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It welcomes original articles, interesting case reports, update articles, book reviews, journal abstracts and research papers in Ophthalmology. Dates of the upcoming conferences and CME’s are also published. Original articles are accepted on condition that they have not been published in any other journal.
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My Swan Song

It is always difficult to put words to a farewell “swan song”, particularly one that has been as enjoyable as my last four years as Editor of the Kerala Journal of Ophthalmology. As with most good songs though, I think my message should be short and sweet. The simple message I would like to convey, therefore, is a heartfelt “Thank You!” to all the people who have helped me in my work with the KJO over the years. The first “thanks” goes to the organization, which has given me tremendous encouragement. In closing, I want to thank all of my friends in the surgical teaching community for their support and their dedication to clinical research and education. Your voluntary contributions to the KJO have been but one more example of your commitment to sharing your experience, wisdom, and enthusiasm with your colleagues.

The majority of ophthalmologists practice in a clinical setting and diagnose and manage a host of ophthalmic conditions. While many of the conditions encountered are common, they are often difficult to manage, requiring tremendous expertise on the part of the treating physician. Our goal was to provide what is called the four Cs of content: information that was current (timely), concise (summarizing), credible (evidence based), and clinically relevant (practical) to benefit the practicing ophthalmologist in his day to day practice. I have at times researched and referenced for articles far removed from my sphere of activity so that we can cater to the needs of the majority. This would not have been possible without the generous voluntary efforts of authors who accepted our invitation to write original articles on a variety of topics. My job was easy, simply to select the topics and the individuals whose opinions I most wanted to read. We and our readership thank you.

It is with very mixed emotions that I am retiring as editor of KJO. I have thoroughly enjoyed the experience of helping to shape this unique publication, but, after 4 exciting years, it is time to bring in fresh editorial leadership. It has been an honor and a privilege to share the editorship with my friends and counterparts. Their insight, imagination, and personalities have made this collaboration a lot of fun, and they have taught me a lot. Our thanks …… To Our Readers ……… To Our Authors ……………… To Our Reviewers ……… and our trade sponsors.

It has thus been my pleasure to serve you as Editor of KJO over these last four years. I know that the journal will continue to flourish under seasoned leadership.

Dr. Meena Chakrabarti  MS DO DNB
Editor, KJO
Steroid-induced glaucoma is a form of open-angle glaucoma occurring as an adverse effect of corticosteroid therapy. It is usually associated with topical steroid use, but it may develop with oral, intravenous, inhaled, or periocular steroid administration by causing decrease in aqueous outflow facility. A number of drugs have been implicated in corticosteroid induced glaucoma including dexamethasone, betamethasone, prednisolone, medrysone, fluomethalone, hydrocortisone, cortisone etc. Glucocorticoids may exert their effect by increased expression of the MYOC (TIGR) gene at Locus GLC1A.

Incidence

Steroid-responsive intraocular pressure (IOP) elevations can occur in people of all ages, although children have frequently reported IOP elevation with steroids. No gender and racial predilection exists for steroid-responsive glaucoma.

Incidence of steroid-induced IOP elevation in patients on systemic corticosteroids is unknown because most of these patients do not have their IOP checked. These patients may be discovered during a routine eye exam while on medication, or the glaucoma may have progressed to the point of causing visual symptoms. Patients taking topical steroid drops usually receive follow-up care by an ophthalmologist who monitors IOP. Approximately one third of individuals experience moderate increase in IOP after topical steroid use. However 5-6 % of normal population will develop a marked increase of IOP after 4-6 weeks of topical steroid therapy. Thus 5 % of the general population is considered to be “steroid responder”, i.e., may develop steroid induced glaucoma when steroids are administered. This is shown by studies conducted by Armaly and Becker. (Table 1)

Table 1. IOP response to topical corticosteroid administration

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Becker</th>
<th>Armaly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>QID</td>
<td>TDS</td>
</tr>
<tr>
<td>Duration</td>
<td>6 weeks</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Type of Responder</td>
<td>IOP (mmHg)</td>
<td>IOP Change</td>
</tr>
<tr>
<td>Low</td>
<td>&lt; 20 (58 %)</td>
<td>&lt; 6 (66 %)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>20-31 (36 %)</td>
<td>6-15 (29 %)</td>
</tr>
<tr>
<td>High</td>
<td>&gt; 31 (6 %)</td>
<td>&gt; 15 (5 %)</td>
</tr>
</tbody>
</table>

Risk factors

Patient related

Persons with preexisting primary open-angle glaucoma have a much greater potential to experience an elevated IOP from topical corticosteroids. On the other hand normal individuals classified as high steroid responders are more likely to develop POAG.

Patients with primary chronic angle closure and patients with secondary open-angle glaucoma behave similarly to normal eyes with regard to steroid response.

There are certain conditions which are associated with increased risk of steroid induced glaucoma such as:

- Patients with primary open angle glaucoma
- First degree relatives of POAG patients
- High myopia
Route of administration

Most cases of steroid induced glaucoma occurs from exogenous steroids which may be given topically, periocularly or systemically. However endogenous steroids can also cause this condition (Table 2).

Table 2 Route of administration leading to steroid induced glaucoma

<table>
<thead>
<tr>
<th>EXOGENOUS CORTICOSTEROIDS</th>
<th>ENDogenous CORTICOSTEROIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular (topical)</td>
<td>Adrenal hyperplasia</td>
</tr>
<tr>
<td>Eye drops</td>
<td>Adrenal adenoma or carcinoma</td>
</tr>
<tr>
<td>Ocular ointments</td>
<td>Ectopic ACTH syndrome</td>
</tr>
<tr>
<td>Inadvertent administration to the</td>
<td></td>
</tr>
<tr>
<td>eye from lids or face</td>
<td></td>
</tr>
<tr>
<td>Periocular / Intravitreal injections</td>
<td></td>
</tr>
<tr>
<td>Systemic</td>
<td></td>
</tr>
<tr>
<td>Oral</td>
<td></td>
</tr>
<tr>
<td>Topical to skin</td>
<td></td>
</tr>
<tr>
<td>Injection</td>
<td></td>
</tr>
</tbody>
</table>

The number of people responding with an elevated IOP varies with the route of administration. More people respond from topically applied drops (including topically applied creams to the periorbital area) 20,21. Periocular steroids, especially repository forms, are particularly dangerous due to their prolonged duration of action 22. A patient’s response to topical steroids does not predict response to periocular steroids 23.

IOP elevation after intravitreal triamcinolone injection is common and may take an extended period of time to manifest. After intravitreal injections of Triamcinolone acetonide, an IOP elevation can develop in about 50 % of eyes, starting about 1-2 months after the injection. In the vast majority, IOP can be normalised by topical medication, and returns to normal values without further medication about 6 months after the injection 24-26.

Systemic administration of corticosteroids is least likely to induce glaucoma. However the IOP elevation may occur as long as weeks to years after treatment 27.

In order of decreasing frequency, incidence of elevated IOP is less with intravenous, parenteral, and inhaled routes of administration. It is reported that the response to systemic steroids does not correlate with the dosage or duration of treatment but is associated with the degree of pressure response to topical steroids 28,29.

Elevated IOP may also be caused by increased endogenous corticosteroids as seen in Cushing’s disease 19.

Steroid formulation

In general the pressure inducing effect of a topical steroid is proportional to its anti inflammatory potency. Commonly used, potent corticosteroids like Betamethasone, Dexamethasone and Prednisolone have a significant tendency to induce glaucoma 30. Less potent steroids such as Fluorometholone and Medrysone are less likely to induce IOP elevations 31-32.

The concentration or dose of a steroid is also related to the likelihood of producing an intraocular pressure elevation. In a study of high topical steroid responders, 0.01 % Betamethasone caused significantly less pressure elevation than the 0.1 % concentration 33.

Duration of steroid administration

Patients who receive corticosteroid therapy may develop IOP elevations in days, weeks, months or years after initiating treatment. The period required and the magnitude of IOP rise depends on the various factors described above. Topical corticosteroids typically produce IOP elevation within 2 to 6 weeks 4-7. Systemically administered steroids, however, may take longer duration to elicit an IOP rise 25.

Pathophysiology

Corticosteroids cause elevation of the IOP by decreasing the facility of aqueous outflow 9,34. Steroid specific receptors on the trabecular meshwork cells may play a role in the development of steroid induced glaucoma 35. Recent research has elucidated the possible role of genetic influences in the pathophysiology 2.
The main mechanism of action of steroids that is responsible for glaucoma is their membrane stabilizing action. Hyaluronidase sensitive glycosaminoglycans (mucopolysaccharides) are normally present in the aqueous outflow system.

These glycosaminoglycans in the polymerized form may undergo hydration producing a “biologic edema”. Hence these are constantly degraded by the hyaluronidase within the lysosomes of the goniocytes.

The steroids stabilize the lysosomal membrane of the goniocytes and thus lead to an accumulation of polymerized glycosaminoglycans in the trabecular meshwork, producing an increased outflow resistance. Glucocorticoid administration increases expression of collagen, elastin, and fibronectin within the trabecular meshwork and induces expression of sialoglycoprotein.

Another mechanism proposed is that steroids inhibit phagocytosis by the endothelial cells lining the trabecular meshwork. This leads to an accumulation of debris within the meshwork. There is also extracellular deposition of fingerprint like material.

Steroid use decreases expression of extracellular proteinases including fibrinolytic enzymes and stromolysin.

A decrease in the synthesis of prostaglandins by corticosteroids, that regulate aqueous facility has also been proposed as one of the mechanisms leading to increase in IOP.

**Genetic influences**

In an experiment involving exposure of cultured trabecular meshwork cells to dexamethasone, delayed increase in expression of a gene product was observed. This protein was termed “trabecular meshwork inducible glucocorticoid response” protein, initially localised to the GLC1A locus on chromosome 1q25 and subsequently linked to the myocilin gene (MYOC).

The MYOC gene spans approximately 17 kb and contains three exons transcripting a 2.3 kb gene product. Within the trabecular meshwork, it is equally expressed in the trabecular meshwork cells from the juxtacanalicular, corneoscleral and uveal layers. Normal myocilin expression is increased in response to elevated IOP dexamethasone exposure and other forms of trabecular stress implying that it may have a protective role in the outflow pathway.

Myocilin gene mutations result in the formation of abnormal gene products which when produced in larger concentrations may lead to trabecular meshwork clogging and increased IOP. In human trabecular meshwork cell cultures treated with dexamethasone the TIGR/MYOC protein co-localises with components of the extracellular matrix like fibronectin and laminin. This could alter cell matrix interactions in the trabecular meshwork. The mutated gene product also suppresses normal myocilin secretion. However a recent study conducted in steroid responders failed to identify a statistically significant association between myocilin variations and steroid response.

**Ultrastructural changes in the trabecular meshwork**

The main finding in steroid-induced glaucoma is an accumulation of basement membrane-like material staining for type IV collagen. These accumulations are found throughout all layers of the TM. Glucocorticoids affect TM cell morphology by increasing synthesis of endoplasmic reticulum, golgi complexes, secretory vesicles, and increased cell and nuclear size. There is an increased deposition of extracellular matrix, thickened trabecular beams and increased expression of fibronectin and laminin. Formation of cross-linked actin networks, microtubule tangles, increased actin binding proteins and an altered gap junction morphology have also been noted. There is an increased expression of MYOC (TIGR) gene and decreased expression of matrix metalloproteinases. This results in altered TM cell function, namely, inhibition of phagocytosis, proliferation & migration, resulting in altered outflow facility.

**Clinical features**

In steroid-induced glaucoma, the pressure elevation is gradual. Therefore, like primary open-angle glaucoma, very few symptoms exist. History of systemic or ocular disease, which could require chronic corticosteroid use (eg, uveitis, collagen vascular disease, asthma, dermatitis) should be elicited in patients having open angle glaucoma.
The age of the patient may determine the clinical form of corticosteroid induced glaucoma. Infants may present with features of congenital glaucoma having tearing, photophobia, blepharospasm, cloudy corneas, buphthalmos, elevated IOP and optic disc cupping. Unlike congenital glaucoma, however, the anterior chamber angle is normal. Teenagers and adults usually present with features of primary open angle glaucoma with decreased outflow facility. Clinical evaluation reveals an elevated IOP, open and normal appearing angles on gonioscopy, painless white eye, optic disc cupping and visual field defects.

Steroid induced glaucoma may mimic low tension glaucoma when the steroid induced pressure elevation has damaged the optic nerve head and visual field in the past, but the IOP has subsequently returned to normal with cessation of the steroid. Steroid induced glaucoma may be masked following refractive surgery due to central corneal thinning, ocular rigidity changes, corneal edema or fluid accumulation beneath the LASIK flap. Additional ocular findings from use of topical steroids include mydriasis, increased corneal thickness, corneal ulcers, posterior subcapsular cataracts, delayed wound healing, ptosis and skin atrophy of eyelids.

Differential Diagnosis

POAG, uveitic glaucoma, glaucomatocyclitic crisis, normal pressure glaucoma, traumatic glaucoma (esp. unilateral cases) and juvenile glaucoma need to be excluded. Steroid treatment of acute uveitis can suppress inflammation and lead to recovery of aqueous production with resultant increase in IOP, which should not be mistaken as steroid induced glaucoma.

Management

Steroid-induced IOP elevation typically occurs within a few weeks of beginning steroid therapy. In the majority of cases, the IOP lowers spontaneously to the baseline within a few weeks to months upon stopping the steroid. In rare instances, the IOP remains elevated.

The most effective management is discontinuation of the drug and administering antiglaucoma medications till the IOP is reduced. If the patient’s underlying medical condition can tolerate discontinuation of corticosteroids, then cessation of the medication usually will result in normalization of IOP. In the case of topical corticosteroid drops, a lower potency steroid medication, such as the phosphate forms of prednisolone and dexamethasone, rimexolone, loteprednol etabonate, fluorometholone, or medrysone, may be substituted. These lower potency drugs have a lesser propensity to raise the IOP, but they usually are not as effective as anti-inflammatory drugs. Topical nonsteroidal anti-inflammatory medications (eg, diclofenac, ketorolac) are other alternatives that have no potential to elevate IOP, but they may not have enough anti-inflammatory activity to treat the patient’s underlying condition. If subtenon depot steroids are causing an elevation of IOP they should be excised and removed. It is important to remember that steroids may also cause a rise in the IOP after a filtering surgery and in such patients low potency steroids should be substituted and rapidly tapered.

When medical therapy is ineffective laser or surgery can be tried. In patients with an open angle and the absence of ocular inflammation, laser trabeculoplasty can be attempted to lower the IOP. Selective Laser Trabeculoplasty is a temporizing procedure to consider in patients with steroid-induced elevated IOP. Repeat SLT treatments may be necessary for IOP control. In patients, whom both medical and laser therapy have failed to lower the IOP adequately, surgical therapy is warranted. Usually, trabeculectomy with or without intraoperative antimetabolites, is the primary procedure. In cases of eyes with active neovascularization or inflammation, a glaucoma drainage implant may be used as the primary procedure.

In eyes with steroid induced glaucoma and vernal keratoconjunctivitis, prostaglandins should be avoided as they can lead to an exacerbation of symptoms with an increase in the conjunctival inflammation.

Anecortave acetate is a synthetic derivative of cortisol, but very specific and irreversible chemical modifications to the cortisol structure have resulted in the creation of a potent inhibitor of blood vessel growth with no evidence non-clinically or clinically of glucocorticoid receptor-mediated bioactivity. Thus Anecortave acetate (AA) can be used for the treatment of exudative age related maculopathy and does not lead to increased IOP.
In fact, an anterior juxtascleral depot of AA has been shown to lower IOP substantially in some eyes with medically uncontrolled steroid-related ocular hypertension 59.

**Steroid induced glaucoma and refractive surgery**

Steroid induced glaucoma is known to be masked following refractive surgery as IOP recordings are erroneous due to central corneal thinning, ocular rigidity changes, corneal edema or fluid accumulation beneath the LASIK flap 48-50,60. Early onset steroid-induced elevation of IOP after LASIK may cause corneal edema and a sudden decrease in visual acuity. Rapid diagnosis and treatment can control IOP and recover the visual loss 61.

Steroid induced glaucoma has been reported after photorefractive keratectomy and is known to be underdiagnosed for the same reasons as above 62.

**Conclusion**

Careful monitoring of all patients on corticosteroids (especially those with a family history of glaucoma) is warranted. Self medication and injudicious use of steroids should be avoided. If necessary, steroid therapy must be used with intermittent drug holidays and never on a continuous basis.

**References**

Ocular Tuberculosis- An update

Dr. J. Biswas MS

Introduction

Tuberculosis (TB) is an air-borne disease that affects one-third of the world’s population (approximately 1.9 billion) and is the leading single cause of mortality and morbidity worldwide causing about 3 million deaths annually. According to the WHO estimates, 8 million people are infected with the disease annually and 95% of them are in developing countries. Nearly 3 million people die from TB annually, the highest incidence being in Africa, Asia and Latin America. Thus, WHO has declared TB as a global emergency.

Tuberculosis primarily affects the lungs but may also affect extra-pulmonary organs. Mycobacterium tuberculosis spreads by droplet infection by coughing or sneezing.

Ocular tuberculosis is an extra-pulmonary form of the disease. Ocular tuberculosis includes any infection in or around the eye caused by Mycobacterium tuberculosis or its related species. It may be either an active infection or an immunologic reaction, related to delayed hypersensitivity or an aseptic reaction.

In primary ocular TB, the eye is the initial portal of entry into the body, whereas the secondary one is defined as an infection resulting from contagious spread from an adjacent structure or hematogenous dissemination.

Primary infection of the eye is rare. Secondary ocular tuberculosis is the ocular involvement as a result of hematogenous spread from a distant site or a direct invasion from adjacent areas like the sinus or the cranial cavity. Almost every tissue of the eye and its adnexa can get affected. Ocular tuberculosis may be acute but usually it runs a chronic course with exacerbations and remissions.

Epidemiology

There has been a dramatic change in the epidemiology of ocular tuberculosis. From 1953 through 1984, the number of TB cases fell, mostly in industrialized countries. However, around 1985, there was an increase in number of new cases which was attributed in large part to the occurrence of tuberculosis in persons infected with HIV. High rate of immigration from countries with a high incidence of TB and emergence of multi-drug resistance of TB were other factors responsible for its rise. The incidence of tuberculosis has increased with the increase in the HIV infected population. According to WHO estimates, there are about 42 million HIV-infected people worldwide, with an estimated 2.5 million in India. Mycobacterium tuberculosis is the commonest infecting organism in HIV-infected patients worldwide and one in three people with AIDS will die of TB. Since 1993, the number of new cases has begun to drop again worldwide. This has become possible because of newer and better treatment for HIV, increased awareness, better institution of Direct Observed Therapy (DOTS) and the use of multi-drug therapy (MDT).

Clinical Presentation

The clinical spectrum of ocular tuberculous infection is diverse. It can have variable manifestations depending on the site and severity of infection. Ocular tuberculosis can manifest without obvious involvement...
of other commonly affected organs or an evidence of a systemic illness. The ocular disease can result from haematogenous spread, from direct local extension from the skin, mucous membranes, or sinuses or it can be an immunologic reaction of delayed hypersensitivity in the absence of an infectious agent. Ocular TB is usually a granulomatous process but it may also be non-granulomatous and the involvement may be unilateral or bilateral. Lesions are known to occur in all parts of the uveal tract, but choroid is most commonly involved.

**Posterior segment findings (Fig. 1)**

The most common finding of ocular TB is choroiditis-multifocal choroidal granulomas being the hallmark feature. These tubercles can mimic in appearance with serpiginous choroiditis, multifocal choroiditis, or simulate the panuveitis pattern. The presence of choroidal lesions, with or without inflammation, is strongly correlated with the systemic disease and is an indicator of haematogenous spread of mycobacteria.

a. **Choroidal tubercles** - These tubercles are unilateral or bilateral, greyish-white to yellowish in color with indistinct margins usually less than five but can be several hundred in number. The choroidal tubercles can be active or inactive and are mostly unilateral but can be bilateral. They typically develop at the posterior pole either singly or in a multifocal pattern with sizes varying from one half to several disc diameters. As the infection resolves, these tubercles heal in 12-14 weeks, become pigmented with distinct margins forming an atrophic scar.

b. **Choroidal tuberculoma** - When a choroidal tubercle continues to grow, it forms a solitary mass known as tuberculoma. Intra-ocular tuberculosis may rarely present with these tuberculomas.

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![Mutton fat KPs in Tubercular anterior uveitis](image1)

![Subretinal abscess](image2)

![Conjunctival tuberculosis in HIV patient](image3)

![Fig. 1. Various Manifestations of Ocular Tuberculosis](image4)

![Choroidal tubercles in Tuberculous posterior uveitis](image5)

![Subretinal abscess](image6)

![Tuberculoma of choroid in HIV patient](image7)
without evidence of any systemic disease. These tuberculomas may be seen anywhere in the choroid- posterior pole, macula or they maybe juxta-papillary in location. The tuberculomas are subretinal masses, often mimicking a tumour, 4-14 mm in size and yellowish in color. There may be an overlying exudative retinal detachment seen in the later stages.

c. **Subretinal abscess**-Large tuberculomas may undergo liquefactive necrosis and form yellowish subretinal mass lesions accompanied by exudative retinal detachment. These lesions may present with clinical signs of subretinal abscess and can be seen both in immunocompetent as well as immunocompromised patients. Such patients need to be investigated for the evidence of miliary tuberculosis. Rarely, these lesions can rupture into the vitreous cavity and may lead to endophthalmitis or panophthalmitis.

d. **Serpiginous like choroiditis**-Serpiginous choroiditis is a rare, bilateral, chronic, progressive and recurrent inflammation of the outer retina and inner choroid which is of unknown etiology. Gupta et al have shown that intra-ocular tuberculosis may present as choroiditis simulating serpiginous choroiditis. There is progression of the disease in spite of the patient being administered systemic corticosteroids and immunosuppressants. These lesions begin in the peri-papillary area and spread centrifugally. However, choroidal tuberculosis may also present in the multifocal form where the lesions are discrete and non-contiguous initially but later in the course may form a diffuse, contiguous pattern.

The retina may show features of retinitis, vasculitis, vascular occlusions or serous retinal detachment. Retinal periphlebitis is rarely caused by the direct invasion of the retina by tubercle bacilli. Retinal tuberculosis usually occurs secondary to underlying choroiditis. Cystoid macular edema can accompany intraocular inflammation in ocular tuberculosis. Vitreous may show vitritis and “snowballs” opacities in the anterior and inferior vitreous. Pars plana “snow banking” may sometimes be observed.

**Anterior segment findings**-

The most common anterior segment presentation is anterior uveitis which can be chronic anterior uveitis or panuveitis. Iridocyclitis shows characteristics mutton-fat keratic precipitates (KPs) classically distributed inferiorly in the lower one third of the cornea which is known as the Arlt’s triangle. The iris usually develops posterior or anterior synechiae and/or iris granulomas. Granulomas may be seen at the angle of the iris base and over the trabecular meshwork. HIV patients on retroviral therapy can show an immune recovery uveitis associated with concomitant tuberculosis even if they are not on Rifabutin. Long-standing inflammation can lead to cataract formation and secondary inflammatory glaucoma.

**External ocular findings**

Lupus vulgaris of the eyelids can rarely develop. Tuberculocous conjunctivitis has been reported which is usually unilateral, chronic, may occasionally be associated with conjunctival mass or ulceration. Preauricular lymphadenopathy is occasionally seen in these cases. Conjunctival granulomas may also be seen. Phlyctenulosis is the most common form of external ocular tuberculosis involvement. It is a Type IV Hypersensitivity reaction, presents as an inflammatory mass on the cornea. It is usually occurs due to tuberculosis but can be associated with Staphylococcus aureus. Focal, nodular or diffuse scleritis with or without keratitis can also develop. The tuberculosis keratitis and scleritis may develop as a result of spread of infection and granulomatous reaction from within the eye. These are known to be biopsy-proven cases of TB scleritis. It is usually diffuse, posterior or nodular and associated with localized granuloma formation. Interstitial keratitis and sclero-keratitis is also known to occur.

The orbit may be involved by spread of disease from within the eye. Commonly the spread occurs from orbital periostitis. Orbital periosteal rim, dacyroadenitis, and sinus infections with a non-healing, draining fistula are typical of tuberculosis. Panophthalmitis or endophthalmitis may also occur. Tuberculosis can also present as an orbital mass, or as eyelid abscesses.
There are two other ocular entities that are related to Tuberculosis-

1. **Reactions to tuberculin**- Allergic reactions have occurred in patients with bilateral, granulomatous anterior uveitis associated with tuberculin skin testing. Severe choroiditis progressing to serous retinal detachment has been reported with intra-dermal injection of purified protein derivative (PPD) in patients with pre-existing tuberculous uveitis

2. **Eales’ disease**- The disease is characterized by recurrent vitreous haemorrhages and retinal periphlebitis in young adult males. The true nature of this disease is still a matter of debate though tuberculosis has long been implicated as a cause.

**Pathology**

Tissue destruction from M tuberculosis infection occurs due to the organism’s ability to incite intense host immune reactions to antigenic cell wall proteins. The main feature of ocular TB histopathology is granulomatous inflammation. There occurs granuloma formation in the choroid characterized by lymphocytes, epithelioid cells, and giant cells with caseating necrosis. Rarely are any TB bacilli seen. Overlying retina can also be involved. The scleral involvement can range from mild to frank perforation.

**Diagnosis**

Despite the existence of highly sensitive molecular diagnostic techniques, the diagnosis of ocular tuberculosis is often presumptive, based upon clinical presentation, systemic evaluation and response to treatment. Choroiditis is the most common ocular manifestation in patients with pulmonary and systemic tuberculosis and in the absence of ocular biopsies the diagnosis remains presumptive. The primary screening and diagnostic test is the tuberculin skin testing with purified protein derivative (PPD).

Culture for acid-fast bacilli (AFB) is the most specific test and allows direct identification and susceptibility of the causative organism. The microscopy of specimens can rapidly detect the presence of acid-fast bacilli but requires large quantities of sample material, which is difficult to obtain from ocular tissue. It is less sensitive than culture of specimens in specific media.

Definitive diagnosis is achieved by identifying the M. tuberculosis by Polymerase chain reaction (PCR) which evaluates the presence of the tubercle bacillus DNA in ocular fluids and tissues. Only 0.01 ml of sample is required and both aqueous and vitreous specimens can be used. Nested-PCR has further reduced the antigen density required to obtain a positive result but it has an increased risk of false positivity. Enzyme-linked immunosorbent assay (ELISA) evaluates host immunoglobulin G (IgG) and immunoglobulin M (IgM) levels and helps in identifying recent infection but is not a particularly sensitive test. More recently developed assays are being used to augment the PPD test. Interferon gamma titres correspond to the strength of PPD and correlate more strongly to the risk of disease than PPD.

Quantiferon TB- Gold is the new antigen specific test for the diagnosis of tuberculosis. It is helpful in diagnosing infection with M. tuberculosis, including both tuberculosis disease and latent tuberculosis infection. It utilizes synthetic peptides representing mycobacterium tuberculosis proteins. It is a commercially available test that has been approved by Food and Drug Administration (FDA). It has a higher specificity than tuberculin skin test since it is unaffected by prior BCG vaccination and has equal or slightly more specificity than tuberculin skin test. Also, the result is objective and ready within 24 hours and unlike tuberculin skin test, no follow-up is required. Quantiferon test has also been shown superior to tuberculin skin test in immunosuppressed patients, in HIV patients and in patients with immune-mediated diseases.

Pars plana vitrectomy allows in obtaining intraocular specimens. Chorioretinal endobiopsy using standard three-port pars plana vitrectomy technique has been used for diagnosing TB choroiditis. It is however, associated with significant hazards such as retinal detachment, vitreous hemorrhage, and endophthalmitis.

The diagnosis of ocular tuberculosis is supported by the clinical imaging techniques including a chest x-ray to evaluate for possible associated pulmonary findings, optical coherence tomography (OCT) which is especially useful for the choroidal lesions, Fluorescein angiography, Indocyanine green angiography and
B-scan ultrasonography\textsuperscript{15}. CT scan is useful to evaluate an orbital mass from TB\textsuperscript{16}.

**Treatment**

**Treatment for pulmonary tuberculosis**

Once the tuberculosis is confirmed, the treatment is begun immediately. A combination of four drugs during the first two months- Isoniazid, Rifampin, Pyrazinamide and Ethambutol and two drugs- Isoniazid, Rifampin for next four additional months is given. Due to the prevalence of drug resistance especially to isoniazid (INH) and Rifampin, multi-drug therapy is now used routinely. The most common cause for treatment failure in case of pulmonary tuberculosis is non compliance to the therapeutic regimen. In this regard, Direct-Observed-Therapy (DOTS) has been of great help.

The treatment of active ocular tuberculosis infection differs from prophylaxis in patients with PPD positive but with no evidence of active TB. Here, the onus rests with the ophthalmologist to decide if the uveitis is indeed a sign of active tuberculosis infection. It is probably not indicated to treat every uveitis patient with a positive PPD with long-term anti-tuberculous medication in the absence of other evidence of tuberculosis.

**Treatment for ocular tuberculosis**

Treatment for ocular tuberculosis is the same as that for pulmonary tuberculosis\textsuperscript{17}. CDC has recommended the use of all 4 drugs-isoniazid, rifampicin, Pyrazinamide and Ethambutol for an initial 2 month period. This is followed by a choice of different options for 4-7 months\textsuperscript{18}. The CDC also recommends prolonged treatment for tuberculosis of any site that is slow to respond. Many studies have also recommended a treatment regimen consisting of isoniazid and rifampicin for a period of 9 months\textsuperscript{19,20,21}. It has been shown that the addition of rifampicin or Pyrazinamide to drug regimen containing isoniazid reduces the duration of the therapy\textsuperscript{22}. Low dose steroids given concomitantly with anti-tubercular therapy for a duration of 4-6 weeks has been shown to have a protective effect against tissue damage from delayed hypersensitivity. Few studies have highlighted that the use of steroids may activate a latent infection and cause a flare-up of systemic tuberculosis\textsuperscript{23}. Subretinal tuberculomas have been successfully managed surgically although a report by Gupta et al reports successful medical management of these tuberculomas. Also, Gupta et al have described that the addition of anti-tubercular therapy to corticosteroids in uveitis patients with latent/manifest tuberculosis decreases the risk of developing recurrences of uveitis\textsuperscript{24}.

**TB and HIV**

Tuberculosis is the commonest infection detected in HIV-infected individuals worldwide and the patients with HIV infection exhibit a unique susceptibility to Mycobacterium tuberculosis. These patients are not only more likely to develop an active disease but there occurs a rapid progression to active disease in their case. Also, once the infection is established, the clinical disease is more severe in these patients. They are also susceptible to reactivation of latent tuberculous infection.

There are some challenges in dealing with HIV Patients with TB as far as diagnosis and treatment is concerned. Tuberculin skin testing is not reliable in these cases. The manifestations of ocular tuberculosis are the same as in immunocompetent patients; disseminated choroiditis being the most common manifestation. The immunocompromised status of HIV patients retards recovery. Also, drug malabsorption is seen in HIV patients warranting a longer duration of treatment.

**Treatment of tuberculosis in HIV-infected patients**

The treatment regimen in HIV patients remains the same as that for non-infected individuals and consists of a combination of anti-tubercular drugs\textsuperscript{25}. It has been showed that administration of trimethoprim-sulphamethoxazole to HIV infected tuberculosis patients on being diagnosed as having active tuberculosis, protected them from a variety of infectious causes of death\textsuperscript{26}.

**Rifabutin and uveitis**

Rifabutin is used for the treatment and prophylaxis of Mycobacterium avium complex (MAC) infection in the HIV patients. Uveitis is a rare, dose-related toxicity of this therapy. The risk of Rifabutin-associated uveitis has
been shown to increase in patients receiving concurrent therapy with Clarithromycin or fluconazole because of drug interactions. If any signs of uveitis develop, Rifabutin therapy should be promptly discontinued.

**Ocular toxicity of anti-tuberculular drugs**

Ocular tuberculosis patients should be followed for side effects of anti-tuberculular drugs. Of all the anti-tuberculular drugs used, Ethambutol is the most likely to cause ocular morbidity.

Ethambutol has been associated with retrobulbar optic neuritis. However, it is dose related and usually reversible but may sometimes warrant discontinuation of the drug. Isoniazid has also been implicated in causing peripheral neuropathy. Such patients should take pyridoxine, which has been shown to prevent isoniazid-associated neuropathy. Isoniazid is also known to be hepatotoxic. Liver enzymes should be tested serially while the patients are on this drug. Rifampin is associated with thrombocytopenia. So, complete blood counts should always be done. Pyrazinamide has been associated with causation of hyperuricemia, but acute gout is not common. Streptomycin has been associated with hearing loss.

**Conclusion**

Ocular tuberculosis may occur in the absence of pulmonary disease and the patients may present with a wide variety of clinical signs. Also, the disease can mimic several clinical entities. Tuberculosis may affect all ocular tissues; choroiditis being the most common ocular manifestation. The retinal involvement occurs secondary to the underlying choroidal infection. Treatment for ocular tuberculosis is the same as that for pulmonary tuberculosis. Due to the emergence of drug resistance, multidrug therapy is advocated.

In the present time of the HIV pandemic, there has been a resurgence of tuberculosis and it is the most common opportunistic infection in HIV positive patients. HIV-related TB shows a higher prevalence of ex- pulmonary and disseminated TB. Since the disease is treatable and eyes can be saved using anti-tuberculular treatment if detected early, considerable stress should be laid on its early diagnosis and prompt treatment so as to prevent ocular morbidity and blindness.

**References**

on experimental ocular tuberculosis in the immune-allergic rabbit. AMA Arch Ophthalmol 59:559-78, 1958
The Evolving Story of Aphakic and Pseudophakic Glaucoma after Cataract Surgery in Children: What’s New?

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Glaucome in the aphakic and pseudophakic eye is the third most common cause of glaucoma in children, coming after congenital and traumatic glaucoma.1 Our knowledge regarding its incidence, pathogenesis, risk factors associated with its development and best management options is still evolving. We present here a review of the literature that forms the bulk of knowledge of this currently inevitable complication to pediatric cataract surgery.

Incidence of glaucoma in aphakic and pseudophakic eye of children:

The incidence of glaucoma following pediatric cataract removal has been reported to be as low as 5 % to as high as 41 %.2-7 Comparing incidence from different studies is unreasonable, since studies use a variety of definitions to glaucoma and different instruments to measure the intraocular pressure (IOP). The incidence is further affected by the age, surgical technique, the length of follow up and the presence of risk factors for subsequent glaucoma development.

Francois2 reviewed 13 studies from the international literature on congenital cataract surgery in the 1940’s to 1950’s when the linear aspiration technique was used. Delayed glaucoma occurred in 0-14 % of the cases.

In 1984, Chrousos, Parks, and O’Neill3 reported their 15 year experience with pediatric cataract surgery using both the Scheie’s manual aspiration technique and the Ocutome automated cataract removal technique. Chronic glaucoma occurred in 6.1 % of the eyes, none of the eyes operated with the Ocutome technique developed glaucoma. However, the follow up of the eyes operated using the aspiration technique was for a mean of 6.3 years versus 2 years for the eyes operated with Ocutome.

Simon et al.4, using an IOP of 26 mmHg to define glaucoma, reported an incidence of 7 % for eyes with < 5 years of follow up after lensectomy and an incidence of 41 % for eyes followed up for > 5 years. This further exemplifies how the incidence is affected by the period of follow up.

Rabiah5 reported glaucoma in 118 of 570 eyes (21 %) at a mean age of 5.4 years (range 2 weeks- 15.6 years); average total follow up for eyes with and without glaucoma was 8.5 years and 10.9 years, respectively.

With 71 out of 76 eyes with at least 5 years of follow up, Michaelides et al.6 calculated a 5 year risk for developing aphakic glaucoma after lensectomy of 15.5 %, and a 5 year risk for a patient to develop aphakic glaucoma in at least one eye after surgery of 21.6 %. The onset of glaucoma ranged from one month after...
surgery to 7 years with an average yearly incidence of 5.3 %.

Findings from the British congenital cataract study of patients with at least 6 years of follow up showed an overall annual incidence of postoperative glaucoma of 5.25 %. The median time to development of glaucoma was 1.34 years with a range of 0.39 months to 6.73 years. Closed angle glaucoma was excluded from their analysis.

In the Denmark population based cohort study, ten years after cataract surgery 31.9 % of the children who underwent cataract surgery before 9 months of age developed aphakic glaucoma. They note that glaucoma cases continued to occur even after 10 years from surgery.

We reported that after pediatric cataract surgery, 10/266 (3.8 %) eyes with primary IOL were diagnosed with glaucoma, whereas 8/47 (17.0 %) aphakic eyes were diagnosed with glaucoma. However, when focused on children operated before 4.5 months of age, the glaucoma incidence was 10/41(24.4 %) in children with pseudophakic eyes and 8/42 (19.0 %) in age-matched children with aphakic eyes (risk ratio=1.1, CI=0.7-1.9; P=.555).

Wong and colleagues reported the incidence of glaucoma, with onset within 1 year after cataract surgery (early onset) performed in the first year of life, with or without IOL implantation. At a mean follow-up of 2.51 years, 15.3 % (12.2% within 1 year) of all eyes, 9.8 % of eyes (6.6 % within 1 year) in the planned aphakic group, all four eyes with failed implantation and 13.5 % of the pseudophakic eyes (10.8% within 1 year) developed glaucoma.

Kirwan and colleagues reported the incidence and risk factors for glaucoma in pseudophakic and aphakic eyes following surgery for congenital cataract within the first year of life. The incidence of glaucoma was significantly greater (P = 0.02) in the aphakic (15 eyes, 33 %) compared to the pseudophakic (seven eyes, 13 %) group. However, duration of follow-up was significantly longer (P < 0.001) in the aphakic (113 ± 69 months) compared to the pseudophakic group (56 ± 44 months) and age at surgery was significantly less (P = 0.01) in the aphakic group.

Proposed mechanisms for the development of glaucoma after pediatric cataract surgery

Several theories have been proposed to explain the pathogenesis of glaucoma after pediatric cataract surgery and it is still not clear why glaucoma develops in these eyes; however it appears to be a consequence of surgery rather than cataract itself. Children with unoperated isolated congenital cataract do not tend to develop glaucoma and patients with bilateral congenital cataracts who have cataract surgery in one eye only, tend to develop glaucoma in the operated eye only. In the predisposed eye, surgery to remove the cataract appears to trigger a cascade of events that can lead to glaucoma.

In 1986, Walton discussed pupillary block and chronic angle closure from peripheral anterior synechiae as the typical mechanism following cataract removal by the ‘aspiration’ mechanism. A decade later, David Walton’s American Ophthalmological Society thesis concluded
that the asymptomatic, postoperative glaucoma in aphakic patients was actually an open-angle mechanism and that those that underwent surgery in the first year of life were at highest risk for this complication, but the etiology of the glaucoma was still speculative. Walton studied the angle structure of 65 aphakic children with postoperative glaucoma from modern methods of pediatric cataract removal. Vitrectomy techniques were utilized in the majority (80%) of cases. Preoperatively, the majority of patients with available gonioscopy (19/29 eyes) had no angle abnormalities, while 10 patients did have “anomalous attachments from the iris root to Schwalbe’s line and the trabecular meshwork. Postoperatively, the angles were open in 79 of 80 eyes, but in 76 of 79 (96%) of eyes, “circumferential repositioning of the iris insertion anteriorly at the level of the posterior or mid-trabecular meshwork with resultant loss to view of the ciliary body band and scleral spur” occurred. Windows of visible scleral spur or ciliary body were visible in these eyes, confirming open angles. Walton observed scattered pigment deposits in the exposed anterior trabecular meshwork, and less frequently, white crystalline deposits suggestive of lens protein. Phelps observing similar gonioscopic findings in patients after surgery, implied that the uniformity of the angle findings “throughout its circumference” instead suggested that these findings were congenital and not related to the cataract surgery. There is no way to prove, however, that those angle findings were not indicative of subclinical dysfunction.

It is possible that cataract extraction may indeed damage a growing, vulnerable anterior chamber angle in an eye with a subclinically imperfect trabecular outflow in a way that creates high IOP years later. This may be why patients with a preexisting ocular abnormality (such as trauma, dislocated lens, chronic uveitis, or anterior segment dysgenesis) may be at higher risk for post-operative glaucoma.

Many studies have shown age at surgery to be the major risk for the subsequent development of glaucoma. This would support the theory of cataract extraction damaging a growing, vulnerable anterior chamber, but what factors could be implicated in this damage? Recently, Michael et al. studied the interactions between the trabecular meshwork cells (TMC) and the lens epithelial cells (LEC). They cocultured primary and transformed TMC’s with LEC’s and studied the structural changes, and differential protein and gene expression in the cocultured TMC’s, using TMC’s grown in a low serum medium for the same period as a control. They found the cocultured cells to be larger in size and volume with fewer cell to cell contacts. They also accumulated granules and had fewer vesicles. They had an increase in cytoskeletal protein expression and a differential gene expression with upregulation of 400 genes and downregulation of 566 genes. The most affected genes were the ones regulating cellular processes related to the extracellular space, vesicle and actin cytoskeleton. The changes were similar to changes seen in the ocular tissue of patients with primary open angle glaucoma. They aim in the future to further study the effect of young and adult LEC’s on the TMC’s and suggest examining the difference in the response of infant TMC’s to the presence of LEC’s.

Risk factors associated with aphakic and pseudophakic glaucoma

A number of reports have discussed the following risk factors associated with post-operative glaucoma in children with cataracts: age at surgery, age at cataract diagnosis, microcornea, poorly dilating pupils, the presence of other ocular disease (e.g., congenital rubella syndrome), nuclear cataract, persistent fetal vasculature (PFV), and performance of a posterior capsulorhexis.

Mills reported several risk factors for childhood glaucoma: cataract surgery at an age of < one year (relative risk (RR) = 9.9; P d” 0.001), microcornea (RR=4.4; P d”0.001), poor pupillary dilation (RR=5.2; P d”0.001), and congenital rubella syndrome (RR = 5.8; P d” 0.001). The relative risk (RR) was notably high for patients undergoing surgery before the age of 6 months (RR= 5.4; P d” 0.001) and 1 year (9.9; P d” 0.001). No patient who had surgery after 1.25 years of age developed chronic open or closed angle glaucoma. The authors state, “the time at surgery may not be independent of other pathologic factors as a disproportionate share of those patients who had early cataract surgery had other ocular abnormalities (congenital rubella syndrome 10.1% of 79 eyes operated on before 1 year of age), poorly dilating pupils (22.0%), microcornea (10.1%), or persistent fetal
vasculature (6.3 %))...or more complete lens opacity.”
Congenital rubella syndrome, poor pupillary dilation, and microcornea were also determined to be independent risk factors in this report.

Magnusson\textsuperscript{23} prospectively followed a cohort of 137 patients in Sweden for an average of 9 years and concluded that cataract extraction in children younger than 10 days of life is associated with double the frequency of glaucoma. Twenty-nine percent (4/14) of patients operated on before the age of 10 days developed glaucoma; operations performed after 10 days of life had half the frequency of glaucoma. The immature trabecular meshwork of patients undergoing cataract surgery at a very young age were exposed to inflammation or direct surgical trauma and led to glaucoma.

Rabiah\textsuperscript{5} concluded in a retrospective study of childhood aphakes that age at time of surgery is an important determinant of chronic glaucoma. Potential predictors of risk were entered into a univariate and multivariate model. The vast majority (86 %) of the glaucoma was diagnosed in patients who underwent surgery at or before 9 months of age. Of patients with cataracts in one or both eyes, no unoperated fellow eye developed glaucoma. The significant predictors of glaucoma in the multivariable analysis included: microcornea; primary posterior capsulotomy/anterior vitrectomy; secondary membrane surgery; and surgery at 9 months of age. The risk appeared substantially lower in children operated on after three years of age.

Watts et al.\textsuperscript{24} studied the complications after cataract extraction in the first 12 weeks of life. Their CART analysis showed an increased incidence of glaucoma when surgery is performed between 13.5 and 43 days of life. Vishwanath\textsuperscript{25} and colleagues found that after bilateral lensectomies the 5 year risk of glaucoma decreases from 50 % if cataract surgery was performed in the first months of life to 14 % if surgery was performed later in life. There was no statistical difference between the risk for eyes operated in the first half of the first month and eyes operated in the second half of the first month. There was no difference in the five year visual outcomes for eyes operated before and after the first month. This led them to conclude that it may be prudent in bilateral cases to postpone surgery to after the first month of life to decrease the subsequent risk of glaucoma without compromising the visual outcome.

In their study of the risk factors for the development of glaucoma after congenital cataract surgery, Chen and associates\textsuperscript{26} aimed to study if there is a time period during the first year when the risk for glaucoma after performing lensectomy becomes lower. By a multivariate analysis of 216 eyes that developed aphakic glaucoma and 152 eyes that did not develop glaucoma they found that having lensectomy in the first year and the development of postoperative complications were the risk factors of highest significance to the development of glaucoma. They did not find any time during the first year when the risk of glaucoma decreased significantly. After the ninth month fewer eyes had lensectomy which decreases the power for conclusions made after this period. Other risk factors found to be significantly associated with the development with glaucoma were postoperative cycloplegic use, a corneal diameter < 10mm and having a nuclear or total cataract. Would these factor still be significant after adjusting for age at cataract extraction?

The British congenital cataract study\textsuperscript{7} showed that age at detection of cataract was the only factor significantly associated with the development of glaucoma. They found that a ten fold increase in the age at detection decreases the hazard ratio for the development of glaucoma by 64 %. Microphthalmia, insertion of an IOL, type of cataract surgery, and significant postoperative uveitis were not significantly associated with the development of glaucoma after univariate and multivariate analysis.

In the Denmark population-based cohort study\textsuperscript{8} of 946 eyes undergoing cataract surgery, age at surgery < 9 months was associated with a 7.2 fold increased risk for the development of glaucoma. All the other risk factors (type of surgery, posterior capsulotomy, surgery for secondary cataract, nystagmus, microcornea, etiology, laterality, insertion of an IOL, and morphology of the cataract) were not significantly associated with glaucoma when adjusted for age at surgery. In our recent study of 266 pseudophakic eyes and 47 aphakic eyes\textsuperscript{9}, we found that all of the eyes that developed glaucoma were operated before the age of 4.5 months. Wong and colleagues\textsuperscript{10} reported that excessive surgical trauma influences incidence of glaucoma. Microcornea,
PFV and age 4 weeks at surgery were not significant predictors of early-onset glaucoma in this series.

**How should a clinician use these data?** It may be reasonable to require more frequent anesthetized exams for children operated on at three months of age than those at three years. In our opinion, the data are not of sufficient strength to postpone surgery of a seven month old with a visually significant cataract to lower the presumed risk of future glaucoma. A few authors have discussed the critical period for binocular development beginning at about the 5th or 6th week of life. At our current level of knowledge, we feel it is reasonable to postpone surgeries in neonates with unilateral or bilateral cataracts until about the 5th week of life, which allows one to operate on a firmer, more developed eye.

**Does microcornea appear to be a risk factor for glaucoma?** Parks and colleagues found a 32% incidence of aphakic glaucoma among those eyes with corneal diameters of 10 mm at surgery. By contrast, eyes with corneal diameters >10 mm at surgery had only a 2.9% incidence of glaucoma during the follow-up period. Simon and coworkers found no association between microcornea and the development of glaucoma in their patients. Wallace and Plager noted microcornea to be a significant risk factor for aphakic glaucoma. During our initial analysis, we also observed that eyes that developed glaucoma had a significantly smaller corneal diameter than eyes that did not develop glaucoma. However, when we focused our analysis on eyes in children who underwent surgery at an early age (4.5 months of age), we did not find a significant difference in corneal diameter between those that developed glaucoma and those that did not (pseudophakic eyes, P = .860; aphakic eyes, P = .254).

Different approaches when comparing corneal diameter could have resulted in different conclusions between our and other studies. Wallace and Plager defined microcornea as any corneal diameter smaller than that established by the authors’ age-related curve. They compared corneal diameter in aphakic eyes that developed glaucoma with that of normal corneal diameter. It may be possible that all or most of the aphakic eyes had microcornea (even those eyes that did not develop glaucoma). These authors did not have a control group of aphakic eyes that did not develop glaucoma. In contrast to the most eyes with postoperative corneal diameter in the Wallace and Plager series, we compared preoperative corneal diameter of eyes that developed glaucoma with those eyes that did not develop glaucoma and treated corneal diameter as a continuous variable. In addition, our analysis included only eyes of children who underwent surgery in the first 4.5 months of life. Unfortunately, we do not have comparative age-related data. Ideally, we should compare 3 groups (children with normal, aphakic, and pseudophakic eyes) that developed glaucoma with those that did not. Comparing these 3 groups in age-matched data may help us to give a definitive answer. However, for now, on the basis of the results of our study, we fail to find corneal diameter as a significant and independent risk factor for the development of glaucoma. Eyes operated early in life more often are associated with having microcornea, and age at surgery rather than corneal diameter itself may play a role in the development of glaucoma after cataract surgery.

**Does primary IOL implantation prevent “aphakic” glaucoma in children?** A growing number of surgeons are using intraocular lens (IOL) implantation as the preferred mode of optical rehabilitation in patients after pediatric cataract surgery. However, the effect of IOL implantation on the incidence of glaucoma after cataract surgery is unclear. Several authors have noted a low incidence of glaucoma in children with pseudophakic eyes, and the implication being that pseudophakia in children somehow protects against glaucoma. The reported decreased incidence of pseudophakic glaucoma after pediatric cataract surgery in some studies may be related to a protective effect of the synthetic lens from a vitreous component, alteration of the lens-iris-drainage angle relationship by the synthetic lens, or selection bias (patients most at risk for developing glaucoma simply may be selected not to receive IOLs).

Like other clinicians, during the initial years of our IOL implant practice, we also observed a lower incidence of glaucoma in these children. However, during those years of practice, children who underwent eye surgery in the first year of life and who had microcornea, coexisting ocular anomalies, or PFV often were left aphakic. These conditions are reported risk factors for the development of aphakic glaucoma.
In a multicenter retrospective review, Asrani and coworkers reported a lower incidence (0.3 %, or 1 in 377 cases) of open-angle glaucoma in eyes receiving a primary IOL implant compared with those that remained aphakic (11.3 %, or 14 in 124 cases) after cataract surgery. In our series, we noted that glaucoma developed in 10 (3.8 % of 266) pseudophakic eyes and 8 (17.0 % of 47) aphakic eyes. However, when focused on eyes operated before 4.5 months of age, in an age-matched cohort, we note no significant difference between the rate of development of glaucoma between the aphakic and pseudophakic eyes. We found that among the patients who underwent surgery before 4.5 months, the corneal diameter, keratometry and axial length were significantly different among the aphakic and pseudophakic groups reflecting a tendency to leave the smaller eyes aphakic which may underestimate the incidence of glaucoma in the pseudophakic group. The incidence of aphakic glaucoma has been reported as higher when children are followed for longer period after cataract surgery. We might expect the same trend with pseudophakic eyes and the incidence reported in our series (or any other series) may be higher as we have longer-term follow-up.

Adding challenge and better understanding to the diagnosis of aphakic and pseudophakic glaucoma: Central corneal thickness (CCT)

Central corneal thickness can affect the accuracy of measuring IOP. A thicker cornea can overestimate the IOP. Moreover, in recent studies in adults, a lower CCT predicted the progression to primary open angle glaucoma. Simon et al. in a prospective masked study measured the corneal thickness of 36 aphakic and 6 pseudophakic eyes and used the CCT measurements from the phakic fellow eyes in unilateral cases (14 eyes) as controls. The mean CCT in the operated eyes was 660 microns, significantly higher than the mean of 576 microns in the phakic fellow eyes. They suggest refining the definition of glaucoma based on this finding to include eyes with an IOP above 22mmHg with documented optic disc or visual field changes and use the IOP measurement on its own if it was above 35mmHg. Based on this definition, glaucoma would be diagnosed in 21 % of the eyes in their study group and ocular hypertension in 60 %. If only an IOP of more than 26 mmHg was used as a criterion for the diagnosis, then glaucoma would be diagnosed in 50 % of the eyes.

Is this increased CCT present in all pediatric Glaucomas? Tai et al. found the mean CCT in eyes with aphakic glaucoma (651 microns) to be significantly higher than that in primary infantile glaucoma and glaucoma associated with Axenfeld-Reiger anomaly, even after adjusting for age. Simsek et al., in a randomized masked prospective study used healthy volunteers matched for age and sex as controls. Unlike Simon et al., they included only one eye, randomly chosen, in bilateral cases to further increase the power of their study. They found the median CCT (662microns) in the aphakic and pseudophakic group to be significantly higher than the median CCT (556microns) in the control group. They also found a negative correlation between the age at lensectomy and the CCT. They found a significant difference between the CCT in aphakic eyes and the CCT in the pseudophakic eyes with primary IOL implantation. However, they only had 5 eyes in the pseudophakic group, none of which had glaucoma, which decreases the power of such a result. Further studies are needed to explore the effect of IOL implantation on the CCT measurements.
Is this increase in corneal thickness caused by the cataract extraction or is it that the eyes with congenital cataract start off with developmentally thicker corneas?

Muir et al. \(^{37}\) in their study of the CCT in 369 eyes found that the mean CCT of eyes with cataract was not different from the mean CCT of the controls. Further, the mean CCT of eyes with pseudophakia was significantly higher than that of eyes with cataract and eyes of controls. The mean CCT of eyes with aphakia was significantly greater than the mean CCT of eyes with pseudophakia, cataract and controls. They found a positive correlation between the time since cataract surgery and CCT, while there was no correlation between increasing age and CCT in controls. When comparing the mean CCT of aphakic eyes with glaucoma with the mean CCT of aphakic eyes without glaucoma, they found the mean CCT to be higher in the eyes with glaucoma (they used a cup to disc ration of >0.4, or an asymmetry of >0.2 to diagnose glaucoma, so this increase in CCT in eyes with glaucoma probably is not related to a diagnostic selection bias of eyes with thicker corneas into the glaucoma category). They acknowledge that there might be a selection bias with the eyes with aphakic glaucoma having thicker corneas because they are eyes with microcornea or other structural corneal abnormalities not represented in the study. They discuss that a study that compares the CCT in the same eye before and after cataract surgery may be better able to answer this question.

What causes this increase in CCT after cataract surgery is still unknown. Is it related to endothelial injury at the time of cataract surgery?

Nilforushan \(^{38}\) and associates reported an increased CCT in children with aphakia compared with age-matched control eyes, but with similar endothelial cell counts and morphologic features in both groups. Simsek et al. \(^{36}\) postulate that surgical trauma to the cornea in the early months of life, when the cornea is undergoing a rapid decrease in its thickness may account for an arrest in the process and the development of thicker corneas in aphakic eyes. This would explain their finding of a negative correlation between the age at cataract surgery and CCT. They also postulate that the presence of an IOL would protect the cornea from exposure to vitreous factors affecting corneal development. Is the same mechanism that affects the trabecular meshwork and leads to aphakic glaucoma, the culprit affecting corneal development and leading to increased corneal thickness? Would corneal endothelial cells cocultured with LEC’s show similar changes found in cocultured TMC’s? Further studies are needed to better understand the changes cataract surgery introduces to the developing eye.

How would the emerging data regarding CCT in aphakia modify our clinical practice?

We could probably follow Simon’s recommendations of reserving the diagnosis of glaucoma to eyes that show optic disc or visual field changes and the eyes with an IOP of >35mmHg. When the IOP is elevated it would be recommended to measure the CCT to aid in the interpretation. Lopes et al. \(^{39}\) showed that when a CCT correction formula was applied to the IOP, more than half of the eyes had a 3mmHg difference between measured and adjusted IOP. With a rate of progression from OHTN to glaucoma of 23%, all eyes with elevated IOP should be monitored closely for any changes in optic nerve function that would warrant aggressive medical and surgical management. Would the CCT help us predict which eyes would progress to glaucoma? Further studies are needed to explore this question.

Treatment:

The management of children with post-operative aphakic or pseudophakic glaucoma differs from that of congenital glaucoma. Medical management is often initiated after aphakic glaucoma is diagnosed. There is a paucity of the literature comparing different medical treatment modalities.

When medical management fails, realistic surgical options include seton implantation, trabeculectomy or cyclo-destructive procedures. Aphakia has been previously reported as a significant risk factor for failure of trabeculectomy with mitomycin-C (TMMC) in not only adult patients \(^{40,41}\) but also in patients under one year of age \(^{42,43}\); the latter studies are discussed below. Freedman et al.\(^{42}\) retrospectively evaluated results of
17 consecutive children (21 eyes) under 17 years of age (median age 2.6 years) who had failed maximum medical therapy, prior angle or filtration surgery (goniotomy, trabeculotomy, trabeculectomy), or both. TMMC with or without post-operative 5-Fluorouracil (5-FU) or laser suture lysis or both were performed. Aphakic patients performed worse than phakic patients whether TMMC was performed before or after one year of age. Success was poor in all patients less than a year of age, whether phakic (3/8 eyes, 38%) or aphakic (0/2 eyes). Success rates were higher in patients one year of age, both for phakic (6/6 eyes) and aphakic (2/5, 40%) groups. The authors contend that laser-suture lysis or 5-FU augmentation of TMMC did not improve success in younger, aphakic children and may have increased complication rate. The study is limited by the small number of patients in each subgroup and limited (median 23 month) follow-up of successful cases. Mandal et al. also reported high success rates in older, phakic patients without identifying success in the subgroup of patients who were younger or aphakic.

Beck and colleagues provide another report of failure of TMMC in aphakic patients less than a year of age. Records of 49 patients (60 eyes) 17 years of age or younger (mean age 7.6 years) who had undergone TMMC for various etiologies were retrospectively reviewed. Success (IOP < 22 mmHg without glaucoma progression or visually devastating complications) rates were 67% at one year and 59% at two years. Young age (≥ 1 year) and aphakic status were statistically significant risk factors in multivariate analysis. Failure occurred in 60% of aphakic eyes and in 24% of phakic eyes. Failure occurred in 7 of 8 eyes of children < 1 year old and in 29% of 41 eyes of patients one to 17 years of age. Late onset, bleb-related endophthalmitis occurred in 5 of 60 (8%) eyes. Although TMMC demonstrated considerable efficacy in phakic patients greater than one year old in this and other reports, the authors express concern about the ‘substantial’ risk of infection with TMMC in aphakic infants.

Age less than one year and aphaia are risk factors for failure of TMMC in the two aforementioned retrospective studies. How do aqueous shunt devices compare? For children two years and younger, Beck, Freedman, and colleagues reported greater efficacy of aqueous shunt devices over TMMC. Only the minority of these patients studied were aphakic or pseudophakic. In this retrospective, age-matched comparison of aqueous shunt devices (ASD) and TMMC, Beck et al. determined the likelihood of maintaining an IOP of less than 23 mmHg in 46 eyes of 32 patients under two years of age. According to the authors, pressure below this level provides clinical stability in very young patients with glaucoma. For the 46 eyes receiving aqueous shunts, 16 eyes (34.8%) were aphakic or pseudophakic compared to three of 24 eyes (12.5%) in the TMMC group.

Beck and colleagues employed Baerveldt implants for 32 eyes and Ahmed valves for 14 eyes. After the aforementioned procedures, success achieved at one and three years was 87% and 53% in the ASD group, respectively, compared to 36% and 19% with the TMMC group at the same intervals. Interestingly, although the seton implantation group was comprised of more high risk patients (16/46 (34.8%) eyes aphakic or pseudophakic) than the TMMC group (3/24 (12.5%) eyes), the seton group overall (no separate success rates were reported for aphakic and pseudophakic patients) fared better (72% success versus 21% success in TMMC group) and had no infections (versus 8.3% in TMMC group). Infection is an even larger concern for contact-lens wearing aphakic patients.

The poor success rates and potential for infection with TMMC for young, aphakic patients in the retrospective studies previously discussed corroborate the results of Beck’s work discussed above. For the first surgical procedure for aphakic or pseudophakic patients on maximal medical therapy, seton implantation appears more likely to succeed in controlling IOP than TMMC, especially in infants.

Recently, Chen et al. report a success rate (defined as an IOP of ≥ 21 mmHg with or without medications and no need for further surgery) of 16% for goniotomies or trabeculotomies, 24.6% for trabeculectomy with mitomycin-C (MMC) or 5FU, and 44.1% for seton implants. Pakravan and colleagues performed a randomized prospective clinical trial in which patients were allocated to either TMMC or Ahmed valve with MMC. They did not find a significant difference in the success rates between the two groups. They only had 15 eyes in each group which decreases the power of their study. There was no significant
difference in the rate of complications between the two groups. 6 eyes in the TMMC group had complications which included 4 eyes with choroidal effusions, one with vitreous hemorrhage and one with endophthalmitis. 4 eyes had complications in the Ahmed valve with MMC group with 2 eyes having a choroidal effusion and two eyes a suprachoroidal hemorrhage in the first day after surgery. Ghadhfan and Khan 49 in their literature review of cases of suprachoroidal hemorrhage after pediatric glaucoma surgery conclude that MMC might increase the risk for delayed suprachoroidal hemorrhage and advice against its use with an Ahmed valve without evidence of improved valve function with its use. May be if MMC was not used when implanting an Ahmed valve in Pakravan’s clinical trial, the results would have been different.

Seton implantation size and type are additional surgical considerations. Higher success rates have been reported for Ahmed glaucoma valve implants, Baerveldt implants, and double-plate Molteno implants than single-plate Molteno implants 50-57. An attractive feature of Ahmed valve implants is the immediate pressure lowering effect delivered to the glaucomatous eye without a high risking of hypotony; the non-valved Baerveldt implants will not lower pressure until the temporary tube occluder is removed at least one month after the original surgery. Without this temporary tube occlusion the Baerveldt implant would produce marked early hypotony. Rapid IOP reduction may be less crucial in aphakic glaucoma than in patients with congenital glaucoma who fail angle surgery - these latter patients depend upon rapid clearing of the visual axis from lower pressure. Patients with aphakic glaucoma typically have clear corneas. It is easier to implant an Ahmed glaucoma valve than a Baerveldt in an infant due to eye and orbit size, but aphakic glaucoma is most commonly diagnosed four to five year after the cataract surgery is performed. The valve in the Ahmed implant may fail 58, and there is a greater probability of having a hypertensive phase in an Ahmed valve than in a Baerveldt in pediatric patients. The hypertensive phase tends to peak at a month and resolve by six months after Ahmed implantation in adults 59.

In children, success has been reported with Molteno implants 53, 60-62, Ahmed valve glaucoma implants 52,55,56, and Baerveldt implants 51,63,64. Since all types of glaucoma implants will demonstrate a decline in success rates over time 50, 65, 66, the ideal seton implant for the aphakic or pseudophakic child with glaucoma is not currently agreed upon. In a recent report on the long term outcomes after aqueous drainage device surgery in refractory pediatric glaucoma, Schotthoefer 66 and associates found that there was no significant difference between the success rates of Ahmed and Baerveldt implants in all of the patients with refractory glaucoma as a group (They did use Ahmed valve more commonly in aphakic glaucoma because in this group there is less of a need for a rapid lowering of IOP, it is possible that the success rates of the two implants would have been different if they stratified for the type of glaucoma). They also did not find a significant difference in the motility limitations or strabismus complications between the two implants 67.

Banitt and colleagues 68 report on the insertion of a pars plana Baerveldt implant to decrease the risk of anterior rotation of an initially well positioned tube in the growing pediatric eye. The authors concluded that Baerveldt glaucoma implant surgery with pars plana tube insertion is a reasonable option for managing aphakic and pseudophakic children with uncontrolled glaucoma. Complications of Baerveldt glaucoma implant surgery related to anterior chamber tube placement, such as tube-cornea touch, are minimized with this approach. The incidence of posterior segment complications, although possibly higher compared with limbal tube insertion, was not excessive.

Cycloablative techniques have been generally reserved for refractory cases of glaucoma in children 69-72. Reported success rates have been low if these techniques are used as the initial surgical option 73. Cyclocryotherapy and laser cyclophotocoagulation in children may result in severe complications in some patients. Reported complications include retinal detachment, sympathetic ophthalmia, and phthsis 74-76. Surgical revision or addition of a second tube implant can also be associated with high rates of complications such as new corneal edema 77. Supplemental transcleral laser photocoagulation is a viable alternative for children suffering tube failure 78. Several laser treatments may be required to achieve long term control.
Endocyclophotocoagulation is a relatively recent technique which has demonstrated some promise in treating refractory glaucoma in children and adults. Would this be applicable to children with aphakic glaucoma? Neely and Plager reported on 51 endoscopic diode laser cyclophotocoagulation procedures performed on 36 eyes of 29 pediatric patients. Cumulative success rates after all procedures at a mean of 19 months of follow up was 43%, which is similar to the 50% success rates achieved by Phelan et al and Bock et al with forms of transcleral Nd:YAG or diode laser. Severe visual complication rates were lowest with endocyclophotocoagulation (11% with the endoscope versus 50% or 19% of patients with transcleral Nd:YAG or diode, respectively). In fact, the authors point out that when combining their study with other studies of this procedure, only 1/123 diode endolaser treated eyes progressed to phthisis. In contrast, cyclocryotherapy is historically associated with more morbidity, as 12% to 34% of patients treated with cyclocryotherapy progressed to phthisis in past reports. Nonetheless, for aphakic patients especially, Neely and Plager report that endocyclophotocoagulation is not undertaken without risk, as retinal detachment, hypotony, and decreased vision all have occurred. Long term results are not available, so this procedure should still be used with caution in children with refractory aphakic glaucoma.

Carter, Plager and associates recently reported a 53% success rate with endoscopic diode laser photocoagulation after an average follow up of 44.4 months. They mention that they are increasingly using it as a primary procedure in aphakic glaucoma. 38% of the eyes received only one treatment and were deemed a success. Retinal detachment did develop in two eyes out of 34 in the first month, however, hypotony was not encountered despite 8 eyes having 360° of cycloablation.

Outcome: how well are we doing in the management of aphakic and pseudophakic glaucoma

Chen et al. report a median and mean final VA on the last follow up visit of 20/400 and 20/515 respectively. In their long term outcome study of pediatric aphakic glaucoma, Bhola and associates report a more promising visual outcome. At the time of the last follow up, 54.5% of their patients had a VA of 20/40 or better, 34.5% between 20/50 and 20/200 and 11% less than 20/200. They included all patients with an IOP above 25mmHg, so their outcomes may represent a mixed group of OHTN and glaucoma, though 64% of the eyes had an increase of 0.2 in the cup to disc ratio during the course of follow up and a similar percentage had visual field changes consistent with glaucoma. The percentage of eyes having 20/40 vision or better were equal in the unilateral and bilateral aphakic groups, however the percentage of eyes having less than 20/200 vision was greater in unilateral aphakia.

Summary

Ophthalmologists must be vigilant about assessing for post-operative glaucoma in children left aphakic or pseudophakic when cataract surgery is performed within 1st year of life. We recommend regular follow-up (if needed, examination under anesthesia) for early diagnosis of glaucoma in children operated at early age.

References


33. Leske MC, Heijl A, Hyman L, Bengtsson B, Dong L, Yang Z. Predictors of long-term progression in the early manifest glaucoma trial. Ophthalmology 2007; 114:1965-72.


38. Nilforushan N, Falavarjani KG, Razeghinejad MR, Bakhtiari P. Cataract surgery for congenital cataract:


Photoreceptor integrity following treatment of diabetic macular edema: a prospective OCT study

Dr. Sobha Sivaprasad MS ¹, Dr. Zdenek J Gregor MS ²

Abstract

PURPOSE: To describe changes of the foveal photoreceptor layer using optical coherence tomography (OCT) in diabetic macular edema (DME) treated with argon laser photocoagulation (ALP) or intravitreal triamcinolone (IVTA) and correlate these changes with visual outcome.

DESIGN: Analysis of OCT images from a prospective randomised controlled trial of ALP versus IVTA for DME.

METHODS: We studied the final OCT images of 71 eyes with diabetic macular edema. The tomographic finding of the foveal third hyper-reflective band (HRB) was classified into 2 groups: intact HRB and disrupted or absent HRB. The final visual outcome in these groups were compared in both the laser group and the IVTA group

RESULTS: The presence of the third HRB at the fovea was associated with better visual outcome in both treatment groups with the laser group showing statistically significant correlation.

CONCLUSION: Intact foveal third HRB is a reliable indicator of favourable final visual outcome following treatment of DME.

Introduction

Macular edema is the main cause of visual impairment in diabetic patients ¹. Timely macular (focal or grid) laser photocoagulation remains the principal therapy for sight-threatening diabetic macular edema (DME) and it reduces the risk of moderate visual loss by 50 % ². Due to the limitations of current treatment for DME, new pharmacological therapies such as intravitreal triamcinolone (IVTA) have been tried ³-⁶.

The long-term effects of IVTA can be unpredictable mainly due to the limited half-life of the drug and photoreceptor atrophy associated with advanced disease. Optical coherence tomography (OCT) allows objective, quantifiable, and reproducible measurements of the retinal layers. Evaluation of the reflectance of the posterior retinal structures have demonstrated two well-defined, linear hyper-reflective bands (HRBs) at the level of the outer retina in the macular region of healthy subjects ⁷. The inner HRB (third HRB) is thinner and is believed to correspond to the junction between the inner and outer photoreceptor segments while the outer HRB corresponds to the retinal pigment epithelium-choriocapillaris commonly visualised in the first generations of OCT. The presence or absence
of the 3rd HRB is thought to correlate with visual function.

In this study, we carried out an analysis of the OCT images obtained during a recently completed prospective RCT comparing macular laser with IVTA in the treatment of DME. The aim was to assess the influence of third HRB on the final visual outcome in patients with DME and compare those who were treated with macular laser or IVTA.

Methods

The study protocol adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Moorfields Eye Hospital. Patients were recruited from the Medical Retina clinics in the Hospital. Each eligible patient gave written, informed consent before entering in the study.

Patient Eligibility and Evaluation

Patients were included if they had refractory diffuse DME (defined as biomicroscopic and fluorescein angiographic evidence of clinically significant DME that is unresponsive to focal laser photocoagulation performed at least 3 months before evaluation). Each patient received a detailed ophthalmologic examination, including measurement of best corrected visual acuity (BCVA) according to a standardised refraction protocol using modified ETDRS charts 1, 2, and R, applanation tonometry, and slit lamp biomicroscopic examination every 4 months for 12 months. Investigations including digital colour fundus photography, fluorescein angiography and OCT were also performed at baseline, 4, 8 and 12 months.

Triamcinolone acetonide injection

Four milligrams (total volume, 0.1ml) of IVTA (Kenacort, Bristol-Myers Squibb, Paris, France) was injected into the vitreous under sterile conditions. The injection was performed under subconjunctival anesthesia with a 30-gauge needle. Repeat IVTA was performed at 4 monthly intervals if there was angiographic and OCT evidence of persistent DME.

Grid laser photocoagulation

Patients randomized to the laser arm underwent further macular grid photocoagulation according to the ETDRS guidelines. Treatment was repeated at 4 monthly intervals if there was angiographic and tomographic evidence of persistent DME.

Optical coherent tomography

We used high-resolution optical coherence tomography (Stratus model 3000; Carl Zeiss Meditec, Dublin, CA) with software version 3.0 to measure retinal thickness and assess retinal structure. With this third-generation instrument (OCT3) we recorded from each eye six 6-mm (~20°) line scans in a radial spoke pattern intersecting at fixation. Each tomogram consisted of 512 A-scans, each A-scan comprising 1024 data points spanning a 2-mm depth. The examiner (FI) asked each study participant to look at the internal fixation spot, which was kept in its central location, and confirmed that the image of the macula appeared to be approximately centred with respect to the spot’s image on the fundus monitor. The OCT software was used to position on the screen a vertical line that designated the centre of the scan image. During each scan, the examiner checked whether the fovea in the scan image was centred with respect to the vertical line. The vertical retinal sections of the OCT images at the final follow-up were converted into greyscale raw images. These images were graded for third HRB by two graders (SS and PP) masked to the treatment assignment. The foveal third HRB was classified into two groups: (i) intact or (ii) disrupted or absent so as to be able to assess whether visual acuity varied with the configuration of the third HRB. Patients with absent 3rd HRB band in the non-foveal area were excluded to avoid methodological artefact.

Statistical Analyses

The visual outcome was determined by the change in the number of ETDRS letters read at the final visit compared to baseline. The visual outcome was determined in three categories: all patients irrespective of treatment, post laser group and post IVTA group. The patients were classified into two groups. Group 1 were patients with intact third HRB. Group 2 consisted of patients with absent or disrupted third HRB at the fovea. The data were processed on computer (SPSS version 11.5; SPSS Sciences, Chicago, IL). Paired t-test was used to compare the visual outcome in patients in
group 1 and 2. P<0.05 was considered statistically significant. The inter-grader and intra-grader reliability were calculated using the kappa statistics.

Results

There were 45 patients in the IVTA arm and 43 patients in the laser arm of the study. Nine patients in the IVTA group and eight patients in the laser group were excluded from analysis because they were either lost to follow-up or the third HRB was not gradeable. Therefore, 36 patients in the IVTA group and 35 patients from the laser group were included in the analysis. There were no significant differences in baseline clinical characteristics of the patients studied (Table 1). The mean number of IVTA injections was 1.8 (range 1 to 3) while the mean number of further grid laser sessions was 2.1 (range 1 to 3) in this group of patients.

Table 1: Baseline characteristics of patients randomized to the two treatment groups

<table>
<thead>
<tr>
<th></th>
<th>IVTA group</th>
<th>Grid laser group</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of eyes</td>
<td>36</td>
<td>35</td>
</tr>
<tr>
<td>Mean age in years</td>
<td>60.82</td>
<td>62.43</td>
</tr>
<tr>
<td>Duration of diabetes in years</td>
<td>15.15 years</td>
<td>14.96 years</td>
</tr>
<tr>
<td>Mean previous laser</td>
<td>3.2</td>
<td>3.1</td>
</tr>
<tr>
<td>Proliferative diabetic retinopathy</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Mean HbA1C</td>
<td>7.31</td>
<td>7.58</td>
</tr>
<tr>
<td>Baseline visual acuity (ETDRS letters) mean ± SD</td>
<td>51.60 ± 11.31</td>
<td>53.12 ± 10.84</td>
</tr>
<tr>
<td>Baseline CMT mean ± SD (μm)</td>
<td>438 ± 105</td>
<td>441 ± 98</td>
</tr>
</tbody>
</table>

There were also no significant differences in baseline clinical characteristics of the patients categorised depending on the presence of the foveal third HRB (Table 2).

Table 2: Baseline characteristics dependent on the presence of third HRB

<table>
<thead>
<tr>
<th></th>
<th>Third HRB intact</th>
<th>Third HRB not intact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>61.29 ± 3.2</td>
<td>60.92 ± 2.7</td>
</tr>
<tr>
<td>ETDRS letters at baseline (mean ± SD)</td>
<td>52.31 ± 14.28</td>
<td>53.12 ± 15.32</td>
</tr>
<tr>
<td>Mean foveal thickness (μm) at baseline</td>
<td>467 ± 105</td>
<td>459 ± 112</td>
</tr>
</tbody>
</table>

Intact 3rd HRB was associated with better final visual outcome (table 3). This was statistically significant in the laser group although the IVTA group also suggested a similar trend.

Table 3: Mean change in visual acuity at 12 months follow-up

<table>
<thead>
<tr>
<th></th>
<th>Third HRB intact</th>
<th>Third HRB not intact</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>+4.2 (n=36)</td>
<td>-2.68 (n=35)</td>
</tr>
<tr>
<td>Patients in the laser group</td>
<td>+6.16 (n=18)</td>
<td>-1.05 (n=18)</td>
</tr>
<tr>
<td>Patients in the IVTA group</td>
<td>+2.27 (n=18)</td>
<td>-4.14 (n=17)</td>
</tr>
</tbody>
</table>

+ indicates gain in ETDRS letters; - indicates loss in ETDRS letters

The mean change in central macular thickness in the two treatment groups at 12 months follow-up were not statistically different (p=0.2). Change in central macular thickness were also not significantly different in the two third HRB groups (p=0.09).

Discussion

This study shows that the presence of an intact third HRB is an important determinant of final visual prognosis following treatment of diabetic macular edema. Macular edema can affect all layers of the retina and may even cause a serous macular detachment. However, good visual recovery is independent of the location of the macular edema or the central macular thickness.

The 3rd HRB has been evaluated in many conditions such as retinitis pigmentosa, resolved central serous retinopathy and following the management of macular edema secondary to branch retinal vein occlusion with intravitreal tissue plasminogen activator. 8-10 In all these conditions, the presence of intact third HRB was associated with better visual prognosis. Our study complements these studies and indicates that an intact 3rd HRB may be a better surrogate marker of visual acuity than the reduction in central macular thickness following treatment for DME.

The higher resolution of the new ultrahigh-resolution OCT (UHR OCT) system confirmed that the third HRB detected by Stratus OCT3 represents the junction between the inner and outer segments of the photoreceptors. 11 Damage of photoreceptors may occur...
as a consequence of the macular edema and the treatment and may be responsible for the reduced visual acuity seen in patients despite return to normal macular thickness.

Macular edema, especially long-standing cases and those associated with ischaemia may be more prone to photoreceptor dysfunction and atrophy. The exact mechanisms underlying the beneficial effects of laser photocoagulation are poorly understood but it is thought that laser causes loss of photoreceptors thereby decreasing the oxygen consumption of the outer retina and reducing production and release of angiogenic stimuli. Similarly, animal studies have shown that IVTA produces dose-dependent toxic effects on the retinal photoreceptors and pigment epithelium. Although the edema and the treatments may cause photoreceptor atrophy, it is unclear why the loss of the third HRB is noted in some and not in others.

Further studies are required to determine the factors that cause the loss or disruption of the 3rd HRB.

References


LMI-A New Mirror Telescopic IOL
(A New Solution For The Optical Rehabilitation Of Patients With Age Related Macular Degeneration And Other Macular Pathologies)

Prof. Amar Agarwal MS FRCS FRCOPHTH, Dr. Isaac Lipshitz MD

Introduction

Macular pathologies cause a great amount of morbidity and mortality world wide and have significant impact on community health. Age related macular degeneration (ARMD) is the leading cause of legal blindness in the industrial world. ARMD has been divided into dry or exudative and wet or nonexudative types. Recently the AMD prosthetic device, Implantable Miniature Telescope (IMT- by Dr. Isaac Lipshitz), was tested. The drawbacks encountered in the IMT included loss of peripheral vision in the implanted eye, difficult surgical technique, endothelial compromise (Fig 1), blocked peripheral retinal visibility, difficulty in future retinal laser treatments, difficulty due to the size & weight of the implant, severe aniseikonia due to disparity of images of two eyes etc.

To solve these problems, we designed a new IOL, which magnifies the image on the retina based on a mirror telescope: the LMI-Lipshitz Macular implant. The implant was designed by one of us (Dr. Isaac Lipshitz). We aimed to test this IOL not only on patients with dry or wet ARMD but also other diseases which affect the macula thus affecting central vision. This was the first experimental trial of this novel surgical implant.

LMI-Mirror Telescopic IOL

The LMI (Fig 2) is a regular IOL that incorporates two miniature mirrors in Cassagrain telescopic configuration. These mirrors act by modifying the image on the retina (Fig 3) The IOL has a dual optical system which ensures that light passing through the center of the optic is magnified by the Cassagrain telescope whereas the light passing through the periphery passes through the normal IOL configuration. Overall diameter
of the IOL is 13mm and the size of the optic is 6.5 mm. The anterior, central mirror size is 1.4 mm. The posterior mirror is doughnut shaped and 2.8 mm in diameter with a central clear area of 1.4 mm diameter. The peripheral zone of the optic is similar to a normal IOL for undisturbed peripheral vision. The reflecting surfaces of the LMI are coated with multiple layers of TiO2 & SiO2 (dielectric coatings) thus creating the mirror effect. The thickness of these mirrors is only 1-2μ. The entire IOL is also coated with Parylene C (poly-para-xylylenes) for the reasons of biocompatibility.

This LMI was designed to have x 2.5 magnification i.e. it magnifies the central image on the retina 2.5 times (Fig 4). The subject thus sees a magnified central image through the mirror telescope and a normal non-magnified image through the periphery of the IOL, thus increasing the magnified central vision while maintaining the orientation in space due to normal peripheral vision. Testing was done on the lab while preparing the IOL (Fig 5).

![Fig. 2- The new mirror telescopic IOL –LMI (Lipschitz macular implant) (US patents filed)](image)

![Fig. 3- Illustration depicting the LMI-mirror telescopic IOL.](image)

![Fig. 4- The IOL magnifies the central image on the retina](image)

**Patient Selection Criteria**

Patients with bilateral macular pathologies with visual acuity less than 20/200, cataract less than NS grade II and having no other ocular or systemic diseases and in whom the vision improved when tested with x 2.5 external telescope preoperatively were selected. Informed consent was taken from all patients after explaining to them the potential benefits and possible complications of the procedure. Patients’ motivation, communication skills and availability for follow-up of upto 12 months was considered before including them in the study.

**Surgery**

All surgeries were performed by same surgeon (Am A). Conventional phacoemulsification or 700 micron cataract surgery (Microphakonit) (7) was performed (Fig 6 and 7) or coaxial phaco was done. The corneal tunnel was increased with diamond knife or regular keratome to 6.5mm and the IOL was placed in the bag. One patient was pseudophakic and in that case explantation of existing IOL was performed followed by implantation of LMI (Fig 8-10).

![Fig. 5- Lab studies done while designing the LMI](image)

![Fig. 6- Microphakonit- 700 micron cataract surgery](image)
2 of the patients had initial loss of lines in the operated eye when measured 1 week postoperatively which had improved at the 1 month follow-up in one patient and at the 6 month follow-up in the other patient. At the end of 6 months, none of our patients had any decrease in distance visual acuity. The mean postoperative distance visual acuity in decimal equivalent at the end of 6 months was 0.133 as compared to 0.067 preoperative values.

**Endothelial density**

The eyes were evaluated for endothelial cell density and loss. The mean endothelial cell count in operative eyes was $3018.33 \pm 513.09$ which at the end of study was found to be $2842.66 \pm 593.01$. The mean change in the operated eye was $-5.79 \% \pm 4.07 \%$.

**Postoperative corneal endothelial-LMI distance**

All the patients were found to have anterior chamber depth within normal range. Photos of anterior segment OCT (Fig 11) shows normal position of LMI and normal anterior chamber dimensions.

**Ease in fundus evaluation**

Fundus evaluation of all patients was done by the same retina specialist in order to grade the difficulty in fundus examination using indirect ophthalmoscope and to assess the possibility of future retinal photocoagulation for peripheral retinal pathology. It was found that the difficulty level encountered was of Grade I in all the quadrants. Good central fundus view was also possible in all the patients.
Grading system for assessing ease of fundus evaluation

Grade 0  No difficulty
Grade I  Ora Seen
Grade II  Ora seen but with problem of glare
  View upto mid-periphery only
Grade III View upto equator only
Grade IV  Only central fundus seen (disc & macula)

Discussion

Patients with ARMD usually have difficulty in reading and also difficulty in seeing near objects like inability to recognize faces clearly. Other macular pathologies will also cause similar difficulties with varying degree of severity. Optical modalities available to improve the size of the image on the central retina in these patients like low vision aid loops, magnifiers etc. can be used. But this is all at the expense of loss of field of vision and depth of focus. Also the short reading distance, distortion of images, weight & large size are the problems associated with these devices. Some new devices like head mounted video-based image processing system are also available. But the problem of handling, which is the most common cause of failure of low visual aids 16, is associated with them also. Implantable Miniature Telescope (IMT by Dr. Isaac Lipshitz) was used previously with limited success. The new implant is free from the complications associated with IMT.

The LMI is similar to an usual IOL used after phacoemulsification and is fully placed in the bag in a similar way. It provides magnified central image upto 2.5 times the normal while maintaining the normal peripheral vision through the peripheral portion of the lens unlike IMT 17. Because of this it can be used in both eyes of a patient. If there is any further deterioration of the macula, increased magnification can be achieved by adding the plus eyeglasses up to +4.00 D range. There is no relative movement between the eyes and the LMI unlike an external telescope. It requires 6.5 mm corneal incision unlike more than 10mm in the case of IMT thus reducing surgically induced astigmatism 18. In this study we found the postoperative examination of these patients easier with only minimal glare problem due to inadvertent reflection from mirrors. This provides no difficulty for future retinal photocoagulation in contrast to IMT which has limited possible fundus view. Fluorescein angiography results of patients show good visibility of retina upto mid periphery in experienced hands as shown in the photos. Photographs taken through the center of the lens had reflexes due to reflection from the posterior mirror which blocks the visibility of half of the view but those taken from the periphery of the optic after complete dilatation of the pupil had satisfactory retinal view. No significant endothelial loss was noted as the surgery was similar to conventional surgeries for IOL implantation after phacoemulsification and the size of the LMI was quite small as compared to IMT.

References

9. Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) Study Group. Photodynamic Therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin; One- year results of two randomized


Refraction abnormalities prevail in the world profile of ophthalmic diseases and require timely correction, including surgery. Both ophthalmologists and patients have shown increasing interest to different keratorefractive interventions. However, some authors consider that in patients with ametropia, routine methods, i.e. spectacle and contact lenses, can provide high functional results. It means that surgery aims at a cosmetic effect. And only in astigmatism, keratorefractive operations (KRO) are considered to be pathogenetically substantiated. Thus, the requirements of the results of correction should be rather high.

Despite high level of modern KRO, adequate equipment and minimal possible trauma, any operation causes complex biochemical, immunological, and morphological alterations in eye tissues, that can provoke in certain conditions development of postoperative complications. In all cases, compensatory mechanisms start which are directed towards restoration of homeostasis but in some cases they appear to be insufficient.

In this case, postoperative complications of KRO caused by failure of regenerative process develops which includes the following:

- neurotrophic epitheliopathy
- edema and non-infectious inflammation of corneal flap
- non-specific diffuse intralamellar keratitis
- early subepithelial fibroplasias – haze
- certain forms of secondary syndrome of dry eye
- allergic kerato-conjunctivitis
- retardation of re-epithelialization of the zone of surgery
- hyperplasic processes (for example, epithelial hyperplasia) and some other effects.

Epidemiological data about KRO complications vary within a wide range because of, in particular, different approaches to interpretation of the term “complication”. Routine criterion for development of KRO complication implies deterioration of corrected visual acuity as compared to preoperative values. Thus, published data on postoperative complications are large. Lately, more rigid criteria have been formulated for the term: “KRO complication” which means any aberration in the normal course of surgery or postoperative period, which requires additional manipulations or drug therapy even without deterioration of final result of the surgery.

According to this approach, the rate of complications is rather higher:

1) The rate of subepithelial fibroplasias (haze) one month after PRK achieves 60% (in patients with high degree of ametropia). Under the influence of intense drug therapy (corticosteroids, enzyme therapy (Lidaza), and application of antiproliferative agents such as mytomycin) and as a
result of spontaneous regression, rate of residual fibroplasias one year after PRK does not exceed 9 % (in initial mixed or stromal forms of haze) and requires repeated surgery in not more than 3 % of cases 5,36,53.

2) Neurotrophic epitheliopathy (NE), according to different authors, is found in 11.2-48 % of cases. Some authors do not distinguish NE as separate complication but include it into complex of symptoms of secondary dry eye induced by KRO on the basis of the fact that the rate of NE is significantly higher in the group of patients with impairment of lacrimation. However, in some cases, signs of secondary dry eye do not accompany NE. The cause of more frequent detection of NE in this group of patients is common etiology of complications: development of both NE and secondary impairments of lacrimation are caused by mechanical damage to intrastromal corneal nerves in the course of KRO. The difference is that NE is mainly caused by failure of neurotrophic function of intrastromal nerves, while development of secondary dry eye is mainly caused by separation of neuronal connections of receptor areas and glands, which produce lacrimal fluid 9,54,59.

3) Transitory secondary dry eye forms in 8.2-45 % of cases after LASIK and somewhat rarely after PRK (up to 17% of cases) 18,39,44.

4) Non-specific diffuse lamellar keratitis (DLK) – syndrome “Sahara sands” develops in 1.3-1.9 % of cases. Till now, there is no generally accepted concept of DLK etiology, it is supposed to be caused by powder from surgical gloves, metal microparticles from cutting edge of microkeratome, lipid and mucin secretions of conjunctival glands, autoimmune reactions, and recently there are some articles about failure of local metabolic processes induced by KRO as important factor of DLK development 33,55,60.

As a rule, complications, listed above, are rather successfully cured but they require long-term application of drugs, which are cumbersome for the patient on the whole 5,27. This prolongs significantly the period of visual and social rehabilitation of patients, deteriorates life quality of active working people, and prolongs sick-list time 42.

It was noted that these KRO complications are recorded more frequently in patients with certain ophthalmic and system diseases.

This was the base for determination of the following risk factors for KRO complications.

- long-term application of contact lenses;
- preceding surgeries on the cornea;
- aggravated ophthalmic anamnesis (particularly, infectious keratoconjunctivitis);
- age before 18 years and after 40 years;
- long-term hormone substitutive therapy;
- inclination to keloid formation;
- allergic and autoimmune diseases (bronchial asthma, neurodermatitis, psoriasis, atopic dermatitis, rhinitis, etc.)

Due to different mechanisms, these risk factors interfere in general and local (in eye tissue) metabolic, hormonal, and immune processes. This decreases significantly compensatory abilities of the organism to restore homeostasis after the influence of exogenous destabilizing factors such as surgery or trauma. Initiation and persistence of metabolic and immune misbalance cause development of certain postoperative complications of KRO 1,4,14,31,40.

Many authors have shown that excimer laser ablation of the cornea is accompanied by development of surgically induced oxidative stress (SIOS) at the level of tissue. It aggravates the course of posttraumatic inflammatory reaction and is one of the main pathophysiological mechanisms of disregenerative postoperative complications 16,21,28.

SIOS is the impairment of balance between pro- and anti-oxidative systems in tissues of the anterior eye segment. Among causes of SIOS, the main one is generation of free radicals and active forms of oxygen under the influence of excimer laser.

Besides, influence of excimer laser leads to inhibition of glutathione-dependent antioxidative system of the cornea. In the case of insufficient activation of other chains of anti-oxidative protection, it leads to aggravation of SIOS 16.
SIOS is intensified by chronic psycho-emotional tension and unbalanced nutrition with deficiency of bioantioxidants typical of urbanization.

SIOS produces multifactor pathological influence on eye tissues.

1) Intensification of lipid peroxidation (LPO) leads to increased cell membrane permeability, ion misbalance, separation of tissue respiration and oxidative phosphorylation in mitochondria, and, as a result, decreases ATP production. Energetic starvation interferes into all energy-dependent processes. Impairment in function of transport protein aquaporin-5, which provides energy-dependent trans-membrane transportation of water molecules, results in long-term aseptic edema of the corneal flap. Regeneration of quickly renewing tissues is affected that is accompanied by retarded re-epithelialization of corneal erosions, long-term neurotrophic epitheliopathies, etc.

2) Oxidative modification of DNA causes abnormal regeneration of corneal cells with altered cytophysical and antigenic properties. This initiates cascade of autoimmune reactions, which play the role in formation of DLK. Besides, altered keratocytes synthesize abnormal collagen, which is deposited chaotically and is visualized as the component of early haze.

3) Lipoperoxidation of proteins of cytoplasmic membranes and direct cytotoxic influence of LPO induces cytolysis of epithelium and keratocytes that is manifested by retardation of re-epithelialization and formation of so called acellular zone along both sides of interface lacking in keratocytes. This phenomenon was first diagnosed with the help of confocal microscopy. There are hypothesis that long-term existence of acellular zone alters biomechanical properties of the cornea and may be the cause of iatrogenic keratectasia.

4) Irreversible conformation of glycosaminoglycans molecules, for example, increase of number of cross-links in hyaluronic acid, causes alteration in mucin layer of lacrimal film that leads to alteration of its stability and induces development of a special form of secondary dry eye.

The factors mentioned above indicate that SIOS plays the main role in formation of certain postoperative complications of photorefractive surgery. Impairment of protein metabolism with prevalence of catabolic reactions over anabolic ones is another factor induced by KRO and aggravated by secondary alteration by SIOS. This leads to impairment of the balance between cytolysis and cellular regeneration, synthesis and inactivation of enzymes and other protein-containing substances playing an important role in cellular metabolism.

Thus, KRO has multifactor influence, which causes the development of the complex of alternative-regenerative processes. They are reflected in deep biochemical reconstructions at the regional level, first of all in the cornea. They are specific and precede the development of clinical picture of postoperative complications.

Lacrimal fluid is an available diagnostic medium for evaluation of metabolic processes in the eye as it is constant, dynamically renewing micro-medium of the anterior segment of the eye. It is tightly connected with local metabolic processes. On the other hand, non-invasion method of lacrimal fluid collection is an important advantage.

Besides, objective evaluation of dynamics of regenerative processes after KRO and search for subclinical signs of postoperative complications are impossible without precise methods of visualization of corneal ultrastructure. Confocal microscopy, which is recently widely introduced into different fields of ophthalmology, provides valuable assistance in examination of corneal morphology in vivo. Confocal microscopy allows examination of biological tissues at the cellular level at the state of physiological activity and demonstration of results in three dimensions – height, width, depth, and time.

For the first time, principle of confocal microscopy was described by Minsky in 1957. He proposed the system, where the lenses of illuminator and objective focused in one point (had common focal points) that gave the name of “confocal” microscopy (Fig. 1). Confocal microscopy allowed significant increase of axial (5-10 um) and lateral (up to 1-2 um) resolution of microscopy due to exclusion from focal points of
information from adjacent areas. This makes possible 600 times magnification of image without the lost of contrast and clearness\textsuperscript{30,43}.

White light passing through the first perforation in the disk is focused on the focal plane in the cornea with the help of collecting (convex) lens. Reflected ray is refracted on the lens of the objective and, passing through the outlet in the disk, achieves camera-detector. All rays, which are focused above and under the focal plane, are cut off with the help of perforations in the disk and do not achieve the camera.

Increasing interest to KRO and successes in the study of histomorphology of the cornea in vivo using confocal microscopy open wide prospects for the study of the cornea after different types of surgery: evaluation of cellular reactions related to healing process, migration of different types of cells and cornea remodeling, process of re-innervation of the cornea, formation of Haze, and cicatrisation of the cornea, reasons of formation of iatrogenic keratectasia in the case of preservation of sufficient thickness of residual stroma and several other questions that can be answered by confocal microscopy\textsuperscript{15,30,34,35}.

Modern confocal microscopes allow one to visualize cellular composition of different corneal layers, to measure thickness of the corneal valve and residual stroma, to determine localization and length of subepithelial fibroplasia, to measure thickening of the cornea, which causes regress of refractive effect after PRK, and to analyze the type of inclusions in the interface\textsuperscript{22,49,50,56}.

Although several studies on this topic have been published, there are no integrative studies connecting histomorphological alterations in the cornea of patients in vivo with metabolic processes in eye tissues in the course of reparation after KRO and during the development of complications.

All facts mentioned above, and twenty years experience of active scientific and surgical activity in the field of excimer laser surgery gave us an idea to study morphological and metabolic features of typical and pathological regenerative process in the cornea after different keratorefractive interventions, to develop objective methods of evaluation of individual reaction of eye tissues on surgical intervention, and to propose algorithm of diagnosis, prophylaxis, and correction of disregerenerative complications.

**Materials and Methods**

**Clinical characteristics of examined patients**

We studied 213 patients (394 eyes) with myopia to solve different tasks of this study (table 1).

There were the following principles of formation of groups:

1. **Control group** included patients with myopia who used spectacles for optic correction.

2. **The first main group** was formed to study specific features of typical postoperative course of different KRO. It comprised patients with myopia, initially unaltered cornea, and uncomplicated postoperative period. Based on the type of surgical correction, the group was divided into two subgroups:
   - 1a – patients with myopia, who have undergone LASIK;
   - 1b – patients with myopia, who have undergone PRK.

3. **We formed the second main group** to study specific features of atypical postoperative period of different types of KRO. This group comprised patients with myopia, initially unaltered cornea, and disregerenerative postoperative complications recorded three days to four months after surgery. Based on the type of surgical correction, the group was divided into two subgroups:
   - 2a – patients with myopia, who have undergone LASIK;
   - 2b – patients with myopia, who have undergone PRK.

4. **We formed the third main group** to prove effectiveness of the algorithm of prediction,
diagnosis, and correction of dismetabolic complications of KRO, developed in the course of the study. It comprised patients with myopia and initially altered cornea because of long-term history of contact lenses with development of neovascular keratopathy or KRO, who were intended for LASIK.

5. Additionally, we examined healthy volunteers with emmetropia (to develop the method of examination and to determine normal biochemical parameters of lacrimal fluid).

**Screening system for studying functional tear complex**

Lately in refractive surgery, much attention is paid to examination of condition of functional tear complex (FTC), which is implied to consist of eye surface, tear-producing organs, and their neuroreflexive interactions. We used the following diagnostic tests to evaluate condition of FTC:

1. **Schirmer test-1** – evaluation of total (basal and reflexive) tear production. The test is based on moistening of standard sterile strips of filter paper during a certain time. We used ready-to-use test strips “Bausch&Lomb” (USA). Results were evaluated in millimeters of moistened part of the strip during five minutes.

   We used the following criteria to interpret the data obtained:

   - more than 25 mm during 5 minutes – hypersecretion;
   - 15-25 mm during 5 minutes – normosecretion;
   - 10-15 mm during 5 minutes – intermediate condition;
   - less than 10 mm during 5 minutes – hyposecretion of lachrymal fluid.

2. **Schirmer test-2 (modification by Jones)** – examination of value of basal tear production.

   Method of testing: after preliminary instillation of anesthesia, lacrimal fluid and residual anesthetics were accurately absorbed by cotton tampon from inferior fornix of conjunctiva. Then filter paper strip was placed under the lower lid of the patient for 5 minutes (as in Schirmer test-1). Moistening of more than ten millimeters of standard test strip during five minutes was considered to be normal.

3. **Test for evaluation of tear film break-up time (Norn’s test)** – examination of tear film stability indicating condition of its mucin and lipid layers.

   Method of testing: 0.2 % sodium fluorescein solution was instilled into conjunctival cavity with subsequent examination of patient’s eye using slit-lamp with cobalt filter. Time interval between the last blinking and appearance of first dry spots was evaluated. Parameters for evaluation of results: norm – from 15 to 45 sec., 10-15 sec. – intermediate
values, less than 10 sec. – instability of tear film. In cases of intermediate or decreased values of break-up time test it was repeated three times, accepting the average value as the result.

4. **Evaluation of the corneal condition** is based on the ability of fluorescein solution instilled into conjunctival cavity to indicate epithelial defects.

Method of testing: condition of the corneal epithelium is evaluated after instillation of 0.2 % sodium fluorescein solution into conjunctival cavity using biomicroscopy with cobalt filter. For quantitative evaluation of epithelial damage, the cornea was divided into five zones. Staining in each zone is evaluated using four-points scale:

1 – dotted defects (to ten spots);
2 – moderate;
3 – average;
4 – severe alteration. Then marks for each zone are summarized. Maximal mark is twenty.

**Method of investigation of biochemical composition of lacrimal fluid (LF).**

LF was collected from inferior fornix of conjunctiva using laboratory micropipette with disposable sterile tips or glass microcapiller without preliminary stimulation of lacrimation (Fig. 3).

To exclude influence of drugs on composition of lacrimal fluid, samples were collected at the same time in all patients (from 8.30 to 9.00 a.m.).

Biochemical examination of LF was performed using automatic analyzers “Express Plus” (Bayer, USA), “Hitachi-912” (F Hoffmann-LA Roche LTD, France), and spectrophotometer. The following parameters were studied: parameters of free-radical oxidation (malonic dialdehyde), anti-oxidative protection (superoxide dismutase), protein synthetic activity of cells (total protein), and activity of protein degradation (urea).

To evaluate severity of damage to the cornea after KRO, in all patients pre- and postoperatively, we calculated values of earlier developed biochemical coefficients of SIOS and degree of impairment of synthesis/ degradation of protein (SDP) using the following formulas:

1) \( K_1 \) – coefficient of evaluation of SIOS degree in tissues of the anterior eye segment:

\[
K_1 = \frac{MDA \times 1000}{SOD} - 54.0
\]

where

- MDA – content of malonic dialdehyde, parameter of activity of free-radical oxidation;
- SOD – activity of superoxide dismutase, the most active enzyme of anti-oxidative protection of the cornea;
- 54 is the mean ratio of MDA x 1000/SOD in healthy people.

If \( K \) lower than 8, corneal damage is absent, \( K \) is from 8 to 38 – light damage of the cornea, \( K \) is from 38 to 55 – average damage, \( K \) is from 55 to 75 – severe damage, \( K \) is from 75 and higher – extremely severe damage.

2) \( K_2 \) – coefficient of evaluation of degree of impairment in the system of SDP:

\[
K_2 = 4.9 - \frac{P}{U}
\]

where

- \( P \) – content of the protein, an indicator of protein-synthetic activity of cells;
U – content of urine – the product of biodegradation of proteins,
– average value of ratio P/U in tears of healthy people;
If K lower than 0.7, corneal damage is absent,
K is from 0.7 to 1.4 – light damage of the cornea,
K is from 1.4 to 2.8 – average damage,
K is from 2.8 to 4.1 – severe damage,
K is from 4.1 and higher – extremely severe damage.

Method of confocal microscopy of the cornea
We used confocal microscope Confoscan 4 (Nidek, Japan) with the following parameters: lens for examination through immersion gel – 40x, NA 0.75, WD 1.98, Zeiss; examined zone of the cornea was 460x345 um, image obtained was 768x576 pixel, lateral resolution – 0.6 um/pixel, and speed of scanning was 25 images per second. We used automatic mode for examination of the whole thickness of the cornea, manual mode for visualization of certain corneal structures, automatic calculation of density of endothelial cells with evaluation of polymorphism and size of cells, and optic pachymetry (using Z-ring).

Examination was performed after one instillation of local anesthetic through immersion gel.

All the special examinations was performed in all patients before surgery and one hour to 12 months postoperatively.

Technology of keratorefractive surgeries
Leading ophthalmosurgeons of excimer laser refractive department of the Center of Laser Surgery of Eye Microsurgery Complex operated all patients in the various groups.

Standard preoperative preparation in all types of KRO was identical and consisted in antibiotic installations three times a day two days prior to operation.

Technology of LASIK procedure
LASIK procedure was performed using standard technology accepted in Eye Microsurgery Complex with the use of modern home excimer ArF laser “MicroScan” created in collaboration with the Center for Physics and Instrument-making Industry of the Institute of General Physics of Russian Academy of Sciences. The device functions at frequency of 100 Hz, it is equipped by formation system according to the technology of “flying spot” with diameter of 1.0 mm and highly sensitive system of control over the movements of patient’s eye – “eye tracking system”.

The corneal flap was formed by microkeratome “Zyoptix” (Bausch & Lomb, USA) with head “120”, which allows one to form the flap 100±20μm thick, according to the data of the producing company. Our previous studies on flap thickness with different microkeratomes performed with the use of optical coherence tomograph “OCT Visante” (Carl Zeiss Meditec Inc., Germany) showed that thickness of the corneal flap, which is formed by keratome “Zyoptix” with the head “120” is 105.3 μm, on average (95 to 110 μm) (Fig. 5).

Standard postoperative therapy consisted of regular instillations of :
- antibiotics three times a day up to seven days postoperatively (3-5 days, on average);
corticosteroid medicines during 2-3 weeks postoperatively according to a decreasing scheme beginning with three times a day.

**Technology of PRK operation**

PRK was also performed using excimer laser “MicroScan”. In all patients, we used an original transepithelial technology of ablation – without preliminary scarification of epithelium. We have developed special algorithm of the first stage of PRK, which allows us to achieve even removal of epithelium on the whole area of correction (area of de-epithelialization zone depends on the diameter of transition zone of operation) The system of interactive control over the process of epithelial ablation provides total differentiated removal of epithelium without refractive effect. This allows us to use standard nomograms of the laser for refractive keratectomy itself at the second stage of correction.

Transepithelial technology of PRK decreases the risk of development of subepithelial fibroplasia due to decrease of stimulating effects of products from destroyed epitheliocytes on synthesis of non-organized collagen by stromal fibroblasts. Conical microscopy showed that corneas were intact in all patients. This indicates homogeneity of groups and gives grounds for further correct comparison and interpretation of results.

The operation was completed by application of bandage contact lens, which decreases postoperative pain syndrome and stimulates re-epithelialization.

Standard postoperative therapy consisted of two stages:

1) the first stage (before re-epithelialization of the corneal erosion) during 3-5 days:
   - antibiotic – three times a day;
   - non-steroidal anti-inflammatory drug – three times a day;
2) the second stage – up to two months postoperatively:
   - corticosteroid medicines in tapering doses scheme.

**Results and discussion**

At first examination, parameters of FTC and biochemical tests of LF of control group and the first main group did not differ significantly (p<0.5) (Tables 2, 3). Confocal microscopy showed that corneas were intact in all patients. This indicates homogeneity of groups and gives grounds for further correct comparison and interpretation of results.

All patients of the first and second main groups underwent KRO without intra-operative complications.

Results of complex dynamic examination of patients of the first main group after KRO:

**Investigation of FTC**: In all patients in early postoperative period (from one hour to three days), we found intensification of reflexive tear production that distorted results of examination of basal secretion of LF and Break-up Time Test, and different degree of damage to corneal epithelium (from 4.9 points after LASIK to 12.3 points after PRK according to twenty points scale). Later on, we noted general tendency to decrease of total (Schirmer test-1) and basal (Schirmer test-2) tear production (maximally pronounced after

**Table 2.** Results of FTC analysis in patients of control group and the first main group at first examination (M±s)

<table>
<thead>
<tr>
<th></th>
<th>Control Group</th>
<th>1&lt;sup&gt;st&lt;/sup&gt; Main Group</th>
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<tbody>
<tr>
<td></td>
<td>1a</td>
<td>1b</td>
</tr>
<tr>
<td>Shirmer-1 Test, in mm for 5 min (I±o)</td>
<td>20,5±1,5</td>
<td>21,0±1,2</td>
</tr>
<tr>
<td>Shirmer-2 Test, in mm for 5 min (I±o)</td>
<td>12,3±0,5</td>
<td>12,2±0,3</td>
</tr>
<tr>
<td>Break-up time test, sec (I±o)</td>
<td>19,1±0,7</td>
<td>18,9±0,7</td>
</tr>
<tr>
<td>Corneal Epithelium Assessment, points (I±o)</td>
<td>1,9±0,5</td>
<td>2,1±0,4</td>
</tr>
</tbody>
</table>

**Table 3.** Results of biochemical analysis of LF in patients of control group and the first main group at first examination (M±s)

<table>
<thead>
<tr>
<th></th>
<th>Control Group</th>
<th>1&lt;sup&gt;st&lt;/sup&gt; Main Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1a</td>
<td>1b</td>
</tr>
<tr>
<td>Total Protein, g/l</td>
<td>19,1±1,8</td>
<td>18,8±2,0</td>
</tr>
<tr>
<td>Urea, mmole/l</td>
<td>3,87±0,5</td>
<td>3,90±0,3</td>
</tr>
<tr>
<td>Malonic dialdehyde, μmole/l</td>
<td>1,39±0,22</td>
<td>1,41±0,22</td>
</tr>
<tr>
<td>Superoxide Dismutase, Un/l</td>
<td>25,1±2,0</td>
<td>25,6±2,2</td>
</tr>
</tbody>
</table>
LASIK) accompanied with decrease of stability of tear film (Break-up time test) (also maximally pronounced after LASIK) with gradual normalization of parameters by 6 (after PRK) and 8 months (LASIK) postoperatively. Degree of damage to epithelium after all types of KRO gradually decreased and reached initial values by month 1-3 of postoperative period (Figs. 6-9).

The study showed that analysis of FTC allows quick (to 15 minutes) evaluation of severe alterations of eye surface but has low specificity and does not meet the requirements of subclinical diagnosis of postoperative complications.

Investigation of biochemical coefficients of degree of corneal damage in dynamics of postoperative period of KRO was most interesting for us. It was noted that acquisition of reliable data on metabolic status of the anterior eye segment is possible from the second day after LASIK and third day after PRK (i.e. after cessation of pronounced reflexive tear production, which coincide with re-epithelialization of the area of surgery).

Results of dynamical coefficients in patients with uncomplicated postoperative period after KRO are presented on figures:

Dynamic study of coefficients in patients after KRO showed the following:

1) In uncomplicated course of PRK, values of coefficient evaluating SIOS (K1) in early postoperative period were within ranges of severe degree, impairments of SDP were of average degree. Values of coefficients reached norm by eight (K1) and six (K2) months postoperatively.

2) After LASIK, alterations of metabolic status (K1 and K2) are minimal, and achievement of initial level was observed by eight months postoperatively (Fig. 10, 11).
Confocal microscopy in dynamics of uncomplicated postoperative period allowed us to visualize the following features of corneal regeneration.

After LASIK, foreign inclusions of different origins were visualized in the interface of 97% of eyes (in 91.2% of cases they were metal, in 33.4% - lipid and mucin, and in 12.3% there were inflammatory macrophage-like cells and erythrocytes) (Fig. 12).

By days 10-14 of postoperative period, acellular zone began to form along both sides of the interface. It represented the area lacking differentiated cells, which gradually decreased in length and disappeared by 6-8 months postoperatively (Fig. 13).

a – hypercellular stroma due to inflammatory cells migration first postoperative days

b – acellular intrastromal zone since 10-14 days up to 6-8 months after surgery

c – rarefied fibrocellular stromal net after 8 months postoperatively

In 78% of cases, microstrias of the corneal flap were visible (Fig. 14).

Re-innervation of the central zone of the cornea occurred by 8-12 months postoperatively. However, abnormal branching of newly formed nervous fibers and abundant anastomoses did not allow one to consider it to be full (Fig. 15).
a – “scraps” of the nerve fibers of the superficial nerve plexus (arrow) damaged by microkeratome during corneal flap creation

b – re-innervation of the central corneal optical zone

Quantitative and qualitative analysis of endothelium revealed cell loss within 2.2-2.6 % without alteration of cellular morphology.

After PRK, epithelial defect was substituted by migration of wing-shaped epitheliocytes from intact zone of the cornea (Fig. 16).

Fig. 16. Substitution of epithelial defect with wing-shape epitheliocytes.

Thickness of newly formed epithelium was significantly higher (76.3±9.8 mm) as compared to intact cornea (52.1±6.5 mm).

Length of acellular zone was less (to 68 mm) than that after LASIK (to 160 mm), and re-innervation of the central optic zone occurred earlier (by 5-6 months). Loss of endothelial cells was 2.5-2.7 % by one year postoperatively.

Complex dynamic examination of patients with disregenerative KRO postoperative complications (main group 2) gave the following results:

1. Study of FTC parameters allowed us only to register complications but did not have essential prognostic value.

2. Calculation of values of biochemical coefficients of degree of corneal damage degree showed their significant difference from values typical of uncomplicated postoperative period: coefficient of SIOS (K1) was increased in 97.9 % of cases, coefficient of SDP (K2) – in 84.0 % of cases, both coefficients (K1+K2) – in 76.6 % of cases, that confirms important role of these pathophysiological mechanisms in pathogenesis of disregenerative complications of KRO. Besides, we noted that in all cases, increase of these coefficients preceded clinical manifestation of complications that allowed us to include them in predicting system of disregenerative complications of KRO.

3. Almost in all cases, confocal microscopy of the cornea in patients with disregenerative complications revealed specific pathomorphological signs of the forming complication at subclinical stage (Fig. 17-19).

Fig. 17. Confocal microscopy of the cornea of the patient with aseptic edema of the corneal valve (day 3 after LASIK).

Fig. 18. Confocal microscopy of the cornea of the patient with neurotrophic epitheliopathy (day 7 after LASIK).

Fig. 19. Confocal microscopy of the cornea of the patient with subepithelial fibroplasia (one month after PRK).

4. Based on the pathophysiological mechanisms revealed, we include the following medicaments into complex therapy:
Table 4. Specific features of complex examination in patients with disregenerative complications of KRO as compared to uncomplicated course (printed in blue)

<table>
<thead>
<tr>
<th>Complication</th>
<th>eye N</th>
<th>Time of finding</th>
<th>K1/K2 (average)</th>
<th>FTC in (uncomplicated course) (average)</th>
<th>Specific features</th>
<th>Specific features of confocal microscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurotrophic epitheliopathy (NE)</td>
<td>22</td>
<td>Day 7-14</td>
<td>59,6 / 2,6</td>
<td>21,7 / 1,04</td>
<td>Epithelium ↓</td>
<td>↓ number of basal epitheliocytes, local defects of epithelium</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2,9 points</td>
<td></td>
</tr>
<tr>
<td>Aseptic edema of corneal flap</td>
<td>2</td>
<td>Day 3</td>
<td>59,0 / 1,4</td>
<td>28,8 / 1,05</td>
<td>EC: 4,1 points</td>
<td>Diffuse edema of all layers of the cornea, thickening of the flap to 150 um</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3,6 points</td>
<td></td>
</tr>
<tr>
<td>Dry-eye syndrome (DES)</td>
<td>19</td>
<td>Day 7 – one month</td>
<td>62,3 / 1,8</td>
<td>14,1 / 0,8</td>
<td>Schirmer test-1 (ST-1): 8,2 / 17,4</td>
<td>Increase of number of inflammatory cells</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NE+DES</td>
<td>13</td>
<td>Day 7-14</td>
<td>64,3 / 2,5</td>
<td>64,3 / 2,5</td>
<td>EC / ST-1: 6,2/ 9,5</td>
<td>Local defects of epithelium + many inflammatory cells in stroma</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2,9 / 16,8</td>
<td></td>
</tr>
<tr>
<td>Subepithelial fibroplasia of the cornea</td>
<td>38</td>
<td>1-3 months</td>
<td>69,2 / 2,6</td>
<td>13,3 / 0,7</td>
<td>No specific features</td>
<td>There is an additional pike on the curve of optic density (behind epithelium), ↑ reflective ability of extracellular matrix, ↓ of cell number in stroma</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4,4 points</td>
<td></td>
</tr>
</tbody>
</table>

- antioxidants in patients with high values of coefficient of evaluation of SIOS;
- antioxidants + reparative drugs in patients with combined increase of both coefficients.
- reparative drugs in patients with high coefficient of evaluation of SDP evaluation;
- In all patients, we recorded quick regress of clinical signs of complications accompanied by decrease of biochemical coefficients.
Analysis of results obtained proposed the following diagnostic algorithm of early detection of complicated postoperative course (scheme 1).

Final section of the study is a clinical proof of effectiveness of the proposed algorithm of predicting and correction of excessive lesion of the cornea resulted from KRO.

We selected group of patients (50 patients – 100 eyes) with myopia who were intended for LASIK (main group 3). To increase probability of signs of atypical postoperative course, patients with initially altered cornea because of long-term use of contact lenses (neovascular keratopathy) or previous KRO were included into the group. Patients were divided into two equal subgroups. LASIK was uncomplicated in all patients.

Design of the study: in all patients, pre- and postoperative examination was performed according to the proposed algorithm but in patients of the first subgroup, drug therapy was carried out in standard way and in patients of the second subgroup, we carried out differentiated correction of revealed lesions (scheme 2).

Results of the study represent at the scheme 3 and 4.

Thus, in the first subgroup with initially altered cornea, average degree of corneal lesion revealed by calculation of biochemical coefficients on day 2 postoperatively was accompanied by development of complications in 83.3 % of cases, while severe degree of corneal lesion – in 100 % of cases. In all cases, confocal microscopy confirmed the diagnosis.

In the second subgroup, drug correction (antioxidants and reparative drugs) was performed according to
Table 5. Algorithm of prophylaxis of complications after KRO

<table>
<thead>
<tr>
<th>Algorithm of prophylaxis</th>
<th>Criterion of effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Before KRO in patients with unaltered cornea: study of FTC and correction of deviations revealed</td>
<td>Normal value of FTC parameters</td>
</tr>
<tr>
<td>2. Before KRO in patients with initially affected cornea: FTC + biochemical coefficients + confocal microscopy of the cornea and correction of deviations revealed</td>
<td>Normal value of all examined parameters</td>
</tr>
<tr>
<td>3. After KRO in all patients: FTC and in the case of deviations of parameters and/or unclear clinical picture biochemical coefficients confocal microscopy In all patients with excessive corneal damage (even in absence of clinical signs – metabolic correction)</td>
<td>Decrease of biochemical coefficients to values typical of uncomplicated postop course</td>
</tr>
</tbody>
</table>

scheme described above in patients with average and severe degree of corneal lesion revealed on day 2 postoperatively by data of biochemical coefficients. This allowed us to achieve uncomplicated course during the whole period of observations in 94.4 % of patients with initially altered cornea and excessive corneal damage by KRO.

The results obtained suggest the following algorithm of preventing dismetabolic complications of KRO based on early detection and correction of excessive damage to the cornea (table 5).

Thus, the study revealed morphological and metabolic features of uncomplicated course of PRK and LASIK and specific subclinical markers of excessive corneal damage causing disregenerative postoperative complications. Algorithm of prediction and correction of postoperative disregenerative complications of KRO, developed on the basis of these markers, will improve quality of rehabilitation of young socially active patients with ametropia who decide to get rid of spectacles or contact lenses with the help of excimer laser correction.

References


58. Wachtlin J., Blasig I.E., Schrunder S., et al. PRK and LASIK-their potential risk of cataractogenesis: lipid peroxidation changes in the aqueous humor and crystalline lens of rabbits, Cornea, 2000, ?1, P. 75-79
61. Wilson S.E. Role of apoptosis in wound healing in the cornea, Cornea, 2000, ?3, P7-12
Dry Eye–A Hospital Based Incidence Study

Dr. Nita S. MS DO DNB, Dr. Amita Verghese MS, Dr. Verghese Joseph MS DO

Abstract

Aim: To find out the incidence of Dry Eye in patients with standard symptoms and to identify the risk factors in them.

Methodology: By applying the standard objective tests required for diagnosis, patients with standard symptoms of Dry eye were evaluated and categorized. The study included 474 eyes of 237 patients. All patients who volunteered with symptoms of dry eye were included in the study.

Results: On the basis of the Schirmer’s test and tear break up time, out of the 237 patients included in the study, 149 patients (62.8%) were diagnosed as Dry eye and 88 (37.13%) did not have dry eye. The mean age was 60 years and Female: Male ratio was 2.5:1. Maximum number of patients were housewives (53%). 27% of dry eye subjects had diabetes mellitus; 5% had arthritis and 1% had thyroid disease.

Conclusion: Dry eye is not a vague entity. Its etiopathogenesis has been defined and specific treatment modalities are available. To correctly label a patient as dry eye and to identify the level of the disease it is important to do objective tests so that proper treatment can be started.

Keywords: Dry Eye, Standard Symptoms, Objective Tests.

Introduction

Dry eye is a disease with varied presentations and numerous definitions. Prevalence of the disease as well as morbidity from this disease is on the rise.¹ Research suggests that impact on quality of life is approximately equal to that of angina.² The International Dry Eye Workshop (DEWS) defines Dry eye as “A multi-factorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability, with potential damage to the ocular surface”. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface. Dry eye is also recognized as a disturbance of the Lacrimal Functional Unit (LFU), an integrated system comprising the lacrimal glands, ocular surface (cornea, conjunctiva and Meibomian glands) lids, and the sensory and motor nerves that connect them.

Several studies of dry eye prevalence rely only on reports of symptoms for the definition of the disease. The Shihpail Eye study and the Salisbury Eye evaluation were two prominent studies which used objective tests along with symptoms to evaluate dry eye.³ ⁴

Studies on dry eye are based on pre-designed questionnaires. These involve answers to leading
questions which are given in a printed format. The Mcmonnies questionnaire and the ocular surface disease index [OSDI] are questionnaires commonly used to diagnose or to evaluate symptoms of dry eye.

Incidence of dry eye in symptomatic patients has not been extensively studied. We decided to study the incidence of dry eye based on the symptoms which patients volunteered and then applied the objective tests to confirm the diagnosis. This was to help us decide the proper line of management of the group of patients, who very often present with a vast array of vague symptoms in a general out patient practice.

**Materials and Methods**

This hospital based cross sectional study was conducted from January 2007 to June 2008. We first defined 13 symptoms as standard for dry eye after analyzing various dry eye questionnaires. All of them were subjected to objective tests to confirm the diagnosis. All patients above 20 years of age, who attended the outpatient department of our hospital with any one of the symptoms, for more than one month duration, were included in the study (Table 1). Patients who had undergone any extra ocular or intraocular surgery within one month, contact lens wearers and those with active ocular infection or inflammation were excluded from the study.

All patients underwent a through history taking by an ophthalmologist. The active complaints were recorded. The presence of any systemic disease, history of ocular surgeries, trauma or contact lens use and the use of any ocular medications were noted. After the history taking the same ophthalmologist did a complete ocular examination. The lids were examined for presence of any anatomic abnormalities that interferes with normal spread of tear film.

Slit lamp biomicroscopy was done and the presence of mucus strands in the tear film, and corneal filaments were noted. Lid margins were examined for irregularity or thickening.

Meibomian orifices were examined for pouting, presence of foam, secretion and plugging. Tarsal conjunctiva was examined for the presence of papillae.

Objective tests were done by another ophthalmologist who was masked to the above information. Tear break up time with Fluorescein and staining with Fluorescein and Lissamine Green were done first. This was followed by Schirmer test with local anesthetic. Tear Break-up Time (TBUT) was done by instilling a 2 % fluorescein strip wetted with saline into the conjunctival sac of either eye. Patient was asked to blink once. The time taken for the appearance of the first dark spot on the cornea was noted under the blue filter of the slit lamp. A value of less than 10 seconds was taken as abnormal. Staining pattern with fluorescein, of conjunctiva and cornea were noted and recorded as Nil, Mild and Diffuse.

Lissamine green staining was done next after washing the conjunctival sac and introducing saline wetted Lissamine green strips. Staining pattern of the conjunctiva was noted and graded as Nil, Mild and Extensive.

Schirmer test with local anesthetic was done. Patient was seated in a dark room with fans and Air conditioner switched off. Proparacaine Hydrochloride 0.5% was instilled into both eyes. Excess local anesthetic was gently wiped off with cotton. After 2 minutes, standard Schirmer test strips were applied to the inferior conjunctival sac at the junction of the lateral 1/3 & medial 2/3. Patient was asked to look straight and allowed to blink. After 5 minutes, the test strips were removed and the amount of wetting was noted. Value less than 10mm and tear breakup time less than 10 seconds was taken as dry eye. Patients were classified on the basis of age, sex, occupation, symptoms prevalence, ocular and systemic associations.

<table>
<thead>
<tr>
<th>Table 1: List of Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 FB sensation</td>
</tr>
<tr>
<td>2 Non sticky eye discharge</td>
</tr>
<tr>
<td>3 FB sensation</td>
</tr>
<tr>
<td>4 Heavy sensation</td>
</tr>
<tr>
<td>5 Dry sensation</td>
</tr>
<tr>
<td>6 Discomfort</td>
</tr>
<tr>
<td>7 Ocular pain</td>
</tr>
<tr>
<td>8 Watering</td>
</tr>
<tr>
<td>9 Temporary blurred vision</td>
</tr>
<tr>
<td>10 Itching</td>
</tr>
<tr>
<td>11 Photophobia</td>
</tr>
<tr>
<td>12 Redness</td>
</tr>
<tr>
<td>13 Burning / Stinging</td>
</tr>
</tbody>
</table>
Dry eye was graded into four levels based on the Delphi panel consensus listed as follows:
Level I: TBUT less than 10 seconds
No conjunctival or corneal stain.
Level II: TBUT less than 10 seconds, mild corneal fluorescein stain
Mild Conjunctival Lissamine stain
Level III: Diffuse corneal stain with Fluorescein
Extensive Conjunctival Lissamine stain
Level IV: Corneal ulcer, epithelial breakdown

**Results:**
A total of 237 patients were included in the study. On the basis of the objective tests, 149 were classified as having dry eye and 88 patients did not fulfill the criteria for the diagnosis of dry eye. Their age ranged from 29 years to 80 years, the mean age being 60 years (Fig. 1).

There were 106 females & 43 males; female: male ratio was 2.5:1 (Fig. 2).

By profession, 80 (53 %) were house wives, 20 (13 %) were nurses, 20(13%) computer professionals, 15(10%) drivers, 8( 5 %) outdoor workers and 6 (4 %) teachers (Table 3). On analysis of the symptoms that the patient presented with, 40 patients (26.85 %) had itching, 39 patients (26 %) had symptoms of foreign body sensation, 26 (17.4 %)had ocular pain, 23 (15.4 %) non sticky discharge, 22 (14.7 %) had watering and 20(13.4%) burning or stinging. 17 (11.4 %) had symptoms of dryness, 13 (8.7 %) temporarily blurred vision, 11 (7.4 %) feeling of heaviness, 10 (6.7 %) redness, 2(1.3 %) patients had photophobia and 2(1.3 %) had ocular fatigue (Table 2).

On analysis for systemic associations of patients with dry eye 41 patients (27 %) had Diabetes Mellitus, 15 patients (5 %) had arthritis and 5 patients (1 %) had thyroid disease, 1 (0.6 %)each had parkinsonism, Steven Johnson syndrome and primary Sjogren's syndrome (Fig. 3).
Associated ocular diseases were found in 38 eyes (14.2 %). Of these 13 eyes (34 %) had undergone cataract surgery, 12 eyes (31 %) had healed Viral Keratitis, 9 eyes (24 %) had Blepharitis and 3 eyes (7.8 %) had filamentary keratitis (Fig. 4).

Out of the total of 268 eyes of 149 patients, 83 eyes (31 %) had level I disease; 42 eyes (15 %) had level II disease; 137 eyes (51 %) had level III disease and 6 eyes (2 %) had level IV disease (Fig. 5).

Fig 4: Ocular Associations

Out of 237 patients 88 (37.13 %) did not have dry eye. Among these patients 30 had ocular allergy, 27 had blepharitis and 22 had refractive error.

Fig 5: Levels of disease

Out of 237 patients 88 (37.13 %) did not have dry eye. Among these patients 30 had ocular allergy, 27 had blepharitis and 22 had refractive error.

Discussion

Dry eye tends to be ignored as a disease entity because of the vast array and non specificity of symptoms. Some of the symptoms are common to other disease entities. The prevalence of dry eye in the general population is still not precisely known. It has ranged from 6 % of an Australian population 40 years and older to 15 % of a population over 65 years of age in Mary Land, USA. The prevalence was lower when a combination of signs and symptoms were used as diagnostic criteria as in the Salisbury eye study. Prevalence in clinic population is usually higher than that for general population and varies between 0.6 % and 57 %.

Due to the difficulty in carrying out longitudinal studies on dry eye on a sufficiently large population group, cross sectional prevalence studies have been reported in literature. The Shihpai eye study, which studied the Chinese population in Taiwan, reported dry eye incidence of 62.5 % in symptomatic patients. In an Italian Eye Centre, of 1200 patients reporting dry eye symptoms, 57.1 % had dry eye diagnosed by objective tests.

In the present study we found that out of the 237 patients who presented with standard symptoms of dry eye, 63 % of patients were diagnosed positive for the disease. This is comparable to both the other studies conducted in the Chinese population and the Italian eye Centre.

We found a peak occurrence of dry eye in the age group of 60-70 years. 76 % (113 patients) of dry eye patients were, over 50 years of age. Other studies also show increasing prevalence with age. The Beaver Dam Eye study which was one of the first to report the incidence of dry eye, found a peak at 70-80 years of age. With aging, all cellular structures of the body undergo progressive apoptosis. This affects all exocrine glands, the lacrimal gland being no exception. Lacrimal fluid secretion becomes insufficient for normal situations by about 60 years. Females are more prone for dry eye. An epidemiological study conducted at Schepens Eye Research Institute and Brigham Women's Hospital shows a prevalence of 7.8 % in women over 50 yrs.

Salne's eye study reports that 11.9 % of women and 9 % of men suffered from dry eye. Our study also
reports a higher incidence in the female population. There were 106 (71%) females as compared to 43 (29%) males. The female: male ratio being 2.5:1.

Meibomian gland dysfunction & evaporative dry eye frequently occur during menopause. As menopause sets in, an imbalance between oestrogen and androgens, due to decrease in androgen levels occur. Androgens modulate the immune system and tropic functions of the lacrimal glands and the functioning of the meibomian glands. Meibomian gland dysfunction results in lipid layer instability and evaporative dry eye. The most common complaints of dry eye patients are foreign body sensation, burning, redness, itching, blurred vision and light sensitivity. Foreign body sensation and itching were the commonest symptoms in our series. 39% of patients had 2 symptoms and 29.53% presented with 3 or more symptoms.

Dry eye is known to be associated with certain systemic conditions. In the present study 27% of dry eye subjects had diabetes mellitus. 5% had arthritis and 1% had thyroid disease. The Beaver Dam Eye study also showed similar associations. Mechanism for increased occurrence of dry eye in Diabetes Mellitus is unclear. Autonomic dysfunction has been suggested. Aldose reductase, the first enzyme of the sorbitol pathway, may be involved. The oral administration of aldose reductase inhibitors has been shown to improve the tear dynamics significantly.

Systemic immune diseases like arthritis and thyroid disorder disrupt the lacrimal functional unit by lymphocytic infiltration. Autoimmune diseases causing dry eye can be classified into four categories, the first type preferentially affecting glands as in primary Sjogren’s syndrome and the second affecting the exocrine glands and connective tissue as in rheumatoid arthritis and Systemic Lupus Erythematosis. The third variety is that which attack the ectodermal and mesodermal tissues and cause secondary destruction of non attacked glands as in Steven Johnson syndrome.

Lastly there is the type which affects other tissues and cause secondary destruction of exocrine glands.

Dry eye is also associated with certain ocular conditions. Beaver Dam Eye Study cohort found that lens surgery was related to increased prevalence of dry eye. Postoperative corneal desensitization is the most important factor responsible for dry eye in this category. In the present study lens surgery was an association in 34% of eyes.

Blepharitis was another association in 24% eyes of our patients. Other studies have reported an association as high as 56%. The frequent association of dry eye with blepharitis has been documented by several investigators. A large proportion of patients with chronic blepharitis show marked changes in meibomian gland structure. The changes in lipid layer leads to increased evaporation of tear and resultant dry eye.

In this study 31% eyes had previous viral keratitis. It has been reported that herpetic keratitis causes decreased corneal sensation. The resultant afferent neurodeprivation results in decreased tear secretion.

The Delphi panel and the DEWS panel have graded dry eye into levels based on severity and have charted out treatment accordingly. In the present study we found that of the 63% of symptomatic dry eye patients, 83 eyes (31%) had level I disease, 42 eyes (15%) had level II, and 137 eyes (51%) had level III disease. More than half the patients had level III disease which is quite substantial.

Artificial tears and lubricants are the mainstay in the treatment of dry eye. In the present scenario there are treatment modalities like immune-modulators which are specific to the etiology and severity of dry eye. Surgical approaches are also available like mechanical occlusion of the lacrimal puncta for blocking tear drainage and thereby prolonging the action of natural tears. An analysis of the various treatment modalities adopted for different levels of dry eye is beyond the scope of this article but needs to be studied further.
Conclusion

Dry eye is a common disease with innumerable symptoms which are often vague and confusing. Despite this, a confirmation of diagnosis can be arrived at after conducting simple and low cost tests in the outpatient department without consuming much time. Since the etiopathogenesis and treatment modalities are now well defined for different levels of diseases, it is important to confirm diagnosis and grade the severity before starting appropriate treatment.

Treatment being long term and varied depending on the severity of the condition, it is important to rule out other disease processes in patients who present with symptoms of dry eye but do not fit into the diagnosis. These patients need to be evaluated for conditions like ocular allergies, refractive errors, lid infections and other pathologies.

References:
8. Ashok Garg, John D. Sheppard, Eric D Donnenfeld, David Meyer et al. editors Clinical Diagnosis And Management Of Dry Eye And Ocular Surface Disorders, chapter 3 pages 49-50. chapter 5 pages 69-70
Macular Hole Surgery Sans Gas

Dr. Sonia Rani John DNB, Dr. Meena Chakrabarti MS DO DNB, Dr. Arup Chakrabarti MS DO

Introduction

Macular holes affect one in every 1,000 individuals, 72% of them are women between 60 and 70 years of age \(^1\) with a bilaterality ranging between 6 and 22%. Eyes with idiopathic macular hole have reduced vision, secondarily to the loss of tissue, cystic retinal changes, detachment of the retinal ring surrounding the hole and photoreception degeneration \(^2\). In 1988, Gass described the pathogenesis of idiopathic macular hole, considering tangential vitreoretinal traction as the cause \(^3\). Also in 1988, Smiddy et al performed this surgery without being able to define the usefulness of vitrectomy and due to the progression of lens sclerosis and potential retinal complications; concluded that conservative management in this stage would be a better option \(^4\). Subsequently, studies were made in patients with stage 3 or 4 idiopathic macular hole in which pars plana vitrectomy with removal of the posterior vitreous and tamponade with expandable gas induced a healing of the macular hole in 58 - 97% of cases, with visual improvement between 42 and 85% \(^2,5,6\).

The first report of successful macular hole surgery was published by Kelly and Wendel in 1991 \(^1\). In recent years, a number of authors have attributed increased success rate of surgery to the use of healing adjuvants (autologous serum, transforming growth factor \(\beta\), platelets or thrombin), the initial stage and duration of macular hole \(^2-8\).

The surgical technique necessitates post operative face down posturing in order to achieve effective tamponade of the macular hole. Indeed, there is evidence to suggest that longer duration of intraocular gas tamponade may have a favorable effect on the outcome of macular hole surgery \(^9,10\).

Although 2 studies have reported comparable results with no face-down posture \(^11\) and four days of posture \(^12\) postoperatively, most studies advocate strict face-down posturing for at least one week after surgery as this is believed to be an important factors in closure of the hole. Because of this, macular hole surgery has been restricted to patients who are able to comply with the postoperative face-down posturing.

A number of patients however are unable to maintain posture because of positioning difficulties due to neck, back, spine, chest, other diseases or social reasons. This study reviews our experience of macular hole surgery without gas tamponade in a consecutive series of 25 patients and presents the results of a comparative analysis of patients undergoing macular hole surgery with and without postoperative gas tamponade.

Clinical Objective

To study whether gas tamponade was necessary to improve anatomic and functional outcomes in macular hole surgery.

Materials and Methods

This was a comparative case control study in which a retrospective analysis of 50 patients who underwent macular hole surgery at our centre between 2007 and 2009 June. They were divided into 2 groups. Group I which included 25 patients in whom surgery was...
performed with intra operative gas tamponade and Group II which included 25 patients without gas tamponade. In both groups ILM peeling had been performed intraoperatively.

The inclusion criteria comprised patients between 50 and 80 years of age, males and females with macular hole diagnosed and evaluated based on clinical features, digital fluorescein angiogram and Optical Coherence Tomography (OCT) scan of stage 3 and 4 with a duration of greater than 6 months.

The exclusion criteria were vitreous or retinal pathology, aphakia, uveitis, glaucoma, corneal pathology, high myopia and previous vitreoretinal surgery. In all cases, a detailed evaluation was made, including assessment of visual acuity, slit lamp evaluation, assessment of lenticular changes, non contact tonometry and indirect ophthalmoscopy. All patients also underwent digital fluorescein angiography, fundus imaging and OCT Scan.

**Infusion of air-perfluoropropane gas (C₃F₈) mixture at a non-expansible concentration of 17 %.** A thorough examination of 360° of the peripheral retina was performed with indirect ophthalmoscope and scleral indentation. The sclerotomies were then closed.

### Post operative management

The post operative visits were scheduled on day 1, weekly for the 1st 1 month and then monthly for the second, fourth, sixth and 12th months. The post operative evaluation comprised of best corrected visual acuity, non contact tonometry, slit lamp evaluation (to evaluate the condition of the cornea, lens, macular hole), indirect ophthalmoscopy and presence of complications, if any. OCT scans were performed on the 1st, 6th and 12th month after the procedure.

### Results

The study included 50 eyes of 50 patients, 17 males and 33 females, between 52 and 80 years of age with an average of 61.4 ± 11.9 years. (Table: 1)

The pretreatment best corrected visual acuity ranged from 6/9 to counting fingers at half meter distance. The post operative visual acuity ranged from 6/9 to hand movements.

Distribution of the sample patients according to duration of the macular hole is shown in table 2. 32% of the patients had a duration of < 5 months while 42% between 5-8 months and 26% of the patients had macular holes of more than 9 months duration.

The average duration of holes prior to surgery was 6.9 m ± 5.6 m.

58% of the patients had a macular hole size of > 400 micrometre while 42% had macular hole sized < 400 micrometers (Table 3)

Associated findings included cystoid macular edema (CME) 6%, epiretinal membranes (ERM) 22%, subretinal fluid (SRF) 4% and Berlin's edema 2%. 56% of the cases with macular hole did not have any other associated findings. One patient had an associated peripheral hole which was lasered intraoperatively.

Retinal tears and postoperative retinal detachments are the most serious posterior segment complications and they occurred in 12% of cases (Table 4) 88%
of patients did not encounter any intra operative problems.

36 % of the patients underwent staining of the internal limiting membrane (ILM) with indocyanine green dye while 4 % of the ILM was stained with brilliant blue green (BBG) and 60 % with trypan blue dye.

50 % of the patients underwent perfluoropropane (C$_3$F$_8$) injection following ILM peeling while the remaining 50 % did not received any gas.

Patients who received C$_3$F$_8$ gas underwent post operative positioning for a period of 3 weeks. (6 hrs / day X 1 week ; 4 hrs / day X 2$^{nd}$ week ; and 2 hrs / day in the 3$^{rd}$ week). They were instructed to maintain face-down posture for the prescribed duration and to sleep on either sides avoiding supine position.

In 80 % of the patients in both the groups, the macular hole closed completely while the hole remained open in 20 % of the cases in both groups (Table 5)

Post operative complications included cataract in 40 % of patients who underwent macular hole surgery with gas and only 8% in those without gas. Glaucoma was encountered in 4 % of patients with gas while none of the patients in the other group developed glaucoma.

Table 1. Distribution of the sample patients according to age

<table>
<thead>
<tr>
<th>Age</th>
<th>Without gas</th>
<th>With gas</th>
<th>Total</th>
<th>(\chi^2)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Count</td>
<td>Percent</td>
<td>Count</td>
<td>Percent</td>
<td>Count</td>
</tr>
<tr>
<td>&lt; 50</td>
<td>2</td>
<td>8.0</td>
<td>3</td>
<td>12.0</td>
<td>5</td>
</tr>
<tr>
<td>50-59</td>
<td>5</td>
<td>20.0</td>
<td>4</td>
<td>16.0</td>
<td>9</td>
</tr>
<tr>
<td>60-69</td>
<td>12</td>
<td>48.0</td>
<td>26</td>
<td>52.0</td>
<td>70-79</td>
</tr>
<tr>
<td>24.0</td>
<td>10</td>
<td>20.0</td>
<td>10</td>
<td>20.0</td>
<td>Average</td>
</tr>
</tbody>
</table>

Table 2. Distribution of the sample patients according to duration

<table>
<thead>
<tr>
<th>Duration</th>
<th>without gas</th>
<th>With gas</th>
<th>Total</th>
<th>(\chi^2)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Count</td>
<td>Percent</td>
<td>Count</td>
<td>Percent</td>
<td>Count</td>
</tr>
<tr>
<td>&lt;5m</td>
<td>9</td>
<td>36.0</td>
<td>7</td>
<td>28.0</td>
<td>16</td>
</tr>
<tr>
<td>5m-8m</td>
<td>8</td>
<td>32.0</td>
<td>13</td>
<td>52.0</td>
<td>21</td>
</tr>
<tr>
<td>9m+</td>
<td>8</td>
<td>32.0</td>
<td>5</td>
<td>20.0</td>
<td>13</td>
</tr>
</tbody>
</table>

Table 3. Distribution of the sample patients according to hole size

<table>
<thead>
<tr>
<th>Hole size</th>
<th>Without gas</th>
<th>With gas</th>
<th>Total</th>
<th>(\chi^2)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Count</td>
<td>Percent</td>
<td>Count</td>
<td>Percent</td>
<td>Count</td>
</tr>
<tr>
<td>&gt; 400</td>
<td>11</td>
<td>44.0</td>
<td>18</td>
<td>72.0</td>
<td>29</td>
</tr>
<tr>
<td>&lt; 400</td>
<td>14</td>
<td>56.0</td>
<td>28.0</td>
<td>21</td>
<td>42.0</td>
</tr>
</tbody>
</table>

Table 4. Distribution of the sample patients based on intraoperative complications encountered.

<table>
<thead>
<tr>
<th>Intra OP Problem</th>
<th>Without gas</th>
<th>With gas</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Count</td>
<td>Percent</td>
<td>Count</td>
<td>Percent</td>
</tr>
<tr>
<td>Nil</td>
<td>22</td>
<td>88.0</td>
<td>21</td>
<td>84.0</td>
</tr>
<tr>
<td>Retinal Tear</td>
<td>2</td>
<td>8.0</td>
<td>3</td>
<td>4.0</td>
</tr>
<tr>
<td>Peripheral Hole</td>
<td>0</td>
<td>0.0</td>
<td>1</td>
<td>4.0</td>
</tr>
</tbody>
</table>

Table 5. Distribution of the sample patients according to closure.

<table>
<thead>
<tr>
<th>Closure</th>
<th>Without gas</th>
<th>With gas</th>
<th>Total</th>
<th>(\chi^2)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Count</td>
<td>Percent</td>
<td>Count</td>
<td>Percent</td>
<td>Count</td>
</tr>
<tr>
<td>closed</td>
<td>20</td>
<td>80.0</td>
<td>20</td>
<td>80.0</td>
<td>40</td>
</tr>
<tr>
<td>open</td>
<td>5</td>
<td>20.0</td>
<td>5</td>
<td>20.0</td>
<td>10</td>
</tr>
</tbody>
</table>

*Statistically significant at \(p < 0.05\).
Discussion

The rate of closure of idiopathic macular hole depends on many factors like size of the hole (measured by OCT scan), duration of symptoms, ILM peeling, type of tamponade used (air, SF6, C3F8, silicone oil) and length of face-down positioning (2 weeks, 1 week, 5 days, 1 day or more).

Majority of the surgeons use gas tamponade. A 2006 survey by Mittra and Pollack showed that 63 % of surgeons use C3F8 while 33 % use SF6 as 6 weeks of visual disturbances with C3F8 is disabling for most patients. The patient compliance to postoperative positioning is also poor as indicated in a patient survey conducted by the AAO (Pollack J.S, Packo J 2000). Only 3 % (4 weeks), 8 % (3 weeks), 63 % (2 weeks) and 25 % (1 week) compiled with the postoperative positioning.

So if buoyancy of the gas is small and the patients are generally unable to comply with the positioning, then what are we positioning for? A metanalysis of relevant studies on shortened post operative positioning is given below (Table 6).

Park in 1999 conducted a study in 58 patients with macular hole and concluded that 91 % of the macular holes closed with gas tamponade and positioning for 4 days.

Isomac in 2002 studied the effect of C3F8 tamponade and 1 day post operative positioning in 21 eyes with recent onset macular holes which also had a hole closure rate of 91 %.

Sato in 2003 also attained 91 % hole closure rate with air tamponade and 1 day face down positioning in a case series of 23 patients with small macular holes.

Krohn in 2005 studied 24 eyes with full thickness macular hole who underwent pars plana vitrectomy along with C3F8 tamponade and 3 days post operative face down positioning and showed that 87.5 % of the macular holes closed well while Wocks in 2006 achieved 95 % closure rate (21 eyes case series) with C3F8 gas tamponade and 3 days face down positioning.

Toruambe in 1997 achieved 79 % closure rate with C3F8 tamponade alone without any face down positioning, while Simcock in 2001 with C3F8 tamponade alone achieved 90 % closure rate.

Tranos and Merkur in 2007 used C3F8 alone for tamponade and had a hole closure rate of 88 % and 92 % respectively.

Thus smaller, recent holes will likely close with ILM peeling and minimal or no positioning (as long as patient avoids the supine position). Most holes will close with ILM peeling, SF6 gas and 1 day of positioning. For chronic or larger holes or if there are doubts regarding the patients ability to position, 3 or more days of face down positioning or C3F8 gas can be considered.

Clinical studies have shown that small holes that are of recent onset will have high success rates using almost any technique. Tadayoni et al (Br J Ophthalmol 2006) has shown that 100 % hole closure can be obtained for holes < 400 micrometre, with or without ILM peel.

Table 6. Metanalysis of published articles on MHS with shortened duration of posturing.

<table>
<thead>
<tr>
<th>STUDY</th>
<th>PATIENT</th>
<th>SIZE/DURATION</th>
<th>GAS</th>
<th>POSITION</th>
<th>CLOSURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>PARK 1999</td>
<td>58</td>
<td>ALL</td>
<td>AIR</td>
<td>4 DAYS</td>
<td>91 %</td>
</tr>
<tr>
<td>ISOMAC 2002</td>
<td>21</td>
<td>RECENT</td>
<td>C3F8</td>
<td>1 DAY</td>
<td>91 %</td>
</tr>
<tr>
<td>SATO 2003</td>
<td>23</td>
<td>SMALL</td>
<td>AIR</td>
<td>1 DAY</td>
<td>91 %</td>
</tr>
<tr>
<td>KROHNS 2005</td>
<td>24</td>
<td>ALL</td>
<td>C3F8</td>
<td>3 DAYS</td>
<td>87.5 %</td>
</tr>
<tr>
<td>WICKENS 2006</td>
<td>21</td>
<td>ALL</td>
<td>C3F8</td>
<td>3 DAYS</td>
<td>95 %</td>
</tr>
</tbody>
</table>

Table 7. Hole Closure Rates for macular holes without positioning.

<table>
<thead>
<tr>
<th>STUDY</th>
<th>PATIENT</th>
<th>SIZE/DURATION</th>
<th>ILM</th>
<th>GAS</th>
<th>POSITION</th>
<th>CLOSURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>TORNABE</td>
<td>33</td>
<td>20 % CHRONIC</td>
<td>-</td>
<td>C3F8</td>
<td>NONE</td>
<td>79 %</td>
</tr>
<tr>
<td>SIMCOCK</td>
<td>20</td>
<td>STAGE II/III</td>
<td>-</td>
<td>C2F6</td>
<td>NONE</td>
<td>90 %</td>
</tr>
<tr>
<td>TRANOS</td>
<td>16</td>
<td>ALL</td>
<td>+</td>
<td>C3F8</td>
<td>NONE</td>
<td>88 %</td>
</tr>
<tr>
<td>MERKUR</td>
<td>72</td>
<td>RECENT</td>
<td>+</td>
<td>C3F8</td>
<td>NONE</td>
<td>92 %</td>
</tr>
</tbody>
</table>
100% closure could be obtained with ILM peel in macular holes > 400 micrometre while only 73% of the macular holes closed without ILM peel.

Although ILM peel remains controversial, most surgeons peel ILM for idiopathic holes. ILM peeling allows for complete removal of perifoveal vitreous traction.

Most surgeons use C$_3$F$_8$ for gas tamponade. However 6 weeks of visual disturbance with C$_3$F$_8$ is disabling for most patients.

The buoyant pressure and interfacial tension of the gas tamponade reattaches retina. C$_3$F$_8$ allows for 2-3 weeks of contact between hole and gas if supine position is avoided. Longer acting gas allows for more leeway in positioning. Shorter acting gas requires more positioning to achieve hole/gas contact as bubble dissipates. Positioning may actually be more critical as the bubble dissipates.

Hole closure rates for macular holes without positioning has been studied by several workers and the results show that it does not affect closure rate or functional outcomes (Table: 7)

The anatomic and functional outcomes in macular hole surgery are similar irrespective of whether intraoperative gas tamponade was used or not in the present study. Face down positioning is burdensome for the patient with reported side effects like ulnar neuropathy.

We decided to conduct our study without gas to tamponade the macular hole in 20 consecutive cases of idiopathic 3 and 4 macular holes and compared our results with our own series where C$_3$F$_8$ was used for postoperative tamponade. The rate of hole closure was similar in both groups, with the added advantage of fewer complications in the group where gas was not used. The patients were also saved from the discomfort of postoperative positioning, lesser progression of cataract and negligible postoperative glaucoma. However for repeat procedures and large chronic holes, tamponade should still be considered.

References
Efficacy of Combining Internal Limiting Membrane Peeling with Epimacular Membrane Surgery

Dr. Meena Chakrabarti MS DO DNB, Dr. Sonia Rani John DNB, Dr. Arup Chakrabarti MS

Epiretinal membranes are seen in 6.4% - 11.8% of the general population and can vary in severity from a mild alteration of the light reflex over the macula to thick scrolled membranes producing underlying pathological changes in the retina over which it lies. Surgical treatment should be considered for any epiretinal tissue severe enough to account for the patients complaints.

ERM surgery has been shown to be associated with improvement of vision in 80%-90% of cases. There is controversy regarding 1) Role of ILM in pathogenesis of ERM 2) Necessity of ILM peel during ERM peel, 3) Final outcome after combined ERM – ILM peel 4) Rate of Recurrence.

Sivalingam A et al (1990) correlated visual prognosis with the presence of ILM in histo pathological specimens obtained from ERM surgery and postulated that ILM peel was associated with poor visual recovery. This finding has been disproved subsequently by several authors.

Surgical results and benefits include measurably appreciable visual improvement in 78% to 87% with less micropsia and distorsion, progressive reduction in retinal thickness, unfolding of retinal striae and less tortuosity of retinal vessels.

Complication of Vitrectomy and ERM peel includes peripheral RT (4-9%), Macular breaks (<1%), retinal hemorrhages, retinal detachment (3-6%), progression of nuclear sclerosis (50%) and recurrence of ERM in (4% to 31%).

The aim of our study was to assess the efficacy of comparing ERM peeling with ILM peel during epimacular membrane surgery in 20 consecutive patients who underwent epimacular membrane surgery at our centre from 2006-2008 and were followed up for a period of 2 years.

Materials And Methods: We conducted a prospective case controlled study on the the efficacy of combining ERM peeling with ILM peel during epimacular membrane surgery in 20 consecutive patients who underwent epimacular membrane surgery at our centre from 2006-2008 and were followed up for a period of 2 years.

The patients were randomized to undergo either ERM peel alone or in combination with ILM peel

1. ERM PEEL ALONE 9 EYES (ILM PRESERVED GROUP) 2. COMBINED ERM & ILM PEEL 10 EYES (55%) (ILM PEELED GROUP)

All 20 patients had significant epiretinal membranes producing visual symptoms and pathological macular changes (Table 1) (Fig 1 a and b)

The fundus findings included a glinting, shifting light reflex in all patients, vitreo-macular traction syndrome in 40%, swiss cheese dehiscence of membrane (10%) pseudo hole formation in 20%, true macular hole
Table 1. Pathological Macular Changes Responsible for Visual Symptoms

<table>
<thead>
<tr>
<th>Symptomatic</th>
<th>20 EYES (100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ERM Opacities Overlying Fovea</td>
<td>20 Eyes (100%)</td>
</tr>
<tr>
<td>Vitreo Macular Traction</td>
<td>8 Eyes (40%)</td>
</tr>
<tr>
<td>Macular Oedema</td>
<td>6 Eyes (30%)</td>
</tr>
<tr>
<td>Tr. Induced Macular Ischaemia</td>
<td>2 Eyes (10%)</td>
</tr>
</tbody>
</table>

Fig. 1. (a) Fundus Red free photograph showing dragging of vessels and vascular Tortuosity in a patient with an epimacular membrane (b) Dense Epimacular membrane with vitreomacular traction causing visual loss.

30 %. Dilatation and tortuosity of vessels, and tethering and straightening of vessels were seen in all cases. Foveal ectopia 20 %, subtle shallow table top retinal detachment 10 %, retinal edema, thickening, foveal cysts 30 %, with cotton wool spots 10 %, retinal pigment epithelial changes 10 %, and macular pucker in 20 % were the other fundus findings observed.

A baseline fluorescein fundus angiography was performed in all patients. The fluorescein angiographic findings are given in Table 2 and Fig. 3.

Table 2: Showing the correlation between pre and postoperative central retinal thickness and visual function in the Group I patients (ILM preserved group)

<table>
<thead>
<tr>
<th>Retinal Thickness</th>
<th>Visual Acuity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre operative 400 -690 Micron</td>
<td>3/60 - 6/12</td>
</tr>
<tr>
<td>Post operative 200 -490 Micron</td>
<td>6/60 -6/9</td>
</tr>
</tbody>
</table>

Fig. 3. a-c Fluorescein angiographic features of epimacular membranes showing straightening and tethering of vessels, (b) choroidal neovascular membrane and (c) macular ischemia

Preoperative optical coherence tomography showed the following findings: Pseudohole 20 %, cystoid macular edema (CME) 20 %, retinal striae 40 %, true macular hole (MH) 30 %, vitreomacular traction (VMT) 30 % and diffuse edema in 30 % (Fig 4 a&b).

The preoperative retinal thickness by OCT varied from 400 micron to 690 microns with a visual acuity ranging between 3/60 to 6/12. Following surgery the OCT was repeated at one month. A significant reduction in the retinal thickness was observed in both groups, but was more in the ILM peeled group (Mean difference of 200 μm vs 390 μm) Table 2&3.

Table 3: Showing the correlation between preoperative and postoperative central retinal thickness and visual function in Group II patients (ILM peeled group)

<table>
<thead>
<tr>
<th>Retinal Thickness</th>
<th>Visual Acuity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre operative 400 -690 micron</td>
<td>3/60 - 6/12</td>
</tr>
<tr>
<td>Post operative 200 -300 micron</td>
<td>6/18 – 6/6</td>
</tr>
</tbody>
</table>

Prognostic indicators associated with poor vision included history of poor pre-operative visual acuity, longer duration of symptoms, older age of patient, evidence of VM Traction, pre-operative CME, RPE window defects, macular hole, partial PVD and absence of ILM peeling.

Discussion

Epimacular membranes have been known by various terminologies such as primary retinal folds, secondary...
retinal gliosis, surface wrinkling retinopathy, silkscreen retinopathy, cellophane maculopathy, preretinal gliosis or fibrosis, macular pucker and epimacular proliferation. However the most accepted terminology for this condition has been epiretinal membrane abbreviated as ERM.

Epiretinal membranes are characteristically seen in ages > 50 years with a preponderance in women. Bilateral membranes occur in 20 % - 30 % of patients.

Primary epimacular membranes are thought to be congenital in origin or could develop later on in life from persistent adherence of the primary vitreous or as a sequel of shaken baby syndrome or vitreous hemorrhage.

Secondary epiretinal membranes occur in 32 % of epimacular membranes. Their occurrence may be associated with of a myriad of causes given in Table 4.

Table 4. Incidence of Secondary ERM’s

<table>
<thead>
<tr>
<th>Cause</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDR</td>
<td>39.5%</td>
</tr>
<tr>
<td>Retinal Vein Occlusions</td>
<td>18%</td>
</tr>
<tr>
<td>Following Cataract Surgery</td>
<td>28.3%</td>
</tr>
<tr>
<td>RD repair</td>
<td>28%</td>
</tr>
<tr>
<td>Ocular Inflammation</td>
<td>2%</td>
</tr>
</tbody>
</table>

In the earlier stages of its evolution, epiretinal membranes are asymptomatic and are only recognized as a peculiar reflex over the macula on fundus examination. Thus thin transparent membranes, and membranes peripheral to the macula (eccentric ERM’s) are usually asymptomatic.

Symptomatic epiretinal membranes produce micropsia, and metamorphopsia as well as varying degrees of visual disability. Visual loss in the presence of an epiretinal membrane could be due to 1) ERM opacity overlying the fovea 2) Vitreomacular traction 3) Macular oedema 4) Traction induced macular ischemia.

Slit lamp biomicroscopy with a contact lens is a very essential part of evaluating a patient with ERM. This method of examination helps in assessing 1) density and extent of the membrane 2) Pathological changes in the underlying and surrounding retina 3) presence or absence of a pseudo or true macular hole 3) swiss cheese dehiscence of the membrane and 5) severity of vitreomacular traction.

Fluorescein fundus angiography can best be utilized to demonstrate the degree of retinal vascular tortuosity, distortion of perifoveal capillary bed, degree of vascular leakage and severity of macular edema, differentiate between true and pseudo holes and rule out macular ischemia and underlying CNVM.

Optical Coherence Tomography is a new and very handy tool in the evaluation of epimacular membranes. OCT demonstrates the presence of a highly reflective layer over the retina. This membrane may be globally adherent or it may be separated in places from the underlying retina. There is loss of foveal contour as well as a variable amount of retinal thickening. Associated findings of pseudo and true macular holes, CME, VMT, retinal striac as well as diffuse retinal thickening can be easily demonstrated and is of great value in preoperative evaluation and prognostication in a given case. Preoperative evaluation with OCT directs operative approach and also gives an idea about whether membrane peeling will be easy or difficult. It helps the VR surgeon to anticipate difficulty white peeling globally adherent membranes and helps assess the friability of the underlying retina. Postoperative OCT evaluation helps to document the completeness of ERM removal and helps to monitor reduction in retinal thickness and correlates it with visual recovery.

Role of PVD in the pathogenesis of Epiretinal membrane has been put forward by Schepens et al (1995). PVD acts by generating a peripheral retinal tear, leading on to RPE migration. PVD may induce micro trauma to the ILM which can stimulate subsequent secondary glial cell proliferation. PVD also stimulates migration and proliferation of cells by generating ONH trauma, precipitating intraocular hemorrhage and inflammation.

Spontaneous separation and scrolling of membrane away from fovea have also been demonstrated to occur in conjunction with PVD, relieving the patient of symptoms and improving his visual acuity.

Surgical treatment should be considered for any epiretinal tissue severe enough to account for the patients complaints.

ERM surgery has been shown to be associated with improvement of vision in 80 % -90 % of cases. There is controversy regarding 1) Role of ILM in pathogenesis
of ERM

2) Necessity of ILM peel during ERM peel,

3) Final outcome after combined ERM – ILM peel

4) Rate of Recurrence.

Sivalingam A et al (1990) correlated visual prognosis with the presence of ILM in histopathological specimens obtained from ERM surgery and postulated that ILM peel was associated with poor visual recovery. This finding has been disproved subsequently by several authors. In our study the reduction of central retinal thickness and visual recovery was significantly associated with ILM peeling.

The poor prognostic indicators include:

1. Poor pre-op Visual acuity
2. Longer duration of symptoms
3. Older age
4. Evidence of VMT
5. FFA evidence of preoperative CME
6. Presence of macular RPE window defects
7. Presence of Macular hole
8. Partial PVD
9. Diffuse retinal thickening.

Surgical results and benefits include measurably appreciable visual improvement in 78% to 87% with less micropsia and distortion, progressive reduction in retinal thickness, unfolding of retinal striae and less tortuosity of retinal vessels.

Complication of Vitrectomy and ERM peel includes peripheral RT (4-9%), Macular breaks (<1%), retinal hemorrhages, retinal detachment (3-6%), progression of nuclear sclerosis (50%) and recurrence of ERM in (4% to 31%) which should be borne in mind while advising surgery.

References

Introduction
The advent of intravitreal therapies such as Ranibizumab and Bevacizumab have revolutionised outcomes for the majority of patients with neovascular or ‘wet’ age related macular degeneration (wAMD). However there is a small group for whom these pharmacologic treatments are not suitable (Figure 1), those who do not respond to these drugs or indeed have sustained complications of treatment with these agents (Figure 2). For these patients, who are loosing the last of their central vision to wAMD, macular translocation surgery (MT360) may offer the only realistic option for restoration of vision.

Macular translocation with 360 degrees retinotomy was first introduced by Machemer in the early 90s and later popularised by Eckhardt, Toth and other workers.

Indications
MT360 surgery is reserved for patients who have poor vision in one eye already and present with recent loss of vision in the second eye. If intravitreal anti-VEGF (Ranibizumab or Bevacizumab) is thought to be appropriate, it is offered first, and surgery reserved for non-responders.

Surgical Procedure
Surgery is a two stage procedure. In the first operation a phacoemulsification with IOL implantation procedure is done (for phakic patients). Following this a complete pars plana vitrectomy with thorough vitreous base shaving is performed. This can be achieved by external indentation combined with vitreous base excision under direct visualisation with the operating microscope. Triamcinolone staining of vitreous is useful in visualising the vitreous base (Figure 3). The conventional light-pipe may be used as an indenter to trans-illuminate the vitreous base, thus facilitating identification and removal (Figure 4).

Once the vitreous has been totally removed, the retina is detached. This can be done by injecting fluid into the subretinal space through three point retinotomies in the mid peripheral retina using a 41 gauge cannula (Figure 5), or using a wider cannula to inject fluid through a retinotomy adjacent to the ora serrata (Figure 6).

The temporal retina is now reflected nasally and the subretinal neovascular membrane is removed (Figure 9) and the base treated with diathermy. The retina is then reopened and partially reattached using perfluorocarbon liquid (PFCL). The retina is then rotated with the attachment at the optic nerve acting as a fulcrum. The fovea is moved onto an area of healthy retinal pigment epithelium (Figure 10).

PFCL is then used to completely fill the posterior segment, thereby reattaching the retina. Endolaser is applied adjacent to the retinotomy edge, 360 degrees around. Direct PFCL to silicon oil exchange is then done. Silicon oil tamponade is then left in-situ for two months.
Fig. 1. Large sub macular haemorrhage in right eye. This patient already has poor vision in the left eye due to advanced disciform scar. Intravitreal drugs are unlikely to be successful in this setting. The patient was offered MT360 and had a good outcome, vision was restored to 6/9 NS and has maintained this for over 3 years after surgery.

Fig. 2a. A: Right eye has a vision of 6/36 from dry AMD. B: Left eye has a wAMD process reporting recent loss of vision to 6/60 at presentation. C: Red free fundus photo of left eye. D: Late frame from fluorescien angiogram of left eye showing an occult subretinal neovascular membrane. Intravitreal Ranibizumab was recommended.

Fig. 2b. Same patient as in Figure 2a. After first injection of intravitreal Ranibizumab developed a large tear of the retinal pigment epithelium with drop in vision. MT360 was done with good outcome.

Fig. 3. Intra-operative view of triamcinolone stained vitreous base being excised.

Fig. 4. Vitreous base excision using trans-illumination to highlight the vitreous base.

Fig. 5. The retina is detached using fluid injection through a 41 gauge cannula, one point has been injected already, this frame shows injection through the second point retinotomy.

Fig. 6. Injection of fluid through a retinotomy adjacent to the ora serrata to detach the retina. Multiple fluid air exchanges are then performed to push the recently injected subretinal fluid posteriorly and complete the detachment (Figure 7). A peripheral 360 degree retinotomy is then made using scissors to create a cut parallel and adjacent to the ora serrata (Figure 8). The retina is avascular here and therefore no bleeding is encountered.
Two months later the second stage of the operation is performed. This consists of surgery to extraocular muscles to counter-rotate the globe, by the same amount as the initial macular rotation together with removal of silicon oil. This resolves most of the distortion and diplopia which the patient initially experiences due to rotation of the retina.

Outcomes are encouraging with about 40-70 % of patients gaining over 3 lines of vision, although 10 % of patients have worse vision after the operation than they had at presentation.
Conclusion
Macular translocation surgery involves the detachment of the entire retina from the RPE by a subretinal infusion of fluid and creating a 360° circumferential retinotomy followed by the rotation of the retina. Although postoperative complications such as recurrent retinal detachment have been reported in about 10-30% of cases after macular translocation, a large proportion of patients benefit from significant visual improvement. Thus for the patient losing central vision in the second eye from AMD which is not responding to intravitreal pharmacotherapy, this is the only approach which offers a reasonable chance of visual improvement. Further insights and refinements of this surgical procedure are likely to improve outcomes even more in the near future.

References
Surgical Pearls: Biaxial Microincision Cataract Surgery

Dr. Arup Chakrabarti MS

Standard Coaxial VS Bimanual Phaco

Standard Coaxial Phaco :
(a) Irrigation/ aspiration incorporated into the same handpiece.
(b) A 2.5 to 3.0 mm Phaco Incision is employed.
(c) A 1.0 mm sideport incision is employed.

Bimanual Phaco :
(a) Irrigation /aspiration via separate instruments.
(b) Two microincisions of approximately 1.5mm.

Benefits of Bimanual Phaco :
(a) Potentially astigmatic neutral incisions.
(b) Enhanced chamber stability.
(c) Better followability of nuclear fragments due to separation of I/A.
(d) Better control of fluid dynamics by separating I/A.
(e) Access to 360° of the anterior segment with either irrigation or aspiration by switching instruments between hands.
(f) Less traumatic surgery.
(g) Can use the flow of irrigating fluid as a tool to move material within the capsular bag or anterior chamber.
(h) Associated with a significantly reduced chance of Vitreous prolapse in the case of a posterior capsular tear or rupture.

(i) Seen as a next generation cataract surgical procedure with sub 2mm incision.
- An advanced procedure that will allow its full benefits to be realized once a true micro incision IOL is introduced.

Bimanual Phaco –Disadvantages:
(a) There is a learning curve.
(b) Less fluid flow into the anterior eye chamber
   Instability when high vacuum levels are utilized and occlusion from nuclear material as the phaco tip is cleared.
(c) Need for additional equipments.
   - Small incision Keratomes
   - Capsulorhexis forceps.
   - Irrigating Choppers.
   - Bimanual I/A handpieces.
(d) Current limitations in IOL technology
   Special Instrument- Requirements for Bimanual Microphaco

Keratomes: The keratomes are chosen according to the wound size which in turn depends on the gauge of the irrigating chopper or the Phaco tip. In general Keratome size of 1.2 to 1.6 have been used to fashion the incision.

Microrhexis Forceps: Special Rhexis forceps that can be introduced through the small wound size are required.
Irrigating Chopper: These are again available in 19 and 20 G size. These are basically the front irrigating and side irrigating types. The choppers are designed for both vertical as well as horizontal chopping.

Phaco Tip: The 19 or 20 G tips may be used depending on the surgeon’s preference. Bausch and Lomb has come out with the unique stableflow design for the specific purpose of Microphaco.

Cut Sleeve: An infusion sleeve cut close to the hub may be attached to the phaco tip. This prevents fluid spray which may otherwise be encountered during Microphaco.

Phaco machine: Bimanual Microphaco can be performed with any basic phaco machine. However a higher generation phaco machine with sophisticated fluidics and higher order phaco power modulations are more desirable.

Issues with BMICS:

(a) Tissue/Wound Damage.

- Abrasive Effect.
- Distortion.
- Thermal Damage.

The best way to manage heat build up in Phaco Surgery is to prevent it.

- Use low Phaco Power.

(b) Stability of Anterior Chamber

The inflow should never be less than the outflow.

Factors Governing Outflow:

- Vacuum Setting.
- Diameter (Phaco Tip & Aspiration Cannula).
- Sensible Fluid Loss (Desired).
- Insensible Fluid Loss (Undesired).
- Aspiration Controllers (Cruise Control, Vacuum Surge Suppress of ABS System, Coiled Supervac Tubing).

Factors Governing Inflow:

1. Passive Infusion (Not Forced).
   Gravity:
   - Height of Infusion Bottle
   - Extended
   - Height of OT Roof
   - Dia of irrigating line/ Cannula.
   - Type of Infusion Bottle.
   - Amount of Fluid in the Bottle.
   - Capacity of the bottle.
   - Level above sea level.

2. Forced Infusion

External (EFI)

- Fish tank Pump

Internal (IFI)

- AVGFI
- Bottle Infusion Tool.
Binocular Indirect Ophthalmoscope

Dr. Sonia Rani John DNB, Dr. Meena Chakrabarti MS DO DNB, Dr. Arup Chakrabarti MS DO

Binocular indirect ophthalmoscope has become an indispensable tool to diagnose and manage a variety of vitreoretinal disorders. The instrument has a rich history evolving through many generations to yield the current diagnostic marvel. Sophisticated additions to the basic technology include high magnification lenses built in to the ophthalmoscope, video adapters that facilitate patient and student education as well as open up an array of telemedical possibilities and laser photocoagulation systems mounted on to the indirect ophthalmoscope to treat peripheral tears through a 20 diopter lens.

The first binocular indirect ophthalmoscope was invented by Marc Antonie Giracid Tenlon of France in 1861. The first reflecting ophthalmoscope was invented by Helmholtz in 1850. Since Helmholtz first described the ophthalmoscope hundreds of variants have been described.

Perhaps the most useful, successful variant of the ophthalmoscope is the binocular indirect headband ophthalmoscope, first described by Charles Schepens in 1945 (Fig 1). It soon became the standard method of clinical ophthalmoscopy by ophthalmologists. They are indispensable in diagnosing and managing vitreoretinal disorders including lattice degeneration, retinal holes or tears, retinal detachment, retinopathy of prematurity, retinoschisis, sickle cell retinopathy and an array of other diseases.

Modern indirect ophthalmoscopes come with a myriad of features, which may include adjustable inter pupillary distance, portable power packs, adjustable mirrors, dust sealed optics and red free and cobalt blue filters. Video capture capabilities built in to some indirect ophthalmoscopes allow the patient to see his or her fundus on video and students also greatly benefit from this feature.

Optics

We can see an object only if it lies in line with the observing eye, provided that the object is illuminated. If a flat surface is to be illuminated and visualized, there may be a wide angle between the source of light and the observer. When the access to the object is limited, as in the eye by the pupil, the angle between the source of light and the observer is smaller. The source of light and the observer need to be practically overlapping. The illuminating and observing beams are optically aligned in an indirect ophthalmoscope, to make this possible. When both the illuminating and reflecting beam pass through the pupil, that area of fundus is seen.

The principle of indirect ophthalmoscopy is to make the eye myopic by placing a strong convex lens in front of it. This forms a real inverted image of the fundus in the air between the lens and the observer. The usual powers used are +20 D and +13 D. The lens is
positioned in such a way that it changes the direction of diverging rays emanating from the subjects’ eye and brings them to a point focus within the pupillary plane of the observers eye. Thus the pupils are in conjugate places.

If the patient is emmetropic, the rays of light from the subjects’ eye are parallel, but this changes once these rays pass through the condensing lens. As the rays of light enter the lens with zero vergence, they are brought to a focus in the focal plane of the condensing lens. Considering all rays of light emerging from the patient’s eye together, an aerial image of the patients’ fundus is formed in the focal plane of the lens (aerial image plane). Beyond this, the rays of light are divergent which are brought into focus by the observed eye. To focus this image on his own retina, the observer must accommodate for the aerial image plane and hence cannot approach too closely.

The magnification of the image is calculated by dividing the power of the eye by the power of the condensing lens. A 20 D lens should give a magnification of 3 times where the power of the emmetropic eye is 60 D. The stronger the power of the condensing lens, the closer it must be held toward the eye, since it is based mainly on the focal length of the condensing lens.

**Procedure**

The patient should be preferably in supine position, with pupils maximally dilated. The patient should be explained about the procedure before hand. Room light should be turned off making sure that all extraneous sources of light are eliminated. The illumination should be kept minimum initially with the beam size maximum and filters out. The headband keeps the indirect ophthalmoscope anchored to the head preventing any further movement. The crown strap rests snugly over the vertex of the head. The headband should fit approximately one finger width above the eyebrow with the rear strap straddling the inion (Fig 2a). The oculars should be as close to the examiners’ pupil as possible and the optical axes kept parallel to the line of the examiners’ vision. The view through both the eyes should completely overlap each other. The mirror should be aligned in such a way that the light is anteriorly directed. The light from the ophthalmoscope should enter the patient’s pupil in a plane higher then the image of the examiners visual axes.

The light should be adjusted in such a way that the vertical portion of the light fills the upper half of the field of view. This adjustment can be done on the back of the fist held at arm’s length or on the eye of the patient.

The interpupillary distance should be adjusted properly to avoid diplopia and achieve stereoscopic view of the fundus image. This can be accomplished by adjusting the oculars which slide horizontally. The oculars should be made to slide approximately in the right direction by the same amount in both eyes till a unified binocular field is obtained. The condensing lens should be held properly to perform various aligning maneuvers of the lens efficiently. The lens should be held with the convex side facing the examiner.

The thumb of the index finger should be diametrically opposite to each other with the middle finger supporting a point on the rim midway between the thumb and the index finger. While the ring and the little fingers rest on the cheek of the patient they can also be used to retract the lid.

The lens can be moved antero-posteriorly, side ways, tilted across the visual axes or tilted across the eye. The lens is moved to and fro in the antero-posterior direction in order to find the correct focal plane. Side to side movement helps to centre the image on the lens and is part of the basic movement for aligning the lens. This movement also helps in verifying the meridional localization of a pathology. Tilting of the lens across the visual axis helps to create a reflex free area through the fundus can be seen clearly. Tilting the lens across the eye helps to shift the viewing area from an area to the adjoining area.

If the image of the fundus is filling only the centre of the lens, the lens should be moved either towards the observer or the patient, till a clear image is obtained. Crescent image formation at the edge of the condensing
lens can be avoided by tilting the lens towards the crescent shadow.

Initially the illumination should be kept low with gradually increasing the voltage once the patient has become light adapted. The routine examination begins with superior nasal position of the patient.

The examiner is positioned 180° opposite the patient's direction of the gaze (Fig 2b). Initially the ophthalmoscope light is directed into the pupil and the red reflex is observed. Then the +20 D condensing lens is inserted into the light path about 2” from the eye. The superonasal area of the fundus of right eye is viewed first by standing to the right of the patient. Then the examiner moves progressively to the head end. The 12 0’ clock position corresponds to the head end of the patient and 6 0’ clock towards the feet. For the right eye 3 90' clock points to the nose and 9 0’ clock towards the nose. This orientation remains the same irrespective of the position of the head. A low power lens (14D) may be used where the distance of the lens from the eyes is sufficiently large to prevent any disturbance from the nasal bridge.

To examine the extreme periphery of the fundus, the patient is instructed to move his eyes maximally in the direction to be examined. For viewing through oval pupil in extreme peripheral gaze, the examiner can tilt his head towards either shoulder and view through the widest apparent diameter of the oval pupil. The posterior pole is examined finally by asking the patient to look at the examiner's ear. By shifting the thumb of the patient on which the patient’s gaze is fixed by the other eye, the examiner can move the eye under observation into various positions of gaze, thereby scrolling the entire posterior aspect of the fundus in detail. The macula should not be exposed to more than 40 seconds of continuous bright light to avoid the risk of the photic injury. The patient should be allowed brief respirations for blinking since the lens increases the intensity of light by focusing it onto an area and also to prevent corneal dryness.

The binocular indirect ophthalmoscope gives an inverted image of the fundus. The image is upside down and reversed right for left. Only the image is reversed and not the location of the fundus. The periphery of the fundus is imaged towards the observer or inferiorly as seen in the lens and the posterior aspect is imaged superiorly or away from the examiner. Movement by the examiner in one direction produces a movement of the fundus image in the opposite direction. When the patient moves the eye, the fundus image in the condensing lens also moves in the same direction.

**Colour coding**:

All the fine details of the lesion, for eg. the size of a tear, the direction of the flap, relation to adjacent lesions like, relation to the blood vessels and their branching should be drawn.

**Colour coding for retinal diagrams**:

<table>
<thead>
<tr>
<th>Colour</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blue</td>
<td>Retinal vessels, subretinal fluid, detached retina edema</td>
</tr>
<tr>
<td>Red</td>
<td>Attached retina, haemorrhage (preretinal, retinal or subretinal), retinal tears, micro aneurysm, panretinal neovascularization, occasionally normal retinal arterie</td>
</tr>
<tr>
<td>Yellow</td>
<td>Exude, inflammation (retinal), amelanotic</td>
</tr>
<tr>
<td>Green</td>
<td>Media opacity (corneal calcification, cataract vitreous debris or haemorrhage), panretinal fibrosis or preretinal membranes, vitreous detachment (weiss ring)</td>
</tr>
<tr>
<td>Brown</td>
<td>Melanocytic lesions</td>
</tr>
<tr>
<td>Orange</td>
<td>Orange pigment</td>
</tr>
<tr>
<td>Black</td>
<td>RPE (retinal pigment epithelium), pigment clumping, lattice degeneration, melanocytoma</td>
</tr>
</tbody>
</table>

The technique of scanning in indirect ophthalmoscopy is important to identify the exact orientation of lesions and to get an overall view of the fundus and makes scleral indentation possible. In this technique, the posterior pole of the eye is scanned first. Then rotate a retinal vessel and follow it from the disc to as far anterior as can be readily observed. Then follow the vessel of the disc. This exercise is to be repeated until a continuous scanning portrait of the fundus can be seen.
for all positions of gaze within the eye. This overlapping view review strategy also assures that nothing is missed.

For scleral indentation, the 3 O’clock and 9 O’clock positions can be indented by placing the depressor slightly above on the upper lid (2 O’clock and 10 O’clock) and sliding the probe downwards to move it into the inner or outer canthal positions. Indentation can also be done by applying the probe to the sclera without the intervening lid, but topical anesthesia should be used to make the patient comfortable.8 A better peripheral view can be obtained using +28 D or +30 D lenses.

Cleaning of the condensing lens may be achieved by using hard contact lens cleaner and warm water and then dry with a soft lint free cloth. Sterilization of the condensing lens can be done by placing the lens in cidex for 5-10 minutes, by ethylene oxide sterilization or by placing it in formalin chamber9. The lens can also be autoclaved in a steel chamber with perforation for steam10.

Advantages of binocular indirect ophthalmoscopy

- The biggest advantage of indirect ophthalmoscopy is the wide field of view. It crystallizes the spatial topography and the relative size, shape and positions of different structures in the fundus.

- Stereopsis is essential for depth perception and a three dimensional reconstruction of an object. The stereopsis rendered by the indirect ophthalmoscope offers an invaluable and unmatched evaluation of the relative plane of different structures and lesions in the fundus.

- The periphery of the retina can be examined only with a binocular indirect ophthalmoscope.

- The binocular indirect ophthalmoscope helps to view the retina through a hazy media.

- Indirect ophthalmoscopy is not affected by the refraction state of the subject’s eye.

In short, binocular indirect ophthalmoscopy opens up a whole new world of exciting clinical images that cannot be appreciated without mastering this technique.

References


Artificial Human vision

Dr. Ashad Sivaraman MD, Dr. Haj Ismail H. MD, Dr. Tariq Al-Rawasdeh MD

The goal of artificial vision research has been to create an implantable medical device that provides useful vision for those patients who are left with no alternatives. Analogous to the cochlear implants for some forms of hearing loss, these devices could restore useful vision by converting visual information into patterns of electrical stimulation that excite the remaining viable inner retinal neurons in these patients.

It is the conversion of light energy to electrical energy which is happening at photoreceptors in a healthy eye. Electrical signals from these photoreceptors are then processed through layers of bipolar and ganglion cells within the retina, before passing it to the optic nerve. Photoreceptors will be almost completely absent in the retina of end-stage RP and in macula of AMD patients, while the bipolar cells and ganglion cells survive at high rates. In the groups with severe RP 30% of ganglion cells and in moderate RP 88% of the inner nuclear layer cells were preserved. As the ganglion and bipolar cells remain intact, and due to the anatomy of the retina, they are in a position where they may respond to electrical stimulation. So if the work of damaged photoreceptors can be replaced by an artificial exciting device, then the rest of the connections should help the patient to see. This is premise of therapy with visual prosthesis implantation in RP.

Artificial retinal prosthesis can be implanted in any of the four sites in the visual pathway which includes subretinal, epiretinal, optic nerve or in the visual cortex. This is a dream project for researchers and patients with retinal degenerative diseases all over the world.

Latest development in this field is always heard with much anticipation and enthusiasm by all of them. The most impressive gains in vision in this field have been reported from the subretinal device project. Initial subretinal devices were developed by the Optobionics Corp (Allan Chow) and the sub-ret project (Eberhart Zrenner). But there are concerns that the success results of this device may not be related to the microphotodiode device used and can be due to activation of a growth factor which in turn rescues the remaining photoreceptors and thus exerts a neuromodulative effect.

The prosthesis

The development of an artificial human vision (AHV) system is a multidisciplinary field, involving inputs from ophthalmology, biomedical engineering, and neuroscience. Most AHV systems have similar system requirements with the exception of subretinal prostheses which is more simple when compared to other devices. The main components, which will need to function in real time in the AHV system includes a camera, an image processing unit, transmitter, stimulator and electrodes.

- Camera is required to capture and digitize image information from the environment with an adaptive mechanism to function in different levels of illumination.
- Image processing – there will be more data retrieved from the camera than that can be used in an artificial vision device. The image data will usually be preprocessed to reduce noise, (unwanted frequency) an information reduction (such as edge detection or...
segmentation) or a scene understanding approach, attempting to extract information that can be used.

- Transmitter is the link from the camera/image processing components to the stimulator and electrode array, which are usually located inside the body. Percutaneous or transcutaneous connections can be used for this connection. A transcutaneous connection uses radiofrequency telemetry to send data and power to the embedded stimulator whereas percutaneous devices use direct cables. The transcutaneous devices have the advantages of reduced risk of infection. Even though earlier devices were made for percutaneous connections the new generation ones are transcutaneous. This is being used in the current trials of new generation intelligent medical implant systems and by other researchers.

- Electrodes are thin wires, which allow a small amount of precisely controlled electrical current to pass through it to stimulate the neurons. There are two main types of electrodes discussed in the literature; surface electrodes, which lie flat against the stimulation target and penetrating electrodes, which are inserted inside the stimulation target.

Stimulator, located outside the body receives information from the transmitter and sends through multiple electrodes.

Subretinal Prosthesis are different from all other forms of artificial vision devices in terms of location of implantation, its energy needs, proximity to the inner retinal layers, existence in the subretinal atmosphere, heat generation etc. the details of this will be described later in this article.

**Types of artificial vision devices**

Different methods of implants are tried in different parts of the visual pathway starting from retina, optic nerve and optic radiation.

(a) **Cortical prosthesis**; (photograph)

In 1929, Forester noticed that cortical stimulation with electrodes caused the subject to see a spot of light in a position that depended on the site of stimulation. Later in sixties and early seventies Brindley and Lewin worked on this and implanted an array of 80 platinum electrodes in a 52-year-old legally blind. Stimulation of these electrodes produced discernible phosphenes and also found that phosphenes moved with eye movements and that phosphene perception usually (but not always) stopped when stimulation ceased.

Dobelle worked on this and came out with similar reports of stimulus perception. In late seventies he used a 64-channel platinum electrode surface stimulation prosthesis and showed that it can allow blind patients to recognize 6-inch characters at 5 feet (approximately 20/1200 visual acuity). Patients in these initial experiments complained of an inability to appreciate distinct phosphenes, but rather reported seeing “halos” surrounding each of these phosphenes. This approach has advantage of the potential to restore vision to the largest number of blind patients as it bypasses all diseased visual pathway neurons rostral to the primary visual cortex. But the disadvantages includes the difficulties encountered in controlling the number of phosphenes induced by each electrode, and interactions between phosphenes, need for high currents and large electrodes that can induce pain due to meningeal stimulation and occasional focal epileptic activity following electrical stimulation.

There are two methods for cortical stimulation discussed. The one with surface stimulation electrodes and other with intra cortical electrodes. Intra cortical stimulation was introduced in the hope of remediing the shortcomings of surface cortical stimulation via a lower current and higher fidelity system. This employed smaller electrodes closer to the target neurons, therefore requiring less current and resulting in a more localized stimulation. Initial studies, during which the intra cortical prosthesis was implanted in humans for a trial period of 4 months, demonstrated the ability to produce phosphenes which exhibited colour. Current models of the intra cortical prosthesis which are being studied in animal models include the Illinois Intra cortical Visual Prosthesis project and the Utah Electrode Array.

In 2000 Dobelle reported a case report of a patient who has stayed implanted with his cortical prosthesis for 20 years. This cortical implant system from the Dobelle institute was made commercially available (not approved by the FDA) and there was an article in the Wall Street Journal, which reported a 33-year-old
female recipient who paid US$100,000 for the Dobelle system and was only able to use it for 15 min per day (as it was tiring and caused severe headache). But the future of this device is in question as the major emphasis is on other types of artificial vision devices like epiretinal subretinal or optic neuronal. 

b. Optic Nerve Prosthesis

The optic nerve is an interesting and appealing site for the implementation of a visual prosthesis where the electrodes can be implanted on the temporal side of the optic nerve and the simulator placed on the orbital cavity.

Advantages of this approach are that the entire visual field is represented in a small area and this region can be reached surgically. The disadvantages being that the dura mater has to be dissected with a possible risk of infection and possible interruption to the blood flow to optic nerve. Also the optic nerve being a dense neural structure with approximately 1.2 million axons confined within a 2-mm diameter cylinder with the entire visual field represented, it can be difficult to achieve focal stimulation of neurons corresponding to the needed visual areas. Again it can be used only when intact retinal ganglion cells are present and therefore limited to the treatment of outer retinal (photoreceptor) degenerations only. Thus it can only be substitute to subretinal or epiretinal prosthesis.

Reports of such a chronically implanted optic nerve electrode connected to an implanted neuro stimulator and antenna that resulted in phosphene perception in a volunteer with no residual vision due to retinitis pigmentosa was there. It was encouraging as the blind volunteer was able to adequately interact with the environment while demonstrating pattern recognition and a learning effect for processing time and orientation discrimination. Further works are being carried out in this approach by various scientific groups. One such approach (fig. 1) in its early phase is being conducted by prof Quinshi Ren in China where they have successfully implanted their prosthetic device in animal models and are planning for human experiments.

c. Intraocular Approaches

(i) Epiretinal Prosthesis

Epiretinal implants specifically target surviving ganglion cells by positioning stimulating electrodes in close proximity to the inner surface of the retina (fig 2).

The electrodes will be implanted on the retinal surface after a pars plana vitrectomy with a retinal tack to hold it in position. Some surgeons fix the electrodes after an ILM peeling and others without.

The electrodes which are connected to the simulator can either be sewn outside the sclera with wire connections traversing through the pars plana wound (Prof Richard) or it can be secured in the capsular bag of the lens after lens removal, making it completely intra ocular (Prof Walter).

As the electrodes are implanted near to nerve fiber layer the image processing work which is usually taken care of by inner retinal cells and its connections have to be addressed. Also the energy send to the nerve fibers should be ideally corresponding to natural out flow. This stays technically difficult as much of the details regarding image processing inside the retinal layers are unknown. To overcome this issue at least to a certain level, image processing is being done by the image processors.
The work on successful epiretinal prosthesis is guided by the requirements like, preserving as much the normal anatomy/physiology of the eye as possible while minimizing the amount of implanted electronics required to power the device. Several groups worldwide have developed different designs of epiretinal implants that vary in terms of the intraocular and external elements. Listed in Table 1.

Dr Mark Humayun at the Doheny Eye Institute and University of Southern California started working with artificial vision initiative, IRP; since early 1990 with Second Sight Medical Products, Inc (Sylmar, CA.) Their system consisting of an externally mounted camera visual processing unit and magnetic coils was implanted in the temporal skull, which provide the inductive link telemetry system. The microelectrodes on the array use these pulses to stimulate any viable inner retinal neurons. The array is positioned just temporal to the fovea and is attached to the inner retinal surface using a single tack, which is inserted through the electrode array into the sclera \(^{13,14}\).

After it was demonstrated in several different animal models that epiretinal stimulation could reproducibly elicit neural responses in the retina, preliminary tests of acute (<3 hours) epiretinal stimulation were performed on humans in the operating room using hand-held electrodes as well as multielectrode arrays not affixed to the patients’ retina. These patients perceived phosphenes in response to the electrical stimulation to the retina and were even able to detect motion as well as identify shapes, amounting to crude form of vision \(^{15,16}\).

Their Clinical trials of chronic, long term implantation of the IRP with 16 electrodes began in 2002 at the Doheny Retina Institute as part of a Food and Drug Administration (FDA) Investigational Device Exemption study. It has been implanted in 6 subjects for more than 5 years. Report of this 16 electrode implant in a patient showed spatial pattern recognition corresponding to 2.3 logMar \(^{17}\). Later they have improvised their device by increasing the number of electrodes to 60 and recently reported (Argus II trials www.clinicaltrials.gov) its early outcome. Till July 2009, 32 patients have been implanted at 11 centers and reports of the first 17 among them who completed a minimum of 6 months follow up were addressed. There were no device failures and no explants, 5 cases of conjunctival erosion, 4 hypotony, 3 endophthalmitis. But all resolved after the early post op period. They reported that “100% of the subjects were seeing phosphenes and significant improvements in the spatial localization, motion detection, orientation and mobility and other measures were there \(^{18}\). They are expected to come out with the detailed reports soon.

Joseph Rizzo and John Wyatt at the Harvard Medical School was working on another epiretinal prosthesis. (Boston group) Their version of an implant is similar to that of the IRP group in that it consists of distinct intraocular and extra ocular modalities. The intraocular components are composed of a photodiode panel and a stimulator chip that are affixed, away from the retinal surface, onto a modified intraocular lens \(^{19}\). The extra ocular unit is composed of a charge coupled device (CCD) camera, a signal processing unit, as well as a laser, all mounted onto a pair of glasses. The battery back which powers the device is also located external to the eye. The photodiode panel acts to capture the processed signal from a laser pulse emitted from the

<table>
<thead>
<tr>
<th>Table 1. Details of work on Epiretinal prosthesis</th>
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<tbody>
<tr>
<td>Surgeon, University, Country</td>
</tr>
<tr>
<td>Dr M Humayun, University of California, USA</td>
</tr>
<tr>
<td>Dr J Rizzo, Wyatt, Harvard medical school, Massachusetts eye and ear infirmary, USA</td>
</tr>
<tr>
<td>Dr Eckmiller, Dept of computer science, Uty of Bonn, Germany</td>
</tr>
<tr>
<td>Dr G Richard, University of Hamburg, Germany</td>
</tr>
<tr>
<td>Dr Walter, University of Aachen, Germany</td>
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In order to study the acute effects of electrical stimulation on visual perception, they implanted this device in 5 blind patients with RP and 1 normal-sighted patient who was scheduled for enucleation due to orbital cancer. Three different types of electrode arrays, varying in the number, size and spacing of the peripheral electrodes, were tested. Similar to the results found by the IRP group, they observed that higher charge densities were required to stimulate the retinas in patients with worse vision. No apparent damage as a result of electrical stimulation of the retina was evident in histological specimens from the retina of the enucleated eye of the normal-sighted patient. But their results were mixed and inconclusive. While stimulating a single electrode above threshold levels, multiple phosphenes were often perceived by the blind subjects. Simple pattern vision was not achieved by either the blind or the normal sighted patients when multi electrode patterns of electrode stimulation were applied in trials with multiple electrodes. On average, 3 of the 5 blind RP patients accurately described the percepts that corresponded to the correct stimulation pattern only 32% of the time, compared to 43% for the normal-sighted patient. Driving the same electrode with the same stimulus parameters at different times showed relatively good reproducibility, which was achieved 66% of the time in the 5 patients. Later, due to the inability of getting good or consistent results with epiretinal stimulation, Rizzo and Wyatt have abandoned the epiretinal approach and then started developing a subretinal approach very similar in nature to the Zrenner group (commented later in this article).

In 1995 a consortium of 14 expert groups in Germany directed by Rolf Eckmiller has started working for the development of the Learning Retina Implant. Like the previous 2 epiretinal prostheses, their implant also consists of intracocular and extra ocular components.

Their retina encoder (RE) (processor), which approximates the typical receptive field properties of retinal ganglion cells, replaces the visual processing capabilities of the retina by means of 100 to 1000 individually tunable spatiotemporal filters. The processing of visual information that occurs in the RE simulates the filtering operations performed by individual ganglion cells. The RE output is then encoded and transmitted via a wireless signal and energy transmission system to the implanted retina stimulator (RS). The REs not only simulate the complex mapping operation of parts of the neural retina, but also provide an interactive, perception-based dialogue between the RE and human subject. The purpose of this dialogue is to tune the various receptive field filter properties with information “expected” by the central visual system to generate optimal ganglion cell codes for epiretinal stimulation.

They successfully tested their retina encoder/stimulator in several different animal models as well as normally sighted subjects (later this group spread up and started working as independent groups).

At University of Hamburg Professor G Richard is working on another epiretinal prosthesis with Intelligent medical implant system in their European trial. This device, similar to the other epiretinal designs has got a visual interface (spectacle) a pocket processor, the retinal stimulator and 49 electrodes (Fig. 3). The Visual Interface which looks like a standard pair of glasses consists of a camera to capture images and the electronics to provide energy to the Retinal Stimulator/electrodes implanted in the eye via wireless transmission. The Pocket Processor with the size of a walkman, contains rechargeable batteries that supply energy for the entire system and a microcomputer that translates the image data into stimulation commands for the Retinal Stimulator. The acute trial results of this group in 4 subjects with an implanted 49-electrode epiretinal array in a trial designed to last 18 months (clinicaltrials.gov identifier: NCT00427180; recruiting) were encouraging regarding the phosphene production and the feasibility of a long term intra ocular implant. For the chronic trials the company has come

Fig.3. Epiretinal prosthesis of IMI. (image courtesy Dr Hornig)
out with a new generation device having 49 electrodes. This trial named as the ‘Europe trial’ is going on in different universities in Europe including Hamburg, Parris, Austria, London. Reports of the outcome can be expected by early next year.

The project named EPI RET3 of Prof Walter et al. at University of Aachen reported results of a 25-electrode epiretinal array implanted for 4 weeks in 6 blind subjects (Fig. 4).

![Camera chip embedded in goggle, epiretinal chip in position with stimulator in the posterior chamber. (image courtesy, IMI, Dr Hornig.)](image.png)

(ii) Subretinal Prostheses

In the subretinal approach a micro photodiode array is implanted between the bipolar cell layer and the retinal pigment epithelium, either through an abexterno (scleral incision) or abinterno approach (through the vitreous cavity and retina).

This was first described by Alan and Vincent Chow of Optobionics Corp, who believed that a subretinal implant could function as a simple solar cell without the need for a power or input source of any type 27,28,29. Their Artificial Silicon Retina (ASR) Microchip is powered entirely by light entering the eye, without batteries or other ancillary devices. Two millimeters in diameter, the ASR contained approximately 5000 microelectrode-tipped micro photodiodes which convert incident light into electrical signals similar to those normally produced by the retina’s own photoreceptors. These electrical impulses, in turn, stimulate any viable retinal neurons, which then process and send these signals to the visual processing centers in the brain via the optic nerve. This chip was implanted in 6 patients, with a follow-up of 6 to 18 months and reported gains in visual function in all patients as well as unexpected improvements in retinal areas distal to the implantation site. They hypothesized this as an effect due to the neuro modulation of the existing neurons due to the electrical activation.

But later works demonstrated that the idea behind this simple approach is not feasible because it lacks a source of viable power 30. Gabel et al showed that cortical activation secondary to retinal stimulation with such a device required brightness comparable to 2 to 3 times sunlight levels (energy) 31. Simple photodiodes will also not produce charge balanced pulses, which are the safest form of electrical stimulation of nerve tissue. 32

Across time, pulses that are not charge balanced will lead to dissolution of metal with toxicity to neural tissue and loss of electrode function. Methods to amplify these signals and produce charge balanced pulses are proposed but these add significant complexity 31.

In fact, Chow et al too have abandoned the notion that their ASR Microchip is efficacious as a prosthetic device and later thought that the low levels of current delivered from the implant, although insufficient to electrically activate any remaining retinal neurons in a retina with damaged photoreceptors, may act as therapeutic as well as neuro protective to otherwise dying retinal photoreceptors. Hence, it is thought that this type of an implant works through a “growth factor” that then rescues the remaining photoreceptors. Thus, some of the researchers claimed that this device is not a true retinal prosthesis but should be best classified as a therapeutic device. Studies by Pardue et al were on to determine whether these effects are indeed neuro protective as well as if they are persisting and reproducible 33, 34. In addition, studies are also ongoing to determine whether an electronically inactive implant can have similar effects.

In Germany another design for a subretinal implant has been under development since 1996 by a consortium of research universities under the guidance of Eberhart Zrenner. They have demonstrated in various animal models with comparable retinal degenerations that subretinal stimulation elicits neuronal activity in retinal ganglion cells. Also they were successful in defining parameters necessary for successful electric stimulation and then incorporated these data into the development of their photodiode arrays 35,36.

Having identified that the subretinal approach to a retinal prosthesis is not practical without an additional
source of energy to power the implant, the feasibility of polyimide film electrodes in a cat model was demonstrated and further exploration of film-bound electrical stimulation was studied \textsuperscript{37}. Prototypes of this subretinal device have an external power source that supplies energy to the subretinal implant by means of very fine wires that are run outside of the eye.

Dr Zrenner’s present device designed and manufactured by IMS Stuttgart with dimensions (3×3×0.1 mm) comprising one photodiode activated by light associated with one stimulation electrode (TiN 50×50 μm, 70 μm grid spacing) to be placed subretinally under the macula. For initial testing purposes in the pilot study, they also added an array of 4 x 4 electrodes which are powered and controlled centrally allowing the exact determination of thresholds for visual sensations and electrode impedances. The power supply was connected by a retroauricularly placed cable \textsuperscript{38}. The outcome of such an implant in a 44 year old retinitis pigmentosa patient with no residual vision was presented recently at 2\textsuperscript{nd} Bonn Dialogue on Artificial retina. It has shown that the patient was able to appreciate Landolts C patterns and grating patterns (fig 5) shown at 62.5 cm distance corresponding to a visual acuity of 1.68 logMar and was able to read the cut out near vision letters like OIL, NUT, LOVE, MOUSE etc after scanning eye movements of about 5-200 s per letter (expected due to small visual field of the chip). To provide the control condition they switched off the power supply unknown to the patient where he completely failed to identify or localize the letters. This is the most promising and the latest report in this field and gives much inspiration to the researchers \textsuperscript{39}.

A third type of subretinal prosthesis is being developed by Rizzo and Wyatt (commented in the epiretinal prosthesis group). Minimally invasive surgical techniques utilizing a posterior, ab externo approach to implant the prosthesis and to insert the stimulating electrode array in the subretinal space, have been tested and studies regarding the long-term biocompatibility of materials in the subretinal space as well as methods to protect the retina upon insertion of the prosthesis during surgery were going on with their group \textsuperscript{40}.

Advantages of the subretinal project includes that, unlike epiretinal prostheses, external cameras or image processing units are not required and the patients’ eye movements can still be used to locate objects. Placement of the subretinal prosthesis in closer proximity to any remaining viable inner retinal neurons in the visual pathway may be advantageous in possibly decreasing currents required for effective stimulation, then in addition to the relative ease in positioning and fixing the micro photodiodes in the subretinal space, the lack of mechanical fixation allows for less surgically induced trauma upon implantation. Also the micro photodiodes of a subretinal prosthesis directly replace the functions of the damaged photoreceptor cells while the retina’s remaining intact neural network is still capable of processing electrical signals \textsuperscript{41}. However, disadvantages like the limited area of the subretinal space which will contain the microelectronics predisposes the contacted retinal neurons to an increased likelihood of thermal injury resulting from heat dissipation and if the subretinal implant is composed only of an electrode array with the electronics outside the eye, the prosthesis must have a cable piercing the sclera leading to potential tethering on the cable. The tethering effect on the electrode array in the subretinal space leading to possible movement after implantation can lead to subretinal bleeding. Again the more invasive trans choroidal incision too can lead to extensive subretinal bleeding. Also simple photodiodes will also not produce charge balanced pulses, which are the safest form of electrical stimulation of nerve tissue \textsuperscript{32}. Across time, pulses that are not charge balanced will lead to dissolution of metal with toxicity to neural tissue and loss of electrode function. Methods to amplify these signals and produce charge balanced pulses will add significant complexities \textsuperscript{42}.

Other projects includes the Japanese subretinal project by prof Jun Ohta, Nara where light controlled retinal
stimulator based on multiple microchips have been tried on animal experiments, another Japanese project based on supra choroidal –trans retinal stimulation, the minimal invasive retinal project of Prof Heinrich Gerding in Switzerland, the Seoul Artificial project of Prof Hum Chung etc.

Conclusion

With ongoing advances in technology, surgical techniques and treatment options, there has been significant advancement towards restoring some vision to patients suffering from RP.

Although many advances have been made, the field of artificial vision is still young. We hope within another five years, patients with retinitis pigmentosa will be able to receive a retinal prosthesis, suitable to their needs, and possess vision allowing them to possibly perform. The management options of AMD has changed a lot since the retinal prosthesis started developing in nineties. In the dawn of anti VEGF era, the number of patients who needs prosthetic vision due to this disease is expected to fall according to many researchers.

Future research by all AHV groups will need to address more on the energy needs, its supply, long-term biocompatibility of microelectronics in the saline environment of the eye in terms of hermetic packaging of the micro fabricated electrode arrays, minimization of the heat generated and dissipated with its use, effect of chronic electrical stimulation on the retina etc. In addition to this, significant attention needs to be given to the manner in which visual images will be encoded and delivered in patterns of electrical stimulation to the retina. Plasticity of the visual system in response to electrical stimulation as well as how the brain interprets a pattern of stimulation resulting from thousands of, electrodes has to be understood well and will be crucial in the evolution of better prosthetic design.

We can thus tell our patients with outer retinal degenerations that there is progress toward an electronic retinal prosthesis but fully functional, long-lasting devices are not on the immediate horizon.

References

4. Arturo Santos, MD; Mark S. Humayun, MD, PhD; Eugene de Juan, Jr, MD; Robert J. Greenburg; Marta J. Marsh, MS; Ingrid B. Klock; Ann H. Milam, PhD. Arch Ophthalmol. 1997;115(4):511-515.
12. Xinyu chai, Liming li, Kajjie wu, Chuangqing zhou, Pengjia cao, and Qiushi Ren IEEE Engineering in medicine and biology magazine
18. Brian; second sight medical products Inc; Abstract; 2nd Bonn dialogue on artifitial retina.
38. Walter Wrobel, Reutlingen, Germany. Active subretinal implants: design, functionality, and operational experience. 2nd Bonn Dialogue on Artificial retina abstract.
39. Zrenner, Tubingen, Germany. Blind retinitis pigmentosa patients can read letters and combine them to words. 2nd Bonn Dialogue on Artificial retina abstract.
40. Rizzo JF. Biological considerations for a subretinal prosthetic implant. Presentation given at Second DOE International Symposium on Artificial Sight; 29 April 2005; Fort Lauderdale.
Role of MRI and CT in Ocular and Orbital Diseases

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Abstract

CT and MRI have made significant contributions to the field of ophthalmology. Familiarity with salient imaging features of conditions affecting the eye and orbit will help the ophthalmologist to better understand disease process and evaluate response to therapy. The article outlines important diagnostic features with an algorithmic approach which would help in making a diagnosis.

Introduction

The eye and the orbit constitute a unique and complex region of the nervous system which poses a challenge to the ophthalmologist and neuroradiologist. While history and clinical examination are invaluable, CT and MR provide an insight into the retrobulbar area, the orbital apex and the brain. CT was the preferred investigative modality with its faster acquisition times and lack of sensitivity to eyeball motion which were seen as major problem areas in MR imaging. With the advent high-tesla MR systems and small diameter dedicated surface coils, the skepticism against MR has receded and despite the limitations, MRI is now the modality of choice and can provide information that is unavailable on CT because of superior soft tissue resolution. The article focuses on salient MRI and CT findings of few commonly encountered conditions in the eye and orbit, and also aims to provide a systematic approach to these conditions.

Techniques

MRI Technique:

MRI is performed using a head or preferably a surface coil with the patient in supine position. The common pulse sequences used for orbit are Spin Echo T1 and T2, Fat suppression and Short Tau Inversion recovery. These help in tissue characterization. Post contrast T1 sequences help in assessing the vascularity of lesions, the enhancement patterns of some of which may help in reaching a definitive diagnosis.

CT Technique:

With the advent of Multi Detector row CT, the images obtained with the patient scanned in supine position and can be reformatted to coronal and sagittal planes in slice thickness of as low as 0.6 mm.

Radiological Anatomy of The Globe and Orbit:

To identify and characterize the lesions of orbit and globe one should be aware of normal structures and their signal intensities on various MRI sequences. Representative image with anatomical structures is shown below. (Figs 1a, 1b)
Lesions In The Globe

The lesions in globe and orbit can be summarized in Table 1 and 2. The classification system followed is based on pathology. The imaging approach to each disease entity is dealt with at the end of the discussion.

### Table 1. Approach to lesions in Eye

<table>
<thead>
<tr>
<th>Congenital</th>
<th>Microphthalmia</th>
<th>Macrophthalmia</th>
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</thead>
<tbody>
<tr>
<td>Staphyloma</td>
<td>Coloboma</td>
<td></td>
</tr>
<tr>
<td>Ocular Detachments</td>
<td>Posterior subhyaloid</td>
<td>Retinal</td>
</tr>
<tr>
<td>Posterior Vitreous</td>
<td>Choroidal Detachment</td>
<td></td>
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<tr>
<td>Inflammation</td>
<td>Scleritis</td>
<td>Uveitis</td>
</tr>
<tr>
<td>Laukocoria</td>
<td>Retinoblastoma</td>
<td>Persistent primary hyperplastic vitreous</td>
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<tr>
<td>Coats Disease</td>
<td>Retinopathy of prematurity</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumours</td>
<td>Melanoma</td>
<td>Lymphoma</td>
</tr>
</tbody>
</table>

### Table 2. Approach to Orbit

<table>
<thead>
<tr>
<th>Congenital</th>
<th>Dermoid/epidermoid</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory</td>
<td>Orbital cellulitis</td>
<td>Subperiosteal abscess</td>
</tr>
<tr>
<td>Cavernous sinus thrombosis</td>
<td>Fungal Sinmsisitis</td>
<td>Pseudotumor</td>
</tr>
<tr>
<td>Graves</td>
<td>Sarcoidosis</td>
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<tr>
<td>Neurofibromatosis</td>
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<tr>
<td>Vascular</td>
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<tr>
<td>Capillary Hemangioma</td>
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<td></td>
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<tr>
<td>Cavernous Hemangioma</td>
<td></td>
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<tr>
<td>Lymphangioma</td>
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<tr>
<td>Orbital varix</td>
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<tr>
<td>Caroticocavernous fistula</td>
<td></td>
<td></td>
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<tr>
<td>Neural</td>
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<tr>
<td>Schwannoma</td>
<td>Neurofibromatosis</td>
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<td>Optic nerve sheath</td>
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<td>Optic neurotis</td>
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<tr>
<td>Optic N glioma</td>
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<tr>
<td>Optic N meningioma</td>
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<tr>
<td>Lacrimal gland lesions</td>
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</table>

**Congenital Microphthalmia**

It is defined as a globe with AP diameter of less than 21mm in adult or less than 19 mm in an infant. The condition may be isolated or may present with other ocular and craniofacial anomalies, congenital rubella,
leukokorias. If the embryological insult occurs before the complete invagination of the optic vesicle then an orbital cyst in formed and is referred to as microphthalmos with orbital cyst. (Fig 2).

**Staphyloma and Coloboma**

Staphyloma results due to diffuse thinning and stretching of the sclera-uroal coats of the eyeball. The causes include progressive myopia, glaucoma, post infectious and inflammatory conditions. Coloboma on the other hand is a notch, gap or a fissure in which a tissue or portion of tissue is lacking. The cleft appears in the inferonasal quadrant of the globe with optic disc excavation in a typical Coloboma. Retinal detachments are well documented with Colobomas. Ocular colobomas may involve iris, lens, ciliary body, retina, choroid, optic nerve or sclera.

![Fig. 3. Coloboma. Axial CT section demonstrating ectasia of the globe and a defect in its inferonasal aspect.](image)

**Ocular Detachments**

**Posterior hyaloid detachment (PHD)**

These are seen when fluid fills the posterior hyaloid space and appear as layered abnormality in vitreous chamber that shifts its location in decubitus position. As opposed to hyaloid detachment, hemorrhage with posterior vitreous detachment mixes with the vitreous and thus does not show layering which helps it to be differentiated from posterior hyaloid detachment.

**Retinal Detachment (RD)**

RD is seen as a characteristic V shaped membrane with its apex at the optic disc and its extremity towards the ciliary body with underlying protein rich subretinal fluid.

RD can be caused by pathology in the vitreous or the choroid. RD can result due to a mass causing retraction or any fibroproliferative disease caused by diabetes in the vitreous or choroid such as malignant melanoma and choroidal hemangioma.

Therefore imaging plays a larger role in detection of underlying cause, if any than just identification of type of detachment. (Fig. 4a, b)

**Choroidal Detachment**

Choroidal detachment occurs due to accumulation of fluid or blood in the potential suprachoroidal space. CD can be caused by trauma, inflammatory diseases or post surgery. CT is indicated when a ferromagnetic foreign body is suspected and appears as a semilunar or a ring shaped area of variable attenuation with underlying hemorrhage density of which depends on its age. A serous CD appears as a smooth elevation of the choroid, is hypodense on CT and mimics an exudate on MR. CD is difficult to differentiate from RD but a rapidly shifting fluid in the wall of the eye would favour a diagnosis of RD.

**Ocular Inflammatory Disorders**

Majority of the inflammatory disorders of the globe such as infectious conditions, papilledema, episcleritis and uveitis are usually a clinical diagnosis. Imaging does not play a significant role except when there is an abscess or space occupying lesion like a cysticercus which is causing the symptoms.

**Leucokoria**

Leucokoria is a white, pink white or a yellow white pupillary reflex and results from any intraocular abnormality that reflects the incident light back to the observer. Causes of Leucoria are Retinoblastoma, Persistent fetal vasculature, Retinopathy of prematurity, Cataract, Coloboma (fissure or cleft) of choroid or optic
disc, Uveitis, Toxocariasis, Coats’ disease, Vitreous hemorrhage, Retinal dysplasia

The radiological approach to common causes of leucokoria can be summarized as in Table 3.

**Retinoblastoma**

It is the most common intraocular tumor of childhood. Imaging plays a crucial role in differentiating it from benign mimics and evaluating the extent of retrobulbar spread of the lesion. It rules out tri/tetralateral lesions in the pineal gland or suprasellar region. Punctate or finely speckled calcification is seen in 90-95 % cases on CT. MR is useful for assessing extraocular and intracranial disease as extension beyond the eye signifies close to 100 % mortality. (Fig 5.)

**Coats’ disease**

Coats’ disease also known as primary retinal telangiectasias, is seen as subretinal exudates. Calcification is not a feature. It is important to differentiate this from a non calcified retinoblastoma which is not possible on CT. On MRI Coat’s disease shows hyperintense signal on T1, T2 and proton density images whereas retinoblastoma appears hyper on T1 and proton density, and hypointense on T2W images. Enhancement may be seen which is attributed to idiopathic intraretinal telangiectasia and microaneurysms.

**Persistent hyperplastic primary vitreous (PHPV)**

PHPV is caused by failure of embryonic hyaloid vascular system to regress normally. On CT the globe is small,

Fig. 5. Retinoblastoma. CT image reveals a hyperdense calcified mass in right globe of a 2 year old child.

Fig. 6. a, b: PHPV. CT shows hyperdense retrolental soft tissue in posterior chamber of right eye. Colour doppler demonstrates the persistent hyaloid artery in the right globe coursing anteriorly in the vitreous chamber.
calcification is absent and a generalized increased
density of vitreous chamber may be visible. The
enhancement of abnormal intravitreal tissue (the
retrolental tissue stalk) may be seen. There may be an
associated small and irregular lens with a small and
shallow anterior chamber. (Fig. 6a, b).

**Retinopathy of prematurity (ROP)**

ROP is seen in premature low birth weight babies
due to prolonged exposure to oxygen therapy. Spontaneous regression is seen in 85-95 % with the
disappearance of neovascularisation and formation of
dense membrane or a vascularised mass that is left
back as a permanent evidence of active phase.
Calcification is rare. Involvement is bilateral and often
asymmetric. There may be associated massive
persistent hyaloid vascular system. Clinical history
plays a crucial role in differentiating these from other
causes of bilateral leukokoria.

**Uveal Masses: Uveal melanoma**

Malignant uveal melanomas are more frequent in
whites than blacks. Less than 2 % of patients affected
are under 20 years. Dynamic CT may help to
differentiate it from a choroidal hemangioma. They
appear as elevated hyperdense sharply marginated
lenticular or mushroom shaped lesions and show a
moderately high signal on T1W and PD images and
low on T2W sequences. Lesions smaller than 3 mm
are better detected on ultrasound. They show moderate
post contrast enhancement which is important in
defining the extraocular extent of the disease. Other
mass lesions which are difficult to differentiate from
each other are uveal metastasis, choroidal hemangioma
and retinal astrocytoma.

**Orbital Diseases**

**Congenital Dermoid/Epidermoid**

These are choristomas which are among the most
common orbital tumor in childhood and are seen
superior or temporal in location. Both appear as well
circumscribed smoothly marginated low density
masses. Fatty tissue or calcifications are a feature of
dermoids. On MR both are seen as hyperintense on T1
and T2 depending upon the content of fat and are of
negative HU values on CT. Minimal enhancement of
capsule may be seen. On CT they show negative
Hounsfield values typical of fat (Fig. 7).

**Inflammatory**

The majority of acute inflammatory disorders are of
paranasal sinus origin. Inflammatory disorders can be
classified as inflammatory edema, subperiostal
phlegmon and abscess, orbital cellulitis, orbital abscess
and ophthalmic vein and cavernous sinus thrombosis.
Imaging in inflammation is aimed at detecting the
underlying cause if any, intraocular and intracranial
extension and bony involvement. In post septal orbital
cellulitis, orbital imaging with contrast enhanced study
is indicated to differentiate inflammatory edema,
cellulitis, phlegmon and orbital abscess. Subperiosteal
phlegmons (Fig. 8) may result from collection of
inflammatory tissue and edema beneath the periosteeum seen as diffusely enhancing soft tissue and
this may progress to abscess (Fig. 9a, b) formation when

Fig. 7. Angular dermoid. Well defined lesion in the region of
medial canthus of left eye showing negative
Hounsfield values values within.

Fig. 8. Subperiosteal phlegmon due to right ethmoidal
sinusitis. T2W sequence showing extraconal
hyperintense soft tissue with mucosal thickening of
adjacent right ethmoidal sinus.
it shows peripheral enhancement with a non-enhancing centre.

Complications such as cavernous sinus thrombosis is seen as low attenuation non enhancing structure on contrast scans. Engorgement of cavernous sinus ophthalmic veins and extraocular muscles is seen. MR Venography is more sensitive than CT and MR angiography reveals deformity of cavernous portion of internal carotid artery.

**Mycotic infections**

Mucor and aspergillus are the most common fungal organisms incriminated and usually affect diabetics and immunocompromised. Spread to orbit occurs usually from paranasal sinuses. Hypointensity of the mycetoma on T2W images due to the paramagnetic materials produced by the fungi is an important finding and helps to distinguish from other lesions which are frequently iso to hyperintense on T2.

**Pseudotumors**

Orbital pseudotumours are part of a non-granulomatous inflammatory process in the orbit or eye and are without known local or systemic causes. Patients present with acute onset orbital pain, restricted eye movement, diplopia, proptosis or impaired vision. This acute presentation helps to differentiate other lesions that are similar in appearance but have a chronic presentation. Pseudotumours can be classified as follows.

1. Acute and subacute idiopathic orbital inflammation seen as thickening of uveal-scleral rim with obscuration of optic nerve junction and post contrast enhancement.

2. Acute and subacute idiopathic diffuse orbital inflammation seen as a diffuse lesion which fills up the retrobulbar space and moulds itself around the globe while respecting its shape. No bony erosions are seen even in large masses. (Fig. 11a, b)

3. Acute and subacute idiopathic myositis orbital inflammation which present as enlargement of muscles of superior complex and medial rectus. The enlargement extends anteriorly to involve tendon insertion. The ragged fluffy borders of involved muscles with infiltration of the fat with an inward bowing of the medial contour of the muscle belly help in diagnosis. (Fig. 12a, b)

4. Acute and subacute idiopathic apical orbital inflammation is seen as irregular infiltrative process at the orbital apex that may extend anteriorly along the posterior aspect of extraocular muscles (EOM’s) or optic nerve.

**Fig. 9.** a,b: Right orbital abscess. Pre and Post contrast T1W images showing a peripherally enhancing lesion in right orbit displacing the right globe.

**Fig. 10.** a,b: Fungal sinusitis – Mucosal thickening with hyperdense areas within opacifying the left maxillary sinus extending into the extraconal space of left orbit with destruction of floor and medial wall of orbit. On MRI, the soft tissue displays predominantly hypointense signal on T2 WI.

**Fig. 11.** a,b: Patient with acute onset retro-orbital pain. Pre and post contrast T1W image shows diffusely enhancing intraconal soft tissue moulds itself posterior to the globe suggestive of diffuse orbital inflammation (Pseudotumor).
5. Idiopathic dacryoadenitis is seen as enlargement of the gland. A viral etiology, sarcoidosis, Sjogren’s disease, lymphoproliferative disorders, cysts, neoplasia has to be ruled out by biopsy if required. (Fig. 13a, b).

is presumed to be an autoimmune disease. Initially the extraocular muscles are infiltrated by lymphocytes, and later they undergo fibrosis resulting in restrictive myopathy. Exophthalmos and limitation of ocular motility are the most common presenting symptoms, and exophthalmos results mainly from enlargement of the EOMs and/or increased orbital fat volume. Inferior rectus muscle is involved most commonly, and the exophthalmos is almost always bilateral, usually being relatively symmetric. Imaging in the early stage may reveal bilateral proptosis with markedly swollen retrobulbar contents. Later on the muscle bellies start enlarging, with coronal sections being especially valuable in their evaluation. However, axial views are best to see the strangulation of the optic nerve. On CT or MRI, the characteristic finding is enlarged muscle belly with normal anterior tendinous insertion. (Fig. 14a, b). Another helpful finding is the presence of hypodense areas within the muscle bellies. Additional findings are excessive orbital fat, enlargement (engorgement) of lacrimal glands, lid edema, anterior displacement of orbital septum, and stretching of the optic nerve with or without associated “tenting” of the posterior globe. In chronic stages, when fibrosis of the EOMs occur, CT and MRI may show fatty replacement or a string-like appearance of the EOMs.

6. Perineuritis seen as ragged edematous enlargement of the optic nerve sheath complex.

**Tolosa-Hunt Syndrome (THS)**

THS is unilateral recurrent painful ophthalmoplegia involving 3rd, 4th, 5th and 6th cranial nerves. It is considered as a regional variant of idiopathic orbital tumor and is located in the superior orbital fissure or cavernous sinus. The cavernous ICA may show adventitial thickening with a cuff of inflammatory tissue surrounding it on MR and the superior ophthalmic vein may be occluded.

**Thyroid Orbitopathy**

Grave’s dysthyroid ophthalmopathy is the most common cause of uni- and bi-lateral exophthalmos in the adult population. Generally more common in women and orbital manifestations appear approximately 2 to 5 years after onset of thyroid disease. Thyroid orbitopathy is presumed to be an autoimmune disease. Initially the extraocular muscles are infiltrated by lymphocytes, and later they undergo fibrosis resulting in restrictive myopathy. Exophthalmos and limitation of ocular motility are the most common presenting symptoms, and exophthalmos results mainly from enlargement of the EOMs and/or increased orbital fat volume. Inferior rectus muscle is involved most commonly, and the exophthalmos is almost always bilateral, usually being relatively symmetric. Imaging in the early stage may reveal bilateral proptosis with markedly swollen retrobulbar contents. Later on the muscle bellies start enlarging, with coronal sections being especially valuable in their evaluation. However, axial views are best to see the strangulation of the optic nerve. On CT or MRI, the characteristic finding is enlarged muscle belly with normal anterior tendinous insertion. (Fig. 14a, b). Another helpful finding is the presence of hypodense areas within the muscle bellies. Additional findings are excessive orbital fat, enlargement (engorgement) of lacrimal glands, lid edema, anterior displacement of orbital septum, and stretching of the optic nerve with or without associated “tenting” of the posterior globe. In chronic stages, when fibrosis of the EOMs occur, CT and MRI may show fatty replacement or a string-like appearance of the EOMs.

**Sarcoidosis**

Granulomatous systemic disease affecting both sexes and all ages. Ophthalmic lesions are seen in approximately one fourth of the cases, and any part of the globe may be involved. The most common form of orbital involvement is chronic dacryoadenitis, which may mimic a lacrimal gland tumor. MRI is the modality of choice, with post contrast images being essential for the diagnosis. Multiple enhancing granulomatous lesions which can involve any part of optic tract and
globe along with pituitary stalk involvement is known. Chest x-ray maybe helpful in diagnosis especially in the active stages of the disease 18.

TUMOURS

Orbital Lymphoma

Lymphoid tumours account for approximately 10% to 15% of orbital masses. Imaging cannot reliably differentiate benign from malignant lymphoid tumours. The CT and MRI findings are usually nonspecific, and based solely on imaging, it may be impossible to diagnose lymphoma confidently. Orbital lymphomas are well defined relatively high density homogenous masses and are often seen in the anterior portion of orbit, the retrobulbar area, or in the superior orbital compartment. Mild to moderate enhancement is usually present. All orbital lymphoid tumours tend to shape themselves around the orbital structures with no associated bony erosions 19. However, frank destruction of bone may be seen in aggressive malignant lymphomas. (Fig. 15a, b, c). Deformity of the globe shape is rare. Both pseudotumours and lymphoma may have intermediate to low signal intensity on T1-weighted and proton density MR images, and appear iso to hypointense to fat on T2-weighted images 20.

Secondary Orbital Tumours

Tumours may invade the orbit from its vicinity such as those arising from sinonasal cavities, skin of the face etc. The orbit may also be involved by metastases, especially from breast carcinoma in women, and carcinoma of the lung, kidney, or prostate in men. These may involve any of the orbital contents. (Fig. 16a,b)

Orbital Vascular Conditions

Capillary hemangioma

They are tumours of infancy show a rapid growth followed by gradual decrease in size 21. They derive their blood supply from either external or internal carotid arteries and are capable of bleeding profusely. These tumours can extend intracranially through the superior orbital fissure, optic canal and orbital roof. On CT they appear as fairly well marginated, irregular intensely enhancing lesions most of which are extraconal. On MR, they appear hypointense on T1 and hyperintense on T2 with intense enhancement on contrast injection. (Fig. 17a, b)

Cavernous hemangioma

It is the most common orbital vascular tumor of the orbit in adults and tends to occur in second to fourth
decade and progressively increase in size. They have a fibrous pseudcapsule and are well defined masses majority of which are intraconal. On CT they are smoothly marginated homogenous masses that respect the contour of the globe. (Fig. 18a, b, c) On MR they are hypo on T1 and hyper on T2. Dynamic MRI can help differentiate cavernous hemangioma from intraconal schwannoma. Hemangiomas show typical pattern of enhancement that starts from a point and then spreads to the entire mass whereas schwannomas show homogenous enhancement that involves a large area of the mass in the early phase. Prominent arterial supply is usually absent which is in contrast to capillary hemangiomas.  

Lymphangioma

Lymphangiomas are tumours of children and young adults and also progressively enlarge during the first two decades. On CT they are poorly circumscribed heterogeneous masses often of increased density in intra or extraconal space with varying degree of enhancement. Bony remodeling may be present. On MRI fluid-fluid levels related to hemorrhages are characteristic. (Fig. 19a, b)

Orbital varix

These are congenital venous malformations characterized by proliferation of venous elements and massive dilatation of one or more orbital veins. A tortuous enhancing structure which changes form and gets distended on valsalva is confirmatory for orbital varix. (Fig. 20a, b) MRI can be performed with patient in supine and then prone to increase the venous pressure. They can present as thrombosis and hemorrhage.

Caroticocavernous fistula

Caroticocavernous fistula can be post traumatic or spontaneous secondary to osteogenesis imperfecta, Ehlers-Danlos syndrome and pseudoaxanthoma elasticum. CT and MR imaging helps in identifying engorgement of superior ophthalmic vein. Angiography is the gold standard and helps in categorizing the fistula and deciding further management.

Neurogenic Tumors

Schwannoma and Neurofibromas together form approx 4% of all the orbital tumors. Schwannomas in the orbit arise from 3rd, 4th, 5th, 6th, 7th and the autonomic nerves and appear similar to cavernous hemangioma differing
its enlargement. Imaging should include evaluation of the entire visual pathway. On MRI they are isointense to cortex and hypointense to white matter on T1 and hyperintense on T2.

**Perioptic meningiomas**

These benign tumors arise from the meningoendothelial cells of the arachnoid. They occur in the 4th and 5th decades with a female predominance. They present as an eccentric mass at the orbital apex or as a well defined tubular thickening or fusiform enlargement of the optic nerve sheath. Moderate to marked enhancement of the tumor gives a tram track appearance due to circumferential enhancement of the meningioma around an optic nerve and may simulate a pseudotumor. MRI displays the tumor as an abnormally enlarged optic nerve sheath and appear hypointense to grey matter on both T1 and T2. Calcification may be seen.

**Other rare tumours**

Fibrous histiocytoma is a mesenchymal tumor and are seen as well circumscribed masses that may be intraconal and appear moderate to markedly hypointense on T2 images. These may not be able to differentiate from neurofibromas and other fibrous tumours. Rhabdomyosarcomas, although rare still remain the most common primary orbital malignancy of childhood. CT and MRI play an important role in staging. Imaging should include the possible metastatic sites. On CT they appear as enhancing tumours with bone destruction and invasion of surrounding structures. They can appear heterogeneous due to hemorrhage within the tumor. Findings are nonspecific and tissue diagnosis is required to differentiate it from other aggressive lesions.

**Lacrimal Gland Lesions**

Lacrimal gland lesions may be broadly classified as inflammatory or neoplastic. Inflammatory lesions cause diffuse enlargement of the gland. There may be associated features of myositis and scleritis. Inflammatory processes tend to involve all parts of the gland including the palpebral lobe. Pleomorphic adenoma account for 50% of the tumors and appear as well defined and rounded (Fig. 23a, b, c) whereas...
Fig. 23.a,b,c: Lacrimal gland mass lesion: Coronal and Axial T2 weighted fat sat images (a,b) show hyperintense mass lesion involving orbital lobe of lacrimal gland. The lesion is enhancing on post-contast fat sat T1-weighted image (c). Histopathological correlation revealed a pleomorphic adenoma.

adenoid cystic carcinoma is the commonest malignant tumor to affect the orbit tend to have microserrations. Table 4a,b.

**Conclusion**

Cross sectional imaging plays an important role in identifying and characterization of lesions in eye and orbit. Awareness of the usual location of the lesions, their density and signal intensities frequently help in clinching the diagnosis. The algorithmic approach provided in the article may help reach a diagnosis in most situations.

**References**


Viscoelastics in Cataract Surgery

Dr. B. Ganesh MS

OVDs (viscoelastics) are substances that exhibit both viscous and elastic properties, and are most commonly used in cataract surgery, in other ophthalmic intraocular surgical procedures and as components of artificial tears and rewetting drops.

Since not all of the lower viscosity products are particularly elastic, and since some of the devices are elastoviscous rather than viscoelastic, the International Standards Organization (ISO) coined the term ophthalmic viscosurgical devices (OVD), harmonizing it with other device nomenclature in medicine and surgery. Healon (Sodium Hyaluronate 1 %,) was the first viscoelastic agent developed, and brought a revolution to the way traditional cataract surgery was performed.

OVDs provide essential protection of the corneal endothelium, and create and maintain working space during cataract and other intraocular surgery. With the advent of phacoemulsification, the need for OVDs possessing different physical properties for different surgical phases became apparent, leading to the development of the Soft Shell technique. Choosing the most effective OVD for a particular use is based on a thorough understanding of the properties and functions of the various products, and the physical nature of what the surgeon is trying to achieve.

Introduction

The use of viscoelastics for anterior segment surgery was introduced by Balazs in 1979 with Healon 3. Healon was the first viscoelastic substance introduced commercially (1980) for use in human intraocular surgery. Previously, air, balanced salt solution, and the patient’s plasma were used in cataract surgery to maintain space and to attempt to minimize contact of surgical instruments and the IOL with the corneal endothelium during intraocular lens implantation. Unfortunately, these substances lack sufficient viscosity and elasticity to prevent their escaping from large surgical wounds, often resulting in collapse of the anterior chamber at inopportune times.

Home-made hydroxypropylmethylcellulose 1% (HPMC), sourced from wood pulp, was then trialed as an OVD and for lubricating the implant during intraocular surgery. HPMC often contained impurities, possesses the lowest viscosity of all OVDs, and is poorly elastic, and minimally pseudoplastic. Poor pseudo plasticity (lack of decline in viscosity with increasing shear rate) causes it to require a large-bore cannula and increased infusion pressure for injection, thereby causing decreased feedback sensation for the surgeon.

In pursuit of an ideal OVD, various viscoelastic agents have been manufactured by modifying the rheologic components, their molecular weights, concentrations and mixtures, and thereby, their biomechanical properties. An ideal OVD should be biocompatible with ocular tissues, should be able to create and maintain space during intraocular surgical manipulation and should protect the corneal endothelium. It should also be able to be easily removed from the anterior chamber at the end of surgery, and should have little effect on post operative intraocular pressure (IOP) rise. It follows directly from the fact that the rheologic properties of an OVD are the result not only of its rheologic
polymer(s), but also of the molecular weight(s) of those polymers and their concentrations, included buffers, etc. that OVDs cannot be adequately referred to generically by their chief rheologic polymer and its concentration, but must be referred to by their trade names for full characterization of their makeup and surgical behavior, as for example, many companies may manufacture a 1% sodium hyaluronate product, but they are all different in their rheologic properties.

Rheological properties such as elasticity, viscosity, pseudo plasticity and cohesion determine the performance of an OVD in surgery. Elasticity is the property of a substance to return to its original shape after being stretched, compressed or deformed.

Viscous fluids possess internal friction caused by molecular attractions resisting flow. Viscosity is the measure of this resistance to flow. Viscosity of a viscoelastic substance at rest is called zero shear viscosity, which is the only consistent measure of viscosity in a pseudoplastic fluid. Zero shear viscosity of an OVD is a function of its rheologic polymer, its molecular weight and concentration.

Pseudoplastic fluids demonstrate a decline in viscosity with increasing shear rate, and at very high shear rates, the viscosities of pseudoplastic fluids may dramatically decrease and become independent of the molecular weight, and is determined mainly by concentration. Viscoplasticity provides ocular protection against high frequency mechanical insults associated with phacoemulsification.

Pseudoplasticity is a property of non-Newtonian fluids, such as sodium hyaluronate. Some highly pseudoplastic fluids can be easily extruded through a thin cannula despite very high zero shear viscosities. Chondroitin sulfate, like air and water, is a Newtonian substance, as it does not change its viscosity at different rates of shear. Pseudoplastic behavior of OVDs is often confused with surgical retention. Research has demonstrated that retention of an OVD within the anterior chamber during phaco is enhanced by three factors: greater dispersive properties, negative charge, and the presence of hyaluronic acid in the OVD, for which Madsen (1989) had earlier found specific endothelial binding sites. Of all OVDs marketed only Viscoat (Alcon, Fort Worth, Texas) and Discovisc (Alcon) score well on all three counts, as they possess hyaluronic acid, and the chondroitin sulfate component makes them more dispersive and enhances their negative surface charges.

Free radical formation has been related to ophthalmic phacoemulsification devices. OVDs reduce the oxidative damage caused by free radicals produced during phacoemulsification surgery. Both hyaluronic acid and chondroitin sulfate are known free radical scavengers. The antioxidant effect of the OVD depends on its molecular makeup and its retention in the anterior chamber during phacoemulsification; the more dispersive the agent the more retention is seen during and after phacoemulsification and irrigation-aspiration of cortex.

**Current Classification**

Initially, OVDs were classified into two kinds: higher viscosity cohesive and lower viscosity dispersive. Cohesion is the degree to which long-chain polymeric molecules entangle and is a function of the nature of the molecule and its chain length. Cohesive HA OVDs are high molecular weight (greater than 1 million Daltons) and possess high zero shear viscosity. Higher viscosity cohesive OVDs are best at creating and preserving space and inducing pressure in the eye.

A major advantage of higher viscosity cohesive OVDs is their ability to induce and sustain pressure in an eye despite an incision, enabling pressure-equalized cataract surgery. This is important in performing consistent capsulorhexes, preventing the tear from running outwards, as it would when the pressure behind the anteriorly convex anterior capsule exceeds that in front of it, and to implant IOIs in stabilized open capsular bags.

They are also easily removed from the eye as a bolus during irrigation and aspiration especially in the presence of a large incision. Currently available viscous-cohesive OVDs include Healon (1% sodium hyaluronate, 4 million Daltons), Provisc (1% sodium hyaluronate, 2.4 million Daltons), Amvisc Plus (1.6% sodium hyaluronate, 1.5 million Daltons, Bausch and Lomb, B&L, Rochester, N.Y.), Amvisc (1.2% sodium hyaluronate, 2 million Daltons, B&L), and many others. Healon GV is a super viscous cohesive OVD (1.4% sodium hyaluronate, 5 million Daltons) with a zero
shear viscosity of 2,000,000 milli Pascal seconds (mPaS), about 10 times the zero-shear viscosity of regular viscous cohesive OVDs, which results in it being able to perform all of the tasks above of a viscous-cohesive OVD better.

While any OVD, if retained in the anterior chamber after surgery, can result in increased postoperative IOP, very high IOP spikes can occur if a large amount of a highly viscous cohesive OVD is left in the eye. When appropriately removed, post-op IOP spikes are similar with different OVDs.

Lower viscosity dispersive OVDs are lower molecular weight and have low zero shear viscosity (less than 100,000 mPaS). The advantage of these OVDs is that they are retained better in anterior chamber during high level of fluid turbulence such as during phacoemulsification. They are capable of partitioning spaces such that there is a viscoelastic occupied space and a working space with circulating balanced salt solution, which makes lower viscosity dispersive OVDs particularly useful in managing complications. When aspirated, lower viscosity dispersive OVDs, even under low vacuum, lack internal cohesion and break apart, thus they are vacuumed out in smaller pieces, leaving most of the OVD mass behind and thus provide added endothelial protection in prolonged or difficult phaco cases.

It follows that it takes longer to completely remove dispersive OVDs from the eye at the completion of surgery, when compared to cohesive OVDs, resulting in small amounts of dispersive OVDs usually being left behind at the end of surgery, causing small IOP spikes, whereas with highly viscous cohesive OVDs, either a larger amount of OVD is left, or almost none.

Currently available dispersive OVDs in the United States include Viscoat (sodium hyaluronate 3 %, 600,000 Daltons & chondroitin sulfate 4 %, 50,000 Daltons), Ocucoat, (HPMC 2 %, 80,000 Daltons, B&L) and Cellugel (Modified HPMC 2%, 300,000 Daltons, Alcon), among many others.

Healon5 (AMO), which is 2.3 % sodium hyaluronate, is a viscoadaptive OVD with a molecular weight of 4 million Daltons (it is made up of the same hyaluronic acid chains as Healon, but differs in concentration). Viscoadaptive OVDs are different from the traditional dispersive and cohesive OVDs in that they are extremely highly viscous and cohesive under low shear conditions; at low flow phacoemulsification, they do not fracture and remain undisturbed while phacoemulsification continues. By design, they also exhibit pseudo dispersive characteristics under high shear conditions, because they begin to fracture under stress, much as a solid would. They may therefore be referred to as pseudo dispersive. Like other OVDs, complete removal of viscoadaptives is essential to reduce the risk of high post operative IOP. In the late 1990s, a systematic OVD method of usage scheme the ultimate soft shell technique was proposed with the use of viscoadaptive OVDs. It was an extension of the previous soft shell technique, but the extremely high zero shear viscosity of viscoadaptives enabled the soft shell to be performed with a viscoadaptive and balanced salt solution the ultimate low zero shear viscosity OVD, with essentially the same viscosity as water.

OVD classification has recently been modified to accommodate DisCoVisc (Alcon), the first viscous dispersive OVD.20 (Figure 3) DisCoVisc is a combination of hyaluronic acid 1.6 % and chondroitin sulfate 4 %, and is a higher viscosity dispersive OVD (1.7 million Daltons). DisCoVisc possesses zero shear viscosity similar to Provisc, but is dispersive, similar to Viscoat. DisCoVisc combines the advantage of both a cohesive and a dispersive OVD. It provides dual function; space maintenance (cohesive) and superior retention (dispersive) in the same syringe.

Optimizing surgical outcomes

In order to maintain space and protect tissues, the OVD should possess high viscosity at low shear rates; but low viscosity at high shear rates is also important to permit passage through a small bore cannula. For phacoemulsification and I/A, some OVD should be retained throughout the procedure in the anterior chamber, protecting the endothelium; and for IOL implantation and movement of instruments, the OVD should possess moderate viscosity at medium shear rate.

It is hard to meet all the above requirements by a single OVD, and different newer OVDs (Healon5 viscoadaptive & pseudodispersive, DisCoVisc higher viscosity dispersive), and OVD techniques (soft shell, ultimate...
soft shell) have been designed to try to achieve these apparently contrary and mutually exclusive goals. Consequently, some surgeons prefer using different OVDs during different phases of phacoemulsification surgery.

To cater to this need, several OVDs come packaged in pairs. DuoVisc is an OVD system containing Viscoat and ProVisc in U.S. Similarly, Healon D+H and Healon D+GV both provide the surgeon with a two OVD system.

In contrast, surgeons who prefer to use only one OVD during surgery may find the newer DisCoVisc, or Healon5 particularly effective. Depending on individual style, for example, a tendency towards more rigorous I/A versus a gentler, slower approach a more dispersive or a more viscous OVD may be preferred. Some surgeons prefer the higher zero shear viscosity of Healon5 and use of the ultimate soft shell technique. In all of these techniques, the common goal of devising a method to enhance OVD retention during the turbulent phases of surgery, and a second method to enable easy removal of all the OVD at the termination of surgery prevails.

There are various products in the Indian market sold under various brand names. They are Intavisc, Hyvisc, viscomet, Moisol-R are substances containing HPMC. They are marketed in prefilled syringes. Chances of contamination are much reduced. Other companies are trying to bring Healon (Hiluron) and chondroitin sulfate. (Viscocel).

OVDs are essential tools in cataract surgery. The choice of best OVD is based on personal surgical technique as well as individual surgical case physical requirements. With the availability of so many OVDs possessing diverse rheological properties that influence their surgical behavior, it is tough to make a selection. Detailed knowledge of OVDs and their biomechanical properties is important in order to make the right choice.

References
Correcting Presbyopia With Soft Contact Lenses

Dr. Pravin Tellakula MS

Why fit presbyopic patients with contact lenses?

The answer is that they want contact lenses. Those who have enjoyed single-vision contact lens correction for years appreciate the multitude of benefits and don’t want to give them up just because they’ve become presbyopic. Many of those who aren’t contact lens wearers have a strong interest in contact lens correction and many of them can be successful with them.

In India, the greatest untapped source of future growth in the contact lens field is the fitting of the presbyopic patient. As demographics continue to shift over the next decade, more patients will be in the over-40 group widening the market. Satisfying this population of patients who make health care decisions for themselves, their children and their elderly parents as well, secures ones position as the eye care provider for the entire family.

The evolution of materials and lens designs have provided a powerful array of contact lenses for presbyopes, who need to wear their lenses full-time, part-time or just for social occasions. The challenge is to identify the viable candidates and match them with the most appropriate corrective option.

Understanding the Aging Eye

Certain special physiologic changes that take place in the aging eye that make fitting contact lenses in a presbyope challenging should be noted.

· There is a reduced elasticity in the lids,
· aging of the meibomian glands,
· the marginal tear meniscus is inadequate,
· lacrimal glands become less productive and there is
· reduction in acuity and contrast sensitivity.
· pupils are smaller and sluggish,
· crystalline lens loses transparency and also
· synchisis of vitreous is present.

The Psyche of the Presbyope

For many people, presbyopia is one of the first indications that they are not going to escape the ravages of aging. Their search for the fountain of youth often leads them to beauticians, personal trainers and cosmetic surgeons. So as these patients hit presbyopia, there are psychological as well as physiological changes that affect their personalities. The presbyope wants to avoid the stigma attached to bifocals and how they relate to a person’s age. Many patients want to see and feel as they did when they were in the twenties.

Compromises present in various systems used to correct Presbyopia

· Spectacles: difficulty is experienced while walking or using stairways, fogging occurs and even slips off during vigorous activity.
• **Translating Bifocals** - near vision is gaze dependent; there can be an image jump at the segment.

• **Simultaneous Bifocals** - degraded retinal image, haloes at nights, reduced contrast sensitivity, ghost images has been reported\(^1\).

• **Monovision** - reduced central visual acuity in one eye, reduced binocular comfort, reduced visual quality at night has been noted.

• **Refractive surgery** - has also not addressed this issue efficiently.

Every presbyopic correction be it eyeglasses, monovision or bifocal contact lenses is a compromise. Vision will never be as natural or as efficient as it was in the twenties. Usually, unwillingness to compromise is a contraindication to the fitting of contact lens for presbyopia \(^1\). The goal of presbyopic contact lens fitting is to provide reasonably good vision for most of the activities most of the time. If patient and practitioner both accept this, they are more likely to reach success. Patients and practitioners should understand at the outset that fitting for presbyopia is not instant, automatic or particularly predictable. Successful modern presbyopic fitting is a process that results from an understanding of the lens designs and their appropriate application as well as adjustments and compromises that allow a balance to be achieved.

Presbyopes can be broadly divided into two groups, the emerging presbyopes (in the age group of 35 – 49) referred to as “Gen-X” and the mature presbyopes (in the age group 49-60) referred to as baby-boomers. For the next generation of new and emerging presbyopes Technology is a key component. This generation is highly motivated to preserve both vision function and youthful appearance. Not surprisingly the mindset, visual requirements and life style demands of early presbyopic Gen-Xers are different as indicated in the table below \(^2\). Likewise the method of correction of presbyopia and lens types will vary between the two groups.

Soft Lens Options available to manage Presbyopia.

1. **Reading Glasses**— Patients who have adapted to single-vision contact lenses may prefer reading glasses over their contact lenses, especially if they’re early presbyopes, where assistance with near tasks is required only occasionally.

2. Alternatively, regular soft contact lenses can be prescribed using the **Monovision** principle in which one eye is corrected for distance and the other for near.

3. Special Bifocal contact lenses with **translating designs** (segmented), which provide distance and near vision by alternating the gaze between the segments of the lens is another form of correction.

### TABLE 1

<table>
<thead>
<tr>
<th>GENERAL PRESCRIBING FACTOR</th>
<th>EARLY/EMERGING PRESBYOPES (AGE 35-49)</th>
<th>MATURE PRESBYOPES (AGE 50-64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiology / ocular health</td>
<td>Relatively fewer challenges / healthy ocular surfaces</td>
<td>Chronic ocular disease conditions (especially dryness) may hinder successful contact lens wear.</td>
</tr>
<tr>
<td>Vision tasks / demands</td>
<td>Greater use of mobile technology, more demanding visual-motor tasks (greater use of texting/personal computing). Greater task variability.</td>
<td>Less use of mobile technologies. Comparatively less demanding, stationary near vision tasks (reading). Relatively less vision task diversity.</td>
</tr>
<tr>
<td>Refractive error</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Function vs Cosmesis</td>
<td>Strong motive to preserve both vision function and youthful appearance</td>
<td>Generally greater functional orientation</td>
</tr>
</tbody>
</table>
4. In **Simultaneous Vision** lens designs the distance and near vision is perceived simultaneously and the brain selects the image of interest. They come in different types, concentric ring or bull's eye design (annular), aspheric design, multi-zone or diffractive design.

5. **Modified monovision** is a method where single vision lens is used in one eye and a bifocal in the other.

6. Other **Combinations** like different designs of multi/bifocal lenses in each eye are reserved for mature presbyopes and those having higher demands in vision.

A good **patient evaluation** is required, prior to selecting a method of correction, noting the amount of refractive error and visual sensitivity, occupation, visual needs, personality, previous contact lens experience, motivation and expectations. Ocular examination would include the routine for any contact lens fitting with special attention to the pupil size and dynamics, tear function, lid position and lid tonicity. Low error and high adds may be problematic, as may high sensitivity to small lens changes during refractive testing and acuity not correctable to 20/20 in each eye.

**Selecting the method of correction** will depend on the ocular health and needs of the patients. The visual demands vary widely and could be any of the following

- Good distance vision
- Reasonable distance and near vision
- Good distance and near vision
- Occasional good vision without specs
- Cosmetic value

In general, in patients where assistance with near tasks is required only occasionally (e.g., reading medicine bottles or threading a needle) spectacles over their contact lenses is preferred. As presbyopia progresses and near tasks become more and more challenging, this form of correction becomes unacceptable and inconvenient.

For an emerging presbyope over-plussing the non-dominant eye will work well. While early presbyopes are well served this way it can be tried in all presbyopes.

**Simultaneous / Aspheric lenses** are good for good intermediate vision e.g. Computer professionals and in occupations like accountant, mechanic, plumber, electrician requiring “arm’s length” vision range. It is also the recommended lens type for the emerging presbyopes.

**Translating designs** are best suited for patients with “near to far” demands, like teachers and truck drivers. It is also the recommended lens type for the advanced presbyopes.

When the pupil size is more than 4.5 mm in mesopic conditions do not attempt bifocal contact lenses.

**Monovision**

Monovision provides the simplest method of correcting both distance and near vision with contact lenses. A distance contact lens is fitted to one eye and a near contact lens is fitted to the other. The Dominant eye is corrected for distance and the other for near. This concept of over-plussing the non-dominant eye was first proposed by Westsmith more than 30 years ago. The induced imbalance is minimal and often well tolerated. While this method of correction works well with emerging presbyopes, it can be used for all presbyopes with any lens material and any replacement schedule. It can also be used with toric lenses in patients with astigmatism by exercising caution.

The advantage with monovision correction is that it provides consistent near and distance vision independent of gaze position. It does not cause aberrations or distortion of the peripheral vision. Patients with an add of less than +2.00 Dioptres theoretically attain well focused image for any intermediate viewing distance. It is easy to fit comparatively, it is less time-consuming and less expensive for both patients and practitioners than bifocals and has shown a high success rates with patients.

A more complex monovision approach uses a bifocal lens in one eye and a single vision contact lens in the other, i.e. so-called modified monovision. Usually, the single vision lens is used to correct the patient’s vision for their most critical viewing distance, i.e. distance or near, and then base the multifocal lens for the other range.

The alternative is to use bifocals in both eyes.
Monovision Fitting

A fundamental dictum to successful monovision prescribing is to demonstrate benefits of monovision before describing how it works. Some patients may not be comfortable with the idea of monovision. A few key tests can help identify a patient who can successfully adapt.

Patient Selection - The key tests

1. While the patient is wearing his distance correction, determine his dominant eye (The dominant eye can be determined by methods such as the simple “hole in the hand” test or fogging techniques where plus power over-correction is added to each eye in turn, and the eye that accepts the most plus is considered the non-dominant one.)

2. Next, evaluate his near acuity by holding the appropriate power spectacle trial lens over the non-dominant eye. Unacceptable near vision is usually indicative of a poor monovision candidate.

3. If the response is positive, ask him to shift his gaze to a detailed distant object and evaluate the distance acuity. Most patients accept some compromise of distance vision if near is acceptable.

4. Dispense a trial lens for patient to test monovision in everyday situations, if the response is positive.

5. When distance or near vision is unacceptable, explore bifocal options.

Adaptation

Abrupt onset of anisometropia presents a significant challenge to presbyopic visual system. Hazy vision and occasional loss of balancing can be experienced during this time. Some patients possess strong blur suppression skills and can adapt very easily. No clinical tests available to confirm the time taken for monovision adaptation (usually 2-3 weeks)

How does Monovision work?

Cortical processing of Monovision Images

Several cortical processes like Suppression, Adaptation and Binocular Unmasking are involved while generating monovision images.

Suppression- Visual system preferentially processes output from dominant eye even so it has been shown that the output from the suppressed eye still contributes to binocular summation. The suppression of blur in monovision is different from that in retinal rivalry. Thus under normal monovision viewing conditions, the blurred eye makes substantial contribution to binocularly perceived image and should be capable of sustaining useful levels of binocular function in most patients. However, under certain conditions inter-ocular suppression is not constant. This momentary loss can increase the risk of loss of confidence or of efficient judgment. 20 % of monovision patients are unable to achieve second degree fusion.

Adaptation- is another cortical process present in varying degrees in patients. Some patients inherently possess strong blur suppression skills that may be absent in unsuccessful monovision patients.

Binocular Unmasking- The ability to assess the organization of visual space is impaired when information to one eye is reduced. Also there is evidence that indicates the ability to detect visual signals in the presence of noise (blur secondary images) is significantly enhanced under binocular conditions. These findings suggest that cortical processing of complex images generated by presbyopic contact lenses involves higher order functions and requires further study.

Controversies of Monovision

Both monovision and bifocal contact lens modalities have been criticized for the visual quality they provide compared to spectacle bifocal lenses.

Anisometropia- Some clinicians find the intentional anisometropia created by Monovision to be unacceptable ethically. In reality if one observes the aniseikonia with monovision contact lens is typically insignificant compared to that of spectacle correction. E.g. for a difference of +2.75D between the two eyes, aniseikonia is 6% for spectacles compared to 0.5 % in the case of contact lens.
Other binocular performance concerns with monovision include its possible effects on stereopsis, fusion and complex spatial-locomotor tasks (especially driving).

**Effects on Static Functions**

Various Static functions like stereopsis, contrast sensitivity and peripheral vision have been assessed. **Stereopsis** - 94% exhibit stereopsis within norms with an average stereoacuity of 58 seconds as information from suppressed eye continues to be processed. Under dynamic conditions, such as driving the contribution of stereopsis is minimal beyond 20 ft, instead other clues such as perception, speed of motion, overlapping contours & dynamically changing disparities tend to indirectly enhance the perception.

**Contrast Sensitivity** - As add increases binocular contrast sensitivity approaches that of monocular contrast sensitivity. Binocular summation not seen for adds greater than +2.00 D as reported by electrophysiological data. For low contrast targets, monovision provided better visual acuity than simultaneous vision bifocals lenses. For adds greater than +2.0 D it reduces the ability to make background figure judgements and affects posture and movement.

**Peripheral Vision** - Monovision does not reduce the size of the binocular field or peripheral visual acuity. Detection acuity is better than resolution acuity in the peripheral retina.

**Effects on Dynamic Functions**

**Motion perception and Spatial Localization** - Of all the visual functions performed by the peripheral retina, motion perception is least affected by blur. Peripheral blur essentially has no effect on spatial localization and perceived egocentric movement. Thus, monovision should have no significant impact on these vital peripheral functions.

**Dynamic Activities** - No difference in reaction time is seen in various lens types, however, in near point occupational tasks, resolution tasks suffered most with monovision as it was for certain eye hand co-ordination procedures at close range. Ghosting and momentary diplopia have been reported. The secondary images cause distraction and have been reported to contribute to nearly 33% of pilot errors in accidents and hence may not be a choice for patients requiring very high visual demands.

**Night Driving** - Monocular blur of bright objects, during night driving, such as headlights against a dark background is extremely difficult to suppress and the patient should be cautioned regarding the risk. It is also to be noted that night-driving conditions appear to present significant problems for most presbyopic contact lens treatment modalities.

**Monovision - Conclusion**

Currently available information indicates that monovision is an effective and reasonable prescription for correcting presbyopia. Patients should be fully informed of all correction alternatives, visual limitations and precautions and an informed consent should be obtained. Properly selected patients can obtain good vision for most viewing distances under most circumstances.

**Soft Bifocal / Multifocal Contact Lenses**

Soft bifocal contact lenses can be considered for previous soft lens patients who are already accustomed to the handling and care of these lenses. It is also ideal for those who consider comfort or lens stability a priority, such as sportspersons. It is also an excellent option for occasional wearers as immediate comfort is achieved. It works best in patients who have no more than 0.75D of spectacle astigmatism and on low to moderate (+0.75D to +1.50D) presbyopes. One can achieve higher add effects with a modified monovision approach, adding more plus to the bifocal lens on the non-dominant eye.

When approaching a presbyopic patient for bifocal contact lenses it is important to know their needs and expectations. The patients should be aware that contact lenses also have limitations and the goal for fitting would be to meet most of their visual needs most of the time. The presbyope must accept certain visual compromises which will vary depending on the individual patient and the type of contact lens correction he wears.

The best candidates for fitting bifocal contact lens would be those with low visual demands, low visual sensitivity,
adapted contact lens wearers and those with realistic expectations and good ocular health. Fitting patients with high visual demands at more than one distance, high visual sensitivity, patients who have never worn contact lens before, flaccid lids, dry eye and unrealistic expectations would be more challenging.

The ideal candidate for a beginner in fitting bifocal contact lens would be a patient who is symptomatic during near tasks and requires distance correction of at least –0.50D of myopia or +0.75D of hyperopia and an add of at least +0.75D.

### The Multifocal Milieu

No other aspect of contact lens practice offers the variety that is available with multifocals.

Soft bifocal lenses mostly are simultaneous vision designs, which present distance and near optical portions within the pupil at the same time. Some aspheric and multi-zone designs also provide optics for intermediate distances. Alternating (translating) soft lens designs, available in fewer numbers, have mostly been unsuccessful because translation is usually insufficient to displace one optical portion of the lens for another. However this design has performed well in RGPs (Fig 1).

Simultaneous designs are classified as

- **center near**
- **center distance**
- **full aperture designs**

The above designs use one of the following optics

- **aspheric**
- **concentric**
- **combinations of aspheric and concentric diffractive optics.**

Fig. 2. (Left) Translating Design with near power at the bottom (Midele) concentric design with near prescription in the middle and for correction at the periphery (Right) Aspheric design

Fig: 2. Left: In this example of a translating design the near power is on the bottom. The bottom edge is flattened to keep the lens from rotating on your eye when you blink. Middle: In this concentric design the near prescription is in the middle and far is on the outside, but they can be reversed. Right: In this aspheric design the near and distance prescriptions are both near the pupil.

With a concentric design, a central zone of distance or near power focus is surrounded by one or more rings that contain the opposite power (Figure 2, 3). Some even alternate distance and near in a repeating pattern which helps to improve pupil coverage and visual input with variations of illumination and pupil size.

Aspheric designs use an aspheric front or back surface to create the multifocal effect (Figure 2). Most often, front surface aspheric designs are center-near and back surface aspherics are center-distance. Each type has its own merits, as center-near designs tend to favor near and intermediate vision, while center-distance lenses usually give better distance focus. Which one to choose depends on the patient's individual needs and ocular characteristics.
Multi-zone lenses usually have distance correction in the center and also provide optics for intermediate distances and could even be a combination of aspheric and concentric zones.

With diffractive design (Figure 5), light entering the eye is diffracted to produce the images the retina receives. The diffractive design has a distance center and a series of diffractive phase-plates that surround it. As the add power increases, the number of phase-plates increases, and they get closer together.

**Design of the various categories**, clinical application, their advantages and disadvantages are discussed below. Few of the locally available lenses have been described in more detail.

**Aspheric Center Near Designs**— Aspheric center near designs have maximum plus power centrally. The graduated front surface curve change, results in a progressive increase in minus or decrease in plus toward the periphery.

Clinically, the anterior aspheric multifocals not only create a progressive power effect, but they may also reduce optical aberrations and increase depth of focus. They should be fitted as flat as possible without compromising comfort or lens centration.

Even with good centration, many aspheric center near designs require more plus or less minus than expected in the non-dominant eye of more mature presbyopes in order to achieve adequate near vision. If this provides unacceptable distance acuity, a concentric design on the non-dominant eye and an aspheric design on the dominant eye may better balance distance and near vision.

The locally available **Bausch & Lomb Soflens Multi-Focal** lenses fall in this category of front aspheric center-near design. These lenses come in two base curves, 8.5 and 8.8 mm, and in two profiles, low add and high add. It is a cast moulded lens made from low water content non-ionic material Polymacon.

By and large the low add profile is used for spectacle adds of +1.50D or less and the high add profile for spectacle adds of +2.50D or more. For the intermediate range between +1.50 and +2.50D low add on dominant eye and high add on non-dominant eye is used. In case of unacceptable vision trouble shooting should be done as per the manufacturer’s fitting recommendations initially.

**Natra-Sight Optics incorporated in this Soflens multifocal** provides a broad near to distance power transition to provide crisp, clear and natural vision. Equalised mass distribution facilitates lens centration essential for effective functioning of the aspheric optics. Comfort blend geometry reduces the back surface mass, creating a consistent peripheral zone and enhancing comfort. Round edge profile provides smooth movement over conjunctival tissue for excellent comfort.

The **Air Optix Aqua Multifocal** lens from Ciba Vision is another proven aspheric back surface design and will be shortly launched in the Indian market. This lens has shown good centration and excellent fitting characteristics. While there are definitive near, intermediate and distance zones in the lens, the design allows for a smooth transition from each zone.
This unique presbyopic lens system with 3 ADD powers is designed to successfully fit emerging presbyopes and smoothly transition patients through the different stages of presbyopia so they can stay in contact lenses longer. Air Optix Aqua Multifocal has a base curve of 8.6mm and a diameter of 14.2 mm. It will be available in spherical powers of +6.00 to -10.00D in 0.25 steps with LOW, MED and HIGH Adds

**Concentric Center Near Designs**— Pupil size assessment is critical for success with concentric center near lenses. Small pupils require small add zone diameters to provide adequate distance viewing, while larger pupils require larger add zones on each eye. With any pupil size, it’s often beneficial to use smaller central near zones on the dominant eye to enhance distance viewing and larger central near zones on the non-dominant eye to enhance near viewing. A significant part of fitting these designs is determining the proper add zone size for each eye to optimize visual performance.

Excellent centration is important with any center near contact lens design. Patients who are exposed to a wide variety of light levels and who have extreme variations in pupil size may experience some fluctuation in vision. Most concentric center near designs available internationally offer multiple near zone sizes.

**Aspheric Center Distance Designs**— Aspheric center distance designs have maximum minus or minimum plus power centrally, and the graduated back surface curve change results in a progressive increase in plus or decrease in minus toward the periphery. Generally, they provide very good distance acuity, and adapted single-vision soft contact lens wearers convert easily to them. Near acuity is often best accepted by the early presbyope. A patient with large pupils may have better near vision with these designs, as increased light rays from the more plus peripheral portion enter the pupil.\(^\text{12}\)

Centration is also key to success with back surface aspheric multifocals. A decentered lens places a more plus peripheral portion of the lens along the line-of-sight with distance fixation. This over-plussing requires more minus to compensate, which diminishes the near add effect.

**Concentric Center Distance Design**— Only a few concentric center distance soft lenses are widely available internationally. While this lens generally provides very good near vision, the peripheral near zone may interfere with distance vision, especially in patients with large pupils. This can be particularly problematic with night driving.

**Multi-Zone Designs**— All current multi-zone designs feature distance correction in the center of the lens. The locally available Acuvue Bifocal from Johnson & Johnson, is a multi-zone concentric lens having PUPIL INTELLIGENT DESIGN™ which consists of 5 alternating zones with optimized size and spacing.

Center distance zone: when pupil miosis occurs under extreme bright light conditions, center zone delivers distance correction. Multiple alternating concentric zones: Three middle zones, together with the center zone deliver equal amounts of near and distance vision under intermediate light conditions. Outer distance zone: Provides added distance correction to optimize vision during night driving, and other low light situations. Precision junctions are designed to reduce blurs and haloes in low lighting. The modified Edge design promotes an exceptional comfort.

Acuvue Bifocal has significantly improved my success with presbyopes and soft bifocal lenses. This simultaneous design, two-week replacement lens is approved for daily wear and has ultraviolet filtration and a light blue handling tint. Its unique design features alternating distance and near zones (Fig. 4). Contrary to most simultaneous vision designs, this lens performs quite well, even in the absence of ideal centration, and is relatively independent of pupil size. Although a large range of ametropes can achieve success with the lens, myopes with low to moderate adds are very enthusiastic wearers.

Fitting is very straightforward, but you must follow specific guidelines to achieve optimal success. Initial lens power selection is equal to the vertexed spectacle prescription. Following insertion of the lenses, verify that they are properly orientated by viewing an inversion indicator on the lens. Some patients don’t feel an inverted lens, which makes the inversion indicator even more valuable in assuring proper vision. Finally, allow patients to assess their vision outside of the examining room for 10 to 15 minutes. When they return to the exam room, ask them how their vision is.
Their comments guide you to which, if any, lens power adjustments to make. As with nearly all soft multifocal contact lenses, higher adds in the Acuvue Bifocal tend to degrade distance vision. A lower add lens or possibly a single-vision distance lens on the dominant eye, combined with a higher add lens on the non-dominant eye often provides an acceptable balance of distance and near vision. A good supply of Acuvue Bifocal diagnostic lenses are available, allowing both doctor and patient to efficiently explore the feasibility of this lens with little or no economic risk.

**Full Aperture Design**—This design uses a diffractive phase plate which extends effectively across the entire pupil. The phase plate is formed by back surface echelettes which split the light to form the near image. The add power of a diffractive lens is determined by the number of diffractive rings. Higher adds have more rings with shorter radii. Optical performance of diffractive lens is less dependent on pupil size.

Approximately 20 percent of the light is lost to higher orders of diffraction, so lens performance is often reduced in low light conditions. Good centration is necessary to achieve adequate near acuity. These lenses work best on hyperopes, and pushing plus to create a distance over-refraction of -0.50D usually enhances near vision without compromising distance vision significantly.

Preparing patients for initial awareness of halos at night and a 3-D effect with near printed material helps reassure and ease them through adaptation. The diffractive lens can significantly limit oxygen transmission, particularly in higher powers, so careful slit lamp examination for striae and other signs of hypoxia is indicated.

**Emmetropia.** Patients who are emmetropic for distance may be dissatisfied with the compromise in distance vision associated with nearly all bifocal contact lens designs. They need to be to be told that a little of their distance vision will be stolen to improve their near vision. If need be they could wear a “driving glass” fully correcting distance vision while wearing the bifocal contact lens.

**Myopia.** Most low to moderate myopes can wear either a simultaneous or alternating design, depending on their visual needs and lid position. Alternating designs are the best for high myopes.

**Hyperopia.** Although hyperopes can wear either simultaneous or alternating vision bifocal designs, aspheric simultaneous designs are recommended.

**Presbyopia.** Add needs are important in choosing correction. Patients with a low add and only transient symptoms during near tasks are best managed with reading spectacles over their distance contact lenses. When they need the spectacles more frequently and the hassle becomes unbearable, bifocal contact lenses can be suggested. For the incipient presbyope who is reluctant to wear any form of spectacle correction aspheric soft bifocals would be a good choice. These lenses generally perform well in correcting low presbyopia (low adds +0.75D to +1.00D) and often require little adaptation. For adds ranging from 1.25D to 1.75D, soft multifocals will work, but the patient may need unequal adds or slight over-plussing of one lens for adequate near correction while maintaining satisfactory distance vision. For add needs 2.00D or greater alternating lens designs can be tried. Soft multifocal lenses may need some degree of monovision for success.

**Astigmatism.** Most soft bifocals don’t provide satisfactory vision if the patient has an astigmatic error exceeding 0.75D. When corneal astigmatism is present or if the astigmatism is more than 2.00D alternating designs are preferred. Internal astigmatism should do well with either simultaneous or alternating design. Astigmatism correction with soft contact lenses has improved. Ignoring astigmatism and fitting with equivalent sphere correction often creates too much compromise when attempting multifocal correction.
Matching Patients with the Right Option

With so many options, even just finding a starting point can be overwhelming. On the other hand, evaluating a presbyopic patient for contact lens correction is similar to evaluating single vision correction; however, accurately correcting each eye becomes more significant.

Factors like Refractive error, amount of Presbyopia and Pupil size would determine the type of lens to be used.

Astigmatic patients who want or need soft lenses should anticipate some compromise in vision. Monovision with toric soft lenses can work, but is more likely to fail. A few soft bifocals are available internationally in toric designs with concentric center near designs and a toric back surface, but fitting them is a lengthy process. Some patients will present with significant astigmatism in only one eye. In such cases, try fitting a single vision toric lens on one eye (usually for distance vision) and a multifocal sphere on the other.

The pupil factor. Patients with very small pupils will have difficulty utilizing anything but the central portion of a relatively stationary lens. A lens that centers well over the pupil is advantageous, but may also be limiting. Consider pupil size in determining whether to use a center-near or center-distance design. Patients with exceptionally large pupils are more likely to have night vision problems with multifocal lenses and may be more suited to monovision. Multi-zone lenses are the least pupil dependent. When the pupil size is more than 4.5 mm in mesopic conditions do not attempt bifocal contact lenses.

Pupils are almost always slightly decentered nasally. Most multifocal lens designs are symmetrical, and if they center on the cornea they will not center over the patient’s pupil. Observe the red reflex through a retinoscope or direct ophthalmoscope to check for position of the multifocal components relative to the pupil.

General Fitting Guidelines

As stated, good lens centration is critical to success with most soft bifocal contact lenses, especially concentric center near and diffractive designs. Although centration is still desirable, some aspheric designs perform adequately with small decenteration, especially for early presbyopes. The Acuvue bifocal seems to be relatively independent of lens centration. With most simultaneous vision multifocals, minimal movement is desired to provide a stable optical system over the pupil. However, enough lens movement must occur to flush debris from beneath the lens and to prevent limbal binding. As with all soft lenses, it’s necessary to allow the lenses to settle at least 15-20 minutes before assessing visual performance.

With most designs, other than the true alternating bifocals, distance vision and near vision tend to compete such that the better one is, the worse the other becomes. This challenges the fitter to find the balance point appropriate for the patient. Break from the idea that both eyes need full near correction. At least half of the successful soft multifocal fits consist of lenses with unequal adds (the so-called modified bifocal), and in the majority of both rigid and soft lens fits, the degree of add is less than what the spectacle correction called for. Just as with monovision, the less near correction one employs, the less one interferes with the distance vision.

Assessing Vision— The first golden rule is to assess vision binocularly both at far and near, which provides a better and more realistic evaluation than the monocular testing. Monocular acuity assessment does not accurately reflect what patients experience during their habitual binocular state and will often be disappointing. The second golden rule is to measure success as meeting most of the patient’s visual needs most of the time. Success is achieved when the patient is able to perform most of his visual tasks comfortably. If the patient is happy, the practitioner should be too. Do not get locked in to the need to achieve 20/20 vision. Many bifocal contact lens wearers are successful with binocular distance acuity 20/25 and binocular near acuity of 20/30.

It should be noted that changes as small as 0.25D in distance lens power can have a profound effect on near vision when working with presbyopic lenses. If near vision is inadequate, add additional plus to the lens on the non-dominant eye or switch designs. In some cases, success can be achieved with a different design on each eye. For example, an aspheric lens on the dominant eye and a concentric center near design on the non-dominant eye may provide the proper balance needed.
to provide adequate vision at distance and at near. Another way to assess near vision is to have the patient move a near target in and out to locate the distance of clearest vision. If this “tromboning” locates a best vision area within the patient’s habitual reading zone, the patient will likely be pleased with his near vision.

**Conclusion**

No given bifocal lens design or brand meets the needs of all presbyopic patients. Emerging presbyopes or those requiring maximum visual performance at distance and at intermediate may do best with aspheric designs. High add patients may do best with over-plussing the distance correction in the non-dominant eye in order to achieve adequate near vision. High add patients with detailed distance demands may do best with a single-vision distance lens on the dominant eye and a bifocal lens on the non-dominant eye. Of course, many patients, particularly those with low or intermediate add strengths, do quite well with straight monovision.

The wealth of options and the development of some of the newer multi-zone multifocals affords the opportunity to provide a higher level of visual correction to presbyopic patients today. The ability to provide clear vision at distance and at near in a more natural binocular state is within the practitioner’s grasp. Nothing about multifocal or bifocal contact lens fitting is difficult as it is really a progression of standard contact lens practice.

**References**

15. IACLE Contact lens teaching Module 8: Unit 8.3
A Case of Diffuse Ocular Muscle Enlargement

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Dr. Elizabeth John MS DO

Case Report

A 2½ year old male child presented to our outpatient department with bilateral proptosis of two weeks duration. There was no history of fever or upper respiratory tract infection. Child attained milestones normally. He was immunized for his age.

On examination, there was bilateral axial proptosis, without any evidence of inflammation. Extra ocular movements were full in all directions. Anterior segment examination was normal. Pupil was brisk. Fundus examination was also normal [Fig. 1].

Thorough systemic examination was done.

Wt of the child was 12kg. There was no hepatosplenomegaly.

Investigation report

Hb -11.2 gm %, TC -6000, DC -P-31, L 69, E: nil, ESR - 16mm/hr

Peripheral smear

Large lymphocyte with scanty cytoplasm and increased nuclear cytoplasmic ratio with open chromatin and prominent nucleoli - suggestive of germ cell tumour or leukemia (Fig. 2-4).

CT scan

Diffuse muscle enlargement with involment of tendon. The radiologist suggested the possibilities of
neovascularisation, peripheral retinal hemorrhages & central retinal vein occlusion can occur. Corneal manifestations are less due to its avascularity, but limbal infiltrations have been reported. Anterior segment manifestations are iritis, hypopyon, spontaneous hyphema & heterochromia iridis. Sclera may show perivascular infiltration 1,2,3,4.

Aetiologies to be considered for B/L proptosis in a child are:

Orbital cellulitis, neuroblastoma, rhabdomyosarcoma, leukemia, eosinophil granuloma, Burkitt’s lymphoma & pseudotumour 6.

Causes for B/L diffuse extra ocular muscle enlargement:

Acromegaly, amyloidosis, carotico caurneous fistula, Graves disease, leukemia, lymphoma, metastases, orbital cellulitis, orbital myositis, Plexiform neurofibroma, polyneuropathy, sarcoidosis & trichinosis.

ALL is a condition producing bilateral proptosis due to orbital infiltrates. Proptosis due to diffuse muscle infiltration has been described in AML. Review of literature did not reveal any reports of extraocular muscle involvement. So we are reporting this case as a rare presentation.

References

3. T. Sharma,J.Grewal, S.Gupta,P.I Murray;Ophthalmic manifestation of ALL,ophthalmologist role; Eye; 2004; 18;663-672
4. S.C.Reddy,N.Jackson,B.S.Menon.ocular involvment in Leukemia;Ophthalmologica;vol 2003;217;441-445
5. Albert Jakobiec,Timothy .J.Murtha ;Hematologic Disorder:Leukemia,Dysprotenimia and Aneamia;vol 5; 353;4968-4976
6. Duane Gerald .J. Harin, Bruce.M.Marraro;acute proptosis in childhood;vol 2;46
Leukaemic Retinopathy with Serous Macular Detachment – A Case Report

Dr. Rajesh P* MD, Dr. M A Safarullah* MS, Dr. Syed Basheer Ahmed* DO

Hematological disorders can occasionally present with ocular symptoms. In the setting of an established systemic illness, it is easy to explain the ocular findings. But when ocular involvement is the primary presentation of the systemic disease, the diagnosis can be difficult, especially when the presentation is atypical.

We report a 36 years old male, who presented with sudden decrease in vision in both the eyes, right more than the left, of four days duration. He gave history of fever with joint pain 2 weeks prior to the presentation. On examination the Best Corrected Visual Acuity was 1/60 in right eye and 6/9 in the left eye. The pupils were normal and briskly reacting to light with no RAPD. AC and vitreous were quiet. Fundus examination showed a serous detachment of the macula in the right eye and retinal hemorrhages and dilated tortuous veins in both the eyes. Some of the hemorrhages were white centered (Fig. 1 & 2). B scan of the right eye showed macular detachment with peripapillary choroidal thickening (Fig. 3). Fluorescein angiography showed blocked fluorescence corresponding to the areas of hemorrhage in both the eyes and segmental leakage from the arterioles and capillaries with late staining in the right eye (Fig. 4, 5).

Haematological work up was also done. Hemoglobin was 4.5 gm % and total count was 1,16,000 cells/ cumm. Peripheral smear showed microcytic hypochromic RBCs with many polychromatic cells and occasional nucleated RBCs. WBCs showed blast cells.
Confused with CRVO. Involvement of vitreous and optic nerve are rare happenings in ocular leukemia.

Histopathologically, choroid is the most commonly involved structure in leukemia. Choroidal involvement can lead to hyperplasia of overlying RPE and pigment clumping which leads to “leopard spot appearance”. Serous detachment of overlying retina has been attributed to the decreased blood flow in the choriocapillaries, leading to disruption of retinal pigment epithelial barrier and accumulation of choroidal fluid in the sub-retinal space. Serous detachment occurs only in 0.3% of the patients.

Our patient had sonological evidence of choroidal thickening in the eye with the serous detachment, signifying choroidal involvement. Fluorescein angiography showed leakage from arterioles and capillaries in the eye with serous detachment. Hence leakage from the vessels could also have contributed to the serous detachment in this patient in addition to the mechanism already described.

In conclusion, leukemic retinopathy may be asymptomatic in many patients and serous detachment causing visual disturbance could be one of the presenting features of the disease.

References

Optic pits are congenital excavations of the optic nerve head that may be associated with other abnormalities of the optic nerve and peripapillary retina. Optic pits occur in about one in 10,000 people, with no gender predilection, and are usually sporadic. Optic pits are usually incidental findings on fundus examination and remain asymptomatic unless complicated by macular lesions such as edema, schisis or serous detachment. A patient with macular involvement generally presents with visual acuity of worse than 20/70 in the affected eye, and 80 percent of these eyes lose visual acuity to 20/200 or worse. It has been suggested that these patients have a greater propensity to develop normal-tension glaucoma, although the arcuate visual field defects may be caused by the optic pit itself rather than by glaucomatous damage.

A 17 year old male patient presented with progressive defective vision of 6 months duration in his left eye. Ocular examination revealed a best corrected vision of 6/60 not improving further with glasses or pinhole. Ocular examination was within normal limits except for abnormal fundus findings. Fundus examination revealed the presence of congenital optic disc pit with a serous macular elevation in the left eye. (Fig 1)

**Laser photocoagulation** was used to produce several rows of laser burns between the area of the serous retinal detachment and the optic disc. The objective was to achieve a very light white laser burn with little collateral damage to the nerve fiber layer. This presumably creates a wall of scar tissue to block the passage of fluid from the optic pit to the inner retinal schisis cavity and subretinal space.

**Vitreous surgery and internal tamponade:** Combinations of posterior vitrectomy, photocoagulation and gas tamponade was suggested for treating optic pit–associated maculopathy. Successful macular reattachment and improved central vision can be achieved using vitrectomy with induction of PVD and gas tamponade.

**Discussion**

Congenital pits of the optic nerve head vary in size, shape, depth and location. They appear as small, hypopigmented, grayish, oval or round excavated depressions in the optic nerve head. They are usually about 500 μm in size and may be bilateral in 10 to 15 percent of cases. Optic pits are most commonly located on the temporal side of the optic disc, but they may be situated centrally or anywhere along the margin of the optic disc. Optic pits along the rim of the optic disc are most likely to lead to serous detachments of the retina, with associated full-thickness or laminar retinal holes, retinal pigment epithelium mottling and general cystic changes. The retinal detachments are usually confined between the superior and inferior vascular arcades and are contiguous with the optic disc, sometimes through a visible isthmus of subretinal fluid. The elevated retina contains cystic cavities in the outer plexiform layer.

**Optical coherence tomography** - OCT of an optic pit usually shows a schisislike separation...
between the inner and outer retina and a larger retinal detachment.

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

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

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

**Electrophysiological testing** An electroretinogram (ERG) may show poorly defined and low-amplitude waveforms, consistent with schisis and serous detachment. Preoperative evaluation of macular function is important for predicting the likelihood of central vision recovery after successful macular reattachment. Patients with a poor ERG response are less likely to experience visual acuity improvement even after anatomical reattachment.

**Differential Diagnosis** A dilated biomicroscopic fundus examination is essential for differentiating optic pits from the following conditions:

- Optic disc anomalies such as choroidal and scleral crescent.
- Tilted disc syndrome.
- Circumpapillary staphyloma.
- Hypoplastic disc.
- Glaucomatous optic neuropathy. (Any change in the appearance of the optic pit over time suggests that the lesion may be an acquired notch of the neuroretinal rim secondary to glaucomatous damage.)
- Central serous retinopathy and subretinal neovascular membranes. (These conditions are alternative considerations for serous macular detachment).

**Pathophysiology**

Congenital optic pits result from an imperfect closure of the superior edge of the embryonic fissure. They are asymptomatic unless complicated by secondary macular changes. They typically lead to a two-layered maculopathy consisting of a primary inner retinal layer schisis and a secondary outer layer detachment. Although the exact mechanism by which optic pits cause macular detachment is not known, various theories about the source of fluid and the macular changes have been proposed, including:

**Subretinal fluid.** It has not been established conclusively whether the subretinal fluid originates from the vitreous cavity, from the subarachnoid space or from leakage from the retinal vessels around the optic disc. Studies involving intrathecal fluorescein injections and histological tissue analysis have failed to provide any evidence of the optic pit acting as a conduit between the subarachnoid and subretinal spaces. The lack of dye leakage from retinal vessels
makes it unlikely that the retinal vasculature is the source of the fluid. Brown and colleagues suggested that there may be a connection between the vitreous and the submacular fluid, based on the findings in their canine model of optic pit. Using India ink they found a direct communication between the vitreous, the optic pit and the subretinal space in three collie dogs with congenital optic pits.

**Two-layer separation.** Serous macular detachment associated with optic pit was thought to be due to direct communication between the optic pit and the subretinal space, facilitating fluid accumulation under the macula. However, Lincoff and colleagues suggested that the primary communication from the optic pit may be to the retina. Fluid may move into the retina, causing a schisislike separation of the inner and outer layers, with the neurosensory serous retinal detachment occurring secondary to this schisis. Recent OCT findings confirm this separation.

**Vitreous traction.** Vitreous traction appears to be an important factor in the pathogenesis of optic pit-related macular detachment. Traction, vitreomacular or vitreopapillary, may permit entry of fluid into the retina through the optic pit.

**Management**

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

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

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

**Macular buckling.** Macular buckling has been reported as a treatment option for serous detachment associated with optic pit. Scleral buckling converts the posterior hyaloid traction from an inward to an outward vector, promoting reattachment of the macula.

**Vitreal surgery and internal tamponade.** Combinations of posterior vitrectomy, photocoagulation and gas tamponade are used for treating optic pit–associated maculopathy. Successful macular reattachment and improved central vision can be achieved using vitrectomy with induction of PVD and gas tamponade. A complete PVD helps relieve vitreous traction. Indeed, spontaneous macular reattachment has been observed in eyes undergoing posterior vitreous separation. Gandorfer and Kampik advocate internal limiting membrane peeling in addition to removing the posterior vitreous for relieving all tractional components.

**Conclusion**

Maculopathy caused by optic pits has an overall poor prognosis, and long-term studies involving large groups of these patients are lacking. Given that the exact pathophysiology is still a matter of debate, management should be tailored to the visual disability and macular changes of the specific patient.

**References**

Surgically Induced Necrotizing Scleritis – A Case Series

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Abstract

Surgically induced necrotizing scleritis (SINS) is a rare complication of ocular surgeries like cataract extraction, strabismus correction, scleral buckle, trabeculectomy, pterygium excision, pars plana vitrectomy and diode laser cyclophotocoagulation. It is associated with systemic collagen vascular diseases like rheumatoid arthritis, polyarteritis nodosa, Wegener's granulomatosis etc. It can occur on the first postoperative day or forty years after surgery. We report four cases of necrotizing scleritis, three following cataract extraction and one after pterygium excision with amniotic membrane transplantation, with no associated systemic illnesses. Autoimmunity, multiple surgeries, local ischemia have been implicated in its pathogenesis. Prompt diagnosis and treatment with non-steroidal anti-inflammatory drugs or immunosuppressives can prevent morbid complications.

Keywords: Surgically induced necrotizing scleritis (SINS), cataract surgery complication, pterygium, amniotic membrane transplantation.

Introduction

Surgically induced necrotizing scleritis (SINS) is a rare sequelae of various ocular surgeries like cataract extraction, strabismus correction, scleral buckle, trabeculectomy, pterygium excision, pars plana vitrectomy and diode laser cyclophotocoagulation. This entity is known to occur commonly in patients with systemic illnesses like rheumatoid arthritis and various other collagen vascular diseases. We report four cases of necrotizing scleritis, three following cataract extraction and one after pterygium excision with amniotic membrane transplantation, with no associated systemic illnesses. It is important to diagnose this condition as early diagnosis and prompt treatment with non-steroidal anti-inflammatory drugs (NSAIDs) or immunosuppressives can prevent morbid ocular sequelae in most of the patients. The various etiological mechanisms put forward for this clinical entity and treatment are discussed.

Case Report

CASE 1

Seventy year old lady presented eight weeks after extracapsular cataract extraction with severe pain and decreased vision in right eye. She gave no history of diabetes mellitus, hypertension and collagen vascular diseases. Her best corrected vision in the involved eye was 3/60. Slit lamp examination showed a 5 × 3 mm area of scleral necrosis overlying the section with iris prolapse and severe tenderness (Fig. 1). There was mild
corneal edema, no evidence of cells and flare in the anterior chamber. On indirect ophthalmoscopy the media was fairly clear, no vitreous exudates were seen. Investigations showed a raised erythrocyte sedimentation rate (ESR) of 40 mm/hr. C-reactive protein, Rheumatoid factor and Anti-Nuclear Antibody (ANA) were negative. She was treated with topical antibiotic-steroid eye drops (gatifloxacin 0.3 % & 0.1 % Dexamethasone) Q 4th hourly and oral Indomethacin 75 mg od. The area of scleral necrosis stabilized on follow up after 4 weeks and vision improved to 6/18.

**Case 2**

An 80 year old male was referred as a case of scleromalacia perforans (LE) following cataract surgery. Three weeks after small incision cataract surgery he presented with a sudden drop in vision when iris prolapse was noted and underwent iris repositioning with suturing of the wound. Two and a half months later he presented to us with severe pain, redness and poor vision in the same eye. On ocular examination visual acuity in the right eye was found to be 6/9 and 2/60 in the left. Slit lamp examination of the left eye showed mild corneal edema with 2+cells. The anterior chamber was shallow superiorly with an area of scleral thinning 10×6 mm at the section with iris prolapse (Fig2). A fibrinous membrane was also noted on the surface of the IOL. On fundus examination disc was hazily seen and details were unclear. Investigations showed a raised ESR of 46 mm, RA factor was negative, ANA negative. He was treated with oral prednisolone 60 mg/day and 0.1% dexamethasone eye drops with which he improved.

**Case 3**

Young lady 40 years of age presented with fleshy pterygium in both eyes. She underwent pterygium excision with amniotic membrane transplantation which was sutured with 6-0 vicryl. Until the second postoperative week the amniotic membrane was in situ and the underlying sclera was healthy. On the third postoperative week scleral thinning and uveal tissue exposure was noted. Her ESR was 40mm, RA factor negative, ANA negative. She was treated with topical (1 % prednisolone acetate 4th hourly) and systemic steroids (prednisolone 1mg/kg). She responded well to treatment and in two weeks the scleral thinning stabilized.

**Case 4**

Young lady 40 years of age underwent cataract extraction in the right eye. Four weeks after an uncomplicated small incision cataract extraction painful scleral thinning at the section was noted on follow up. There was no drop in vision (V/A 20/20 OD) and no reaction in the anterior chamber. Her ESR was 30mm, RA factor negative, ANA negative. Her topical steroid was maintained at Q 4th hourly. Oral NSAID (Tab Ibuprofen 400mg TID) was also started. In three weeks the scleral thinning stabilized and the congestion decreased.

The four cases are summarized in table 1.

**Discussion**

The hypothesis put forward for the pathogenesis of surgically induced necrotizing scleritis is varied and complex. Autoimmunity is a well accepted etiological factor in the development of SINS. Clinical or serological markers for connective tissue disorders are present in as many as 62 % of cases. Episcleral vessels are affected in systemic vasculitis and immune complexes have been found to be deposited in and around episcleral vessel walls by immunofluorescence techniques. The time of onset of the condition ranges from first postoperative day to as long as forty years. Causative factors resulting in local ischemia due to disruption of episcleral vasculature in squint surgery, scleral buckle and excessive use of cautery have been implicated in the pathogenesis of necrotizing scleritis especially in patients developing it in the early postoperative period. But then their rapid response to immunosuppressive agents also supports the view of immunological reaction involved in the pathogenesis.

Multiple ocular surgery is one of the predisposing factors for necrotizing scleritis. Hence it may be due to a hypersensitivity reaction directed against the antigen revealed or altered following tissue damage due the first surgery.
SINS occurring after pterygium surgery has been frequently reported following the use of adjuvant mitomycin/ thiopeta or beta irradiation or bare sclera technique. In our scenario it occurred following use of amniotic membrane transplantation which has not been reported before. Use of irradiation or antiproliferative agents causes obliterative endarteritis or inhibition of endothelial proliferation resulting in local ischemia and necrosis. In the absence of above, excessive use of cautery has been implicated as the cause for scleral necrosis especially in bare sclera technique.

When treated early and when not associated with systemic diseases SINS responds well to topical and oral NSAIDS or steroids as in our case series. Patients who are positive for ANA and other serological markers for autoimmunity may require systemic cyclosporine or azathioprine for response. Surgical treatment with scleral or corneal patch graft is considered when there is no response to medical therapy with impending perforation.

### Conclusion

Though SINS is a rare postoperative complication, prompt diagnosis and early treatment has good prognosis and can avoid need of toxic systemic immunosuppressive drugs.

### References


### Table 1. Case Summary

<table>
<thead>
<tr>
<th>S No</th>
<th>AgeYrs</th>
<th>Sex</th>
<th>Surgery done</th>
<th>Time of presentation</th>
<th>Visual acuity</th>
<th>Treatment</th>
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<tr>
<td>1</td>
<td>70</td>
<td>F</td>
<td>ECCE</td>
<td>8 wks</td>
<td>3/60</td>
<td>Dexamethasone eyedrop 0.1 % &amp; oral Indomethacin</td>
</tr>
<tr>
<td>2</td>
<td>80</td>
<td>M</td>
<td>SICS</td>
<td>3 wks</td>
<td>2/60</td>
<td>Topical 0.1 % Dexamethasone &amp; oral Prednisolone</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
<td>F</td>
<td>Pterygium</td>
<td>3 wks</td>
<td>20/20</td>
<td>1 % Prednisolone acetate eyedrop &amp; oral Prednisolone</td>
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<tr>
<td>4</td>
<td>40</td>
<td>F</td>
<td>SICS</td>
<td>4 wks</td>
<td>20/20</td>
<td>Topical Dexamethasone 0.1 % &amp; oral Ibuprofen</td>
</tr>
</tbody>
</table>

ECCE – Extracapsular cataract extraction, SICS – Small incision cataract surgery.
Health Research: Some aspects of Methodology and Statistics

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Research is a systematic and rigorous process of enquiry that aims to describe phenomena and to develop and test explanatory concepts and theories with the aim of contributing to a scientific body of knowledge. Health research, specific to the field of ophthalmology or otherwise, aims to improve health, health outcomes and health services through providing evidence to inform policy, direct practice and develop products.

As with any investigation or enquiry, adequate planning prior to commencing the process is essential to ensure a well-organized and efficient research study that generates constructive evidence. While the first part of this paper outlines the essential steps through which a study should be planned, the second section briefly covers commonly disregarded but important considerations related to sample size and data management.

A. Planning a research study

Research Question

A research idea is born of the need to know more. It must be developed into a research question, the answer to which is sought through conducting systematic study.

The first step is to find out what is already known about the question of interest through a review of literature and discussion with experts. This also helps to focus on identifying the scope of the proposed research, often through three broad areas of inquiry.

- What aspects would warrant a more detailed study?
- What ‘new’ thoughts about the issue / possible explanations have arisen?

Since the purpose of conducting a study is to add to the body of scientific knowledge, a response to questions such as these provides the core of the research question your study will be designed to answer. Often, a ‘good’ research question would be one of public health interest (make a significant difference to a [large] group), a question that tests a hypothesis about cause/risk factors and effect, or one that assess an intervention.

Aim and Objectives

The aim is directly derived from the answer sought to the research question (e.g. Randomized controlled trial of safety and effectiveness of intravitreal bevacizumab). The objectives are specific goals that will be achieved in the process of fulfilling the stated aim, and are characteristically framed along the lines of being ‘SMART’: Specific, Measurable, Attainable, Relevant and Time-bound. Being precise and concise are key characteristics of the sentence stating an objective (e.g. one objective could be ‘to compare the effectiveness of intravitreal bevacizumab injection in reducing blindness after three months, with that of standard therapy (vitrectomy and endolaser)’).

Objectives that are consistent with the research question guide design, conduct and analysis and therefore are the framework upon which the study is built.

• What gaps in information have been identified?
Definitions

Lucidity of meaning and clarity of context are crucial for effective communication. This is achieved in scientific investigation by defining all variables, such as defining a ‘case’ when studying a disease, or ‘cure’ when that is the outcome being investigated. Definitions are usually in alignment with universally accepted and previously validated norms (e.g. Visual acuity less than 3/60 when tested with the best possible refractive correction, using Snellen’s optotypes is defined as ‘Blind’).

Going on to refining the research question in the context of the study design, objectives and definition, it could now be framed so as to include the PICOT (Population sampled, Intervention(s) tested, Comparator for the intervention, Outcome(s) of interest and study Timeframe) something along these lines – Among a group of diabetics with poor glycemic control (glycated hemoglobin over 7) and uncomplicated fresh vitreous hemorrhage resulting from diabetic retinopathy, but with no other ocular or systemic morbidity, how safe and efficacious is intravitreal bevacizumab in reversing blindness (at three months from the intervention) as compared with standard therapy?

Methodology

Questionnaire Development

Data collection is the most resource intensive part of the study. It is worthwhile remembering the Information Technology catchphrase ‘GIGO’, an acronym for “garbage in; garbage out” to keep in perspective the rigor required during data collection.

Collecting data that is meaningful and doing this in an efficient manner requires framing valid questions, and ensuring that the question elicits reliable responses. The other aspect that sometimes proves to be the most difficult is to collect only what one NEEDS to know, and resist adding data that is only NICE to know. The process of piloting and validating a questionnaire or other tool of data collection therefore needs to be done in a systematic manner, and every tool should be pre-tested before being finalized.

Questionnaires are typically used for survey research to record the status of variables involved in research. For the purpose of this article, the term ‘questionnaire’ is used interchangeably with any form used to collect primary data or data that will be subjected to analysis for the particular research study. A well-designed questionnaire gathers information effectively. Questionnaire designing is commonly done using Microsoft Word or PageMaker. When developing a questionnaire, a (unique ID) serial number is provided for each form, to enable tracking the forms for errors or verification.

Important points in developing the questionnaire are that each question should be directly related to the survey objectives, and the researcher should avoid unnecessary questions. Instructions should be precise and sufficient, so that every respondent is able to answer every question in a self-administered questionnaire. It is wise to avoid ‘double-barreled questions’; ones that have more than one question embedded within because participants may answer one question, but not both, or may disagree with a part of or the entire question (imagine your plight if entrance exam MCQs were double barreled). Clear indication of answer choices in the questionnaire also reduces incorrect data entry. Provided below are some examples of improper designing of questionnaire and recording of data:

- Categorizing variables such as age:
  Categorizing age and other continuous variables like IOP is not advisable during data collection and data entry; it is best to categorize only when analyzing the data. The reason is simply that re-categorization and calculating the mean is not possible once data is categorized. For example, if age is collected in categories like ‘under 15’; ‘15-40’ and ‘over 40’, then it is not possible to elicit information on how many persons were 50 years old, or how many were below 18 years of age.

- Writing gender in words
  Data needs to be recoded before analysis because text like ‘male’ cannot be subjected to mathematical manipulation like addition, for example, unlike the code ‘1’ for ‘male’, which can. If left to the data entry operator, this can lead to data entry errors, and cannot be checked for accuracy of transcription.

- Recording Visual Acuity
This is an error that happens frequently while recording the data. For example, pinhole visual acuity being recorded instead of presenting visual acuity (due to misunderstanding instructions by the examiner) will lead to incorrect results and interpretation of outcome. The other instance is where an inappropriate tool is used to measure visual acuity (such as the Snellen’s chart, which provides categorical data vis a vis the LogMAR charts that measure visual acuity as a continuous variable).

If the researcher is not directly involved in the data collection, then appropriate training should be given to the person who is collecting data and the researcher must ensure quality checks during data collection. Regular follow-up at data collection team meetings is one way of ensuring that ‘garbage’ does not get in at this level. Systematic and rigorous pre-testing and a pilot study go along way in avoiding the hassles brought by changing the questionnaire or protocol during the main study. Problems encountered through the pilot study should be discussed with study team members including the data collection team.

Responsibilities of each member of the study team should be described, and equipment for measurement should be standardized during the planning phase. The final protocol is passed on to all members of the study team before embarking on data collection, usually through a training workshop during which the principal investigator communicates and clarifies methodological details.

It is good practice to put down the standard operating procedures, codebook for data being collected, and other such useful information in a ‘ready-reckoner’ manual that is distributed to all members of the study team.

**Ethical issues and Consent**

It is essential to abide by the tenets of the Helsinki Declaration when conducting any research that involves human beings as subjects. Most institutions that conduct health research also have ethics committees and an (independent) Institutional Review Board (nomenclature varies), from whom approval is mandatory before the study commences. In India, the Indian Council for Medical Research has clearly laid down guidelines for the conduct of research on human subjects in its 2006 publication. As a norm, informed consent is to be obtained in writing from all participants at enrollment in the study, and a clear statement of how adverse events will be handled should be provided.

It is also good practice to ensure that inducement for participation in the study or conflicts of interest are carefully avoided or declared, and that the outcomes of the study (results) are disseminated to the participants at the end of the study.

**Budget**

This is a subject that is often neglected, though inadequate planning of resources can bring the study to a grinding halt. Budgeting is planning of finances. It includes planning for persons who will be involved in the study and their time, materials and machinery, transportation and logistics and sometimes training costs and other such intangibles such as consultation with technical experts, all of which can be translated into monetary terms. All such ‘line items’ that are vital to conduct of the study should be listed and costed.

**B. The role of Biostatistics in research activities**

Statistics is an integral part of modern medical research, and is a science applied while planning study methodology - it is the process of simplifying data, identifying or predicting how data falls into patterns, measuring relationships between variables and interpreting these through description or comparison. Statistical analysis involves data organization and mathematical manipulation of data. It is NOT manipulation of data to obtain intended results. Writing a statistical analysis plan for studies a priori (during the stage of planning the study itself) is the best way to finish the analysis in time. A statistical analysis plan should clearly state objectives and list the most important tasks, providing a detailed description of exactly what we want to do and why.

The people and processes involved in statistical applications and data management is described here. Participation of the ‘statistical’ people commences early in the planning phase with development of the study protocol. It continues into conducting the study, through
analysis of data, to writing a report of the analysis. Therefore, every researcher needs basic biostatistical knowledge to understand and work with the biostatistics personnel, lest one may find that they have to completely rely on and blindly accept the inferences provided by the statistician.

**Data Entry System Development**

Data Entry System (DES) is used to integrate data, and is needed for handling large volumes of data. A pre-programmed system plays a role in entering data faster and without confusion whereby errors can be minimized, especially in research studies involving a large number of variables and it ensures easy data retrieval. Data redundancy can also be avoided by reducing the database size. When the DES is developed and designed by the person who is going to enter data it becomes easier to understand and make modifications when the need arises.

The data entry programmer ensures that the structure of the database is designed for easy analysis, and meaningful variable names are given to variables. This is one reason why the programmer should be involved at the stage of questionnaire development, and the DES should be pre-tested and piloted. Software testing is the process by which the appropriateness, completeness, security and quality of computer software developed for the study is evaluated. Software testing is an absolute requirement for studies that used DES created by someone outside the study team. Often, the DES is developed in Visual Basic as front end and Access as backend for most of the studies. EpiInfo is also used for designing DES.

**Data Entry**

The process of entering data into a computerized database or spreadsheet is called data entry. Data Entry Operators (or programmers) are well trained in entering data, and have to be made familiar with the clinical terms and other such jargon used in each study. This is extremely important while entering clinical details. Data is stored in databases like MSAccess, MSExcel, FoxPro and EpiInfo. Selection of a database to store the data depends on sample size of the study, and the type of data collected. If the study is small, then MSExcel is used and when the sample size of the study is large, MSAccess is most commonly used. To improve the quality of data entry forms should be thoroughly checked by the person who is responsible for data collection (the researcher and data collection team) before being handed in for data entry. It is normal practice not to modify data once it has been entered except to correct inconsistencies picked up through comparing datasets when double data entry is done.

For high volume data entry, “Double Entry” method is strongly advocated, where data is entered twice, each time by a different person. Then a special program is written to compare each variable; the program generates values showing a discrepancy, and those values are checked manually by going back to the proforma/questionnaire. Thus double entry method significantly reduces data entry errors.

**Data Management**

Data management is the process of monitoring and improving the quality of data. This is the interface between data entry and data analysis. The success of a study is often dependant on data management since one of the major roles of data management is to minimize error in all stages of the study, not just at the computing stage.

The data manager is responsible for maintaining and monitoring the database on an ongoing basis for large studies, including sending out queries for missing data and incorrect entries periodically. It involves setting up appropriate data collection systems for coding, cleaning, reshaping and editing the data.

**Data checking and data cleaning**

For all studies, data cleaning, or data checking, needs to be undertaken prior to any analysis being performed. If the accuracy of the data is assumed and no checks undertaken, it is highly likely that data queries will result whilst attempting the analysis and these will need to be resolved and the analysis re-run, resulting in unnecessary delay.

Even with small studies, it is very unlikely that absolutely no data entry errors have occurred. Despite the data being entered as it appears on the
questionnaire, it still could be incorrect. (e.g. right eye vision entered under the column for left eye at presentation could be picked up as an inconsistency if the initial vision is worse than the final vision in one of the eyes, in a study on the benefit of spectacles for correcting refractive errors).

Data checks may involve range checks or logical checks, but every variable should have been checked. Examples of checks to be undertaken include:

- Checking that age in years does not exceed 16 in a study of children
- Checking that sex takes the value 1 (for males) or 2 (for females), if that is how it is coded, and no other value
- Checking that date of discharge from hospital is not before date of admission to hospital
- Checking that those who state they never drink alcohol have zero or “not applicable” quantities listed for the amount drunk in the last month.

Reshaping database

Reshaping or restructuring is one of the methods to modify data into an analyzable form. This requires some foreknowledge about statistical methods to be applied.

Labelling and Codebook

In every research project, a codebook should be generated. A codebook is a document that describes data and indicates where and how it can be accessed. At the minimum, the codebook should include for each variable, the Variable name, Variable description, Variable format (number, date, text) and explanatory notes where required. The codebook is an indispensable tool for the analysis team. Together with the database, it should provide comprehensive documentation that enables other researchers who might subsequently want to analyze the data to do so without the need to seek any additional information.

Statistical Analysis

Statistical analysis is the process through which data becomes knowledge and is a science to assist one in arriving at a decision under conditions of uncertainty. It is not a process of torturing results out of numbers, but rather a scientific method that uses data meaningfully, to make comparisons and generate evidence within limits of probability.

A researcher requires the help of a statistician in order to design and conduct the study and to analyze the data collected in an appropriate manner such that the research problem is solved. Consulting the biostatistics team in the preparation of questionnaire will avoid questions that are incomplete, ill conceived or inadequately answered, because no statistical analysis can compensate for the resulting defective data collected.

Two other situations where the help of a biostatistician is sought are in calculating a sample size, and in allotting numbers for randomization. Randomisation is a process eliminates predictability by allocating research participation to either the investigational group or the control group through chance rather than by choice. Randomization is done by the toss of a coin, using a random number table or by using a range of software, so long as masking is ensured to eliminate selection bias. Choosing an appropriate sample pre-empts the need for surveying the entire target population. Sample size should be given due consideration in any research proposal, as an inadequate sample size invariably leads to wasted resources. Though sample size calculations are done early in the planning phase, we present here some empirical facts behind the rationale of sample size calculation.

The most common aim with which a research study is conducted is probably that of determining some difference between two groups so we will continue thinking through the bevacizumab example. The calculation of an appropriate sample size should be based on estimates of from a rigorous review of literature, though it often relies on a subjective choice or crude estimates of certain factors making it appear to be a well educated guess. Nevertheless, this guesstimate is more useful than a completely arbitrary choice. There are three main factors that must be considered in the calculation of an appropriate sample size – P value, Power and Effect. The difference between two groups in a study will usually be explored in terms of an estimate of effect, appropriate confidence interval
and P value. The confidence interval indicates the likely range of values for the true effect in the population, while the P value determines how likely it is that the observed effect in the sample is due to chance. A related quantity is the statistical power of the study, which is simply the probability of correctly identifying a difference between the two groups in the study sample when one genuinely exists in the populations from which the samples were drawn.

If the ‘clinically significant’ P value is small (usually set at 0.05 to 0.01), it is difficult to achieve significance unless a large sample is used because of the stringent criterion for measuring effectiveness.

The ideal study for the researcher is one in which the power is high – where the study has a high chance of detecting a difference between groups if one exists; consequently, if the study demonstrates no difference between groups the researcher can be reasonably confident in concluding that none exists in reality. The power of a study depends on several factors but as a general rule higher power is achieved by increasing the sample size; often studies are reported that are simply too small to have adequate power to detect the hypothesized effect. In other words, even when a difference exists in reality it may be that too few study subjects have been recruited, and therefore the ‘truth’ remains hidden; P values are higher and confidence intervals wider than would be the case in a larger study, and the erroneous conclusion may be drawn that there is no difference between the groups. Since ‘absence of evidence is not evidence of absence’, an apparently null result that shows no difference between groups may simply be due to lack of statistical power, making it extremely unlikely that a true difference will be correctly identified. A study that is designed to be powerful (conventionally, power is set at 80 % to 95 %) makes it more probable that the ‘true’ effect is measured, but requires a larger sample size compared to a less powerful study.

A small effect size (e.g. small difference in visual acuity expected with bevacizumab above that expected with vitrectomy and endolaser) is difficult to identify and therefore requires sensitive tools and a large sample size. Ideally, the size of the effect will be based on clinical judgement. It should be large enough to be clinically important but not so large that it is implausible.

Once these three factors have been established, there are tabulated values (as normograms) and formulae available for calculating the required sample size. Even in the simple example we are using, the choice of an appropriate formula will vary depending on whether the groups are equally sized and on whether the measure of effect is a difference in means (continuous outcome variable) or a difference in proportions (categorical outcome variable). Since certain outcomes and more complex study designs may require further information, calculation of the required sample size is best left to someone with appropriate expertise. However, it is important to remember that it is the duty of the researcher to provide values that will be plugged into the formula and that the sample sizes obtained from these methods are intended as approximate guides rather than exact numbers.

Although the most common criticism of the size of a study is that it is too low, having a study that is too large raises more issues beyond being a waste of resources. Recruiting an excessive number of participants may be unethical, particularly in a randomized controlled trial where a larger number of patients end up receiving placebo or potentially inferior care, than is necessary to establish the worth of the new therapy under consideration.

Any sample size calculation is based on the total number of subjects who are needed in the final study. In practice, eligible subjects will not always be willing to take part and it will be necessary to approach more subjects than are needed in the first instance. In addition, even in the very best designed and conducted studies it is unusual to finish with a dataset in which complete data are available in a usable format for every subject. Subjects may fail or refuse to give valid responses to particular questions, physical measurements may suffer from technical problems, and in studies involving follow up (e.g. trials or cohort studies) there will always be some degree of attrition. It may therefore be necessary to calculate the number of subjects that need to be approached in order to achieve the final desired sample size. It is particularly important to account for nonparticipation in the costing of studies when initial recruitment costs are likely to be high.

In conclusion, if the researcher asked the wrong question, asked the wrong group of people or was
subject to major bias, there is no statistical analysis method in the world that can create meaningful information from the raw data. There are some techniques that can correct small errors, but the more 'small errors' are corrected, the less accurate the results will be. The key to good research is planning, piloting and more meticulous planning. Teamwork is the key throughout, from developing and reviewing the study protocol, questionnaire and other study materials. A tight design works only when the study is conducted systematically and with rigor. Including a statistician is necessary in order to ensure correct statistical representation of data and results.

References
3 Whitley E, Ball J. Statistics review 4: Sample size calculations. Critical Care 2002, 6:335-341
6 Whitley E, Ball J. Statistics review 4: Sample size calculations. Critical Care 2002, 6:335-341
Idiopathic Central Serous Retinopathy With Bullous Retinal Detachment

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Classically Central Serous Retinopathy presents as a round or oval serous detachment of the retina at the macula that is localised and well delineated from the surrounding normal retina. The detachment invariably involves the fovea, and may rarely be outside the macula. The fluid under the sensory retina may be clear or turbid, and may sometimes contain protein deposits, or fibrinous exudates. More than one such localised detachment may be occasionally found in different areas of the same fundus, and could be located peripherally as well. The sensory detachment may sometimes be extensive and bullous, with shifting subretinal fluid that may extend to the fundus periphery. Eyes with fibrin in the subretinal space or eyes with extensive detachments may develop subretinal fibrosis. Serous detachments of the retinal pigment epithelium (RPE) may often be found in eyes with localised or extensive retinal detachments. These appear as smooth, round or oval, dome-like elevations of the RPE with clear fluid and distinct margins. RPE detachments are usually around ¼ disc diameter in size, but can be much larger. They may be found within the area of serous retinal elevation, at its border, or outside it. RPE tears and choroidal neovascularisation are rare in ICSC, but have been described. It is also important not to over look a congenital pit of the optic nerve head that may be associated with a serous detachment of the macula. When ICSC resolves or becomes chronic, there may be alterations in the fundus such as RPE atrophy in different patterns, RPE hyperpigmentation, subretinal yellow deposits, or retinal neovascularisation. An atrophic tract in the RPE might be noticed in eyes after absorption of fluid that had gravitated inferiorly from the macula. While acute ICSC may not pose a problem in diagnosis, the chronic stages can be easily misdiagnosed unless one is familiar with the fundus changes associated with it. ICSC may sometimes be bilateral with symptoms developing days or weeks apart in each eye. Fellow eyes may be normal, may show localised serous detachments of the retina away from the fovea, RPE detachments, or evidence of previous ICSC.

The natural course of ICSC is favourable in most patients, with resolution of the serous detachment and return of visual activity, with sustained long-term visual gain. About 5% will be left with a visual acuity of less than 6/9, 20 to 50% will have one or more recurrences, with most recurrences occurring within one year, and about 20% can develop ICSC in the other eye. Recurrences were most often seen within one disc diameter of the original site of fluorescein leakage. Eyes with serous bullous detachments can also reattach spontaneously with recovery of vision. In spite of clinical resolution and improvement in visual acuity, other tests of macular function determined by Amsler’s grid, visual field charting, colour vision testing, contrast sensitivity determination, multifocal electroretinograms, and electro-oculograms could be abnormal. Morphological changes in the retinal pigment epithelium such as pigment epithelial atrophy, and hyperpigmentation may be seen in eyes after resolution of the serous detachment. These areas of atrophy may be located...
within, or even outside the area of serous detachments that had resolved. Serous pigment epithelial detachments associated with ICSC in younger patients can spontaneously flatten and show some pigmentation, without the development of geographic atrophy or choroidal neovascularisation. Hyperfluorescence on the ICG, and foveal thinning on the OCT may be evident long after the sensory detachment subsides.

We present a case of central serous retinopathy with atypical features in an young patient who gave a history of chronic use of a steroid skin cream for allergic dermatitis.

Spontaneous resolution on conservative treatment was slow and took place over a period of 3 months. The patient was weaned off steroids and an emollient cream was given for local application. Although the resolution was dramatic, it was not accompanied by a corresponding increase in visual acuity.

**Management**

Patients with ICSC can be reassured and observed because of the favourable natural outcome that has been consistently documented. In patients taking steroid for an ocular problem, the drug may be tapered off and stopped if there are clear indications that it is not necessary. In patients taking steroids for other medical conditions, a careful consideration of the reason for steroid intake must be made, and any plans to reduce the dosage or withdraw the steroid must be made in consultation with the patient's physician. There may be patients with systemic disorders who need the drug for prolonged periods. There is no proved medication for ICSC at present. Resolution of the serous detachment has been reported after discontinuation of steroids and institution of anti-tubercular drugs, and beta blockers have been found to be useful in a small number of patients. Psychosomatic assessment of patients with ICSC did not reveal any conspicuous abnormality that warranted psychotherapy.

Photocoagulation using different wavelengths, and different techniques can bring about a quicker resolution of fluid, amelioration of symptoms, and improvement in vision. Such a response to laser treatment is seen in eyes with bullous serous detachments as well. However, some residual defects in macular function, and chronic changes in the RPE may remain, and recurrences are possible. The most important indication for laser treatment is the patients’ intolerance to symptoms, inability to perform daily tasks because of symptoms, or the need for normal vision in each eye that is mandatory in certain professions. Other considerations include the duration of the serous...
detachment, location of leakage on the fluorescein angiogram in relation to the fovea, and recurrences. Laser photocoagulation consists of identifying the origin of dye leakage at the RPE from a recent fluorescein angiogram, and treating these sites directly with burns that are just visible. Associated RPE detachments may be treated entirely in the same manner. Such direct treatment was found to be superior to indirect treatment, and is the most common method adopted. However, disappearance of a foveal leak after treatment of other leaks, and resolution of serous detachment after a grid pattern of treatment in eyes with diffuse RPE changes have been reported. Apart from the argon green laser, effective treatment of ICSC has been reported with other wavelengths, and with the subthreshold technique as well. The krypton red has been successfully used to treat leaks much closer to the fovea. An accidental foveal burn is a potential complication with laser treatment of ICSC, and laser burns may enlarge over a period. Choroidal neovascularisation is rare, but may occur at the site of laser treatment, and care must be taken not to overlook a small choroidal neovascularisation prior to treatment.

More recent approaches in the treatment of CSCR include the use of photodynamic therapy, sometimes guided by indocyanine green angiography, and transpupillary thermotherapy. These procedures, performed on patients who had chronic CSCR, or fluorescein leaks at or close to the fovea, resulted in resolution of serous detachment, decrease or cessation of dye (fluorescein and indocyanine green) leakage, and stabilisation of vision in most patients, though one developed choroidal neovascularisation. Vitrectomy using perfluorocarbon liquid and endolaser was successful when a bullous serous detachment did not allow adequate laser treatment.

References
chronic central serous chorioretinopathy. Retina 2003; 23: 752-63.


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### In lighter vein

RRV

#### NO TITLE

If you look at it closely, conducting an Ophthalmic Conference is very much like undertaking a cataract surgery with only minor differences. You don’t think so? Look at it this way.

<table>
<thead>
<tr>
<th>Cataract Surgery</th>
<th>Ophthalmic Conference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient selection</strong></td>
<td><strong>Organising committee selection</strong></td>
</tr>
<tr>
<td>Beware of hypertensives, diabetics, ones with</td>
<td>Beware of ones with short tempers, “ladies’ men”, ones</td>
</tr>
<tr>
<td>systemic problems and ones with prominent eyes</td>
<td>involved with other associations and ones who look too</td>
</tr>
<tr>
<td></td>
<td>much into protocols and precedence.</td>
</tr>
<tr>
<td><strong>Anaesthesia</strong></td>
<td><strong>Anaesthesia</strong> (read ‘Fellowship’)</td>
</tr>
<tr>
<td><strong>Local preferred</strong></td>
<td>‘Local’ is OK; but ‘foreign’ is preferred.</td>
</tr>
<tr>
<td><strong>Pupils</strong></td>
<td><strong>Pupils</strong> (and teachers &amp; all else)</td>
</tr>
<tr>
<td>Should be well dilated</td>
<td>Should be well dilated (with food and drinks)</td>
</tr>
<tr>
<td>(Operation) Theatre ambience</td>
<td>(Lecture) Theatre ambience</td>
</tr>
<tr>
<td>Patient should be comfortable</td>
<td>Delegates should be comfortable</td>
</tr>
<tr>
<td><strong>Visco-elastics</strong></td>
<td><strong>Visco-elastics</strong> (read flattery)</td>
</tr>
<tr>
<td>Use in plenty</td>
<td>Use in plenty, on faculty, staff, delegates, everyone in</td>
</tr>
<tr>
<td></td>
<td>general</td>
</tr>
<tr>
<td><strong>Implant</strong></td>
<td><strong>Implant</strong> (read complement kit)</td>
</tr>
<tr>
<td>1. Foldable preferred</td>
<td>1. Foldable is alright; but a rigid ‘VIP’ brief case will</td>
</tr>
<tr>
<td></td>
<td>be preferred</td>
</tr>
<tr>
<td>2. ‘In the bag’ preferred</td>
<td>2. As many things ‘in the bag’ as possible preferred</td>
</tr>
<tr>
<td><strong>Congestion (ciliary)</strong></td>
<td><strong>Congestion (of creditors)</strong></td>
</tr>
<tr>
<td>Is not preferred on the next day</td>
<td>Is not preferred on the next day</td>
</tr>
</tbody>
</table>

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An Interesting Case of Scleritis

Dr. Mahesh P. Shanmugham MS, Dr. Rajesh P MS, Dr. Sunil Neelakantan MS, Dr. Meena Chakrabarti MS

Case History
A 30 year old female patient presented to our outpatient department on 23-5-09 having been referred with a diagnosis of ? choroidal detachment /? subretinal hemorrhage. This diagnosis was made from a CT Scan taken by an ENT consultant to evaluate headache and ocular pain.

The patient complained of chronic low grade pain and redness of atleast a months duration. She also complained of moderate visual loss. Her systemic history was uncontributory and she had been on oral nonsteroidal anti-inflammatory agents for the preceeding three weeks.

Your valuable opinion on investigations and management is solicited

Dr. Rajesh P.

The clinical picture of pain, deep scleral congestion, solid sub retinal elevation and exudative detachment

Ocular examination revealed the following findings :

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Uncorrected vision</td>
<td>6/60</td>
<td>6/6</td>
</tr>
<tr>
<td>2. Near Vision</td>
<td>N36</td>
<td>N6</td>
</tr>
<tr>
<td>4. Anterior segment</td>
<td>Deep scleral congestion and tenderness</td>
<td>Localised Normal</td>
</tr>
<tr>
<td>5. Fundus (Fig 1 a&amp;b)</td>
<td>Solid subretinal elevation temporal to macula. Macular edema, Inferior exudative RD</td>
<td>Clear Media, Normal</td>
</tr>
<tr>
<td>6. B Scan</td>
<td>Solid Hyper reflective elevation. No definite T Sign</td>
<td>Normal</td>
</tr>
<tr>
<td>7. FFA (Fig 2 a&amp;b)</td>
<td>Hypofluorescence to pinpoint leaks with pooling</td>
<td>Normal</td>
</tr>
<tr>
<td>8. OCT</td>
<td>CRT 525 microns.presence of subretinal fluid</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Investigations:

Hb, TC, DC, Peripheral Smear, Toxo NEGATIVE
S. Calcium 9.5 mg/dl MANTOUX negative
ESR 62 mm/hr TB Ig M POSITIVE
Plain x ray Chest : prominent hilar markings Consultation with chest physician : non-contributory
with B scan findings of sclerochoroidal thickening and FFA picture of pinpoint areas of leakage with pooling suggest a diagnosis of posterior scleritis. Although T sign on B scan is classical of posterior scleritis, at times localized thickening of sclerochoroidal complex with overlying subtenon fluid can also occur in posterior scleritis. History as well as clinical features of rheumatoid arthritis, SLE, relapsing polychondritis, Wegeners, tuberculosis and sarcoidosis will also be sought for. I also would have suggested the same set of investigations for the patient, probably with the exception of ELISA for TB. The reason why ELISA would not have been done is because of its poor reliability in diagnosing active tuberculosis particularly extra pulmonary TB. A positive IgG which is the most common result even in active tuberculosis does not carry much significance in Indian population. IgM which suggests recent infection is not often positive in extra pulmonary TB. Other investigations I would have liked to do in this patients are rheumatoid factor (rheumatoid arthritis), anti ds-DNA (SLE), cANCA (wegener’s), pANCA (PAN) ACE (sarcoidosis) VDRL and FTABs (Syphilis).

The patient under consideration has positive IgM, but has a negative mantoux. This is a difficult situation to make a decision regarding starting ATT. A TB patient with -ve mantoux could be either immunosuppressed or have miliary form of the disease. In an immunosuppressed state the chances of a positive ELISA is also less. The test like Quantiferon –TB gold test which helps to pick up latent and active TB is not available to us and would have been of greater significance in making a decision regarding starting ATT.

Treatment with oral prednisolone is started at a dose of 1mg/kg body weight and is gradually tapered over 3-6 months. Azathioprine or methotrexate is added if the response is poor with steroids alone or as a steroid sparing agent. Any underlying connective tissue disorder is managed in consultation with a physician.

Dr. Mahesh P. Shanmugham

This is a case report of a 30 year old lady with one month history of ocular pain, redness and loss of vision of indeterminate duration. There is no known systemic disease. Information such as loss of weight, appetite, cough, genitourinary, gastrointestinal disease, sinus disease, joint pain and such is not available. It would be necessary to know if there is any evidence of anterior segment or vitreous inflammation.

Fundus photography of the right eye shows a single, grey white subretinal lesion temporal to the macula with macular edema. The borders are irregular and ill-defined in some areas. The color and surface of the lesion are inhomogeneous. Fundus fluorescein angiogram shows initial hypofluorescence with areas of pin-point leaks and late staining with few suspicious areas of leakage and indication of disc staining. Posterior pole photograph of the left eye is normal. Significant anterior segment finding is presence of deep sclera congestion and tenderness; however the location of the scleral congestion is not mentioned. Ultrasound intralesional characteristics of the lesion are not mentioned – high reflective scleral thickening, regular internal structure, tenon’s space edema presenting as “T” sign.

The differential diagnosis would be
1. Inflammatory lesion
2. Neoplastic lesion
3. Neovascular lesion

The young age of the patient, short history, pain, presence of anterior scleral inflammation, tenderness, posterior, unilateral, single, subretinal choroidal lesion, macular edema, disc staining on FA, elevated ESR point.
to the possibility of an inflammatory lesion. It is necessary to look for vitreous reaction, particularly overlying the mass using slit-lamp biomicroscopy. Absence of intense overlying reaction is obviously absent indicating that this unlikely to be a choroidal abscess in an immunocompetent patient. Elevated lesion with characteristics mentioned above with anterior scleral inflammation points to a posterior scleritis.

Choroidal metastasis can also be a possibility with cream colored mass associated with secondary retinal detachment in the absence of vitreous inflammation. Points against metastatic tumor are the age of the patient, short history, presence of anterior scleral inflammation. Intraocular lymphoma can also present similarly, rarely in a young patient.

Altered subretinal hemorrhage can appear grey white but should be hypofluorescent on FA with identifiable site of leakage such as a choroidal neovascular membrane or polypoidal choroidal vasculopathy.

**Management**

Mantoux is negative, prominent hilar markings on X-ray, elevated ESR and TB IgM positive. It is essential to rule out pulmonary and extrapulmonary tuberculosis in this patient with a thorough systemic examination. Investigations to rule out connective tissue disease may identify the causative factor for the scleritis.

**Treatment**

Once an infective etiology is ruled out a course of systemic steroids at 1 mg/kg body weight should be instituted and tapered based on response. The patient has been on non-steroidal anti-inflammatory agents without much of a response and hence the need for systemic steroids. If the lesions (the anterior and posterior) do not respond adequately, an incision biopsy of the anterior scleral lesion will be necessary.

Dr Sunil N

The primary complaint is pain, followed by defective vision. There is sclera congestion and tenderness

Fundus shows a subretinal, yellowish irregular lesion, mainly appearing intrachoroidal.

There is no evidence of retinitis. FFA shows pinpoint leaks with pooling in the subretinal space, the leakages are from Choriodal level. ESR is elevated, significantly.

I feel it is a case of POSTERIOR SCLERITIS with anterior scleral involvement. Posterior Scleritis has various clinical presentations, like- Subretinal mass lesions, Disc oedema, annular CD, etc. T-Sign if present indicates that the site of involvement is near the disc, as the subtenons oedema is continuous with the optic nerve sheath.

**Absence of T-sign does not rule out posterior Scleritis**

As it has feature of pan Scleritis, Connective tissue disorders have to be ruled out. A high ESR is also suggests this possibility.

TB IgM positivity should be further investigated to rule out TB Scleritis, or TB Granuloma.

However even in cases of TB, we have to rule out Scleritis due to Connective tissue disorders, as TB involvement is mostly a diagnosis of exclusion.

A therapeutic trial course of systemic steroids, if gives relief, also will help in diagnosis, as it will definitely point towards Scleritis.

Dr. Meena Chakrabarti

The patient was treated with tapering dose of systemic steroids starting with a dose of 1mg/kg body weight. She responded well to therapy with complete resolution of the lesions and return of normal visual acuity TB IgM positivity was further investigated and a second opinion sought. Based on the pulmonologist’s suggestion a course of 3 drug ATT was started and is to be continued for 9 months.

Compiled by Dr. Meena Chakrabarti, Editor, KJO
The History of Vitrectomy: Innovations and Evolution

Dr. Meena Chakrabarti MS DO DNB

Each of the innovators featured here has a story to tell that often combines an exceptional understanding of disease, foresight, perseverance, and an ability to obtain funding for an unrecognized technology. Going through the works of these innovators will definitely serve as a source of inspiration to us as they are standing examples of how hard work and perseverance pays.

A narrative of the evolution of vitrectomy

The history of vitrectomy is a story of the interrelated development of a vast array of techniques and evolution of technique-driven technology. David Kasner developed open sky cellulose sponge vitrectomy prior to machine-based vitrectomy; initially to address the problem of vitreous loss at cataract surgery. He later used the technique to remove opaque vitreous through a penetrating keratoplasty incision. Many surgeons had injected air, various gases, silicone oil, and saline in the vitreous, aspirated liquid vitreous, and used scissors in the vitreous cavity prior to development of a mechanized vitreous cutter.

Cutter Technology

Robert Machemer developed closed, pars plana vitrectomy to eliminate the need for keratoplasty and operate with a closed system with controllable intraocular pressure.

Machemer did the first clinical cases of pars plana vitrectomy and was the crucial element resulting in the development of a systematic approach to vitreoretinal surgery and a distinct vitreoretinal surgery subspecialty. A vitreous cutter with infusion and aspiration was developed and used clinically in Japan prior to development of vitrectomy in the United States but this was published in the Japanese literature and apparently not known in the United States. Anton Banko patented a vitreous cutter including aspiration and infusion prior to the development of the VISC by Jean Marie Parel and Machemer but never commercialized the device. Banko, who developed the fluidics for the initial phacoemulsification machine for Charles Kelman, had knowledge of mechanized lens removal systems invented by Kelman prior to the application of ultrasound, and saw vitreous often during the development of clinical phacoemulsification. Jean Marie Parel developed the VISC, fiberoptic endoillumination, and the solenoid operated MPC vertical scissors. Working with Machemer, Douvas developed the RotoExtractor which, like the VISC, was a full-function, large incision, rotary cutter but incorporated an oscillatory mode to address the vitreous winding problem of the VISC. O’Malley and Heinz developed three-port vitrectomy with a 20-gauge (0.89 mm) system as well as a lightweight, reusable, bellows-driven, pneumatic, axial cutter driven by the Ocutome 800 console (Berkley Bioengineering, 1972). Gholam Peyman developed the electric solenoid driven axial (guillotine) cutter at about the same time R. Kloti in Europe developed a three port system with an electric cutter.
Tamponades

**Steve Charles** invented internal (through the retinal break) drainage of sub retinal fluid to address the many complications of transscleral drainage: incarceration, bleeding, and incomplete drainage. He developed simultaneous internal fluid-air exchange, now just called fluid-air exchange, to eliminate the problems of sequential exchange: hypotony, incomplete exchange, and having a needle in a deflated eye. He also developed air-gas exchange and air-silicone exchange to produce a complete exchange of air for so-called tamponade substances without fluctuation in intraocular pressure. **Brooks McEwen** developed the air pump which replaced using a syringe for fluid-air exchange. The air pump produced a controllable intraocular pressure and was never depleted. Carl Wang and Steve Charles developed the first power gas injector and first power silicone injector. Steve Charles also invented vacuum cleaning using a straight cannula with a fingertip side port to control fluid egress (flute needle) but soon switched to Conor O’Malley’s technique of extrusion, using the console aspiration system and foot pedal to control fluid egress. **David McLeod and Peter Leaver** combined John Scott’s technique of injecting silicone oil with fluid-air exchange, internal drainage of subretinal fluid, and endophotocoagulation technique; creating the currently utilized paradigm. **Edward W. D. Norton and Harvey Lincoff** independently developed the use of gas injection in conjunction with scleral buckling leveraging much earlier, independent work by **Ohm and Rosengren**.

**Gary Abrams** developed the concept of using an iso-expansive gas concentration leveraging Steve Charles’ techniques of fluid-air exchange, internal drainage of subretinal fluid followed by air-gas exchange. The use of iso-expansive gas-air mixtures produced near full fill bubbles without producing elevated intraocular pressure. **Stanley Chang** developed the use of perfluorocarbon (heavy) liquids to unfold giant breaks and stabilize the retina during PVR membrane dissection. **Machemer and Steve Charles** independently and simultaneously developed both retinectomy (relaxing retinotomy) as well as subretinal surgery.

Endophotocoagulation

**Steve Charles** developed endophotocoagulation to allow retinopexy, hemostasis, and pan retinal photocoagulation without corneal or iris damage and adapted the technique to three-port vitrectomy. His first system used the Zeiss xenon source while his first commercial system used a xenon source (Patrick O’Malley’s Log III photocoagulator); subsequently **Maurice Landers, Jay Fleischman, and S. Charles** simultaneously and independently developed endophotocoagulation systems using an argon laser source, later **Yasuo Tano** developed the near-IR diode laser source and finally Alcon and Iridex developed 532 nm, diode pumped sources.

Membrane Peeling

**Machemer** developed membrane peeling using a bent needle. **Conor O’Malley** developed the pic for membrane peeling which was safer because it did not have sharp point. Steve Charles developed end-grasping forceps membrane peeling to enable safe, one-step epiretinal membrane peeling without the need for needles, pics, dyes, or viscosdissection. Steve Charles developed diamond-coated membrane peeling forceps and conformal forceps which afforded a better purchase than earlier forceps designs. He developed scissors segmentation to shear adherent, epiretinal membranes that could be peeled into separate epicenters to reduce tangential traction. And also developed scissors delamination of epiretinal membranes to completely remove adherent epiretinal membranes without dangerous peeling. **Yasuo Tano** developed the diamond-dusted membrane scraper and **Brooks McEwen** developed the micromanipulator which combined a pic with a light source and diathermy. **Stanley Chang** developed the end-aspirating laser probe which allowed simultaneous drainage of subretinal fluid and laser retinopexy.

Twenty-gauge Vitrectomy Technology

**Steve Charles** developed linear (proportional) control for the Ocutome 8000 working with engineers at Coopervision after they had acquired Berkley Bioengineering, the developers of the Ocutome 800. Linear suction was developed to enable control of
vacuum by the surgeon rather than the circulator. **Carl Wang** subsequently left CooperVision (Fairport, NY) to start the original MidLabs; working with Wang and his engineers to develop the disposable, 20gauge, pneumatic, axial cutter and higher cutting rates and faster aspiration fluidics.

In the mid-80s Steve Charles started InnoVision and invented the Ocular Connection Machine, the forerunner of the Alcon Accurus and subsequently the Alcon Constellation. He used the OCM in the operating room as did several other surgeons but it was never commercialized; the technology was acquired by Alcon Laboratories, Inc., in 1991 and he became a consultant for Alcon Laboratories, Inc. The OCM had a xenon light source, servo-controlled intraocular pressure (IOP), global functions, a smart key graphical user interface, tool ID, a tubing management system incorporated into a sterile articulated arm, the dual actuation InnoVit (no spring), 1.500 cpm, push prime, and proportional diathermy all of which are implemented on the new Alcon Constellation. The Constellation uses RFID instead of the more primitive tool ID system on the OCM. The OCM began the revolution of system integration, a steadily increasing number of functions in one console under unified control using a graphical user interface.

**Microincision Vitrectomy Systems**

The Accurus took 5 years to develop and included global functions, a smart key driven graphical user interface, the dual actuation InnoVit, a halogen light source, power silicone injector, fragmenter driver electronics, power scissors and ultimately supported 23- and 25-gauge vitrectomy as well as 2,500 cpm vitrectomy. In addition to servo-controlled IOP, global functions, a smart key graphical user interface, tool ID, a tubing management system incorporated into a sterile articulated arm, dual actuation, and proportional diathermy described above the Constellation has variable duty cycle control, auto-gas fill, auto-stopcock for fluid air exchange, dual xenon illumination sources, power silicone injector, and supports over 5,000 cpm.

**Dyson Hickingbotham** developed the first trocar-cannula system for 1.0 mm tools but it never became popular until **Eugene DeJuan** working with Bausch & Lomb brought us sutureless, transconjunctival, 25-gauge vitrectomy. Alcon developed a better trocar-cannula system and a disposable 25-gauge cutter. Dutch Ophthalmic Research Centre (DORC) first introduced 23-gauge vitrectomy working with **Klaus Eckardt** and Alcon subsequently developed a single step 23-gauge trocar-cannula system. The introduction of 23 gauge after 25 gauge implied to many surgeons that 23 gauge combined the best attributes of both systems; in my view 25 gauge is better for all cases. The Constellation 25-gauge UltraVit has much less fluidic resistance than previous 25-gauge systems and provides the same performance as current 23-gauge systems. All the Constellation tools have greater stiffness than the previous generations of tools which also makes the case for 23 gauge less tenable.

The original approach to wide-angle viewing was contact-based using the Rodenstock panfundoscope without an inverter. Subsequently, **Manfred Spitznas** developed the BIOM noncontact system and Stanley Chang developed the AVI contact-based wide-angle system, which uses a Volk lens and an inverter. Contact-based wide-angle visualization provides 10º greater field of view than noncontact systems (BIOM and EIBOS), eliminates corneal asphericity, and decreases the need for ocular rotation (tool flex) to view the periphery.

The future will bring a greater understanding of fluidics, the physics of vitreous removal and tissue cutting, providing greater safety and utility for the cutter when working near the retinal surface. Can non-mechanical cutting or enzymatic vitrectomy replace mechanical devices? .................. the question remains unanswered.
Intraocular Tuberculosis – An Update

Vishali Gupta MD, Amod Gupta MD, Narasing A Rao MD

The World Health Organization (WHO) has declared ocular tuberculosis as a global emergency as it remains the most common single cause for morbidity and mortality worldwide, causing nearly 3 million deaths each year. Intraocular tuberculosis represents an extra pulmonary form of tuberculosis. The proportion of cases with extra pulmonary form of tuberculosis has increased in the recent years in immunocompromised individuals.

The lack of an uniform diagnostic criteria for intraocular tuberculosis in both immuno compromised and immunocompetent individual has contributed to the confusion regarding diagnosis and management. However recent studies addressing the clinical significance of purified protein derivative test results, computerized tomography of the chest and molecular diagnostic procedures have provided a new insight into the diagnosis and management of ocular TB.

This review article on ocular tuberculosis was published a decade after the previous major review. This article focuses on diagnostic modalities and criteria, various clinical features, and treatment recommendations. The spectrum of clinical manifestation of ocular tuberculosis, manifestations in AIDS patients and management of drug resistant tuberculosis is addressed in this review. An analysis of the clinical presentations in 158 patients of ocular tuberculosis between 1994 and 2004 showed that 66 (42 %) had posterior uveitis, 57 (36 %) anterior uveitis, 18 (11 %) panuveitis, 17 (11%) intermediate uveitis. The authors have published data on ocular imaging studies carried out on these patients. Fluorescein angiography was the most commonly used imaging technique, however other modalities which were also helpful in the diagnosis includes ICG angiography, OCT, USG and ultrasound biomicroscopy.

The increasing use of PCR for detection of M. tuberculosis from the intraocular fluids has helped in the diagnosis of tuberculous vasculitis, serpiginous like choroiditis, neuroretinitis and posterior scleritis.

Drug resistance for ocular tuberculosis described in this article are similar to those for pulmonary and extra pulmonary tuberculosis and a complete 4 drug regimen should be given because of concerns of developing drug resistance.
A Randomised Trial Comparing Intravitreal Triamcinolone Acetonide and Focal/Grid Laser Photocoagulation for Diabetic Macular Edema

Diabetic Retinopathy Clinical Research Network
Ophthalmology 2008, 115: 1447-1459

The paper published in the Ophthalmology journal presents the results of a multicentre randomized clinical trial to evaluate the efficacy and safety of 1mg and 4mg doses of preservative free intravitreal triamcinolone acetonide in comparison with focal/grid photocoagulation for the treatment of diabetic macular edema.

The participants were 844 study eyes of 693 subjects with DME involving the fovea and with a visual acuity of 20/40 to 20/320.

Eyes were randomized to focal/grid laser photocoagulation (n=330), 1 mg of intravitreal triamcinolone acetonide (n=256) or 4 mg intravitreal triamcinolone acetonide (n=254). Retreatment was given for persistent or new edema at 4 months intervals. The primary outcome was evaluated at 2 years.

Visual acuity measured with the electronic Early Treatment Diabetic Retinopathy Study method (primary), optical coherence tomography-measured retinal thickness (secondary), and safety.

At 4 months, mean visual acuity was better in the 4 mg triamcinolone group than in either the laser group (P<0.001) or the 1mg triamcinolone group (P=0.001). By 1 year, there were no significant differences among groups in mean visual acuity. At the 16-month visit and extending through the primary outcome visit at 2 years, mean visual acuity was better in the laser group than in the other 2 groups (at 2 years, P=0.02 comparing the laser and 1mg groups, P=0.002 comparing the laser and 4-mg groups, and p+0.49 comparing the 1mg and 4-mg groups). Treatment group differences in the visual acuity outcome could not be attributed solely to cataract formation. Optical coherence tomography results generally paralleled the visual acuity results. Intraocular pressure increased from baseline by 10 mm Hg or more at any visit in 4 %, 16 %, and 33 % of eyes in the 3 treatment groups, respectively, and cataract surgery was performed in 13 %, 23 % and 51% of eyes in the 3 treatment groups, respectively.

Over a 2-year period, focal/grid photocoagulation is more effective and has fewer side effects than 1-mg or 4-mg doses of preservative-free intravitreal triamcinolone for most patients with DME who have characteristics similar to the cohort in this clinical trial. The results of this study also support that focal/grid photocoagulation currently should be the benchmark against which other treatments are compared in clinical trials of DME.
Diseases of the Macula: A Practical Approach

JACK J. KANSKI & STANISLAW A. MILEWSKI
Mosby International Limited

Despite great advances in medicine, macular diseases still remain a very common cause for severe visual impairment particularly in the elderly. A practical and didactic approach to the management of macular disease is essential as a quick reference to the practicing specialist as well as the novice trainee.

In this book the term ‘macula’ is used quite liberally. The authors have included a variety of commonly encountered macular diseases as well as those that have an indirect bearing on the macular function such as vascular and inflammatory diseases.

The first introductory chapter covers briefly but comprehensively the applied anatomy of the macula, and touches on the relevant aspects of clinical evaluation. Investigatory modalities such as fundus fluorescein angiography, indocyanine green angiography and electrophysiological tests are described. However newer modalities such as optical coherence tomography, macular microperimetry and fundus autofluorescence imaging have not been covered.

The body of this book is divided into four sections: Acquired macular diseases, vascular diseases, inflammatory fundus disorders and heredomacular fundus dystrophies. The beginning of each chapter gives a list of the disorders covered in order of clinical importance. Relevant aspects of history, heredity, symptomatology and clinical features are covered in the usual crisp and comprehensive format with beautiful fundus photographs and illustrative line diagrams. The various management options are discussed briefly but succinctly and the conclusion is short and relevant. This book can be used as a ready reckoner for post graduate students as well as practicing ophthalmologists.

Clinical Pathways in Vitreoretinal Diseases

Scott M. Steidl & Mary Elizabeth Hartnett
Thieme Publications

Development of a clinical pathway is absolutely essential for the assessment and treatment of patients with a similar diagnosis. In this text book the authors have successfully assembled a group of accomplished vitreoretinal specialists to write clinical algorithms for the assessment and treatment of vitreoretinal diseases.

The format of this book has certain unique characteristics. The book is divided into 5 sections. The first section on history, physical examination and diagnosis poses key questions for a focused history, gives clues on sorting out a possible diagnosis from the history, and how to expand on the primary complaint
to get to the diagnosis. Clinical examination of the ocular fundus and the section on how to use the instruments for examination of the posterior segment are relevant and useful to both general ophthalmologists and vitreoretinal surgeons alike.

The remaining section deals with commonly encountered clinical findings such as areas of whitening in the fundus, pigmented lesions, hemorrhages etc. The text makes use of evidence based medicine to develop management strategies. Decision trees and descriptions in the text highlight these strategies. The decision trees present a focused ‘yes-or-no’ approach to a problem and will definitely have a role in aiding current and future eye care specialists in managing the daunting challenges posed by vitreoretinal diseases. This publication present a broad glimpse of what is new and current in the field of vitreoretinal disease management and will help as a tool to navigate this rapidly changing field providing us with a glimpse of the road ahead.

Compiled by Dr. Meena Chakrabarti
CME Programmes

STATE CONFERENCES

DRISHTI 2009
36th Annual Conference of Kerala Society of Ophthalmic Surgeons
27-29th November 2009
Dinesh Auditorium, Thana, Kannur
Dr. Sreeni Edakhlon
9895618170

NATIONAL CONFERENCES

VISTA 2009
XIX Annual Conference of the Glaucoma Society of India
November 6 – 8, 2009
Nimhans Convention Centre
Bangalore
Dr. Gowri J Murthy: 080-26722215

KSOC 2009
28th Karnataka State Ophthalmic Conference
November 27-29, 2009
J.J.M Medical College, Davangere
Dr. Rajesh.P: 9845568791

AIX 2010
68th Annual conference of All India Ophthalmological Society &
15th Afro Asian Congress of Ophthalmology
21-24th January 2010
Science city Kolkata
Dr. Ashish K. Bhattacharya
www.aioc2010.com

INTERNATIONAL CONFERENCES

ASCRS.ASOA
Boston 2010
9-14th April 2010
www.ascrs.org / www.asoa.org
References for the Editorial Sept. 2009 were inadvertently omitted. Enclosed here are the list of the references for the article titled “In the grip of the python”.

1. Kant I. Foundations of the Metaphysics of Morals. Beck article titled “In the grip of the python”.
30. Cole KC, Hotz RL. Science, hype and profit: a perilous mix; with "newsy" or moneymaking research often eclipsing worthy studies, some say highly touted findings that don’t hold up are eroding public trust. Los Angeles Times. January 24, 1999:A1.
35. Hampton T. Experts debate need to improve quality and oversight of continuing education. JAMA. 2008;299(9):1003-1004
WHAT IS CVS?
A Series of Visual Symptoms Which Are A
Byproduct of Excessive Viewing of VDT
Screens Without Proper Attention To Practical Visual
Hygiene
75% - 90% Of VDT WORKERS
Vs
22% Musculoskeletal disorders
(NIOSH SURVEY)

<table>
<thead>
<tr>
<th>Symptoms</th>
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<tbody>
<tr>
<td>• EYE STRAIN (ASTHENOPIA)</td>
<td>• DRY EYES</td>
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<tr>
<td>• HEAD ACHE</td>
<td>• DOUBLE VISION</td>
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<tr>
<td>• FOCUSING DIFFICULT</td>
<td>• BLURRED VISION</td>
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<tr>
<td>• TIRED EYES</td>
<td>• LIGHT SENSITIVITY</td>
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<tr>
<td>• ACHING EYES</td>
<td>• NECK &amp; SHOULDER PAIN</td>
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- Headache during / after Work on Computer
- Overall bodily fatigue & Tiredness
- Burning Eyes
- Distant vision Blurry on Looking up From Screen
- Dry, Tired & Sore Eyes
- Squinting Helps while looking at the computer
- Neck, Shoulder & Backpain
- Double vision
- Letters on screen run together
- Driving/Night Vision Worse After Computer Use
- Halos Around Objects On Screen
- Need To Interrupt work Frequently

WHY DOES EYESTRAIN OCCUR?
- THE HUMAN FOCUSING SYSTEM: Well defined images with good contrast
- VDT: Characters depicted in PIXELS
- PIXELS: Brightest at centre with increasing intensity to periphery

WHY DOES EYESTRAIN OCCUR?
- LIGHT AMPLITUDE GRAPH
  (LIGHTMETER)
  PRINT: SQUARE WAVE ABC
  PIXEL: GAUSSIAN WAVE

RESTING POINT OF ACCOMODATION
- Sustaining Focus on the Pixels Of
  A Computer Is Difficult
- Eyes Relax To A Point Behind The Screen Called RAP

HEADACHE
- Typical Pattern: Frontal / Hemicranial
- Browache
- Onset in middle / end of day
- Different patterns on Weekends
- Precipitating Factors!

Precipitating Factors
- Tension & stress
- Numerous Eye Conditions
- Improper Work Place Conditions (Glare, Poor Lighting, Improper work Station Setup)

BLURRED VISION
- REFRACTIVE ERRORS
- IMPROPER PRESCRIPTION LENSES
- AGE RELATED FOCUSING PROBLEMS
- DIRTY SCREEN
- POOR VIEWING ANGLE
- POOR QUALITY MONITORS
- REFLECTED GLARE

DES IN CVS
- Reduced Blink Reflex Rate
- Larger Size of Palpebral Aperture (To view VDT: Upgaze)
- Greater Evaporative Dryness
- Greater No: Of Incomplete Blinks

Blink more often
- Computer users should make a conscious effort to blink more often:
- They should try out the suggested formula 20: 20: 20
- Every 20 mins: for 20 seconds: blink 20 times
- OR
- BLINK EVERYTIME U HIT THE “ENTER” KEY
- LUBRICANTS & TEAR SUBSTITUTE
- Headache during / after Work on Computer
- Overall bodily fatigue & Tiredness
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COMPUTER RELATED ACHEs & PAIN
TO EASE STRAIN ON VISUAL SYSTEM A COMPENSATORY BODY POSTURE IS ADOPTED: THE EYE LEADS THE BODY

INCREASED LIGHT SENSITIVITY
• DISPARITIES IN BRIGHTNESS IN THE FIELD OF VIEW
• OVERHEAD LIGHT FIXTURES
• BRIGHT OPEN WINDOWS
• DARK BACKGROUND DISPLAY SCREEN
• WHITE PAPER ON THE DESK
• LIGHT COLOURED DESK SURFACES
• DESKLAMPS DIRECTED TOWARDS SCREEN

DOUBLE VISION
• Excessive Convergence to view near object
• Weakness Of Convergence
• Inability To Focus
• Suppression Of Image Of One Eye

COMPUTER GLASSES: WHO NEEDS CORRECTION?
• Pseudomyopia / Increased Nearsightedness
• Onset Of Age Related Focusing Problem (Presbyopia)
• Lag Of Accomodation
• Inappropriate Prescription glasses

WHY DO THEY NEED CORRECTION?

REGULAR GLASSES
• DISTANCE VISION GLASSES
• READING GLASSES
• BIFOCALS
• TRIFOCALS & PROGRESSIVES
THE WORK ON THE COMPUTER IS IN YOUR INTERMEDIATE ZONE

COMPUTER LENS DESIGN
• OCCUPATIONAL PROGRESSIVE LENSES: (ZOLA ACCESS’ Zeiss R” Web.com)
NO LINE MULTIFOCAL
LARGER INTERMEDIATE ZONE
DISTANCE SEGMENT: VIEWING ACROSS LENGTH OF A ROOM
0 LINED TRIFOCAL WITH LARGE INTERMEDIATE SEGMENT
0 BIFOCAL – I & N / I & F
0 SINGLE VISION INTERMEDIATE
0 CLIPONS

ADDED OPTIONS FOR LENSES
• TINTS To Reduce Perceived Brightness of screen & Filter out Unwanted Blue Light: Beige; Gray; Pink
• UV Coating To Eliminate Blue Light
• AntiReflective Scratch Proof Coating
• Prisms

9 STEPS TO REDUCE CVS
• GET AN ANNUAL EYE EXAMINATION
• USE PROPER LIGHTING
• MINIMIZE GLARE
• ADJUST SCREEN BRIGHTNESS
• BLINK MORE OFTEN
• EXERCISE & STRETCH YOUR EYES
• TAKE FREQUENT BREAKS
• MODIFY WORK STATIONS
• EXERCISE WHILE SITTING

LIGHTING SUGGESTIONS
BRIGHT LIGHTS IN YOUR PERIPHERAL VISION CAN CAUSE GLARE AS LIGHT DIRECTLY ENTERS THE EYE

AVOID FULL BRIGHTNESS OF OUT DOOR LIGHT: USE BLINDS

WEAR A VISOR TO WORK: IT BLOCKS OVERHEAD LIGHTS

FIT ANTIREFLECTION SCREEN

✓ VIEWING DISTANCE OF 25 – 28 INCH
✓ CENTRE OF SCREEN 4-9 INCHES BELOW EYE LEVEL
✓ DON’T ALLOW CHAIR TO BE LOWER THAN KNEECAP
✓ KEEP YOUR FEET ON THE GROUND

EXERCISE & STRETCH (Your Eyes !)
✓ Look Away From Screen Every 30min & Focus On A Distant Object For 5 -10 Sec
✓ Rock Your Focus Back & Forth Between Near & Far
✓ TAKE FREQUENT BREAKS
✓ 10-MINUTES Break for Every 1 Hour Of Work
✓ Sitting, Stretching Or Joint Rotating Exercises
✓ Blink Every Time You Hit “ Enter “ Key

Compiled by
Dr. Meena Chakrabarti, Editor, KJO
GENERAL INSTRUCTIONS TO AUTHORS

The Kerala Journal of Ophthalmology (KJO) is a quarterly; peer reviewed one, devoted to dissemination of the latest in ophthalmology to the general ophthalmologists as well as to specialists in the various subspecialties of this discipline. It invites submission of original work dealing with clinical and laboratory materials.

Authors submitting materials to this journal are requested to adhere STRICTLY to the norms laid down below. The matter must be typed on one side of the paper. A margin of 1” must be left all around and the material must be double-spaced. A page should contain not more than 25 lines. Two copies of the text in paper and one copy in a CD must be submitted to the Editor and the corresponding author is advised to keep another copy with him. The corresponding author must give it in writing in his covering letter that the same matter will not be submitted elsewhere if accepted. He must also enclose the copyright transfer of his work to this journal. The papers sent will be subjected to peer review. The accepted manuscripts become the permanent property of this Journal. The author is informed that, if his work is returned to him for correction / clarification after peer review, he should effect the same and send the manuscript back to the Editor within one month. Each manuscript component mentioned here under must begin with a new page and the pages are to be numbered at the right tip corner starting from the Title page.

1. **TITLE:** The title of the work must be brief and precise. It should not exceed two lines and 40 characters (including comma, period) Author (s) full name (s) must be given along with his (their) degree and the affiliations. Corresponding author's name, correct address (including e-mail and Fax, if available) and phone number must be mentioned at the bottom left hand corner of the first page.

2. **ABSTRACT:** The abstract is to be given in the beginning itself. It should not exceed 200 words. It must contain the aim, methodology, results and conclusion. For case report, summary / conclusion alone is to be given.

   **KEY WORDS** (maximum five) in capitals are to be included at the end of Abstract.

3. **INTRODUCTION:** Describe the aim of the study, along with the hypotheses that were tested. Only necessary references are to be given

4. **METHOD:** Give in detail the materials used and the methods employed. Describe the type of study. Pharmacological names only must be mentioned for the drugs used and, if proprietary name is used, then the manufacturers name must be given in parentheses. Except for standard, well-accepted abbreviations (Including SI Units), all others must be introduced in parentheses when the full term is used for the first time in the article.

5. **RESULTS:** Give only the results obtained by the study under discussion. State the statistics in the correct scientific form (P value, mean etc). Results based on assumptions must not be given. Indicate in the text the place where the tables have to be inserted

6. **DISCUSSION:** The discussion should be to the point and relevant to the subject under discussion. This section can be combined with the previous one if the author desires. Avoid speculations. Use only standard abbreviations or the abbreviations already introduced.

7. **ACKNOWLEDGEMENT:** This is to be made only to those who were directly and scientifically involved with the preparation of the paper. Permitting authorities, technicians, photographers who assisted in the work need not be mentioned.
8. REFERENCES: The references should be given in numerical order in which they first appear in text and not in alphabetical order (Citation Order System). It should be numbered consecutively in the text. The references will not be checked by the Editor or by the Peer reviewer and hence the author is solely responsible for its completeness and the accuracy. Period should not be employed anywhere in the references. Personal communication, unpublished data and poster references, if mentioned, should be in the text itself and the source mentioned in parentheses. References should be in the following form:-

Journal reference: Author(s) full title, Journal name (as abbreviated in Index Medicus), volume number, pages and year. If there are more than three authors, then mention the first three authors and then ‘et al’.

Book reference: Authors(s) (& Editor, if any), title of book (and chapter), publisher, place of publication, page number (s) of the cited portion and year.

9. THE LEGEND: The legend for the illustrations (and tables, if necessary) must be given in a separate sheet of paper and should be typed double-spaced.

Illustrations: The photos and figures should be prepared in glossy prints with good contrast and of the size 6” x 4”. Only salient details should be included. On the back of the illustration, the figure number in text, title of the paper, the first author’s name and the top side (marked with an arrow) must be specified. Except for arrows, no text is to be on the photos. It is the duty of the author(s) to get the patient’s written permission when the subject is identifiable in the photo. Submit two sets of illustrations. Illustrations from other Journals and books are usually not accepted. If used, it rests with the author(s) to get the copy right permission from the original author / publisher and this permission letter must be sent to the Editor at the time of submitting the manuscript. For Histological figures the stain and magnification used should be noted e.g.: - H & E Stain x 70.

10. TABLE: It should be in double space. Each table must have an Arabic numeral (except for single table) and a title both in a single line. Each column in the table must have a short heading. If a table is large, then it must be continued in a second page, which also must have the table number and the title. Avoid vertical lines in the tables. Two sets must be submitted.

The manuscripts are to be sent to The Editor by Courier Mail or by Registered post. The corresponding author will receive communication from the Editor within two weeks of receiving the manuscript.

11. All manuscripts are subjected to editorial board review.

12. Other Categories of Manuscript

a) Original Articles should generally not exceed 3,000 words or 12 double – spaced pages.

b) Review Articles: can be on topics of relevance to clinical practice, research methodology, community ophthalmology or investigative work, of relevance to visual science. These articles should include up to date review of existing literature, and summarize the current status / preferred practice for that particular topic.

Brief reports are short communication of new instruments, new laboratory techniques or surgical techniques as well as interesting case reports with unique findings. These should not exceed 1000 words with a maximum of 2 illustrations. They should follow the format - introduction, case, and discussion. No more than 8 references should be cited. Each brief report must begin with a 75-100 word summary that highlights the significance of the articles.
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