insight

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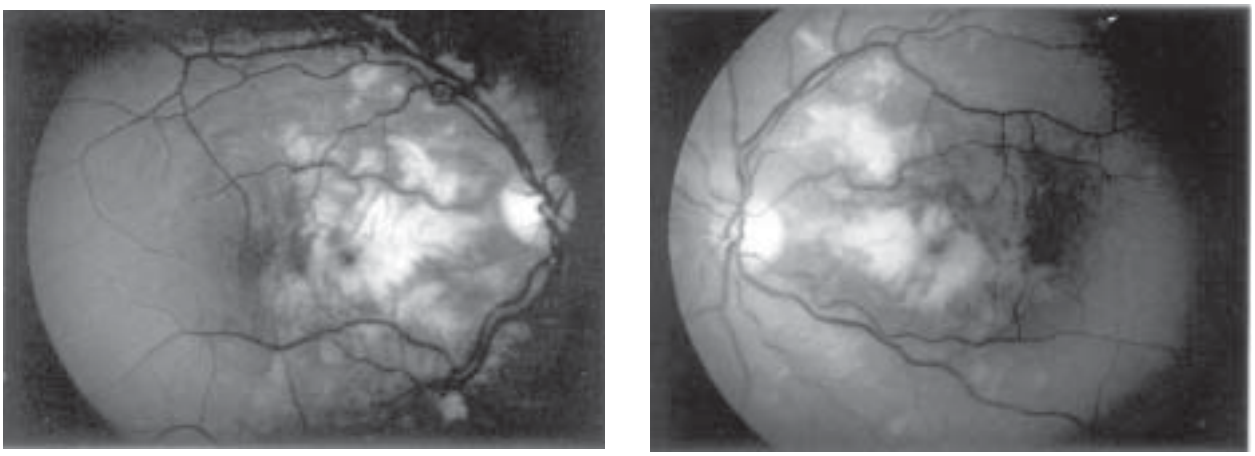

Fundus picture of both eyes showing multiple white patches of soft exudates in the posterior pole.

EDITORIAL

Amblyopia is a very important cause of monocular blindness in children and young adults. Accurate diagnosis of amblyopia is possible with a few simple and easy to practice clinical methods. Timely management of these patients is critical in ensuring good recovery of vision. Our perspective article in this issue deals with this topic, which is of great importance to the practicing ophthalmologist.

Several unusual, interesting clinical cases seen at our tertiary centre have been reported, which include purtscher's retinopathy, frosted branch angiitis, and conjunctival siderosis.

Preoperative fasting is essential to prevent life threatening complications during anesthesia, especially general anesthesia.We look at an anesthesiologist's view on current trends of preoperative fasting.

Vital genes regulate the development of the human eye. This issue carries an article that provides some basic information regarding the same, and the various developmental eye diseases that occur as a result of mutation of these regulatory genes.

Brachytherapy is the process of delivering precise radiation to an intraocular tumor, with limited exposure of normal surrounding tissue to radiation, thus avoiding unnecessary radiation to the periocular structures. This treatment is used for treating intraocular tumors such as retinoblastoma and malignant melanoma. This treatment facility has recently started at Sankara Nethralaya. Our last page article provides detailed information regarding this modality of treatment of intraocular tumours.

Dr Rajesh Fogla

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Editors

Perspective:

Amblyopia : diagnosis and management

S. Meenakshi and T. S. Surendran

Amblyopia, one of the most important causes of childhood blindness, is a treatable condition in most children, using simple time tested methods. Let us first very briefly review the definition and pathogenesis of amblyopia, to enable us to diagnose and treat it better.

How do we define amblyopia?

Amblyopia is an acquired defect in monocular vision that is due to abnormal visual experience early in life. It is usually unilateral but may be bilateral.

Why does amblyopia occur?

Abnormal early visual experience can affect monocular vision through either or both of two amblyogenic mechanisms:

In the first, lack of exposure to the sharply focused images necessary for normal development disturbs and limits the maturation of form vision.

In the second, marked disparity in the quality and directionality of inputs from the two eyes prevents binocular fusion and results in abnormal competitive binocular interaction. This leads to exclusion or interference with one eye's input to higher visual centers, which persists during monocular viewing

What are the known causes?

Classically these are due to the following:

1. Strabismus
2. Anisometropia
3. Ametropia (usually in hyperopia more than myopia)
4. Form deprivation (secondary to cataracts, lid tumors, ptosis etc.)

How does one test vision in children?

Since the diagnosis depends on visual acuity level, this is the single most important step in the clinical exam. However, visual acuity testing in children is not without its challenges. Children will often memorize lines, peek around the occluders and guess freely. Their intent is not to falsify but to perform and please.

Traditional testing methods such as Snellen acuity do not work in preverbal and illiterate children. Children are often shy or wary of the examiner and sometimes frankly uncooperative. This calls for creativity and innovation. So let us look into what methods are easily available to the general ophthalmologist without resorting to expensive charts and equipment.

Monocular and Binocular fixation pattern:

This is useful in very young infants and children. It is better to use one's thumb, which is gently lowered in front of one eye, while the child is made to fixate on something interesting, which the parent or the examiner holds up. A note is made if the fixation is *central or eccentric*. The latter implies vision less than 6/60.

The next step is to make note, if the fixation is *steady or unsteady*. Nystagmus in bilaterally vision-deprived infants tends to be horizontal, with a symmetrical pendular quality in primary gaze and jerky in lateral gaze. Especially in strabismic patients bilateral motor nystagmus may coexist with unilateral amblyopia. Many children with very poor vision may have manifest latent nystagmus on occlusion of one eye, which reduces the acuity further. In these kids it may be better to use a plus lens or translucent occluder while testing fixation.

Most amblyopic eyes with better than 6/60 acuity, have fixation that is grossly central and steady. So this does not rule out amblyopia. In such cases when acuity cannot be measured directly, it is possible to

document amblyopia by finding a significant unilateral *fixation preference*. This is done with the help of fixation devices described below and occluding each eye with a thumb, or occluder. This works well in strabismic patients.

Fixation pattern	Visual acuity
Eccentric fixation	6/240 or less
Unsteady fixation	6/240-6/90
Central fixation but will not hold	6/60-6/30
Central fixation-will hold OU but prefers one eye	6/21-6/9
Alternates spontaneously	6/6 OU

(These are conversions from the original numbers in feet)

16Δ or 10Δ Base down test:

This test is useful if the child has no manifest strabismus. A 16 or 10 loose prism is held in front of one eye and any upward refixation movement is noted. If the eye with the prism spontaneously shifts upwards to pick up fixation then it is *maintained*. If it does not then the eye without the prism is covered to force the prism covered eye to fixate. Then the cover is removed. If the eye with the prism maintains fixation through a blink it is termed *maintained*. If the eye with the prism does not maintain fixation through a blink then it is termed *unmaintained*. If the child holds briefly, then a significant amblyopia is present. If the child holds upto but not through a blink, then mild amblyopia of atleast two lines are present. This is repeated with the prism in front of the other eye.

The visual acuity testing described above, is ideally done at both distance and near, with interesting fixation targets. The distance fixation targets could be in the form of motorized toys which light up and move with the flip of a switch or foot pedal. These are mounted at six metres. It could also be a cartoon played on a video.

As far as the near toys, sky is the limit. But the more you have the better will be your exam. Remember the old adage "One toy, one look".

There are a few charts that are useful even in preverbal but cooperative children. We have found the *Lea symbols* more easily comprehensible than the Allen, which is popularly used in the West. The Lea symbols uses four objects, a house, an apple, a square and a circle, which are recognizable by most children. Whereas some of the objects depicted on the *Allen* e.g. a cake, may not be familiar to all children. Some others like the man on the horse are abstract and difficult sometimes even for adults to comprehend.

A hand held photocopy card of the reduced original chart can be made and the shy child can be taught to match the optotypes. The shy but verbal child can also whisper the answer to the parent. It also helps for the other parent or helper to point the letters out on the screen or the chart individually, but taking care not to cover the others. Covering the other letters will artificially improve the vision by eliminating the crowding phenomenon seen in amblyopia.

We often will send the parents home with the Lea symbols drawn on a piece of paper. This makes the child more compliant with vision testing in the follow up visits.

Snellen acuity is quite adequate in older children. The Tumbling E and Landolt C are again useful in illiterate children who are cooperative.

Other tests such as neutral density filters, Teller acuity may not be available to the general ophthalmologist and actually could be later added if a large number of children with amblyopia are seen and managed in the practice.

What else is needed to complete the exam?

A good cycloplegic refraction is the next important step, which helps uncover refractive errors including anisometropia as the cause. This is the time to look for media opacities like cataract. A good look at the posterior pole to rule out organic causes like optic nerve

hypoplasia that may explain the decreased vision will conclude the exam. Usually by this point you should have a good idea as to the density of the amblyopia and its cause, in most cases.

How do you manage amblyopia?

Just like many things in medicine, there is nothing carved in stone. But here are some guidelines. If you are not sure as to the presence of amblyopia, then re-examine the child and only when sure, initiate amblyopia therapy. At the outset we recommend a sound discussion with the parents. They need to understand that amblyopia treatment is a long and arduous task. It needs to be impressed on them that compliance with treatment is the single most important factor affecting outcome. They also need to know that the prognosis for vision recovery is fairly good before nine years of age.

The two important components of amblyopia treatment are

First, optical correction of the amblyopic eye to provide the best possible vision

Second, patching or penalization of the "good eye". Or in other words, by some method force the amblyopic eye to work

Optical correction of the amblyopic eye is usually in the form of spectacles. The prescription depends on other factors such as presence of strabismus. But usually whatever provides the best vision in the amblyopic eye is given as the prescription.

Sometimes in anisometropic amblyopia when there is a very high degree of anisometropia or when glasses have been tried in high hyperopia or high myopia and the vision does not improve, contact lenses may be an alternative worth trying. Many other considerations such as the ability of the parents to afford and maintain them may play a role in that decision.

There are a few situations in amblyopia treatment when simply giving glasses alone may usually suffice. Ametropic amblyopia, i.e. high myopia, high hyperopia or high astigmatism (also known as meridional amblyopia when oblique axis are involved), is one such situation.

In anisometropic amblyopia, when there is no manifest squint, you could give only glasses as a trial before deciding on further therapy.

For all other amblyopes some form of forcing the amblyopic eye to work has to be adopted. The gold standard treatment is occlusion of the "good eye" or the eye with the better vision. The next question is **HOW** and **HOW MUCH**.

First decide how severe is the amblyopia. Occlusion with a patch applied to the skin for ten or twelve hours a day is considered *full time occlusion*. Full time occlusion is the best treatment for large differences in vision. But these patients need to be followed very closely due to the risk of inducing occlusion amblyopia. The patch can be a precut one with adhesive, available by the brand name of Opticlude®. Some patients find these expensive, especially if the therapy involves many months. An inexpensive option is a sterile eye pad like the ones used in postoperative patients. This is secured with some micropore tape. Other occluders like the slip on ones for wearing over the glasses are more popular nowadays. But a word of caution about these and any form of patching. The whole point of the patching therapy is that no light should enter the "good eye". A lot of effort is needed on the parents' part to ensure no peeking around the patch is going on. We have on several occasions sent letters to teachers requesting their cooperation in this matter. We have also found it useful to demonstrate to the parent exactly how the patch is applied and on which eye. This leaves no room for confusion.

Occluding the amblyopic eye for six days and the normal eye for one day may have a role to prevent occlusion amblyopia especially in situations where follow-up is difficult.

For uncooperative children who tend to rip the patches off, some type of arm restraint

(one can use one's imagination, but a rolled up old x ray slipped around the elbow and tied with strings works like a charm!), may also help reinforce compliance.

Is there any role for frosted glasses?

The use of frosted glasses is part of methods known as optical penalization. Some others do not prescribe the hyperopic correction for the better eye, leaving it blurred, which works like a frosted glass. These are useful in mild to moderate amblyopia. It has the advantage of preserving binocularity. But the children are prone to peek on top of the glasses, which is its drawback. But with poor follow-ups it may be a safer alternative to full time occlusion provided there is parental supervision.

What about Atropine?

Otherwise known as pharmacological penalization, is useful in a limited number of patients. Again it can be used in mild to moderate amblyopia. It is useful only in hyperopia. The results of one of the arms of the Amblyopia Treatment Study revealed, in moderate amblyopia (20/40 to 20/100) in the age group of 3 to 7 years, 10 hours or more of patching seems to cause a more rapid improvement in vision than atropine or part time patching initially, but at six months there was no difference. The problem of atropine side-effects has to be kept in mind. Also in a sun drenched country like ours long term use of agents that dilate a pupil raises questions of safety for the lens and the retina. We use it selectively for those who are completely non compliant with patching or optical penalization.

How does you follow these patients?

Patients following full-time occlusion need close careful follow-ups to avoid occlusion amblyopia. A general guideline is, one week for every one year of the child's age, e.g. a one year old is followed every one week, a two year old every two weeks and so on to a maximum of four weeks. Each such period is described as an episode.

What is the endpoint for full time occlusion?

1. Less then two lines difference in vision between the two eyes
2. No improvement after three consecutive episodes with good compliance.

Several important points to remember during these follow-ups are

1. The amblyopic eye is always checked first.
2. If memorization is suspected then the vision is double checked with another chart such as the E chart.
3. Near vision is always checked to make sure the child glasses are not too hyperopic.
4. Also if the glasses were broken and remade in the interim it is better to verify them, as it is not too uncommon for prescriptions to be reversed.
5. If the child's vision should improve given the clinical situation and has not, then it is better to repeat a cycloplegic refraction and look again for organic causes such as subtle posterior lenticonus, optic nerve hypoplasia etc., which may have been missed on an earlier exam especially in a difficult child.
6. It also is often helpful in repeating the cycloplegic refraction especially in cases of high astigmatic errors to make sure that the axis of the cylinder has been appropriately detected and prescribed.

What about part-time occlusion?

As the Amblyopia Treatment Study's preliminary results have recently revealed, when the amblyopia is of mild to moderate level i.e. 20/40 to 20/80 then one can use just two hours of patching and this may all that is necessary. This should be combined with one hour of near activity.

Part-time occlusion is also used to maintain the gain after the end point of full time occlusion has been reached. This is usually done about four to six hours a day till the child is eight to nine years old. Part

time occlusion is also helpful when there are amblyogenic factors like a large anisometropia, or ptosis and can be used to prevent the development of amblyopia. Part time occlusion also has a role when the child is very young and follow-up is very difficult. After instituting part time occlusion, the child will still need close observation to make sure he or she does not *slip*. The younger the child and more severe the anisometropia and more different the acuities the closer the follow up needs to be.

Are there any drugs that can be used?

Levodopa has been tried and found to be effective in even older amblyopes, but the effect does not seem long lasting. It is likely that after a randomized clinical trial proves its benefit, it may gain widespread acceptance.

In conclusion, amblyopia and its treatment can be easily mastered with a mixture of patience and diligence. You can provide the child with lifelong good vision if you catch them in that window of opportunity before time passes by.

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Purtscher's retinopathy following childbirth

Vikas Khetan and Lingam Gopal

Purtscher's retinopathy was first described by Omar Purtscher in 1912 in five patients with visual loss following head injury[1]. Classically they were seen to be having superficial white retinal patches and retinal haemorrhages. The fluorescein angiography is known to reveal patches of capillary nonperfusion and variable degree of leakage from involved retinal vessels[1].

Case report:

A 22 yr old lady came to us with complaints of sudden diminution of vision in both eyes a day following caesarean section at 8 months of pregnancy. There was a history of moderate blood loss during the surgery. There was no history of altered sensorium. There was no preceding history of eclampsia or diabetes mellitus during the pregnancy.

On examination the best-corrected visual acuity was counting fingers ant 1 meter in both eyes. The anterior segment examination did not reveal any abnormality and the applanation tonometry revealed an intra ocular pressure of 7mm/Hg in both eyes. Fundus examination revealed normal discs and blood vessels in both eyes. There were multiple white retinal patches in the peripapillary area and the posterior pole (Fig 1). Fundus fluorescein angiography showed focal areas of hypo fluorescence in the corresponding areas (Fig 2). The patient was on tab. Prednisolone 60mgs per day when she presented to us. The same was tapered off in the course of next few days. No other specific treatment was administered. 10 days later the vision improved to 6/200. At this stage the fundus picture was unaltered. Flash VEP showed delayed latency for P1 while pattern VEP showed extinguished response for all check sizes. Two months later the vision improved to 20/40 in the right eye and to 20/80 in the left eye. At one-year follow-up the right eye vision improved further to 20/30. Fundus at this stage revealed nerve fibre layer atrophy in the peripapillary region. Visual fields with Humphrey field analyser using the 30-2 programme did not identify any field defects.

Discussion:

Purtscher's retinopathy has been classically described after trauma. The present-day understanding of the pathogenesis is one of complement activation leading to leukoemboli that cause the retinal

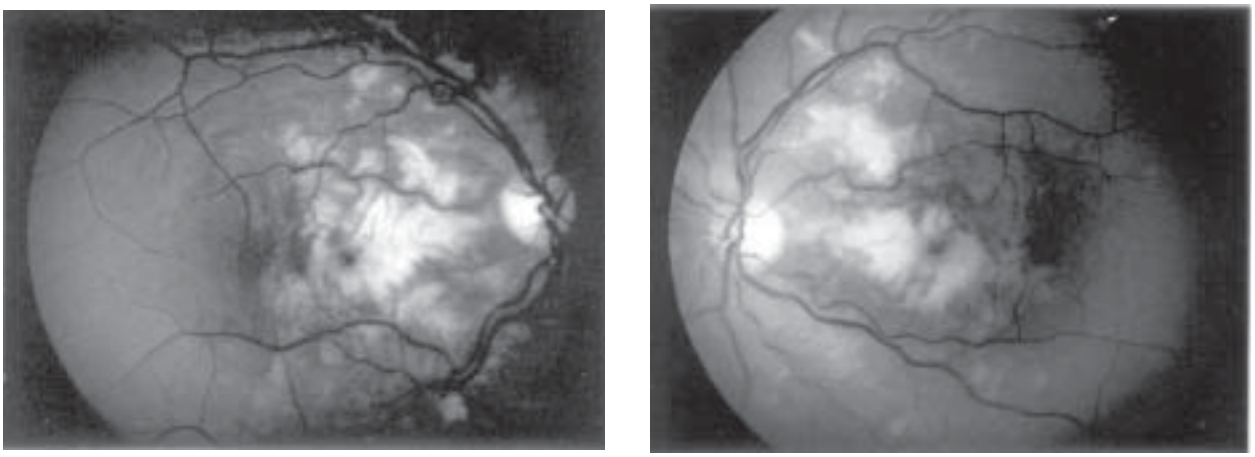

Fig 1. Fundus picture of both eyes showing multiple white patches of soft exudates in the posterior pole.

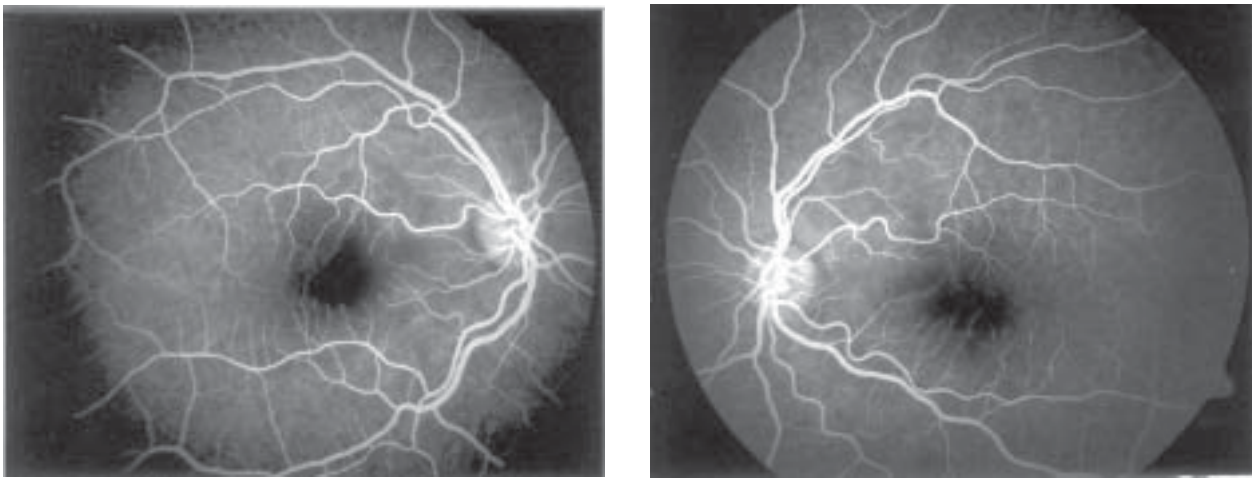

Fig 2. Fundus fluorescein angiography showing focal areas of hypofluorescence.

arteriolar infarction. Reports of the occurrence of Purtcher's retinopathy following childbirth are very rare. Table 1 lists the 4 cases of Purtscher's like retinopathy after childbirth reported by Blodi et al. One of them also had pancreatitis, which is also known to produce this fundus appearance. The others also had some additional problem such as uncontrolled hypertension. In two cases evidence of intra cranial micro embolism in the form of seizure or cerebral infarction were present. Similar fundus picture has been described after amniotic fluid embolism, but this case had several other systemic features of amniotic fluid embolism. Our case had no other attributable cause for the Purtscher's retinopathy except child delivery. The pathogenesis in this regard is hard to explain. The clinical appearance in our case and others reported, clearly point to the occlusion of arterioles of the retina. The nature of the occluding material is however conjectural. Micro embolism of amniotic fluid has been suggested but can never be proved. The visual improvement in the four cases reported by Blodi et al was variable with one patient suffering permanent damage. Our patient recovered good visual acuity but consistently complained of poor quality of vision and poor contrast sensitivity. In the absence of a better

Table. List of reported cases of Purtscher's retinopathy following childbirth

S. No.	Author and Year of Publication	Age	Obstetrical history	Weeks of gestation	Type of delivery	Additional features	HTN	Onset of Visual loss	Initial V.A	Final VA
1.	Blodi et al (1990) Case-1	29	G3P2	32	Vaginal	Pancreatitis	+	8 hrs	OD-20/30 OS-CF	OD-20/20 OS-20/60
2.	Blodi et al (1990) Case-2	24	G1P0	32	Caesarian	Pre eclampsia	+	12 hrs	OD-20/400 OS-20/400	OD-20/40 OS-20/30
3.	Blodi et al (1990) Case 3	16	G1P0	40	Vaginal With Pitocin	Post patum seizure	-	18 hrs	OD-HM OS-20/200	OD-20/40 OS-20/20
4.	Blodi et al (1990) Case 4	22	G1P0	37	Caesarian	Eclampsia, Cerebral infarct	+	6-12 hrs	OU-CF 1mtr	OD-20/30 OS-20/80
5.	Present case	22	G1P0	42	Caesarian	Uneventful	-	24 hrs	OU-CF 1mtr	OD-20/30 OS-20/80

G- Gravida; P- Para; HTN- Hypertension; V.A- Visual acuity: mtr- meter; CF- Counting fingers; HM- Hand motions

understanding of the pathogenesis of this disease, a scientific approach to the treatment or prophylaxis does not seem to be possible in the context of women developing Purtscher's retinopathy after childbirth.

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AN APPEAL

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COME, GIVE THE GIFT OF SIGHT

Unilateral frosted branch angiitis in a patient with abdominal tuberculosis

Mamta Agarwal and Jyotirmay Biswas

Tuberculosis is one of the most common systemic disease in India. Intraocular tuberculosis is however rare.[1] Various ocular lesions caused by tuberculosis includes scleritis, iritis, iridocyclitis, choroiditis, chorioretinitis, retinal vasculitis, choroidal tuberculoma, subretinal abscess and panophthalmitis. Choroiditis is the most common ocular manifestation. Retinal vasculitis is relatively rare.[2] Frosted branch angiitis is a rare vasculitis where severe sheathing of retinal vessels are seen. It has been reported in cytomegalovirus retinitis in AIDS and various other infectious entities. The diagnosis of intraocular tuberculosis is made 1) by demonstrating Mycobacterium tuberculosis from ocular fluids or tissue specimens by microbiological or histopathological study, 2) presumed ocular tuberculosis with proven active systemic disease 3) presumed ocular tuberculosis without any active systemic disease. We report a case of unilateral frosted branch angiitis in one eye and healed choroiditis in other eye in a patient with abdominal tuberculosis.

Case report

A 17 yr old girl came to emergency with complaints of sudden diminution of vision in both the eyes since morning. There were no other ocular complaints. She gave a history of chronic abdominal pain since 5 months. She also had loss of appetite associated with weight loss, since past 2 months. She was also suffering from chronic cough since 3 months. Gynaecological history revealed amenorrhoea in the last 3 months. The patient was extensively investigated elsewhere. Ultrasound abdomen showed free fluid in the cul de sac and retroperitoneum. Chest X ray and barium meal study were normal. Mantoux test was 13 mm x13mm positive. Haemoglobin was 7.7mg/dl and peripheral blood smear showed microcytic hypochromic red blood cells. Stool test for occult blood was negative. ESR was found to be 45 mm at 1st hour. The patient underwent duodenal biopsy, which showed features consistent with granulomatous colitis with areas of necrosis suggestive of tuberculosis. On examination, her vision in both eyes was counting fingers at 2 meters. Extraocular movements were full. Anterior segment evaluation with slit lamp biomicroscope was normal. There were few anterior vitreous cells in the right eye. Fundus examination in the right eye showed disc odema, dilated tortuous vessels with perivascular sheathing and macular odema. There were scattered areas of superficial and deep retinal hemorrhages. (Fig 1) The left eye showed areas of healed choroiditis in the posterior pole and along the superior temporal arcade. (Fig 2) The patient underwent gastrointestinal endoscopy which showed ulcers in the ascending colon and was diagnosed as tubercular colitis. Laboratory investigations revealed RA and antinuclear antibody to be negative. But C reactive protein and serum angiotensin converting enzyme was raised i.e 24 mg/l and 37.0 units. Hematological work up was with in normal limits. A diagnosis of retinal vasculitis secondary to tuberculosis was made and she was started with antitubercular therapy (Tab. isoniazid 300mg, tab rifampicin 600mg, tab ethambutol 800mg and tab pyrazinamide 1000mg) along with low dose oral steroids in the tapering doses. She was monitored every month and after 6 months of treatment, fundus examination in the right eye showed resolution of retinal vasculitis.(Fig 3) At the last follow up, her best corrected visual acuity in both the eyes was 6/36.

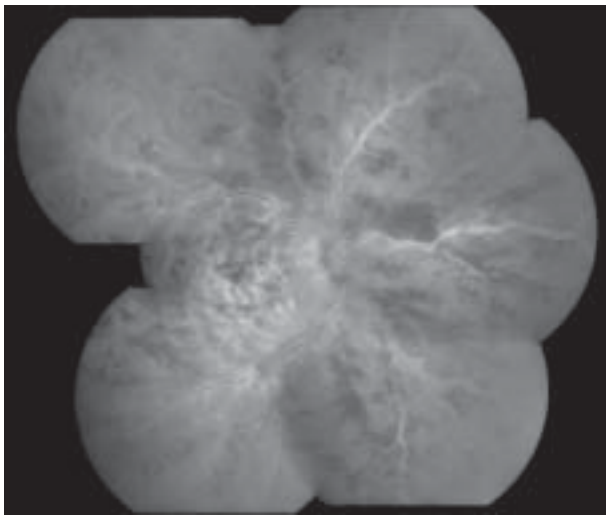

Fig 1.Montage fundus photograph of the right eye showing frosted branch angiitis, disc odema and scattered retinal hemorrhages.

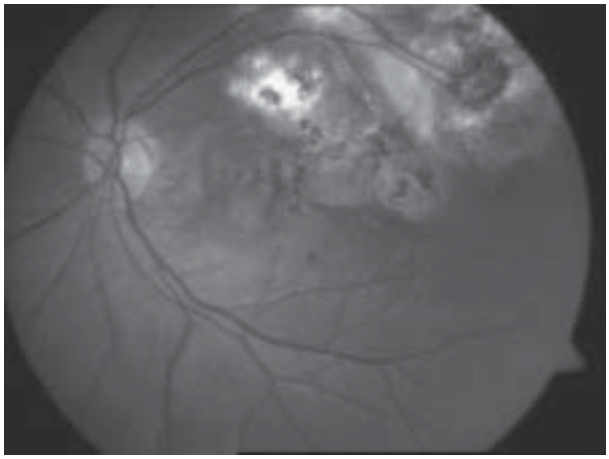

Fig 2. Fundus photograph of the left eye showing areas of healed choroiditis

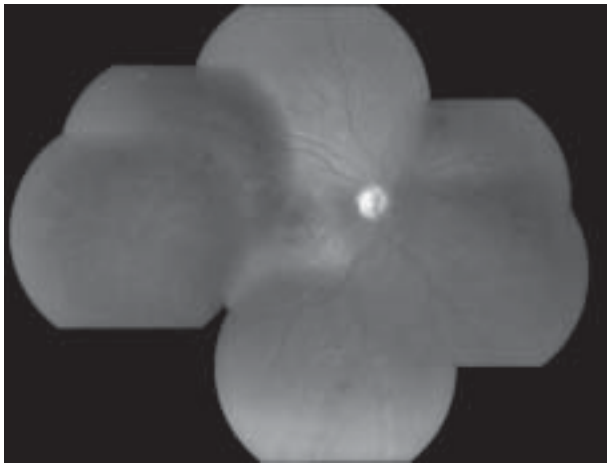

Fig 3. Montage fundus photograph of the right eye showing resolution of vasculitis after 6 months of antitubercular treatment

Discussion

Frosted branch angiitis is described when retinal vascular sheathing is so extensive that the underlying vessels are obscured. The condition has been described in cytomegalovirus retinitis, herpes simplex virus infection, rubella[3] and even neoplastic diseases. There are several reports of retinal vasculitis due to tuberculosis. Gupta and co workers described 13 patients of retinal vasculitis.[4] In all patients, polymerase chain reaction of intraocular fluid (aqueous and vitreous) was positive for Mycobacterium tuberculosis. Rosen and coworkers described in a series of twelve patients with intraocular tuberculosis, 9 of them had florid ischaemic retinal vasculitis.[5] Hoh et al reported a case of bilateral retinal periphlebitis which responded promptly to 2 months of antitubercular treatment.[6] Eales disease is another form of retinal vasculitis predominantly affecting the peripheral retina of young and otherwise healthy adults between 15 - 40 years. Recently in a study by us, Mycobacterium tuberculosis DNA has been demonstrated by nested polymerase chain reaction supporting the association of Mycobacterium tuberculosis in this disease.[7]

Our case is the first report of frosted branch angiitis due to tuberculosis. The evidence favouring tubercular aetiology in this case is associated abdominal tuberculosis and positive Mantoux test. In addition the patient had healed choroiditis in other eye suggestive of tuberculosis. The vasculitis in this patient responded to a course of antitubercular treatment with low dose of systemic steroids. Differential diagnosis in our case was collagen vascular disease, sarcoidosis and hematological disorder. Rheumatoid arthritis factor and antinuclear antibody were negative. Although serum angiotensin converting enzyme was elevated (37.0 units), there was no other evidence suggestive of sarcoidosis. Hematological work up was with in normal limits. Anti tubercular therapy in a patient of suspected tubercular retinal vasculitis should be four drug regimen which includes isoniazid 5mg/kg/day, rifampicin 450 mg daily if body

weight is less than 50 kg and 600 mg /day if body weight is more than 50 kg, ethambutol 15mg/kg/day for first 4 months followed by rifampicin and isoniazid for 9-14 months. Our report indicates that frosted branch angiitis can be a rare manifestation of intraocular tuberculosis. Prompt treatment with antitubercular therapy can preserve vision in such cases.

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Conjunctival Siderosis

Geetha K Iyer and Rajesh Fogla

A variety of foreign bodies both metallic and non-metallic can be retained on the ocular surface. The tissue response to these foreign bodies depends mainly on their chemical composition. Metal and stone fragments are more common in the industrial setting, whereas seeds, thorns, and insect fragments are more common in agricultural surroundings.[1] Conjunctival granulomas have been reported to occur with retained synthetic and non-synthetic fibers in the fornices.[2,3] Conjunctival siderosis is a rare condition that occurs secondary to retained iron particles or preparations.[1,4]

We report the occurrence of conjunctival siderosis with pyogenic granuloma formation following accidental instillation of an iron containing preparation into the conjunctival fornix.

Case report

A 5-year-old male child presented to the outpatient department with complaints of a reddish mass lesion in the left eye since last two months. His parents informed that an accidental instillation of an iron and folic acid combination medication (Fesovit, SmithKline - ferrous sulphate 150mg, folic acid 1mg, nicotinamide 50mg, vitamin B-6 2mg, and vitamin B-12 15mg) into the left eye had occurred four months back. This happened when the parents were away and the children were playing doctor patient game at home. The older sister acted as the doctor and instilled the iron tablet into the left eye of this patient. This was retained in the upper fornix for almost three hours till the parents returned back home. The medication was finally removed from the eye by the local ophthalmologist under general anaesthesia. At review two months later, he was noted to have developed symblepharon involving the superior fornix medially in the left eye. Surgical release of the symblepharon was performed by the local ophthalmologist. Subsequent to this he presented to us two months later with a progressively increasing reddish mass lesion in the left eye. On examination his best corrected visual acuity was 6/6 in the right eye and 6/9 in the left eye. A fleshy, pendunculated, reddish-brown mass lesion measuring 6 - 7mm in diameter was noted at the 9'o clock nasal limbus. (Fig 1) The lesion was also associated with loss of limbal palisades of Vogt, besides symblepharon extending into the superior and inferior fornices. The adjacent conjunctiva revealed presence of brownish pigmentation. Rest of the ocular examination was normal and did not reveal any features suggestive intraocular siderosis. The right eye did not reveal any abnormality. Extra ocular motility testing revealed restricted abduction in the affected eye. A clinical diagnosis of conjunctival pyogenic granuloma was made. Surgical excision of the conjunctival mass was performed along with release of symblepharon, followed by conjunctival autografting from the unaffected fellow eye. The conjunctival graft measured 10mm x 8 mm.

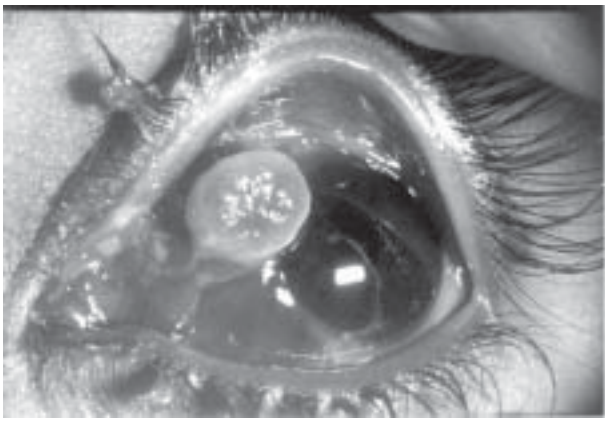

Fig 1. Slit lamp photograph of the left eye showing the reddish brown mass lesion at the limbus in the left eye.

Histopathological examination of the excised mass revealed features consistent with

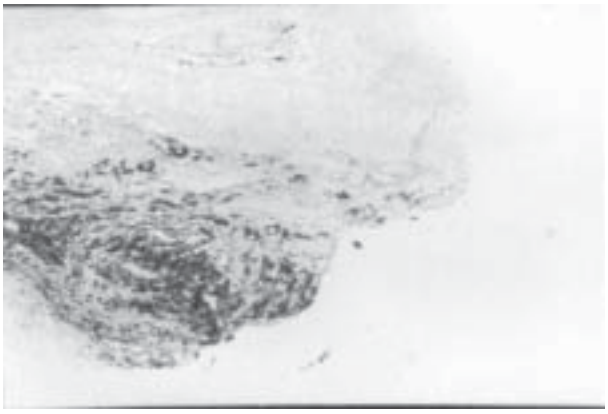

Fig 2. Histopathology of the mass lesion showing positive stain for iron (Perls' stain, original magnification x 100)

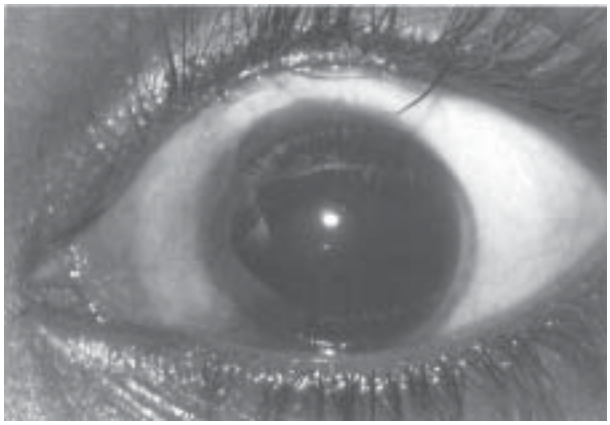

Fig 3. Slit lamp photograph of the left eye showing a healthy conjunctival graft with diffuse brownish pigmentation

diagnosis of pyogenic granuloma along with secondary dilatation of blood vessels. Special staining for iron (Perls' stain) was positive, indicating possibly conjunctival siderosis. (Fig 2)

Four months later he was asymptomatic, and examination of the left eye revealed a healthy conjunctival graft with diffuse brownish pigmentation and no restriction of ocular movements. (Fig 3)

Discussion

Conjunctival siderosis was first described by Reich in 1881, in a soldier who suffered a self inflicted injury with iron sulphate.[1] Salmien et al reported epibular siderosis in a 5-year-old boy, induced by iron containing tablets.[4] Our case also had findings similar to their patient. Foreign bodies are often swept up by the upper lid in the violent movements of blinking, excited by its impact on the ocular surface. These then progressively move upward and reside in the recesses of the upper fornix.[1] The bivalent iron (ferrous) is more toxic to the ocular tissues than the trivalent iron (ferric).[5] Siderosis is the deposition of iron ion as ferritin or cytoplasmic siderosomes in many tissues throughout the eye. Toxicity is mainly caused by interference of excess intracellular free iron with some essential enzyme process leading to various changes throughout the eye.

In the earlier report on epibulbar siderosis[4], the initial reaction to the iron tablet was characterized by inflammation and necrosis of the involved conjunctiva, and corneal de-epithelialization with dark brown discoloration of the stromal layers. It is possible that our patient also had similar clinical features initially following the injury. This represents a form of chemical injury which leads to tissue destruction and may involve the limbal stem cell population if situated close to the limbus. Due to diffusion of the iron ions, continued tissue damage may occur especially if the foreign body is retained for a longer duration. The pyogenic granuloma in our case could have been the result of initial surgical intervention. Positive stain for iron in the excised conjunctival tissue, and post operative brownish discoloration of the conjunctival graft harvested from the unaffected fellow eye, both support the clinical diagnosis of conjunctival siderosis.

Due the presence of extensive symblepharon, restricted ocular movements, and associated conjunctival damage, a conjunctival autograft was performed from the unaffected fellow eye to restore the ocular surface in our case.

In conclusion, iron containing preparations commonly used for treatment of anemia, if accidentally instilled into the eye can result in tissue damage and conjunctival

siderosis. These preparations should be kept out of reach of children at home. Conjunctival autografting may be required if there is extensive conjunctival damage and symblepharon formation.

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Comparison of Conventional Refractive Technique and Automated Refractor (Topcon Rm-A 7000) in Pseudophakic Eyes

Ramesh S Ve, Deepa B M S, Manish J Shelat, Kumari B, Ramya S, Pradeep G Paul, Sripriya Krishnamoorthy and Smita Praveen

Autorefractors have become common place in ophthalmic examination in the recent times. The popularity stems from, that they can be operated by relatively less trained technicians, leaving the professional clinician time to deal with more specialized examination techniques. The main draw back of these autorefractor machines is that they are less able to detect patient reliability as compared to refraction done by a clinician.

Theoretically an individual who had intraocular lens implantation following cataract extraction should be an ideal patient when it comes to comparing Autorefractors[1,2] ,since pseudophakic eyes have very less or no accommodation. In normal patients, with active human lens, proximal accommodation to the targets projected inside a autorefratometer can produce erroneous readings[3], thus in pseudophakic eyes the readings that are obtained can be trusted to be the actual refractive error of the patient. But in reality, the noise caused by the intraocular lens interferes with the reading of the autorefractor. Most manufacturers compensate for this by providing an "intraocular lens setting" algorithmn in their machines. These machines are advertised to be as accurate as conventional refraction when it comes to pseudophakic individuals and a possible alternative to the conventional refracting techniques in phakic and aphakic individuals too[4,5]. So to determine Topcon RM-A 7000[7] (Topcon Co-corporation, Tokyo, Japan) autorefractor's efficiency and accuracy in a clinical situation, comparison was made between conventional refractive technique and automated refractor.

Previous studies have shown that the Canon Model RK – 1 autorefractor provides reasonably accurate postoperative refraction for patients who have undergone posterior and anterior chamber intra-ocular lens implantation following extra-capsular extraction[1,2]. While the Nikon autorefractor NR1000F tended to overestimate myopia (or under estimate hyperopia) in younger patients, it gave reasonably accurate reading in patients above the age of 40 as well as aphakic individuals and individuals with mixed astigmatism. Cylinder axis was found to be accurate in all cases[3]. The refraction reading obtained by using model 6600 showed a high degree of accuracy in determining the refractive error, but the errors were sufficient enough to perform subjective refinement before prescribing[4].

Previous studies have indicated that the IOL setting algorithm holds true for some devices[1,3,4]. As different machines use different algorithm, we were interested to ascertain the level of agreement between the Topcon Model RM-A 7000 and conventional refraction in an effort to simplify the Outpatient procedure regarding the refraction of pseudophakic patients in a tertiary eye care center.

MATERIALS AND METHODS

Objective retinoscopy was performed using streak retinoscope (Beta 200, Heine, Germany), Retinoscopy is based on Foucault's principle, where the patient's refractive error is obtained by coinciding the subject's farpoint with the examiners nodal point. The Topcon RM-A 7000[7] (Topcon Co-corporation, Tokyo, Japan) uses infra red light to obtain patients

refractive error. It measures spherical refractive errors from –25.00diopter to +22.0 diopter in 0.25 diopter steps. For cylindrical power it is capable of measuring refractive errors from –7.00 diopter to +7.00 diopter in 0.25 diopter steps and axis from 1º to 180º in one-degree steps.

The study was carried out at a tertiary eye care center from November 2002 to January 2003. All subjects enrolled for the study had undergone extra-capsular cataract extraction with posterior chamber intraocular lens implantation. Criteria for inclusion were best-corrected visual acuity of 6/12 and no posterior capsular opacification. Post suture removal subjects were excluded. All subjects who fulfilled the inclusion criteria underwent refraction in the 6th postoperative week, which followed conventional techniques like objective retinoscopy following by subjective refinement. Retinoscopy was conducted at a working distance of 66 cm using streak retinoscope (Beta 200, Heine, Germany). This was followed by full subjective refraction- spherical fogging and refinement of cylinder using a Jackson's Cross Cylinder.

All these procedures were conducted in the same room, with a constant illumination to reduce any bias. The conventional refraction technique was conducted by only one of the authors. Subsequently every subject underwent automated refraction using the Topcon Model RM-A 7000. These readings were taken by one of the authors. Three readings were taken using the autorefractor, the final reading being the average of the three. Only the magnitude of cylindrical error was taken for analysis and the axis was not included in analysis. All measurements were grouped into three groups for separate analysis.

Group A: Measurements of Objective refraction (OR) and the readings from the Autorefractors (AR) were compared.

Group B: Measurement of Objective refraction and Subjective acceptance (SA) were compared.

Group C: Measurements of subjective Refraction and the readings from the Autorefractors were compared.

Analysis of the data was carried out using the Altman-Bland method[6] to ascertain the limits of agreement, correlation coefficient and coefficient of variation.

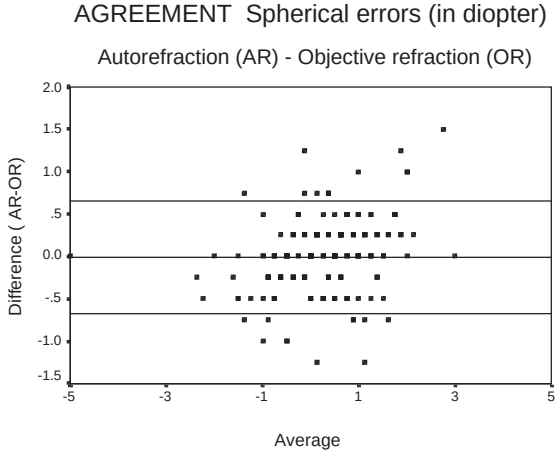
RESULTS AND ANALYSIS

A total of 161 subjects (216 eyes), with mean age of 58.54 ± 9.3 years passed our inclusion criteria.

GROUP A

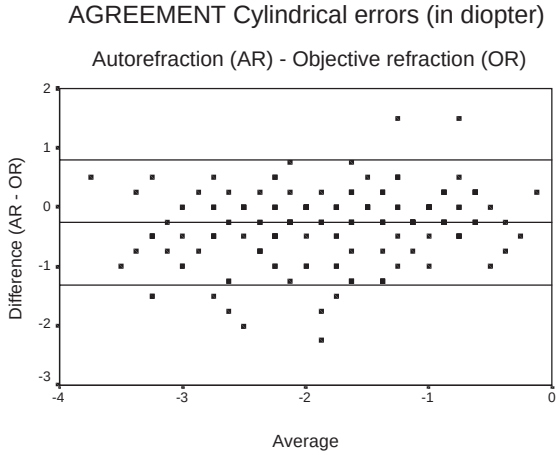
Sphere: the mean difference between OR and AR was –0.01 ±0.42 diopter. The 95% limits of agreement were 0.66 diopter and -0.68 diopter. There was significant positive correlation between OR and AR (r=0.92, p=0.01) and the 95 % CI was 0.04 diopter and –0.07 diopter. The coefficient of variation of OR and AR were 337.7 and 336.2 respectively. (Graph 1)

GRAPH 1



Cylindrical correction: The mean difference between OR and AR was -0.26 ±0.54 diopter. The 95% limits of agreement were 0.8 diopter and -1.32 diopter. There was significant positive correlation of the cylindrical errors between OR and AR (r=0.79, p=0.01) and the 95 % CI was 0.19 diopter and 0.34 diopter. The coefficient of variation of OR and AR were 47.63 and 47 respectively. (Graph 2)

GRAPH 1



GROUP B

Sphere: the mean difference between OR and SA was 0.08 ±0.24 diopter. The 95% limits of agreement could were 0.55 diopter and –0.39 diopter. There was significant positive correlation of the cylindrical errors between OR and SA (r=0.97, p=0.01) and the 95 % CI was 0.05 diopter and 0.11 diopter. The coefficient of variation of OR and SA were 337.7 and 444.43 respectively.

Cylindrical correction: The mean difference between OR and SA was –0.15±0.30 diopter. The 95% limits of agreement were 0.44 diopter and -0.74 diopter. There was significant positive correlation of the cylindrical errors between OR and SA (r=0.92,0.01) and the 95 % CI was –0.19 diopter and -0.11 diopter. The coefficient of variation of OR and SA were 47.63 and 52.73 respectively.

GROUP C

Sphere: the mean difference between AR and SA was –0.09± 0.44 diopter. The 95% limits of agreement were 0.77 diopter and –0.95 diopter. There was significant positive correlation of the cylindrical errors between AR and SA (r=0.91, p=0.01) and the 95 % CI was -0.15 diopter and -0.04 diopter. The coefficient of variation of AR and SA were 336.28 and 444.43 respectively.

Cylindrical correction: The mean difference between AR and SA was 0.42±0.55 diopter. The 95% limits of agreement were 1.5D diopter and -0.65 diopter. There was significant positive correlation of the cylindrical errors between AR and SA (r=0.78, p=0.01) and the 95 % CI was 0.34 diopter and 0.49 diopter. The coefficient of variation of AR and SA were 47 and 52.73 respectively.

DISCUSSION

All three groups showed correlation between the two techniques. However, as one would expect good correlation between techniques that measure the same parameter, the Altman and Bland technique of assessing agreement is more appropriate. Using this technique there was a clinically acceptable level of agreement between the autorefractor readings as well as conventional refraction when it comes to spherical errors. The magnitude of difference in spherical measurement could range between 0.55 diopter to -0.39 diopter in Group B to 0.77 diopter to -0.95 diopter in Group C.

But when it comes to cylindrical error, the large limits of agreements for Groups A (0.8 diopter to -1.32 diopter) and C (1.5 diopter to -0.65 diopter) is probably not clinically acceptable and has moderate correlation in Group A(r=0.79) and C(r=0.78). Group B (0.44 diopter to -0.74 diopter) on the other hand shows a strong correlation (r=0.92) with an acceptable level of agreement. Thus the conventional technique of OR and SA shows good agreement but the cylindrical measurements obtained with AR did not show good agreement when compared with OR and SA. Both the spherical and cylindrical errors in Group B show good agreement as expected because objective refraction was the starting point for subjective acceptance.

Depending on the clinical situation, the clinician could consider replacing conventional retinoscopy with the Topcon Model RM-A 7000 Autorefractor, thus enjoying the speed that comes with use of an autorefractor, keeping in mind that in case of cylindrical error it is advisable to follow the current philosophy of conducting retinoscopy followed by subjective refraction, as these two readings (Group B) show an acceptable agreement.

The decision on prescribing spectacle lens would depend on the clinical situation. In this study the auto refraction data in pseudophakes were all acceptably accurate especially as far as objective refraction was considered. If this level of agreement is acceptable and the clinician conducts a full subjective refinement following autorefraction it is possible to achieve the optimum correction as required by the patient as well as saving time by conducting autorefraction instead of manual objective retinoscopy.

Overall, the Topcon Model RM-A 7000 autorefractor is capable of replacing manual retinoscopy as long a proper subjective refraction is conducted as well. In conclusion this autorefractor is capable of providing a reasonably accurate starting point for subjective refraction.

CONCLUSION

There was good agreement in the spherical correction between both the conventional refractive techniques (objective refraction and subjective acceptance) and autorefraction. The spherical correction between objective refraction and subjective acceptance shows good agreement. But only a reasonable agreement was seen in the cylindrical correction between both the conventional refractive techniques and AR. The Topcon Model RM-A 7000 autorefractor can replace manual retinoscopy as long as a proper subjective refraction is conducted as well.

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"MUCH ADO ABOUT NOTHING?"

ANAESTHESIOLOGIST'S INSISTENCE ON PREOPERATIVE FASTING

Ian Sundararaj

Starvation, refusing to eat, hunger strikes are not new to us. Each one is observed with a specific motive, be it to save our environment or press demands for better working conditions!

At home the sulking grandchild or grandfather refusing to eat is not uncommon!

Fasting for religious purposes is observed by many.

But when fasting is advised before anesthesia and surgery **why** is the "nil per oral"schedule not strictly observed? This is the plaint of the anaesthesiologist!!

A crying baby or an adamant boy may eat during the recommended fasting period inspite of parent's objection. An elderly patient whose surgery is postponed, waiting anxiously, hungry, may be irritable and may want to eat or drink.

So why so much fuss about preoperative starvation?

General anaesthesia produces loss of consciousness, muscle relaxation and analgesia. The physiology of bodily functions are altered. Any ingested food or drink partially digested may be regurgitated, vomited or aspirated at the time of induction of anaesthesia, at the conclusion or when the patient recovers. Aspirated particulate matter can block the respiratory passages resulting in respiratory distress. Aspiration pneumonia or a chemical pneumonitis can occur if gastric pH is 2.5 or less. This can sometimes prove fatal.[1]

To prevent pulmonary aspiration during general anaesthesia the traditional practice of NPO (nulla per os) or nothing by mouth after midnight, prior to elective surgery was followed by anaesthesiologists and surgeons throughout the world.

In recent years several studies have been conducted regarding gastric volume and pH of gastric secretions and the consequences of pulmonary aspiration in order to formulate acceptable fasting guidelines. As a result of these studies fasting guidelines have been re-formulated in many centers throughout the world.

NPO after midnight is applied only to solids. Clear fluids are now allowed until 3 hours before the scheduled time of surgery or 2 hours before the actual time of surgery. This allows for any change in surgery timing and still allows for the 2 hour fasting regime..

Clear fluids include apple juice, water, carbonated water, tea or coffee without milk. Milk is considered as a solid which takes 3-4 hours to empty from the stomach.

Children may be allowed to have clear fluids upto 2 hours before surgery to avoid hypoglycaemia and dehydration. This is especially important in children with

American Society of Anaesthesiologists Fasting Guidelines (1999)

Ingested material	Minimum fasting (hrs)
Clear fluids (water, fruit juice without pulp, tea, coffee without milk)	2
Breast milk	4
Infant formula	6
Non human milk	6
Light meal (dry toast & clear fluid)	6
Solid food (fried & fatty food)	8

homocysteinuria when thrombosis can occur if dehydration is present.

When a patient does eat solid food, the *quantity* and *time* of ingestion should be noted.

An early breakfast with clear liquids is permissible for cases scheduled in the afternoon.

In 1999, the American Society of Anaesthesiologists formulated certain guidelines for preoperative fasting.[2]

Anaesthesiologists insist on strict adherence to fasting guidelines to enhance the quality and efficiency of anaesthetic care and to reduce the morbidity and mortality associated with anaesthetic complications such as vomiting and pulmonary aspiration of gastric contents, should they occur.

The change from the traditional NPO from midnight for both solids and liquids to NPO from midnight for solids only, allowing liquids until two hours before the actual time of surgery has increased patient satisfaction, decreased incidence of complications of undue starvation such as dehydration or hypoglycaemia and minimized preoperative morbidity.

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Development genes and eye

Sarangapani Sripriya and Govindaswamy Kumaramanickavel

The development process of eye is controlled through a network of regulatory genes that are conserved throughout evolution. Studies on drosophila models and mouse models have led to the identification of vertebrate homologue for the developmental genes. The vertebrate eye comprises tissues from different embryonic origins. Most of the regulatory genes are expressed throughout the eye compartments during the early stage of eye development.[1] Later, the expression of the genes are regulated according to tissue specification. The identification of different developmental genes of the eye is based on the drosophila and mouse models. In the fruit fly, cluster of genes with similar domain (helix loop helix domain) that are required for the development of the different organs are identified. These genes encoding homeodomain proteins are also found to interact during the eye development process. Based on this, vertebrate homologue to these proteins are then identified to understand the molecular regulation during eye development. The vital regulatory genes that are identified in the fruit fly and the vertebrate homologue to the same are discussed.

***Pax* genes**: *Pax-6* is a member of the paired box gene class and encodes a transcription factor containing a paired domain and a homeodomain and act as the master controller of eye morphogenesis.[1] Pax *6* regulates eye development process by activating/repression of downstream targets. The gene is expressed in head ectoderm and in optic vesicle during the early stages of morphogenesis and later restricted to the lens placode, vesicle and optic vesicle. In retina, *Pax-6* regulates the proliferation of retinal progenitor cells. [2] Homologue for the vertebrate *Pax 6* genes are the eyeless (*ey*) , twin of eyeless (*toy*) in Drosophila and small eye (*sey*) gene in mouse.[1] In human, *Pax6* gene mutations have been found to result in many developmental eye diseases. Haploinsufficeincy of *Pax6* gene results in aniridia, foveal hyperplasia, accompanied by cataract, corneal opacificaiton and progressive glaucoma while homozygous mutations result in anophthalmos, nasal hypoplasia and central nervous system defects.[3] In mouse mutation in the *sey* gene results in small eye with characteristics similar to that in aniridia.[4] This similarity suggests that human and mouse *Pax6* genes function in a similar way to regulate eye development. In Xenopus, ectopic induction of the Pax6 gene results in formation of ectopic retinal and lentoid structures.[1] This suggests that Pax6 gene also plays an important role in the development of both retina and the lens. Loss of functional mutation seen in the *Pax6* gene in association with the disease explains the function of the disease. *Pax2* gene is another member of the *Pax* family that is involved in patterning the optic stalk during development. Mutations in *Pax2* gene in human and mouse are found to result in kidney and ear defects.[5]

***Six* family genes:** *Six* family of genes are homologue to the sine oculis (*so*) homeobox gene of drosophila. This gene regulates the initial events of eye disc formation and also the optic lobe and is also expressed in the anterior neural plate. The gene is expressed even in the non-ocular tissues.[1] In drosophila three genes are present in the *six* family: *so*, *Optix* and *Dsix4*. In mouse six homologues are identified. Many of these are expressed in the retina. Another member of the six family called the *Optx2* gene (six6 and six9) identified in mouse is found to express the lens placode and optic vesicle. In human being, 6 *six* genes, are identified : (1). *SIX3* and *SIX6* gene orthologous to *Optix*, (2) *SIX1* and *SIX2* genes orthologous to sine oculis and *SIX4* and *SIX5* gene closely related to

DSix4.[6] In human mutations in the *Six3* gene leads to holoprosencephaly and microphthalmia.[7] Human chromosomal deletions of the *Optx2* containing region is found to result in bilateral anophthalmia.[1] The misexpression of this gene in Xenopus eyes induces expression of neural retina-specific markers and increases the proliferation of the retinal cells.[1]

Eya (Eye absent genes): Eye absent genes (*eya*) encodes a member of a network of nuclear transcription factors that promotes eye development in both vertebrates and invertebrates. The mouse homologue of the *eya* gene are expressed in lens placode.[1] The *eya* protein is found to regulate transcription by binding to other DNA binding proteins. .Even though the role of *eya* gene is unclear, human mutations in eya genes results in cataracts and anterior segment defects. Recent studies have demonstrated that *eya* gene triggers programmed cell death at inappropriate levels.[8]

Daschand (Dach1 and 2): In drosophila, misexpression of the *Dach 1* and *2* genes induces ectopic eye formation. Two homologues to fly *Dach1* and *2* genes are identified in mouse which are related to the ski and Sno genes that negatively regulate the TGFb signal transduction. In mammals, these genes are suggested to have a possible function in retinal development.[1]

BMP (Bone morphogenetic protein): These are a large family of proteins with more than 20 proteins of the TGFb superfamily. The functions of these proteins are regulated according to the gene dosage. Bmp2 and Bmp4 genes of this family are closely related to the Drosophila dcapentaplegic. . The Bmp4 gene is expressed in multiple tissues during embryonic development including the heart, lung, kidney, brain and eye. Decreased functional dosage of the Bmp4 genes are found to contribute to anterior segment dysgenesis and elevated intra ocular pressure.[9,10] Bmp7, another member of this family is found to regulate the lens palcode formation along with PAX6 gene.

***Otx* and *Crx* gene genes:** These family of genes in vertebrates share homology with the drosophila orthodenticle gene.[1] These genes are members of transcription factor that are necessary for head and photoreceptor development in the fly. Recent studies have suggested that *Otx* genes are required for tissue specification. The gene is expressed in different stages of eye development. Heterozygous and homozygous mutant for *Otx* gene are found to have ocular malformations including, lens, pigment epithelium, neural retina and optic stalk defects.[11] Mutations in the human Otx1/2 genes are not yet reported but mutations in CRX genes are shown to be associated with cone-rod dystrophy[12] and retinitis pigmentosa and Lebers congenital amaurosis.[13]

REIG/PITX family: PITX2 and PITX3 are the two human homologues to the mouse PITX/REIG family. The members of this family are found to be mutated in developmental disorders of the eye. PITX2 is transcription factor located in the human chromosomal loci 10q25. This gene encodes for transcription factor, which is expressed throughout eye ontogeny and also left-right axis determination. In human, this gene is mutated in Rieger syndrome, a haploinsufficiency disorder affecting eyes and teeth. Pitx2 also has a postulated role in left-right axis determination. Heterozygotes for either allele have eye abnormalities consistent with Rieger syndrome. Analysis of mutations in this gene are associated with distortion in right left symmetry of the abdominal organs.[14] Homozygotes are found to exhibit septal and valve defects, and null homozygotes are found to have a single atrium proving that a threshold level of Pitx2 is required for normal heart development. Null homozygotes exhibit arrest of pituitary gland development at the committed Rathke pouch stage and eye defects including optic nerve coloboma and absence of ocular muscles. Another gene of this PITX family, the PITX3 is also found to be expressed in lens. The rat homologue to this gene is Ptx3. Mutations in this gene is recently reported in Rieger syndrome, Axenfeld-Rieger

anomaly, glaucoma, various anterior chamber anomalies, anterior segment mesenchymal dysgenesis (ASMD) and congenital cataracts.[15]

Foxc1and 2 (Mf1 and Mf2): These are the forkhead transcription factor genes that are expressed in the mesenchyme from where the ocular drainage system is derived.. The human homolgoue for Foxc genes are the FKHL7 (Foxc1) and FKHL14 (Foxc2) genes.[16] Mutant mouse model for Foxc genes are found to have anterior segment abnormalities. Similar abnormalities are found associated with FKHL7 mutations in patients with anterior segment abnormalities as in Axenfeld-Reiger syndrome.[16] Mouse embryos homozygous for null mutations in Mf1 show severely abnormal development of the anterior segment. The cornea fails to separate from the lens, resulting in the complete absence of the anterior chamber.

Other homologues to the Drosophila eye genes: Several other developmental genes in droshophila are identified for which the vertebrate homologues are also identified. These are the Prox1 gene which is responsible for lens fiber elongation. The human homologue to the Drosophila crumbs gene are found to be mutated in retinitis pigmentosa.[1] The Rx/Rax homeobox gene (retina and neural fold homeobox) required for the optic vesicle and neural patterning in mice is expressed in the eye primordia regulates the proliferation of the cells that forms the retina.[17] Over expression of this gene is found to induce ectopic retinal tissue formation.

Regulation of eye development is through a complex cascade of the above mentioned developmental homeobox genes. In drosophila , the epistatic interaction of the *ey* , *toy* with the *so*, *eya* and *dac* genes controls the eye development process. Pax6 mediated genetic cascade act as the master regulator of eye development.[1] *Six3* expression is found to be specifically reduced in lenses of Pax6 heterozygous mouse embryos. Both the transcription factors *(Six3* and *Pax6)*[18] bind regulatory sequences from the counterpart gene and mutually activate their expression. *SOX 2* is yet another protein with which the Pax6 transition factor binds to form a complex. This complex binds to the enhancer element of crystalline during the lens development.[19] Thus it is demonstrated that Pax6 is the master regulator of the eye development.

To summarize, the developmental genes of the eye determines the fate of the embryonic tissues during eye development by forming a complex network system. Table 1 summarizes

Table1:
Vital development genes of eye, their site of expression and associated diseases

Developmental genes	Expression in the eye	Disease in human
CRB1	Retina	Retinitis pigmentosa (RP)
Crx	Neural Retina	Cone-rod dystrophy, RP, Lebers congenital amaurosis
Pax6	Lens placode, optic vesicle	Aniridia
Pax2	Optic stalk	Optic nerve coloboma
Bmp4	Optic vesicle	Anterior segment dysgenesis
Bmp7	Optic vesicle	
Eya1	Perioptic mesenchyme	Cataract, anterior defects
Six3	Lens palcode, optic vesicle	Holoprosencephaly, microphthalmia
Pitx/REIG family	Lens, anterior segment	Reigers' syndrome
FKHL-7	Mesenchyme (drainage system)	Anterior segment dysgenesis
Optx2	Optic vesicle	Anoptholmos

the different genes involved in eye development and the disease associated with them. Understanding the roles of these genes will thus help to probe in the different ocular abnormalities which will further help to manage the disease effectively.

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(contd. from page 74)

chemotherapy is currently the preferred primary modality of treatment in retinoblastoma, brachytherapy would still be a viable option in unilateral solitary retinoblastomas, tumors that do not show adequate response to chemoreduction and those resistant tumors which have not responded to chemoreduction or external beam radiotherapy.

The limitation to I-125 brachytherapy in India was the short half life of the isotope which until recently had to be imported. Currently, BRIT (Board of Radiation Isotope Technology), isotope arm of BARC, Bombay, has been able to manufacture the seeds indigenously which has made I-125 brachytherapy possible in India. We have recently begun the clinical trial of these seeds at Sankara Nethralaya.

Tumors that can be treated with I-125 Brachytherapy

1. Malignant melanoma of the choroid 2.5 - 10 mm thick / <16 mm in diameter
2. Retinoblastoma
   a. Post chemoreduction residue that is too large for local resection
   b. Post chemoreduction / EBRT persistent, recurrent tumor that is too large for local treatment
   c. Primary brachytherapy in unilateral unifocal retinoblastoma in an eye with visual potential
3. Solitary choroidal Hemangioma with secondary retinal detachment precluding laser photocoagulation
4. Selected solitary or one quadrant von Hippel Lindau retinal angiomatosis

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I-125 Brachytherapy

Mahesh P Shanmugam

Brachytherapy is the process of delivering radiation as precisely as possible to the tumor, the main advantage being the limited exposure of normal surrounding tissue to radiation. This form of treatment is particularly attractive for treating intraocular tumors such as retinoblastoma and malignant melanoma. Growing children with retinoblastoma are particularly susceptible to the adverse effects of external beam radiation therapy such as impaired growth of the orbital bones, delayed dentition etc., By limiting the area of irradiation by taking the radioactive source close to the eye as in brachytherapy, unnecessary radiation to the periocular structures can be avoided. Melanomas are not particularly radio sensitive and need large dose of radiation to achieve regression. Delivering large doses precisely to the tumor by external beam radiation machines is not possible without delivering inadvertent radiation to the adjacent structures. This is however possible with particle beam therapy machines which are available in very few centers in the world. Brachytherapy hence has become the widely used treatment option for intraocular melanoma.

Various radioisotopes such as Cobalt 60, Iridium, Ruthenium105 and Iodine 125 / 131 have all been used to treat intraocular tumors, but Iodine 125 is most widely used isotope and has come to be accepted as safe and effective.

Iodine-125 has the advantage of good depth penetration, which makes it suitable to treat tumors up to 10 mm in height. This isotope can be easily shielded with a thin plate of gold, unlike the cobalt plaque which enhances its safety. The low radioactivity also limits its depth penetration thereby avoids damage to the periocular structures. Iodine - 125 is available in the form of seeds. The seeds are glued on to a gold carrier, which is then sutured on to the sclera for a specified period of time to deliver the required dose of radiation. The gold carrier can be fabricated in various sizes to suit the particular tumor. The number of seeds per plaque and the design of the plaque can be custom designed to suit a given patient. This flexibility is another advantage of I-125 brachytherapy. Custom made plaques to treat ciliary body tumors or pars plana seeding in retinoblastoma have been achieved with I-125 seeds. Similarly, I-125 seeds have also been used to treat select orbital malignancies such as orbital recurrence of retinoblastoma, residual orbital tumor after resection etc.,

Results with brachytherapy have been gratifying. COMS found that the mortality rate in medium sized choroidal melanomas to be similar to enucleation, the advantage of brachytherapy being that most patients may retain the eye with some vision as well. Cure rate of >90% has been reported in treating retinoblastomas with brachytherapy. Though

(contd. on page 73)

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