV, systemic malignancies	Generalised immunosuppression						
Severe Malnutrition with Acute gastro enteritis (AGE)/ pneumonia in 0 -5 yrs age	Keratomalacia sequelae						
Alcoholic liver disease	Klebsiella						
Recurrent episodes of redness, pain	Viral keratitis						
Cataract surgery	Tunnel infection with commensals, fungi						
Keratoplasty surgery	Staphylococcus epidermidis and other commensals						
LASIK	Atypical mycobacteria, Nocardia, Fungi, Staphylococcal species						



Figure 1: Flow chart for guideline to management of a case of corneal ulcer

Table 2 Clinical examination	
Eyeball and orbit	Proptosis
Eyelids	Entropion Ectropion Trichiasis Distichiasis
Lacrimal sac	Chronic dacryocystitis
Cornea	Epithelial defect Infiltrates Corneal thinning (Central / peripheral) Descemetocele Perforation (with iris prolapse) Corneal edema Corneal opacity Neovascularisation (superficial/ deep)
Anterior chamber	Depth Hypopyon Cells/ flare
Lens	Clear /cataractous
Sclera	Abscess / thinning
Fundus	Endophthalmitis Choroidal detachment Retinal detachment Chorioretinal thickening

location (quadrant) and extent needs to be noted. Anterior chamber examination is done to look for any hypopyon, cells, flare, hyphaema. Intraocular pressure should be ascertained digitally and fundus examination should be done wherever the media clarity permits.

Investigations

Corneal scraping of infiltrates is one of the most important investigations in the work up of a case of corneal ulcer.

Table 3 Specific clinical feat	ures of the different types of keratitis
Disease	Specific clinical feature
Bacterial Keratitis	Well defined infiltrate with moderate inflammation in anterior chamber
Fungal Keratitis	Dry looking ulcer with feathery margins, satellite lesions, ring ulcer, endothelial plaque, pigmentation in dematiatious keratitis
Acanthamoeba Keratitis	Epithelial haze with pseudodendrites, radial perineuritis, ring ulcer
Microsporidiosis	Multifocal punctate raised epithelial lesions with clear underlying stroma
Pseudomonas Keratitis	Rapidly sloughing ulcer, ring ulcer, with evident corneal edema in the uninvolved cornea, rapid melting with perforation of cornea
Viral Keratitis	Dendrites, geographic ulcer, annular stromal edema with KPs

Scraping can be done using a no. 15 blade on B P handle / Kimura spatula from the margins and the base of the ulcer after clearing the eye of discharge or slough. The material collected is used to prepare smears for gram stain and KOH and for bacterial and fungal culture and sensitivity. Direct plating on blood agar is preferred due to the better yield of the organism.

Ultrasound of the posterior segment will have to be done to rule out any endophthalmitis / retinal or choroidal detachment. Orbital ultrasound is done in presence of orbital cellulitis to rule out any pus pocket. Confocal scan can be done to prove the presence of fungal hyphae and acanthamoeba cysts.

Treatment of corneal ulcer

Patients with corneal ulcer are many times treated with a cocktail therapy of antibacterial, antivirals and antifungal (Figure 1). Such a practice should not be done as it exposes the patient to unnecessary toxicity of medications along with the emergence of resistance to the medication. Specific treatment should be given depending on the clinical findings aided with the microbiological diagnosis. (Table 3) This also improves the patient compliance.

Bacterial corneal ulcer

Patient with corneal ulcer is started on empirical therapy using fortified cefazolin 5% and tobramycin 1.3% eye drops. Cefazolin covers the gram positive organism while the tobramycin gives gram negative coverage. Patients with suspected pseudomonas keratitis must be started empirically on ciprofloxacin as this organism is found to be resistant to the other conventionally used antibacterial



Figure 2: Ring ulcer caused by fusarium infection



Figure 3: Fungal keratitis: feathery margins of infiltrate, endothelial plaque

agents. Intensive therapy is given in the early phases of infection – every half hourly round the clock for the first 48 hours, followed by the same frequency in waking hours. Then the medications are tapered to 1 hourly and 2 hourly every 3 days. A cycloplegic like homatropine or atropine is prescribed TDS to QID. Oral antibiotic is prescribed in the cases with perforated corneal ulcer, limbal / scleral involvement and endophthalmitis. Intravitreal injections of vancomycin (1 mg/0.1 ml) and Ceftazidime (2.25 mg/ 0.1ml) are given in the presence of endophthalmitis It is important to look for the clinical signs of improvement while continuing with the above medications. There will be decrease in the symptoms along with decrease in the size of the epithelial defect and infiltrates, decrease in density of infiltrates, and development of neovascularisation towards

the ulcer suggesting clinical response to the treatment given.

Fungal corneal ulcer

It is common in the developing nations with hot humid climate. They are also the most difficult infections to treat in view of poor penetration of anti fungal agents. The symptoms and signs for a fungal corneal ulcer are quite characteristic. Most commonly, the infection occurs following trauma with vegetative matter or indiscriminate use of topical steroids over the counter. Candida infection is common in diabetics and patients with systemic immunosuppression. The diagnosis of a fungal ulcer is predominantly based on the clinical findings. On slit lamp examination, appearance of a dry looking ulcer with feathery margins, presence

Table 4 Herpetic Eye Disease Study (HEDS)		
Study Group	Intervention	Recommendation
HEDS - 1		
Stromal keratitis not on steroids; onTFT	Topical prednisolone phosphate	Faster resolution and fewer treatment failures
Stromal keratitis on steroids and TFT	Oral acyclovir 400 mg 5 times a day	No added benefit
HSV iridocyclitis on steroids	Oral acyclovir 400 mg 5times a day	Fewer patients recruited but potential benefits noted
HEDS - 2		
HSV epithelial keratitis trial	Oral acyclovir 400 mg 5 times a day for 3 wks	No benefit in preventing subsequent stromal keratitis / iridocyclitis
Acyclovir prevention trial	Oral acyclovir 400 mg BD	Reduced the risk of any form of ocular herpes by 41% and stromal keratitis by 50%
Ocular HSV recurrence study	Studied the association between psychological and other forms of stress with HSV recurrence	No association noted

of a ring ulcer, satellite lesions, endothelial plaque are all quite characteristic of fungal keratitis (Figures 2 &3). In corneal scraping, the presence of fungal hyphae on smear (grams / KOH wet mount) or growth in saborauds dextrose agar medium is confirmatory. Natamycin (5%) is the drug of choice for filamentary keratitis. In the Mycotic ulcer treatment trial (MUTT), it is shown to be superior to voriconazole in smear proven filamentous fungal keratitis. Topical Amphotericin B (0.15%) is the drug of choice for proven yeast infection. All the topical antifungals must be used hourly till complete epithelisation and then tapered to four times a day for the next three weeks. Systemic therapy is indicated in large and severe ulcers (involving more than two thirds of stromal depth), hypopyon, limbal / scleral involvement, corneal perforation, endophthalmitis. Among the systemic antifungals, oral ketoconazole (200 mg BD) is the drug of choice. Systemic voriconazole is used in patients refractory to ketoconazole therapy and there are not many studies comparing the efficacy of these two antifungal agents. Care must be taken to monitor the liver function parameters during ketoconazole therapy.

Viral keratitis

HSV – 1 and 2, HZV, CMV can cause keratitis. Of these, infections caused by HSV – 1 are the most common. The major burden of this infection is due to recurrence of the disease. The manifestation can be epithelial, stromal/ endothelial keratitis, necrotising stromal keratitis each with typical clinical presentation (Figure 4). The treatment guidelines given by HEDS form the standard of care for these patients and is given in Table 4.



Figure 4: Dendritic ulcer in graft

Acanthamoeba keratitis

Acanthamoeba is a free living protozoon found in air, water and soil. It exists in trophozoite (50 micron) and cystic form (15 – 30 microns). The highly specific corneal findings include ring infiltrates and radial perineuritis. The diagnostic modalitites involve the identification of acanthamoeba DNA by PCR (90 % sensitivity, 100% specificity), corneal smear by Giemsa stain (31% positivity), culturing of the organism on non – nutrient agar with E Coli overlay (57% positivity), identification of cyst on confocal scan (63 - 90% positivity)¹. The diamidines (propamidine isethionate 0.1%, hexamidine 0.1%) and the biguanides (PHMB 0.02%,



Figure 5: Post LASIK fungal infection with sloughing of flap from edges



Figure 6: Flowchart for management of a case of infectious keratitis following LASIK

Chlorhexidine) are the most effective cysticidal antiameobic agents. Of these two the biguanides have the least corneal toxicity and the most effective cysticidal activity. Treatment is usually started using combination of these two agents hourly and then tapered after 5 days to prevent the drug related epithelial toxicity. Oral itraconazole is added in cases with severe disease. Topical antibiotics are also given and oral antibiotic in preperforating injuries. Oral NSAID is used to reduce inflammation and corticosteroids are adde d only after 2 weeks of intensive biocidal agent. In one study by Bouheraoua et al², the indications for surgical treatment in proven cases of acanthamoeba keratitis were the following:

Table 5

Risk factors for graft infection

- 1. Donor related problems
- 2. Host related problems
 - i) Ocular surface disorder
 - ii) Recurrence of previous infection
 - iii) Topical medications (steroids)
 - iv) Use of contact lenses
 - v) Systemic diseases
 - vi) Socioeconomic status
- 3. Graft related problems
 - i) Loose suture
 - ii) Persistent epithelial defect
 - iii) Decompensated graft
 - iv) Wound leak / late dehiscence
 - v) Recent rejection episode
- Late presentation > 30 days after the onset of symptoms
- Initial visual acuity of $\leq 20/200$
- Large infiltrate > 3mm
- Pre perforating keratitis
- Presence of corneal neovascularisation

Post lasik keratitis

Microbial keratitis following LASIK has become an increasingly recognized sight threatening complication of refractive surgery (Figure 5). The reported incidence varies from 1: 1000 to 1: 5000 of which majority of them present within the first week of LASIK surgery³. A high degree of suspicion with rapid diagnosis and appropriate therapy can result in eradication of infection and visual recovery. Any focal infiltrate following LASIK should be considered infectious and it should be differentiated from Diffuse lamellar keratitis (DLK) - the other non infectious entity presenting in the same time period. Unlike DLK, the inflammation associated with LASIK associated infectious keratitis persists and sometimes worsens with the use of topical steroids. The appearance of an interface inflammation more than 1 week after LASIK should be presumed to be of an infectious etiology until proven otherwise. The management guidelines recommended by ASCRS for post LASIK infection is illustrated in Figure 6. All measures must be taken to prevent this devastating complication in patients undergoing refractive surgery.



Figure 7: Post keratoplasty PED leading to graft infection

Post surgical keratitis

Infectious keratitis has also been reported to occur after cataract surgery, pterygium surgery, keratoplasty, collagen crosslinking in keratoconus patients and posterior segment surgeries. The occurrence of keratitis following cataract surgery is usually localized to the tunnel attributed to the improperly constructed wound. Tunnel abscess caused by fungi is typically resistant to treatment.

The incidence of infectious keratitis after keratoplasty varies from 1 - 7.5% in developed nations to 12% in developing countries and most of these infections occur within the first year of surgery. Three common sources of infection are contamination of the donor tissue, incomplete excision of infected recipient tissue and infection from organisms acquired from the environment. The risk factors for graft infection has been listed in Table 5, of which the most common cause is the persistent epithelial defect (PED). Graft infection related to loose suture lead to smaller peripheral keratitis whereas PED leading to secondary infection produce much larger central and paracentral ulcers (Figure 7). The occurrence of herpetic keratitis after PK may present as classic dendritic ulcer or as non healing large epithelial defects. Many times, it becomes difficult to distinguish between graft rejection and herpetic keratouveitis, however presence of typical endothelial pigment line of Khodadoust and differential stromal edema points towards graft rejection. The most common organisms isolated are the coagulase negative Staphylococcal species and Staphylococcus aureus. In a study by Vajpayee et al⁴, 74% of the eyes that developed graft infection responded to medical therapy. Various studies have reported that long term prophylactic antibiotics are not useful in the prevention of graft infection because the infections that ultimately occur usually involve bacterial strains resistant to them.

The overall visual outcome in eyes with graft infection is very poor even after appropriate medical / surgical therapy. Vajpayee et al studied the impact of presence or absence of sutures in cases of graft infection and found that though both groups shared the similar indications and risk factors, infection with indolent micro organisms were more common in the grafts without suture

Infections after corneal collagen crosslinking (CXL) for keratoconus has been reported. The various causative organisms reported include Pseudomonas aeruginosa, E.coli, S. aureus, Acanthamoeba and HSV. The likely factors predisposing these patients to infection include breakdown of epithelial barrier, use of topical steroids, use of contact lens and the possible role of apoptosis.

Surgical management

The indications for surgery in a case of corneal ulcer includes the presence of severe thinning, descemetocele, perforated corneal ulcer, sloughing corneal ulcer and ulcers not responding to medical management. The surgical options available are

- *Tissue adhesives:* in perforations < 3mm, using cyanoacrylate glue
- *Tenon's patch graft:* for peripheral ulcers, inexpensive, seals the defect by the fibroblastic response of the tenon tissue
- Multilayered amniotic membrane graft (AMG): in cases of severe thinning
- Tectonic Patch graft: in perforations 3 5mm in size
- Therapeutic penetrating keratoplasty: in perforations > 5mm / large corneal ulcers

- Therapeutic DALK (viscoelastic assisted): in descemtoceles where the infection is not involving the deeper layers nor the anterior chamber.
- *Conjunctival flap:* to stabilize the ocular surface, does not provide any tectonic support.

Therapeutic keratoplasty

- It is worthwhile to consider the following points while doing a therapeutic keratoplasty
 - Complete excision of the diseased tissue with atleast 1 mm of healthy cornea all around
 - Thorough AC wash to remove all the exudates from the angle
 - Use of intracameral vancomycin / amphotericin B
 - Oversizing the graft by atleast 1 mm for adequate angle formation
 - Surgical PI to prevent pupillary block from membranes owing to the anticipated excessive postoperative inflammation
 - In proven cases of fungal keratitis: to withhold topical steroids for atleast 2 weeks in the postop

and to continue topical (6 - 8 wks) and systemic (4 wks) antifungal therapy

Recent advances

- 1. Ganciclovir gel for HSV keratitis
- 2. *CXL in infectious keratitis*⁵ mechanism by which it is found to be clinically useful is first by oxidative damage to the pathogens by non specific means and also that cross linked cornea become more resistant to the degradative enzymes of the organisms.

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Diagnostics





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E arly and reliable diagnoses in ophthalmology usually depend on the recognition of minute changes in normal structures. The demands of modern ophthalmology have evolved from descriptive findings from the slit lamp to in vivo assessment of cellular level changes.

Confocal microscopy is a bioimaging technique which allows non invasive in vivo analysis of corneal microstructure and function. The confocal microscope was first described by Goldmann in 1940¹ and later published as a patent by Minsky in 1957². It creates sharp images of a specimen that would otherwise appear blurred when viewed with a conventional microscope. This is achieved by excluding most of light from the specimen that is not from microscope's focal plane. It has been used to investigate numerous corneal diseases: epithelial changes, stromal degenerative or dystrophic diseases, endothelial pathologies, corneal deposits, infections and traumatic lesions.

Principle

When examining the cornea using light biomicroscopy, the resolution is decreased by interference of light reflected





from structures above and below the plane of examination. For instance, when examining a corneal lesion located at a certain stromal depth using a slit-lamp, light reflection from the stroma proximal and distal to the lesion, the epithelium, the tear film, and the endothelium is also perceived by the examiner.

The confocal microscope incorporates the idea of point by point illumination of the specimen and rejection of out of focus light. To understand it, consider a pair of lenses that focuses light from the focal point of one lens to the focal point of the other. All light from the focal point that reaches the screen is allowed to go through. Light away from the focal point is mostly rejected (Figure 1). In confocal microscopy, the aim is to see only the image of the focused point. At a time only one point is in focus; thus, complete image of cornea is never obtained in single view.

Current confocal microscopes use a point light source that scans the cornea and a point detector to further increase the resolution. The point light source and the detector use conjugate pinholes that work in tandem. As a result, the optical resolution is increased and it is possible to optically section the cornea at the cellular level. White light or a focused laser beam may be used as the light source. In clinical use, white light is preferred, because of the risk of damaging living tissue with laser beams.

Types

The three most common confocal microscopes in practice today are: 1) the Tandem Scanning Confocal microscope [TSCM] (Tandem Scanning, Reston, Virginia, USA), which is no longer commercially available, 2) the ConfoScan 4 slitscanning confocal microscope [SSCM] (Nidek Technologies, Greensboro, North Carolina, USA) and its similar earlier versions, and 3) the Heidelberg Retina Tomograph Rostock



Figure 2

Corneal Module laser scanning confocal microscope (HRT or HRT3; Heidelberg Engineering; GmbH, Heidelberg, Germany).

Tandem scanning-based confocal microscopy

A real-time tandem scanning CM was developed by Petran and Hadravsky. The basic part of the system was contributed by Nipkow. A modified Nipkow disk contains thousands of optically conjugate (source/detector) pinholes arranged in Archimedean spirals. Light from a broadband source passes through the pinholes on one side of the disk, and is focused onto the specimen. Detector pinholes on the opposite side of the disk prevent light from outside the optical volume from reaching a camera or eyepiece. Rotation of the disk results in even scanning of the tissue in real time. So, the illumination and detection of light through conjugate pinholes occurs in tandem. This confocal design provides excellent lateral and axial resolution³.

The small pinhole diameters of the TSCM significantly limit light transmission (range, 0.5% to 1%)⁴, which produces images with relatively poor contrast compared to those of confocal microscopes with larger apertures. Limited field brightness and contrast makes visualization of small structures (<5 μ m diameter) difficult. Also, although the illumination is inefficient, it appears very bright to the patient and patient discomfort can limit examination times. The TSCM system is no longer commercially available.

Slit-Scanning Confocal Microscope

SSCMs, such as the ConfoScan 4 (Nidek Technologies; Figure 2), use vertical-slit apertures for illumination and observation of the field. A rapidly oscillating two-sided mirror scans the confocal image of the illumination and observation slits across the field. The wide slit aperture (300 μ m for ConfoScan 4) allows increased light throughput, which improves field brightness and contrast

when compared to the TSCM. As a result, structures appear brighter, sharper, and with more detailed. Increased light throughout also means that illumination need not be as bright as that of the Tandem Scanning microscope, and this lower intensity improves patient comfort and extends examination time. The increased field brightness and contrast provided by SSCMs is accomplished in part at the expense of an increased depth of field. The depth of field of the ConfoScan 3 and ConfoScan 4 is approximately 26 μ m⁵.

Laser Scanning Confocal Microscope

The laser scanning confocal microscope (LSCM), such as the HRT or HRT3, incorporates the laser scanning optics of the Heidelberg Retina Tomograph with the Rostock Cornea Module for imaging the cornea. High-contrast, high-quality images of the cornea are produced by using laser light at a wavelength of 670 nm. Lateral resolution and depth of field as reported by the manufacturer are 1 μ m and 4 μ m.

Confocal Microscopic Examination of Normal Corneal Anatomy

The images obtained in confocal microscopy generally consist of 10- to 20- μ m optical sections that are oriented parallel to the surface of the microscope objective (i.e., to the surface of the cornea). The confocal microscope provides images of all layers of the cornea: superficial corneal epithelium, basal epithelium, Bowman's membrane, subepithelial nerve plexus, stromal keratocytes, deep nerves, Descemet's membrane, and, finally, the corneal endothelium⁶⁻⁸.

Epithelium: Superficial cells (Figure 3a) are characterized by a polygonal cell pattern, bright illuminated cytoplasm, reflecting nucleus and perinuclear dark halo. Cell size is up to 50 μ m in diameter and about 5 μ m thick with individual variations. The cells of the epithelial intermediate layer, or wing cells (Figure 3b,c), form a regular mosaic with sharp and reflecting cellular borders. The wing cells are smaller in size (about 20 μ m) but regular in form⁹. Basal epithelial cells (Figure 3d) have a smaller diameter (8–10 μ m) and appear as a layer of cylindrical cells where nuclei cannot be remarked by a reflecting border. The ratio between superficial, intermediate and basal cells (accordingly to the cell density) is approximately1:5:10¹⁰

Sub-basal nerve plexus (SNP) (Figure 3e) is characterized by the presence of hyper-reflective fibres of $4-8 \ \mu m$ length¹¹⁻¹², connected with anastomoses and organized in a vortex pattern in the lower nasal quadrant of the paracentral cornea.

Bowman's layer (Figure 3f) is an 8–10 μ m thick zone consisting of randomly arranged collagen fibrils located in between the basal cells and the stroma. Moreover, in vivo CM shows polymorphic structures composed of fibrillar materials (K-structures) beneath the Bowman's



Figure 3: In vivo confocal images of the normal cornea. (*a*) Superficial cells. (*b*) Upper wing cells. (*c*) Low wing cells. (*d*) Basal cells. (*e*) Sub-basal nerve plexus. [*Courtesy:* Rudolf F Gutboff et al. Clinical and Experimental Ophthalmology 2009; 37: 100–117]



Figure 3: (f) Bowmane's membrane. (g) Anterior stroma. (b) Posterior stroma. (i) Endothelium [Courtesy: Rudolf F Gutboff et al. Clinical and Experimental Ophthalmology 2009; 37: 100–117]

layer in normal human subjects. It was presumed that these microstructures (5–15 μ m in diameter) may be responsible for the formation of the anterior corneal mosaic¹³.

Stroma (Figure 3g,h) forms around 80–90% of the whole corneal volume. It consists of three main histological components: cellular, acellular and neurosensory. The

keratocyte nuclei are visible as egg-shaped reflecting light corpuscles, whereas the connective lamellae appear black (that is transparent) because of their optical properties. Patel et al. presented a review of 18 studies of keratocyte density in normal corneas¹⁴. Taken together, keratocyte density is highest in the anterior stroma, clearly declines toward the central stroma, and increases again slightly in the posterior. The density of keratocytes decreases with age¹⁵. The stromal nerve fibres, which are thicker than the subepithelial ones, run along the stromal tissue along a straight pathway, although it is sometimes possible to find dichotomous branches (T and Y shapes).

Descemets membrane is a thin $(6-10 \ \mu\text{m})$ homogeneous layer, located in between the posterior stroma and endothelium, and is not visible with CLSM.

Endothelium (Figure 3i) is a monolayer of cells arranged in a hexagonal pattern of honeycomb regular mosaic, where the cells are normally identical in size and shape. Sometimes it is possible to visualize the nucleus of the cells. The total number of cells is about 500 000 in a healthy subject with a normal cell density of 2500–3000 cell/ mm^{2 9,10}. The cell density decreases with age¹⁶.

Light scattering phenomenon determines the reflectivity of cells. The main factors influencing the interaction of light beam and its transmission and absorption are cellular organelles and membranes, microvilli, microplicae and glycocalyx¹⁷. It was postulated that the presence of microdesmosomes in the epithelial layers could explain why the cell membranes of epithelial cells were more brightly illuminated (Figure 3a,d) than those of the endothelial cells (Figure 3i).

Pathological cornea

Cell types

Leucocytes present as hyper-reflective oval-round cell bodies, located at the level of the wing or basal sells or SNP.

Erythrocytes are non-nucleated, biconcave discs averaging 7 μ m in diameter. The presence of hyper-reflective reflex in the middle of the disk is a typical sign and underlines the biconcave cell morphology⁹.

Dendritic cells or Langerhans cells (LCs) are a critical factor in antigen presentation in the cornea and conjunctiva¹⁸. LCs present as either large cells with long processes or smaller cells lacking cell dendrites, supposedly indicating mature and immature phenotypes, respectively.

Corneal Diseases

Infectious Keratitis

The confocal microscope is capable of providing corneal epithelial, intrastromal, and endothelial cellular detail. This detail makes it possible for the investigator to observe



Figure 4: Typical hyper-reflective Acanthamoeba cysts up to 20 µm diameter.

microorganisms in vivo without the use of stains, dyes, or tissue fixation.

Acanthamoeba represents a ubiquitous protozoan organism. Early detection of the organism in its trophozoite or cystic form is helpful, because early initiation of treatment for amoebic keratitis yields a better prognosis. The confocal microscope may provide the best diagnostic means to detect the organism early and to evaluate the effectiveness of treatment. Primarily the cystic form of the organism is documented, which generally presents as a double-walled, hexagonal, hyper-reflective structure that is 10 to 25 μ m in diameter (Figure 4).

Although the trophozoite form can also be seen, it is often difficult to discern from the normal corneal keratocyte nuclei, because both appear as ovoid, S-shaped, or irregularly shaped structures within the corneal stroma. A radial keratoneuritis has been described in association with amoebic keratitis. Pfister et al¹⁹ demonstrated the association of the amoebic organism with corneal nerves.

Like amoebic keratitis, fungal keratitis can be difficult to diagnose. Although cultures are still the primary diagnostic tool, cultures generally require several days to weeks to obtain growth. Furthermore, culture results can be negative if the organisms are deeply embedded within tissue. Winchester et al²⁰ have described the in vivo appearance of Aspergillus fumigatus within the stroma of a human cornea and confirmed the diagnosis by corneal scraping and staining.

Moreover, it offers the in vivo possibility of fungal differentiation. Fusarium solani typically displays the presence of multiple highly reflective linear formations (hyphae) up to 300 μ m in length and 5 μ m in width, with



Figure 5a: Reis Buckler dystrophy showing distinct deposits in the epithelium and Bowman layer. The deposits in the basal epithelial cell layer show extremely high reflectivity from small granular material. Bowman layer is replaced by highly reflective irregular material

branches at 90° angles in the anterior stroma. In contrast to hyphae, the Candida pseudo-filaments are characterized by numerous hyperreflective particles from 10 to 40 μ m in length and from 5 to 10 μ m in width located in the anterior stroma.

Thus, confocal microscopy offers the potential for instantaneous diagnosis of fungal keratitis and the ability to monitor the effectiveness of the antifungal treatment even in the presence of deep fungal infections.

Bacteria - 1.5- to 2 μ m, hyperreflective bodies in the cornea. Type of bacteria cannot be identified. Most bacteria are far smaller and are never observed with routine confocal microscopy.

Viruses: not amenable to detection by confocal microscopy

Corneal Dystrophies

Each corneal dystrophy evaluated has a unique appearance when observed by confocal microscopy (Figure 5a). Fuchs' dystrophy has the same characteristic appearance as that seen with specular microscopy; however, guttata and corneal endothelial pleomorphism can be detected within grossly edematous corneas due to the unique optics of the confocal microscope (Figure 5b).

With the exception of Fuchs' dystrophy, it is unlikely that corneal dystrophies can be diagnosed exclusively with confocal microscopy. The confocal microscope could be useful in *monitoring the progression* of a corneal dystrophy over time by comparing the relative intensity curve, counting the structures per high-power field (HPF), or measuring the depth of the abnormal structures.

ICE syndrome

Visualization of the corneal endothelium is also useful in diagnosing cases of iridocorneal endothelial syndrome.

Chiou et al²¹ described the confocal microscopic features of this syndrome. Epithelial downgrowth of the corneal endothelium results from epithelial cells that gain access into the eye and proliferate. As in iridocorneal endothelial syndrome, examination of the corneal endothelial surface demonstrates the presence of epithelial or epitheliallike cells with hyper-reflective nuclei on the endothelial surface. This differential appearance between corneal epithelial cells and endothelial cells, which do not have visible cell nuclei, facilitates identification of the irregular corneal endothelial cells.

Corneal Deposits

Corneal deposits other than those in corneal dystrophies can be viewed at high magnification with the confocal microscope. One study by Ciancaglini et al²² discussed the appearance of amiodarone-induced keratopathy in 11 patients. The authors described observed abnormalities in the corneal stroma as well as in the endothelium. It is generally not possible to perform specular microscopy when moderate corneal edema or other corneal opacification is present, but with the confocal microscope the corneal endothelium can be visualized through cloudy corneal stroma.

Side-effects of topical medication

Various side-effects of topical medication can be visualized with in vivo CM and utilized in research and practice.



Figure 5b: Fuch's Dystrophy with numerous micro-bullae in the basal layers

Influence of preservatives on the ocular surface

BAC solution 0.01% induces marked epithelial changes: complete loss of microvilli, degenerative membrane changes and desquamation of the two superficial epithelial cell layers after three hours' exposure. CM has revealed desquamation of the surface layer within 30 min of exposure to 0.005% BAC²³.

Topical side-effects of mitomycin C on cornea after pterygium surgery

It has been reported²⁴ that after application of MMC 0.02%, complete epithelialization of the operated zone was found 2 weeks post surgery. In vivo CM revealed signs of superficial punctate keratitis for 2 weeks in the central cornea only after application of MMC. The presence of epithelial and stromal oedema in this group was noted for up to 2 weeks in the central cornea and for up to 4 weeks in the operated zone. Nevertheless, in vivo CM shows that these changes are reversible 4 weeks after application of MMC 0.02%.

Contact lens wear

Eckard et al. quantified the changes in the epithelium of contact lens wearers as follows: cell bodies of superficial cells are generally smaller (30 μ m in contact lens wearers and up to 50 μ m in the normal cornea)⁹. A significant increase in superficial cell density existed both centrally and peripherally. Structures of intermediate and basal cells were found to be identical to the normal probands. The cell counts of both cell types were significantly reduced only in the periphery. Corneal thickness in the corneal periphery decreased in proportion to the duration of contact lens wear.

Typical changes observed in the stroma are the presence of hyper-reflective panstromal microdot deposits. An increased number of microdot opacities compared with the non-lens wearing eye is apparent and has been associated with the duration of contact lens wear. These microdots are thought to be granules of lipofuscin-like material.

Signs of polymegethism, pleomorphism and endothelial precipitates are the most common findings in the corneas of contact lens wearers.

Corneal cross-linking

Collagen cross-linking with riboflavin and UVA light is considered to prevent or delay the progression of keratoconus²⁵. CLSM enables visualization of the photopolymerization effect²⁶ as well as possible complications of the procedure. Rarefaction of keratocytes in the anterior and intermediate stroma, associated with the stromal oedema, was observed immediately after treatment²⁶. *Complete repopulation of the keratocytes was found 6 months after the crosslinking*. No endothelial damage (change of the endothelial cell count or morphology) was observed at any time.

Corneal refractive surgery

Cellular changes after refractive surgery are often not visible using the normal slit-lamp technique, which is why the CLSM may be useful²⁷. Wound healing after photorefractive keratectomy (PRK) as well as laser in situ keratomileusis (LASIK) could be reliably controlled, and haze development, interface zone, activated keratocytes, reinnervation and possible complications, such as epithelial ingrowths or fibrosis, can be identified. Another useful measureable parameter is the real flap depth. The depth of the flap can be quantified as the distance between the superficial cell layer and the interface zone. The latter is characterized by the presence of multiple hyper-reflective spots in the interface zone, as well as hyper-reflective (activated) keratocytes. These signs of the interface zone decrease over time, but still present many years after LASIK²⁸ and act as a landmark for CM. Moreover, Kaufman et al.²⁷ described a decline in the keratocyte cell count within the flap zone during the 3-year follow-up period.

Reinnervation of the cornea is a cornerstone question in refractive surgery. CLSM allows easy detection of the SNP. The literature review shows that re-innervation in the central cornea starts somewhere between the first and sixth month.

Imaging of the filtering bleb

One advantage of the recent advancement of CM is the ability to image the filtering bleb²⁹. It allows the analysis of bleb microstructures that are invisible under a slit lamp, as well as estimation of the bleb function. Thus, the epithelial microcysts, total stromal cyst area, absence of encapsulated stromal cysts and minimal vascularisation, as well as the absence of tortuous conjunctival vessels, are the signs of a good bleb function. The sub-epithelial connective tissue is widely spaced in functioning blebs, whereas the tissue is dense in nonfunctioning blebs. Moreover, Guthoff et al. classified the stromal structure into four patterns (trabecular, reticular, corrugated, compacted). The trabecular structure occurs only in functioning blebs, particularly in the early postoperative period. In contrast, corrugated, reticular or compact stromal patterns in early blebs tend to indicate a less favourable functional status³⁰.

Ocular manifestations of systemic disorders

The ocular manifestations of systemic diseases have been examined by confocal microscopy. In a study by Rosenberg et al³¹ examined the corneas of 45 eyes of diabetic patients and compared the cellular and structural morphology with that of 9 control eyes. The mild to severe groups of diabetic eyes were found to have fewer long subepithelial corneal nerves than the control eyes; however, corneal sensation was not affected in the mild to moderate diabetic group. Thus, confocal microscopy demonstrated diabetic neuropathy before it was clinically evident. The corneal epithelium was also noted to be thinner in a group of diabetic eyes.

Conclusion

In addition to providing qualitative data, confocal microscopy is valuable for quantitative analysis of the cornea and enables the investigation of pharmacologic and surgical modifications of corneal wound healing, nerve regeneration, and cellular responses. Thus, in vivo CM provides a universal tool to assess corneal architecture and morphology with properties similar to that provided by conventional histopathology, without the invasive preparation and need for biopsy.

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DOSP Ophibalmologieal BOCKETT Society			
Monthly Clinical Meeting,	, (August 2013	
Venue: Jawaharlal Nehru Auditorium, AIIMS, N Date & Time: 25th August 2013 (S	lev	/ Delhi - 110029 dav)	
Annual General Body Meeting: 9:30 A.	м.	Onwards	
Breakfast & Registration: 10:30 a.m.	Or	nwards	
Clinical Session: 11:00 a.m. onwards			
Clinical Cases:			
1. Glaucoma Masquerade	:	Dr. Shikha Gupta	10 Min.
2. Choroidal Osteoma with CNVM	:	Dr. Anil B. Gangwe	10 Min.
Guest Case Presentation from G.T.B. Hospital, New Delhi:			
Intramuscular Myxoma of Orbit	:	Dr. Pragati Gupta	10 Min.
Clinical Talk:			
Collagen Cross Linking : The current status	:	Prof. Namrata Sharma	15 Min.
Mini Symposium: Recent Advances in O Chairpersons: Prof. R.V. Azad, Prof. Y	pht '.R.	halmology Sharma	
 Emerging practice patterns in premium IOL surgery Conjunctivo-DCR: Current Status Recent Trends and approaches in Vitreoretinal Surgeries Surgical management of late complications after trabeculectomy 	: : :	Prof. Jeewan S. Titiyal Prof. Neelam Pushker Prof. Pradeep Venkatesh Prof. Tanuj Dada	12 Min. 12 Min. 12 Min. 12 Min.
Lunch 50 Early Bird	d P	rizes	
Sponsored by: Abbott Medical C	Ppti	ics	

Miscellaneous

Complications and Management of Regional Blocks in Ophthalmology



Lp.

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Regional Eye Blocks may lead to a number of complications and if not managed promptly may lead to cardiorespiratory arrest requiring resuscitation. Complications may be oculocardiac reflex (OCR), seizures, brainstem anesthesia, or an allergic response. Generally these complications occur within 15 minutes of regional block. Vasovagal reaction is the most common minor complications associated with local anesthesia. Hypotension, bradycardia, cardiac arrhythmias, diaphoresis occur within seconds of manipulation of the eyeball are usually responses to fear or pain of injection. Systemic toxicity may occur due to overdose of local anaesthetic or intravascular injection. Hyaluronidase and local anaesthetic may cause allergic reactions.

Scenario -1

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A 70 year old man after giving peribulbar block develops shivering followed by tachycardia. Gradually his breathing became shallow and then he stops breathing which was followed by loss of consciousness. On examination there is dilatation of the contra lateral pupil of the eye!

Shivering occurs in approximately 0.64% of patients, probably because of absorption of local anesthetic along the optic nerve sheath into the CNS (brainstem anesthesia) with retrobulbar block. Clinical picture of brainstem anesthesia can include amaurosis, gaze palsy (ductional defects), dilatation of the contralateral pupil, shivering, apnea, tachycardia, hypertension, loss of consciousness, dysphagia and cardiac arrest.

The local anaesthetic can be inadvertently injected under the dura matter sheath of the optic nerve resulting in its subarachanoid spread. Symptoms depend on the amount of drug that gains access to the CNS and the specific area to which it spreads. The signs and symptoms may include violent shivering, contralateral amaurosis, loss of consciousness, apnea, hemiplegia, paraplegia or quadriplegia. Blockade of the eighth to twelfth cranial nerves will result in deafness, tinnitus, vertigo, dysarthria, dysphagia, and aphasia.

The onset of symptoms may be delayed 2 to 40 minutes after injection. Apnea occurs within 20 min and resolves within an hour.

Treatment: it is mainly supportive

- Call for help of anaesthesiologist
- Insert intravenous cannula, give intravenous fluid
- Oxygen supplementation
- Monitor ECG, NIBP, SpO2 may need positive- pressure ventilation and intubation to prevent hypoxia and aspiration
- IV Atropine 0.3-0.6mg to treat bradycardia (HR < 50-60/min) with hypotension Vasopressor: Dopamine at 5-15mcg/kg/hr
 - It usually permit complete recovery after the spinal block wears off (a few hours). If recognized early and treated promptly, patients usually recover within 1 to 3 hours and do well. Brainstem anesthesia has not yet been reported with the peribulbar method of eye anesthesia.

Scenario 2

A 50 year old man complained about tingling sensation on the tongue while administration of peribulbar block. After completion of block he develops generalized tonic clonic seizures with biting of tongue and frothy sputum coming out from the mouth!

He had an intra-arterial injection of local anesthetic: retrograde flow through the ophthalmic artery into the cerebral circulation and midbrain area. Inadvertent intraarterial injection of the anaesthetic agent can result in retrograde flow of the agent from the ophthalmic artery to the cerebral or internal carotid artery resulting in CNS spread of anaesthesia. The onset is usually immediate and may be associated with seizure activity.

Treatment: Call for help of anaesthesiologist

- Oxygen supplementation
- Monitor ECG, NIBP, SpO2
- Bite block to protect tongue bite
- Insert intravenous cannula, give intravenous fluid
- IV midazolam: 2-3mg stat, may need additional doses
- IV Thiopentone sodium: 50-100mg or Propofol 30-50mg
- Protect airway, Positive- pressure ventilation and intubation to prevent hypoxia and aspiration
- IV Atropine 0.3-0.6mg to treat bradycardia (HR < 50-60/min) with hypotension Vasopressor: Dopamine at 5-15mcg/kg/hr
- May need cardiopulmonary resuscitation (CPR)
- Recovery from LA-induced cardiac arrest may take >1 h.
- Arrhythmias are common and refractory to treatment if bupivacaine is used for block. Lidocaine should not be used as antiarrythmic.
- Consider the use of cardiopulmonary bypass if available.
- Intralipid may be consider for refractory cardiac arrest.

For a 70-kg patient, an initial intravenous bolus injection of 20% lipid emulsion 100 ml over 1 min then start an intravenous infusion of 20% lipid emulsion at 1000 ml/ hr. Give a maximum of two repeat boluses of 100 ml. Continue infusion at same rate but double rate to 2000 ml /hr after 5 mins. Cumulative dose should not exceed dose of 840 ml.

Prevention of complication

- Explain about symptoms of intra-arterial injection to the patient before injection
- Have vital monitoring at the time of injection
- Always aspirate before and in between administration of injection
- Stopping the injection of LA once patient starts complaining tingling sensation on tongue or uneasiness
- Have emergency drugs available in the OT along with facility of oxygen supplementation.

Scenario 3

A 60 year old man after giving peribulbar block develops severe pain in the eye.

There may be increase in intraocular pressure. Intraocular Injection a large volume (8 to 10 mL) of fluid into the orbit (e.g., a peribulbar block) may significantly increase IOP. If IOP reaches the level of retina arterial pressure, retinal ischemia can result. This increase is not seen following sub-Tenon's blocks.

IOP is generally reported to increase immediately after injection. Direct relationship exists between central venous pressure and IOP.

Slight head-up tilt during intraocular surgery helps counteract the effects of central venous pressure.

Ocular massage may be attempted via in-and-out movement with a Goldmann contact lens or digital pressure

Repeated pressure for 10 to 15 seconds, followed by a sudden release has been recommended. This technique may produce retinal arterial dilation, with the improved perfusion. To reduce the IOP, agents like acetazolamide and mannitol can be administered. The total volume of the drug can be reduced by selection more potent drug or addition of adjuvant for early onset and to increase the intensity of the block.

Alternative block which will not affect IOP can be used in patients with high IOP.

Scenario 4

A 60 year old female after giving peribulbar block suddenly develops red rash, with hives/welts, has sudden onset wheezing, Chest tightness and trouble breathing with hoarseness of voice and difficulty in swallowing with feeling of impending doom.

These are the symptoms of drug allergy and this patient had an anaphylaxis reaction. Anaphylaxis is a severe, life-threatening, generalized or systemic hypersensitivity reaction. Warning signs typically affect more than one part of the body. Local anaesthetic esters are more likely than amides to provoke a Type IV allergic reaction. Preservatives such as methyl-paraben or metabisulphites may be responsible in some cases. It has been suggested that inadvertent intravascular injection of a local anaesthetic or the systemic absorption of adrenaline may also be responsible. Hyaluronidase may also lead to orbital swelling, allergic reactions.

Treatment:

- Call for help of anaesthesiologist
- Oxygen supplementation
- Monitor ECG, NIBP, SpO2

- Epinephrine-do first and fast IV is preferable. If no IV then intramuscular at 0.3-0.5mg (1:1000) repeated every 15 to 20 minutes Insert large bore intravenous cannula
- If there is no clinical improvement, IV epinephrine 0.1mg (1:10 000) slowly over 5 minutes. Epinephrine may be diluted to a 1:10 000 solution before infusion.
- Aggressive fluid resuscitation isotonic crystalloid (eg, normal saline) if hypotension is present and does not respond rapidly to epinephrine. A rapid infusion of 1 to 2 L or even 4 L may be needed initially.
- *Antihistamines* Administer antihistamines slowly IV or IM (eg, 25 to 50 mg of diphenhydramine).
- *Corticosteroids* Infuse high-dose IV corticosteroids early in the course of therapy. Beneficial effects are delayed at least 4 to 6 hours.
- *Atropine* when relative or severe bradycardia is present, there may be a role for administration of atropine. Protect airway, as there may be airway swelling and odema with difficulty of respiration.
- *Positive* pressure ventilation and intubation to prevent hypoxia and aspiration
- IV Atropine 0.3-0.6mg to treat bradycardia (HR < 50-60/min) with hypotension Vasopressor: Dopamine at 5-15mcg/kg/hr
- May need cardiopulmonary resuscitation (CPR)

Scenario 5

A 60 year old female after giving a peribulbar block was made to lie supine and pressure was applied on the eye ball using a soft rubber ball suddenly stops responding!

She had an OCR and had cardiac arrest. OCR could have developed at the time of injection or due to the pressure application on the eyeball. OCR may manifest as cardiac arrhythmias and hypotension.

- I. Prevention
 - 1. explanation of the procedure to the patient,
 - 2. monitoring of vitals while performing the block
 - 3. good surface anesthesia,
 - 4. gentle technique,
 - 5. slow injection of warm local anaesthetic agent
 - 6. Reassurance
- II. Treatment
 - 1. IV atropine 0.3-0.6mg
 - 2. Oxygen
 - 3. May need CPR

These signs may present themselves in various combinations and the ophthalmologist and anesthesiologist must be alert and prepared to provide cardiopulmonary resuscitation as an emergency, when there are apparent signs of local anesthesia spreading to the CNS, intra-arterial injection, vasovagal response or an anaphylaxis reaction. While symptomatic and proper treatment can lead to total recovery of the patient, delay in diagnosing and treating could be fatal.

Guidelines from The Royal College of Anesthetists and the Royal College of Ophthalmologists (2012)

- 1. Pre-operative checks must be made on the day of surgery to evaluate recent changes in the patient's condition or therapy.
- 2. Local orbital blocks should be administered by a trained anaesthetist or ophthalmologist.
- 3. For difficult cataracts and complex procedures, sub-Tenon's blocks should only be administered by a trained anaesthetist or ophthalmologist.
- 4. Intravenous sedation should only be administered under the direct supervision of an anaesthetist, whose sole responsibility is to that list.
- 5. An anaesthetist is not essential when topical, subconjunctival or sub-Tenon's techniques without sedation are used.
- 6. When peribulbar or retrobulbar techniques are used the responsibility for the immediate management of complications lies with the ophthalmologist or anaesthetist administering the local anaesthetic. An anaesthetist should normally be available in the hospital for further management if necessary.
- 7. No LA or surgical technique is entirely free from the risk of serious systemic adverse events, although these events may not be always a consequence of the technique itself.
- 8. The patient should be continuously monitored, from before the administration of the LA to the end of the operation. Monitoring should be by clinical observation, pulse oximetry and using other equipment as appropriate.
- 9. A suitably trained individual must have responsibility for monitoring the patient throughout anaesthesia and surgery.
- 10. All theatre personnel should participate in regular Basic Life Support (BLS) training, and there should always be at least one person immediately available who has Immediate Life Support (ILS) training or equivalent. Where the unit is free-standing and there is no immediate access to a formal cardiac arrest team there should be at least one person with Advanced Life Support (ALS) or equivalent.

Isolated Orbital Neurofibromatosis



Miscellaneous

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Neurofbromatosis is a rare condition characterized by hamartomas of neural crest origin (phakomatosis). The condition is autosomal dominant, though spontaneous new mutations are not uncommon. The National Institute of Health (NIH) divides neurofibromatosis into type 1 (NF1 or von Recklinghausen syndrome) and type 2 (NF2, acoustic neurofibromatosis, or central neurofibromatosis)¹.

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Orbital neurofibromas are rare, accounting for 0.5 to 2.4% of all orbital tumors². Isolated neurofibromas of the orbit are relatively uncommon, representing less than 1% of orbital neoplasms^{3,4}. The 3 typical ocular manifestations of neurofibromas are plexiform, diffuse and localized. Isolated

(localized, circumscribed, or solitary) neurofibromas are distinct from plexi-form and diffuse neurofibromas and are less frequently associated with neurofibromatosis type I (also known as Von Recklinghausen' s disease).

The orbit contains two types of nerves: the optic nerve (a tract of the central nervous system) and peripheral nerves (both branches of sensory nerves, such as the fifth nerve, and motor nerves, such as those that innervate the extraocular muscles). Oligodendrocytes produce and maintain the myelin of axons within the central nervous system. In contrast, the Schwann cells produce the myelin that surrounds the axons of nerves within the peripheral

Table 1 Prevalence of Peripheral Nerve Sheath Tumours of the Orbit ²						
Studies	No	Schwannomas (%)	Neurofibromas (%)	Others*(%)		
Handerson	764	8 (1.0)	18 (2.4)	2 (0.3)		
Rootman	1409	14 (1.0)	7 (0.5)	4 (0.3)		
Shields	645	5 (0.8)	5 (0.8)	4 (0.6)		
Kennedy	820	4 (0.5)	25 (3.0)	0 (0.0)		
*Amputationneuroma Granular cell tumour, and Malignant Schwannoma						



Figure 1: Patient with proptosis right eye



Figure 2: Hertel's Exophtalamometry measuring amount of proptosis



Figure 3: CT scan of right orbit showing an intraconal mass with displacement of globe

nervous system. Isolated neurofibromas of the orbit are one of the nerve sheath tumors (NSTs) which are derived from the Schwann and perineurial cells of the peripheral nervous system. These are benign, solitary and slowly growing tumors.

Figure 4: Histpathology of excised masswavy cells with eosinophilic cytoplasm and comma-shaped nucleishowing confirminglocalised neurofibroma

The isolated (localized) neurofibroma is named because it generally grows as a circumscribed lesion. Although circumscribed, it usually is not encapsulated, as is the schwannoma. Isolated orbital neurofibromas tend to appear in the superior aspect of the orbit during the third to fifth decades.

A number of isolated cases of intraorbital solitary neurofibroma have been reported since 1985⁴. Isolated orbital neurofibromas associated with systemic neurofibromatosis is relatively rare and may be difficult to clinically differentiate from other orbital tumors. Radiation induced intraorbital neurofibroma has been seen in a case with cranial irradiation in childhood.

Decreased visual acuity is an uncommon symptom of localized neurofibroma confined to the anterior compartment of the orbit. The most common site is superior orbital location as the tumor often arises from branches of the frontal nerve^{6,7}. Bony involvement has been reported in previous literature⁷. When the posterior aspect of the orbit is affected, compression of the optic nerve may lead to decreased visual acuity and visual field defects and may produce a relevant afferent pupillary defect. Diplopia, which also may develop in isolated neurofibromas of the posterior aspect of the orbit, more likely is the result of mass effect rather than direct involvement of the innervating nerves. Orbital involvement can lead to malposition of the eveball outward, also called proptosis (Figure 1&2). If the tumor is large enough, it can put pressure on the eyeball or optic nerve causing glaucoma or optic neuropathy, which leads



Figure 5: Excision of intraconal mass by lateral orbitotomy

to vision loss. If sensory nerves are involved, patients may experience pain or discomfort. Pulsations of the eyeball or eye socket may also be felt or observed by the patient. This phenomenon may occasionally occur because of bony defects within the socket adjacent to the intracranial cavity. This leads to a transmission of the normal brain pulsations to the eye socket.

Multiple localized orbital neurofibromas have been reported in patients who do not have neurofibromatosis^{4,5}. It is unclear whether these cases actually represent a formefruste of neurofibromatosis.

The best imaging technique for diagnosis of orbital neurofibroma is controversial. Computerised Tomography (CT) appears to be most useful for delineating bony involvement, while Magnetic resonance imaging is most useful for defining the ultra-structure of the tumor and relationship to adjacent tissue. A variety of radiologic patterns have been noted such as cystic lesions, solid lesions and mixed cystic-solid lesions (Figure 3). Such findings may result from a large spectrum of complex cellular differentiation modalities with the resulting variability in stromal composition⁶. Incisional biopsy with tissue pathology is required for definite diagnosis.

Histologically, the localized neurofibroma is characterized by wavy cells with eosinophilic cytoplasm and commashaped nuclei. Collagen can be present in variable quantities. Commonly, there is no palisading of the nuclei, in contrast to the Schwannoma. Ultrastructurally, the neurofibroma is



Figure 6: Patient after surgery showing resolution of proptosis



Figure 7: Post operative CT scan showing no residual intraconal mass and globe displacement

composed of cells that more characteristically have features of the perineurial fibroblast. Conversely, schwannomas have long-spacing collagen and abundant basement membrane, seen on electron microscopic evaluation (Figure 4).

Most cases do not need specific management, and surgical excision is considered depending on the size of the tumor and the degree of severity of the symptoms, such as clinical diplopia, severe proptosis and its complications, or optic nerve compression (Figure 5). Preoperative imaging studies are helpful in surgical planning. Total tumor removal can be achieved without serious complications (Figure 6&7).

Radiation therapy is not advisable because a transformation into a neural sarcoma has been reported during radiation therapy⁸. It has been suggested that some neurofibromas may be related to somatic mutations or mosaicism, producing a segmental pattern of involvement as in isolated orbital neurofibroma⁹. Genetic analysis of surgical specimens may prove it.

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Evolution of Penetrating Keratoplasty



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Corneal transplantation surgery has evolved rapidly since 1905, when Edward Zirm¹ completed the first successful penetrating keratoplasty (PKP) procedure on a 45-year-old farm laborer in what is now the Czech Republic. However the pioneers stumbled across countless failures before they gave this procedure the distinction of being the most successful as well as the most frequently done organ transplant worldwide. It is the vision and determination of these pioneers that has given PKP not only the tag of a curative procedure but of refractive as well.

The evolution of PKP can be divided into five periods:-

- 1) Inspiration (1789-1824)
- 2) Trials and Frustration (1825-1872)
- 3) Conviction (1873-1905)
- 4) Achievement (1906-1965)
- 5) Refinement and Innovation (1966-present)

At the start of the Inspiration period a French surgeon, Pellier de Quengsy in 1789 actually suggested that a glass cornea could be used to replace the human cornea. Erasmus Darwin in 1797 suggested that by surgically removing corneal pathology the scar might grow back clear. This, of course, was wishful thinking.

In the next period of Trials and Frustration, Reisinger suggested that living tissue grafts might be used to perform a corneal transplant. However, most attempts at transplantation in the 19th century used corneas of different species or hetrografts and they failed.

The third period, that of Conviction saw Henry Power² recommend transplantation within the same species. In 1877, von Hippel started publishing his studies using circular mechanical trephines (Figure 1) to remove the donor and recipient corneas. This principle is same for

keratoplasty even today. Other factors leading to success of corneal transplantation included the development of general anesthesia and asepsis.

The period of Achievement actually started with Edward Zirm's successful transplantation of Alois Golgar's cornea



Figure 1: Von Hippel's clockwork trephine

in 1905. Despite Zirm's success with a single penetrating keratoplasty, this operation was not accepted in the first two decades of the 20th century. The lamellar graft was more often used. Direct suturing was years away and penetrating grafts almost always failed. More research into keratoplasty was carried out by Magitot³, Elschnig⁴ and Vorisek. At the same time Vladimir Filatov⁵ popularized the use of cadaver corneas for corneal transplant purposes changing the whole scenario of availability of the tissue. Castroviejo's⁶ investigations of keratoplasty (Figure 2), his design of unique instruments and his exquisite skill almost single-handedly improved the techniques and popularized PKP in 1950s. By the same time Barraguer⁷, a pioneer in keratoplasty was using donor tissue up to 6.5mm in diameter and utilized direct suturing with fine silk sutures. As the corneal transplantation grew to be more successful, the need for corneas from cadavers became greater. Eye banking began in 1940, when Paton established the first eye bank in the USA.

In the present period of Refinement and Innovation corneal transplantation has become well established for numerous indications with high success rates. The introduction of nylon suture and microsurgery has taken PKP from being a therapeutic procedure to a refractive one. Corneal graft rejection was the greatest limiting factor in graft survival and Edward Maumenee was the one to recognize this clinical entity. It was followed by classic scientific description and experimental models were elegantly designed by Khodadoust. The concept of corneal storage in artificial media was introduced by McCarey and Kaufman⁸ in the early 1970s. The media have improved continually so that corneas may now be stored for atleast a week. Various models of suction trephine have been designed to provide complete or partial keratotomy for keratoplasty procedures. Hessburg-Barron Vacuum Corneal Trephine is one such trephine that is self-contained with its own suction source and designed with crosshairs which assist with centration over the cornea.

It is very exciting to study the changes in PKP from the beginning of its evolution and even more exciting to see the current explosion of ideas in the field dealing with endothelial transplantation and anterior lamellar transplantation. Femtosecond laser application is the "excitement of today" in microsurgery of the cornea.

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Figure 2: Ramon Castroviejo in 1930's designed a square graft "watermelon plug" to have better wound coaptation

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PG Corner

Workup of a Case of Corneal Opacity



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Any disease which interferes with corneal clarity leads to an opacity which may be partial or total and may or may not interfere with visual acuity.

Workup and management is subdivided into following headings.

History

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- Congenital or acquired
 - Causes and management differs
- Onset- early onset in childhood has chances of amblyopia esp if opacity is unilateral.
- Recurrent episodes- of redness and pain is suggestive of viral etiology
- Laterality- bilateral involvement may indicate dystrophies, viral etiology



Figure 1: Corneal opacity in a case of Peter's anomaly

- Trauma- look for injury to other ocular structures which may affect final visual recovery .
- Systemic illness in childhood may indicate keratomalacia
- Socioeconomic status-if poor, post operative treatment and follow up after PK will be affected

Symptoms

- Vision loss
- Handicap, affecting day to day activity- if present intervention needed even in presence of poor visual potential
- One eyed patients, if ambulatory-guarded approach is needed
- Pain, photophobia- suggestive of ongoing activity which needs treatment before definitive therapy

Examination

- Visual acuity- near and distance with and without correction
- Refraction- may allow functional acuity without any surgical intervention
- Ocular deviation- may suggest poor visual potential
- Fixation, nystagmus- assessment of visual potential
- Intra-ocular pressure if raised, needs to be treated
- Depth of opacity- a partial thickness opacity may be amenable to lamellar keratoplasty
- Vascularisation- superficial, deep. Affects choice of keratoplasty and graft survival

- Anterior segment evaluation
- Pupillary reaction is indicative of optic nerve health
- Posterior segment evaluation is must

Investigations

- Assessment of visual potential- VA prior to opacity, Macular function tests, Laser interferometry, VER
- USG- assessment of posterior segment
- ASOCT- depth of opacity, evaluation of anterior chamber. Affects decision of choice of surgery
- UBM- angle of anterior chamber is visualised

Treatment

Treat any on-going disease process as an infectious etiology, ocular surface problem or raised IOP, and then only plan a definitive therapy

- 1. Cosmetic treatment if there is a poor visual potential
 - Tattooing
 - Cosmetic contact lens

2. Visual

- Non surgical
 - Refraction and glasses
 - Rigid gas permeable contact lens- if VA is less because of irregular astigmatism
- Surgical
 - *Optical iridectomy-* in case of central opacities with clear periphery, preferably in children and one eyed individuals, poor visual potential cases to salvage some vision.
 - Phototherapeutic keratectomy/ photorefractive keratectomy in cases of superficial opacities
 - Lamellar keratoplasty
 - Penetrating keratoplasty
 - Keratoprosthesis in patients with poor ocular surface where chances of graft survival are bleak specially if patient has poor vision in other eye also.

Monthly Meeting Corner



Diagnostics on Wheels

Dr. Shroff's Charity Eye Hospital, Daryagunj, New Delhi

urs is a diverse country with varied population and the population to doctor ratio is skewed with more doctors in the larger cities. Along with this the awareness of the chronic and largely asymptomatic diseases like glaucoma is very limited in the low socioeconomic sections of India.

We see many patients who would rather tend to their livelihoods than to visit a doctor and this results in the disease being very advanced when they are eventually seen. Various factors which account for this are cost of medical care, distance to the proper medical care, and most of all awareness.



Figure 3: Measuring the Intraocular Pressure





Figure 1: The Eye Diagnostic Van



Figure 4: Slitamn Examination



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Figure 5: Fundus Photograph



Figure 7: Talking to the Community and Awareness Building



Figure 6: Visual Field by FDT

Our way to decrease this would be to reach the people at their doorsteps and this was the idea behind the diagnostic van project. The diagnostic van is equipped with comprehensive eye examination instruments including refraction station, slit lamp with applanation tonometer. There is a fundus camera and an FDT machine. The patient undergoes a complete eye examination with glaucoma as a focus.

The team includes a doctor, optometrists and paramedical workers and the team actively works to spread awareness about various eye diseases and glaucoma in particular.

The advantages of this system

- Patient convenience
- Reduced patient cost (Indirect : travel, loss of earnings)
- Optimum utilization of specialty services
- Better data for future planning of health service
- Awareness building
- Marketing tool

We plan to extend the services to more areas and also increase the equipment to be able to pick up diseases other than glaucoma.

Forthcoming Events

AUGUST 2013

(Saturday - Sunday) 17th – 18th August, 2013 Refractive Surgery 360 degree: includes a no. of hands on skill transfer courses

Venue: Hyderabad International Convention Center, Hyderabad **Contact:** Dr. Pravin Krishna Vaddavalli, Cornea service, Head, Refractive Surgery, Cataract, Contact Lens service, L.V. Prasad Eye Institute (LVPEI), Hyderabad

Email: pravin@lvpei.org, *Phone:* +91-40-30612632 *Website:* www.lvpei.org/refractivesurgery360/index.html

SEPTEMBER 2013

(Saturday - Sunday) 31st August – 1st September, 2013 Corneologue 2013 - A Kerato Refractive Symposium Venue: The Metropole Hotel, Ahmedabad

Contact: Ms. Meera Zala, Retina Foundation and Eye Research Centre, Near The Underbridge, Shahibaug, Ahmedabad-380004 **Email:** meera@retinafoundation.com **Phone:** +91-79-22865537, 22860086

(Friday, Saturday, Sunday) 6th – 8th September, 2013 24th Annual Conference of Oculoplastic

Association of India

Venue: Bangalore, India Contact: Dr. Gagan Dudeja, Phone: +91-9902680000, Email: gagan.dudeja@gmail.com, Website: www.opai.in

(Friday, Saturday, Sunday) 20th – 22nd September, 2013 The Glaucoma Fest 2013: 23rd Annual Conference of Glaucoma Society of India

Venue: Indore, Madhya Pradesh, India
Contact: Dr. Aditya Agarwal, Dr. Prateep Vyas, Eye Site, 109-111, Trade House Above HDFC Bank, 14/3, South Tukoganj Dhakkanwala Kuan, Indore 452001
Email: glaucomafest@gmail.com
Website: www.glaucomafest2013.com
Phone: + 91-0731-2528378; + 91-9826064746

OCTOBER 2013

(Thursday - Sunday) 3rd – 6th October, 2013 **SAARC Academy of Ophthalmology Conference** *Venue:* Bhurban, Pakistan

Contact: Dr. Amer Yaqub, Secretary Organizing Committee, Associate Professor of Ophthalmology, Army Medical College, Armed Forces Institute of Ophthalmology, Rawalpindi,Pakistan Email: ospfederaleye@gmail.com Website: saarccongress2013.com Phone: 0321-5365434

(Friday, Saturday, Sunday) 18th – 20th October, 2013 37th Annual conference of MPSOS

Venue: Sadguru Netra Chikitsalaya,Chitrakoot (MP) Contact: Dr. Elesh Jain Organizing Secretary Email: dreleshjain123@gmail.com Phone: +91-9993741000

(Friday, Saturday, Sunday) 25th – 27th October, 2013 UP State Ophthalmological Society: Annual Conference

Venue: Jhansi (Orchha), Uttar Pradesh Contact: Dr. D. Nath, Geeta Netra Chikitsalaya Sirsaganj, UP, AND Dr Prakash Gupta, Dr Jiya Lal Memorial Hospital Pvt Ltd Opp Medical College Jhansi, UP Email: dr.dnath@yahoo.com

(Monday - Thursday) 28th – 31st October, 2013 ASIA-ARVO 2013

Venue: The Ashok, Chanakyapuri, New Delh, India Contact: Conference Secretariat, Room No. 474-475 Dr. Rajendra Prasad Centre for Ophthalmic Sciences, AIIMS, New Delhi-110029, India, Phone: 011-26593144-45, Email: asiaarvo2013@gmail.com Website: www.asiaarvo2013.org

(Saturday- Tuesday) 16th – 19th November, 2013 American Academy of Ophthalmology : 117th Annual Meeting 2013

Venue: Ernest N. Morial Convention Center in New Orleans Email: meetings@aao.org Website: www.aao.org/meetings/annual meeting/index.cfm

(Saturday- Sunday) 30th Nov. – 1st Dec., 2013 Delhi Ophthalmological Society Winter Conference Venue: New Delhi

Contact: Dr. Rajesh Sinha, Secretary, Room No. 479, 4th Floor, Dr. Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, Ansari Nagar, New Delhi – 110029 Ph.: 011-65705229, E-mail: dosrecords@gmail.com Website: www.dosonline.org

(Thursday- Sunday) 6th - 11th February, 2014 72nd Annual Conference of All India Ophthalmological Society (AIOC-IJO Diamond Jubilee Conference 2014) Venue: Agra, Uttar Pradesh, India

Contact: Dr. S.K. Satsangi, Professor, Department of Ophthalmology, SN Medical College, Agra, *Mobile*: +91-9897069441, *Email:* sksatsangi@gmail.com *Website:* www.aioc2014.com

DOS ²	Delhi Ophthalmological So	ociety	
The Photo Identity Card will be issued after your Membership is ratified by the General Body during the next Annual DOS Conference	(LIFE MEMBERSHIP FO	RM)	Paste Photo
Name (In Block Letters)			
S/D/W/o		Date of Birth	
Qualifications		Registration No	
Sub Speciality (if any)			
ADDRESS			
Clinic/Hospital/Practice		Phone	
Residence			
		Phone	
Correspondence			
		Phone	
Email		Mobile No.	
Proposed by			
Dr	Membership No	Signature	
Seconded by			
Dr	Membership No	Signature	
[Must submit a photocopy of	the MBBS/MD/DO & State Medical Cou	Incil / MCI Certificate for	our records.
Declaration: I hereby declare that the abo by the Rules, Regulation & Bye-Laws of <i>(Life membership fee Rs. 5100/- paya</i> <i>Society)</i>	ive details are correct. I wish to be Life member. I have the Society as in force and any subsequent amendm able by DD for outstation members. Local Cheque	e carefully read the instructions over nent(s) made from time to time <i>is acceptable, payable to Delhi</i> C	erleaf. I shall abid Dphthalmologica
Please find enclosed Rsin	words	by Cash	
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with Date	I hree specimen signatures fo	or I.D. Card.	
Dr.	FOR OFFICIAL USE ONLY	has been admitted as I	ife Member o
the Delhi Ophthalmological Societ	ty by the General Body in their meeting hel	d on	
His/her membership No. is	. Fee received by Cash/Cheque	/DD Noda	ated_
drawn on			

(Secretary	DOS)
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INSTRUCTIONS

- 1. The Society reserve all rights to accepts or reject the application.
- 2. No reasons shall be given for any application rejected by the Society.
- 3. Every new member is entitled to received the Society's Bulletin (DOS Times) and quarterly Journal DJO (Delhi Journal of Ophthalmology) of the Society free.
- 4. Every new member will initially be admitted provisionally and shall be deemed to have become a full member only after formal ratification by the General Body and issue of Ratification order by the Society. Only then he or she will be eligible to vote, or apply for any Fellowship / Award, propose or contest for any election of the Society.
- 5. To be proposed and seconded by Ratified Life Member only. No application form will be accepted unless it is complete in all respects. Proposed and Seconded by existing Member of the Delhi Ophthalmological Society.
- 6. Photo ID Card will be issued only after the membership is ratified by the General Body.
- 7. Documents to be attached with application form:
 - 1. Copy of Degree (MBBS / MD / DNB)
 - 2. Copy of Registration Certificate Medical Council of India or State Medical Council
 - 3. Copy of PAN Card
 - 4. One Stamp size Coloured Photograph to be pasted on the Application Form and one stamp size coloured photograph to be attached with form for issue of Laminated Photo Identity Card (to be issued only after the Membership ratification by GBM).
 - 5. For Delhi members only : Copy of Passport/Licence/Voters Identity Card/Ration Card/ Electricity Bill/MTNL (Landline) Telephone Bill (Delhi Life Member should either reside or practice in Delhi.
- 8. Membership Fee

There is only membership on one Time Payment of Rs. 5,100/-

- 1. Life membership fee Rs. 5,000/- (This money will be part of corpus of Society)
- 2. Admission fee Rs. 100/-

The application form should be complete in all respects and accompanied by a Demand Draft of Rs. 5,100/- in favour of "Delhi Ophthalmological Society" payable at New Delhi should be sent:

Dr. Rajesh Sinha, Secretary,

Delhi Ophthalmological Society,

Room No. 479, 4th Floor, Dr. R.P. Centre for Ophthalmic Sciences, AllMS, Ansari Nagar, New Delhi – 29

9. For update address for sending application, please visit website www: dosonline.org

DOS Community Programme

Sunday, 30th June, 2013



The **DOS Community programme** had the first social initiative by DOS for the year 2013-14. A diabetic screening camp was organised in conjunction with the Delhi Diabetic Forum in Central Delhi on the 30thof June 2013.

The diabetic screening camp saw the participation of 16 ophthalmologists who screened over 200 patients over a 3 hours period. The patients were offered free blood sugar and blood pressure checking by the physicians of the Diabetic forum, while the participating



DOS members provided fundus screening for all patients. Forty diabetics had evidence of retinopathy and five were refreed to a higher centre for laser treatment. Baseline fundus photographs of the patients with retinopathy were taken for record on a handheld fundus camera. Refractive error correction was advised to eighty patients and they were referred for the same to ophthalmic setups around the area. Counselling with regard to ocular changes in diabetes was provided and patients with other ocular diseases such as glaucoma and cataract were also counselled with regard to their ailment.

The effort of the ophthalmologists was

appreciated by the Delhi diabetic forum and emphasis was laid on the need for further screening camps in view of the large number of undetected retinpathy cases. The DOS executive expresses gratitude towards all the members who participated and gave their valuable time to this social cause.



Instructions:

- 1. Please return your answers to dostimes10@gmail.com or mail them to **"The Quizmaster**, DOS Times Quiz, Dr. Rajesh Sinha, Room No. 479, Dr. R.P. Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029". Please write your DOS membership number along with your answers.
- 2. The answers should reach not later than 23rd September, 2013.
- The quiz can also be viewed and directly answered on our website www.dosonline.org
- 3. The results will be announced at the DOS monthly clinical meeting on 29th September 2013. The correct entry will be given a prize of Rs, 2,500. If there are more than one correct entries, the winner of the prize will be decided by draw of lots. **Quiz compiled by Dr. Digvijay Singh**

Quiz Prizes Sponsored by M/s. Syntho Pharmaceuticals Ltd.

What's in a name?

Instructions:

Fill in the blanks below to reveal the names of persons related to ophthalmology. The clues will help you narrow down in the names. Then unscramble the highlighted alphabets and answer the final question.

Answers are included on the last page after the tear sheet.

A. I am part of the trinity of ophthalmic disorders involving the corneal endothelium and causing glaucoma. I share my name with that of a popular Sitcom's fictional character. What is my name?



B. I share my first name with the nick name of the 26th American president. Guess my surname, which defines a principle on which a popular ophthalmic device is based.

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C. The first part of my name is snake in Sanskrit and the second part is a lost cause. I developed a technique and instrumentation which helped to break. Who am I?



D. The first half of my name is precious to all, I help measure something the glaucoma specialists are happy to see fall. What is my name.

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Unscramble the highlighted alphabets to make a word which refers to a finding seen in papilledema.

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Membership No Name :	
Mobile No	_Email:
Answer to DOS Times Quiz July 2013	
A	B

D.

Keratoconus

Definition- it is an ectatic non inflammatory condition in which cornea assumes a conical shape because of thinning and protrusion.

Prevalence-

- 0.5-2/1000 population.
- Usually bilateral, may be asymmetric.
- Onset at puberty, progress over 1to 2decades and then stops.

Systemic Associations-

- Atopic disease,
- Down's syndrome,
- Connective tissue disorders (Ehler Danlos syndrome, Osteogenesis Imperfecta)
- Mitral valve prolapse

Ocular associations-

- Retinitis pigmentosa,
- Leber's congenital amaurosis,
- Vernal conjunctivitis

Etiology-

- Genetic predisposition (Autosomal dominant inheritance with incomplete penetrance, high risk in first degree relatives)
- Microtrauma due to eye rubbing or contact lens wear

Symptoms-

- in a patient in teens or twenties
- Progressive visual blurring/ distortion, photophobia, glare, monocular diplopia, ocular irritation

Signs-

- High, irregular myopic astigmatism
- Eccentrically located ectatic protrusion of cornea, cornea thinned most at apex of protrusion
- *Munson's sign-* indentation of lower lid in downgaze due to conical cornea
- *Rizutti's sign-* conical reflection on the nasal cornea when a penlight is shone from the temporal side

- Scissoring reflex on retinoscopy
- *Fleischer's ring* iron deposition in epithelial basement membrane at the base of the cone.
- Subepithelial scarring
- Prominent corneal nerves
- **Vogt's striae** fine vertical lines in deep stroma and descemet's membrane parallel to the axis of the cone, disappear on gentle pressure
- **Retroillumination-** oil droplet reflex (Charleaux sign)
- In more advanced cases, deeper opacities can be seen at the apex of the cone resulting from ruptures in Descemet's membrane.
- Acute keratoconus or corneal hydrops results from stromal imbibition of aqueous through these defects.
- Photokeratoscopy signs:
 - Compression of mires inferotemporally
 - Compression of mires inferiorly or centrally
- Videokeratography signs:
 - Localized increased surface power

Table: Ams	ler-Krumeich classification		
Stage I	Eccentric steeping		
	Myopia and astigmatism < 5.00 D		
	Mean central K readings < 48.00 D		
Stage II	Myopia and astigmatism from 5.00 to 8.00 D		
	Mean central K readings < 53.00 D		
	Absence of scarring		
	Minimum corneal thickness >400 μ m.		
Stage III	Myopia and astigmatism from 8.00 to 10.00 D		
	Mean central K readings > 53.00 D		
	Absence of scarring		
	Minimum corneal thickness 300 to 400 μ m.		
Stage IV	Refraction not measurable		
	Mean central K readings >55.00 D		
	Central corneal scarring		
	Minimum corneal thickness 200 μ m		



Figure 1: Management algorithm of Keratoconus

- Inferior-superior dioptric asymmetry
- Relative skewing of the steepest radial axes above and below the horizontal meridian

Investigations- diagnosis is mainly clinical however topographic evaluation is needed for diagnosis in subclinical (forme fuste keratoconus) and for follow up

- Video keratography (VKG)
- Orbscan
- Pentacam
- ASOCT- very useful for diagnosis, localization of fluid clefts and follow up of hydrops
- Pachymetry

Management-

- Spectacles- only initial mild cases
- Contact lens-
 - Soft, Toric
 - Rigid Gas Permeable lens
 - Special designs- Rose K lens-It's complex geometry can be customized to suit each eye and can correct all of the myopia and astigmatism associated with Keratoconus
 - Rose K 2 lens

- Collagen Cross Linking (CXL) -a one-time application of riboflavin solution to the eye that is activated by illumination with UV-A light for approximately 30 minutes. The riboflavin causes new bonds to form across adjacent collagen strands in the stromal layer of the cornea, which recovers and preserves some of the cornea's mechanical strength. It stabilizes progression in most treated eyes, improves contact lens fitting and a slight correction in visual acuity in most patients. Minimal corneal thickness (CCT) needed is 400 microns, hypo- osmolar riboflavin can be used upto 350 microns.
- CXL combined with Toric IOL or ICRS
- Intra Corneal Ring Segment(ICRS)
 - Minimum corneal thickness > 400
 - Avg K < 53D (mean reduction of 3-4 D)
- Keratoplasty
 - ALTK-CCT > 380 microns
 - DALK-CCT < 380 microns
 - PK-Central descemet's scar



Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi