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Editorial

Goodbye to a legend

“Better than a thousand days of diligent study is one day with a great teacher.”
— Japanese Proverb

Respected Seniors & friends,

Ophthalmology has produced some of the greatest clinicians and researchers. It is their commitment and hard work that ophthalmology can boast of the rapid advances and changes like no other field in medicine can. Cataract surgery itself has changed from ICCE to ECCE to Phaco, all in one generation! But it is our teachers, whose selfless contributions in building the surgeons of tomorrow, the researchers of the future and the insightful doctor that have ensured that this knowledge and advances reaches to all. And these great teachers are everywhere. Every institution boasts of a master teacher who has molded and sharpened minds. This editorial is dedicated to one such master, one who inspired, coaxed, cajoled and sometimes reprimanded yet it was just a day’s work for him.

Prof S P Garg who will be attaining superannuation at the end of October, is such a legend. And if anyone knew that the philosophy of life should be “to make friends and influence people” it was him. The number of lives he influenced, touched and molded often without even knowing, is awesome. His modus operandi was his simplicity and his uncanny ability to blurt out the painful truth without giving the other person the opportunity to mind it.

There cannot be a single ophthalmology resident passing out of R P Centre over the past many decades who has not been whiplashed by him for a hour in the rounds yet not remember him for his helpful nature and simplicity. Future generations of R P Centre residents will surely not be the same having never passed through one of his rounds.

He may leave this hospital but we all will forever remember this great human and teacher of Ophthalmology who could never been seen with his ophthalmoscope.

Thank you Prof Garg for being what you were. We all wish you the best.

Rohit Saxena
Secretary,
Delhi Ophthalmological Society
An MBBS degree is just a passport for Post graduation in Ophthalmology. How well you will be placed academically, financially and socio-politically depends largely upon your learning during PG and few years thereafter. Your competence will depend upon your hard work, desire to excel and pride in yourself. Your aim should be to get the best out of the institution and its faculty, earning goodwill and making an active attempt to learn from the strength of your teachers. However it is more of your responsibility to learn, than of your teachers to teach you. A common OPD scenario: you see a patient, write the treatment, finish work and leave. But imagine if you would have discussed the case for a few minutes, how much you would have gained in three years. When you are preparing a case its very important to be your own examiner? If you ask yourself, if I was the examiner, what questions I would ask, you will be surprised that most of the questions put up by the examiner would be the same. This will give you an opportunity to go back to the case and check what you have missed in the history and examination and will make your reply prompt and clear. While studying or reading try to analyse where that particular knowledge is going to be useful – for exams, viva, patient care etc. Also it is not the reading time that matters, but how much time that subject occupies your mind when you are not studying. Try to go through that subject in your mind again and again.

Have you mastered the ophthalmic techniques? If an optical shop owner or technician can do better refraction than you, then it should hurt your ego. Lets take indirect ophthalmoscopy. What it takes to master it, is a little bit of knowledge, may be some clarification from your seniors but largely hard work and a desire to excel. An overcrowded OPD or lack of equipment is not an excuse. If needed, buy one with your own money. Lost money can be regained but time and learning opportunities cannot.

Lets go to the operation theatre. Have you gone through the text of surgery which you are going to see and assist. If you are mentally there you should be slightly ahead of the surgeon i.e. you should know beforehand where he is going to place the instrument, what he is going to do and what’s going to happen in an ideal situation. If there is any deviation you should be able to analyse why it happened, so that you don’t repeat the same mistake and what are the options to correct it. In other words, mentally soak in the surgery. Every surgery has many steps and you need to master all of them one by one, to be a perfect surgeon. Lets take phacoemulsification. It involves incision, CCC, hydroprocedures, nucleus, epinucleus and cortex removal, implantation of IOL and securing the wound. Every step has got further sub steps. Lets take wound construction. What is the ideal incision in terms of external site, internal site, width, length and depth for a routine case? Have you mentally analysed if there is any variation? What are the advantages and disadvantages? Will it remain the same, if we are operating a hard cataract, floppy iris or high myopia? A majority of the patients will be alright even in a poorly constructed wound but the pleasure of doing a perfect surgery should give you a kick. You should enjoy your surgery just as an artist enjoys his creation and work, whether others appreciate it or not. When you get an opportunity to work with many surgeons do you compare or not? Can you identify the mistakes of not so good a surgeon? Have you gone through the surgery in your mind even before getting the opportunity to lay your hands on the patient? Believe me, if your mind has got an exact picture of what is to be done you will learn very, very fast. The mind gives all the commands for the work. So train your brain and your hands will follow.

It pays to be an academician. If initially you are not able to publish in indexed journals keep on sending well written articles to various state journals. It pays even more to be a good clinician. Suppose a patient comes to you for headache, do you take a relevant history to know whether the headache is cervical, neurological, ENT related, psychological or aggravated by ocular factors? When prescribing small spectacle numbers, not for vision but for eye strain, do you tell the patient that we are giving a therapeutic trial of spectacles? Are you aware what it is? Keep your mind alert, and mentally analyse and optimize your knowledge to be a smart learner.

Dr. Harbansh Lal
President, DOS
Central Retinal Vein Occlusion

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Q1. What is central retinal vein occlusion (CRVO)?
Ans: CRVO is the occlusion of central retinal vein at or just behind the level of the lamina cribrosa, which occurs typically in individuals aged greater than 50 years.

Q2. What is the pathogenesis of CRVO?
Ans: At the level of the lamina cribrosa, there are certain anatomic factors that predispose the central retinal vein to occlusion. First, the lumina of the central retinal artery and central retinal vein are narrower than they are in the orbital optic nerve, and the vessels are bound by a common adventitial sheath.

The flow of blood through the central retinal vein becomes increasingly turbulent as the vein progressively narrows at the lamina cribrosa, where it also may be further impinged upon by arteriosclerosis of the adjacent central retinal artery. This turbulence damages the endothelium in the retrolaminar vein, which exposes collagen and initiates platelet aggregation and thrombosis.

Q3. How does a patient of acute CRVO present?
Ans: A patient of acute CRVO presents with sudden painless loss of vision. This usually occurs on waking and can be mild or very severe.

Q4. What are the fundus findings in CRVO?
Ans:
• Flame-shaped, dot and blot hemorrhage, and dilated, tortuous vein involving whole of retina. (Figure 1)
• Cotton-wool spots, macular edema, and optic disc edema.
• Signs of old occlusion are vascular sheathing and venous collaterals.
• The diagnosis is based on clinical examination with slit lamp biomicroscopy and fundoscopy.

Q5. What are the risk factors of CRVO?
Ans: An increased risk of central retinal vein occlusion was found in patients with
• Systemic hypertension
• Diabetes mellitus
• History of open-angle glaucoma

The risk of central vein occlusion was decreased for patients with increasing levels of physical activity.

For women, the risk decreased with the use of postmenopausal estrogen and increased with a higher erythrocyte sedimentation rate.

Q6. How is CRVO classified?
Ans: CRVO is classified into Ischemic (non-perfused) or Non ischemic (perfused) CRVO.

<table>
<thead>
<tr>
<th>Nonischemic</th>
<th>Ischemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild vision loss, usually better than 20/120</td>
<td>Marked visual loss, usually 20/200 to only hand motion</td>
</tr>
<tr>
<td>Rare afferent pupillary defect</td>
<td>Afferent pupillary defect</td>
</tr>
<tr>
<td>Variable dot and flame hemorrhages, cotton wool spots are few</td>
<td>Extensive retinal hemorrhages in all 4 quadrants, retinal vein markedly edematous and engorged, several cotton wool spots</td>
</tr>
<tr>
<td>Macular edema less severe</td>
<td>Macular edema is often severe.</td>
</tr>
<tr>
<td>FA &lt; 10 DA of non perfusion</td>
<td>FA &gt; 10 DA of non perfusion</td>
</tr>
<tr>
<td>NVI/NVA decreased risk</td>
<td>60% will develop NVI/ NVA risk</td>
</tr>
<tr>
<td>ERG – b-wave amplitude normal or slightly decreased</td>
<td>Amplitude of b-wave is &lt;60%</td>
</tr>
</tbody>
</table>

Q7. How will you manage a patient presenting with CRVO?
Ans: All patients with central retinal vein occlusion should have a comprehensive ophthalmic evaluation, including an appropriate evaluation for glaucoma. In addition, they should be referred to their primary care physician for an evaluation of cardiovascular risk factors, including hypertension and diabetes.

Detailed examination on every follow – up (every month for 6 months)
• Visual acuity
• IOP
**Q10. What are the complications of CRVO?**

Ans:

- Undilated examination to look for NVI and NVA
- Dilated fundus examination

34% of non-ischemic CRVO get converted to ischemic CRVO

Systemic conditions are mostly associated with CRVO and should be evaluated and managed.

**Q8. When will you perform Fluorescein angiography (FA) and what is it role?**

Ans: FA is usually performed after 4 weeks until the haemorrhages clear. It also takes time for the retinal capillaries to obliterate completely.

Fluorescein angiography (Figure 2) shows:

- Delayed retinal vascular filling and marked increased retinal arteriovenous transit time
- Non perfusion areas – classifying ischemia
- Macular nonperfusion
- Macular leakage/edema
- Retinal neovascularization

**Q9. What is the role of OCT in management of CRVO?**

Ans:

- Used to measure macular thickness (cystoid macular edema or sub-retinal fluid)
- OCT can detect even subtle macular edema in the presence of significant hemorrhages, which is not evident by fluorescein angiography because of blockage from hemorrhage.
- Follow-up post therapy to measure response to treatment

**Q11. What are the causes of visual loss in CRVO?**

Ans:

- Chronic macular edema
- Macular ischemia
- Vitreous hemorrhage
- Neovascular glaucoma

**Q12. What are CVOS study guidelines?**

Ans:

- Once neovascularization in the anterior segment is detected, panretinal photocoagulation should be
instituted promptly. This will often result in regression of the iris vessels and prevent complete angle closure; this is also true in patients with some increase in intraocular pressure but in whom the angle is not occluded for 360°.

- Although grid photocoagulation lessens macular edema both angiographically and clinically, there was no difference in visual acuity between the treated and untreated patients. For treated patients, there was a trend toward decreased visual acuity in patients older than 60 years and visual improvement in patients younger than this; this effect was not seen in untreated patients.
- Although this study suggests a possible benefit to visual acuity in younger patients with macular edema who are treated compared with untreated controls, the number of patients in this subgroup is too small for a statistically valid comparison of treated versus untreated eyes.

Q13. What are the newer treatment modalities available for management for CRVO?

Ans: Steroids: Intra-vitreal Triamcinolone (Figure 3), Ozurdex (dexamethasone implant) Anti-VEGF drugs: Ranibizumab and Bevacizumab.

Q14. What were SCORE guidelines?

Ans: Standard Care vs. Corticosteroid for Retinal Vein Occlusion (SCORE) study. The SCORE study evaluated the clinical benefits of intravitreal triamcinolone for treating macular edema associated with vein occlusion. In the SCORE CRVO trial patients in the corticosteroid treatment groups were five times more likely to have a substantial visual gain at one year.

However, participants who received the 4 milligram dose had the highest rates of cataract formation, cataract surgery, and elevated pressure within the eye, indicating that the 1 milligram dose is safer for patients.

Q15. What were CRUISE guidelines?

Ans: The CRUISE trial (A phase 3, multicenter, randomized, sham injection-controlled study of the efficacy and safety of ranibizumab injection compared with sham in patients with macular edema secondary to CRVO) assessed the safety and efficacy of ranibizumab in patients with CRVO.

At six-month follow-up, a visual acuity improvement of three or more lines was observed in 46% of the subjects in the 0.3mg ranibizumab group, 48% of the subjects in the 0.5mg ranibizumab group, and 17% of the subjects in the sham group.

Additionally, subjects in the 0.3mg ranibizumab group gained an average of 12.7 letters from baseline best-corrected visual acuity; subjects in the 0.5mg ranibizumab group exhibited gained 14.9 letters; and subjects in the sham group gained just 0.8 letters.

Improvements were maintained in both treated groups at 12 months. Though subjects in the sham group did show some relative improvement in both visual acuity and macular thickness by month 12, the findings were not as significant as those from either treatment group.

Q16. What is CRVO of young?

Ans: CRVO occurring in less than 40 years of age is categorized as CRVO of young. Ischemic form is present in 20% of cases. Disc edema is more common finding at the onset, while macular edema is less frequently seen.

Inflammation of the central retinal vein has been proposed as a cause of the occlusion in young adults and for that reason it has been called papillophlebitis. The appearance of unilateral optic disc edema, dilatation, and tortuosity of the major retinal veins with a variable amount of retinal hemorrhage in young, healthy adults with complaints of blurred vision or photopsias has been called, in addition to papillophlebitis, benign retinal vasculitis, optic disc vasculitis, big blind spot syndrome, and presumed phlebitis of the optic disc.
Systemic or ocular disorders are often found. The visual prognosis in CRVO of young people is often poor; the more frequent cause of the reduced visual acuity is chronic cystoid macular edema.

Q17. What additional investigations are required?

Ans: In young patients, laboratory testing may be tailored depending upon individual findings, to include the following:

- Complete blood cell (CBC) count
- Glucose tolerance test
- Lipid profile
- Serum protein electrophoresis
- Hematologic tests - Underlying hyperviscosity states should be considered

In addition, thrombophilic screening, activated protein C resistance, lupus anticoagulant, anticardiolipin antibodies, protein C, protein S, and antithrombin III may be completed.

Polycythemia, Waldenstrom’s macroglobulinemia, Multiple myeloma, Leukemia, High homocysteine levels, and Antiphospholipid syndrome should be ruled out.
Penetrating keratoplasty has been the gold standard for treatment of endothelial dysfunctions for last 100 years\(^1\). Although results of penetrating keratoplasty have been excellent, its disadvantages are well known\(^2\). These are delayed visual rehabilitation and poor visual quality due to high and irregular astigmatism. Surface and suture related problems include graft infection, graft rejection, risk of wound dehiscence, long follow-up visits and problems of long term use of steroids. This caused a demand for suture less keratoplasty and replacing only diseased endothelium. Melles gave the key breakthrough in endothelial transplants in 1998 and called it Posterior Lamellar Keratoplasty (PLK)\(^3\). His work was supplemented by Mark Terry (Deep lamellar endothelial Keratoplasty, DLEK)\(^4\) and Francis W. Price (Descemet's Stripping and Endothelial Keratoplasty, DSEK)\(^5\). The basic difference in DLEK/ PLK and DSEK is recipient dissection. In DLEK, posterior stroma along with Descemet’s membrane is removed while in DSEK; only Descemet’s membrane is removed. Because of technical ease, DSEK has become the treatment of choice for endothelial dysfunctions like endothelial decompensation after cataract surgery (Pseudophakic or aphakic bullous keratopathy), Fuch’s endothelial dystrophy, congenital hereditary endothelial dystrophy (CHED), ICE Syndrome and previous failed grafts\(^6-9\).

Endothelial keratoplasty (DSEK) patients regain vision much sooner than penetrating keratoplasty patients. Better visual quality is achieved because of minimal astigmatism\(^6-9\). The eyes are structurally stronger and more resistant to postoperative traumatic injury, and surgery is performed with self-sealing incisions, so the risk of losing the eye from intra-operative suprachoroidal hemorrhage is virtually eliminated. There is no suture related graft infection or graft rejection and frequent visits are no longer required as in Penetrating Keratoplasty.

**Pre-operative assessment & Contraindications**

Pre-operative assessment is required mainly to rule out glaucoma and posterior segment abnormality. Anterior chamber depth is an important factor since this space is used to manipulate the donor graft. Careful slit lamp examination is required to rule out anterior synechiae, vitreous and irregular AC depth. In initial cases, it may be prudent to avoid DSEK in such cases, but as the surgeon gains experience, DSEK can be performed in almost all cases of endothelial decompensation. Anterior segment OCT and UBM can be helpful in patients having very hazy view. Appropriate method should be used to check IOP. Ultrasound B Scan helpful to rule out gross posterior segment abnormality and disc excavation.

**Procedure**

The procedure of DSEK will be discussed under following headings:

- Preparation of Donor Tissue
- Preparation of recipient
- Implantation of Donor tissue in recipient eye

**Preparation of Donor tissue**

**Tissue Requisites**

Any donor corneal tissue that is suitable for optical penetrating keratoplasty may qualify for DSEK. Corneal tissue with good endothelial cell count that has anterior stromal scar cannot be used for PK but can be used for DSEK. In early cases, surgeon may choose ‘very good’ to ‘excellent’ donor tissue (Endothelial cell count more than 2500 cells/mm\(^2\)) since the manipulation of donor lenticule may be more during the learning curve.

**Procedure**

The target is to prepare a donor disc of required diameter having posterior 1/3rd stroma and Descemet’s membrane with healthy endothelial cells. Preparation can be manual

**Figure 1:** Straight end of blunt dissector to dissect the cornea up to the done
or automated (Microkeratome). The latter has been termed as Descemet’s Stripping and Automated Endothelial Keratoplasty (DSAEK). Femtosecond Laser can also be used to prepare donor lenticule (FS-DSEK). With the present data, all these methods seem to be comparable in clinical outcome. Since manual dissection is most cost effective, we perform manual dissection in all our cases. Many eye banks in western world supply precut donor disc. However, the corneal surgeon should be well versed with donor tissue preparation.

**Instruments required for Manual dissection**
- Artificial Anterior Chamber
- Blunt dissectors
- Diamond knife or prefixed depth blade

**Steps of manual preparation of donor disc**
- Donor tissue is mounted on artificial anterior chamber. It is important to keep the optimum pressure. Too low pressure tends to make dissection irregular and higher chances of cut through. Too high pressure increases the chances of perforation. Also, one tends to get thinner lenticule with high pressure in artificial chamber and a thicker one with low pressure.
- Epithelium is removed to improve the view.
- Disposable blade with prefixed depth (300 microns) is used to make 3-6 mm limbal incision. The length of incision depends on technique of graft insertion. If forceps insertion or Sheet’s glide is used for graft insertion, it is important to use larger incision to avoid compression forces on graft. The incision size may be smaller for glide (Busin’s Glide, Tan’s Glide etc.) assisted graft insertion. The incision site may be scleral especially in cases with larger incision. We prefer limbal incision and clear corneal tunnel to avoid iris prolapse during graft insertion since we use anterior chamber maintainer in all our cases.
- Manual lamellar dissection is carried out at approximately 2/3rd depth with 2 blunt dissectors. Initial plane is created with Crescent’s knife used for small incision cataract surgery. The dissection is completed with blunt dissectors. One can use double-sided blunt dissectors in which one end is straight and the other is curved to match the curve of cornea.
- Straight end of blunt dissector is used up to the dome of cornea. (Figure 1)
- Curved end of blunt dissectors is used beyond the dome and up till opposite limbus. (Figure 2) It is important to dissect into the opposite limbus, which ensures the complete separation of posterior lamellae throughout.
- While dissecting right or left from the center, the dissector is tilted towards right or left respectively so that side of dissector facing center is lifted upwards. While dissecting beyond corneal dome, foot (junction of handle and main dissector) of dissector is lifted. Both these maneuvers help to achieve a donor lenticule with almost homogenous thickness.
- Donor tissue is removed from artificial anterior chamber and desired diameter is punched.
- Sinskey’s hook is gently inserted just inside the dissected plane to check the complete dissection all around. In case, few fibers are still attached, Vanna’s scissors can be used to cut these fibers.

**Figure 2: Curved end of blunt dissector to dissect the cornea into the opposite side of limbus**

**Figure 3(a): Fibro vascular pannus covering the long-standing corneal edema**

**Figure 3(b): Clear view to perform endothelial keratoplasty after removal of pannus**
Preparation of Recipient Bed

- **Anesthesia:** Surgery is done under conventional peribulbar anesthesia, although it can be done under topical anesthesia as well.

- **Pupillary constriction:** Preoperatively pilocarpine 2% is used to constrict the pupil. This is done just before implantation of donor disc. The rationale for the same is to protect the crystalline lens in phakic DSEK and to prevent any chance of IOL dislocation in pseudophakic eyes during graft insertion.

- **Epithelial Debridement:** Epithelium in these cases is edematous and loose and removing the epithelium improves the view. In case of long standing pannus, it is removed by dissection. Plane is reached just below the fibro vascular scar and it is removed in total. Figure 3a shows a case of pseudophakic bullous keratopathy with fibro vascular pannus. Note the removal of pannus intraoperatively in (Figure 3b). Most of the times view below is good enough to carry out the whole procedure.

- **Surface Marking:** Circular mark of desired diameter can be made with gentian violet on surface, which serves as a reference mark for Descemet’s stripping. This step is not necessary and it can be planned to remove most of the Descemet’s membrane.

- **Side Ports:** Three 1-mm side-ports are made at 6, 10 and 2 o’clock positions. 10 and 2 o’clock incisions are for Descemet’s stripping and to manipulate and unfold the donor lenticule. 6 o’clock incision is used for anterior chamber maintainer (ACM).

- **Viscoelastic Agent:** It is better to avoid any kind of viscoelastic substance. In case the surgeon is not comfortable with ACM, only cohesive viscoelastic agent should be used. Dispersive viscoelastic agents tend to interfere with graft adhesion. We prefer to do the procedure under ACM only.

- **Descemet’s Stripping:** Circular scoring of the Descemet’s membrane is carried out with a reverse Sinskey’s hook (Figure 4) corresponding to epithelial template mark, if made. Scoring (touching the membrane with optimal pressure) can be done in a complete circle form (Descemetochorhexis) or in a can opener form. Scoring makes a cut in the Descemet’s membrane, which can later be completely stripped off with the help of the hook. Trypan blue (0.06%) solution is used to stain DM after scoring or the procedure can be performed under red glow from fundus, depending on view available for surgery. DM stripping may be avoided in patients with previous failed graft (Penetrating keratoplasty).

- **Corneal Tunnel:** 3 to 6mm clear corneal tunnel is created starting at limbus. The site of main port is superior or temporal if Forceps or Sheet’s glide is used for graft insertion. It is superonasal when Busin’s Glide is used because it is easier to pull the graft from inferotemporal port.

- **Additional Surgery:** Cataract surgery, anterior vitrectomy or IOL exchange, if required, is done at this stage since the view is comparatively better after removing Descemet’s membrane and epithelium. If there is no capsular support, ACIOL can be implanted if the AC is deep. Posterior iris claw lens or scleral fixated IOL are other options that can be considered depending on case and surgeon expertise.

- In case Viscoelastic agent is used, it is washed out thoroughly and carefully with balanced salt solution (BSS) using an irrigation/aspiration cannula and AC is then well formed with BSS.
The posterior lamella of the donor tissue is folded into an asymmetric ‘taco-shape’, in a 60:40% ratio with a fine forceps grasping only the edge of the donor lenticule. This ‘taco’ is gently held at the leading edge with capsulorrhexis forceps with 60% side up and inserted through the tunnel into the AC like a foldable IOL. The platforms of the capsulorrhexis forceps do not oppose thereby minimizing the crush injury to the donor endothelium.

Unfolding the donor disc: Unfolding the donor tissue is very crucial step and is biggest challenge, particularly during the initial learning phase. The time used and manipulation should be minimal to protect endothelial cells. Various methods can be used for the same.

- A bent 30-gauge needle (reverse cystitome) on a 2-cc air syringe is used to gently engage the posterior edge of the anterior flap of the folded donor lenticule and fixate it against the host corneal stroma. While maintaining fixation, an air bubble is injected posterior to the graft, causing it to unfold.

- A ‘hitch suture’ is taken through the peripheral edge of the donor lenticule before folding it and inserting it into the recipient eye. A Sinskey’s hook is inserted through a limbal stab incision is then used to grab the suture loop and unfold the donor tissue.

Busin’s glide assisted graft insertion: Posterior stromal donor tissue is loaded onto the plate of Busin’s glide with endothelial side facing upwards. It is coated with cohesive viscoelastic substance and was pulled into the tunnel of Busin’s glide with a forceps touching only stromal side. The tip of Busin’s glide is kept at the external opening of main wound and the graft is pulled into AC by an internal limiting membrane pealing forceps from the clear corneal side port on the opposite end. The tip of the Busin’s glide doesn’t go into the main port at any time of surgery and it helps if the port for pulling the graft in inferotemporal quadrant of cornea. The bottle height of irrigation is kept low while pulling the graft into the anterior chamber. We prefer this method and found this to be repeatable in almost all the cases.

Sheet’s glide assisted graft implantation: The main wound is enlarged and a Sheet’s glide is placed inside the wound. Both Sheet’s glide and endothelial side of donor tissue is covered well with cohesive viscoelastic substance and the donor tissue is slid inside the eye using Sinskey’s hook or modified 30G needle.

- Centering the donor lenticule: It is done by massaging over the cornea with an iris repositor or round cannula after filling the anterior chamber completely with air. Interface fluid is removed by gentle massage of corneal epithelial surface with a flat cannula. We had been using 2-4 mid peripheral stromal punctures (venting incisions) to drain the interface fluid in our initial cases. It has been found not to be of much additional use because once the graft sticks to the host stroma, endothelium starts pumping fluid out and ensures further adhesion. Venting incisions may be helpful in cases, which are more predisposed to graft dislocation e.g., aphakes, children and failed graft.

- After 30 min, 40-50% of the AC air bubble is replaced with BSS. The intraocular tension is checked digitally. Apart from antibiotics and steroids, topical homatropine should be given at the end of the surgery to prevent the secondary glaucoma. A bandage contact lens is placed till epithelium is healed.
The eye is patched and the patient is instructed to lie supine for at least 12 hours.

**Postoperative Medications**

Postoperative patient can be discharged after 48 hours. Postoperative medications include topical steroids (Prednisolone acetate or betamethasone) in tapering doses starting from 8 times per day to 1 time per day over one year and finally on topical fluoromethalone 1 time per day indefinitely.

**Outcomes**

Visual Acuity: Mean best spectacle-corrected visual acuity (BSCVA) of 20/40 is generally achieved within 3–6 months of surgery. Pictures 5-7 show the outcomes of endothelial keratoplasty in different conditions of endothelial dysfunctions. Very few patients gain 20/20 vision and the cause can be minimal interface haze which is not detectable clinically. DMEK is an attempt to solve this problem although it has its technical difficulties.

Endothelial cell loss: Mean endothelial cell loss at 6 months after DSEK has been found to be 34% in 2 different studies. Factors contributing towards higher endothelial cell loss are compression of donor tissue during insertion and any donor reattachment procedure. Coating of donor tissue with viscoelastic substance and use of single point fixation forces minimize endothelial cell loss. Glide assisted donor insertion is associated with lesser endothelial cell loss than forces assisted one because of lack of graft compression forces in the former technique.

**Complications & Management**

- **Graft Dislocation**: The recipient interface exposed after stripping Descemet’s membrane is extremely smooth and provides little traction for the donor graft, so graft dislocation is the most frequently reported complication after DSEK (10-34.7%). A detached graft can usually be reattached by repeating the air injection procedure. It is good to leave the air in longer the second time to ensure firm attachment. Drainage of interface fluid after filling the anterior chamber completely with air is most important factor to prevent graft dislocation.
  - **Graft rejection**: Incidence of graft rejection in DSEK is reported to be 7.5% within first 2 years. Author feels it is important to continue topical steroids indefinitely.
  - **Pupillary block glaucoma**: This can be relieved by letting some air out and dilating the pupil. Removing 40-50% of air after surgery and dilating the pupil prevents pupillary block.
  - **Graft failure**: Primary graft failure can be a complication mainly during learning curve because of excessive manipulation of donor lenticule or reattachments. In such a scenario, replacing a fresh donor lenticule after stripping off the older one can be easily performed.

**Conclusions**

There has been a paradigm shift in management of endothelial dysfunctions in last few years and DSEK is now a widely accepted as treatment of choice for decompensated corneas. In US, donor corneas used for endothelial keratoplasty has gone from 4.5% to 45% in 3 years. Main reason for this paradigm shift is quicker visual rehabilitation and an improved safety profile compared with standard penetrating keratoplasty. Many innovations are expected in coming years especially to minimize endothelial cell loss and achieving 20/20 vision.

**References**

Senior Ophthalmic Surgeons for our Nabi Karim (Qutab Road) and Hauz Rani (Saket) hospital to perform phaco cataract surgeries with IOL Implant.

Ophtalmic Specialists for OPD at hospitals and dispensaries.

Ophthalmic Specialist for camps organized mostly on Sundays.

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Managing subluxated lens by phacoemulsification reminds us of Funambulism (Tight rope walking) and it remains a challenge for cataract surgeons. It complicates at each step of the procedure therefore, it has been an enigma for all ophthalmic surgeons. Thus proper preoperative planning and careful surgical approach is required. By using Capsule Retractors (CR) at capsulorhexis margin and Capsular Tension Ring (CTR) in the bag, safe phaco is possible in visually rehabilitating patients with subluxated lens.

To recapitulate, partial displacement of crystalline lens from its central position in the pupillary area is known as subluxation of lens. This could also be called as zonulopathy or zonular weakness. Etiologically it could be congenital (inherited), or acquired. Inherited forms do not necessarily manifest at birth and are present in conditions like: Marfans syndrome, Homocysteinuria, Weill Marchesani syndrome. Other associated conditions are Retinitis pigmentosa and pseudoexfoliation syndrome.

The acquired subluxation of lens may occur due to hypermaturity of cataract, blunt or penetrating trauma, previous eye surgery, high myopia etc. leading to degeneration or weakness of zonules.

**Signs of zonular damage**

**Subtle signs of zonulopathy**
- Focal Iridodoneses.
- Iridolenticular gap.
- Visibility of lens equator during eccentric gaze.
- Decentred nucleus in primary position.
- Changes in contour of lens periphery.

**Obvious signs of zonulopathy**
Includes phacodonesis, Vitreous prolapse, iridodonesis and lens subluxation.

Even without development of cataract, subluxation of the crystalline lens can induce significant visual symptoms such as large refractive errors, anisometropia or amblyopia during childhood.

Even though surgical techniques have evolved considerably, intervention continues to have a reserved visual prognosis depending on associated co morbidity.

**Indication of surgery**

**In Ectopia Lentis:**
- When margin of lens is seen in pupillary area.
- In progressive subluxation.
- Threatened posterior or anterior subluxation.
- In the presence of significant cataract.

**Preoperative evaluation**
- Note the area of zonular dehiscence under full dilation of pupil.
- Vitreous herniation in the anterior chamber.
- Presence of phacodonesis.
- Posterior shifting/ displacement of lens in lying down position in cases of gross zonulodialysis.
- Look for the presence of co morbid conditions affecting visual outcome viz. corneal opacity, pseudoexfoliation, anterior/posterior synaechiae, traumatic mydriasis, vitreous hemorrhage, retinal or macular pathology etc.
- Systemic examination and family history is to be taken properly. A complete cardiovascular and musculoskeletal evaluation is required in Marfans syndrome and Sodium Nitroprusside test for homocystenuria before subjecting the patient for general anaesthesia in cases of Ectopia Lentis.

**Surgical Approach**

**Anaesthesia:** General anaesthesia is recommended in paediatric age group patients. In adults, peribulbar anaesthesia is suggested, keeping in view the longer duration of surgery.

**Incision:** Clear corneal incision is to be given, away from the area of zonular dialysis. If incision is made in the region of zonular tear, a slightest leak of Ocular viscoelastic device (OVD) from the anterior chamber during the subsequent steps of surgery will cause the vitreous to come into the anterior chamber and then out through this wound. The zonular defect will enlarge further; all this is enough to jeopardize the whole surgery.

Initially a small incision, less than the size of 15° blade is made. The size of incision is sufficient enough to enter fine OVD cannula, cystitome and microhexit forceps. This avoids aqueous leak, shallowing of the anterior chamber and vitreous disturbance.

**Capsulorhexis:** It is suggested to use high molecular weight OVD with good retention & tenonape property. This is required to prevent shallowing of the anterior chamber and vitreous herniation.
Capsulorhexis is relatively difficult to perform than the routine cataract cases with intact zonules; this is because of the instability or laxity of capsule. Equal amount of radial traction provided at the circumference of the normal lens by the zonules maintains anterior capsule as a taut membrane. The lack of zonular circumferential traction due to tear or diffuse zonular weakness will create difficulty in incising the anterior capsule as if the cystome is blunt (Figure 1).

Sometimes in post traumatic cases due to inflammation, thickening or fibrosis of the anterior capsule is observed which causes extra trouble in performing capsulorhexis successfully in already lax anterior capsule. With weak zonules the risk of radial anterior capsular tear significantly increases because of pseudoelasticity.

A capsulorhexis of 5-5.5 mm size would be ideal. Making an initial small opening which is enlarged at a later stage is also a good option, as it reduces the risk of a peripheral extension. One should remember that use of capsular retractors (CR) or a capsular tension ring (CTR) requires a continuous curvilinear capsulorhexis. For creating and maintaining an intact capsulorhexis, erring on the side of a smaller diameter that can be secondarily enlarged after IOL implantation is better than risking for a large incomplete capsulorhexis with a radial tear.

Proper centering of capsulorhexis is extremely important in relation to the circumference of the lens more so in a cases of ectopia lentis where the lens is markedly displaced or decentered. For this sometimes we may have to reach under the iris to avoid eccentric capsulorhexis.

Worthy to mention, that a firm grip provided by microrhexis forceps which entails small incision is a useful tool to aim for a successful capsulorhexis.

**Capsule Retractors:** Fixing of capsular retractors at the capsulorhexis margin after filling the chamber with high molecular weight OVD is the next useful step. This is more so in a case of significant circumferential zonular weakness where you observe gross phacodonesis. These cases have marked phacodonesis and are different from other variety of cases as the lens is central with no displacement on any side.

The clock hours of subluxation determines the number of capsule retractors to be placed. Larger the area, more the number of retractors to be placed in order to provide adequate support to the capsular bag (Figure 2).

Limbal stab incision is given in the area of subluxation; capsule retractor is then fixed at the intact capsulorhexis margin. Use plain forceps to hold the retractor, slide it inside through the incision. One can use any second instrument like iris spatula from inside to stabilize the iris retractor at the margin of capsulorhexis in case of difficulty.

Gently apply traction by slipping the stopper of the self retaining retractor. A sudden forceful traction should be avoided, as this can tear the capsulorhexis margin and jeopardize whole case.

Gradually increasing the traction on each retractor one by one starting from one end of the area of subluxation is recommended. This will uniformly pull the lens and bring it to the site of normal anatomical position. Thus, it creates a barrier for the prolapse of vitreous in anterior chamber; it also prevents further damage of the adjacent zonules. It provides necessary radial traction on the capsular bag which counteracts the aspiration forces of phacoemulsification and cortex. All this is mandatory for the successful phaco outcome.

External radial fixation by CR provides anchoring and fixing of the lens bag this is similar to the stability provided by the trampoline which is stretched on all side by equal traction. This can counteract variety of unequal forces encountered in all directions during the course of hydrodissection, nucleus rotation, nucleus emulsification and cortex aspiration. Finally, they restrain the capsule from being aspirated and dehisced by the phaco and I/A tip.

The author has specially designed Iris Retractors to suit the need for ease and efficacy of the surgical technique and because of its use on capsulorhexis margin they are called, Modified Capsule Retractors (MCR) (Figure 3).
To compare, for severe zonular deficiency capsule retractors are significantly more effective than capsule tension ring for safe & successful phacoemulsification outcome. This is because CTR can only redistribute the variety of forces on the remaining intact zonules. Larger or more the area of zonular defect, the less effective a CTR is at stabilizing the bag, this can be observed in a case video of phacodonesis with no displacement of lens. CTR is helpful in focal zonular dehiscence by redistributing the mechanical forces to areas of stronger zonular support.

**Nucleus Emulsification**

A slow motion phaco keeping lower than normal parameters as would have been used by the surgeon for the particular grade of cataract is recommended. Direct Phaco chop technique is preferred as it significantly reduces the stress placed on the zonules and capsule. As forceful sculpting or rotation of the nucleus, may shear zonules in the oppositely located quadrants.

One should always remember to perform minimum movements inside the capsular bag so as to avoid any undue traction on the remaining zonules and stretching of the capsular bag. Flipping and prolapse of nucleus and epinucleus from the periphery to the centre is very helpful where they can be further chopped and removed.

Low vacuum and low aspiration flow rate is useful for successful phaco outcome. This is all the more important when you are removing the last nucleus fragments and epinucleus. Repeatedly filling the anterior chamber by high molecular weight OVD is beneficial during the entire course of phacoemulsification procedure. This helps by preventing trampolining of the flaccid posterior capsule towards the aspirating instrument. Pushing dispersive OVD in the region of zonulodalysis keeps the anterior vitreous face behind and prevents vitreous disturbance.

During entire procedure of phacoemulsification, avoid collapse of anterior chamber while removing any handpiece. To achieve this leave irrigation hand piece ‘ON’ inside the chamber, remove aspiration hand piece, and with this hand simultaneously fill the chamber with OVD.

**Cortex Aspiration**

With caution and care one can successfully do cortex aspiration which is different and risky in these cases. As emphasized earlier complete & proper hydrodissection leaves little epinucleus sheet adhered to posterior capsule. One has to be very careful in separating cortical sheet adhered to the redundant posterior capsule.

Bimanual Irrigation and aspiration (I/A) is useful in such cases. It increases the access in all areas including the sub incision region. Also, any misdirection of the irrigating fluid towards the anterior vitreous in area of zonulodalysis could be avoided. Always keep an eye on the aspirating port for any inadvertent holding and pulling of anterior or posterior capsule.

Always keep an eye on the aspirating port for any inadvertent purchase of anterior or posterior capsule.

After cortex aspiration bag is filled with OVD and CTR is carefully implanted in the bag. I prefer implanting CTR through the small side port incision by gently sliding or pushing it inside with the help of plane forceps. The side of side port incision is so selected that the advancing tip of the CTR is directed inside the capsule bag towards the area of intact zonules. There should be no anterior or posterior capsule tear. The CTR is pushed inside firmly and carefully using bimanual hand on hand technique. The terminal end of ring is next pushed inside the bag with the help of sinskey hook and with another sinskey hook from main section the trailing end is tapped inside the bag; otherwise the trailing end slips in the ciliary sulcus outside the capsular bag which is then difficult to retrieve. Throughout one should keep an eye on the advancing tip of CTR so that it does not pierce or push the capsule bag and damage it.

I feel, when zonulodalysis is less than 5 clock hours, CR along with CTR is useful. In more than 5 clock hours’ zonulodalysis, CR with modified CTR (MCTR or Cionni’s Ring) is recommended which is fixed along with bag by 10’0 prolene suture to the sclera.

**Technique of fixing Modified CTR (MCTR)**

Before inserting MCTR (Cionni’s Ring) in the bag, one end of the 10’0 prolene suture is tied to the extra haptic which is placed above the plane of MCTR so that it remains above the capsulorhexis margin (Figure 4). The other end of this
prolene suture has got a long straight, fine needle. Gently push MCTR inside the lens bag through the main wound pushing towards the area of intact zonules after feeling the bag and anterior chamber with OVD.

A 27G hollow needle is then passed inside through sclera, 1-1.5mm away from limbus through the floor of scleral tunnel/ scleral flap. This emerges inside from ciliary sulcus region under the iris and above the capsulorhexis without piercing the bag. Guided by this hollow 27G needle, long needle along with proleene suture is brought outside. After pulling out, proleene suture is tied to the sclera. This fixates the lens bag for the future.

Next the retractors are removed and foldable IOL with square edge is injected inside the bag. A single piece foldable IOL is preferred as these IOL’s opens up slowly and gently without creating extra stress on the bag and zonules.

Automated anterior vitrectomy should be performed whenever one feels it necessary, in the presence of vitreous disturbance. At times the vitreous is already present in the anterior chamber before the case is begun, then one has to clear all the vitreous from the anterior chamber by performing automated anterior vitrectomy in the beginning itself.

The author has a personal experience of more than 5 years of using this technique of combined CR and CTR in a variety of cases with excellent immediate and long term results. Use of CR is very helpful in providing excellent surgical control during all steps of phacoemulsification as compared to the technique of using CTR alone. Implantation of CTR at the end of phacoemulsification is necessary in maintaining stability, shape and integrity of the capsular bag and centration of IOL in long run. The technique is simple and reproducible in majority of cases of subluxated lens. Excellent visual rehabilitation is achieved in most our cases, although visual recovery depends on the comorbid conditions of the eye.
When you think of modern day cataract surgery, Phacoemulsification (PE) immediately comes to your mind. It is time tested, best cataract surgery in the world. So every eye surgeon in India and abroad wants to learn this technique. Medical education in India is such that not many of the post graduate medical colleges are teaching this technique practically. Most of our postgraduates pass their exam without doing even a single case of Phacoemulsification (PE). Manual Small Incision Cataract Surgery (SICS) is the most commonly done eye surgery in India. Most of the eye surgeons and post graduates are able to do it. So everyone who is not doing Phacoemulsification (PE) wants to graduate from SICS to Phacoemulsification (PE).

Manual SICS is a simple surgery. First of all two side port incisions are made at three and nine o’clock positions. Chamber is filled with visco-elastic and capsulorhexis is performed from the side port. Though capsulorhexis is preferred, Manual SICS can be performed even without complete rhexis or even after “Can-opener” capsulotomy. Here after undermining the conjunctiva, homeostasis is done. A frown incision is given just behind the limbus. It is astigmatic neutral zone. Using crescent knife a sclero-corneal tunnel is made. Here we make deep pockets on both sides. Cornea is entered by 2.8 mm keratome and tunnel is extended on both sides by enlarging keratome. Hydro dissection is done to prolapse out the nucleus. Nucleus is rotated to make it free from the bag.

There are various methods to bring the nucleus out of AC. I prefer ‘Sandwich technique’. In this, after putting viscoelastic (OVD) above and below the nucleus, Wire vectis is kept behind the nucleus and Sinskie hook above it. They are gently pressed together and withdrawn slowly. They come out with nucleus in between them. Viscous-expression of cortical matter is done. Rest of cortical matter is removed by Simcoe canulla. OVD is put again to form the chamber. IOL is inserted in the bag. After hydrating the wound on both sides, OVD is removed by Simcoe canulla and chamber is formed. We press on top the cornea to check the integrity of wound. It is padded for at least 3-4 hours.

On the other hand, Phacoemulsification is a totally equipment based surgery. In Phacoemulsification after making side port incision, chamber is filled with OVD. In supero-temporal part of the limbus, a scratch incision is made at the 11 o’clock position. From this incision, we make about 2mm of corneal tunnel by 2.8 mm keratome. Rhexis is performed from side port. Some people prefer to do rhexis from main corneal tunnel using Utrata’s forceps. Hydro dissection is performed to separate the nucleus from the capsule. Here we perform cortical cleavage hydro dissection. We press the centre of nucleus after each hydro dissection. We see the fluid wave travelling behind the nucleus. After this, a central trench is made in the nucleus. Nucleus is divided into two halves. Finally, they are emulsified one by one.

If you are not already doing capsulorhexis in all your cases of SICS, start doing it in all cases. Here is how you should start. After making side port incision trypan blue dye is put in to the AC under Air (that is first air and then dye is put in the AC) after 5 seconds dye and air is replaced by OVD put into the eye from the side port. A cystitome is made from 26G-27G needle. Cystitome is taken into eye from side port and 2.5mm incision is made on the anterior capsule of the lens starting from centre towards periphery. Then this is lifted up to make a flap which is engaged by the tip of cystitome and rotated circumferentially to complete the capsulorhexis. Ideally capsulorhexis should have 5.5mm diameter.

Before entering with phaco probe into the eye of a patient one should have feel of doing phacoemulsification eb externo. For this remove various density of nuclei by SICS and try to emulsify them in a bowl of water. If you keep rubber cap of
a injection vial in bowl and keep nucleus inside its cup, then this simulates as you are working in anterior chamber (AC). You should try different density nuclei and have the feel how easy or tough is to emulsify these nuclei. Other method is using Kimura eye. This has been developed by a Japanese scientist. In this you can practice rhexis as well as actual phacoemulsification.

The third method is to practice on goat’s eye. Get fresh goats eyes from a butcher. Keeping it under microscope, we make side-port incisions fill it up with OVD and do the rhexis. Make the tunnel Incision as Phacoemulsification and do some central sculpting so that it can accommodate human cataract nucleus. Open the eye from the other side as ECCE and put Nucleus previously removed by SICS. Close the incision by sutures. Now do the Phacoemulsification from the other incision we made for this purpose. This way it is closest to doing Phacoemulsification in human eye.

Another way of transit to phaco can be through “Modular Training” but it has to be carried out under supervision. Here the learning surgeon initially starts with I/A and starts getting friendly with the machine. Also he/she develops the feel of foot pedal in the meanwhile. Thereafter he learns to “eat up” the broken pieces of nucleus and finally takes up the job of breaking up of nucleus into pieces. Wound construction and capsulorhexis is done by the experienced surgeon till the last so that inadvertent complications can be managed well and there are lesser chances of conversion back to SICS/ECCE.

There are a few mental and technical prerequisites before making the transit from SICS to Phacoemulsification.

**Mental prerequisites**

- Remove fear & gain confidence.
- Back up of experienced surgeon in OR (preferable)
- Master one technique (copy one surgeon)
- Case selection

Let’s elaborate on this- When one decides to take a leap ahead and shift to Phacoemulsification, it is best to introspect first. Am I prepared? One must ensure what exactly he/she is going to do and preferably start in presence/guidance of an experienced surgeon. One should have no confusion regarding the technique he is going to opt, rather try to copy the senior’s technique and then try to innovate later.

Imagine your plan A for the whole case and introspect after every case for further improvement. Plan B must always be ready to take care of catastrophe. One must be able to identify the complications early and should be prepared to convert the case back to SICS or ECCE.

Before choosing a case for Phacoemulsification, co-morbidities must be seen before hand. A Typical patient should be a 60+ female (Figure 1) Ensure a clear cornea, well dilated pupil and a NS grade III cataract. Have an eagle’s eye for deep set eyes, zonular dialysis, pseudo exfoliation, and high myopia, posterior polar and very soft/hard cataracts.

The surgery should not be kept on a busy day. You should attempt when you are relaxed and not tired at all. Patient should be having good vision in his other eye and should not be very demanding.

It would be a piece of cake if you plan your OT with a senior surgeon, as his/her presence would not only boost up your confidence but also help you out in situation of crisis if any.

**Technical prerequisites**

- Hand, eye and foot co-ordination
- Amphi-dexterity
- Being friendly with machine
- Ability of good wound construction & capsulorrhexis
- Good microscope and phaco machine
- Choice of anesthesia it should be Peribulbar or posterior sub tenon’s

SICS/ECCE surgeon must start making side ports, using instruments in the non-dominant hand and doing good capsulorrhexis.

I would suggest beginners not to start on a 2nd or 3rd hand machine as this makes our journey further difficult. The machine should be user friendly and the surgeon must understand the parameters for every step he/she is going to do. The simple tip here is again to copy someone whom you have seen operating and have an access to discuss the same.

Always use sharp blades, and be liberal with the use of viscoelastics, trypan blue and other consumables if required.

Start as you do in SICS. After doing rhexis and making incision, make a sclero-corneal tunnel as you do in SICS. Enter the Anterior Chamber with kerotome and do not enlarge it. After Hydro-dissection and rotation of nucleus enter with Phaco-probe and make a deep trench in the center of nucleus (Figure 2). The depth of trench should be at least 2/3 of thickness of nucleus. Now enlarge the tunnel and withdraw the nucleus by SICS. Now check the depth of the trench (Figure 3), initially when you think you have made a deep trench it is not at all deep. This way you will know how deep the trench should be. In initial few cases of Phacoemulsification whole case can be done, starting like this, without extending the sclero-corneal tunnel (Figure 1). This way, in case of any mishap, it will be easy to convert into SICS.

Now you are ready for Actual modern day Phacoemulsification.

After cleaning and draping, speculum is inserted. Two side port incisions are given at 9 o’clock and 2 o’ clock positions. Chamber is filled with OVD and a corneal tunnel incision is given at 11 o’clock is 2.8mm keratome. Length of tunnel ideally should be 2mm. Now rhexis is done through side port
There are few common problems that a beginner encounters or main incision. Cortical cleavage hydro dissection is done to separate the capsule and cortex. Nucleus is rotated and a deep central trench is made in the nucleus. Now the nucleus is divided into two halves using two Sinskie hooks or one Sinskie hook and a chopper. Rotate the nucleus to bring one half at six o’clock position.

Take phaco-probe and impale in the centre of nucleus half and from the other hand (Holding Sinskie hook or chopper) divide this into two segments. Take the segments one by one and emulsify them. Now bring the other half at six o’clock position and do the same. Now take the I-A hand piece and remove the cortical matter. Otherwise initially you can use Simcoe canulla to remove the cortical matter. Now fill the chamber with OVD and inject a foldable IOL in the bag. As the first haptic goes in the bag and later you dial the trailing haptic into the bag. Using I-A Canulla OVD is removed. Tunnel is hydrated on both sides. Side port incisions are also hydrated. Wound is checked for any leak (Figure 4).

There are few common problems that a beginner encounters and surgical pearls-

- Often, there is a premature entry with iris prolapse. It is suggested neither to postpone the case, nor to continue from the same port. Iris should be repositioned, wound sutured and another site should be chosen for wound construction.
- Ballooning of conjunctiva is another annoying yet trivial issue. The wound should not be constructed too posteriorly and if it happens cut the conjunctiva on both sides of tunnel incision.
- Tight wound leads to hydration of cornea leading to visibility problems. The wound should be revised instantaneously.
- Hypotony and shallow chamber should be avoided at every step.

- Too much push and pull should be avoided with the injector. It is better to slightly enlarge the wound and push the IOL smoothly.
- Adequate size of capsulorhexis is of primordial importance in phaco. One should aim for a rhexis between 5 and 6 mm. It is suggested not to proceed with a compromised/ extended capsulorhexis in beginning. The case should be converted to SICS/ECCE.
- It must be clearly understood that our aim is not just to complete phacoemulsification, but to do a better surgery with better visual rehabilitation. Hence, corneal protection is a must and maneuvering in the AC must be away from cornea.
- Choice of main port (supero-temporal) is better. I would suggest an ECCE/SICS surgeon to initially go with this, to have a more habitual environment.
- Choice of I/A (coaxial/bimanual) is again personal. It is just a matter of comfort of surgeon.
- Trying fancy things like direct/vertical chop, chip and flip, iris hooks/CTRs, polishing the capsule should be attempted after the sample size crosses the 100 mark. There would be innumerable occasions to innovate, improvise and improve.
- In case of large PCR, a sulcus PCIOL can be attempted by the beginner, but things like ACIOL should always be kept handy. Things like SFIOL should be taken up as a secondary procedure.

Never treat yourself as a beginner. Stick to your plan, give respect to the tissues and graduate step by step as you studied one class after the other. In no time you will see that you have become the master of the Phacoemulsification. All the best!
Epidemiology

The spectrum of paediatric orbital tumours differs from that of adults and further varies according to age. Tumours seen in adolescence are similar to those seen in adults while congenital space occupying lesions like colobomatous cyst and teratoma form an entity unique to infancy and early childhood.

The incidence of various space occupying lesions of paediatric orbit, as reported in literature, is extremely variable. The reporting facility (pathology or ophthalmology), location of the facility and interest of the treating specialist affect the outcome of such studies. However, most studies show that benign lesions are more common; most common being cystic lesions comprising mainly of dermoids and/or vascular lesions. Studies from developing world report a greater percentage of malignant lesions in paediatric orbit as compared to North America and Europe. This could be explained because most inflammatory causes of proptosis like orbital cellulitis are not biopsied and/or there is in fact a greater incidence of paediatric orbital malignancies; for example orbital retinoblastoma constitutes nearly 50% of all cases of retinoblastoma in India while in the western world, it constitutes less than 10%. Therefore, orbital retinoblastoma constitutes a large percentage of childhood orbital lesions in our country. A report from tertiary care centre of our country shows that rhabdomyosarcoma and orbital retinoblastoma are the most common malignant lesions in the paediatric orbit while lymphangioma constitute the most common benign lesions.

Diagnosis

Urgency of diagnosis

Although benign lesions are more common in the paediatric orbit, if not managed on time they may cause severe morbidity from amblyopia, corneal exposure or optic nerve damage. Malignant lesion on the other hand if not diagnosed and treated in time will affect survival.

Difficulties peculiar to paediatric orbital lesions

The examining ophthalmologist faces difficulties that are typical to paediatric age, for eg the child may not be able to report all the symptoms and investigations like imaging (MRI and CT scan) and biopsy may require general anaesthesia. Apart from these problems, the risk of amblyopia is typical to children less than 9 years of age and is a major cause of morbidity in cases of benign lesions of paediatric orbit.

When a child presents with proptosis, following may indicate malignancy:

- Acute onset/ rapidly progressing proptosis
- History of leucocoria
- History of recurrent fever, bone pains, bleeding or any other extra-orbital masses like in the abdomen
- Family history of childhood malignancy

However, one should remember that acute onset proptosis may also result from benign lesions such as orbital cellulitis.

Table 1: Incidence of pediatric orbital space occupying lesions

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<tr>
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<tr>
<td>Dermoid cysts</td>
<td>46%</td>
<td>23%</td>
<td>58%</td>
</tr>
<tr>
<td>Inflammatory lesions</td>
<td>16%</td>
<td>Vascular processes (hemangioma and lymphangioma): 18%</td>
<td></td>
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<tr>
<td>Adipose tissue (either orbital fat or dermolipomas):</td>
<td>7%</td>
<td></td>
<td></td>
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<tr>
<td>Rhabdomyosarcomas or secondary orbital malignancies:</td>
<td>4%</td>
<td>7%</td>
<td></td>
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<tr>
<td>Lymphoid tumors and optic nerve tumours:</td>
<td>2.4%</td>
<td>Optic nerve and central nervous system: 16%</td>
<td>Bone lesions 9%</td>
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Ultrasound (USG): Imaging

Ultrasound (USG): Ultrasound imaging is a very useful tool in making differential diagnosis. Ultrasound reveals the nature and location of the lesion. The lesion may be cystic, solid or mixed; infiltrative, or well defined. In case of solid space occupying lesions, USG reveals the internal architecture of the tumour (regular or irregular, high or low internal reflectivity), presence of calcifications and its relation to and effect on other orbital structures (whether the space occupying lesion conforms to the shape of the globe or causes globe indentation, if the mass is arising from the globe or is confined to one of the orbital structures like extra ocular muscle, lacrimal gland or optic nerve).

On USG, Cystic lesions like cysticercus cyst and hydatid cyst have characteristic features [Figure 1(a),(b)]. Dermoid cysts are seen as cystic lesions with irregular, high internal reflectivity. An infiltrative lesion with multiple, variable sized cysts on USG and a typical history of recurrent proptosis associated with upper respiratory tract infection is diagnostic of lymphangioma.

Computed Tomographic scan: CT scan of orbit must be done in all cases of orbital tumours. It provides useful information about the bony orbit. It demonstrates whether the lesion is arising from bone or is causing secondary bone changes like erosion (sign of malignancy) or remodelling (seen in long standing masses). The exact location, internal architecture and calcification may be better appreciated on CT scan. Any extension from or into adjacent intracranial space, paranasal sinuses or nose may be detected. The effect of contrast on the lesion provides information regarding vascularity of the tumour, for eg: lymphangioma usually enhances minimally with contrast while capillary haemangioma will show feeder vessels with good contrast enhancement.

The list of benign and malignant orbital lesions of paediatric age group

The list of paediatric orbital space occupying lesions is long, but here is a brief clinical, imaging and treatment outline for the most commonly encountered lesions of paediatric orbit.

Cystic lesions

Dermoid cyst: These are the most common cystic lesions of paediatric orbit. They present as long standing, slowly growing hard masses that are located at the external angle of eye (lacrimal fossa). Occasionally, they may rupture secondary to trauma and present with acute inflammation. On USG, they are characteristically seen as cystic lesions with variable internal reflectivity that is high to moderate and often harbour areas of calcification. CT scan is performed to look for bone remodelling and rule out intracranial involvement, fat shadows are usually seen as dark areas within the cyst. Simple excision of the intact cyst is the treatment of choice.

Parasitic cysts: Parasitic cysts of ocular adnexa and orbit are commonly seen in developing world. Cysticercosis of orbit typically affects young individuals and has a wide spectrum of clinical manifestations. It most commonly involves anterior orbit (extraocular muscles), followed by sub-conjunctival space, eyelid and posterior orbit. The affected child presents with acute onset, painful diplopia, squint or proptosis. Visual acuity may be affected when the cyst involves the orbital apex or the globe. There may be single or multiple cysts. On USG, they appear as cystic lesions with a single spec of high (100%) reflectivity. A CT scan of the brain and indirect ophthalmoscopy should be done in all cases to rule out neurocysticercosis and intraocular cisticercosis respectively. A stool test may be done to rule out autoinfection. The choice of treatment is medical therapy with the antihelmintic drug albendazole (15 mg/kg body weight in two divided doses for 6-8 weeks) given under the cover of oral steroids. The changes in the USG characteristics of the cisticercus cyst in response to medical therapy have been described in literature. In case of subconjunctival cisticercus cysts or residual cysts after medical therapy, one may excise the cyst. The inflammation associated with cisticercus cysts may be clinically confusing

Figure 1(a): Ultrasound orbit showing a cystic lesion in an extraocular muscle with central calcific spec s/o cysticercosis.

Figure 1(b): Ultrasound orbit showing cystic orbital lesion with “double wall sign” (arrow) characteristic of hydatid cyst.

Figure 1(c): Clinical photo of a child with cystic orbital lesion due to cysticercus.

Figure 1(d): CT scan orbit of the same child showing cystic lesion in lateral orbit s/o hydatid cyst.

Figure 1(e): CT scan orbit (axial cut) showing orbital mass lesion with multiple cystic areas in a child with history of recurrent proptosis associated with upper respiratory tract infections s/o orbital lymphangioma.

Figure 1(f): CT scan (axial cut) showing retrobulbar cystic lesion with fluid-fluid levels (arrow) in a case of orbital lymphangioma suggestive of chocolate cysts.

Figure 1(g): Clinical photo of a child with rapid onset proptosis of left eye. Figure 1(h): CT scan orbital (axial cut) of the same child showing intraocular mass with calcification extending into the orbit posteriorly s/o locally advanced retinoblastoma.

Figure 1(i): Clinical photo of a child with acute onset proptosis on left side with history of fever, bone pains and anemia.

Figure 1(j): CT scan orbital (axial cut) of the same child showing homogenous well defined lesion in superomedial orbit that is moulding to globe, suggestive of orbital granulocytic sarcoma or orbital cysticercosis or haemorrhage in a pre-existing orbital lymphangioma.

Imaging

Ultrasound (USG): Orbital USG is a very useful tool in making differential diagnosis. Ultrasound reveals the nature and location of the lesion. The lesion may be cystic, solid or mixed; infiltrative, or well defined. In case of solid space occupying lesions, USG reveals the internal architecture of the tumour (regular or irregular, high or low internal reflectivity), presence of calcifications and its relation to and effect on other orbital structures (whether the space occupying lesion conforms to the shape of the globe or causes globe indentation, if the mass is arising from the globe or is confined to one of the orbital structures like extra ocular muscle, lacrimal gland or optic nerve).
and a misdiagnosis of orbital cellulitis is often made64. Therefore, in all cases of orbital cellulitis, imaging should carefully be evaluated to rule out any cysticercus cyst, in which case, there will be no/poor response to systemic antibiotics and anti-inflammatory medications alone. In cases associated with neurocysticercosis, the treatment is guided by the neural involvement. Despite resolution of cysticercosis with medical management, a significant proportion of patients will have residual functional deficits13.

**Hydatid cyst:** Hydatid cyst of orbit may be seen in paediatric orbit, especially in countries endemic for this disease. Around 1% of all cases involve orbit. The affected child presents with a long standing, slowly increasing, painless proptosis [Figure 1(c)]. Ultrasound features are characteristic and reveal an anechoic cyst with two highly reflective linings (double wall sign) [Figure 1(b)]17. A history of contact with dogs is usually present. CT scan shows a cystic lesion with orbital expansion and bone remodelling due to long standing nature of the lesion [Figure 1(d)]. Globe indentation leads to refractive changes, which, if not taken care of may lead to anisometropic amblyopia. Unlike in cysticercosis, where the management of choice is medical therapy, the treatment of choice for a single orbital hydatid cyst is surgical excision. Hydatid cyst is lined by three layers: the endocyst, the ectocyst and the pericyst. The aim of surgical excision is to remove the endocyst (that harbours the daughter cysts) intact after incising the pericyst and the ectocyst. Cryoprobe is helpful in holding and delivering the endocyst which has very thin and delicate walls17. A leak from the endocyst during the surgery will invariably lead to daughter cyst implantation and result into multiple recurrences in the orbit. In cases of recurrence or multiple cysts, oral treatment with albendazole may be tried as complete surgical excision is difficult18,19.

**Vasculogenic tumors:** These include lymphangioma, capillary haemangioma, varicose veins and cavernous haemangioma. Of these, lymphangioma occurs most commonly in paediatric orbit and is discussed here.

**Lymphangioma / combined venous - lymphatic vascular malformation:** Apart from cystic lesions, lymphangioma is the common vasculogenic benign orbital space occupying lesion of paediatric orbit, reported from our country6. The patient usually presents with a long standing proptosis or eyelid swelling that has suddenly increased in size. The swelling characteristically increases in size following an episode of cough and cold and responds dramatically to oral steroids. Sometimes massive haemorrhage may occur within the lymphangioma that may require urgent surgical intervention in order to decompress the orbit20. Indications for such an urgent surgical drainage include optic nerve compromise (suggested by appearance of RAPD and / or deterioration of vision) or corneal exposure due to lagophthalmos. The acute presentation in such cases may often confuse the treating clinician who may misdiagnose it as a malignancy. However, a careful history taking and clinical examination will usually lead to correct diagnosis.

Clinical examination on slit lamp may reveal clear lymphatic fluid filled cysts in the sub-conjunctival space. USG shows diffuse infiltrative lesion with multiple variable sized cysts. CT scan orbit, similarly, shows an infiltrative, ill-defined orbital lesion with minimal / no contrast enhancement, as it is isolated with respect to the vascularity [Figure 1(e)]. Many times large cysts may be seen with fluid-fluid levels [Figure 1(f)].

Being an infiltrative lesion complete surgical excision is usually not possible. Surgical intervention may cause more haemorrhage in the lymphangiomatous tissue. People have tried using sclerosing agents for a non surgical ablation of lymphangiomas, but there is limited data21-22. Most of the times any increase in size of a lymphangioma can be managed with oral steroids, surgical drainage is required when large haemorrhagic cysts are present and surgical excision is restricted for large orbital lymphangiomas that are cosmetically disfiguring. As patients reach the second decade of life some lymphangiomas may show regression or may stabilize.

**Orbital malignancies**

**Rhabdomyosarcoma:** It is the most common orbital malignancy of childhood. Around 5% of cases occur in orbit. It usually presents at a mean age of 7.5 years23. The patient presents with a rapidly increasing proptosis or an upper eyelid mass. Clinical examination reveals a firm orbital mass with variable consistency, usually involving superior orbit. Clinically, it may mimic orbital cellulitis. On imaging, a well defined heterogeneous mass can be seen that involves the extraocular muscle, may have calcification and is usually associated with erosion of adjacent bony orbit. There is variable contrast enhancement and globe indentation but intraocular structures are normal.

An incision biopsy confirms the diagnosis in most cases. Sometimes histopathology may only reveal features of a round cell tumour; in such cases further immunohistochemical staining is required to reach a diagnosis. Other round cell tumours that are differentiated on immunohistochemical staining include: retinoblastoma, medulloepithelioma, ewing’s sarcoma, granulocytic sarcoma and neuroectodermal tumor. Of these, retinoblastoma is a common cause of orbital tumour in paediatric orbit in developing countries.

The current standard of treatment for rhabdomyosarcoma is chemoradiotherapy. The majority of patients are cured with the use of both chemotherapy and radiation therapy, but considerable number experience late sequel of treatment. The 10 years event-free and overall survival reported are 77% and 87% respectively for primary orbital RMS24. The challenge with current therapy is to reduce undesirable effects of radiotherapy.

**Retinoblastoma:** Retinoblastoma is the most common intraocular malignancy of childhood worldwide; also it is an important cause of orbital malignancy of paediatric orbit in developing world6. Along with rhabdomyosarcoma, it constitutes the most common cause of orbital malignancy in paediatric age group in India6. The clinical presentation is similar to rhabdomyosarcoma that is a rapidly increasing proptosis [Figure 1(g)]. However, parents will usually give history of leucocoria preceding the orbital symptoms. Such a history should always be taken in all the cases of rapidly progressing childhood proptosis.

USG reveals an intraocular mass filling the globe with intratemporal calcification. CT scan orbit and brain should be done in all cases and reveals a heterogeneous mass lesion within the globe with areas of calcification and extending into the orbit either as an extraocular mass or as thickened optic nerve [Figure 1(h)]. It may also reveal any intracranial extension. Locally invasive and malignant retinoblastoma constitute nearly half of all cases of retinoblastoma in our country6. The survival prognosis is only 50% at 5 years for locally invasive retinoblastoma25,26. Diagnosis is evident on imaging and is confirmed by histopathological examination in cases of doubt.
Currently, the standard line of treatment of locally invasive retinoblastoma comprises of neoadjuvant chemotherapy (3 cycles) with standard VEC regimen followed by limited surgery (enucleation) and adjuvant chemotherapy (9 cycles) and radiotherapy. Malignant retinoblastoma is treated using high dose chemotherapy and stem cell transplant.

Granulocytic sarcoma: Leukemia is the most common malignancy of childhood. Around 15%–20% cases of leukemia are myelogenous and 8% of these develop extramedullary solid tumours of primitive granulocyte precursor cells known as granulocytic sarcoma/myeloid sarcoma/ chloroma. These occur more commonly in children, are typically multifocal and have a predilection for occurrence in orbit and orbital bones. They present as a rapidly expanding orbital mass at a mean age of around 7-8 years [Figure 1(i)]27. The temporal association with systemic disease may be variable but they usually presents 2 months to 3 years before systemic disease becomes advanced. Symptoms of systemic disease, such as paleness, lethargy, or epistaxis may suggest the diagnosis. Orbital granulocytic sarcoma may occur bilaterally in 10% of cases. They usually arise in the subperiosteal region of the osseous wall of the orbit. CT scan shows homogeneous mass usually in the lateral orbit which is iso/hypodense to extraocular muscle and hypodense to sclera and enhance uniformly with contrast [Figure 1(j)]. They usually do not cause bone destruction and mould to one or more orbital walls26,29. Incision biopsy is diagnostic and may show features of small round cell tumour. Staining for auer rods in the cytoplasm is diagnostic.

In cases of acute onset bilateral proptosis/orbital masses in children, granulocytic sarcoma should be suspected. In such cases a peripheral blood film and/or bone marrow biopsy should always be done to rule out leukemia. This may preclude the need for a biopsy. Although granulocytic sarcoma is highly responsive to chemotherapy and local radiotherapy, survival prognosis is universally poor. Sometimes orbital granulocytic sarcoma may occur in isolation30.

Other causes of acute proptosis in setting of acute leukemia include haemorrhage and orbital abscess. But these can be differentiated on imaging. Less commonly acute lymphocytic leukemia may also infiltrate orbit or eyelid.

To conclude, paediatric orbital tumours constitute a clinically distinct entity from that of adult orbital tumours and pose some unique challenges to the treating ophthalmologist. The treating ophthalmologist/oculo-plastic surgeon should be aware of conditions that may require early medical/surgical intervention.

References

Management of Involutional Entropion

Involutional entropion is often seen in elderly patients, particularly women, and causes great discomfort as well as problems with clear vision due to constant watering. It occurs due to a combination of factors which are seen in the ageing eyelid, including – a) weakening of lid retractors, which allows the lower border of tarsus to swing outwards, b) pre-riding of the preseptal orbicularis over the pretarsal orbicularis, further pushing in the upper border of the tarsal plate, c) vertical shortening of the posterior lid lamella and d) horizontal lid laxity, which is further aggravated by the orbital fat atrophy that also occurs with age; this horizontal lid laxity may result in either entropion or ectropion depending on the condition of the other structures like the tarsal plate and the retractors. Involutional entropion almost always affects the lower eyelid because the lower lid tarsus is of much lesser width and is therefore easily rotated in or out due to a change in the supporting tissues.

Management

When managing a case of lower lid entropion, we must first assess the factors responsible for the entropion in the given case. At the same time, it is important to rule out any cicatricial changes as the management will be different for cases of cicatricial entropion. Horizontal lid laxity and medial or lateral canthal tendon laxity is assessed by pulling on them, precluding of the preseptal orbicularis can be seen as a band or ridge of tissue through the skin, where the muscle is overriding. The lid retractors are assessed by asking the patient to look down. If the lid retractors are functioning properly, the lower lid margin moves down slightly in down gaze and the lower lid skin crease becomes more prominent.

Surgical Options

The choice of surgery depends on the most important factor causing the entropion as also the surgeon’s preference. Transverse sutures are the mildest form of correction and provide temporary relief. Weakening of the lid retractors is corrected by tightening or plication of the lid retractors as in the Jones procedure, horizontal lid laxity is corrected by shortening or tightening the lower lid and pre-riding of the preseptal muscle is prevented by creation of a scar tissue between the preseptal and the pretarsal muscles e.g. in the Wies procedure. Wheeler orbicularis surgery also creates a transverse scar and a band of tissue to support the lower border of the tarsus. The Quickert procedure, which is our preferred technique for most cases, is a combination of everting sutures, which transfer the pull of the retractors to the upper border of the tarsus, as well as transverse lid split with creation of a scar tissue and horizontal lid shortening. The Jones procedure is another popular procedure, but in cases with obvious horizontal lid laxity, a Jones procedure should be combined with a lateral tarsal strip or any other lid tightening procedure, to prevent a recurrence or a late ectropion.

In the Quickert procedure, we first make a vertical incision mark of about 5mm length, perpendicular to the lid margin and 5mm medial to the lateral canthus (Figure 1). From the bottom of this mark, we make another horizontal incision mark, parallel and 5 mm below the lid margin, extending just short of the punctum, and also laterally up to the lateral canthus (Figure 1). We then make full thickness incisions along all these marks (Figure 2), which gives us a medial and a lateral lid strip. We approximate the two lid strips to assess the horizontal lid laxity and excise the excess tissue (Figure 3). We then pass 3 double-armed 4-0 chromic catgut sutures through the lower lid retractor and conjunctival layer (in the inferior edge of the incision, Figure 4) and pass them through the lid strips superiorly to emerge in the skin 2 mm below the lash line. All these three everting sutures are passed before tying any of them to ensure that all the sutures can be passed properly under visualization. The lid margin is sutured in a normal fashion taking care to ensure good approximation without lid notching. The everting catgut sutures are then

Figure 1: Video Grab. Skin incisions being made along the marks as described
tied to result in slight overcorrection, and the skin incisions are closed taking care to avoid any dog ear formation.

The incisions heal well in the postoperative period and there are very few complications. Overcorrection may occur, but usually corrects over a period of time. However, if there is significant overcorrection, the sutures may be selectively removed earlier, at about 1 week, rather than the normal 2 week period. Interest readers can view the video of Quickert procedure at following link: http://www.youtube.com/watch?v=FFzjN7gOgY

**Conclusion**

To summarize, lower lid entropion occurs due to a combination of factors found in the ageing eyelid, and we need to assess these factors to decide the most appropriate management in a given case. A variety of surgeries are available but the Quickert procedure is a good choice for most routine cases as it takes care of many of the contributory factors. Alternatively, a Jones procedure is another popular choice but needs to be combined with a lateral tarsal strip to take care of any associated horizontal lid laxity.
References


Forthcoming Academic Events

**International DOS Conference**

21st November to 24th November, 2012

**DOS Teaching Programme**

Saturday & Sunday 16th & 17th February, 2013
at Jawaharlal Nehru Auditorium,
AIIMS, Ansari Nagar, New Delhi

**DOS Annual Conference**

Friday, Saturday & Sunday 12th, 13th & 14th April, 2013
at Hotel Ashok, Chanakaya Puri, New Delhi
Visual loss is a challenging neuro-ophtalmological problem that is routinely encountered in any ophthalmological practice. It could be due to innumerable reasons which can be different depending on the age and sometimes very subtle. Hence, any type of visual loss would need a meticulous and thorough work-up to reach to a diagnosis. In this section I shall be discussing the approach one should have in any case of visual loss that cannot be explained in adults.

History plays an important role to start with. One should find out if the visual loss is unilateral or bilateral, the onset of visual loss and any associated symptoms to aid in localization. For example, in unilateral loss of vision, the lesion is suspected to be anterior to the chiasma while in bilateral visual loss a bilateral retinal/optic nerve disease or a chiasmal/retrochiasmal lesion should be suspected. The onset would point to the etiology, such that a sudden loss within minutes suggests an arterial occlusion while a delayed loss over months is suggestive of a compressive lesion. Presence of pain on eye movement would suggest optic neuritis while headache may indicate intracranial lesion.

**Classification**
Where is the pathology? (Figure 1)

**Optical**
These include refractive errors or any disturbance of ocular media like the tear film, cornea, lens or vitreous.

**Evaluation**

- **Visual acuity for distance and near vision** – A disparity between the two would point to an optical disturbance.

- **Pinhole test** – An improvement in vision with the pinhole would be likely due to optical disturbance.

- **Retinoscopy with subjective refraction** – Especially for high refractive errors and irregular astigmatism.

- **Colour vision** – Is always normal and if found abnormal, may rule out optical or media related abnormalities.

- **For tear film and corneal lesions** – Detailed slit-lamp examination, corneal topography, aberrometry can identify any abnormalities in the cornea like keratoconus, post-LASIK ectasia etc. Rigid Gas Permeable (RGP) contact lens with over-refraction would improve the vision significantly in such cases.

- **For lenticular problems** – Inaddition to a detailed slit-lamp examination for cataract and lens ectopia, use of a direct ophthalmoscopy will pick up subtle irregularities like lenticicon or oil droplet cataract.

- **Dilated visual acuity or the use of a potential acuity meter can estimate the potential vision.**

**Retina**
These include lesions involving the macula, retina and the choroid.

**Evaluation**

- **Amsler grid** – Picks up any distortion pointing to macular lesions. In addition one should also ask leading questions to pick up any history describing metamorphopsia like wrinkled or distorted vision.

- **Colour vision** is a strong weapon to pick up macular related abnormalities. Of all the tests, Hardy Rand Rittler (HRR) is relatively more sensitive but Ishihara charts can also be used especially for poorer vision.

- **Pupil examination** – It is always normal and abnormal pupillary reaction will help differentiate retinal from neural causes.

- **Other investigations:**
  - **Non-invasive tests:** Optical Coherence Tomography, Electrophysiological tests like electroretinography (ERG), multifocal ERG for macular lesions and EOG (latter reserved for Best’s disease), visual fields (may get small central scotomas)of the central 100 field test
  - **Invasive test:** Fundus Fluorescein Angiography and Indocyanine Green Chorioangiography

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**Figure 1**

*Image of an approach to unexplained visual loss diagram.*
Neural
These include lesions affecting the optic nerves and the visual pathways.

Evaluation
- Detailed history of systemic illness like hypertension or diabetes mellitus can help in reaching a diagnosis of an ischemic optic neuropathy while a history of trauma in presence of optic disc pallor could confirm traumatic optic neuropathy.
- Color vision is a very helpful tool to differentiate neural cause from optical causes. Also in some form of optic neuropathies like optic neuritis the color vision may not parallel the visual acuity loss and may be more severely affected.
- Pupil examination, though a very important and specific test to pick up any optic nerve problem has always been under-utilized. Presence of an RAPD (relative afferent pupillary defect) performed with a swinging-flashlight test strongly correlates with ipsilateral optic nerve pathology.
- B-scan ultrasound of the disc aids to differentiate a disc drusen from a true disc edema (Figure 2).
- Confrontation test in office setting can anatomically localize the neuroretinal lesion. This can be confirmed by visual fields testing that include programs on automated perimetry (10-2, 24-2 and 30-2) and manual perimetry (Goldmann)
  - VEP: Visual Evoked Potential testing detects a delay in the latency confirming an optic neuritis against a reduction in the amplitude suggesting other forms of optic neuropathy.
  - Neuro-imaging (Magnetic Resonance Imaging and Magnetic Resonance Angiography or Computed Tomography Angiography) can localize the etiology like the presence of enhancing plaques on the optic nerve is suggestive of optic neuritis.
  - Detailed fundoscopy is very vital and the disc, macula, retinal vessels and retina have to be examined very carefully.

The following parameters can be used to classify any unexplained visual loss to help us reach a diagnosis (Figure 3 & Figure 4):
- Central visual acuity
- Appearance of the disc (normal or abnormal)
- Presence of RAPD

Presence of disc edema with normal central vision and RAPD (Figure 3) could be seen in infiltrative or compressive neuropathy, optic neuritis, anterior ischemic optic neuropathy or chronic papilloedema.
Amblyopia is a diagnosis of exclusion and needs to be suspected when there is decreased central vision with normal disc and no RAPD. In such cases one needs to rule out any anisometropia or strabismus in the affected eye. One should also investigate for monofixation syndrome or microtropia, which will have subnormal stereopsis with positive 4-prism base out (4ΔBO) test in the ipsilateral eye. In addition, the Worth’s four dot test will show suppression of the affected eye for distance but will be normal for near (Figure 5).

Nonorganic visual loss is suspected when a patient with unexplained visual loss has a normal eye examination. It is a diagnosis of exclusion and needs to be investigated once an organic cause is ruled out. In order to prove that the vision loss is nonorganic, it is imperative to show that the vision of the patient is better than what she or he claims. There are many tests described to confirm non-organic visual loss like development of optokinetic nystamus, mirror test, stereopsis test, binocular visual field test, monocular vertical prism dissociation test, etc.

In summary, a detailed history and thorough examination is mandatory for a work-up of any visual loss that cannot be explained. Appropriate tests like color vision, pupil examination, direct opthalmoscopy, slit-lamp etc. should be carried out for localization. Once localized, correct investigation should be ordered. Non-organic visual loss is a diagnosis of exclusion and should be thought of once an organic cause is rule out.

References
Pupil evaluation is an important part of the complete eye examination, as well as the neurological eye exam. Although examination of pupils help us to diagnose and follow up many neurological and oculal pathologies.

**Assessment of pupil size/shape & function**

Clinical evaluation of pupil to be done as follows

- Assess size of pupils – equal or anisocoria
  - If anisocoria → assess in light & dark
- Whether constricts with same velocity – pharmacologic, Adie’s/tonic pupil.
- Whether dilate equally with same velocity
- Light near pupillary assessment
- Whether RAPD present or not

**History**

- Patients are often unaware of pupil abnormality
- Spouse, friend or physician brings attention

**Symptoms**

- Light sensitivity
- Difficult in focusing while adjusting
- Visual blurring

**Past history**

- About previous injection, trauma, surgery or migraine
- Occupational history – Farmer / Gardner
- Physicians are at risk

**Medication history**

- Opiates, Inhalers

**Examination of pupils**

Anterior segment examination for

- Corneal injury
- inflammations leading to miosis
- Iris sphincter atrophy Vs tear
- Transillumination defect

**Measurement**

**Assessing pupillary size**

- Hand held pupil gauge
- Hand held pupil camera
- Infrared pupillometry (Most sensitive)

Diameter or both the pupils’ should be estimated & measured in light (room light) using a hand held light source. Diameter of pupil then should be assessed in darkness (Dimmest room light in which examiner can still see edge of pupil)

Pupil size should be assessed during near stimulation with an accommodative target to achieve maximum constriction of pupil. This measurement in light and dark should determine if anisocoria is >0.4mm. 20% of normal population has minimally detectable anisocoria (<0.4mm) called as physiological anisocoria.

**Testing pupillary reaction to light**

Pre-requisites:

- The direct pupillary light reactions: it is important to have a quiet & dimly lit room. (Figure 1a, 2)
- Patient must be fixing on distant target to eliminate any effect of accommodation on pupillary size.
- Light source used should be bright enough to produce maximum constriction & re-dilatation. If light source is too bright a prolonged constriction lasting several seconds will occur making determination of normal light reflex difficult.
- Secondary dim light source with oblique illumination of pupil may assist in visualization of dark pigmented iris. The light source should be directed straight into the eye

**Figure 1(a): Testing direct light reflex**
for few seconds & then moved downwards away from eye to eliminate stimulation.

Response to bright light is constriction called “pupillary capture”. “Pupillary escape” is a phenomenon in which pupils initially constrict and then slowly redilate and return to its original size. It occurs most often on side of diseased optic nerve or retina and in normal person tested with low intensity right source. Larger pupil is more likely to show “pupillary escape” and smaller pupil is more likely to show “pupillary capture”.

When light is shined in one eye, contralateral pupil constricts as well in so called consensual light response (Figure 1b). It is assessed using a light source for illumination of pupil of one eye and a dimmer light source that is held obliquely to contralateral eye being obscured. This consensual pupillary response should be approximately equal in both velocity and extent to the direct response because the pupillary decussation in the midbrain is about 50% to each eye.

**Pupillary near response testing**

The near response is tested in room with light that is adequate for the patient to fixate on accommodative target. A non accommodative target such as pencil may not be a sufficient stimulus to produce a normal near response even in normal person. Also the near response should not be induced in bright light because light itself produces pupillary constriction.

**Pupillary dilation assessment**

Pupils usually dilate after they have constricted to light or near stimulation. In patient with certain retinal and less often optic nerve disease they may actually dilate when light is shown in one eye, called as paradoxical pupillary response. Reflex pupillary dilation can also be tested by sudden noise or pinching back/nape of neck (ciliospinal reflex).

While assessing pupillary dilation, look for dilation lag which is present when there is more anisocoria 4 to 5 seconds after pupillary constriction to light than there is 15 seconds after pupillary constriction e.g. Horner’s pupil, some normal subjects.

Dilation lag may be tested by observing both pupils simultaneously in a very dim light after a bright light has been turned off. It can be more easily tested on a slit lamp. Normal pupil returns to the widest size within 12-15 seconds, with most of their dilation occurring in the first 5 seconds.

Pupil that show dilation lag & take up to 25 seconds to return to maximum size in darkness with most of dilation about 10-12 seconds after the light goes out.

**Testing for light near dissociation**

Dissociation between pupillary response to light and to near stimulation occurs in variety of disorders. In almost all cases, pupillary reaction to light is impaired where as pupillary response to near remains normal. Thus light near dissociation should be considered in any patient with an impaired pupillary light reaction.

**Swinging flash light test**

The swinging flash light test which accentuates the difference in pupillary light response is probably the most valuable clinical test of optic nerve dysfunction available to an ophthalmologist / a general physician.

The test is performed with a bright hand light in a darkened room in order to maximize the amplitude of pupillary movement. A direct ophthalmoscope using distant direct technique can be used to detect a milder RAPD.

Too bright light will produce an after image that may keep pupil small for several seconds obscuring pupillary dilation in abnormal eye. In patients with strabismus or distorted globe care must be taken to shine the light along visual axis. The light should remain on each eye for 3 to 5 seconds to allow pupillary stabilization. The initial pupillary constriction response should be observed.

However, the light should never be left longer on one eye than on other. This might create an appearance of an RAPD in the eye with longer light response, because the longer the light is kept on the eye, the more pupillary dilation occurs as the eye adapts to the light. Also if retina becomes bleached in one eye and not in the other, a small apparent RAPD will be produced.

Finally, the swinging flash light test can be performed as long as there are two pupils, even when one pupil is non-reactive and dilated or constricted from neurological disease,
Anisocoria greater in dark

Physiologic

In dim light ~20% of the normal population has an anisocoria of 0.4mm or more. In room light, this number drops to 10%. It is rarely >0.6mm, but may be as much as 1.0 mm. This anisocoria is almost same in darkness and light, but there is tendency for it to decrease in light because smaller pupil reaches zone of mechanical resistance first, giving the larger pupil a chance to catch up. It is also called as simple, central or benign anisocoria.

Horner’s syndrome

When sympathetic innervation to eye is interrupted, dilator muscle of iris is weakened, allowing pupil to become smaller. A combination of ptosis, miosis and anhidrosis is called Horner’s syndrome. (Figure 4a)

Horner’s syndrome based on localization is diagnosed as first order (central), 2nd order (pre-ganglionic) and third order (post ganglionic) based on the order of sympathetic neurons affected. (Figure 5)

Central / first order type

First order sympathetic neurons begin in the ipsilateral hypothalamus and extend to ciliospinal centre of Budge and Waller in intermediolateral gray column of the spinal cord C8-T1. The pathway seems to stay laterally in the brain stem

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**Table 1**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Quantification of RAPD (log units)</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optic neuritis</td>
<td>0.3 to 3</td>
<td>If no RAPD, suspect b/1 disease</td>
</tr>
<tr>
<td>Optic tract disease</td>
<td>0.4 to 0.6 contralateral eye</td>
<td>Look for temporal visual field defect</td>
</tr>
<tr>
<td>Pretectal lesion</td>
<td>Contralateral RAPD without VF loss</td>
<td></td>
</tr>
<tr>
<td>Amblyopia</td>
<td>&lt;0.5</td>
<td>If &gt;1.0 log unit, look for other disease, test in light</td>
</tr>
<tr>
<td>Anisocoria</td>
<td>0.1 log unit for every mm</td>
<td>Test in light</td>
</tr>
<tr>
<td>Macular disease</td>
<td>VA &gt;20/200 no more than 0.5 log unit</td>
<td>Worse macular disease &lt;1.0 log unit</td>
</tr>
<tr>
<td>CSR</td>
<td>&lt;0.3 log unit</td>
<td></td>
</tr>
<tr>
<td>CRVO</td>
<td>-Ischemic 0.9-1.2</td>
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<tr>
<td></td>
<td>-Non-ischemic &lt;0.6</td>
<td></td>
</tr>
<tr>
<td>Retinal detachment</td>
<td>1 quad- 0.3, 2 quad- 0.6, 3 quad- 0.9, total upto 2</td>
<td></td>
</tr>
<tr>
<td>Retinitis pigmentosa</td>
<td>&lt;0.3 log unit</td>
<td></td>
</tr>
<tr>
<td>Patching</td>
<td>Upto 1.5 log unit in unoccluded eye</td>
<td>If dense, expect RAPD in opposite eye</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>Varies</td>
<td></td>
</tr>
<tr>
<td>Cataract</td>
<td>None/Small contralateral RAPD</td>
<td></td>
</tr>
</tbody>
</table>

---

**Table 2**

<table>
<thead>
<tr>
<th>Drugs used for pharmacological testing</th>
<th>Improve</th>
<th>Dose</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilute pilocarpine</td>
<td>Super sensitivity testing</td>
<td>0.125%</td>
<td>30 min</td>
</tr>
<tr>
<td>Pilocarpine</td>
<td>Pharmacological pupil blockade</td>
<td>2%</td>
<td>40 min</td>
</tr>
<tr>
<td>Cocaine</td>
<td>To demonstrate sympathetic defect</td>
<td>10%</td>
<td>60 min</td>
</tr>
<tr>
<td>Hydroxyamphetamine</td>
<td>To detect post ganglionic sympathetic defect</td>
<td>1%</td>
<td>50-60 min</td>
</tr>
</tbody>
</table>

---

trauma, and topical drugs. Recall that as light is shifted from the normal to abnormal eye, the total pupil motor input is reduced. Thus afferent stimulus for pupillary constriction is reduced in both eyes so that both pupils dilate. Thus if one pupil is mechanically or pharmacologically non-reactive one can simply perform a swinging flash light test observing only reacting pupil.

Abnormal eye is eye with fixed pupil: pupil of normal eye will constrict briskly when light is shone directly on it and will dilate when light is shone in opposite eye.

Abnormal eye is eye with reactive pupil- pupil will constrict when light is shone on opposite eye and dilate when light is shone directly on it.

This is extremely helpful in attempting to determine if a patient with an oculomotor nerve paresis or traumatic iridoplegia also has an optic neuropathy or retinal dysfunction.

Quantification of RAPD- using graded neutral density filter (NDF) that are calibrated in percentage of light transmission. After determining that a RAPD is present, the examiner balances the defect by adding successive neutral density filter in 0.3 logarithmic steps over the normal eye while performing the swinging flash light test until the defect disappears. The most useful NDFs are those ranging in transmission from 80% (0.1 log unit) to 1% (2.0 log unit).

A number of ocular diseases cause a measurable RAPD. (Table 1)

**Pharmacologic testing of pupils (Table 2)**

If a judgment is to be made about pupillary response to a drop of drug instilled into the conjunctival sac, then whenever possible one pupil should be used as an internal control.

**Disorders of pupillary function**

These abnormalities are usually unilateral and thus produce a difference in the size of pupil called anisocoria. If it’s present, there is something wrong with one or both irides or with innervations of the iris muscles. The physician should determine if the degree of anisocoria is greater in darkness or light. (Table 3, Figure 3)
and spinal cord so the Horner’s syndrome caused by damage to central neurons is almost always unilateral.

There is no pharmacological test to diagnose central Horner’s syndrome, so associated clinical signs must be looked for.

- **Hypothalamic lesions**- associated with contralateral hemiplegia and some may have contralateral hypesthesias.
- **Wallenberg’s syndrome**- Due to lateral medullary damage there is ipsilateral impairment of pain and temperature sensation over face, limb ataxia, and bulbar (nuclear) disturbance causing dysarthria and dysphagia and Horner’s syndrome. Contralateral pain and temperature sensation are impaired over trunk and limbs.
- **Horner’s syndrome and contralateral 4th nerve palsy** - Indicate involvement either of trochlear nerve nucleus on side of Horner’s syndrome or of ipsilateral fascicle before decussation.
- **Cervical spondylosis** - They may not have signs and symptoms of spinal cord disease but have neck pain and Horner’s syndrome.

**Pre-ganglionic (2nd order) neurons**

These neurons exit from ciliospinal centre of Budge and passes across the pulmonary apex, turn upward and pass through stellate ganglion, go up the cervical sheath to the superior cervical ganglion, near the bifurcation of common carotid artery.

Prolonged impotence of preganglionic Horner’s is non-specific, but disturbance of anhydrosis is characteristic. The entire side of head, face and neck down the clavicle are usually involved.

**Causes**

- Malignancy, most common being lung and breast cancer. Tumors spread behind carotid sheath at C6 level associated with phrenic, vagus and recurrent laryngeal nerve palsy called as “Rowland Payne” syndrome.
- Schwanoma of Sympathetic chain.
- Accidental or surgical trauma (e.g. disc herniation at C8, T1) brachial plexus injuries, pneumothorax, CABG or pacemaker insertion.
- Transient blockade of the preganglionic neurons by anaesthetic technique.
- Chest tubes, vascular catheters and strong bullets can directly injure the pre-ganglionic sympathetic neurons.

**Post-ganglionic (3rd order) neurons**

The neurons of the sympathetic pathway to iris dilator muscle extends from the superior cervical ganglion behind the angle of mandible and up along the internal carotid artery (ICA) where it is called as “The Carotid plexus” or “Carotid nerve”.

---

*Figure 3: A flowchart for evaluation of a case of anisocoria*
ophthalmic division of the trigeminal nerve, entering the nasocilliary nerve divide into two long ciliary nerves that travel with the lateral and medial suprachoroidal vascular bundles to reach the anterior segment of the eye and innervate the iris dilator muscle.

Within cavernous sinus, the sympathetic fibers from the ICA join briefly with abducent nerve and leave it to join the ophthalmic division of the trigeminal nerve, entering the orbit with its nasociliary branch. Sympathetic fibers in the nasociliary nerve divide into two long ciliary nerves that travel with the lateral and medial suprachoroidal vascular bundles to reach the anterior segment of the eye and innervate the iris dilator muscle.

Causes of postganglionic Horner’s syndrome may be extracranial and intracranial

**Extracranial**

- Traumatic and spontaneous dissection of ICA can produce sudden ipsilateral face and neck pain associated with postganglionic Horner’s syndrome.

- Raeder’s trigeminal neuralgia, the name given to headache syndrome with persistent trigeminal pain, post-ganglionic Horner’s likely represents unrecognized carotid dissection in many patients.

---

**Table 3**  
**Disorders of pupillary function**

<table>
<thead>
<tr>
<th>Anisocoria greater in dark</th>
<th>Anisocoria greater in light</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple anisocoria (physiologic)</td>
<td>Damage to parasympathetic outflow to the iris sphincter muscle.</td>
</tr>
<tr>
<td>Inhibition of sympathetic pathway</td>
<td>Oculomotor nerve paresis</td>
</tr>
<tr>
<td>Horner’s syndrome</td>
<td>Tonic pupil syndromes (including Adie’s)</td>
</tr>
<tr>
<td>Pharmacological (Dapiprazole, thymoxamine)</td>
<td>Intermittent dilation of one pupil caused by inhibition of parasympathetic pathway</td>
</tr>
<tr>
<td>Stimulation of sympathetic pathway</td>
<td>Trauma to iris sphincter</td>
</tr>
<tr>
<td>Tadpole pupil</td>
<td>Acute Glaucoma</td>
</tr>
<tr>
<td>Sympathetic hyperactivity causing intermittent dilation of one pupil</td>
<td>Siderosis</td>
</tr>
<tr>
<td>Pharmacologic (cocaine, adrenergic drugs)</td>
<td>Pharmacologic inhibition of parasympathetic pathway (atropine, scopolamine)</td>
</tr>
<tr>
<td>Pharmacological stimulation of parasympathetic pathway (Eserine, organophosphate esters, pilocarpine methacoline, arecoline).</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 4(a): A case of Horner’s syndrome with ptosis and small pupil**

**Figure 4(b): A case of 3rd nerve palsy with ptosis and mydriasis pupil (with limited eye movements)**

**Figure 5: Oculosympathetic pathway involved in Horner’s syndrome**
Other causes are tumors, inflammatory lesions, and other masses and metastasis to cervical lymph nodes.

**Intracranial**
- Tumors of nasopharynx or jugular foramen—associated with paralysis of the tongue, anaesthesia of the pharynx and dysphagia, all on same side.
- Tumors, aneurysms, infection and other lesions in cavernous sinus may produce post-ganglionic Horner's syndrome usually ipsilateral ophthalmooplegia, pain or dysaesthesia of face due to involvement of ocular motor nerves and trigeminal nerve within cavernous sinus.
- Abduccens nerve palsy and post ganglionic Horner's together with other neurologic signs-cavernous sinus lesion.
- Middle fossa lesion encroaching Meckel's cave and on ICA at foramen lace rum- postganglionic Horner's with pain.
- Basal skull fracture, cluster headache, giant cell arteritis.

**Clinical features**
- Small or sunken affected eye (apparent enopthalmos)
- Dropped upper lid which is slight
- Slight elevated lower-eye lid - upside down Ptosis (smooth fibers in lower lid loose their nerve supply)
- **Miosis** due to dilator muscle palsy (pupil will dilate widely after adrenergic stimulation due to denervation hypersensitivity). This weakness of dilator muscle is more apparent in dark because in light both pupils constrict due to normal sphincter pupillae.
- Dilation lag can be detected when the lights are turned out, Horner’s pupil dilates more slowly than normal pupil.
- Depigmentation of ipsilateral iris is not usually seen in acquired Horner’s but is a typical feature of congenital Horner’s syndrome.
- Vasomotor and sudomotor changes of facial skin on affected side is seen with patients of central and pre-ganglionic Horner’s syndrome and not with post-ganglionic type because post-ganglionic sudomotor fiber for face, synapsing at superior cervical ganglion, follow the external carotid artery to face, whereas sympathetic fibers to the eye travel via ICA, carrying only a few sweat fibers for forehead skin.
- Acute preganglionic sympathetic denervation-temperature of skin rises on side of lesion because of loss of vasomotor control and subsequent dilation and blood vessels.
- Acutely there may be some flushing and some conjunctival hyperemia, epiphora and nasal stuffness.

**Diagnosis**

**Cocaine test (10%)** - it blocks the re-uptake of nor-epinephrine at the sympathetic nerve endings. In normal eye 10% cocaine causes dilation of pupil to 8mm or more within 4-5 min.

In Horner’s syndrome- pupil fails / minimally dilates because continuous action potential required for release of norepinephrine does not occur in a sympathetically denervated nerve endings Post cocaine anisocoria of 0.8mm is sufficient to diagnose Horner’s syndrome. Cocaine affects only sympathetic system (dilator muscle) and not parasympathetic system. If patient is observed in a lighted room pupil may fails to respond due to unopposed sphincter action leading to miosis.

Hydroxyamphetamine test can be used to differentiate between post ganglionic and pre-ganglionic or central Horner’s syndrome. This test is performed only after 24-48 hour after cocaine test which has established the diagnosis, to allow cornea and pupil to recover from cocaine effect.

2 drops of hydroxyamphetamine hydrobromide 1% are placed in the lower cul-de-sac of each eye and the pupils are measured in dim light after 45 min. In normal subjects, hydroxyamphetamine releases norepinephrine from the stores in adrenergic nerve endings, producing variable but usually significant mydriasis.

With Preganglionic or central sympathetic lesion, pupils will dilate fully and may be even larger than fellow pupil, presumably because of up regulation of the post-synaptic receptors on dilator muscle.

In Post-ganglionic lesions, nerve endings themselves are destroyed due to anterograde degeneration (no stores of norepinephrine to release), so hydroxyamphetamine will have no mydriatic effect. Recent onset Horner’s syndrome may produce false negative response i.e. within 7 days probably because nor-epinephrine stores were not depleted. So a pupil that fails to dilate to cocaine and subsequently does not dilate after topical hydroxyamphetamine-postganglionic sympathetic neuron lesion.

**Congenital Horner’s syndrome:** It is uncommon. In its fully developed form, the syndrome consists of ptosis, miosis, facial anhidrosis and hypochromia of the affected iris. Brachial plexus injury at birth, congenital tumor and viral infection may account for few cases. Parents of infant with congenital Horner’s syndrome sometimes report that the baby develops a hemifacial flush when crying or nursing, opposite to side of Horner’s syndrome lesion. If’s a normal response which appears more obvious because of impaired facial vasodilatation on the side of congenital Horner’s syndrome.

**Sympathetic hyperactivity**

A tadpole pupil is an intermittent and benign phenomenon in which the pupil of one eye becomes distorted for a minute or two. The pupil is pulled in one direction like the tail of a tadpole. It is thought to be caused by repeated bursts of sympathetic innervations (segmental sympathetic spasms).

Some patients who sustain trauma (whiplash injury) to low cervical or high thoracic spinal cord experience episodes of unilateral pupil dilation associated with sweating. Pharmacological testing reveals mydriasis that is caused by episodic sympathetic irritation.

**Pharmacological stimulation of iris sphincter**

Almost all cases of acute anisocoria in which one pupil is non-reactive are caused by pharmacologic blockade of iris sphincter. Anisocoria is worse in dark because the affected pupil cannot constrict.

In instances where anisocoria is due to parasympathetic stimulation then blockade with 1% tropicamide will dilate the large, reactive pupil but will fail to dilate small, non-reactive pupil.

**Pharmacological stimulation of iris dilator**

Cocaine, oxytetracycline, phenylephrine may dilate pupil leaving sphincter intact. Also here dilation will be obvious in dark than light.
More anisocoria in light

**Damage to parasympathetic outflow to iris sphincter**

Final common pathway for pupillary reaction to light and near stimulation begins in the mesencephalon with the visceral oculomotor nuclei – to ciliary ganglion via oculomotor nerve – their short ciliary nerve – iris sphincter.

Lesion anywhere in this pathway can produce absolute paralysis of pupillary constrictor – pupil is then dilated and non-reactive. In many cases all parasympathetic input to the eye is damaged simultaneously so that accommodation is lost. This combination of iridoplegia and cycloplegia is often called internal ophthalmoplegia to distinguish it from external ophthalmoplegia when the extra-ocular muscles are paralyzed in setting of normal pupal response.

Isolated iris paralysis can be difficult diagnostic problem, so consider lesion of mesencephalon, oculomotor nerve, ciliary ganglion, the short ciliary nerve and the eye itself.

**Edinger Westphal Nucleus damage**

Lesions of rostral mesencephalon almost never produce an isolated unilateral, non-reactive, dilated pupil. Bilateral pupillary abnormalities are the rule with damage to Edinger Westphal nucleus. Most lesions in this region that produces pupillary abnormalities also affect other parts of oculomotor nucleus- ptosis, ophthalmoplegia or both.

**Damage to pupillomotor fibers in the oculomotor nerve fascicle**

Fascicles of oculomotor nerve can be damaged within mesencephalon due to ischemia, inflammation and infection leading to complete or incomplete isolated 3rd nerve palsy or a syndrome in which an oculomotor nerve paresis is associated with neurological signs. Because the fibers emerging from the Edinger Westphal nucleus are among the most rostral in the oculomotor group, it is possible for a lesion to damage just fibers serving pupillary function thus- unilateral, dilated non-reacting pupil.

In other patients, a lesion affecting the oculomotor fascicle may damage only fibers destined for extra ocular muscle-pupil sparing complete or incomplete oculomotor nerve palsy.

**Damage to pupillomotor fibers in the sub-arachnoid portion of oculomotor nerve**

Separate bundles of the oculomotor nerve that leave the mesencephalon merge to from oculomotor nerve in the subarachnoid space. The nerve fibers take short course between posterior cerebral and superior cerebellar arteries and then enter cavernous sinus.

In this path, pupillary fibers are superficial which migrate from superomedial portion to inferior part of nerve. In basal meningitis, noxious influence may cause hazard to superficially located pupillary fibers.

Intracranial aneurysm located at posterior communicating artery and ICA junction will produced dilated, non-reacting pupil which is nearly always associated with other evidences of oculomotor nerve dysfunction. Aneurysms at the tip of basilar artery are more likely to produce isolated pupillary dilation than are aneurysms of internal carotid artery.

**Damage to cavernous part of 3rd nerve**

It is very rare to observe an isolated dilated non-reactive pupil from damage to pupillo motor fibres in this region.

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**Damage to ciliary ganglion and iris root in the orbit- tonic pupils**

Damage to postganglionic parasympathetic innervations of intraocular muscles- initially isolated internal ophthalmoplegia. Later there may be a poor pupillary reaction to light as regional palsy of iris sphincter by slit lamp, paresis ofaccommodations, cholinergic supersensitivity of denervated muscle, near reflex with miosis that is unusually strong and tonic and a slow tonic redilation after construction of nerve stimuli.(Figure 6) This pupil is called tonic pupil.

**Causes:** Damage to ciliary ganglion, damage to short ciliary nerves in retrobulbar space or in intraocular / suprachoroidal space.

Slowness and tonicity of pupillary movement is caused by aberrant regeneration of ciliary nerves into iris sphincter.

**Types of tonic pupil**

**Local**

It occurs due to a variety of inflammation, infection and infiltrative process of ciliary ganglion in isolation or as part of systemic process. e.g. herpes zoster, chicken pox, measles, diphtheria, syphilis (congenital and acquired), sarcoidosis, scarlet fever, pertussis, small pox, influenza, sinusitis, VKH, rheumatoid arthritis, viral hepatitis, choroiditis, primary and metastatic choroidal and orbital tumors, blunt injury to globe and penetrating orbital injury. Siderosis damages nerve more than muscles and may produce iron mydriasis.

**Neuropathic tonic pupil**

It is a part of a generalized widespread, peripheral or autonomic neuropathy that also involves the ciliary ganglion, the short ciliary nerves or both e.g. syphilis, chronic alcoholism, diabetes mellitus, spinocerebellar ataxia, Guillan Barre syndrome and Miller fisher syndrome.

SLE patient may develop tonic pupil as a part of generalized autonomic neuropathy as are many patients with Sjogrens syndrome.

Tonic pupil may also develop in patients with systemic amyloidosis, hereditary sensory neuropathy, a paraneoplastic syndrome and hereditary motor- sensory neuropathy (Charcot Marie tooth disease).

**Holmes-adie tonic pupil syndrome**

It consists of unilateral or bilateral tonically reacting pupils developing in otherwise healthy persons.

**Clinical features**

- Disturbance in deep-tendon reflex without any generalized / peripheral autonomic dysfunction
- Always sporadic, can be familial
- 20-50 years of age
- 70% females,
- 80% unilateral
- **Symptoms:** Photophobia, blurred near vision, enlarged pupil, headache
- Other eye affected (4% of cases/year) with fewer symptoms.
- Segmental contraction or “vermiform” movements are observed in all forms of tonic pupil which is a critical
Features of Adie’s pupil that changes over time-

- There is tendency for patients with unilateral Adie’s syndrome to develop a tonic pupil in opposite eye with time.

The cause of Adie’s syndrome is obscure. Pharmacologic and pathologic studies indicate ciliary ganglion, short-ciliary nerves, or both as the location of lesion.

Ross’ syndrome (tonic pupil plus) is a combination of Adie’s syndrome (tonic pupil and hyporeflexia), and segmental hypohidrosis.

 DAMAGE TO IRIS SPHINCTER

Blunt trauma to eyes- tears in the iris sphincter or in the iris base – cause a dilated non-reactive pupil that can be mistaken for dilated pupil of oculomotor nerve palsy.

Pharmacologic blockade and parasympatholytics

- Pharmacological mydriasis is extreme usually >8mm.
- Pupil of oculomotor palsy is rarely widely dilated and is associated with other signs of oculomotor nerve palsy
- Tonic pupil may have somewhat similar appearance. 1% pilocarpine solution eye drop will distinguish as follows
  - Pupil with pharmacological blockade-constrict poorly/unchanged
  - Tonic pupil will construct to even weaker pilocarpine solution
  - Pupil of oculomotor dysfunction- constricts maximally

TOURNAY’s phenomenon

When some normal person looks in extreme lateral gaze-pupil on that side becomes larger than opposite pupil which becomes smaller. This phenomenon is called as TOURNAY’S phenomenon. It is of no clinical significance.

Thus proper examination of pupil can lead us to diagnose many important ocular and neurologic pathologies as well as to exclude them.

References


Figure 6: Pupils of a patient of left Adie’s pupil in dim light, bright light and with the use of 0.5% pilocarpine ( supersensitivity to pilocarpine)
Mitomycin C in Ophthalmology

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Dr. Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, Ansari Nagar, New Delhi

Mitomycin C (MMC) is a chemotherapeutic agent used to treat upper gastro-intestinal tumours, anal cancers, and breast cancers because of its antitumour and antibiotic activity. MMC was first used in ophthalmology in 1969, in Japan, where recurrent pterygia were successfully treated with the drug. Its use and application in ophthalmology has been increasing in recent years because of its modulatory effects on wound healing. With its widespread use in ophthalmology it has become an integral part of the ocular pharmacological armamentarium. This article reviews the current trends and uses of mitomycin C in the eye and its complications.

Clinical pharmacology
MMC is an antineoplastic antibiotic agent isolated from the soil bacterium Streptomyces caesipotosus. The other variants of this drug are Mitomycin A and B which are also produced by Streptomyces caesipotosus. It is an anti-metabolite with anti-proliferative effect on cells showing the highest rate of mitosis by inhibiting DNA synthesis and interferes with RNA transcription and protein synthesis. DNA is inhibited by cross-linking at the N position of Adenine and at 06 and N position of Guanine. The cell cycle is most affected during the late G-I and early S-phase. The chemical formula is C15 H18 N4 O5 (Figure 1).

Mitomycin is delivered in a solubilized form. It has a high bioavailability in the target tissue. Because of its hydrophobic character, it can penetrate into the epithelially denuded cornea and conjunctiva.

Drug reconstitution
MMC should be reconstituted in sterile water at neutral pH, the drug is inactivated in an acidic solution. The drug should be stored under refrigeration to preserve its potency and under these conditions, it is potent for a period of two weeks only.

The drug is available in a vial (2mg/ml). It is further reconstituted with normal saline(5ml) to make 0.4mg/ml or in 10 ml to make 0.2 mg/ml.

Clinical uses of MMC in ophthalmology
- Glaucoma filtering surgery
- Pterygium surgery
- Dacryocystorhinostomy

Figure 1

Figure 2
• Squint surgeries
• Refractive surgeries
• Ocular surface tumors
• Allergic conjunctivitis

Glaucoma filtering surgery

The high failure rate of trabeculectomy surgery is partly due to subconjunctival or scleral scarring at bleb. Mitomycin C inhibits the fibroblasts proliferation and subsequent scarring of filtering bleb. Intraoperative MMC applied at a concentration of 0.2 mg/ml controlled postoperative IOP as effectively as a 0.4-mg/ml concentration in high-risk cases of congenital glaucoma, but with a lower incidence of complications and thin-walled blebs.

No significant difference was seen in overall success or complication between subconjunctival and intrascleral application of MMC-augmented trabeculectomies in glaucomatous eyes at high risk of surgical failure.

In selected paediatric cases of primary or secondary glaucoma in which visualisation of the trabecular meshwork is poor, trabeculectomy augmented with MMC and 5-FU is a good treatment option.

• **Dosage:** 0.02% - 0.04%
• **Method:** Merocel sponge soaked in the desired concentration is kept for 1-5 minutes generally subconjunctival and sometimes sub scleral. It is then thoroughly washed with BSS.
• **Complication:** The main complications and side effects of antimetabolite-enhanced filtration surgery comprise development of thin-walled cystic blebs, late bleb leaks, bleb infections, endophthalmitis, chronic hypotony, hypotony maculopathy and corneal epithelial toxicity.

Success rate in trabeculectomy cases with MMC in various studies is given in Table 1.

Pterygium surgery

A single intraoperative application of 0.02% MMC for 30 seconds after pterygium excision is associated with minimal complication and effectively reduces the recurrence rates after excision of primary or recurrent pterygium. In comparison with conjunctival autografting, low-dose application of MMC after bare sclera procedure is less efficacious in preventing recurrence of pterygium, but simpler and produces a similar proportion of patients with satisfactory final appearance.

Its use has reduced the proliferation of fibroblasts and thus regrowth of pterygium.

Intraoperative administration of mitomycin C at 0.05% is safe and effective in preventing pterygium recurrences.

• **Dosage:** 0.2 - 0.4 mg / ml applied intraoperatively over bare sclera for 1 - 5 minutes.
• **Complications:** secondary glaucoma, corneal melting and perforation, corneal edema, sclera calcification. Other complications of MMC in pterygium surgery includes, pain, excessive tearing, prolonged hyperemia, late hemorrhage, chemosis lid edema, ptosis, wound dehiscence, photophobia, corneal blood staining, pigment accumulation, superficial punctate keratitis and delayed wound healing.

<table>
<thead>
<tr>
<th>Study</th>
<th>Dosage of MMC</th>
<th>Success rate of trabeculectomy</th>
<th>Success rate with MMC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Harish Agarwal, Ramanjit Sihota al³</td>
<td>0.02% vs 0.04%</td>
<td>IOP control with medication 86.7% with both dosages (lower incidence of complications seen with 0.04%)</td>
</tr>
<tr>
<td>2</td>
<td>Harish Agarwal, Ramanjit Sihota et al³</td>
<td>0.02%</td>
<td>Sub-conjunctival MMC 90.5% and sub scleral MMC 75%</td>
</tr>
<tr>
<td>3</td>
<td>R Ehrlich, M Snir et al³</td>
<td>0.02% - 0.04%</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>Kitazawa et al³</td>
<td>0.04%</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Mutsch YA, Grehn F³</td>
<td>0.04%</td>
<td>76%</td>
</tr>
</tbody>
</table>

Dacryocystorhinostomy

The most important cause of failure of DCR surgery is fibrosis occurring under the flaps near the osteotomy sites. MMC in these cases tends to suppress fibrous proliferation and scar formation. Intraoperative mitomycin C application is effective in increasing the success rate of DCR surgery in standard nasolacrical duct obstruction, and no significant complications resulted from its use⁴. The non-patency rate in the mitomycin C group is 4.5% compared with 11.4% in the conventional group. Intraoperative mitomycin C is effective in maintaining a larger osteotomy size. This modification may possibly improve success rates over the traditional dacryocystorhinostomy procedure⁵. A piece of cotton soaked with 0.2 mg/ml mitomycin C was applied to the osteotomy site for 30 minutes.

**Dose:** 0.02 to 0.04% for 5-30 minutes

Squint surgery

Topical mitomycin C may enhance the success rate of strabismus surgery with delayed adjustment and reduce postoperative adhesions⁶. Intraoperative application of mitomycin C in reoperated cases and restrictive squints helps to reduce fibrosis and scarring under the tenons layer⁷. **Dose:** 0.2 mg / ml for 5 minutes between the conjunctiva and the sclera after adhesion release

<table>
<thead>
<tr>
<th>Success rates</th>
<th>Study</th>
<th>Dosage of MMC</th>
<th>Recurrence rate with conjunctival autograft</th>
<th>Recurrence rate with MMC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Singh et al⁸</td>
<td>0.04%</td>
<td>88.9%</td>
<td>2.2%</td>
</tr>
<tr>
<td>2</td>
<td>Young et al⁹</td>
<td>0.02%</td>
<td>1.9%</td>
<td>15.9%</td>
</tr>
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</table>

13 /g07/g71/g01/g07/g01/g00/g91/g3 /g06/g70/g60/g05/g76/g01/g74/g3 /g01/g73/g3 /g40/g40/g30/g3 /g60/g01/g71/g3 /g06/g00/g69/g06/g71/g04/g00/g71/g01/g07/g3 /g76/g01/g3 /g01/g09/g71/g05/g60/g79/g79/g3 /g06/g00/g70/g70/g71/g06/g06/g3 /g01/g05/g3 /g07/g75/g71/g3 /g07/g75/g71/g3 /g191/g69/g05/g01/g69/g79/g60/g06/g07/g06/g3 /g03/g05/g01/g79/g76/g73/g71/g05/g60/g07/g76/g01/g01/g3 /g60/g01/g71/g3 /g06/g00/g69/g06/g71/g04/g00/g71/g01/g07/g3 /g76/g01/g3 /g01/g09/g71/g05/g60/g79/g79/g3 /g06/g00/g70/g70/g71/g06/g06/g3 /g01/g05/g3 /g07/g75/g71/g3 /g07/g75/g71/g3 /g191/g69/g05/g01/g69/g79/g60/g06/g07/g06/g3 /g03/g05/g01/g79/g76/g73/g71/g05/g60/g07/g76/g01/g01/g3 /g60/g01/g71/g3 /g06/g00/g69/g06/g71/g04/g00/g71/g01/g07/g3 /g76/g01/g3 /g01/g09/g71/g05/g60/g79/g79/g3 /g06/g00/g70/g70/g71/g06/g06/g3 /g01/g05/g3 /g07/g75/g71/g3 /g07/g75/g71/g3 /g191/g69/g05/g01/g69/g79/g60/g06/g07/g06/g3 /g03/g05/g01/g79/g76/g73/g71/g05/g60/g07/g76/g01/g01/g3 /g60/g01/g71/g3 /g06/g00/g69/g06/g71/g04/g00/g71/g01/g07/g3 /g76/g01/g3 /g01/g09/g71/g05/g60/g79/g79/g3 /g06/g00/g70/g70/g71/g06/g06/g3 /g05/g60/g07/g71/g3 /g01/g73/g3 /g40/g40/g30/g3 /g76/g01/g3 /g03/g07/g71/g05/g91/g74/g76/g00/g00/g3 /g06/g00/g05/g74/g71/g05/g91/g3
Refractive surgeries

Haze formation with loss of corneal transparency and surface irregularities and myopic regression are the major complications after corneal refractive surface surgery. The use of mitomycin C (MMC) with its antibiotic and antineoplastic properties is intended to inhibit wound healing mechanisms leading to subepithelial fibrosis.

Mitomycin C is an alkylating agent with cytotoxic and antiproliferative effects that reduces the myofibroblast repopulation after laser surface ablation and, therefore, reduces the risk of postoperative corneal haze. It is used prophylactically to avoid haze after primary surface ablation and therapeutically to treat pre-existing haze. There is no definite evidence that establishes an exact dioptr limit or ablation depth at which to apply prophylactic mitomycin C. It is usually applied at a concentration of 0.2mg/ml (0.02%) for 12 to 120 seconds over the ablated stroma, although some studies suggest that lower concentrations (0.01%, 0.002%) could also be effective in preventing haze when treating low to moderate myopia. This dose of mitomycin C has not been associated with any clinically relevant epithelial corneal toxicity.

Single application of diluted mitomycin C 0.02% solution following scraping of the corneal surface was effective and safe in treating haze and regression after PRK for myopia.

Ocular surface tumors

MMC treatment following surgical excision appears to decrease the recurrence rate of localized conjunctival-corneal intra-epithelial neoplasia (CCIN), and should be considered as adjuvant therapy in primary treatment. MMC should also be considered as adjuvant therapy in the treatment of localised recurrent disease. MMC may be used as sole therapy in more diffuse disease, but close ongoing follow-up is recommended in view of the significant risk of persistent or recurrent disease.

Dose: Topical mitomycin 0.4 mg/ml (0.04%) is administered four times a day for three weeks.

Complications of MMC

Major complications

- Necrotizing scleritis
- Scleral ulceration
- Perforation
- Uveitis
- Cataract
- Glaucoma
- Symblepharon formation

Minor complications

- Ocular pain
- Photophobia
- Lacrimation
- Lid edema

Foreign body sensation (secondary to superficial punctate keratitis)

Contraindications for topical use

- One-eyed patients
- Very old patients
- Pregnant women
- Those with predisposing condition to corneal ulceration or poor healing such as immunocompromised patients or patients with Sjogren’s syndrome, atopic keratoconjunctivitis, acne rosacea or herpetc keratitis.

Conclusion: The use of mitomycin in ophthalmology is increasing in every subspecialty but the risk-benefit ratio should be considered keeping in mind its complications.

References

Visual electrophysiology tests are an extension of ophthalmological evaluation and are an important diagnostic tool for a pediatric ophthalmologist. The aim of this article is to present a practical overview of visual electrophysiology, emphasizing patient selection, and the use of test reports in clinical decision making.

Importance of electrophysiologic tests in pediatric ophthalmology practice.

One of the biggest challenges of pediatric ophthalmology practice are newborns’ and preverbal children coming to the outpatient department who appear apparently blind. Knowledge of an exact ophthalmological diagnosis is essential in the rehabilitation of such a visually impaired child.

The diagnosis clarifies
a. Aetiology and consequently the genetics of the disorder
b. Provides an explanation for various visual problems of the child
c. Implies the prognosis.
d. Also contribute to decisions about which forms of education or career are feasible.

What category of patients are candidates for visual electrophysiological tests?

In our pediatric ophthalmology practice we get clinical presentations of newborns and young preverbal children who present with unexplained poor vision with and without nystagmus. This is challenging in terms of finding out the presence or absence of vision, quantifying visual acuity loss, and also finding out the cause of the visual loss.

In several posterior segment disorders visual electrophysiology plays a decisive and diagnostic role, because psychophysical testing in infants and young children is limited, and ophthalmological examination may initially reveal a normal looking retina even in the case of severe retinal dystrophy.

The normal looking eyes with unexplained poor vision may be further classified according to causes into

- Normal looking eyes with Nystagmus
- Optic nerve hypoplasia
- Foveal hypoplasia

- Infectious disease – toxoplasmosis, CMV retinitis
- Photoreceptor dystrophies – congenital achromatopsia, LCA, etc.
- Normal looking eyes with no nystagmus
- Cortical blindness
- Ocular motor apraxia
- Delayed visual maturation

The common presentations of newborns and preverbal children with visual problems presenting in a pediatric ophthalmology practice are:

- Night Blindness (with or without poor vision)
- Nystagmus
- Central Vision Problems
- Unexplained Poor Vision with/without nystagmus
- Part of Systemic Disease / Syndrome
- Color Blindness

What are the electrophysiological tests available for diagnosis?

Batteries of electrophysiological tests are there in our armamentarium, which help in diagnosis and prognosis. To arrive at a correct diagnosis you need a combination of suitable tests at a suitable age and under suitable conditions. The common electrophysiological tests used in pediatric ophthalmologic practice are EOG, ERG and VEP.

EOG is most appropriate for the child in the first or second decade of life with a macular degenerative disease (namely bests’ disease). It gives an idea of the retinal pigment epithelium function but occasionally EOG may be used as an ancillary test to evaluate retinal function in place of or in addition to ERG. The child must be of sufficient age, usually more than 6 years of age, to cooperate with the testing. Patients with marked loss of visual acuity may find performing the test difficult because of inability to adequately see the fixation lights. The sensitivity of the test to localized disease of the retinal pigment epithelium is poor.

The ERG is appropriate at all ages to evaluate the retinal function. Because the ERG response is small in early infancy and grows in size to about 2 years of age, ERGs from infants less than 3 months of age are often difficult to interpret.
Specific indications include unexplained visual impairment or blindness in an infant with or without nystagmus, unexplained progressive loss of vision in early childhood, unexplained but stable subnormal vision in childhood, and at risk children for retinal dystrophies. The ERG essentially gives no information on visual acuity, can be nonrecordable in many different ocular diseases, and can be nonspecific in them. The examination in infants and young children may require sedation. Different types of ERG tests are available by varying the stimulus and recording conditions which can provide information about the rod and cone activity and also about the retinal sites and local topography of disease action. Pattern ERGs and full field ERGs are commonly used to assess the level of retinal activity in children. Both of these tests take about 40 minutes each which includes the time for sedation. The full field ERG has components of a photopic, scotopic, flicker, and oscillatory potential each of which can help to interpret in the type of cell or the layer of affected retina. The flicker ERG is extremely sensitive to cone activity and the oscillatory potentials indicate the function of amacrines of inner retinal layer.

The table 1 gives the expected electrophysiological findings of ERG in various causes of an apparently blind child:

The VEP is appropriate for the assessment of overall intactness of the pathways from the retinal ganglion cells to the visual cortex. The VEP undergoes considerable variations in waveform from neonatal period to the first decade of life and the usefulness of the test is greatest when evaluating unilateral disease process. Information can be obtained on visual acuity, conduction time of the signal from the eye to the visual cortex, and more complex information about intactness of the pathway in front, within or behind the chiasma. A defect anywhere in the pathway may produce an abnormal VEP. As for ERG, various types of VEP tests are available to assess visual acuity in children ranging from Flash VEP which assesses the presence of vision to Pattern VEP which gives us an estimate of the visual acuity in preverbal children. Pattern VEP also takes about 40 minutes to perform which can be difficult to do in infants and young children. A new method of assessing vision in infants, preverbal, and uncooperative children is the sweep VEP which assesses the grating acuity by changing the spatial frequency of the gratings and is a faster reliable method of assessing visual acuity and takes approximately 10 min to complete.

Which tests for which disorder? How to order an electrophysiological test?

Before we go into details of what tests to order we must understand that there is no single magic electrophysiological test which will answer all the questions. On the other hand, because cooperation and attention to task are limited in children, one must target the test to answer the clinicians’ question about the visual system. Thus, it is extremely important that the clinician convey to the electrophysiology laboratory why the electrophysiology test is ordered and what information is desired from the study.

The approach for ordering an electrophysiological test includes the following points to be assessed:

- Type of vision loss (night, central..)
- Analysis of complaint
- Clinical examination (Fundus, Nystagmus..)
- Family history (detailed)
- Interpretation of other tests (VF, FFA...)

* Associated conditions (malignancy, syndromes...)

The ordering of an electrophysiological test is in collaboration with clinical findings and other investigations (Figure 1). The electrophysiological test should provide information about the presence and absence of visual acuity in a child and also to provide the information about the cause of decreased visual acuity whether retinal or post retinal (Figure 2).
The test should also tell the quality and quantity of vision. As mentioned before no single electrophysiological test can provide all the information desired hence a battery of tests are used to give us the relevant information. The most commonly used tests in a tertiary care hospital setting for infants and preverbal children are pattern VEP, Pattern ERG, and full field ERG.

How to interpret an electrophysiological test?

The following is the basic protocol for interpreting electrophysiological tests in a child with unexplained poor vision:

- Retinal versus post-retinal
- Progressive versus stationary

- Associated with peripheral involvement
- Objective VA assessment
- Family history
- The use of electrophysiology protocols (PERG / VEP / ERG)

In conclusion the proper assessment in terms of clinical examination, history taking and testing helps in identifying the category of problem. Knowing the type of expected errors helps in planning the testing strategy and effective preparation for testing both in terms of child preparation and testing conditions and standards helps in identifying the problem location and magnitude. This helps in overall assessment of the problem and evaluating the prognosis.

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7. ISCEV: A guide to procedures
26 year old male was referred to us from Neurosurgery dept. for complete ocular examination. Patient’s NCCT scan brain and CECT scan Brain was suggestive of left sided cerebellar hemangioblastoma with mass effect leading to deviation of vermis towards Rt. side and b/l dilated lateral & third ventricle (Figure 1). Midline sub occipital craniectomy with excision of tumor was done prior to the referral.

At presentation there were no ocular complaints. There was past history of repeated episodes of left sided ear discharge since childhood. Family history was positive as mother died of brain tumour (records not available) and H/o cerebellar hemangioblastoma and pancreatic cyst in one elder brother. Patient’s left sided cerebellar signs were positive and VIII cranial nerve examination was suggestive of conductive type of hearing loss.

Unaided vision was 6/6 in both the eyes, external ocular and anterior segment examination was normal with normal pupillary reflexes. On fundus evaluation bilateral hyperemic optic nerve head of size of 1.7mm with blurring of superior and inferior pole in right eye and blurring of inferior pole in left eye were found. (Figure 2a,b) Veins were dilated in both the eyes with A/V ratio of 2:4. On peripheral examination in left eye in inferotemp. quadrant in midperiphery, a well circumscribed round sessile orange red colored lesion of 1/3 DD (about 600μm) in diameter with a feeder arteriole and draining venule was seen. (Figure 3a) FFA in arterial phase demonstrated feeder arteriole and lesion. (Figure 3b) Venous phase demonstrated feeder arteriole, draining venule and hyper fluorescent lesion (Figure 3c). Late films showed leakage from lesion in retina and vitreous (Figure 3d).

Automated perimetry (Humphrey 30-2 SITA std.) was normal in both the eyes.

Histopathological examination of cerebellar tumor showed a vascular and a stromal component with Stromal component comprising of large round to polygonal vacuolated cells with central nuclei and a foamy cytoplasm suggestive of cerebellar hemangioblastoma (Figure 4).

With a diagnosis of VHL in our minds, we evaluated this patient systematically for other manifestations. CECT abdomen demonstrated multiple pancreatic cysts and bilateral simple renal cysts. ENT reference exhibited conductive type of hearing loss. Examination under microscope showed unsafe type of CSOM (Chronic Otitis Media) but endolymphatic sac tumor was not seen. Spinal MRI, 24 hr urine catecholamine and metanephrines, scrotal USG and routine investigations were within normal limits.

Since the condition is autosomal dominant in inheritance, we carried out family screening for this patient. (Figure 5) Mother died of brain tumor, records for which were not available but it could have been a CNS hemangioblastoma. We saw retinal
capillary hemangioma, multiple pancreatic cyst and bilateral simple renal cyst in our index case and h/o excision of Cerebellar hemangioblastoma was present. In brother elder to him (case B) we saw a retinal capillary hemangioma on FFA (Figure 6) but on systemic evaluation no other manifestations of VHL were found. In the second brother (case c), cerebellar hemangioblastoma and pancreatic cyst were demonstrated but on FFA retinal capillary hemangioma was not seen.

We carried out genetic mutation analysis for this patient. On sequencing analysis of genomic DNA, (extracted from peripheral blood) frame shift type of mutation was seen in one chromosome due to loss of two adenine bases (AA) from 150th codon (Figure 7).

Since the lesion was more than 500 microns and less than 1.5mm in diameter, we carried out argon laser
photocoagulation for this patient with the settings of 300 micron spot size, 0.1 second duration and 300 mW power. Patient was followed up. After 5 weeks, vision was stable, lesion size had decreased but FFA demonstrated a persistent leakage (Figure 8a,8b) so we gave another session with similar settings, patient was followed up after 4 wks. Vision was stable and the lesion showed considerable decrease in size with an afferent arteriole constriction and negligible leakage on FFA (Figure 9a,9b,9c) so we kept this patient under observation.

**Discussion**

RCH is the most frequent and often the earliest manifestation of VHL. But it can remain asymptomatic for years and patient can present with other manifestations as our index case reported to neurosurgery first.

Common manifestation associated with VHL are RCH, Hemangioblastoma of the cerebellum, Hemangioblastoma of the spinal cord, Renal cell carcinoma, Pheochromocytoma, Hemangioma of pancreas, Papillary cyst adenoma of the epididymis and Endolymphatic sac tumour.

About 50% of VHL patients manifest only one feature of disease. RCH is seen in about 68% of patients. App 1/3 of patients have multiple RCH and up to half of them have bilateral involvement. RCH can be Endophytic, exophytic or sessile and may be Peripheral or juxtapapillary in location. RCH usually progresses if not treated and can lead to various complications.

Diagnostic criteria for VHL were given by Melmon and Rosen:
- **With familial history:** One or more of the following lesions are required:
  - RCH
  - CNS hemangioblastoma
  - Organ lesions: Renal carcinoma, pheochromocytoma, renal/pancreatic cysts, pancreatic islet tumors, paragangliomas, epididymal cyst adenomas, endolymphatic sac tumor
- **Without familial history:** RCH and/or CNS hemangioblastoma (if only one of these tumors expresses, a second organ lesion is necessary).

Birth incidence of VHL is 1/36000 live births. 5 VHL is Autosomal dominant in inheritance. There is great

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**Figure 4:** HPE of Cerebral Tumour vascular & stromal component. Stromal component comprises of large round to polygonal vacuolated cells with central nuclei

**Figure 5:**

**Figure 6:** RCH on FFA in elder brother of index case

**Figure 7:** Sequencing analysis of genomic DNA shown frame shift type of mutation in one chromosome due to loss AA from 150th codon
intrafamilial and interfamilial variability in the expression of the disease\(^2\).

Penetrance reaches over 90% by 65 years. Defect in tumour suppressor gene located at 3p25-26 is responsible for this syndrome. Germ line mutation of the VHL gene is present in all cells and susceptible target organ undergo mutation in remaining wild type of allele (Knudsons 2 hit hypothesis). VHL tumour suppressor gene consists of 3 exons, which encodes protein pVHL, consisting of 213 AA. pVHL negatively regulates hypoxia-inducible proteins (VEGF, erythropoietin, PDGF-B, TGF-\(\alpha\))\(^3\).

Over 300 mutations are seen in VHL tumour suppressor gene\(^5\). Complete deletion is less likely to be associated with ocular lesions and renal cell carcinoma (RCC)

Type 1 VHL without pheochromocytoma is associated with micro deletions/insertions, frame shift mutation, nonsense mutation or deletion

Type 2 VHL with pheochromocytoma is associated with missense mutation, it is again divided into:

- Type 2A- Low risk of RCC,
- Type 2B-high risk for RCC,
- Type 2C-Risk for pheochromocytoma only\(^5\,10\,11,12\)

Treatment of RCH is determined by the size, location, and associated findings. Peripheral RCH is kept under observation if the retinal capillary hemangioma:-

- very small (up to 500 microns),
- not associated with exudation or sub retinal fluid
- not visually threatening because of a nasal location
- Presence of sheathing around retinal capillary hemangioma
- lack of prominent feeder vessels\(^6\).

Laser Photocoagulation is used for eyes with RCH in posterior retina and clear media for which Argon laser, Krypton laser, yellow dye laser or Diode laser have been used. It can be used for retinal capillary hemangioma that are up to 4.5 mm in size but is most effective in tumors that are 1.5 mm or smaller. Photocoagulation can be applied directly to the tumor, to the feeder artery or to both. All three techniques were found to be effective\(^13\). Direct photocoagulation has the potential of causing haemorrhage and exudative retinal detachment\(^14,15\). Small spot size and high intensity application can also lead to haemorrhage\(^16\). Larger size burns are utilized with low intensity and extended duration\(^1\). Scatter laser treatment is frequently given to the retina surrounding the capillary.
hemangioma in an effort to prevent post-treatment extension of any exudative retinal detachment.

The response to treatment is usually evaluated 4–6 weeks later. More than one treatment session is often required. Resolution of sub retinal fluid, leakage, tumor shrinkage, change of colour of retinal capillary hemangioma from bright red to pale pink, and narrowing of vessels are indicative of adequate response to treatment. Even in the presence of adequate clinical response observed ophthalmoscopically, on fluorescein angiography residual retinal capillary hemangioma may be observed. Complete obliteration of the retinal capillary hemangioma is not necessary to achieve resolution of vision threatening effects.

Other modalities of treatment includes Cryotherapy, Transpupillary thermotherapy, Photodynamic therapy, Plaque Radiotherapy, External Beam Radiotherapy, Proton Beam Radiotherapy, AntiVEGF strategies and Vitreoretinal surgical intervention.

Lifetime cumulative probability of permanent visual loss in VHL is 60%. The visual outcome is much better in those cases of retinal capillary hemangioma that are diagnosed and treated before the onset of symptoms.

We have seen asymptomatic RCH in our index case and one of his elder brothers. This signifies importance of yearly fundus examination and FFA in all family members with VHL for early diagnosis and treatment of RCH and to reduce morbidity associated with it.

We have seen variable manifestations of VHL in three brothers in our case. This justifies variable expression associated with VHL.

Our case also correlates with previous genotype-phenotype correlation studies which has shown that frame shift type of mutations (and all the mutations associated with truncated protein) are less likely to be associated with pheochromocytoma (type 1 VHL) and multiple retinal capillary hemangioma.

Von Hippel–Lindau disease is associated with significant mortality secondary to either CNS hemangioblastoma or renal cell carcinoma. The life expectancy of affected individuals may be improved by early detection and treatment of varied manifestations with the use of surveillance protocols implying regular monitoring of predictable manifestations. Although retinal hemangioma are benign tumours, their diagnosis can result in the detection of other life-threatening conditions. The ophthalmologist plays a key role in early detection of these tumours and the prevention of significant disability and even death.

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**Forthcoming Events : National**

**November 2012**

**2-4 PATNA, BIHAR**  
**SWARNAJYOTI: 50th Annual Conference of Bihar Ophthalmological Society**  
*Venue:* Hotel Maurya, Patna (India)  
*Organising Secretary*  
*Dr. Subhash Prasad*  
Divyadhri Eye Centre  
Mangal Market, Sheikhpura, Patna-800 014  
*Ph:* 0612-2298456(R), 0612-2296446(C)  
*Mobile:* 09431209747  
*Email:* drspatnaa@gmail.com

**November 2012**

**3-4 JABALPUR, M.P.**  
**36th Annual Conference of MP State Ophthalmic Society**  
*Venue:* Hotel Kalchuri, Jabalpur, Madhya Pradesh  
*Contact Person & Address*  
*Dr. Shabbir Husain*  
Husain Eye Care Centre  
1047, Napier town, Near Fourth Bridge, Jabalpur  
*Mobile:* 09425152651,  
*Ph:* 0761-2451279, 4036452  
*Email:* drhusains@hotmail.com

**December 2012**

**22-23 MORADABAD, UP**  
**Harmony 2012**  
“Update on Pediatric Ophthalmology & Strabismus”  
*Venue:* C.L. Gupta Eye Institute, Moradabad, U.P.  
*Organising Secretary*  
*Dr. Pradeep Agarwal*  
C L Gupta Eye Institute, Ram Ganga Vihar, Phase-2 Moradabad - 244001, U.P.

**Mob. : +91-09411072329**  
*E-mail:* drpradeepagarwal@rediffmail.com, drpradeepnishi@gmail.com  
*Web-site:* www.clgei.org

**January 2013**

**17-20 HYDERABAD**  
**Joint Meeting of 28th Congress Asia Pacific Academy of Ophthalmology & 71st Annual Conference of All India Ophthalmological Society**  
*Venue:* HICC, Hyderabad, India  
*APAO-AIOS Secretariat*  
Room No. 115, OPD Block, 1st Floor  
Dr. R. P. Centre, AIIMS  
Ansari Nagar, New Delhi - 110029  
*Tel:* 011-26588327, 26593135  
*Email:* aiosoffice@yahoo.com,  
*lalitverma@yahoo.com*  
*Website:* http://www.apaoindia2013.org

**April 2013**

**12-14 NEW DELHI**  
**DOS Annual Conference**  
*Venue:* Hotel Ashok, Chanakyapuri, New Delhi  
*Contact Person & Address*  
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Room No. 479, 4th Floor,  
Dr. Rajendra Prasad Centre for Ophthalmic Sciences,  
All India Institute of Medical Sciences,  
Ansari Nagar, New Delhi – 110029  
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**Notice**

This to inform all concerned that the life membership fees for membership of the Delhi Ophthalmological Society has been raised from Rs. 3,100/- to Rs. 5,100/-. This is applicable w.e.f. 14th June, 2012.

*Dr. Harbansh Lal*  
President  

*Dr. Rohit Saxena*  
Secretary
The two volume book “Postgraduate Ophthalmology” by Drs Zia Chaudhuri and M. Vanathi is a revelation. It is one of the more comprehensive books on Ophthalmology covering all aspects of Ophthalmology needed by the residents and practicing ophthalmologists. The book has contributions from some of the best experts in the field from the country. In spite of being a multiauthor book, there is a very good uniformity of pattern and an excellent quality of text.

The strength of the book lies in its beautiful illustrations including clinical photographs which are extremely appropriate and line diagrams which are easy to reproduce. There are a number of tables which summarize the contents. The book has chapters on ocular pathology, pharmacology and radiology, which are very well illustrated. Blindness, low vision, genetics, ocular anatomy, lasers in Ophthalmology, ethical and medico legal aspects, operation theatres as well as ophthalmic emergencies have been dealt with well.

The authors being active post graduate teachers have a pulse on the requirements of the postgraduates and this is the reason the book has already acquired popularity with the residents. The book could however do well to have separate chapters on ophthalmic clinical examination, optical dispensing, instrumentation and embryology.

All in all, an excellent book, which is up to date and comprehensive and would be an ideal material for those learning and practicing ophthalmology.
Instructions:
1. Please return your answers to destimes10@gmail.com or mail them to “The Quizmaster, DOS Times Quiz, Dr. Rohit Saxena, Room No. 479, Dr. R.P. Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, Ansari Nagar, New Delhi - 110029”. Please write your DOS membership number along with your answers.
2. The answers should reach not later than 26th November, 2012.
3. The quiz can also be viewed and directly answered on our website www.dosonline.org
4. The quiz will be announced at the Monthly Clinical Meeting on 2nd December 2012. The correct entry will be awarded a prize of Rs. 2100 along with a certificate. If there are more than one correct entries, the winner of the prize will be decided by draw of lots.

Quiz compiled by Dr. Digvijay Singh

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

Membership No. ____________________ Name: ____________________________________________________
Mobile No. __________________________ Email: _________________________________________________

Answer to DOS Times Quiz October 2012
A. ____________________________ B. ____________________________
C. ____________________________ D. ____________________________
## Esotropia – Tips for Initial and Follow-up Evaluation

### History (Prime elements)

- Ocular symptoms and signs
- History of ocular ailment (date of onset and frequency of the deviation, presence or absence of diplopia)
- Systemic history (review of prenatal, perinatal and postnatal medical factors)
- Family history, including presence of strabismus, amblyopia, extraocular muscle surgery, genetic diseases.

### Initial Physical Exam (Prime elements)

- Visual acuity
- Ocular alignment (at distance and near)
- Extraocular muscle function/Forced Duction test/Active force generation test
- Detection of nystagmus
- Sensory testing/grade of binocularity
- Cycloplegic retinoscopy/refraction
- Fundoscopic examination

### Initial Management

-Prescribe corrective lenses for any clinically significant refractive error (Full cycloplegic correction).
- Manage amblyopia if present to reduce angle of strabismus or increase likelihood of binocularity
- If optical correction does not align the eyes, then surgical correction is indicated

### Follow-Up Evaluation

- Periodic evaluations necessary until visual maturity reached
- Hyperopia should be assessed every 1 to 2 years
- More frequent cycloplegic examinations are indicated in cases with changes in acuity, amblyopia, or unstable alignment
- If the examination has been stable, follow-up evaluations are appropriate every 1 to 2 years during teenage years

### Esotropia Follow-up Evaluation Intervals

<table>
<thead>
<tr>
<th>Age (years) Interval (months)</th>
<th>0-1</th>
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*Note: More frequent visits may be necessary if amblyopia is present or if there is a recent deterioration of alignment*

### Patient Education

- Discuss findings with the patient when appropriate and/or parents/caregivers to enhance understanding of disorder and to recruit them in a collaborative approach to therapy.
- Formulate treatment plans in consultation with the patient and/or family/caregivers.

*Adapted from the Summary Benchmarks for preferred practice guidelines from American Academy of Ophthalmology*

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