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DOS Membership Fee Revision
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**DOS TIMES - SEPTEMBER-OCTOBER 2016**
“Try to learn something about everything and everything about something.”

- Thomas Huxley

Dear seniors & friends

Season’s Greetings on the brink of the festival season.

Between the time of the previous issue and the current issue, may activities of DOS have been on, with our regular monthly meetings happening with much higher academic content and standards than before. The financial accounts of the previous year presented in the annual general body meeting echoes the phenomenal rise of DOS and further emphasis on the need to be able to acquire a DOS HOUSE as soon as possible.

This executive’s iDOS launch was welcomed with warmth with heightened expectations for a wonderful meeting along with the College of Srilanka Ophthalmologists. We encourage more delegates to come forward and participate and reap the benefits of this exciting mix of academics and travel in an exotic tropical location.

The midterm conference of 2016 opens under the umbrella of winterDOS 2016: OPHTHALMIC VISTA and entices all across the country to attend. Attending winterDOS 2016 reflects the commitment to enhanced learning and desire to keep update to the current trends in ophthalmology. This DOS Vista is indeed a promising one which will be a wonderful confluence of academics, ophthalmic exhibition and entertainment which you will not want to miss.

Another highlight is holding of DOS teaching program – DOST 2016 – 2017 in conjunction with the winterDOS 2016. This enables several postgraduates and trainees to also attend winter DOS. This also provides them the benefit of live surgery of all ophthalmic specialities in the teaching program besides the regular didactics and wetlabs.

The Eye donation fortnight spanning over August 24 – September 8 saw wide celebrations across the country with DOS pledging its support to the cause of eye donation though Eye donation awareness walk in partnership with NEB, RP Center, EBAI and ISCKRS.

This second issue of DOS TIMES of 2016 – 2017 comes to you with an excellent academic topics assembly which covers a range of all current interest. It is an optimal mix of ophthalmic coverage on posterior corneal astigmatism, Biometry, FLACS for beginners, capsular opacifications, retinal vasculitis, micropulse lasers, and the AVASTIN DEBACLE, along with all the other captivating regular features.

As this executive works harder on propelling DOS further into greater heights, we are hopeful to see another year of overflowing attendance to our winterDOS meeting and DOST programme as we carve out an academics to learn something about everything and everything about something!

Wishing you all a wonderful and joyous festival season.

With best regards.

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Avastin Debacle - What Do We Learn From It

“All men make mistakes, but only wise men learn from their mistakes.” – Winston Churchill

In recent times, with the advent and increasing use of anti-VEGF agents for intraocular use, there has been a paradigm shift in the management of various medical retinal pathologies including neovascular AMD, diabetic retinopathy, diabetic macular edema and retinal vein occlusion etc. However, the post intravitreal injection risk of cluster endophthalmitis stays either due to failure of proper sterilization techniques adopted for preparing the drug, OT contamination or poor patient preparation, or secondly due to a contaminated agent. The incidence of post-injection endophthalmitis is of great concern as there is dramatic increase in the number of injections performed annually and intravitreal injection being the most commonly performed medical procedure. Also the risk of cluster endophthalmitis is high as multiple patients receive injections in a single session. The time period for occurrence of PIE from injection to presentation is early and ranges from within 24 hrs. to even upto 26 days as reported, with average of 4 days. Unfortunately there has been confirmed reports of series of cluster endophthalmitis from our country after intravitreal injection, especially following intravitreal Avastin® injection leading to the Drug Controller General of India putting use of Avastin on high alert, literally causing a drug ban on the intraocular usage of bevacizumab (Avastin®, Roche), following an incident of cluster endophthalmitis which however was withdrawn later. The intraocular use of Avastin is ‘off-label’ as it is not approved by the Food and Drug administration (FDA, USA). Among the available anti-VEGF agents in India, the multi-dose Avastin proves to be the cheapest and most cost-effective. This has lead to lot of debate and doubt regarding legal implications of use of intravitreal Avastin, procurement of the drug, precautions to be taken and guidelines to be followed while using the vial for multiple patients.

**Causes of Cluster Endophthalmitis after intravitreal injection**
- Counterfeit drug
- Improper storage of drug / lapse in cold chain in case same vial is used more than once.
- Multiple use and multiple puncture of multi-dose vial stopper.
- Failure of aseptic technique.
- Contaminated OT

**Prevention of post-intravitreal endophthalmitis**
- A written-informed consent explaining the procedure and the risks involved. **Off label use to be included in consent and explained to patient.**
- Thorough pre-op screening and control of risk factors like localized adnexal infection or systemic condition is mandatory.
- Proper aseptic precaution including use of **povidone iodine** for adnexe and cul-de-sac are proven preventive measures.
- Prophylactic topical antibiotics: There is **lack of evidence to support pre, peri or post- injection topical antibiotics.** However, short course of post-procedure prophylactic antibiotic is used on surgeon’s personal experience and discretion.

Intravitreal injection should be administered in the operating-room setting only, avoid talking during administering the injection as Streptococcus viridans, a component of human oral flora has been reported to be present three times more often in postinjection endophthalmitis as compared to postsurgical endophthalmitis.
Drug procurement

- Drugs should be purchased from authorized Roche dealers with proper receipt.
- Batch number of each vial should be noted in a register before opening the vial and the records should be maintained which might help to track before opening it.
- Cold chain should be maintained at each stage (2-8 degrees, never freeze the vial), especially at dealer’s storage facility, transport to the hospital and in the hospital with proper temperature log maintenance.

- Multiple injections from one vial – Options
  A) **Ideally** - Compounding pharmacy to prepare *single dose ampoules*/aliquots should be practiced in sterile labs.
  B) Prepare multiple syringes by single puncture of vial under laminar hood. Store the syringes in sterile container. Send 2 such syringes for culture. If culture negative, use the syringes for injection. The stored syringes to be discarded after 2 weeks.
  C) In case facility for above two not available- Pool upto 7 patients on the day of injection. Prepare 7 aliquots of around 0.2 ml per syringe *(one syringe for one patient)* inside the OT by single puncture of the vial after proper scrubbing and using aseptic technique. Re-cap the syringes with fresh sterile needles. Keep these syringes on a sterile surface. Only use these for the patients in the same session. Discard the vial – It is NOT to be re-used or re-punctured.

- Management of post-intravitreal endophthalmitis
  - Post-injection endophthalmitis (PIE) has early presentation and worse prognosis, especially with *streptococcus viridians* as a causative pathogen.
  - The treatment in post-intravitreal endophthalmitis should be more aggressive and early surgical intervention should be preferred in post-intravitreal endophthalmitis.

- Avastin – as a drug.

Numerous trials performed worldwide (CATT trial, IVAN trial, GEFAL, MANTA) on thousands of patients have shown intravitreal Bevacizumab (Avastin®) to be non-inferior to Lucentis (Ranibizumab®) in terms of efficacy and safety. Bevacizumab, on the other hand has the advantage of reducing the cost of therapy especially in our country where population’s access to resources is limited. A recent article in *AJO* on appropriate preparation of bevacizumab for intravitreal injection by compounding pharmacies has been aptly titled – “Avastin does n’t blind people, people blind people.” So lets all follow the Guidelines strictly!

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Padma Shri Awardee

Hon Advisor Ophthalmology, Govt. of India
As the 31st National Eye Donation Fortnight draws to a close culminating in the National Eye Donation Day on 8th September, I take the opportunity to wish all DOS members a very happy and prosperous festival season and best wishes for a healthy, peaceful and enjoyable new year.

This is an exciting time for cornea specialists with lots happening on all fronts. Vibrant NGOs such as SightLife, Netram foundation, Orbis International, SightSavers, Nayan Jyoti and many others have joined hands with the Eye Bank Association of India to take our nation forwards in the endeavor to eliminate the gap between supply and demand for corneas. Innovative approaches by NPCB and NOTTO have sought to facilitate eye banking and corneal transplantation activities by streamlining and facilitating the regulatory process for registration by following an enabling approach. Corneal transplantation surgeons have their own dedicated forums such as ISCKRS and CSI to share ideas, exchange views, enhance knowledge, provide mentorship and skills transfer. Organizations like AIOS and DOS have given support by including adequate representation in scientific sessions and providing facilities for wet labs with master classes and hands on sessions. Our industrial colleagues have risen to the occasion by sponsoring various campaigns, conferences, workshops and CME programmes.

Publicity by media houses and efforts made by eye banks and partner NGOs has spread awareness messages far and wide. Use of social media and mobile phone technology has been harnessed to reach beyond previous limits. The number of donations and corneal transplants has shown a steady increase year after year. The focus on quality eye banking and improvement in utilization rates has been boosted by the availability of indigenously manufactured intermediate term corneal storage media at a reasonable cost. The pilot EBAI-SightLife centralized Cornea Distribution System has fulfilled an unmet need and become very popular with eye banks and corneal surgeons. DOS readers may like to congratulate National Eye Bank at RPC, AIIMS for having completed 50 years of serving the nation and wish it well for continuing its journey to combat needless corneal blindness.

As eye bankers one would like to see the country progress quickly to becoming self sufficient for all eye banking needs. One would wish that efforts be also channelized to reducing our unhealthy demand for corneal transplants by controlling avoidable corneal blindness through education and expansion of hygiene, sanitation and healthcare facilities to the disadvantaged and underprivileged sections of society. All members of DOS are already making a huge contribution in this field, but perhaps engaging paramedical personnel and mobilizing public health resources from all fronts is the need of the hour. We can rely on taking help of our community medicine colleagues and school health services to help strengthen our hand. A little effort can go a long way and a few steps can bridge the gap. I congratulate the DOS Executive and DOS Times team for their forward thinking approach in consistently giving EBAI a platform to promote the cause and the highly successful collaborative walk organized to promote eye donation in Delhi this year. On behalf of all EBAI office bearers and the LOC of the EBAI CME 2016, I take pleasure to invite you all to attend the Annual Corneal and Eye Banking Meet, 8th EBAI CME in Varanasi 1st and 2nd October 2016.

Yours faithfully,

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Posterior corneal astigmatism is increasingly gaining importance as a determinant of the total corneal power. Scheimpflug imagery and swept source anterior segment OCT helps in the measurement of posterior corneal power. The amount of posterior corneal astigmatism varies with the anterior corneal astigmatism; it is up to 0.5D in with the rule and 0.3D against the rule astigmatism. Factoring the posterior corneal astigmatism into intraocular lens power calculations may help in improving the accuracy of the implanted lens.

A. WHAT IS POSTERIOR CORNEAL ASTIGMATISM?

The corneal astigmatism is a sum total of the anterior and posterior corneal power. The posterior corneal astigmatism is calculated from the anterior corneal power by assuming a linear anterior to posterior corneal relationship. The refractive astigmatism of the eye is different from the anterior corneal astigmatism. Until recently the posterior corneal astigmatism was extrapolated from calculating the total corneal power from the anterior corneal keratometry and keratometric index. With advances of technology such as slit scanning scheimpflug imaging swept source anterior segment optical coherence tomography (AS-OCT) and reflective imaging it has been possible to image the posterior cornea. Koch et al found the posterior cornea to be steeper in the vertical meridian in 80% of the eyes causing an against the rule astigmatism (ATR). They also found that with increasing amount of anterior with the rule (WTR) astigmatism there is a corresponding increase in the posterior corneal astigmatism increasing up to a value of 1D. They found the posterior corneal astigmatism to be -0.3D ± 0.15D (range -0.01D to -1.10D). Thus the posterior corneal astigmatism helps offset the anterior corneal astigmatism. However in eyes with increasing amounts of ATR the mean posterior corneal astigmatism remains relatively constant. With increasing age the anterior corneal astigmatism shifts orientation from the vertical to horizontal meridian but the posterior corneal astigmatism remains unchanged. Thus the posterior corneal astigmatism offsets the WTR in younger individuals and adds to the ATR in older age groups. Posterior corneal astigmatism compensates for the anterior corneal astigmatism by 13 to 31%. In a study of corneal thickness profile using a swept source AS-OCT Ueno et al found the vertical cornea to be thicker than the horizontal cornea. Thus this study provides an anatomical correlation to the optical phenomenon of corneal astigmatism. Vector analysis studies have found that calculating the corneal astigmatism alone from the anterior corneal topography underestimates the total corneal power by a factor ranging from 0.22 to 0.28 from 1770 to 1800%. Clinically the refractive astigmatism has been known to be different from the anterior corneal astigmatism. Javal’s rule proposes a mathematical algorithm to calculate the refractive astigmatism from the keratometric astigmatism. The difference in the refractive astigmatism was earlier attributed to the crystalline lens, posterior cornea and the retina. Accurate refraction of the pseudophakic eye will yield the most reliable date of the corneal astigmatism. Posterior cornea is difficult to measure, but with improvement in technology such as the scheimpflug imaging and swept source ASOCT it is possible to calculate the posterior corneal power. Retinoscopic experiments have proven that the tilted retina does not play a major role in ocular astigmatism.

B. HOW DOES POSTERIOR CORNEAL ASTIGMATISM CONTRIBUTE TO TOTAL CORNEAL ASTIGMATISM?

Total corneal astigmatism is calculated as the combined sum of the anterior and posterior corneal power. Most of
the calculations of total corneal power measure the anterior corneal power and extrapolate the posterior corneal power from a built-in keratometric index of 1.3375 and 1.3315 of the Gullstrand schematic eye. These calculations are based on the assumption of linearity and assumption of a fixed ratio between the anterior and posterior corneal curvature. Studies have shown that this approach introduces errors of 0.50 in the estimation of corneal power. This assumption also does not hold true in corneas after refractive surgery where this ratio breaks down completely. In a study using Scheimpflug imaging the posterior corneal power was measured and the keratometric index was calculated to be 1.3281. The authors found that significant deviation from this value of 1.3281 leads to more inaccuracies of the total corneal power estimation. By physiologic measurement of the corneal parameters, Dubelma et al have calculated the keratometric index to be 1.329 ± 0.001 and Dunne et al have estimated a keratometric index of 1.3283. Thus when the IOL power is calculated using standard keratometric index of 1.3375 and 1.3315 instead of the physiologic corneal parameters significant errors into the calculation is introduced. These errors are offset by optimizing the formulae with a surgeon factor and “A constant”. Vice versa if these formulae were also used with the physiologic keratometric index significant errors of the IOL power will be estimated if they are not re-optimized.

Studies have found that the total posterior corneal astigmatism ranges from -0.26D to -0.78D. The amount of posterior corneal astigmatism varies with the anterior corneal astigmatism; approximately it is upto 0.5D in WTR and 0.3D in ATR. The anterior corneal steeper meridian shifts from the vertical to horizontal with increasing age, the posterior steeper meridian remains constant. This explains the age related compensation of the WTR and shifting of the anterior corneal astigmatism to ATR with increasing age with alignment of the anterior and posterior corneal steeper meridians.

In two different studies, Ho et al and Koch et al reported similar values of posterior corneal astigmatism of 0.28 @177.2 and 0.22±0.14 @180. Ho et al reported vertical alignment of the steep meridian n the anterior cornea in 71.8% and 96.1% in the posterior cornea. Koch et al reported a 50.9% and 86.6% vertical orientation of the anterior and posterior cornea. The mean posterior corneal astigmatism of both studies are remarkably similar in spite of different study methodology, the study by Ho et al uses the Pentacam rotating scheimpflug with vector analysis and Koch et al use ray tracing techniques on the Galilei dual scheimpflug analyzer. These findings provide evidence of the entity of posterior corneal astigmatism, its magnitude and orientation irrespective of the technique of measurement and variability of subjects.

The posterior corneal astigmatism offsets the steeper anterior corneal astigmatism in younger subjects and the adds to the corneal astigmatism in older subjects as the anterior steeper meridian shifts from vertical to horizontal with age but the posterior steeper meridian does not change orientation. These considerations are important in calculation of the toric IOL especially if the posterior corneal power is either not measured but derived from the anterior corneal astigmatism or completely ignored.

C. MEASURING POSTERIOR CORNEAL ASTIGMATISM

Cataract surgeons should have an idea of the corneal astigmatism in order to accurately implant an intraocular lens. The calculation of corneal astigmatism from the anterior corneal surface alone extrapolates the posterior corneal power. Such an extrapolation introduces an error of 0.5 to 0.6 D of with the rule and 0.2-0.3D of against the rule astigmatism. Koch et al recommend subtracting 0.5D from with the rule astigmatism and adding 0.3D in against the rule astigmatism from the calculated value in their proposed nomogram.

Several instruments can help measure the corneal power. These include manual keratometer, automated keratometer, partial coherence interferometer, atlas placido based topographer, Orbscan slit topography, i-trace ray tracer, Pentacam scheimpflug imaging, Galilei dual scheimpflug analyzer. All the systems, except the Pentacam and Galilei calculate the anterior corneal power. The posterior corneal power is derived from the keratometric index and the assumption of a fixed anterior versus posterior corneal curvature ratio. The Pentacam scheimpflug imaging measured the anterior and posterior cornea and calculates the posterior corneal power based on the refractive index and location of the principal planes. The Galilei uses Snell’s law to refract rays through anterior and posterior corneal surface and calculates corneal power using ray tracing.

Multiple comparison studies are available to compare corneal measurements using different topographers. Lee et al14 studied preoperative corneal astigmatism prior to toric IOL implantation using six different corneal topographers. They concluded that values obtained from manual keratometry could be used interchangeably with autokeratometry, partial coherence interferometry, i-Trace Orbscan and Pentacam. Shirayama et al15 also reported comparable accuracy of anterior corneal power measured with four different topographers namely, manual keratometer, Partial coherence interferometry, Atlas and Galilei. In a recent analysis of precision and agreement of corneal powers namely flat, steep and mean keratometry measurements by Topcon KR1W, iTrace, topolyzer and IOL master were not good and should not be used interchangeably15.

In a comparative analysis of the Orbscan topographer to the iTrace aberrometer the values obtained for the steep and
flat corneal meridian differed by more than 1D and hence should not be used interchangeably17. For a comparative analysis of corneal pachymetry the Orbscan II measured the lowest central corneal thickness compared to the Pentacam and Galilei. There was a wide variation of keratometry readings in the steep and flatter axis and data from the three instruments could not be used interchangeably. Inter test repeatability was good with Galilei shows the best repeatability18. In a comparative analysis of estimation of the corneal astigmatism and axis location in cataract patients the magnitude of astigmatism measured by total corneal power was more than that obtained by automated keratometry but similar to simulated keratometry, however the axis location was similar except for eyes with high astigmatism19. These findings suggest that the total corneal power follows the simulated keratometry closely as opposed to keratometry readings from the anterior corneal surface alone.

D. CALCULATING TORIC IOL POWER AFTER FACTORING POSTERIOR CORNEAL ASTIGMATISM

Posterior corneal astigmatism significantly contributes to the total corneal astigmatism. Ho et al report a 13.4% reduction of the total corneal astigmatism due to the posterior corneal surface in a Pentacam based study. They report 28.9% of study subjects have a difference of -0.50D and axis >10 degrees of the total corneal astigmatism if corneal powers are calculated ignoring the posterior corneal surface.

Reitblat et al20 in recent comparative study of five methodologies of Toric IOL power calculations estimated Toric IOL power and axis using anterior corneal astigmatism aloneby the Lenstar, Baylor toric nomogram, integrating anterior and posterior corneal astigmatism with the Lenstar; Pentacam derived true net power; and Pentacam derived total corneal refractive power. They reported a decrease of in the residual astigmatism after taking the posterior corneal astigmatism into consideration. This was found to be 81% with the Baylor nomogram, 62% with vector analysis, 64% with true net power and total corneal refractive power. The residual astigmatism decreased from 0.47D with anterior keratometry alone to 0.17D (Baylor nomogram), 0.22D (vector analysis), 0.28D (true net power) and 0.36D (total corneal refractive power), while the calculations based on total corneal refractive power remained unchanged. They recommend combining anterior keratometry with posterior tomography using vector analysis leads to lower residual astigmatism and the steep meridian of the posterior corneal astigmatism should be taken in to consideration of Toric IOL calculation when there is oblique anterior corneal astigmatism.

Savini et al21 in a detailed set of models calculated the error of refractive astigmatism following Toric IOL calculation after estimating the corneal refractive power with a placido based topographer and Scheimplug imaging, they also factored in the surgically induced astigmatism, actual IOL orientation, and effective lens position. They reported a mean cylinder overcorrection of 0.59D for with the rule astigmatism and undercorrection of 0.32D for eyes with against the rule astigmatism. This was statistically not significant when posterior corneal astigmatism was considered into the IOL power calculations. The models evaluating the role of surgically induced astigmatism, IOL orientation and effective lens position was not found to be affect outcomes significantly.

SUMMARY

Posterior corneal astigmatism influences the total corneal power. Accurate estimations of the posterior corneal power is possible by Scheimplug imaging. The posterior corneal astigmatism is oriented vertically and it does not change in orientation with age. Factoring the posterior corneal astigmatism is important in Toric IOL power calculations and cataract surgical refractive outcomes.

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Newer Modalities in Management of Fungal Keratitis

Krutika Boriwal, G.K. Das, P.K. Sahu, Nitish Kumar, Divya Jain

Fungal keratitis is a serious pathological corneal condition that commonly ends in severe visual impairment. The most common causative pathogens are Fusarium spp, Aspergillus spp and Candida albicans, varying geographically among areas. Fusarium spp and Aspergillus spp are common in tropical and subtropical eastern countries and southern US whereas Candida albicans is more common in temperate areas such as the northern US.

The most frequent risk factor for the onset of fungal keratitis is trauma mainly involving vegetative matter. Other risk factors include contact lens use, ocular surgery, ocular surface disease, previous use of topical corticosteroids, a compromised immune system and tropical humid climates.

In most of the developing countries like India, fungal keratitis represents a major problem due to the poor socioeconomic status of many people, lack of proper medical care, unavailability of topical antifungal agents and difficulties in its clinical diagnosis and laboratory work. Ocular infections of fungal etiology still remain a diagnostic and therapeutic challenge for the ophthalmologist. The difficulties are mainly related to establishing the clinical diagnosis, isolation of the fungal pathogen and paucity of effective antifungal agents and the extent to which they can penetrate the cornea.

There is a need of the hour for early detection, prompt and effective treatment of fungal keratitis before devastating ocular damage occurs. To reach this goal, more sensitive and specific diagnostic modalities are required and better treatment methods are desired. This review provides an update on management of fungal keratitis.

**DIAGNOSIS**

Prompt diagnosis and treatment are imperative to prevent vision threatening complications of fungal keratitis. Although clinical signs on slit lamp biomicroscopy such as indolent dry, rough, hyphate branching ulcers, feathery margins, elevated edges, and satellite lesions are significant findings to suspect fungal keratitis, a confirmatory tool is still desired to commence the initial treatment.

Tissue sampling and culture continues to be an imperative utility in diagnosis of fungal keratitis. Because of predilection of fungi to penetrate into deeper layers of the cornea, tissue swabbing is usually inadequate in confirming a fungal agent. A corneal scraping using a surgical blade or platinum spatula is recommended to obtain a tissue specimen. Corneal scraping also helps in debridement of the organisms and of epithelium, which may act as a barrier to penetration of antifungal agents. The material thus obtained is placed on clean microscopic slides and wet mount with 10% KOH are examined allowing direct visualization of fungal cell wall by partial digestion of proteinaceous material of host cells and stromal collagen leaving polysaccharide containing fungal cell walls intact. Sensitivity and specificity of KOH preparation has been reported to range from 62% to 99% and 73% to 99%.

Wet preparations of Giemsa and Gomori methenamine silver stain highlight hyphal fungal elements. Calcofluor white binds to chitin and cellulose on the fungal cell wall and produces a bright green hyperfluorescence on ultraviolet light.

Culture remains a necessary diagnostic step in severe corneal ulcers and suspected fungal keratitis. Sabouraud dextrose agar (SDA), which is considered to be the culture medium of choice for isolation of fungi remains the gold standard for diagnosis. Other culture medias such as blood agar (BA), chocolate agar (CA), brain-heart infusion and thioglycollate broth may also be used. However the drawback of using culture as a means of confirming diagnosis is the delay in early identification and treatment.

In cases of deep stromal keratitis with intact overlying epithelium, a 6-0 silk suture can be introduced through the level of infiltrated cornea to obtain specimens for culture.

**CORNEAL BIOPSY**

A corneal biopsy has a better yield than corneal scrapings for recovering fungi in culture negative cases. Culture of the biopsy tissue specimen is practical and may change antimicrobial therapy, resulting in improved clinical outcomes. 26 gauge needle, sterile blade, microtrephines or femtosecond laser can be used for corneal biopsy.

**IMAGING MODALITIES**

Current imaging means of diagnosis, treatment and follow-up for keratitis are limited to slit-lamp biomicroscopy. Several modalities are currently emerging, allowing for in vivo imaging of cornea.
A confocal microscope uses point illumination and a pinhole in an optically conjugate plane in front of the detector to eliminate out-of-focus signal - the name “confocal” stems from this configuration. As only light produced by fluorescence very close to the focal plane can be detected, the image’s optical resolution, particularly in the sample depth direction, is much better. Confocal microscopy provides the capacity for direct, noninvasive, serial optical sectioning of intact, thick, living specimens with a minimum of sample preparation as well as a marginal improvement in lateral resolution.

Three types of confocal microscopes are available. The tandem scanning confocal microscopy (TSCM) sheds light of high intensity through a pinhole, and a camera generates a two-dimensional image. However, the TSCM is not being produced any longer. In contrast, scanning and examination times are greatly reduced, contrast is greater, and the stroma can be imaged, with the newer slit scanning confocal microscope (SSCM), thanks to its ability to scan, in parallel, many points along the axis of the slit. The newest addition is the laser scanning confocal microscope (LSCM), which uses a coherent light source with the laser beam scanning over the back of the microscope objective by scanning mirrors. The LSCM is commercially available as the Heidelberg Retina Tomograph (HRT) 3 in conjunction with the Rostock Cornea Module (RCM), and has a class I laser that poses no risk of ocular injury. However, the LSCM poses a theoretical risk of epithelial injury as well as the possibility of producing artifacts due to its planaplaning effect. The resolution also varies between the different confocal microscopes, with 1µm/pixel in the newer LSCM HRT 3/RCM. The acquisition time is 30 images/sec in the LSCM HRT3/RCM and 25 images/sec in SSCM. In vivo confocal microscopy can be used for imaging all corneal layers and structures: epithelium, Bowman’s layer, sub-basal nerve plexus, stromal keratocytes, Descemet’s membrane, endothelial cells, and immune cells. Limitations of confocal microscopy are limited accessibility, cost and quality of images depending highly on the experience of the operating technician.

Molecular Diagnostic Techniques

The capacity of molecular methods for detection and identification of genomic material in any type of sample has allowed the diagnosis of many genetic or infectious diseases based on the DNA sequence. Molecular diagnosis of ocular infections is based on DNA detection of microorganisms by polymerase chain reaction (PCR) in ocular samples. The techniques have changed to meet the needs of both ophthalmologists and patients, and the techniques are also easier, faster, and reproducible. A variety of molecular techniques based on amplification, such as nested PCR, real-time PCR, loop-mediated isothermal amplification, and nucleic acid hybridization. PCR allows isolation of DNA fragments from genomic DNA by selective amplification of a specific region of DNA enabling analysis of DNA samples even from very small amounts of corneal sample. Nested PCR increases the specificity of DNA amplification, by reducing background due to non-specific amplification of DNA. Loop mediated isothermal amplification is an isothermal nucleic acid amplification technique in which the reaction is carried out at a constant temperature, and does not require a thermal cycler. The advantage is higher detection rates and identification of fungal pathogens in corneal samples.

Treatment

Once the diagnosis of fungal keratitis has been confirmed, treatment should be started immediately. Prompt treatment may prevent visual loss of the patient. In general, treatment of fungal keratitis is prolonged due to fungicidal activity of the antifungal agents.

Polynenes

Polynenes bind to ergosterol in the fungal cell membrane and thus weakens it, causing leakage of K+ and Na+ ions, which may contribute to fungal cell death and are effective against filamentous as well as yeasts. Natamycin has a broad-spectrum of activity against filamentous organisms. Natamycin is the only commercially available topical ophthalmic antifungal preparation under this group. It is effective against filamentous fungi, particularly infections caused by Fusarium. Used at a concentration of 5% (50 mg/ml), it had good stability and is well tolerated when used topically. However, because of poor ocular penetration, it has primarily been useful in cases with superficial corneal infection. Amphotericin B is the drug of choice to treat patients with fungal keratitis caused by yeasts. Topical administration in concentrations of 1.5 to 5 mg/ml is commonly the first choice in the treatment of fungal keratitis. The product has to be prepared from the intravenous formulation. Periodic debridement of the corneal epithelium is recommended during treatment, because the molecule’s large size hinders penetration into the cornea if the epithelium is intact. Subconjunctival administration can be used in patients with low adherence to treatment. Intracameral administration, provides higher and more sustained corneal concentrations than topical or intracameral administration. Several cases of keratitis unresponsive to topical treatment are successfully resolved after intracameral administration, but further controlled studies are still needed.

Azoles

The azole antifungals inhibit the cytochrome P450 dependent enzyme lanosterol 14-alpha-demethylase, which converts lanosterol to ergosterol, the main sterol in fungal cell membrane. Depletion of ergosterol damages the cell membrane resulting in cell death. Azoles are classified into 2 groups, imidazoles including econazole, miconazole, and ketoconazole; triazoles including fluconazole, itraconazole, voriconazole, and posaconazole.
Various routes of administration of voriconazole (VCZ) include oral, topical, intracameral, and intrastromal delivery. Targeted drug delivery of VCZ has been studied for the management of fungal keratitis not responding to standard topical therapy. Such a method of drug delivery overcomes a major limitation of topical antifungal therapy, which is poor bioavailability of drugs in cases of deep-seated fungal corneal ulcer. It provides a depot of drug, close to the ulcerated area, at a dose of 50 μg/0.1 ml in 5 divided doses, from where the drug is slowly released into the infected tissue.

Posaconazole is a new triazole, a synthetic structural analog of itraconazole. The mechanism of action involves blocking of the fungal cell wall ergosterol synthesis. In vitro and in vivo studies have shown that it has broad-spectrum activity against most Candida species, Cryptococcus neoforms, Aspergillus species, zygomycetes and endemic fungi.

Echinocandins are a group of newer antifungals, which act by inhibiting the synthesis of 1,3-β-d-glucan, leading to cell lysis due to increased permeability of the cell wall. Currently available echinocandins comprise caspofungin, micafungin and anidulafungin. Matsumoto et al. have reported successful use of topical 0.2% micafungin in cases of refractory fungal keratitis. Topical caspofungin has been used in the cases of fungal keratitis refractory to VCZ. There are limited data on the use of echinocandins to treat fungal keratitis in humans.

CORNEAL COLLAGEN CROSS LINKING

The treatment of corneal ulcers with topical antimicrobial agents has been confounded by the ability of microbes to develop resistance to the drugs used. There is therefore a need for an agent which provides complete, rapid antimicrobial activity with a minimum of toxicity. Riboflavin and ultraviolet light (UV) collagen crosslinking of the cornea induces a change in properties of the collagen and has a stiffening effect on the corneal stroma, which stabilizes it and increases its resistance to enzymatic degradation. Spoorl et al. showed that porcine corneas which underwent crosslinking were more resistant to the effects of pepsin, collagenase, and trypsin. The bactericidal and stromal strengthening properties of crosslinking make it a very attractive option for treating bacterial keratitis and this property may be used in future for treating fungal keratitis.

SURGICAL MANAGEMENT

Corneal debridement is the simplest surgical intervention for fungal keratitis. It not only debrides the corneal surface and debulks the fungal load but improves the drug penetration as well. Corneal biopsy is not only a diagnostic tool but therapeutic intervention also. The most frequently performed surgery in fungal keratoplasty is therapeutic penetrating keratoplasty. Permanent conjunctival flaps and amniotic membrane transplantation, and use of tissue adhesives are some of the other surgical methods used for the treatment of various types of fungal corneal ulcers.

CONCLUSION

Fungal keratitis remains a challenging and often elusive diagnosis. It is particularly a public health concern in developing countries where limited access to care and economic barriers can cause visual loss in a demographic that is primarily young. As with all corneal infections, proper identification of the microbe and targeted therapy can mitigate complications. Once a fungal etiology is suspected, traditional techniques of identification may not be sensitive or rapid enough for optimal outcomes. Recent advances in techniques such as in vivo confocal microscopy and the evolution of PCR promise to increase the speed and accuracy of diagnosis and may lead to initiation of prompt treatment with effective antifungals leading to improved prognosis in the management of fungal keratitis.

REFERENCES


Financial Interest: The authors do not have any financial interest in any procedure/product mentioned in this manuscript.

Attention
Those students enrolling as DOS Members between September 10 – November 2, 2016 are eligible for complimentary registration for Winter DOS 2016. (November 12-13, 2016) and DOS Teaching (November 11-12, 2016).
Chloroquine Retinopathy classically presents as a bull’s eye maculopathy but earlier screening can identify subtle changes and help in better management of the disease.

Chloroquine Retinopathy refers to the changes seen in the retina of patients on long term use of chloroquine. The late presentation, classically described as bull’s eye maculopathy, is preceded by a number of subtle changes. With the advent of new investigation modalities and regular screening, it is possible to prevent irreversible retinal damage due to this important and widely used drug. In this article we aim to highlight the ocular manifestations and recommended screening protocols.

HISTORY OF CHLOROQUINE

In the 1600s, it was discovered in Chile that the bark of the cinchona tree can cure malaria and plantations of these trees began for the production of quinine.

Both chloroquine and hydroxychloroquine are alkylated 4-aminoquinolone (4AQs) derivatives of quinine.

Chloroquine was first synthesized in 1934 by Andersag. Hydroxychloroquine was synthesized in 1946 and proposed as a safer alternative to chloroquine in 1955.

CHLOROQUINE METABOLISM

The concentration of 4AQs in different tissues after ingestion varies. In pigmented rats, the concentration of the drug after a single dose is greatest in uvea followed by liver, lung, kidney, vitreous, heart, skin, hair, brain, blood, serum in descending order. The results seen are similar in humans.

For the same dose of hydroxychloroquine and chloroquine, levels of chloroquine are 2.5 times those of hydroxychloroquine in the body tissues.

The 4AQs remain in tissues for years and are mainly excreted by the kidney and the liver.

SIDE EFFECTS OF CHLOROQUINE

Chloroquine can have a variety of ocular and systemic side effects. Long term use of the drug in auto-immune diseases particularly predisposes the patients to these adverse reactions. (Table 2).

RETINAL MANIFESTATIONS OF CHLOROQUINE

Early changes: Fine pigmentary stippling of the macula and loss of the foveal light reflex.

Late changes: This may progress to the development of an annular zone of depigmentation of the retinal pigment epithelium surrounding the fovea classically known as “bulls-eye maculopathy” (Figure 1) (Table 3).

Racial differences: Racial differences exist in the presentation of zone of depigmentation. Although the parafoveal changes remain an excellent and relatively specific clinical finding, especially in a predominantly white population, it is no more the unique presentation of retinal toxicity. There is also a pattern of pericentral retinal damage (seen in the region of the arcades) that primarily affects Asian patients but can be seen in all races.

Other changes: Optic disc pallor and atrophy, attenuation of retinal arterioles, fine granular pigmentary disturbances in the peripheral retina, and prominent choroidal patterns in advanced stage.

The appearance may correspond to the pattern of

<table>
<thead>
<tr>
<th>Table 1: Common Uses of Hydroxychloroquine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria – Treatment and Prophylaxis</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
</tr>
<tr>
<td>Systemic Lupus Erythematosus</td>
</tr>
<tr>
<td>Discoid Lupus Erythematosus</td>
</tr>
<tr>
<td>Polymorphous Light Eruptions</td>
</tr>
<tr>
<td>Solar Urticaria</td>
</tr>
<tr>
<td>Recurrent Basal Cell Carcinoma</td>
</tr>
<tr>
<td>Porphyria Cutanea Tarda</td>
</tr>
<tr>
<td>Antiphospholipid Antibody Syndrome</td>
</tr>
</tbody>
</table>

Figure 1: Right eye of a 52 year old female showing parafoveal zone of depigmentation
lipofuscin accumulation in RPE cells, which in healthy subjects is highest at the posterior pole and shows a depression at the fovea, thus explaining the annular pattern and central sparing.

There are regional variations in the retinal pigment epithelium (RPE) biochemistry. Cathepsin D, Aryl Sulfatase, and Acid Phosphatase enzyme activity is higher in the centre than in the periphery. Some of these enzymes are inhibited by 4AQs pointing to a potential association with the maculocentric distribution of 4AQ receptors.

**OTHER OCULAR MANIFESTATIONS OF CHLOROQUINE TOXICITY**

- Difficulty in near work due to loss of accommodation. This phenomenon is reversible on discontinuation of the drug and is caused by the effect of the drug on the ciliary body.
- Cornea – punctate or whorl like corneal epithelial deposits (cornea verticillata), transient corneal edema, decreased corneal sensitivity. The patient may complain of blurring of vision, haloes around light and photophobia. These changes are reversible.

**DIAGNOSIS OF CHLOROQUINE RETINOPATHY**

**Visual Field**

The earliest signs of HCQ retinopathy on a central visual field may be a cluster of paracentral points with decreased sensitivity. These points may only show mild depression. Progressive HCQ retinopathy leads to a partial bull’s eye scotoma that may resemble an arcuate defect, and in later stages may form a complete bull’s eye scotoma, with a complete ring defect and relative sparing of the fovea. White STTA (Swedish Interactive Threshold Algorithm) testing with pattern deviation plots is recommended. Whereas the 10-2 field pattern is excellent for testing the Non-Asian patients, 30-2 fields must be done for Asian patients who often present with a more pericentral defect rather than parafoveal (Figure 2).

**Optical Coherence Tomography**

High resolution cross-sectional scans of the retina using SD-OCT (Spectral Domain Optical Coherence Tomography) may detect changes in the retinal architecture before the onset of clinically apparent HCQ retinopathy. On SD-OCT, HCQ retinopathy manifests as disruption, or complete loss, of the outer nuclear layer (ONL), external limiting membrane (ELM), inner/outer segment junction (IS/OS), and retinal pigment epithelium (RPE) in the parafoveal region with foveal sparing.

This foveal sparing accounts for the “flying saucer sign” of HCQ retinopathy. Chen et al. first described the “flying saucer sign” as an ovoid appearance secondary to the intact central subfoveal architecture and the loss of adjacent perifoveal outer retinal tissue.

**Table 2: Side Effects of Chloroquine**

<table>
<thead>
<tr>
<th>Category</th>
<th>Side Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular</td>
<td>Difficulty in Reading, Blurring of Vision, Scotoma</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Nausea, Diarrhea, Loss of appetite, Vomiting, Epigastric pain</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Skeletal muscle weakness</td>
</tr>
<tr>
<td>Dermatological</td>
<td>Blue-black discoloration of skin, fingernails, oral mucosa, Bleaching of hair</td>
</tr>
<tr>
<td>Neurological</td>
<td>Headache, Dizziness, Tinnitus, Convulsions</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>Restlessness, Nightmares, Irritability</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Abnormal Liver Function and rarely fulminant hepatic failure</td>
</tr>
<tr>
<td>Others</td>
<td>Bleeding and bruising, Hemolysis reported in patients with G-6-P Deficiency</td>
</tr>
</tbody>
</table>

**Table 3: Differential Diagnosis of Bull’s Eye Maculopathy**

- Cone Dystrophy
- Stargardt’s disease
- Chloroquine Retinopathy
- Age Related Macular Degeneration
- Central areolar choroidal dystrophy
- Benign Concentric Annular Macular Dystrophy
- Fenestrated Sheen Macular Dystrophy
- Leber’s Congenital Amaurosis
- Chronic macular hole
- Inverse Retinitis pigmentosa
- Batten disease
- Bardet Biedl Syndrome
- Clofazimine Toxicity
- Hallervorden-Spatz Syndrome
- Fucosidosis
- Leigh disease

**Figure 2:** VFA 30-2 of a 45 year old lady of Indian origin being treated with hydroxychloroquine for connective tissue disorder, shows partial paracentral scotoma, sparing the foveal area.
Recently, studies have been conducted on the effects of HCQ on the inner retinal layers showed a selective thinning of the ganglion cell layer (GCL) and inner plexiform layer (IPL) without any structural changes to the outer retinal layers and RPE. Thus, developing screening methods to measure the inner layers of the retina may achieve earlier detection of HCQ.

**Multifocal Electroretinography**

Multifocal Electroretinography (mfERG) may be the most sensitive test for early HCQ retinopathy. Unlike full-field ERG, mfERG can localize deficiencies to the central macula, thereby detecting the subtle changes characteristic of early HCQ retinopathy. Specifically, paracentral reductions in amplitude, indicative of depressed retinal function, are the most specific waveform pattern for HCQ retinopathy (Figure 3).

**Fundus Autofluorescence**

Fundus autofluorescence (FAF) imaging is an in vivo imaging method that assesses the distribution of lipofuscin in the outer retina, subretinal space, and RPE.

Preceding the onset of a “Bull’s eye maculopathy” suggestive of the perifoveal outer retina and RPE damage, FAF may show subtle increase in signal intensity in this distribution secondary to early photoreceptor damage. FFA also shows the changes of toxicity but these are often very late changes (Figure 4).

**Fundus Photography**

Visible HCQ retinopathy is often a late clinical finding. It may be done only for documenting the findings and is not recommended for screening.

**Newer Tests**

(a) Microperimetry. This procedure localizes visual field test flashes accurately on the retina.

(b) Adaptive Optics Retinal Imaging. Special cameras with enhanced optics to reduce wave-front distortion can image the cone array directly and show cone damage with early disease.

**2016 GUIDELINES FOR PREVENTION OF CHLOROQUINE RETINOPATHY**

The American Academy of Ophthalmology (AAO) has released recent guidelines for screening of patients who are being treated with chloroquine/hydroxychloroquine for various conditions.

The most critical risk factor for chloroquine retinopathy is the daily dose by weight as opposed to the cumulative dose as was previously thought. The other important risks are listed below (Table 4).

Lesser risk factors include elderly age group, co-existing liver disease and genetic predisposition to HCQ toxicity (eg. abnormalities in ABCA4 gene, polymorphisms in Cytochrome p450).

Rationale for screening – HCQ and CQ retinopathy are not reversible and cellular damage may progress even after the drugs are stopped. When retinopathy is recognized early, before RPE damage, there is only limited progression after discontinuation of the drug and fovea is spared.

**Screening Frequency** – If the patient is not being overdose and does not have co-existing risk factors, AAO recommends that annual screening can be deferred till there has been 5 years of exposure to the drug. (Table 5)

**Recommended Screening Tests** – AAO recommends Automated Visual Fields and SD-OCT be done in all cases being screened for hydroxychloroquine retinopathy. Other tests may aid the diagnosis (Table 6).

**Table 4: Major Risk Factors for Toxic Retinopathy**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily Dosage</td>
<td>Daily dose by weight as opposed to cumulative dose</td>
</tr>
<tr>
<td>Hydroxychloroquine (HCQ) &gt;5.0 mg/kg real weight</td>
<td></td>
</tr>
<tr>
<td>Chloroquine (CQ) &gt;2.3 mg/kg real weight</td>
<td></td>
</tr>
<tr>
<td>Duration of use &gt;5 years, assuming no other risk factors</td>
<td></td>
</tr>
<tr>
<td>Renal disease Subnormal glomerular filtration rate</td>
<td></td>
</tr>
<tr>
<td>Concomitant drugs Tamoxifen use</td>
<td></td>
</tr>
<tr>
<td>Macular disease May affect screening and susceptibility to HCQ/CQ</td>
<td></td>
</tr>
</tbody>
</table>

**Table 5: Screening Frequency**

<table>
<thead>
<tr>
<th>Screening Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Screening</td>
<td>Fundus examination within first year of use</td>
</tr>
<tr>
<td></td>
<td>Add visual fields and SD-OCT if maculopathy present</td>
</tr>
<tr>
<td>Annual Screening</td>
<td>Begin after 5 years of use</td>
</tr>
<tr>
<td></td>
<td>Sooner in the presence of major risk factors</td>
</tr>
</tbody>
</table>

**Table 6: Examination Techniques**

| Primary Tests            | Ideally do both Automated visual fields (appropriate to race) SD OCT         |
|                         | Other Objective Tests (as needed or available)                              |
|                         | mf-ERG                                                                       |
|                         | FAF                                                                          |
| Newer Tests of Possible Value in Future Microperimetry Adaptive Optics Retinal Imaging |

**Table 7: Tests Not Recommended for Screening**

<table>
<thead>
<tr>
<th>Test</th>
</tr>
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<tbody>
<tr>
<td>Fundus examination</td>
</tr>
<tr>
<td>Time-domain OCT</td>
</tr>
<tr>
<td>Fluorescein Angiography</td>
</tr>
<tr>
<td>Full-field ERG</td>
</tr>
<tr>
<td>Amsler grid</td>
</tr>
<tr>
<td>Color testing</td>
</tr>
<tr>
<td>Electro-oculogram (EOG)</td>
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</tbody>
</table>
CONCLUSION

There exists no dietary or medical therapy which has proven effective in preventing, treating, or reducing the risk from HCQ or CQ retinopathy. Even stopping of the drug does not prevent progression of retinopathy, although progression is mild if the toxicity is recognized before there is RPE damage. Once definitive signs of retinopathy are recognized, the decision to stop medication should be made in conjunction with the patient and the prescribing medical physician to ensure that medical risks are managed.

The patient can be advised about the risk of further visual loss depending on the severity of the retinopathy. Screening for retinopathy thus plays a very important role in detecting retinal changes at the earliest before permanent loss sets in.

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Financial Interest: The authors do not have any financial interest in any procedure/product mentioned in this manuscript.
Germain ophthalmologist Gerd Meyer-Schwickerath first pioneered retinal photocoagulation in the 1940s when he focused natural sunlight into the eye. The invention of the argon laser in 1968 by Francis L’Esperance used an ionized gas lasing medium and led to the widespread use of lasers. Contemporary techniques of Neodymium-doped yttrium aluminum garnet (Nd:YAG) and diode lasers use solid-state platforms that utilize crystals and semiconductors respectively. These lasers introduced in the 1980s have become popular because of their portability and ability to deliver laser in both continuous and pulse modes.

The fact that iatrogenic retinal burns are absolutely essential for effective laser treatment of retinal vascular disease has been universally accepted for almost 5 decades, and still remains the popular perception. Considering the time-honoured consistency of opinion regarding the indispensable role of laser-induced retinal damage, the discovery that laser treatment which does not cause any retinal damage can be at least effective as conventional retinal photocoagulation is unforeseen. If using lasers to burn the retina represents the pivotal advance in the treatment of retinal disease, then learning that those retinal burns are unnecessary may fundamentally revise our understanding of not only retinal laser treatment but also the disease process itself.

**MECHANISM OF PHOTOCOAGULATION**

Photocoagulation occurs due to protein denaturation induced by absorption of radiant energy by the ocular chromophores (the melanocytes in the Retinal Pigment Epithelium (RPE) and the choroid). A traditional laser burn creates a heat wave that spreads from the origin of the burn site in the RPE and/or choroid. The grayish-white endpoint in conventional threshold photocoagulation implies that the thermal wave has reached the overlying neurosensory retina with a temperature high enough to alter the natural transparency of the retina, scattering incident light, which creates the white appearance. This appearance is usually associated with a temperature rise of 20°C to 30°C above baseline body temperature. Unavoidably, the thermal damage extends beyond the visible burn as surrounding temperatures rise 10°C to 20°C above the baseline, leading to the phenomenon of laser scar expansion over time.

Full-thickness retinal damage may not be needed to obtain beneficial effects of laser photocoagulation. Contemporary advances show that the benefits of laser photocoagulation may be derived from the regulation of cytokines mediated by the RPE cells leading to the repair of the outer and inner blood-retinal barrier. It is postulated that such regulations are more likely to occur in RPE cells that have only been sub-lethally injured at temperatures lower than those required to produce clinically visible spots. Laser photocoagulation decreases the intraocular concentrations of vascular endothelial growth factor and RPE derived transforming growth factor beta II (TGF-bII) while upregulating pigment epithelium-derived factor.

**THE MICROPULSE LASER**

In 1990, Pankratov reported development of a new laser modality designed to deliver laser energy in short pulses (micropulses) rather than as a continuous wave. In continuous wave mode, the laser energy is delivered as a single pulse of 0.1-0.5 sec that constitutes the exposure duration. In a micropulse mode, the laser energy is delivered with a train of multiple repetitive short pulses of 100-300 msec called the ON time within an envelope of 0.1-0.5 sec. This envelope duration constitutes the exposure duration T. The ratio between the ON time and the period T is called the duty cycle (expressed as a percentage). A lower duty cycle and shorter ON time, lessens the heat build-up, and thus causes less thermal retinal damage and smaller retinal lesions. Dorin noted that the period T should not be shorter than 2 msec (1/500 sec) and the duty cycle should not exceed 15%.

**SUBTHRESHOLD DIODE MICROPULSE LASER (SDM)**

Laser induced thermal elevation that does not result in any visible retinal damage during or after the laser application, is called subthreshold laser treatment. SDM protocols using a micropulse 810 nm diode laser were initially described by Friberg and Hamilton. Thermal retinal destruction using conventional lasers leads to decreased metabolic demand, debulking of the diseased retina, increased oxygenation of the retinal tissue and altered production of vasoactive cytokines. However, with SDM applications, there is no thermal damage to the retinal tissue and thus inflammation and loss of functional retinal tissue are completely avoided.
called subthreshold laser treatment. SDM protocols using a micropulse 810 nm diode laser were initially described by Friberg\textsuperscript{13} and Hamilton\textsuperscript{14}.

Thermal retinal destruction using conventional lasers leads to decreased metabolic demand, debulking of the diseased retina, increased oxygenation of the retinal tissue and altered production of vasoactive cytokines. However, with SDM applications, there is no thermal damage to the retinal tissue and thus inflammation and loss of functional retinal tissue are completely avoided. This is achieved by using exposure durations shorter than the time required for heat to diffuse to the surrounding tissues. SDM thus ends heat production before thermal diffusion can occur. Laser pulses shorter than 100 msec are used in SDM which restrict thermal diffusion to the vicinity of the RPE, sparing the neurosensory retina.

SDM not only selectively targets the RPE but also avoids lethal heat build-up within it. This retains the ability of the RPE to contribute in a therapeutic response. The RPE secretes many factors that may mediate the pathogenesis of retinal diseases. While drug therapy specifically targets a few of these factors, SDM induces alterations in the expressions of multiple factors physiologically by normalizing viable RPE cells\textsuperscript{15–17}.

Also, clinical effects of cytokines follow a U-shaped curve, where small physiologic changes in cytokine production caused by SDM may result in an on/off phenomenon rather than a linear dose-response relationship. This might explain the efficacy of SDM observed at the lowest reported irradiances\textsuperscript{18}. Side effects like reduction in visual acuity, contrast sensitivity, colour vision; poor night vision, choroidal neovascularisation, serous retinal detachments and angle closure glaucoma are significantly reduced and viable retinal tissue is preserved rather than being destroyed. Both extensive clinical experience and in-vitro studies of laser-tissue interactions show that increasing irradiance may simply increase the risk of thermal retinal damage without improving the therapeutic effect\textsuperscript{19}.

Contemporary studies suggest that the therapeutic changes in RPE cytokine production caused by conventional photocoagulation come from cells at the margins of laser burns, affected but not destroyed by laser exposure. With SDM, all areas of the RPE exposed to laser irradiation are preserved, and can contribute therapeutically. SDM contiguously performed over all areas of retinal pathology maximizes the effective surface area of RPE that can functionally contribute to the therapeutic response as compared to conventional laser therapy\textsuperscript{20}.

It is likely that conventional photocoagulation and SDM both have a common final pathway of improved retinal function and therapeutic modulation of cytokine production in viable, sub-lethally affected RPE cells. This effect is produced indirectly by conventional photocoagulation by the spread of thermal energy in, only the non-

Figure 1: Fluorescein Angiography Images of a pt with Chronic serous chorioretinopathy before and after treatment with the SDM laser.

Figure 2: OCT of the same patient before and after treatment. Visual acuity improved from 6/60 to 6/6, 2 weeks after treatment.
targeted RPE cells surrounding the laser burn, while it is produced directly by SDM in all targeted RPE cells irradiated with SDM. Thus, retinal destruction appears to be unnecessary and undesirable for effective laser treatment.

**USES OF SDM**

**Diabetic Macular Edema**

SDM has been shown to be as effective as conventional laser in treating diabetic macular edema. It also permits confluent treatment of the affected areas and also retreatment of these areas in cases of recurrence of edema. Compared to the modified ETDRS protocol, SDM has shown no statistically significant difference in visual acuity, macular thickness and leakage on fluorescein angiography. Mean macular sensitivity as measured by microperimetry has been found to decrease with the modified ETDRS protocol while it improved with the use of SDM21. Many patients with early diabetic macular edema may be asymptomatic, with good visual acuities. The risk of adverse effects of conventional photocoagulation may not be acceptable in these patients. SDM allows us to offer them early treatment, when it is more likely to prevent visual disability and irreversible visual loss.

**CENTRAL SEROUS CHORIORETINOPATHY (CSC)**

Bandello pioneered the use of SDM for the treatment of chronic CSC in 2003. He found 100% resolution of CSC that was maintained at 4 months of follow up in his study. Fluorescein angiography or fundus biomicroscopy did not show any retinal changes resulting from the treatment. Further studies have supported the finding that SDM can be used to treat CSC without producing retinal damage (Figures 1 and 2)22. To deal with the problem of no visible end point of treatment, indocyanine green dye can be used to identify active leaking sites while sparing the neurosensory retina25.

**MACULAR EDEMA IN BRANCH RETINAL VEIN OBSTRUCTION (BRVO)**

Parodi et al were the first to report that SDM was similar in efficacy to conventional laser in treating macular edema secondary to BRVO. This treatment modality did not leave any biomicroscopic or angiographic signs27. SDM preceded by intravitreal triamcinolone injection has shown superior results to conventional laser alone in BRVO associated macular edema29. SDM may reduce macular thickness in patients with visual acuity better than 20/40 in BRVO associated macular edema, without decreasing visual acuity27. A recent study by Parodi et al evaluated the effect of SDM versus intravitreal Bevacizumab injection in BRVO patients having recurrent macular edema following treatment with conventional laser. Bevacizumab showed superior outcomes both anatomically and functionally in these patients26.

**PROLIFERATIVE DIABETIC RETINOPATHY**

Luttrell et al found SDM to be comparable to conventional laser in treating proliferative diabetic retinopathy. The response to SDM was however slow to develop and was without the retinal contraction associated with conventional laser therapy. It may be useful in patients having marked neovascularisation as conventional therapy may cause retinal contracture and detachments.

**CONCLUSION**

The absence of an ophthalmoscopically visible endpoint to guide and titrate treatment regimens is the single most important difficulty in the popular use of the SDM. Also no standardised treatment protocols for SDM have yet been formulated. The evolution of the SDM has lent further credit to the thought that retinal damage is not essential to produce therapeutic effects of laser treatment. As more studies are carried out, our fundamental understanding of basic retinal disease pathology may potentially change. As of now though, Subthreshold Micropulse Diode Laser is still a science in its infancy and many more studies and standardization of its treatment protocols are required for its widespread use.

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Retinal Vasculitis – Approach to Diagnosis and Management

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Retinal vasculitis is a sight threatening inflammatory eye disease which involves the retinal blood vessels, predominantly retinal veins. Clinically, it presents as fluffy white perivascular infiltrates in the retina with aqueous and vitreous inflammatory cells (Figure 1). Fluorescein angiogram shows staining and diffuse leakage from the retinal blood vessels with or without cystoid macular edema. The etiology of the disease is varied. It may occur as an isolated ocular condition, as a manifestation of infectious or neoplastic disorders or in association with systemic inflammatory diseases. Hence, it is essential that a complete history, ocular and systemic examination and a detailed laboratory work up is done in all patients with retinal vasculitis.

CLASSIFICATION
Retinal vasculitis can be classified as follows.
1. Systemic diseases
2. Infectious diseases
3. Ocular diseases
4. Malignancies
5. Drug induced

SYSTEMIC DISEASES
Sarcoidosis, Behcet’s disease, Multiple sclerosis, Systemic lupus erythematosus, Wegeners granulomatosis, Polyarteritis nodosa, Relapsing polychondriitis, seronegative arthropathies, Polymyositis, Dermatomyositis, Antiphospholipid antibody syndrome, Takayasu arteritis, Crohn’s disease

INFECTIOUS DISEASES
Tuberculosis, Toxoplasmosis, Syphilis, Herpes, Cytomegalovirus, Leptospirosis, Cat scratch disease, Candidiasis, Rickettsia, Amoebiasis, Brucellosis

OCULAR DISEASES
Idiopathic, Intermediate uveitis, Eales’ disease, Birdshot retinochoroidopathy, Frosted branch angiitis, Serpiginous choroiditis, Idiopathic retinal vasculitis, aneurysms and neuroretinitis (IVRAN).

MASQUERADERS
Leukemia, Lymphoma, Retinoblastoma

Figure 1: Fundus photograph of a patient with retinal vasculitis showing perivascular cuffing and retinal hemorrhages.

Retinal vasculitis is a sight threatening inflammatory eye disease which involves the retinal blood vessels, predominantly retinal veins. Clinically, it presents as fluffy white perivascular infiltrates in the retina with aqueous and vitreous inflammatory cells with hyperemia in the acute stage. Chronic stage of the disease shows macular ischemia, neovascularization of retina and disc, sheathed vessels and optic atrophy.

Sarcoidosis - This disease typically affects young adults and presents with bilateral hilar lymphadenopathy, ocular and skin lesions. Ocular involvement is seen in 25-50% of patients with systemic sarcoidosis. Retinal vasculitis is a characteristic feature and mainly involves retinal veins. These venules are

DRUG INDUCED
Immunoglobulins, Rifabutin, Metamphetamines

SYSTEMIC DISEASES ASSOCIATED WITH RETINAL VASCULITIS
Behcet’s disease – It is a multisystem inflammatory disease which is diagnosed by the clinical triad of recurrent orogenital ulcers, skin lesions and uveitis. It is strongly associated with HLA-B51. Erythema nodosum, arthralgia and meningoencephalitis are also commonly seen. Ocular involvement is seen in 70% of patients. It usually presents as recurrent vaso-occlusive retinopathy which affects both arterioles and veins in the posterior pole (Figure 2). Fundus examination shows retinal hemorrhages, yellow white retinal infiltrates, retinal edema and optic disc edema.
usually mid-peripheral or peripheral in location and show short segments of perivascular cuffing (Figure 3) associated with retinal infiltrates, sarcoid nodules, snow ball vitreous opacities and optic disc edema. Yellow perivenous exudates, classically described ‘candle wax drippings’ (taches de bougie) may also be seen.

Wegener’s Granulomatosis – It is a granulomatous necrotizing vasculitic condition that primarily affects upper and lower respiratory tracts and kidneys. Ocular involvement occurs in 28-58% of patients with Wegener’s Granulomatosis. In addition to retinal vasculitis, other clinical findings include episcleritis, scleritis, peripheral ulcerative keratitis, dacryocystitis and proptosis.

Systemic lupus erythematosus - Patients present with malaise, fatigue, anorexia and low grade fever. They may also have arthritis, facial rash, alopecia and pleurisy. Fundus examination shows multiple cotton wool spots, dilated, tortuous arterioles and intraretinal haemorrhages (Figure 4). Retinal vasculitis is usually uncommon but very devastating. It causes severe vaso-occlusive disease leading to retinal ischemia and proliferative retinopathy.

Infectious Diseases Associated With Retinal Vasculitis

Tuberculosis – Though choroiditis is the most common ocular feature of tuberculosis but periphlebitis is also commonly present. It occurs either by direct infection or by hypersensitivity reaction to Mycobacterial antigens. It is associated with vitritis and retinal hemorrhages and may lead to branch or central retinal vein occlusion leading to neovascularization and vitreous hemorrhage.

Toxoplasmosis – Toxoplasmic retinochoroiditis caused by the obligate...
intracellular parasite, Toxoplasma gondii, commonly presents with focal necrotizing retinitis associated with retinal vasculitis either near to or distant to the active lesion. Perivasculitis is believed to be caused by an Arthus type reaction. Locally produced antigens diffuse into the vessel walls and react with circulating antibodies, activate complement and recruit inflammatory cells that form a perivascular cuff. Focal perivascular exudates or plaques, called Kyrieleis arteriolitis are also seen near the active focus and these lesions do not cause vascular obstruction or leakage (Figure 5).

Syphilis – Syphilis is a sexually transmitted disease caused by spirochete Treponema pallidum. It can have protein ocular manifestations. Retinal vasculitis though mainly arterial, has been described in secondary and tertiary syphilis causing occlusive vascular disease. Other clinical findings can be vitritis, chorioretinitis, neuro retinitis, optic neuritis, macular edema, subretinal neovascularization and exudative retinal detachment.

Herpes virus – Retinal infections with herpes group of viruses cause necrotizing retinitis, vasculitis, and retinal hemorrhages. Acute retinal necrosis caused by herpes simplex and zoster viruses is a fulminant peripheral necrotizing retinitis with severe vitritis, occlusive vasculitis affecting arterioles in the retina and choroid, optic atrophy and rhegmatogenous retinal detachment. Cytomegalovirus in immunocompromised patients causes fluffy white necrotic lesions along the vascular arcades of the posterior pole with retinal hemorrhages and vasculitis described as ‘cottage cheese with catsup’ or ‘pizza pie’ retinopathy (Figure 6). The vasculitis is caused by perivascular neutrophilic infiltration of both arteries and veins.

**OCULAR DISEASES ASSOCIATED WITH RETINAL VASCULITIS**

Intermediate uveitis is characterized by vitreitis, snowball exudates, peripheral retinal periophlebitis and pars plana exudates.

Eales’ disease is an idiopathic obliterator periophlebitis which commonly occurs in healthy young males between 15-40 years of age. It starts anterior to the equator and progresses posteriorly and ultimately involves multiple quadrants of the retina. This inflammation induced vascular occlusion leads to proliferative vascular retinopathy with sequelae as recurrent vitreous hemorrhage and tractional retinal detachment. The etiology of this disease is still unknown, however it is believed to be due to hypersensitivity to tuberculoprotein.

Birdshot retinochoroidopathy is a bilateral panuveitis where fundus examination shows cream colored, deep, round lesions, retinal vasculitis and cystoid macular edema.

Frosted branch angiitis is a rare vasculitis where thick inflammatory infiltrates surround the retinal arterioles and venules create an appearance of frosted tree branches (Figure 7). The sheathing of the blood vessels is so extensive that the underlying vessels are obscured. Mostly, it is idiopathic, but cases have been reported in herpes, rubella, cytomegalovirus infections and malignancies. It occurs in young, healthy individuals who typically present with acute bilateral visual loss.

**PATHOGENESIS**

Retinal vasculitis is presumed to be an immunologically mediated condition. It is an autoimmune phenomenon and various studies have shown the presence of CD4 +ve T cells within and surrounding the retinal vessels in patients with retinal vasculitis. Thus, cell mediated immunity plays a major role in the pathogenesis, however humoral immunity and immune complex formation can also be involved.

**CLINICAL FEATURES**

**History**

It is very important to elicit a history of systemic complaints in a patient with retinal vasculitis in order to have a tailored investigational approach.

- Orogenital ulcers, arthralgia, skin rash Behcet’s disease
- Weight loss, cough, skin lesions, hilar lymphadenopathy Sarcoidosis
- Night fever, sweats, cough with expectoration Tuberculosis
- Joint pains, backache Seronegative arthropathy
- Neurological symptoms Multiple sclerosis
- Thromboembolic episodes Anti-phospholipid antibody syndrome
- History related to recent infections, foreign travel, sexual habits, contact with animals should also be elicited.

**SYMPTOMS**

Patients usually complain of gradual painless loss of vision except where
vasculitis involves the macula and there is sudden loss of vision. Presence of floaters is due to the inflammatory exudates in the vitreous cavity. Scotomas, photopsias, color vision alterations and metamorphopsia may also be found.

**SIGNS**

Slit lamp examination may show aqueous or vitreous cells, aqueous flare, keratic precipitates, posterior synechiae and posterior subcapsular cataract.

Fundus examination reveals fluffy white exudates around retinal vessels in the form of either continuous or skip lesions. Vascular sheathing, retinal hemorrhages, retinal edema and arteriovenous anastomoses are seen in cases where venous are the site of inflammation. Cotton wool spots which represent nerve fibre layer infarcts are mainly seen in systemic vasculitic diseases. Intra-retinal infiltrates are characteristic of infectious causes of retinal vasculitis except for Behcet’s disease. Vitreous snow ball exudates and cystoid macular edema are seen in intermediate uveitis, sarcoidosis and tuberculosis. Chronic stage of the disease shows vascular occlusion, neovascularization of the disc or retina, vitreous hemorrhage, branch retinal vein occlusion, sclerosed vessels and optic atrophy.

Involvement of retinal venules is more common in conditions like Behcet’s disease, tuberculosis, sarcoidosis, Eales’ disease, multiple sclerosis, inflammatory bowel disease and sero negative arthopathies. Retinal arterioles are involved in systemic vasculitis and viral retinitis. Retinal capillary involvement occur commonly in syphilis and whipple’s disease.

**MANAGEMENT**

**Investigations**

As retinal vasculitis is associated with various systemic, ocular and infectious diseases, a detailed laboratory work up is always essential. A thorough medical history and physical examination should be the basis for a focused diagnostic evaluation. The initial evaluation should include complete blood count, erythrocyte sedimentation rate, C-reactive protein, VDRL, FTA-ABS, mantoux test, angiotensin converting enzyme, rheumatoid factor (RA) and antinuclear antibody (ANA), urine analysis and chest x-ray/computed tomography of the chest.

If an infectious etiology is suspected, especially in retinal vasculitis associated with dense vitreitis, investigations should include ocular fluid cultures, serological tests and polymerase chain reaction. Serological tests are done for toxoplasma, syphilis, lyme disease and cat-scratch disease. Polymerase chain reaction in ocular fluid specimens has been extremely useful in identifying herpes simplex, varicella zoeter, cytomegalovirus and toxoplasma gondii.

In patients with non infectious systemic diseases, diagnostic tests should be focused on systemic vasculitic syndromes. Laboratory work up includes rheumatoid factor, anticardiolipin antibodies, anti-neutrophil cytoplasmic antibodies, complement levels, and imaging studies.

**TREATMENT**

The main goal of treatment in retinal vasculitis is suppression of intraocular inflammation in order to prevent visual loss secondary to macular edema macular ischemia and retinal detachment. The mainstay of therapy is corticosteroids and immunosuppressives. In case of an infective lesion, specific therapy against the infective agent with or without corticosteroids (started 2-3 days after the anti-infective therapy) may be required.

Corticosteroids may be given either systemically or by posterior subtenon's injection. Periocular steroids are useful in patients with unilateral and mild inflammation. Though this route avoids
the systemic side effects, it carries a risk of raised intraocular pressure and globe perforation. Oral corticosteroids (in the dose of 1-1.5 mg/kg/day) are given in patients with moderate to severe bilateral inflammation and a marked decrease in visual acuity. Severe cases of sight threatening retinal vasculitis involving the posterior pole may require intravenous methyl prednisolone (pulse therapy for 3 days) followed by oral corticosteroids and immunosuppressives. Intravitreal steroid injections can also be given in cases of refractory macular edema. Both periocular and intravitreal corticosteroids are avoided in infectious vasculitis including toxoplasmosis and acute retinal necrosis.

In cases, where retinal vasculitis does not respond or shows inadequate control to oral corticosteroids, steroid sparing immunosuppressive agents are useful. These drugs are also used in patients who develop intolerable side effects to oral steroids. Various immunosuppressive agents used for treatment of retinal vasculitis include azathioprine, cyclosporine, cyclophosphamide, methotrexate, mycophenolate mofetil and infliximab. The choice of immunosuppressive agent should be individualized for each patient with a specific systemic disease. Azathioprine, cyclosporine and infliximab are used in Behcet’s disease. Alkylating agents like cyclophosphamide are often used with systemic corticosteroids in vasculitis associated with systemic autoimmune diseases like Wegener’s disease and systemic lupus granulomatosus.

Topical steroids with cycloplegics are given in cases with co-existing iridocyclitis.

Other modalities of treatment in retinal vasculitis are laser photocoagulation and vitrectomy. Laser photocoagulation is indicated in patients with retinal neovascularization, with recurrent or non-clearing vitreous hemorrhage and neovascular glaucoma. As photocoagulation may induce cystoid macular edema, intraocular inflammation must be adequately controlled prior to laser treatment.

Vitrectomy is useful in patients with non-clearing vitreous hemorrhage, tractional retinal detachment and epiretinal membrane removal.

**CONCLUSION**

In summary, retinal vasculitis is not only a potentially blinding intraocular inflammatory condition, it can also be the first sign of a lethal systemic disease. A detailed history, ocular and physical examination with a focused laboratory work up in a patient with retinal vasculitis can help in prompt diagnosis and appropriate management of the disease.

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As we talk about FLACS (Femtosecond laser assisted cataract surgery) the debate starts whether FLACS is superior then conventional phacoemulsification. Are we achieving superior outcomes with FLACS, are the result consistent and so on. Various articles have been published which talk about safety and efficacy of FLACS over conventional phacoemulsification. There are studies, which compared the outcomes of two techniques done by the same surgeon, but they never talked about the experience the operating surgeon had in using FLACS platforms. Most of the time, ophthalmologists start using the FLACS after getting few tips from company engineers and watching a few videos. So when the ophthalmologists start doing FLACS, they face many challenges in terms of patient position, docking, centration, depth adjustment, suction loss, partial cut capsulorhexis, posterior capsular tear, incorrect position of wound incisions and the list goes on. Beginners face these intraoperative challenges more commonly.

When the ophthalmologists start doing FLACS, they face many challenges in terms of patient position, docking, centration, depth adjustment, suction loss, partial cut capsulorhexis, posterior capsular tear, incorrect position of wound incisions and the list goes on. Beginners face these intraoperative challenges more commonly.

This article will talk about various surgical difficulties that can be encountered while doing FLACS and the correct way to deal with it.

The first Femtosecond Laser assisted Cataract Surgery was performed by Dr. Zoltan Z Nagy of Hungary in 2008. The first article on Femtosecond laser assisted cataract surgery dates back to winter of 2009/2010. Since then, various FLACS platforms are available to us. Dr. K P Reddy of Hyderabad did the first study for Victus (B&L) in India in 2009.

**LIST OF FLACS PLATFORMS AVAILABLE WORLDWIDE**

1. LenSx (Alcon Laboratories, Inc.)
2. Lensar (Lensar, Inc.)
3. Victus (Technolas)
4. Catalys (Optimedica)
5. Zeimer Z8 (Zeimer)
6. Intralase (Abbott Medical Optics)

Switching over to a newer technique or newer technology is always a challenge for anyone. As a beginner to FLACS, most of the surgeons are well versed with phacoemulsification techniques. It would not be a correct decision to by-pass the conventional phacoemulsification learning and directly start doing FLACS.

**PRE OPERATIVE PRECAUTIONS**

A thorough pre-operative evaluation is a must for FLACS cases as the surgeon is still in learning phase and encountering an unwanted situation is more common than conventional phacoemulsification. Counseling the patient about FLACS is very tricky. It is a good idea to tell patients the advantages about FLACS like precise corneal incisions, truly bladeless, low ultrasound energy used and faster healing but make sure that the patients’ expectations from surgery are realistic.

Make sure that the patient can lie flat and remain still. This is a unique challenge to the Laser Cataract Surgery. In a manual Cataract surgery it is possible to sedate the patient, but not in Laser Cataract surgery where most of the times the patient has to be shifted to a different sterile theatre and also the patient remaining awake to fixate is necessary for proper central docking.

Special consideration in preoperative planning for FLACS is to look for the deep-set
eyes, as it is difficult to dock these eyes. Many a times its better to go for conventional phacoemulsification in these eyes. Most of the surgeon operates these in cases under topical anaesthesia but few uses peribulbar block also. Chemosis caused by block can cause suction loss.

Alert patient about the postoperative red eye especially in patients on anticoagulants should be aware of postoperative red eye due to subconjunctival hemorrhage. Rarely a large subconjunctival bleed may make it difficult to dock or get a good suction and it is always wise to stop these drugs a few days before FLACS.

Corneal opacity should be looked for because laser doesn’t pass through corneal scars and such cases will have inadequate cuts in areas of scar.

Pupil dilation should be at least 1 mm more then the desired rhexis size otherwise laser would damage the iris and cause intraoperative bleeding. NSAID eye drop instillation 1 hour before Laser helps to maintain pupillary dilation during and after laser procedure. After preoperative preparations, all the patient data is to be fed in the laser machine and machine should be checked for energy delivery.

PRECAUTIONS DURING THE LASER TREATMENT

The first thing to get right is proper docking of eye to laser system. Many a times incorrect docking is the main culprit for the entire problem faced during FLACS. The tip to get the correct docking is explaining the patient where he or she has to look, tell patient not to get scared if things go dark for sometime. Not to move the eye while laser delivery is on. Check for the centration. When docking the patient make sure that the patient’s eye is flat to the patient interface and looking into the fixation light for a central dock. If there is a significant tilt the corneal incisions will be more towards visual axis causing astigmatism and the capsulorhexis will be incomplete. In such situations it’s better not to open those incision and make new incision with a side port knife.

If bubbles are present in the interface, undock and re-dock because bubbles obstruct the path of the laser delivery and compromise its effect on cornea as well as lens. There may be no/incomplete corneal incisions, capsulotomy and nucleus fragmentation.

Make sure you do everything to stop losing the suction. Conjunctiva sucked into the interface or an oblique dock should be recognized early and de-dock - re-dock done.

Another essential point is to note grade of nuclear sclerosis in preoperative evaluation, as the surgeon has to feed this information before starting laser. Laser cannot break hard cataracts with laser settings of soft cataract.

In another situation of corneal incisions becoming more towards Limbus or going into conjunctiva thereby can cause bleeding and difficulty in opening the incisions.

There is an option of designing the corneal incision. Three-step self-sealing wound can be created with laser.

MANAGING THE CAPSULOTOMY

Capsulotomy is usually circular, of desired size and complete.

In a few cases there might be a few areas where the capsulotomy is still attached, recognizing these attachments or incomplete capsulotomy is crucial as pulling them may cause tear in the capsulorrhexis.

The viscoelastic should be injected in such a manner that it flattens the anterior capsule and the surgeon by pressing the center of the anterior capsule can recognize these adhesions or areas of incomplete capsulotomy better and complete it with forceps. If capsule elevates with viscoelastic and folds upon it, incomplete capsulotomy can be missed and by pulling the capsulotomy it may get torn.

An oval bubble underneath the capsule is a pathognomonic sign of incomplete capsulotomy 9 out of 10 times and surgeon should be cautious.

In mature white cataracts with liquefied cortex, as soon as the capsulotomy begins there is release of white fluid into the anterior chamber that interferes with the laser and both the capsulotomy and the nucleotomy remains incomplete. In these cases if energy is increased the results are better. The foot should be removed from the pedal as soon as the fluid starts oozing and pressed after increasing the energy setting.

REMOVING THE NUCLEUS

Pupil constriction immediately after laser treatment is unique to this procedure and could be due to inflammatory response of laser. This makes it difficult to perform the subsequent steps. I put a drop
of tropicamide + phenylephrine immediately after laser and by the time the patient is draped for manual steps, the pupil dilates sufficiently. The effect is quick due to microscopic breakdown of epithelium due to increased IOP during docking. Pupil dilating devices like Malyugin ring can be used with FLACS.

Nucleus fragmentation can be planned in different configuration. There are various options available for lens fragmentation. Most common patterns used are 4, 6, 8 or 16 segments with lens softening. The Gas bubble formed after laser capsulotomy can be trapped behind the nucleus and can cause posterior capsule rupture if hydro dissection is done quickly or with pressure. Gas should be “burped” by gentle hydro dissection along with slow rock-and-roll of nucleus to release the gas into anterior chamber.

Hydro dissection in FLACS is different than after manual capsulorhexis, which separates the capsule from intact cortex, and a nice fluid wave happens. After laser capsulotomy, the underneath cortex is also cut to some depth and to find a cleavage between capsule and cortex is difficult. This leads to partial fluid wave along some depth of cortex and causes the sticky cortex remaining with the capsule needing extra effort to pull it. Also sometimes there are capsule tags from laser capsulotomy, barely visible unless the surgeon is careful, causing a tear in rhexis if pulled inadvertently. As nucleus is fragmented into multiple small pieces, Low or No phaco energy is required to emulsify it.

There are few case reports, which talked about posterior capsular rupture due to laser. This kind of problem occurs due poor docking and not paying attention to intraoperative OCT. Cortical wash is little bit difficult in FLACS because laser cuts anterior cortical plate along with capsulorhexis and in the same zone. Bimanual techniques are useful in this situation.

At the end the surgeon should be careful about tiny cubes of nucleus left behind the Iris or in the capsular bag. Gently irrigating the space behind the Iris and also in the bag will push them out of these hiding areas. These may cause unexplained recurrent anterior chamber reaction and need to be washed later.

FLACS is suitable for most of the cataract cases but still few challenging situation in which FLACS should be deferred. 1. Narrow palpebral aperture 2. Very deep set eyes 3. Advanced glaucoma cases 4. Presence of filtering bleb 5. Post Keratoplasty eyes 6. Posterior synechiae 7. Corneal opacity, Scar, RK incisions

FLACS is a new technology, which has been adopted worldwide. After the initial hiccups and fewer complication the ophthalmologists are adopting the FLACS and utilizing it in various challenging situation like small pupil, subluxated cataract, pediatric cataract and so on. Evolving techniques and better experience of the machines is making FLACS the treatment of choice for cataract surgery across the globe.

It will be appropriate that all patients be informed before surgery that if needed surgery can be converted to conventional phacoemulsification for the safety and better outcomes.

*And Above All Experience Counts.*

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IOL Power Calculations (Part-2) – Formulae and Optimization

Saurabh Sawhney, Ashima Aggarwal

“Mathematics, rightly viewed, possesses not only truth but supreme beauty.”

– Bertrand Russell

The information generated by biometry describes the physical parameters of the eye, most importantly the corneal power and the axial length. This information then needs to be processed to produce the IOL power. To do this, we need to take the help of formulae.

Formulae are like little magic boxes. You put in some input data, they work their magic, and put out an output that you can use. The best part about these magic boxes is that you need not really know how the magic works; they will still work for you. However, there is a particular kind of joy to be experienced if you do, in fact, understand the cogwheels.

There are a lot of formulae that can take your biometry data and produce an IOL power. It is probably impossible to cover all of them in a book, let alone an article, so we will take a lateral look at things. The reason that so many formulae exist is quite simple; none of them work perfectly. This is because the eye is an exceedingly complex piece of optical workmanship, and we cannot yet measure every single aspect of it. So we resort to simplifications, and this produces errors. This chapter will look at the basics of how an IOL power formula is constructed. It also seeks to identify some of the more common problem areas, and strategies for reducing the errors.

A BRIEF HISTORY

The need for calculating lens power dates back to Ridley era, when the very first IOL ever implanted resulted in a large myopic refractive error1. This error led to the immediate realization that an implant was insufficient; it had to be the correct power as well, in order to benefit the patient. The earliest strategy was to factor in Ridley’s result, and reduce the IOL power for the next patient, till reasonably acceptable results were had. Of course, the definition of reasonable back then was considerably more relaxed. This strategy needed no input data. Pretty soon, a standard IOL power was deemed as the panacea for all. In the USA, 18.0 D Binkhorst pre-pupillary lens found favour2. It was supposed to leave the patient with the same amount of refractive error as he had before the cataract developed. This situation continued for close to two decades.

In 1967, Fyodorov developed his theoretical formula, which was based on geometric optics, and required the measurement of keratometry and axial length as input factors. This spurred research in the field, and soon Colenbrander, Thijssen, Van der Heijde and Binkhorst had each published their own version of theoretical formulae. All these apparently disparate formulae were actually structurally identical except for the correction factors used Figure 1. Shows the basic theoretical formula.

The development of these early formulae pushed the development of ultrasonic axial length measurement systems, which improved quickly and dramatically both in ease of use and accuracy. This led to more and more interest in the calculation of IOL power, and emmetropia began to be seen as a realistic goal.

In 1980, independent researchers published data emanating from large IOL series, looking at the results obtained by the implantation of different lenses3-4. The regression analysis of this data threw up several interesting conclusions. All researchers concluded that axial length, followed by keratometry, were the most important determinants of implant power. They also concluded that measurement of preoperative anterior chamber depth had a miniscule effect on improving the prediction, and therefore a 2-variable formula would suffice. The regression formula produced using the data were almost identical, and a collaboration between the authors led to unification of these raw equations, producing the famous SRK formula (Figure 2).

For the first time, this formula introduced the concept of a lens-specific constant, acknowledging the influence of lens design and placement on the calculations.

The early theoretical and regression formulae are also known as first generation formulae.

SECOND GENERATION FORMULAE

It was noticed that for ‘regular’ eyes, the first generation formulae did quite well, but they faltered when extremely long or short eyes were encountered. There was a need to adjust the formulae in some way to allow for the influence of axial length to be accurately factored.

The second generation regression formula, the SRK II, was developed by adding a special value called the C-value, to the original SRK formula (Figure 3). Other approaches, such as Hoffer’s adjustment of ACD, and the modified Binkhorst Formula, also used the measured axial length as a means to apply correction to the theoretical formula. These formulae, theoretical or regression, were termed the Second Generation formulae.

THIRD GENERATION FORMULAE

In 1988, Holladay proposed a direct relationship between
the steepness of the cornea and the positioning of the IOL. The more steeply curved the cornea, the further away from the corneal apex the IOL would be placed (Figure 4). He published the Holladay 1 formula, in which the final IOL placement was determined by the height of the corneal vault, and the distance between the IOL and the iris. The corneal height was calculated using Fyodorov’s equation. The second aspect of the calculation, the distance from the iris plane to the IOL, was recognised as an IOL specific number, since different styles of IOL would finally settle down at different distances behind the iris. Holladay called this distance the Surgeon Factor (SF). He determined the surgeon factor for a series of cases with the same type of IOL. This was done by means of back-calculation of the formula, using complex quadratic mathematics applied to actual post-operative results. Each case had a different SF, and the whole series

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was then averaged to produce a mean SE. This provided a lens-specific surgeon’s factor which could be used prospectively with the Holladay 1 formula.

In 1990, Sanders, Retzlaff and Kraff presented their own version of the theoretical formula, which adopted Holladay’s premise of postoperative AC depth being linked to the height of the corneal vault. This was called the SRK/T formula.

Two years later, Hoffer modified this formula, using the tangent function of the keratometry reading to achieve a similar effect. Since Tan (45) is equal to 1, Tan (40) is 0.84, and Tan (50) is 1.19, this usage of the tangent function by Hoffer is a very clever exploitation of the numerical coincidence that the average keratometry is approximately 45 Dioptres. The new formula came to be known as the Hoffer-Q formula.

The third generation formulae are all two-variable formulae that depend upon axial length and keratometry to provide estimates of the final position of the IOL in the eye, a quantity that has been termed Effective Lens Position (ELP) by Holladay.

FIFTH GENERATION FORMULAE

Haigis introduced his formula in 1999. The formula is built on the same theoretical base as all others, and differs only in the way the ELP is calculated. Haigis proposed using three different constants to better define the ELP. These constants are called the a0, the a1 and the a2 constants. The three constants can be used as standard, optimized, or triple optimized.

In the standard form, none of the constants is optimized. The first constant, a0, is derived from the A-constant using a standard equation (Figure 6). The a1 and a2 constants are set at default values, a1=0.4 and a2=0.1. Single or triple optimization of the Haigis constants can improve prediction accuracy, but requires a large number of cases.

WHICH FORMULA TO USE AND WHEN?

The formulae generations are summarized in (Figure 7). There is obviously a lot of choice, and that calls for a decision making protocol. Based on international experience, a number of suggestions have been put forth. The salient points to be considered are

1. With modern computing resources, ease of calculation is no longer a factor. Once programmed, each formula is just a matter of typing in the input data and reading off the result.
2. For the same input variables, formulae can sometimes produce markedly different results (Figure 8).
3. Formulae seem to perform differently at different axial length ranges. This is because of the underlying assumptions made when the formulae were crafted. These assumptions hold true, broadly, in the middle of the Bell’s curve, but as extremes are tested, they start to buckle under the pressure. Therefore, different formulae have been suggested for different axial length ranges. These recommendations are summarized in (Figure 9).
4. Theoretical formulae are superior to regression formulae. Therefore, the use of SRK and SRK II is not recommended any longer. Many biometry machines still carry these, of course, but they should not be used in the routine course.
5. The performance of any formula will improve after proper optimization.
6. Many surgeons consider outputs from several formulae, instead of relying on just one.

OPTIMIZATION

All formulae were derived from experiences with patients. This meant that any inherent bias in the sample selected got ingrained in the formula as well. So the formula represents a basic calculation structure that needs to be adjusted, so that it can accurately reflect the situation in the surgeon’s own practice. In essence, we are seeking to replace the formula author’s bias
with our own. In addition, different IOLs behave differently in the eye, and that has a bearing on the calculations. This adjustment for various IOLs is also performed by means of optimization.

WHAT DOES OPTIMIZATION MEAN?

With the exception of the Haigis formula, all other currently popular IOL formulae utilize a single ‘lens-constant’ for completion of the calculation, the rest of the terms of the formula being derived from measurable data. These constants are named differently for different formulae. For example, the SRK group of formulae uses the term A-constant, while Holladay employs a different constant called the Surgeon’s Factor (SF), and Hoffer-Q formula is characterized by the pACD, or the personalized anterior chamber depth. Since each of these formulae is constructed differently, the constants are also different and cannot be used interchangeably between formulae.

However, they do share a commonality. Apart from the lens constant, all other terms of a formula are either fixed, such as corneal refractive index and vertex distance, or directly measured, such as keratometry and axial length. This means that lens specific parameters which might influence the IOL power, such as design, haptic angulation, material etc do not have any bearing on the rest of the formula. Therefore, all these factors can only be incorporated into IOL calculations by means of including them in the IOL constant.

Optimization is the process of finding the specific value of a lens constant, which when used for that particular IOL type, will result in the most accurate IOL power calculations. For a group of patients for whom a particular type of IOL has been implanted, optimization is performed by calculating the lens constant in such a manner that the formula produces the exact refractive error that was actually encountered in that eye. Such a value of the lens constant would make that formula ‘perfect’ for that specific case.

AN EXAMPLE

The way to do this is to look at the formula itself. Let us take the example of the basic SRK formula. The equation reads

\[
P = A - (2.5 \times AL) - (0.9 \times K)
\]

This can be rearranged very easily to isolate A, by shifting all other elements from the right side to the left.

\[
P + (2.5 \times AL) + (0.9 \times K) = A
\]

If the terms on the left are known, i.e., ideal IOL power, axial length, and keratometry, then it is possible to calculate the A-constant. The catch here is the ideal IOL power. How does one know what IOL power would be ideal?

To determine the ideal IOL power, the final, stable, postoperative refraction is required. This will tell us how far things went off the prediction. It is important to remember that the refractive error at the spectacle plane is not the same as that at the IOL plane. Therefore, if an IOL of power 20.0 D produced an error of +2.0 D, it would be incorrect to assume that the ideal IOL power would have been 22.0 D.

To calculate the ideal IOL power using spectacle plane refraction, a Refractive Factor (RF) is needed. The RF is a value that needs to be multiplied by the refractive error, to give us an estimate of the error at the IOL plane. Retzlaff et al have used an RF value of 1.25 when the IOL implanted was more than 16.0 D, and a value of 1.0 otherwise. Modern estimates of this value are usually in the range of 1.3 to 1.8, with variations dependent on eye anatomy.

If we take RF = 1.25, then in our example, the ideal power (\(Power_{\text{ideal}}\)) would have been

\[
Power_{\text{ideal}} = Power_{\text{used}} + \text{Refractive Error} \times RF
\]

For myopic errors, the minus sign of the error would result in a lower ideal IOL power.

Now that ideal power is available, the A-constant can be calculated. See (Figure 10) for a sample calculation. Of course, the problem is that the ideal IOL power may not be accurately calculated by means of a presumed RF. This is a limitation of this form of optimization.

This process of back-calculation of the A-constant has to be repeated for several cases involving the same IOL model and surgery type. In each case, the A-constant is likely to be different. All these values are then averaged, and the resultant value is the optimized A-constant. This can be used for prospective calculations in place of the A-constant provided by the manufacturer.

It must be remembered that the A-constant calculated in this manner is specific to the SRK II formula, and cannot be used with the SRK/T.

TACKLING COMPLEX MODERN FORMULAE

Unlike SRK II, modern theoretic formulae such as the SRK/T, Holladay, Hoffer Q or Haigis offer extended scope
of calculations, including calculation for ametropia. Therefore, it is possible to predict the refractive error that is expected when a certain power of IOL is implanted. This is so because the calculation for RF is internalized in these formulae.

This changes the strategy for optimization. There is no attempt to determine the lens constant that would have produced the ideal IOL power, which remains a nebulous entity. Instead, we seek to back calculate the ametropic equation, so that the derived lens-constant would predict a refractive error equal to the actually observed refractive error. This side steps the ideal IOL problem and involves only real, measurable values.

In contrast to the calculation for the SRK II formula, the calculations for these other formulae are complex and require the resolution of quadratic roots, making them difficult to understand and perform manually. It is better to use a free online calculator called the Lens Constants Optimizer v5.1 that performs the task automatically and accurately (see web resources).

The Lens Constants Optimizer v5.1 requires the user to fill in columns on a pre-programmed MS Excel(TM) sheet (Figure 11). For each complete record, the lens constants are back calculated automatically by the software. These constants are then evaluated for outliers, and the extreme individual values truncated. This is important as it ensures that any cases that do not form a part of the general group statistically are eliminated. By eliminating these outliers from the analysis, the performance of the formula for the ‘normal’ cases can be improved. The program calculates the optimized lens constants for five popular formulae, namely the SRK II, The SRK/T, Hoffer-Q, Holladay 1, and Haigis.

To be truly effective, optimization needs to done separately for different types of eyes. Thus, lens constants calculated for myopic eyes will be different from those calculated for hyperopic eyes. This obviously increases the requirement of data. One must also realize that optimization is a continuous process that needs to be repeated periodically for it to remain relevant. A large study by Aristodemou et al shows that when using optical axial length measurements, the benefits of optimization far exceed any differences that the choice of a third generation formula can provide. This clearly underscores the need for all surgeons to optimize.

OPTIMIZATION VERSUS PERSONALIZATION

The process of optimization can be taken further, by only considering data from a specific pool. For instance, one such pool might consists of eyes that have been operated upon by surgeon Dr. X, using biometry device B, keratometry device C, and the measurements having been performed by Mr. D. Such narrow focussing is called personalization, and it refines optimization. Personalization allows the incorporation of systematic errors of the measurement devices, as well as individual bias of the surgeon or technician. This further improves IOL power prediction accuracy to an extent.

DYNAMIC IOL OPTIMIZATION

One of the more recent strategies for IOL power optimization is called Dynamic IOL Optimization. This is a powerful personalized analysis system that bypasses the conventional optimization of the lens constants, and instead focuses on the relative performance of the formulae as a whole. Conceptually, it can compare an infinite number of IOL power calculation algorithms.

The software has a user-friendly interface that runs on the MS Excel(TM) platform. The user is required to fill in the IOL model names, the surgeons’ names etc, as a one-time exercise, with an option for later additions. Following this, the database is created, wherein the user enters case details including biometry, IOL details, and postoperative refraction. A minimum of eleven complete entries are required before the program can generate optimized IOL powers. This is a safeguard to ensure statistical robustness.

When IOL power calculation is required, the user enters the case-specific biometry details and chosen IOL model. The program then automatically scans the database and chooses a niche cohort. This cohort comprises of eyes that have a structural configuration that is similar to the test eye. The parameters for this selection are axial length and keratometry. This ensures that when optimizing the IOL power for an unusual eye, for example a myope, only the matching portion of the database that contains similarly myopic eyes will be evaluated.

Once the niche cohort is chosen, the program then automatically evaluates the relative performance of different
IOL formulae in that cohort. Outliers are automatically excluded. This information is then prospectively applied to the test case, yielding a single, usable IOL power.

Dynamic IOL optimization offers several advantages to the surgeon. First and foremost, it is easy to use. There is no need for additional equipment purchase, as it works to make the most of the existing data. The user need not choose a formula as per the ocular configuration. Instead, there is a smooth surface of prediction based on the surgeon’s own clinical outcomes. Since lens constants are bypassed, there is no need to consider separate values for the contact, immersion or optical methods of measuring axial length.

The program works continuously. As new data is added, the optimization protocol recalculates everything. New information is thus constantly incorporated into the system. This is better than optimizing the lens constants every now and then, doing it for different formulae, and for different axial length ranges. Since cohort selection is continuous rather than discrete, there is zero data wastage. The entire process of DIO is facilitated by a very simple user interface.

AUDITING OF RESULTS

There is no scope for improvement if we don't analyse and introspect. In the context of IOL power calculations, such auditing of results helps to compare formulae and optimization strategies amongst each other. Due to considerable confusion in the past, a clear set of guidelines now exists to report IOL power related data. There are six key measures that are to be reported: In recognition of the fact that comparison of ideal IOL powers is likely to be error-prone, all comparisons are done for actual or predicted refractive errors.

1. Mean Error (ME) and standard deviation (SD) in prediction.
2. Mean Absolute Error (MAE) and standard deviation (SD) in prediction.
3. The percentage of eyes ± 0.5 D from the predicted target refraction.
4. The percentage of eyes ± 1.0 D from the predicted target refraction.
5. The percentage of eyes > 2.0 D from the predicted target refraction.
6. Range of errors from maximum plus error to maximum minus error.

In order to perform an audit, we recommend using software tools. The IOL Formula Audit Calculator v1.6 is a free tool available online (see web resources) which helps you to do just this. It requires the user to enter biometric and postoperative refraction data as input. It then automatically calculates the above mentioned parameters, and displays them in a grid form (Figure 12). SRK/T, Hoffer-Q, Holladay 1, and Haigis formulae are evaluated and compared, with the possibility of adding two more IOL power calculation formulae or protocols as per the user’s choice. Since the use of SRK II is no longer recommended, the audit calculator does not evaluate this formula by default.

OTHER APPROACHES TO IOL POWER CALCULATION

Apart from modifications of the Fyodorov thin-lens vergence formula, several other promising approaches are now being developed. One of these is the Olsen formula with the C-constant, which uses ray tracing and incorporates thick lens optics, thereby presenting a truer picture of the optics of the eye. The use of this formula requires additional measurement of the anterior chamber depth and lens thickness.

Intraoperative aberrometry is another radically different approach, with the strategy of measuring the actual refractive status of the eye during surgery, after the cataract has been removed. This precludes the need for any preoperative measurements, and has been shown to be effective in routine cases as well as surgeries where the eye has previously undergone a refractive surgery.

The Hoffer H-5 uses gender and racial data to tweak the IOL power prediction. The Barrett Universal II formula claims good results across the board. The Ladas Super Formula is another approach that is based on conventional third generation formulae and the Haigis formula. A promising new area of development is the Radial Basis Function formula by Dr. Hill, which employs pattern recognition techniques. This is presently at the beta-testing stage.

These are exciting times for IOL power calculation. As many of these new approaches find acceptance, things can only get better for the cataract surgery patients.
SUMMARY
The process of deriving IOL power from the data collected during biometry is a complicated but rewarding exercise. Understanding the nuances help in achieving better post-operative refractive results. The process of optimization, whether by conventional optimization of the lens constants, or using commercially available software incorporating Dynamic IOL optimization, is absolutely essential if accuracy of predictions is to be improved. Once the surgeon has made efforts to improve the refractive outcomes, the process should be monitored using a systematic auditing protocol.

REFERENCES

WEB RESOURCES
1. The free to use software mentioned in this article can be downloaded from any of these sites. You may also contact OphthalmicCalculators@gmail.com or Facebook/OphthalmicCalculators for the same.
   b. www.softpedia.com/publisher/Dr-Saurabh-Sawhney-Dr-Ashima-Aggarwal-100741.html

FINANCIAL DISCLOSURE: Both authors have proprietary interest in Dynamic IOL Optimization.
With the Vivinex™ intraocular lens (IOL), HOYA has developed a new IOL material platform that is intended to fulfill the following requirements and conditions:

- Hydrophobic acrylate.
- Glistening-free and biocompatible.
- PCO inhibiting.
- Robust and compressible (for safe implantation through incision size as small as 2.0mm).
- Fast and controlled unfolding inside the eye.
- Stable anchoring of the IOL haptics in the capsular bag (for good predictability of the post-operative axial position and refraction with as little dispersion as possible).
- Minimization of aberrations caused by decentration and tilting (coma in particular).
- Rotational stability (as toric IOL).
- Compensation of inherent decentration and tilting of the capsular bag relative to the visual axis by IOL optic.
- Sharp-edged, thin optic edge for inhibition of PCO and prevention of dysphotopsia and volume reduction.
- Preloaded delivery of the IOL in a disposable injector system.

What is particular about the new lens material is the special surface treatment with ozone and UV light, which creates a stronger adhesion of the IOL to the posterior capsule. In animal experimentation, this reduced the layer thickness of the lens epithelial cells in the space behind the lens by a quarter. In this way, the migration inhibiting effect of the sharp optic edge should be enhanced by a direct material effect hindering proliferation.

In the laboratory, the development of glistening, even under stress conditions, was negligible. Decentration and tilting had comparatively few negative effects on the image quality, and there are few cases of dysphotopsia at a diagonal light incidence.

During a pilot study in Japan on 30 eyes, only one YAG capsulotomy was required within three years postoperatively and two thirds of the eyes displayed a completely clear posterior capsular bag.

The new Vivinex™ IOL is currently undergoing systematic clinical testing at the University hospital in Vienna, encompassing all of the criteria previously mentioned. The rotational stability has already been measured exactly, from the end of the surgery on. The regenerative cataract is compared with market-leading IOLs in a bilateral benchmark study utilizing objective, automated scoring of high-quality retroillumination photographs. The indication for a possible YAG laser capsulotomy is standardized and the calculation of the capsulotomy rates is carried out in consideration of the failure of the treated eyes, using an algorithm developed specifically for this purpose. Fibrotic PCO and glistening are quantified using a subjective scoring process.

We were able to certify an outstanding rotational stability to the Vivinex™ lenses: In over 100 eyes, no rotations of more than 5° were measured, with a median of 1.5 ± 1.2° (diagram 1). This is owed to the overall diameter and the haptic tension, such as the adhesive power and coarseness of the haptic surfaces. Right from the first week, the refraction remained stable. The target refraction was reached exactly, with an SD of 0.5 diopters. Most eyes developed a slightly diffuse fibrosis of the rhexis leaf with no shrinking tendency; no increase in lens epithelial cells on the IOL optic was observed. It is still too early for an assessment of the regenerative cataract; up to now, the posterior capsule has remained clear. The injector system is easy to use and works very well if filled with BSS or Ringer; it is activated in 3 steps, it is easy to guide into a 2.0 mm incision and the injection of the implant is very controlled. With gentle counterclockwise rotations, the proximal haptics can be maneuvered in one movement into the fornix of the capsular bag.

In summary, the iSert® injector system, preloaded with the Vivinex™ IOL, combines the possibility of swift, safe implantation in one movement into the capsular bag with highly promising implant performance that could set new standards in rotational stability and cataract performance that could set new standards in rotational stability and cataract prevention.
Posterior capsular opacity (PCO) is the most common late onset complication after cataract surgery. PCO develops after cataract surgery over few months to years. After cataract and secondary cataract are other names for PCO. Incidence of PCO is decreased over past few decades with advancement in surgical techniques, intraocular lens (IOL) material and design. However, it still remains the common cause for suboptimal visual outcome after cataract surgery. Incidence of PCO ranges from 5 to 50% in eyes after cataract surgery for senile cataract. It was reported to be higher in myopic population by Ignjatovic while Vasavada et al reported no significant difference between the myopic and normal population. Hayashi et al reported higher incidence of PCO in diabetic cataract as compared to non-diabetic patients. Visual axis opacification (VAO) caused by PCO is common after cataract surgery and IOL implantation in children and reported to occur in upto 40% of patients seven with posterior capsulotomy during primary surgery. Epithelial cells proliferate on anterior vitreous face along with posterior capsule. Incidence of VAO has been reported to be much higher in patients without primary posterior capsulotomy. Low recurrence was found in patients with Nd:YAG laser capsulotomy.

MECHANISM

PCO is mainly of two types, fibrous (Figure 1) and pearl (Figure 2), sometimes combination of both. PCO develops due to abnormal proliferation and migration of LECs (lens epithelial cells). LECs are located on inner surface of lens capsule at anterior, pre-equatorial and equatorial region. LECs at equatorial region proliferate throughout life to form lens fibres which lay down in concentric manner. Fibrous PCO forms from LECs lining the anterior capsule which is clinically seen as wrinkles on the posterior capsule at the site of fusion of the anterior and posterior capsules while pearl or proliferative PCO forms from LECs lining the pre-equatorial zone of lens capsule which is clinically seen as clusters of swollen, opacified differentiated LECs called as bladder or Wedd cells.

PCO develops mainly by 3 processes - proliferation, migration and differentiation of LECs. Proliferation occurs most frequently in first week following the surgery. Risk factors that promote proliferation include residual cortical matter, iris pigments and cells from blood due to break down of aqueous barrier. In vitro and animal studies have shown that many growth factors and cytokines help in formation of PCO. They stimulate fibroblastic proliferation and attachment of LECs to posterior capsule. Of all, transforming growth factor β (TGF-β) and fibroblast growth factors 2 (FGF-2) are important for development of PCO in humans. Migration of LECs towards posterior capsule is facilitated by various adhesion molecules, integrins and hyaluronan receptors. Abnormal differentiation of LECs forms bladder cells and myofibroblasts and lays down cellular material to form opacification.

PREVENTION

The modifications which could help in prevention of PCO are related to the surgical technique, intraocular lens, and the use of various therapeutic agents.

Surgical techniques related-
Continuous Curvilinear Capsulorhexis (CCC)
Adequately sized, circular CCC is associated with decrease in development of PCO.

Cortical Cleaving Hydrodissection
Cortical cleaving hydrodissection creates gap between the lens capsule and cortical matter and hence helps in complete removal of cortical matter. It is believed that the hydraulic force created during hydrodissection helps to remove LECs. Multi quadrant cortical cleaving hydrodissection helps in early and complete removal of epinucleus and cortical matter.

Hydrodissection with rotation
Cortical cleaving hydrodissection with rotation creates friction force which removes significant amount of LECs and cortical matter fibers.
Figure 1: Fibrous type

Figure 2: Elschnig Pearls
Cortical clean up

Complete removal of cortical matter in areas like sub-incisional part and deep capsular fornices is difficult and necessary. Use of bimanual irrigation and aspiration may aid in complete removal.

Polishing of anterior capsule

Polishing of anterior capsule has a role in decreasing fibrotic type of PCO while it is less effective for proliferative type11.

In the bag fixation of IOL

In the bag fixation of IOL optic with haptics is required to reduce incidence of central PCO. IOL provides barrier for migration of LECs. Incidence of PCO was found to be more in sulcus fixated IOLs as compared to in the bag fixation12.

Buttonholing of posterior capsule

Posterior continuous curvilinear capsulorhexis (PCCC) with posterior buttonholing of IOL haptic through it can be done to prevent development of PCO. IOL optic prevents migration of LECs into retrolental space and posterior capsule over anterior edges of optic prevents formation of anterior capsular fibrosis. But the procedure is skill dependent and needs to be done with caution in selected cases.

Anterior capsule overlap of IOL optic

Difference in size of CCC causes variable anterior capsular overlap of IOL optic. If the size of the capsulorhexis opening is smaller than optic then adhesions will form between anterior capsule and IOL optic which will keep anterior capsule away from posterior capsule and will decrease the posterior migration of LECs. Conversely, if size of capsulorhexis is larger than IOL optic, adhesions will form between peripheral anterior capsule and posterior capsule forming Soemmering ring. It will trap LECs and cortical matter and prevent posterior migration of LECs. The size of this continuous capsulorhexis has not got any significant effect on severity of PCO13.

The anterior capsular overlap leads to variable incidence of PCO formation with different IOL materials. It remains an important factor for eyes with PMMA IOLs and Silicone IOLs14. However, it is not the crucial factor in eyes with the Acrylic IOL implantation15.

IOL related-IOL design and material

IOL optic size, edge, angulation of the haptics and material play an important role in preventing PCO. Meacock WR et al reported less PCO with 6 mm optic size as compared to 5.5 mm optic16. Sharp IOL optic edge can create bend on posterior capsule and forms barrier for migration for LECs. Square edge IOL optic was found to be more effective than round edge IOL optic to exert more pressure on posterior capsule and to reduce PCO formation17. Angulated IOL haptics also decrease PCO formation by inducing more pressure on posterior capsule.

Hydrogel IOLs are associated with maximum occurrence of PCO. Acrylic IOL is associated with lesser amount of PCO formation when compared to PMMA and silicone18. Acrylic material has lesser tendency to induce cellular proliferation and Soemmering ring formation.

Single piece versus multi piece IOL design

No significant difference was seen between development of anterior and posterior capsular opacity with use of single piece and multi piece Acrylic IOLs19.

Therapeutic agents

Many drugs like anti-proliferative, anti-coagulant, anti-inflammatory, anti-adherence, anti-migratory, have been tried to decrease incidence of PCO.

Anti-proliferative:

Drugs like 5-fluorouracil, mitomycin C, duanomycin, octreotide, colchicines and duxorubicin were tried in vitro but outcome was not significant.

Anti-coagulant

Heparin decreases inflammation and reduces PCO formation. Heparin-surface-modified PMMA IOLs were associated with less incidence of PCO formation19. Irrigation of eyes with heparin solution (25 IU/ml) before implantation of IOL was significantly associated with less PCO as compared to non-irrigation group11.

Anti-inflammatory

Indomethacin, diclofenac sodium and cyclosporin A reduce inflammation by decreasing release of cytokines and prevent proliferation of LECs. Topical diclofenac drops were tried in post operative period without any satisfactory results.

Anti-adherence and anti-migratory compounds

These compounds do not allow attachment of LECs to the posterior capsule and prevent migration of LECs to the posterior capsule. The various anti-migrating and anti-adherence compounds tested are ilomastat (a matrix metalloproteinase inhibitor), mibebradil (Ca-channel inhibitor), RGD peptide, EDTA, and coating an acrylic IOL surface with MPC polymer.

MANAGEMENT

PCO involving visual axis can cause cloudiness of vision, glare and decreases visual acuity, and contrast sensitivity. PCO can be managed by invasive and non-invasive methods using Nd:YAG laser capsulotomy.

Invasive method

Surgical removal of capsular opacity is considered in selected cases as Nd:YAG laser capsulotomy is effective alternative and it avoids potential surgery related complications like vitreous loss and endophthalmitis22. Surgical removal is done in cases of visual axis opacification in young children, thick PCO and cases where Nd:YAG laser capsulotomy is ineffective in clearing visual axis.
Posterior capsule can be approached through limbal route or pars plana route. Surgical removal of PCO using 25gauge transconjunctival sutureless vitrectomy in children was evaluated by Lam et al. All cases showed significant improvement in visual acuity.

Pars plana capsulotomy incases with PCO in which the Nd:YAG laser was not successful in clearing the visual axis was performed by Mitra et al and they found success in penetrating the thick pupillary membranes.

Non-invasive method

Aron-Rosa and Fankhauser proposed use of Neodymium:yttrium-aluminum-garnet (Nd:YAG) laser capsulotomy as an effective treatment for PCO in 1980s. Though Nd:YAG laser capsulotomy is an effective procedure, it has many complications.

CONTRAINDICATIONS OF ND:YAG LASER CAPSULOTOMY

Absolute
1. Corneal scarring or edema - inadequate visualization of target aiming beam and interference in Nd:YAG laser optics makes outcome unpredictable and unreliable.
2. Glass IOL: chances of complete fracture of glass IOL.
3. Inability to maintain stability of eye: risk of inadvertent damage to adjacent intraocular structures.

Relative
1. Active intraocular inflammation: procedure induces some inflammation so it is to be better avoided.
2. Cystoid macular edema: cases of CME after capsulotomy have been previously reported due to break down of barrier functions of posterior capsule.
3. High risk of retinal detachment.

TECHNIQUE

Preoperative Assessment
Complete ophthalmological history and examination should be carried out before proceeding.
1. Direct ophthalmoscopic visualization of PCO is most reliable method for assessment.
2. Slit lamp biomicroscopy and retroillumination.
3. Laser interferometry to assess potential vision.

Procedure
1. Abraham central contact lens or Peyman lens can be used to stabilize the eye. Contact lens has added advantages of improved laser beam optics and accurate focusing.
2. Minimum amount of laser energy is desired to create opening and in most cases, capsule can be opened by using 1-2 mJ/pulse.
3. Stress lines in capsule are seen as wrinkles in the posterior capsule and shots are placed at stress lines for maximum effect per shot.
4. Aim laser shots at posterior 150 um from a datum point to avoid IOL damage and effective outcome.

Types of opening
1. ‘Cruciate Opening’ - begin superiorly at 12 o’clock position and proceed downwards towards 6 o’clock position. After creating central opening, shots are given at edges near 3 o’clock and 6 o’clock positions. But pit marks and cracks may happen in visual axial region which can cause glare and also a possibility to increase vitreous floaters by broken pieces of capsule during the procedure.
2. ‘Can Opener Method’ - laser capsulotomy is done along the circumference of the optic. It has the advantage to prevent potential damage to IOL in visual axis, but cut capsular fragment might obscure visual axis.
3. ‘Inverted -U Method’ - capsular fragment remains attached to inferior part of opening. But it is associated with the problem of early visual recovery as time is needed for a flap to sink in intravitreal space due to gravity and get contracted.

5.4 ‘Circular Pattern with Vitreous Strand Cutting’ - this method is expected to improve the drawbacks of conventional procedures. It involves cutting of vitreous strands attached to capsular fragment by laser along with circular pattern.

6. Size of opening - capsulotomy size should be large enough to cover pupil under mesopic conditions and avoid glare from edges that usually occurs during driving at night. Small opening is better in eyes with dense membrane that gives excellent optics as well as eyes at risk of retinal detachment.

Postoperative care
Immediately after the procedure, topical brimonidine, apraclonidine or beta-blocking agents should be administered in eye to minimize post procedure IOP spike. IOP rise is transient in most of the cases. In cases of vulnerable optic nerve head like advanced glaucoma, oral hyperosmotic agents can be used during and after the procedure.

Though most of cases do not require any medications, topical steroids and cycloplegics can be given on individual basis for a few days. Topical antibiotic drops are instilled after the procedure if contact lens is used.

COMPLICATIONS

Rise in intraocular pressure
Elevation in intraocular pressure is most common complication after Nd:YAG capsulotomy. Various mechanisms include trabecular meshwork obstruction by debris, acute inflammatory cells, swelling of ciliary body, pupillary block and liquid vitreous. Peak elevation occurs within first 6 hours of capsulotomy which usually returns to baseline within a week.

Cystoid macular edema (CME)
CME develops in 0.5 to 2.5% of cases. It might be due to shockwave damage to vitreous and release of inflammatory mediators.

IOL pitting/ damage
IOL damage was reported from 9.4 to 33% of cases. Degree of damage depends on nature of IOL material, highest damage occurs to silicone IOLs and lowest to acrylic IOLs. Glass IOL might fracture after Nd:YAG capsulotomy. IOL pitting
in visual axis can cause degradation of image quality and glare.

**Retinal detachment (RD)**

In retrospective analysis of medicare data, retinal detachment occurred in 1.6 - 1.9% of laser capsulotomy cases over 3 years. Increased risk of retinal detachment was found in patients with history of retinal detachment, axial length more than 24mm and lattice degeneration. Exact mechanism for retinal breaks and RD is not known and it might be due to increased rate of posterior vitreous detachment (PVD) after Nd:YAG capsulotomy.

**Other**

Other complications include iritis, pupillary block, malignant glaucoma, endophthalmitis, IOL displacement, macular hole.

**RESULTS**

Improvement in visual acuity was reported in 83 to 96.9% of eyes after Nd:YAG capsulotomy.

**CONCLUSION**

Posterior capsular opacification is a physiological complication of uneventful cataract surgery. Main culprits are LECs that proliferate and form PCO. Appropriate surgical techniques for complete removal of cortical matter and residual LECs along with the use of intraocular lens of different material and edge design helps to minimize occurrence of opacification. Nd:YAG laser remains treatment of choice for managing PCO though correct technique should be used to prevent complications.

**REFERENCES**


**Financial Interest:** The authors do not have any financial interest in any procedure/product mentioned in this manuscript.
Brain metastases represent the most common neurological manifestation of cancer, occurring in 15% of patients with the disease. When patients with brain metastasis were investigated for primary source, it was found that 39% suffer from Bronchogenic carcinoma, 17% Breast carcinoma and 11% melanomas. It is estimated that as many as 1,70,000 cancer patients develop brain metastases per year.

We report 4 such cases, who presented with neuro ophthalmic manifestations due to intracranial secondaries, which lead to the diagnosis of a primary carcinoma elsewhere, explaining the importance of thorough evaluation.

CASE 1

A 28 year old woman presented with a history of headache for one and a half years, loss of vision both eyes for 6 months, left sided limbs weakness for 3 months. Her past history revealed that she had consulted elsewhere for headache two years back. Her vision was no perception of light in both eyes on presentation. Pupils were sluggishly reacting to light and fundus showed features of secondary optic atrophy in both eyes. When old records were checked, CT Brain which had been done earlier, showed an elongated cystic lesion with ring enhancement in the trigonal region. Mantoux was positive then and she had been started on anti tuberculous therapy, which she had taken only for three months and stopped abruptly. We subjected her for repeat neuroimaging (CT Brain), which revealed, right fronto-parietal mixed density lesion 5 x 3.8 cm with perilesional edema and midline shift (Figure 1). Suspecting secondaries, a search was done for the primary lesion. Imaging of chest revealed mixed density lesion in the upper lobe of left lung measuring 8 x 5.08 cm size (Figure 2). A thorough search of whole body showed metastasis in the left adrenal gland also. The final diagnosis was made as Bronchogenic carcinoma or Primitive Neuro Ectodermal tumour of the left lung upper lobe with extensive adrenal and cerebral metastasis with Hydrocephalus. The patient was explained about the poor visual prognosis and referred to an oncologist.

CASE 2

A 43 year old woman presented to the neuro-ophthalmology department with headache for twenty days and giddiness for two days. On examination, best corrected visual acuity was 6|6 in both eyes. Anterior segment was normal in both eyes with briskly reacting pupils. Colour vision by Ishihara chart was normal. Visual fields showed peripheral constriction bilaterally. Dilated fundus examination revealed Established Papilledema (Figure 3). To rule out Malignant Hypertension as the cause of her symptoms and fundus findings, her blood pressure was measured, which was within normal limits. She was advised neuroimaging to rule out a space occupying lesion in the brain. MRI Brain with gadolinium enhanced contrast was done which showed multiple necrotic and hemorrhagic secondaries in both cerebral hemispheres with largest lesion in the left ganglio capsular region. Complete imaging of the suspected organs of primary lesion, revealed evidence of nodular lesion in right lobe of thyroid with calcification measuring 4.4x3.7cm. There was evidence of nodular lesion, also noticed in the middle lobe of right lung measuring 4.29x 4.0cm., suggesting possibility of thyroid malignancy with lung and cerebral metastasis. Patient was referred to oncology and Neurosurgery services.

CASE 3

A 65 year old male, presented with defective vision in right eye of 50 days duration. It was gradual in onset and slowly progressing. He gave no history of associated pain or headache. He also gave history of drooping of right upper eyelid and movement restriction for the past 30 days. On examination, visual acuity in right eye was counting fingers and left eye was 6/9. Right eye revealed ptosis, along with restriction of adduction, depression and elevation. Fundus of right eye showed Gross temporal pallor of the optic disc. Left eye anterior segment and fundus was normal. A probable diagnosis of Right orbito apex syndrome was made and MRI Brain, plain and contrast suggested. It showed a brilliantly enhancing soft tissue lesion in right obital apex, SOF, cavernous sinus region and anterior clinoid process with engulfment of 3rd,4th,5th,6th cranial nerves engulfing the intracanicular and intracranial segment of the right optic nerve. With a suspicion of Intracranial secondaries, Screening of Chest was done to rule out primary, which revealed evidence of nodular lesion noticed in right lung lower lobe (superior aspect). Multiple tiny nodules were noticed in both lungs. A diagnosis of Bronchogenic carcinoma of lower lobe of right lung with mediastinal, lymphnodal, lung and intracranial secondaries was made. Patient was referred appropriately.
A 40 year old woman presented with complaints of headache for the past 6 months and tinnitus for one month. She had 6/6 in both eyes and pupils were normal. Central fields showed enlarged blind spot. Fundus examination unveiled severe established papilledema in both eyes. To rule out the possibility of a tumour or cortical venous sinus thrombosis, which are the common causes of papilledema apart from idiopathic intracranial hypertension, MR Imaging and MR Venogram of the brain was ordered. It showed cerebellar metastasis with transtentorial cerebellar herniation with mild obstructive hydrocephalus (Figure 4,5), with primary in the left breast. Patient was referred to Neurosurgeon/Oncologist. She underwent mastectomy/Chemotherapy followed by Ventriculo peritoneal shunt and is under regular follow up.

**DISCUSSION**

Metastasis to the brain is the most feared complication of systemic Carcinoma. Secondaries are the commonest intracranial tumor in adults. Cerebral metastasis occurs in 15% of patients with cancer. In 15% of the patients, primary site remains unknown. Multiple, large autopsy series suggest that, in order of decreasing frequency, lung, breast, melanoma, renal, and colon cancers are the most common primary tumors to metastasize to the brain. The metastases to the brain accounts for 20% of cancer deaths annually, a rate that can be traced to an increase in the median survival of patients with cancer because of modern therapies, increased availability of advanced imaging techniques for early detection.

In adults, the most common primary tumor responsible for intracranial metastasis is lung. Although in the majority of patients (80%), brain metastasis develops after the diagnosis of primary tumor, in some patients it manifests before the primary tumor is found. The patients who present with neurological symptoms and imaging studies indicative of metastatic lesions, may be investigated for lung cancer. For patients who present with brain metastasis without a known primary, the lung should be the primary focus of evaluation. Sixty percent of these patients will have a primary lesion in the lung. Among the symptoms, headache occurs in 40-50% of patients with brain metastasis.

Metastatic brain tumors have been reported to be at least four times as common as primary brain tumors, and breast cancer is known to be the second most common cause of brain metastasis. Yen et al reported that the incidence of brainstem involvement in patients with breast cancer metastasis to the brain was as high as 12.4%, higher than that in patients with any other type of cancer. Lee et al reported that 28% of cases of brain metastasis in breast cancer showed a single metastatic lesion, supporting the...
idea that a single brain lesion does not necessarily suggest a primary tumor.

Metastatic breast carcinoma is the most common primary tumor to metastasize to ocular structures. The incidence of ocular structures among patients with breast carcinoma in clinical series has been reported to vary between 8 and 10%6. The occurrence of ocular metastases may not be appreciated because of the dominant clinical picture of metastases in other organs.

A clinical study of Mewis and Young8 found an incidence of 9% for choroidal metastasis in asymptomatic patients who had metastatic breast carcinomas. 

Leptomeningeal metastases develop as a complication in 4% to 11% of patients with systemic NHL and in approximately 10% of patients with leukemia. Cranial neuropathy is the presenting feature in 36% of the patients, characterized by facial weakness, numbness and diplopia in most of the patients.

Metastasis to the brain is a devastating and common consequence for patients with malignant melanoma. Cranial nerve palsies and visual deficits are the common presenting clinical features in these patients.

Malignant sinonasal tumors have a reported incidence of 1 in 100000 individuals yearly with only about 9% of these originating in the ethmoidal sinus11. Reported opthalmic manifestation of sinonasal undifferentiated Carcinoma include periocular swelling, pain, Variable Nerve palsies, Visual field loss, Compressive optic Neuropathy. 

Paraneoplastic syndromes are complexes of signs and symptoms in cancer-bearing patients resulting from dysfunction of tissues remote from the site of a malignant neoplasm or its metastases. Paraneoplastic optic neuropathy may produce subacute, progressive, painless bilateral visual loss. Metastasis from Clear Cell carcinoma to eye is uncommon. (Less than 2%). Cancer Associated Retinopathy (CAR) is characterized by slowly progressive visual loss over weeks to months. Large cells, small cell, Oat Cell carcinoma all are associated with CAR.

Metastatic brain tumors spread by hematogenous route either to the skull bones from where it may spread to the subarachnoid space, brain or both or it may metastasize directly to the brain parenchyma or to the subarachnoid space as well as to the orbit.

Tumor cells reach the brain through arterial circulation, most commonly from the lung, by either a primary lung cancer or a lung metastasis. They most commonly involve the gray-white junction12. The location of metastases in the brain roughly correlates with the blood flow to that area. Metastases are found in the cerebral hemispheres (80%), in the cerebellum (15%), and 5% in the brain stem13,14.

When brain metastases are discovered, 29% are found at the time of diagnosis of the primary tumor (synchronous) and in 80% of cases after the primary diagnosis of the cancer (metachronous presentation).

Headache, giddiness, new onset seizures, visual disturbances, should warrant Imaging of Brain. New onset of seizures in a patient older than 35 years is highly suggestive of primary or metastatic disease. Contrast Gadolinium enhanced MRI is more sensitive than CT scan. It detects small brain metastasis, particularly lesions situated in the posterior fossa. Metastases are seen radiologically as ring enhancing lesions located at the grey white matter junction followed usually by significant edema.

A variety of neuro-ophthalmological features including midbrain syndromes, nuclear third nerve palsies, defects in tracking and saccades are known to occur. Neoplasm is known to be one of the causes of abducens nerve palsy and internuclear ophthalmoplegia. Horner’s syndrome may be seen when the posterior fossa is involved. Involvement of the visual pathway may result in visual field defects, loss of colour vision, visual agnosia, and loss of acuity15-21. The pineal gland may be the site of metastases, presenting with parinaud’s syndrome. The most common source is both small and non-small- cell carcinoma of the lung22,23.

The best diagnostic test for brain metastases is contrast enhanced MRI24,25. If the clinical history is typical and lesions are multiple, usually there is little doubt regarding the diagnosis. It is important that metastases be distinguished carefully from primary brain tumours (benign or malignant), abscesses, cerebral infarction, and haemorrhages. One study26 has shown that false positives can be up to 11%.

The treatment for metastatic intraparenchymal brain tumours depend on the nature and extent of the primary process, the nature and severity of the
neurological or visual symptoms and signs, and the life expectancy of the patient. Radiation therapy, stereotactic radiosurgery, chemotherapy, and surgical therapy all may play a role both individually or in combination.27-28.

REFERENCES

Financial Interest: The authors do not have any financial interest in any procedure/product mentioned in this manuscript.

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A 5 month old baby was brought to the OPD (out patient department) of Dr Rajendra Prasad Centre for Ophthalmic Sciences on 17th August 2002. Parents complained of watering from both eyes and closing of eyes to bright light for 2 months; and eye rubbing for 1 month. There was no history of trauma/ preceding acute whitening of the eyeballs.

There was no history of trauma/ preceding acute whitening of the eyeballs. The child was taken to a private clinic where she was started on timolol 0.5% eye drops for 10 days and referred to a higher centre for management. Child was a full term normal delivery. There was no history of any other systemic illnesses. There was no family history of glaucoma or history of consanguinity.

On examination, the child looked healthy and well nourished. The extraocular examination was normal. Child had large corneas with corneal haze. Fundus was not visible due to hazy corneas. Ultrasound B-scan for posterior segment was anechoic in both eyes. Sleeping intraocular pressure by Perkin’s tonometer was 24mmHg on timolol 0.5% eye drops in both eyes.

The child was diagnosed as a case of Primary congenital glaucoma and admitted Examination under anaesthesia revealed the following (Table 1).

The child underwent a trabeculotomy with trabeculectomy augmented with Mitomycin C in right eye followed by the left eye in September 2002. The concentration of mitomycin C used was 0.04% sub-scleral for 3 minutes and sub-conjunctival for 1 minute during the surgery. The child was followed up on subsequent EUAs (examination under anaesthesia) (Table 2).

Serial EUAs showed that the patient had good IOP control on no medication. Corneal diameters decreased 0.5mm in each eye over a period of time. Reversal of cup to disc ratio was also noted. Refraction was done on regular intervals.

Table 1: Findings at first EUA

<table>
<thead>
<tr>
<th>EYE</th>
<th>OD</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>CORNEA</td>
<td>Diameter- H*=13, V#=13mm</td>
<td>Diameter- H*=14, V#=13.5mm</td>
</tr>
<tr>
<td></td>
<td>No Haab’s stria</td>
<td>Haab’s stria present</td>
</tr>
<tr>
<td>LENS</td>
<td>Clear</td>
<td>Clear</td>
</tr>
<tr>
<td>IOP</td>
<td>26 mm Hg with Perkin’s tonometer.</td>
<td>28 mm Hg with Perkin’s tonometer.</td>
</tr>
<tr>
<td>FUNDUS</td>
<td>Vertically oval disc</td>
<td>Vertically oval disc</td>
</tr>
<tr>
<td></td>
<td>Cup to disc ratio 0.5:1</td>
<td>Cup to disc ratio 0.5:1</td>
</tr>
<tr>
<td></td>
<td>Neuroretinal rim pink</td>
<td>Neuroretinal rim pink</td>
</tr>
<tr>
<td></td>
<td>Foveal reflex was sharp</td>
<td>Foveal reflex was sharp</td>
</tr>
</tbody>
</table>

*H-Horizontal corneal diameter; #V-vertical corneal diameter

Figure 1: Flat bleb seen in right eye-OD, thin Cystic bleb seen in left eye-OS.

Figure 2: OD- right eye clear cornea; OS – left eye cornea clear with central Haab’s stria
and glasses were prescribed to prevent amblyopia. The bleb in the right eye had become flat but left eye was noted to have a thin cystic bleb. Child was lost to follow-up in 2009.

Patient again presented to Dr Rajendra Prasad Centre for Ophthalmic Sciences in January 2016, with history of two episodes of redness in left eye that improved with antibiotic drops. At present child is studying class 8th. There was no history of surgical intervention after the primary surgery.

**CASE EXAMINATION**

Child was moderately built and well nourished. The visual acuity in the right eye was 6/6 and in left eye was 6/9. The extraocular examination was normal. The bleb in the right eye was flat and left eye was thin and cystic with a leak on Pressure Seidel’s test (Figure 1). The IOP in right and left eye was 14 mmHg and 8 mmHg respectively. The cornea was clear in the right eye and one central Haab’s stria was present in the left eye (Figure 2). The lens was clear in both eyes. The fundus in right eye had a cup to disc ratio of 0.4:1 and left eye was 0.3:1 (Figure 3). Gonioscopy showed an anteriorly inserted iris in the right eye with fibrosed ostium (Figure 4). The Goldmann visual field was normal in both eyes. Steropsis was present, steroacuity on TNO was 240 sec of an arc.

Bleb revision surgery with Primary Bleb-sparing, epithelial exchange was done. The epithelium over the bleb was peeled off and replaced by the surrounding conjunctiva. The bleb structure was not touched. The child was

### Table 2: Findings on serial EUAs

<table>
<thead>
<tr>
<th>Date</th>
<th>Corneal diameter</th>
<th>IOP</th>
<th>Bleb</th>
<th>Vision</th>
<th>Optic nerve</th>
<th>Refraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>20/9/2002 (4 weeks post-op)</td>
<td>OD-13 OD-13.5</td>
<td>OD-8 mm Hg OS-8 mm Hg</td>
<td>Elevated OU</td>
<td>OD-0.5:1 OS-0.5:1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20/12/2002 (3 MONTHS)</td>
<td>OD-13 OD-13.5</td>
<td>OD-10 mm Hg OS-8 mm Hg</td>
<td>OU bleb relatively avascular &amp; diffuse</td>
<td>OD-0.5:1 OS-0.4:1</td>
<td>- 1 D CYL given at 180° OU</td>
<td></td>
</tr>
<tr>
<td>Feb 2003</td>
<td>OD-12.5/13 OD-13/13.5</td>
<td>OD-10 mm Hg OS-6,8 mm Hg</td>
<td>OU bleb relatively avascular &amp; diffuse</td>
<td>OD-0.5:1 OS-0.4:1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>OD-12.5/12.5 OD-12.5/13</td>
<td>OD-8 mm Hg OS-6 mm Hg</td>
<td>OU bleb relatively avascular &amp; diffuse</td>
<td>TAC-OD-20/190 OS-20/260 AT 55 cm</td>
<td>OD-0.4:1 OS-0.3:1</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>OD-12.5/12.5 OD-12.5/13</td>
<td>OD-8 mm Hg OS-6 mm Hg</td>
<td>OU bleb relatively avascular &amp; diffuse</td>
<td>CARDIF: OD-6/12 OS-6/12</td>
<td>OD-0.4:1 OS-0.3:1</td>
<td>OD: -1D CYL AT 180° OS:+2DS-4DCYL AT 180°</td>
</tr>
<tr>
<td>2006</td>
<td>OD-10 mm Hg OS-6 mm Hg On NCT</td>
<td></td>
<td>OU bleb relatively avascular &amp; diffuse</td>
<td>OD-6/12 OS-6/18</td>
<td>OD-0.5:1 OS-0.3:1</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>OD-14 mm Hg OS-9 mm Hg On NCT</td>
<td></td>
<td>OU bleb relatively avascular &amp; diffuse</td>
<td>OD-0.5:1 OS-0.3:1</td>
<td>OD: -1D CYL AT 180° OS:+2DS-4.5DCYL AT 180°</td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td>OD-12 mm Hg OS-8 mm Hg</td>
<td></td>
<td>OU bleb relatively avascular &amp; diffuse; Thin bleb OS</td>
<td>OD-6/9 OS-6/18</td>
<td>OD-0.5:1 OS-0.3:1</td>
<td>Occlusion therapy: R&gt;L::6:1</td>
</tr>
<tr>
<td>2009</td>
<td>OD-14 mm Hg OS-6 mm Hg</td>
<td></td>
<td>OU bleb relatively avascular &amp; diffuse; Thin bleb OS</td>
<td>OD-0.4:1 OS-0.3:1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
followed up in outpatient department. The conjunctiva remained well apposed (Figure 5). IOP at 6 months was 16mm Hg, for which timolol eye drops 0.5% were advised.

**DISCUSSION**

Congenital glaucoma is a rare disease with an incidence of about 1 in 10,000 in the world1. In Asian countries, esp. India, the incidence is as high as 1 in 3,300 because of various factors such as consanguinity and marriages in close knit communities2. Congenital glaucoma contributes to 4.2% of childhood blindness in southern India2. About 10% of children present at birth, 60% till 1 year of life and rest later. Most of the cases are sporadic, others have an autosomal recessive pattern.

Children usually present with a triad of epiphora, photophobia and blepherospasm although large eye balls or buphthalmos or blepherospasm and hazy corneas are more common in India, epiphora is reported less commonly4 (Figure 6).

The child should be examined under anaesthesia (EUA) for detailed evaluation. The operating microscope should be used to see detailed ocular findings. The following EUA findings should be carefully noted at each followup:

1. **Cornea:**
   a. Corneal diameter: both horizontal and the vertical corneal diameters should be measured using Castroviejo calliper. A diameter more than 12mm under 1 year of age or more than 13mm after 1 year suggests enlargement of the size of cornea, which is highly suggestive of PCG. Enlarging corneal diameters after surgery also suggest increased IOP. Corneal enlargement can be usually seen upto 3 years of age.
   b. Other Corneal findings: examiner should note corneal edema, Haab’s striae or any corneal opacity. A representative diagram should be drawn for future referral. Central Haab’s striae or corneal opacity can be associated with poor visual acuity.

2. **Intraocular Pressure (IOP):**
   IOP can be measured using Perkins applanation tonometer or Tonopen. Anaesthetics have a varied effect on IOP. Fluoranes usually cause artificial lowering of IOP. Succinylcholine and cyclopropane usually elevate the IOP transiently. Even slight bronchospasm can elevate IOP while intubation. The IOP should be measured just before the effect of anaesthetic gases lower IOP further.

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**Figure 4:** Above – superior angle showing fibrosed ostium. Below- inferior angle shows an anteriorly inserted iris with iris prosecces.

**Figure 5:** Above Post-Op 1 month. Below-Post Op at 6 months. conjunctiva is well adhered in place.

**Figure 6:** Children with congenital glaucoma.

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giving a false low reading; i.e. right after intubation of the child. In children less than 3 years, the IOP is usually less than 15mmHg (lesser than adults).

3. Gonioscopy: Koepp’s lens or Swan Jacob lens can be used to view the angle in clear corneas. Dense opacities may preclude angle visualization. In normal eyes the trabecular meshwork and scleral spur are usually visible. In Primary congenital glaucoma, the iris is inserted anterior or over the trabecular meshwork. Prominent iris processes may be present. Postoperative gonioscopy is an essential tool to look at ostium patency.

4. Fundus: Children with PCG usually have a large optic nerve with concentrically enlarged cup. Neuroretinal rim is usually pink. The cup enlarges slowly with glaucoma progression until the NRR thins out and becomes pale. In hazy corneas, the pupil should be dilated beforehand to see the fundus by indirect ophthalmoscopy.

5. Ultrasonography: Ultrasound B scan should be used to look for posterior segment abnormalities if corneal haze precludes the fundus visualization. Axial length can also be measured as it a sensitive indicator of IOP induced enlargement of eye ball.

6. Refraction: Increased IOP causes axial myopia in PCG and the surgery usually induces high cylindrical error in these eyes, which predisposes them for amblyopia. The most important aspect of visual gain is a good refraction and patient counselling for the use of glasses on a regular basis.

After the first EUA, the diagnosis is usually clear. For most of the children, surgery is ultimate management option as the medical therapy has only a supportive role in the treatment of PCG. Combined trabeculectomy with trabeculotomy is the gold standard surgical procedure. It has better surgical results, when augmented with antimetabolites like Mitomycin C or 5 Fluorouracil as children have a vigorous fibrotic response5 after surgery. Serial EUAs should be done until the child is old enough to be examined in OPD. Visual acuity should be assessed with age appropriate tools. A good visual acuity is usually attained unless there is an obvious cause for poor vision like corneal opacity or Haab’s striae or advanced ONH cup or retinal problems. These children have increased risk of retinal detachments than the normal population, which should be kept in mind among other things.

Use of antimetabolites is associated with complications related to bleb like excessive filtration, failure, leak and bleb related infections. Thinning of the bleb is usually seen over the years with predisposition to late-onset bleb related ocular infections like blebitis or bleb-related-endophthalmitis in an otherwise normal eye. Children usually don’t report the infections unless severe, which can lead to loss of vision due to endophthalmitis. Any episodes of conjunctivitis or blebitis or leaks mandate a bleb revision surgery for these patients. Thin blebs without leaks should be carefully followed up.

In a Bleb revision or repair surgery, the bleb area is covered by the surrounding conjunctiva. For many years, bleb revision surgeries entailed excision or cautery of the bleb with advancement of the conjunctiva and possibly sclera. However, an increased IOP and complications were reported in a significant number of patients. Bleb sparing epithelial exchange is done by staining of the dead conjunctiva by Trypan blue dye, peeling of the atrophic conjunctiva from bleb area, without disturbing the bleb and advancement of the adjacent conjunctiva over the bleb (Figure 7). Therefore a bleb sparing epithelial exchange was carried out as it showed promising results in adult bleb revision cases. Other complications include mild ptosis.

In our case the IOP rise was seen from 8mmHg to 16mmHg at 6 months post-op, which is normal for the age of the child. If IOP rises further, an anti-glaucoma drug can be added to control the same.

Lastly, the most important part of patient management is patient counselling. Patients are likely to be lost to followup after a successful surgical outcome also. A life long follow-up has to be explained and emphasized at each followup to the parents as loss to follow-up may lead to worse outcomes.

REFERENCES

Persistent hyperplastic primary vitreous is a term originally coined by Reese in 1949. If the persistent fetal vasculature does not cover the visual axis during the first year of life, the prognosis for patient’s vision is excellent, provided that surgery and treatment for amblyopia of the affected eye takes place as soon as possible. Ultrasound and Color Doppler imaging are informative screening and diagnostic tools.

**CASE**

A 2-year-old baby presented to us with parent noticing whitish reflex from left eye 12 months back associated with eye looking smaller compared to fellow eye. There was no history of trauma during delivery or during perinatal period. Parent took her to local practitioner where she was diagnosed with unilateral congenital cataract and referred to R. P Centre, AIIMS. Physical and mental development was within normal range. Visual acuity, able to follow light in left eye even on patching right eye. On torch light examination, few ciliary processes with unilateral membranous cataract in her left eye and a posterior capsular plaque were identified along with blood vessels (Figure 1).

Ultrasound and Doppler of her left eye revealed the presence of a persistent fetal vasculature (fibrovascular tissue in Cloquet’s canal) (Figure 2). No significant anatomical abnormalities in the vitreous base and peri papillary area were identified.

We proceeded with examination under anaesthesia. The eye was smaller (axial length: 18 mm and K1 = 45 D @ 176, K2 = 47 D @ 86) compared to right eye axial length: 20 mm and K1 = 45 D @ 118, K2 = 45.50 D @ 28), corneal diameter of 10mm in left and 11mm in right eye, while Central corneal thickness, measured with Pachymetry was 581 microns compared to 548 in right eye and IOP of 12mm of hg in both eyes using Perkin’s tonometer. Right eye examination was unremarkable. Under general anaesthesia, we performed anterior capsulorhexis followed by aspiration of the membranous cataract through a clear cornea incision, capsulorhexis of the posterior capsule and cutting of retrolental stalk was done using Fugo’s Plasma blade (Figure 3).

Single piece aspheric hydrophobic lens was put in bag of 29 D with 10% undercorrection (Figure 4). There was no tractional detachment intraoperatively. Superior Peripheral iridectomy was done. On the first day after surgery, the patient’s left eye had a clear cornea with superior buried suture, anterior chamber well-formed and IOL in situ. She was advised to follow a treatment for amblyopia of her left eye (six-hour occlusion of her right eye 2:1 ratio). In addition, she was prescribed topical antibiotic-steroid drops as well as drops for one months. Administration of the antibiotic-steroid drops was tapered appropriately. Suture removal was done at 6 weeks with retinoscopy of +4 D @ 900 and +5d @ 180°. Executive glasses with +3 near add was prescribed for left eye and visual acuity recorded with Cardiff in left eye was 6/48 at 50 cm.

**DISCUSSION**

The reported visual acuity results after surgery for PFV are variable (0-71%)². The patients with strictly anterior PFV have a generally good visual potential, in contrast to patients with posterior PFV in whom visual potential is often limited by coexisting retinal and optic nerve abnormalities. If the persistent fetal vasculature does not cover the visual axis during the first year of life, the prognosis for patient’s vision is excellent, provided that surgery and treatment for amblyopia of the affected eye takes place as soon as possible. Ultrasound and Color Doppler imaging are informative screening and diagnostic tools that show characteristic flow patterns in persistent fetal vasculature.¹¹ A new echo graphic finding of a double linear echo on high frequency ultrasound was observed in the region of the pars plana or plicata only in eyes with PFV. This finding was confirmed intraoperatively to be consistent with a thickened adherent anterior hyaloid face and not to be an anteriorly inserted peripheral retina.¹² This may be the cause of peripheral retinal tears and retinal detachment. PFV may be at risk for the development of vitreous haemorrhage during and even after surgical repair. Intraoperatively presence of ‘salmon pink patch sign’ in centric pink hue is suggestive of active vasculature within the persistent fetal vasculature.¹² The Fugo plasma blade can be used to avoid intra operative bleeding by using pulses of plasma that are generated around the tip to cut and cauterize tissue without extensive collateral tissue damage.¹³ Intra ocular lens implantation should be tried in unilateral cataract to decrease the chance of developing amblyopia.¹⁴
CONCLUSION

Intraoperative complication of haemorrhage can be reduced by the use of plasma blade and diathermy without causing much collateral damage. Persistent fetal vasculature can be
diagnosed early and more precisely with High frequency ultrasound (UBM), Color doppler and Magnetic resonance imaging hence improving the prognosis.

REFERENCES

Financial Interest: The authors do not have any financial interest in any procedure/product mentioned in this manuscript.
Intraocular pressure measurements is an important parameter to diagnose and treat Glaucoma as it is the only modifiable parameter in the Glaucoma treatment. Therefore, it becomes very critical to measure it correctly and reproducibly.

In spite of availability of various recent tonometers, Applanation Tonometry (AT) by Goldmann continues to be considered as the gold standard.

There can be multiple sources of error in the measurement of the IOP including the calibration which often gets overlooked. This article describes and refers the procedure for the calibration of the Goldmann Tonometer 900 series.

**PROCEDURE**

The manufacturers of Haag-Streit Goldmann applanation tonometer provide a calibration error check weight bar. The bar has 5 markings (Figure 1) on it. The central marking corresponds to level 0. Two on either side of it represent level 2 (20 mmHg) and the two outermost markings represent level 6 (60 mmHg). The calibration error of Goldmann applanation tonometer should be measured at all 3 testing levels; the level corresponding to 20 mmHg, being the most important, as many clinical decisions with regard to glaucoma are taken around this IOP.

Next step is to mount the calibration rod on the slot indicated in the (Figure 2). The (Figure 3) shows the mounted rod.

Next step is to set the rod at the mark on the weight bar corresponding to one of the three testing positions. The index mark of the weight holder should be such that the longer arm is towards the examiner and the revolving knob of the measuring drum should be rotated forwards. The reading at which the feeler arm (with the applanation prism in place) moves forward freely should be recorded. The difference of this reading from the actual test position (0, 2 or 6 corresponding to 0, 20 and 60 mm Hg of IOP) indicates the positive error at that level of testing in mm Hg.

Similarly, on rotating the revolving knob in the reverse direction, the reading at which the feeler arm moves backward should be noted. The difference between the latter and the testing position, indicates the negative error at that level of testing. Calibration error testing at level ‘zero’ can be performed even without the calibration error check weight bar (Refer Figure 4).

**ACCEPTABLE TOLERANCE OF CALIBRATION ERROR**

The manufacturers of Haag-Streit Goldmann applanation tonometer define acceptable calibration error to be within...
± 0.5 mm Hg at all levels of testing (0, 20 and 60 mm Hg). But, the South-East Asia Glaucoma Interest Group (SEAGIG) guidelines are less stringent. It recommends the progressively wider acceptable range of calibration error at the higher levels of error testing. By this guideline, the acceptable error can be within ± 2 mm Hg at 0 mm Hg, ± 3 mm Hg at 20 mm Hg and ± 4 mm Hg at 60 mm Hg testing levels.

FREQUENCY

There is no practice guideline in the literature regarding the frequency of calibration error testing. The manufacturer suggests an arbitrary monthly check. Some authors recommend an arbitrary annual check and others suggest an arbitrary monthly check. However it is generally recommended that excessively used or multi-user tonometers should be checked more frequently.

POSSIBLE REASONS FOR THE CALIBRATION ERROR

Sources of calibration error of Goldmann applanation tonometer are rarely investigated. As a part of the study protocol1, the calibration error of a majority of these instruments was found to be the dirt and lubrication related problems.

SUMMATION

Identification of the calibration error in the AT is of utmost importance to take critical decisions in Glaucoma management.

Once the calibration error is found, it is recommended that the instrument should be send back to the manufacturer for correction. However, Chaudhary et al4 have also described the method to fix the calibration error.

REFERENCES


Financial Interest: The author does not have any financial interest in any procedure/product mentioned in this manuscript.
A 37 year old female was referred to the glaucoma clinic for evaluation. She was asymptomatic with no family history of glaucoma. Slit-lamp examination of both eyes was normal. Pupils were acting briskly with no relative afferent pupillary defect. Extra-ocular movements were full and painless. Her visual acuity OU was 20/20 N6. Intraocular pressure recorded by applanation tonometry were 18 mm of Hg in OD and 16 mm of Hg in OS. Diurnal variation of intraocular pressure was recorded in both eyes as phasing at 9am, 2pm and 7pm. The pressures were as follows 16, 14 and 16 mm Hg in OD and 18, 16 and 17 mm Hg in OS.

Gonioscopy showed open angles grade-III 360˚ by Modified Shaffer’s classification. The central corneal thickness was 521 and 516 microns in OD and OS respectively. Colour vision checked with Ishihara’s isochromatic charts was normal in both eyes.

Fundus examination (Figure 1 and 2) revealed normal disc size and shape. Margins were well defined. Vertical cup disc ratio in OD was 0.4 and OS was 0.5. Neuroretinal rim appeared healthy. Wedge shaped retinal nerve fiber layer loss as high-lighted in the red-free photograph (Figure 3 and 4) was seen along the superior & inferior arcuate areas. No disc haemorrhage was present. Blood vessels were normal. Macula was normal.

Both eyes visual fields – G1 Top threshold program by Octopus static perimetry (Figure 5) were reliable and normal. Optical coherent tomography of retinal nerve fiber layer (RNFL) of both eyes by Zeiss Cirrus OCT (Figure 6) was of good signal strength and showed significant thinning of RNFL in the superior and inferior quadrants in OD and thinning of superior, temporal and inferior quadrants in the OS.

Suspecting a non-glaucomatous optic neuropathy, we elicited a detailed history. She was a strict vegetarian, not a smoker or alcoholic. She had no history of trauma, gastric surgeries and was not on any long term use of medications like steroids, chloramphenicol, streptomycin, digitalis, chloroquine. There was no history of headache, refractive error, transient loss of vision and no family history of similar illness.

General examination of the patient was normal. Evaluation of central nervous system was within normal limits. Magnetic resonance imaging of brain was of normal study.

A physician opinion was sought. He suspected vitamin B12 deficiency. Vitamin B12, vitamin D, folic acid assay were all checked. Her vitamin B12 level was 90 pg/ml (Normal levels 200 to 900 pg/ml). Vitamin D and folic acid levels were normal.

Other nutritional deficiency known to cause optic neuropathy like pyridoxine, thiamine, niacin, riboflavin and folic acid were ruled out. Peripheral smear was normal.

She was treated with vitamin B12 injections – 1000µgms daily for one week followed by 1000 µgms once a week for one month & then 1000 µgms once a month for a year. The patient was on regular follow-ups. Visual fields (Figure 7) repeated after one year, was found to be normal. Her blood levels of vitamin B12 improved but her RNFL changes remained unchanged.

DISCUSSION

Vitamin B12 is one of the eight water soluble B vitamins. Vitamin B12 plays key role in the normal functioning of brain, nervous system and haematopoiesis. The most important functions of vitamin B12 are cell differentiation, maturation, DNA synthesis, nervous system integrity and myelin sheath synthesis. Normal blood levels of vitamin B12: 200 - 900 pg/ml...
Vitamin B12 deficiency is a worldwide problem. It affects all ages including children. It is one of the most common nutritional disorders and can cause harmful effects on the nervous system.

Careful history taking is very important to differentiate glaucomatous from non-glaucomatous optic neuropathy. History of sudden or rapid visual loss, headache, double vision, indicates more towards neurological pathology whereas glaucoma is mostly

Figure 3: OD red free fundus photo showing cup disc ratio of 0.4 with classic wedge shaped RNFL loss along the superior and inferior arcuate areas.

Figure 4: OS red free fundus photo showing cup disc ratio of 0.5 with classic wedge shaped RNFL loss along the superior and inferior arcuate areas.

Figure 5: Visual fields OU threshold programme by Octopus static perimetry were reliable and normal.

Figure 6: OU Cirrus OCT of RNFL was of good signal strength and showed significant thinning of RNFL in the superior & inferior quadrants in OD & superior, temporal & inferior quadrants in OS.

Figure 7: OD and OS repeat visual fields after one year-threshold programme by octopus static perimetry were reliable and normal.
asymptomatic. Presence of positive family history favours more towards glaucoma. Currently informations from perimetry, optic nerve head pallor, visual acuity, colour vision, pupillary action are used as aids in differentiating glaucomatous from non–glaucomatous cupping. On examination of the neuroretinal rim: in glaucoma both cupping and pallor of the rim go hand in hand because there is loss of both axons and supporting tissues1. The superior and inferior poles are affected more in glaucoma2, whereas there is no such pattern in non-glaucomatous optic neuropathy. Glaucomatous visual field defects have a pattern; they respect the horizontal meridian whereas non-glaucomatous optic neuropathy visual field defect may not follow a pattern.

Optical coherence tomography a non–invasive imaging modality suggest that, the pattern of RNFL loss in glaucoma is greater in the superior and inferior quadrants while that of non–glaucomatous was more varied depending upon the etiology3. The overall mean RNFL loss occurs in optic nerve damage of any cause and need not be specific for glaucoma. The macular volume and macular thickness measurements by optical coherence tomography was significantly reduced in patients with non-glaucomatous optic neuropathy when compared to patients with glaucomatous cupping.

Özkasap S et al compared the peripapillary retinal nerve fiber layer thickness by Cirrus spectral domain OCT in a healthy control group with children with vitamin B12 deficiency and concluded that the average RNFL thickness and the superior RNFL thickness were significantly lower in patients with vitamin B12 deficiency4.

Cikmazkara I studied the effect of iron deficiency anemia (IDA) on peripapillary retinal nerve fiber layer thickness with by Cirrus high-definition OCT 4000. The average, temporal, nasal, and lower quadrant average RNFL thicknesses of IDA group were thinner than the control group5.

**CONCLUSION**

So to summarize, pathological cupping of the optic nerve head is more commonly associated with glaucoma but it is important to remember that there are various causes of non–glaucomatous optic disc cupping that can mimick glaucoma.

**REFERENCES**

1. Dr. Maneesh Singh Dr, Nikhil S Choudari Differentiating Glaucomatous From Non Glaucomatous Optic Neuropathy Journal of Tamil Nadu Ophthalmic Association, February 2015
2. Diagnosis and Management of Glaucoma First edition 2013. Dr. R. Ramakrishnan, Dr. R. Krishnadas ~ Dr.Alan L. Robin, Dr. Mona Khurana.
3. Gupta PK., Asarani S., Freedman FS., Differentiating glaucomatous from non-glaucomatous optic nerve cupping by Optical Coherent Tomography Open Neurology Journal 2011

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**Financial Interest:** The authors do not have any financial interest in any procedure/product mentioned in this manuscript.
A 62 year healthy male presented with complaints of fluctuations in vision in both eyes since 1 year. The symptoms were more pronounced in left eye.

The BCVA was 6/9, N6: 6/18, N18. IOP – 11mmhg in BE. Slit lamp examination revealed no significant anterior segment pathology. Fundus examination showed a CD ratio of 0.4 and 0.45 with healthy neuroretinal rim and an altered sheen at the posterior pole of the left eye (Figure 1). FFA of the left eye showed delayed filling of the superotemporal arteriole with a horizontal strip of capillary non-perfusion extending from the peripapillary region to the periphery (Figures 2 and 3). The disc was stained. The right

Figure 1: Fundus photograph left eye showing very subtle discoloration at the posterior pole.

Figure 2: FFA image of the left eye showing delayed filling of the superotemporal arterioles.

Figure 3: Late phase of FFA showing highlighting the non perfused retina and diffuse staining of the vessels and disc.

Figure 4: FFA image of the superior retinal periphery showed capillary non-perfused areas and microaneurysms.

Figure 5: FFA image after carotid endarterectomy showing an improvement in the filling of the vessels and reperfusion of the ischemic retina.

Role of Carotid Doppler in Management of Retinal Ischemia

Kapil Sidhu, Shahana Mazumdar, Sugandha Goel
eye showed mild leaks at the macula and the entire peripheral retina of both eyes was ill perfused with small punctate hyperfluorescent microaneurysms (Figure 4). OCT macula BE showed generalised thickening though the contour was maintained.

A diagnosis of both eyes ocular Ischemia with branch retinal artery occlusion left eye was made and patient was referred for cardiovascular evaluation. Carotid imaging revealed complete and 90% stenosis of the internal carotid arteries of the right and left sides respectively.

The right side carotid was inoperable but the left side underwent modified endarterectomy.

Four months after the procedure the patient came for a follow up. His BCVA had improved to 6/6P, N6, 6/9, N6. The fundus looked normal. To our surprise the FFA revealed reperfusion of the retinal arteriole and the capillary non-perfusion areas. The disc showed only a mild staining of the disc and very gentle leaks at the macula. Also the peripheral perfusion of both eyes had improved substantially.

It is interesting and unusual to see reperfusion of the retinal circulation with improvement in vision, so long after arteriolar occlusion and documented ischemia and reperfusion.

Patient had to be referred for carotid Doppler for the diagnosis of the carotid stenosis. This helped in planning the management by endarterectomy which led to retinal reperfusion.

Cornea Services ICARE Eye Hospital, NOIDA, India.

Dr. Kapil Sidhu MBBS
Dr. Shahana Mazumdar MS
Dr. Sugandha Goel MBBS

Financial Interest: The authors do not have any financial interest in any procedure/product mentioned in this manuscript.
1ml of above solution is then added to 3ml distilled water – 0.19% Colistin drops

6. Topical Imipenem–Cilastin eye drops 1%
Method: To parenteral Imipenem(500mg)-Cilastin (500mg), add 10ml sterile water to create a solution of strength 50mg/ml.
Take 1 ml of this solution and add 4 ml sterile water to make topical Imipenem 1% - 1mg/ml
Storage - In amber coloured bottles
Stability – 3 days at 2-8 deg C

7. Topical Amphotericin B 0.15%
Method: Add 10 ml distilled or sterile water to parenteral 50mg of amphotericin B powder for injection. Draw 3 ml of this and add to 7ml of artificial tears eye drops.
Storage: Refrigerate in 4 degrees.

REFERENCES

Dr. Sushmita G. Shah
dos-times.org
DOS Times Quiz 2016-17
Episode-2

Last date: completed responses to reach the DOS OFFICE by e-mail or mail before 5 pm on 10th October, 2016

Q1. What is this investigative modality and what are the structures seen in the image?

Q2. What investigative modality is this and what frequency is utilized in it?

Q3. What surgery has been performed in the image given below and what is its indication?

Q4. The majority of orbital lymphomas are
A. T-cell tumours
B. Polyclonal proliferations
C. Systemic at presentation
D. Involving both orbits
E. Well differentiated

Q5. Goldenhar syndrome includes all of the following findings except
A. Lid notching
B. Cleft palate
C. Epibulbar dermoids
D. Duane syndrome

Q6. What is this retinal lesion and what is the systemic condition associated with it?

Compiled by:

1. Cornea & Refractive Surgery Services, Dr. Shroff’s Charity Eye Hospital, New Delhi
2. Vitreo-Retina Services, Dr. Shroff’s Charity Eye Hospital, New Delhi

Dr. Abhishek Dave  MD, FICO, FMRF
Dr. Prachi Abhishek Dave  MS, DNB, FICO
Q7. Microspherophakia is not associated with
A. Alport’s syndrome
B. Rubella
C. Peter’s anomaly
D. Syphilis

Q8. What is this clinical condition?

Q9. After permanent punctual occlusion with cautery
A. 5-10% rate of recanlization is expected
B. 10-20% rate of recanlization is expected
C. 20-30% rate of recanlization is expected
D. 30-40% rate of recanlization is expected

Q10. Medulloepitheliomas
A. Are congenital lesions often containing cartilage
B. Usually metastasize to the liver
C. Can be caused by trauma to the ciliary body
D. Are tumours arising from the surface ectoderm
E. Are usually malignant in nature

CONTESTANT DETAILS

Name: ___________________________________________ Degree: __________________________

Designation: ___________________________________ Address: __________________________

_________________________________________________ State __________________ Pin ________

Mobile No: ______________________________________ DOS Membership no: ____________

Email ID: ________________________________________ Signature: ________________________

DOS TIMES Quiz Rules

1. DOS TIMES QUIZ will now feature as 5 Episodes (Episode 1: July-August, Episode 2: September – October, Episode 3: November – December, Episode 4: January – February, Episode 5: March – April). Entries will have to be emailed before the last date mentioned in the contest questions form. Late entries will not be entertained.

2. Please email (as scanned PDF ONLY) completed responses for the quiz along with details of the contestant filled in and signed to dostimes10@gmail.com (with cc to dosrecords@gmail.com) or mail to DOS Times Quiz, Dr. M. Varath, Room No. 479, 4th Floor, Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi.

3. Nonmembers may also send in their entries but will be required to send along with their completed entries, the completed membership application (with the required documents) to enroll as member. Failing this their entries into the contest will not be considered.

4. Contestants are requested to attempt all the 5 episodes of the QUIZ contest and send in their applications within the date specified. No entries will be entertained after the last date. The scores of each contestant for all 5 episodes together will be compiled at the end of episode 5 and the winner will be announced in the DOS Annual Conference in April 2017. In the event of more than one winning contestants, a draw of lots will decide the winner. Winner of each episode will also be published in the next episode along with the previous episode answers.

5. Please write to dostimes10@gmail.com/dosrecords@gmail.com for further clarifications if any.

Q7. Microspherophakia is not associated with
A. Alport’s syndrome
B. Rubella
C. Peter’s anomaly
D. Syphilis

Q9. After permanent punctual occlusion with cautery
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Q10. Medulloepitheliomas
A. Are congenital lesions often containing cartilage
B. Usually metastasize to the liver
C. Can be caused by trauma to the ciliary body
D. Are tumours arising from the surface ectoderm
E. Are usually malignant in nature

Q8. What is this clinical condition?
**EPISODE 1**

1. Ida man
2. Choroidal Osteoma
3. (a) Wait for another 5 -6 weeks
4. (c) cotton wool spots represent infarcts of the nerve fibre layer of the retina
5. (d) disciform keratitis
6. (a) outer plexiform
7. (a) Giant papillary conjunctivitis secondary to Vernal Keratoconjunctivitis.
   (b) Shield Ulcer
8. Osteo-odonto keratoprosthesis; PMMA Optical cylinder & biological tooth haptic
9. (a) Macular dystrophy Histological Features: Macular- Aggregations of glycosaminoglycans within keratocytes and the corneal endothelium combined with an extracellular deposition of similar material in the corneal stroma and Descemet membrane that stain with Alcian blue.
(b) Granular dystrophy. Histopathological features: - Amorphous hyaline eosinophilic deposits which stains a brilliant red with the Masson trichrome stain.
10. Neuroretinitis. D/D: Syphilis, multiple myeloma

**EPISODE 2**

1. Arc-Shortening Model after placement of INTACS Inserts for Treating Myopia
2. Implantable Collamer Lens with Nuclear Sclerosis Grade 1-2.
3. Left Superior Oblique Palsy. Tests- Park’s Three step test and Bielschowsky’s test
4. (a) 1mm
5. (c) 0.28 ml bubble of air in an eye of normal volume tamponades 90 degree arc of retina
6. (c) between systolic and diastolic pressure in the central retinal artery
7. Angiod streaks
8. (a) IPPT
9. (a) 6/18-3/60
10. (b) Schwartz-Matsuo syndrome

**EPISODE 3**

1. (a) Blepharophimosis, ptosis, epicanthus inversus syndrome (BPES)
   (b) The usual sequence of surgical treatment is correction of the epicanthic folds and Telecanthus in 1st stage at about the age of 3–4 years followed by correction of the ptosis about 9–12 months later.
2. (d) Injection of air into the vitreal cavity of an aphakic patient causes a hypermetropic shift
3. (a) Limbal dermoid right eye, upper eyelid coloboma-bilateral
   (b) Goldenhar syndrome (also known as Oculo-Auriculo-Vertebral (OAV) syndrome)
(c) Ear, nose, soft palate, lip, vertebrae are usually affected. Development of internal organs like heart, kidneys and lungs may also be affected
(d) Insult occurs in the first trimester and results in an anomalous development of the first and second branchial arch structures
4. (a) CRAO with sparing of cilio retinal artery
5. (a) Lymphangioma of the orbit with chocolate cyst.
   (b) Urgent surgical drainage of the large chocolate cyst

**EPISODE 4**

1. (b) Neurocysticercosis
2. (b) Vision less than 3/60 in better eye with available correction
3. (b) Examination of children less than 9 years for presence of follicles and infiltrate
4. (c) Cataract
5. (a) Rapid assessment of avoidable blindness
6. (a) Macular cornal dystrophy
7. (a) 20%
8. (a) Hoskins-Barksans direct goniolens
   (b) Uses: Diagnostic gonioscopy in children Therapeutic – Intra-operatively used for goniotomy
   (c) Magnification: 1.3x.
9. (a) Aniridic 10L
   (b) Placed in the sulcus
   (c) Size : 12.5-13.5 mm
10. (a) Bleb grading: H3E4V0S0 (Though ‘S’ – Seidels test cannot be commented upon as it is not shown in the clinical photo)
   (b) Bleb classification systems:
   1. IBAGS:Indiana Bleb Appearance Grading Scale
   2. MBGS:Moorfields bleb grading System

**EPISODE 5**

1. Diagnosis: Capillary hemangioma
   Management:
   - Refraction followed
   - Observation
   - intralesional triamcinolone
   - Systemic propranolol
2. Diagnosis: Internal angular dermoid
   Investigation: CT scan
   Management: Excision biopsy
3. (a) Autosomal dominant inheritance
4. (b) This condition is often associated with anterior megalophthalmos, an autosomal dominant disorder
5. Laminar cataract
   Management: Visual axis involvement >3 mm, ACCC+lens aspiration+AV+PCiol.
6. (a) Differential diagnosis – Orbital cellulitis/Orbital abscess/ Orbital cysticercosis/Nonspecific Orbital inflammatory disease/Acute orbital trauma/Carotid cavernous fistula
   (b) Management plan – CT scan, IV antibiotics +NSAIDS if Orbital abscess, Add oral Albendazole (10-15mg/ kg/d) if suspicion of Cysticercosis along with oral steroids
   Indirect ophthalmoscopy to rule out intra-ocular cysticercosis
   (c) Final diagnosis after viewing CT scan – Orbital inflammatory disease likely Orbital abscess or cysticercosis
7. (c) Twins
8. (c) Males affected more frequently than females
9. (b) The likelihood of results occurring as a matter of chance is 3%.
10. (d) 20min
DOS CROSSWORD

Episode-2

Dr. Manish Mahabir MD
Senior Resident,
Dr. R.P. Centre, All India Institute of Medical Sciences,
New Delhi, India

ACROSS

2. High-density porous polyethylene orbital implant (6)
5. Drug for the treatment of keratoconjunctivitis sicca approved by FDA in July 2016 (11)
8. Inability to recognize familiar faces (13)
9. A modified ophthalmoscope to know the type of eccentric fixation (9)
10. Phenomenon in which, tangential incisions lead to flattening in the meridian of incision, and steepening in the meridian 90 degree away (8)
14. Second FDA-approved implantable corneal device for correction of near vision (8)

DOWN

1. IOLs have less posterior capsular opacification (11)
2. Near infrared fundus auto fluorescence using 787 nm excitation and 800 nm emission reveal fluorescence emitted by (12)
3. Is the most common AIDS-related opportunistic eye infection (15)
4. Second Thursday of _____ is celebrated as world Sight day (7)
6. Introduced pneumatic retinopexy (8)
7. First and only biologic approved for the treatment of uveitis (10)
11. Grading of Recommendations Assessment, Development and Evaluation (5)
12. Pattern Scan Laser with increased uniformity and precision of spot placement and reduced pain (6)
13. Hand-held electronic IOP measuring device (7)
DOS Clinical Monthly Meet – I (Dr. R.P. Centre, AIIMS)

The DOS Clinical Monthly Meet – I was held at J.L. Auditorium, Dr. R.P. Centre, All India Institute of Medical Sciences, New Delhi on July 24, 2016 from 11:00 A.M. to 1.15 P.M. The meeting which was well attended by 225 ophthalmologists, commenced at 11.00 AM and concluded on time at 1.15 PM followed by lunch.

DOS General Secretary Dr. M. Vanathi, Padamshree Prof. Atul Kumar, Chief of Dr. R.P. Centre, AIIMS, New Delhi on the dais along with the DOS President Dr. Rishi Mohan and (left to right).

Mini-Symposium: Overviews in OPHTHALMOLOGY
Chair: Prof Atul Kumar
Co-Chair: Prof J.S. Titiyal, Prof. Radhika Tandon

Case Presentations and Clinical Talk

Dr. Talvir Sidhu, Senior Resident presenting the first clinical case of Longterm Management of Congenital Glaucoma and discussant by Prof. Ramanjit Sihota

Dr. Ganesh, Senior Resident, presenting the second clinical case of Pediatric cataract with PHPV and discussion by Prof. S.K. Khokhar

Dr. Saurabh Kamal making the guest case presentation of Nasal Endoscopy and Lacrimal system - What lies beyond routine DCR!

Padamshree Prof. Atul Kumar presenting the Clinical Talk on Retinal OCT and Beyond...

The meeting was supported by Academic Grant from Cipla
Early Bird Prizes were sponsored by Berry & Herbs.
Delhi Ophthalmological Society
DCRS points rating system 2016 – 2017 for DOS MONTHLY CLINICAL MEETINGS

The two clinical case presentations, the clinical talk, and the guest case presentation will be marked for 100 marks each.

Based on the analysis of the attendance in the various institutes in the previous years, the attendance score is given as follows:

<table>
<thead>
<tr>
<th>Marking</th>
<th>Attendance (external delegates only)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&lt; 55</td>
</tr>
<tr>
<td>10</td>
<td>55 - 70</td>
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<tr>
<td>20</td>
<td>71 - 85</td>
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<tr>
<td>30</td>
<td>86 - 100</td>
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<tr>
<td>40</td>
<td>101 - 115</td>
</tr>
<tr>
<td>50</td>
<td>&gt;115</td>
</tr>
</tbody>
</table>

Overall meeting arrangement will be marked by delegates as AVERAGE, GOOD, & EXCELLENT.
(The marking corresponding to these is as follows: AVERAGE-10; GOOD-15; Excellent – 20)

Calculation of overall meeting assessment score
The calculation of overall meeting assessment marks for best institute will be as follows:
(i) The average of the two case presentations and clinical talks out of 300 marks will be calculated and reduced to 30 marks.
(ii) To this will be added the meeting arrangement marks based by the grading (a) given by the delegate. The total will be added up to 50 marks.
(iii) The average of this overall assessment of 50 marks will be totaled for all external delegates and to this will be added the attendance score (as given below), which will be the final score based on which the decision for best institute for the trophy will be awarded.

Example
From DCRS marking sheet of each external delegate:

<table>
<thead>
<tr>
<th>Step 1:</th>
<th>Case presentation I – c1 (100 marks)</th>
<th>Case Presentation II – c2 (100 marks)</th>
<th>Clinical Talk – t (100 Marks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL</td>
<td>- c1 + c2 + t (300 marks)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Step 2: (reduce to 30)

Step 3: 

\[
x \ (\text{out of 30}) + a \ (\text{arrangement grading}) \ (\text{out of 20}) = Y \\
(\text{out of 50})
\]

Step 4:
Take average of Y of all external delegates - av-Y

Step 5: Av-Y + Z (attendance score) = S (FINAL SCORE OF CENTRE)

POINTS TO BE NOTED:
1. All other DCRS rating regulations as before will be continued.
2. DCRS marking sheets will have details of time in of all delegates & marking sheets according to time of entry will be given to the delegate upon signing in the attendance register.
3. ONLY ATTENDANCE OF EXTERNAL DELEGATES UPTO THE START OF THE CLINICAL TALK WILL ONLY BE CONSIDERED for marking purposes.
4. All delegates will be required to hand in their completed DCRS sheets at the conclusion of the meeting, which will be counted by DOS staff, checked and signed by head of the institute/representative holding the monthly meeting and DOS Secretary (President/DOS executive committee representative) & subsequently sealed in their presence.
5. All centers are encouraged required to provide their meeting programme details 4 weeks ahead of their date of programme.
6. All presenters of case reports and clinical talk are required to submit their presentations to the DOS SECRETARIAT within two weeks’ time following the date of the presentation by email (dosrecords@gmail.com and dostimes10@gmail.com) for publication in the “Monthly Meeting Korner” section of the forthcoming DOS TIMES issues failing which a penalization of 5 marks will be made from the final score of the centre. The Heads of the hosting institutes may kindly ensure the same.
7. PLEASE NOTE THAT ALL DOS monthly meetings SHOULD commence by 11.0 am sharp. The number of speakers in the Clinical symposium should not exceed 3.
8. Violation of the recommendations for DOS Monthly meetings will result in penalization of the final DCRS score of the centre.
DOS Travel Fellowship for Partial Financial Assistance to Attend Conferences

Applications are invited for DOS Fellowship for partial financial assistance to attend conference(s).

Conferences

- **International**: Four fellowships per year (two fellowships can be awarded at a time if committee feels that papers are very good)
  - Maximum of Rs. 50,000/- per fellowship will be sanctioned

- **National fellowship**: The winner of the DOS best paper (A.C. Aggarwal Trophy) will be awarded complimentary registration for the DOS Winter Conference and DOS Annual Conference of the subsequent year.

Eligibility

- DOS Life Members (Delhi Members only)
- 75 or More DCRS Points
- Accepted paper for oral presentation, poster, video or instruction course.

Time since last DOS Fellowship

Preference will be given to member who has not attended conference in last three years. However if no applicant is found suitable the fellowship money will be passed on to next year. Members who has availed DOS fellowship once will not be eligible for next fellowship for a minimum period of three years.

Authorship

The fellowship will be given only to presenting author. Presenting author has to obtain certificate from all other co-authors that they are not attending the said conference or not applying for grant for the same conference. (Preference will be given to author where other authors are not attending the same conference). If there is repeatability of same author group in that case preference will be given to new author or new group of authors. Preference will also be given to presenter who is attending the conference for the first time.

Quality of Paper

The applicant has to submit abstract along with full text to the DOS Fellowship Committee. The committee will review the paper for its scientific and academic standard. The paper should be certified by the head of the department / institution that the work has been carried out in the institution. In case of individual practitioner he or she should mention the place of study and give undertaking that work is genuine. The fellowship committee while scrutinizing the paper may seek further clarification from the applicant before satisfying itself about the quality and authenticity of the paper. Only Single best paper has to be submitted by the applicant for review (6 copies). Quality of the paper will carry 50% weightage while deciding the final points.

Poster and Video

The applicant will need to submit poster and video for review.

Credit to DOS

The presenter will acknowledge DOS partial financial assistance in the abstract book / proceedings.

The author will present his or her paper in the immediate next DOS conference and it will be published in DJO/DOS Times.

Points Awarded

1) **Age of the Applicant**
   - a) < 35 years 10
   - b) 36 to 45 years 07
   - c) 45 years plus 05

2) **Type of Presentation**
   - a) Instructor / Co-instructor of Course 12
   - b) Free Paper (Oral) / Video 07
   - c) Poster 05

3) **Institutional Affiliation**
   - a) Academic Institution 15
   - b) Private Practitioner 20

4) The points awarded for DCRS rating in the immediate past year:
   - a) > 150 10
   - b) 75 - 150 05
   - c) < 75 Not Eligible

Documents

- Proof for age. Date of Birth Certificate.
- Original / attested copy of letter of acceptance of paper for oral presentation / video / poster or instruction course.
- Details of announcement of the conference.
- Details of both International & National Conferences attended in previous three years.
- Copy of letter from other national or international agency / agencies committing to bear partial cost of conference if any.
- Original air travel boarding passes and photocopy of the attendance certificate of the conference.
- Fellowship Money will be reimbursed only after submission of all the required documents and verified by the committee.
- Undertaking from the applicant stating that above given information's are true.
- If found guilty the candidate is liable to be barred for future fellowships.

Application should reach DOS Secretary’s office and should be addressed to The President, DOS before March 15, June 15, September 15 and December 15. The committee will meet four times in a year in the month of March, June, September & December within 2 weeks of last date of receipt of applications. The committee will reply within four week of last date of submission in yes/no to the applicant. No fellowship will be given retrospectively, that means prior sanction of executive will be necessary.

Delhi Ophthalmological Society
Room No. 479, 4th Floor,
Dr. R.P. Centre for Ophthalmic Sciences
AIIMS, Ansari Nagar, New Delhi - 110029
FOR KIND ATTENTION OF DOS VOTING MEMBERS

The recommendations of the Electoral Review Subcommittee as approved by Executive of DOS on 5th August 2015:-

I. DISPLAY OF THE LIST OF VOTING MEMBERS ON THE WEBSITE

It was suggested that the name and address of all voting members be displayed as the VOTER’S LIST on the DOS website. The online display of the updated voter’s list on the DOS website is to be ensured by October 15 each year. This is to be performed by the treasurer with the concurrence of the DOS President & Vice President.

II. PROFILE UPDATE BY THE DOS MEMBERS

It was emphasized that all DOS Members be responsible for updating their address change and voting status. Regular email communications may be sent out by the secretary / treasurer requesting for the same. Profile update is possible only on written request / email request from the member to the DOS General Secretary. The same may be acknowledged and profile update status be confirmed to the requesting DOS member within a stipulated time frame. It was suggested that provision for entry of alternate email ids be given in the member profile page so that communications for address change can be sent to more than one email id. Request for update of member profiles may be entertained until 15th January of the following year. Members providing false information/declaration of their address status will be subject to severe punitive action as per recommendations of disciplinary committee assigned to formulate these.

III. CONCERNS REGARDING EXISTING VOTER LIST

a) The committee addressed the apprehension that the current voters list contains names of DOS members who are no longer voting members and how the same be rectified. The committee deliberated upon the best way to ensure that all such members are made to update their address and voting status. It was reiterated that in the current scenario, the onus of address change should be placed on the members and they are required to provide an honest declaration of their current working & residential address and thereby their voter status.

b) It was also stated that senior DOS Members, who retire from practice and are still residents of Delhi, be considered as voting members. In other words working address is not essential if residential address is Delhi.

c) It was also opined that a complaint regarding status of voting member may be sent to the Secretary by any Delhi member (in case of members whose voting status is doubted or if a name is inadvertently omitted). Such complaints to the DOS Secretary should not exceed 25 per DOS member complainant & November 30th will be the last date for filing such complaints.

d) All facts pertaining to such complaints are to be verified by a committee consisting of the President, Vice president and the Treasurer. This could include seeking a clarification from the members and any other step considered appropriate. The committee will implement its decision after due notice to the member.

IV. ELECTION CAMPAIGN

It was agreed upon that non-ophthalmologists will not be allowed to campaign on behalf of the candidates at the conference/ election venue.

V. ELECTORAL PROCESS

a) The CV of all electoral candidates may be displayed on the DOS website following last date of withdrawal.

b) Last date for withdrawal of nomination to be 6 weeks prior to the date of election.

c) It was agreed upon that no DOS office staff be enrolled to participate as officiating staff of the electoral process.

d) The election area be well secured so that no unauthorized person can gain access.

e) Only members on the voter list and producing valid id document will be permitted to vote.

f) No validation by third parties will be permitted / recognized as identification during the voting.

g) A change of address within Delhi will not constitute a reason for disqualification from voting, as long as name is on voter list and there is a valid id.

h) In the event of any misconduct by members / contestants / voters during the electoral process, complaint may be made to the Election Commission / Appellate Committee which will investigate the complaint & if the misconduct is established, graded punitive action will be taken as per recommendations of the Disciplinary Committee assigned to formulate these.

VI. CUSTODY OF ELECTION RELATED DOCUMENTS IN THE EVENT OF DISPUTE

Custody of election related documents will be with the Election Commissioner. These will be handed over to the DOS office within 6 weeks of the date of the election. In the event of any dispute, the custody of election related documents will remain with the election commissioner till resolution of the dispute. Copies will be furnished as required to appropriate authorities.