Frequency Doubling Perimetry
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The goal of perimetry is to establish an accurate estimate of visual field sensitivity. Perimetry is performed to detect early visual field defects, determine specific patterns of visual field loss for differential diagnosis and monitor for evidence of progression of field loss. Conventionally Standard Achromatic Perimetry (SAP) has been used to achieve these purposes but there are certain inherent disadvantages. Newer techniques have developed in need for faster methods of screening, diagnosis and follow-up as compared to conventional perimetry and to examine motion attributes of vision that is involved early in glaucoma and not picked up by conventional perimetry. Frequency doubling technology (FDT) perimetry is such a newly developed technique for the screening and early detection of glaucoma.

Frequency Doubling Theory

The human retina has approximately 1.2-to-1.5 million neurons (also called retinal ganglion cell axons or nerve fibers) that bundle together to comprise the optic nerve. The irreversible loss of these retinal nerve fibers occurs in glaucoma and other ocular conditions, associated with the classic gradual increase in optic nerve "cup" size over time. Some studies have suggested that up to 40 percent of these retinal nerve fibers could die before any notable visual field loss is found, so the patient may be unaware of any visual problem. It may take an average of 3-5 years of gradual nerve fiber loss before varied amounts and patterns of glaucomatous visual field loss become apparent.

Retinal nerve fibers can be simply classified into two main types that transmit signals from the retinal receptor cells by way of the optic nerve to the lateral geniculate body and ultimately to the visual cortex. These are the Magno-cellular (or M) cells, and the Parvo-cellular (or P) cells.

The M-cell pathway is responsible for low-contrast; high temporal frequency (or motion) stimulus detection.10 The P-cell pathway is responsible for high-contrast, low temporal frequency (or static) stimulus detection. The larger diameter M cell neurons constitute approximately 10% of the total number of retinal nerve fibers. It has been found that a particular M-cell neuron sub-set comprising a third to a half of the M-cell neurons (called "non-linear" M-cells) are usually the first to die in glaucoma, and this unique pathological characteristic established the basis for frequency doubling testing. When a low spatial frequency sinusoidal grating with alternating wide light and dark bars undergoes high temporal-frequency counterphase flicker, (i.e., the black bands reverse to become white and the white bands reverse to become black in rapid sequence) the grating appears to have twice as many light/dark bars (i.e., its spatial frequency appears doubled). This phenomenon is called the frequency doubling illusion. (Figure: 1, 2) It is the vulnerable "non-linear" M-cell neurons that are thought to transmit signals related to this illusion. Since these M-cell neurons tend to be among the first to die, selective testing by presenting alternate gratings was developed to attempt to identify earlier retinal neuron loss than by traditional automated perimetry.

Using the frequency doubling illusion as the basis for development, a perimeter was developed that has been called the Frequency Doubling Technology (FDT) perimeter (Welch Allyn & Humphrey Instruments, Inc). In FDT, rather than using a small spot of light as in conventional perimetry, a large low spatial frequency sinusoidal grating (<1 cycle/degree) that consists of black and white bars undergoes a rapid counter phase flicker (>15 Hz) so that the black bars become white and the white bars become black. The use of a low spatial frequency target undergoing rapid flicker leads to the frequency doubling illusion in which, at a certain level of contrast, the number of visible lines appears to double. At this point the person viewing the stimulus will see twice as many bars as are actually present in the grating. Maddess10, 11 in his description of the frequency doubling illusion suggested that M cells, due to their nonlinear properties, are the retinal cells responsible for eliciting the illusion.

There are two different theories as to how frequency-doubling perimetry is able to detect changes in the visual field. In one theory, it is assumed that the large-diameter optic nerve fibers (M) are preferentially damaged in the early stages of glaucoma. In the other theory, referred to as the Reduced Redundancy Theory, it is assumed that a visual field test will be more sensitive to early loss if only a subset of the visual system is tested.

In comparison to conventional perimetry, FDT differs in its use of a target that stimulates a much larger retinal area. The standard FDT target is a square ten degrees in diameter, which is much larger than the size III Goldmann target equivalent that shines a spot of light 0.43 degrees in diameter onto the retina. The size V Goldmann target, the largest size available and usually reserved for conditions
in which the visual field is reduced, is only 1.72 degrees in diameter. Thus, one of the major differences between FDT and conventional perimetry concerns the target size. Since FDT tests larger areas, it may detect certain subtle diffuse changes that may not have been elicited with other perimetric tests but may miss shallow localized defects.

**Methodology**

First generation FDP instrumentation is a portable device which contains a video monitor enclosed in a self contained unit. (Figure 3) It incorporates a moveable binocular cowling piece which shields ambient room light. A viewfinder slides from side to side to allow monocular viewing without the need of patching. A video display unit presents 10-degree square target and a central 5-degree radius target. The patient is asked to fixate a small central spot on video monitor and fixation is monitored at all times by means of a video camera focused on the observer’s eye. Stimulus consists of a monochrome sine-wave sinusoidal pattern of vertical gray stripes of spatial frequency 0.25 cycles per degree and temporal frequency of 25 Hz.

As with conventional perimetry, when evaluating FDT printouts the following areas are evaluated:

- Number of points depressed
- Location of involved points
- Pattern of involved points

- Depth of depression
- Comparison between the two eyes
- Correlate any field loss with ocular examination (lens, optic nerve, and retina)

Reliability indices (fixation errors, false positive errors, and false negative errors) are provided, as well as Mean Deviation (average deviation from a normal visual field based on age-related norm) and Pattern Standard Deviation Indices (a measure of how locations differ from each other in the overall field) for the threshold tests, similar to the indices provided with traditional automated threshold perimetry statistical analyses.

**Testing Modes**

Suprathreshold Strategy. It is used for screening purpose. Test options include a screening field (Screening C-20-1) in which gratings with three contrast levels are shown at locations in the central 20 degree field and it takes about 45 seconds. Other is suprathreshold screening C-30 program.

FDT screening mode perimetry is considered abnormal if there is:

- Any defect in the central five locations
- Two mild or moderate defects in the outer 12 squares
- One severe defect in the outer 12 squares
- Screening test time greater than 90 seconds per eye

*In figure: 4, FDT shows one point abnormal with p<2%
and another point abnormal with p<5% in right eye. In left eye one point is abnormal with p<0.5%, another point is abnormal with p<1% and four points abnormal with p<2%. Standard automated perimetry with HFA 30-2 of the same patient was normal.

Full Threshold strategy: There are two variants in this strategy, one being C-20 and another is N-30. (Figure: 5). In C-20, central 20 degree is examined at 17 locations whereas in N-30 additional 2 nasal points (total 19 locations) are also examined. C-20 takes about 3 1/2 minutes while N-30 takes about 6 minutes.

Here threshold sensitivity is measured using either method of adjustment (MOA) or by modified binary search (MOBS). In method of adjustment, three contrast threshold adjustments are made for each stimulus pattern and the geometric mean of the three trials is used as the final contrast threshold value. Modified binary search (MOBS) procedure is a staircase test strategy which continues until a criterion number of response reversal have occurred and the difference between the upper and lower stack values is equal or less than a specified interval. Final threshold is then defined as the mid point between the upper and lower limits when both of these criteria have been met.

Two other newer strategies are rapid efficiency binary search technique (REBS) and zippy estimation of sequential testing (ZEST). The REBS strategy is based on MOBS but its termination criteria require two response reversals (upper to lower limit interval also within 3 db). In ZEST a probability density function (PDF), which describes the relative likelihood of threshold values within the population, is assumed for threshold before test commencement. Both ZEST and REBS are 40% - 50% faster than MOBS.

Percent correlation to Humphrey 30-2 threshold visual fields has been found to be approximately 100% sensitivity and specificity (area under the curve, 1.0) for detecting advanced glaucomatous visual field loss, approximately 96% sensitivity and 96% specificity (area under the curve, 0.9751) for detecting moderate glaucomatous visual field loss, and approximately 85% sensitivity and 90% specificity (area under the curve, 0.9261) for early glaucomatous visual field loss. Overall sensitivity of FDT in diagnosing glaucoma is 80% to 93% and specificity is 93% to 100%.

Custom 24-2 FDT Perimetry

Commercially available FDT perimeter uses larger targets and smaller number of visual locations. Presuming the possibility of smaller targets and larger number of visual field location to improve the performance Johnson et al. evaluated a custom designed FDT perimeter (Quadravision) with 4 target using 24-2 stimulus presentation pattern. Here 54 stimuli of 40 targets with 6° grid spacing are used in a 24-2 stimulus presentation pattern. They reported that the 24-2 stimulus pattern appears to have modestly higher sensitivity for detection of early glaucomatous loss and provides better characterization of the pattern of visual field loss, but the takes approximately twice as long.

Matrix FDT perimeter

The Humphrey matrix (FDT2) is a second generation instrument using similar small FDT stimuli has recently became available for clinical use (Figure: 6, 7). It provides up to 69 stimuli, 5° x 5° each, to fully characterize visual field defects (Figure: 8, 9) and can also be used to perform a serial analysis to determine progression (Figure 9). Here, except foveal stimulus, the stimuli are 5-degree

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**Fig. 5:** C-20 and N-30 for FDT Perimetry

**Fig. 6:** Humphrey-Matrix

**Fig. 7:** Humphrey-Matrix
square windows of a vertical grating with spatial frequency of 0.5 cyc/deg, counterphase flickered at 18 Hz. It uses a Bayesian strategy specifically ZEST (Zippy estimation of sequential testing), with a fixed number of presentation at each test location and a flat previous probability density function (PDF). By this strategy the test time for full threshold perimetry is reduced to half without affecting the accuracy or reliability of the measurements. Study by Spry et al\textsuperscript{16} suggests threshold testing using the FDT Matrix and SAP is comparable when the 24-2 test pattern is used. Another study comparing test results of second generation FDT and standard perimetry by Artes et al\textsuperscript{17} shows that the global visual field indices mean deviation (MD) and pattern standard deviation (PSD) of FDT and SAP correlate highly and the test-retest variability of FDT\textsuperscript{2} is uniform over the measurement range of the instrument.

**Advantages of FDP**

- Short test duration (4-5 min for full threshold)
- Very tolerant to defocus and blur (+ 6 dioptres sphere)\textsuperscript{18}
- Patients can wear spectacles with bifocals
- Not affected by pupil size
- Useful for glaucoma screening
- Test - retest reliability is good
- Can follow glaucoma progression with MD and PSD values
- Less stringent dark room requirements
- Portable and cheaper
- Easily learned by patient and examiner
- Feasible in children\textsuperscript{19}

**Disadvantages**

- May miss focal defects
- Central 20 degree field may miss nasal steps
- Lack of longitudinal data
- Difficult to follow up early progression

**Clinical studies**

Although FDT has just become visible to the ophthalmic community, it has been studied and developed over many years. Johnson and associates showed that a sensitivity of 82% with a specificity of 95% for early glaucomas, 96% sensitivity and 99% specificity for
that had previously demonstrated abnormalities on FDT visual field loss as measured by SAP occurred in regions as 4 years and the initial development of glaucomatous abnormalities preceded SAP visual field loss by as much follow-up revealed that in 59% of converters, the FDT population. The analysis of FDT examinations during glaucomatous visual field defects, as assessed by standard doubling technology (FDT) perimetry results predict early visual field loss.

They concluded that visual field defects may be detected more often by FDT and SAP-SITA in eyes with perimetry. They found close agreement between clinical examination of neuroophthalmic conditions such as anterior ischemic optic neuropathy, compressive optic neuropathies and pseudotumor cerebri. The sensitivity of FDT was 81.3%, with a specificity of 76.2%. When compared with sensitivity and specificity of Humphrey perimetry 87.5% and 81.0%, respectively, the difference was not statistically significant.

Boden et al21 evaluated relationship of SITA and full-threshold standard perimetry to frequency-doubling technology perimetry in glaucoma. They found FDT detects abnormal fields in more eyes than SAP-FT. Correlations of FDT to standard perimetry global indices were similar regardless of the threshold strategy used for standard perimetry. They concluded that visual field defects may be detected more often by FDT and SAP-SITA in eyes with early visual field loss.

Medeiros FA et al22 evaluated whether frequency doubling technology (FDT) perimetry results predict glaucomatous visual field defects, as assessed by standard automated perimetry (SAP), in a glaucoma suspect population. The analysis of FDT examinations during follow-up revealed that in 59% of converters, the FDT abnormalities preceded SAP visual field loss by as much as 4 years and the initial development of glaucomatous visual field loss as measured by SAP occurred in regions that had previously demonstrated abnormalities on FDT testing.

Landers et al23 investigated whether frequency-doubling perimetry (FDP) predicts future visual field loss with achromatic automated perimetry (AAP), just as it may be predicted with short-wavelength automated perimetry (SWAP) and found that both SWAP and FDP detect field loss earlier than AAP.

To know the agreement in results between frequency doubling technology (FDT) and the conventional automated static perimeter in eyes with normal tension glaucoma (NTG) and high tension glaucoma (HTG), Kogure et al24 in their study found that the best agreement of the results of FDT and HFA was observed in eyes with NTG using threshold of HFA. The eyes with HTG showed lower agreement with more abnormal points in FDT results, which suggest enough sensitivity of FDT in eyes with NTG, and higher sensitivity of FDT in eyes with HTG.

Regarding potential use of FDT as a screening device, Allen et al25 compared the Frequency Doubling Technology (FDT) C20-1 screening algorithm and the Humphrey Field Analyser II (HFA) 24-2 SITA-FAST in a large eye screening. They found low false positive rate and a good positive predictive value comparing the FDT screening algorithm to the HFA 24-2 SITA-FAST in their study.

**Conclusions**

FDT is a promising method for the purpose of screening, diagnosing and monitoring glaucoma which is comparable to SAP with some extra advantages. It is easily learnt by patient as well as by the examiner. It takes shortest duration amongst all perimetric tests. As it is tolerant to blur (+6 dioptres sphere), patients can wear spectacles with bifocals and it is also not affected by pupil size. Only further evaluation and research will be able to illustrate if it is any more sensitive in identifying loss associated with glaucoma and other conditions or is simply another method for the evaluation of the visual field. However due to its ease of use, simplicity, speed, affordability and portability it is an important instrument that is quite useful in the evaluation of the visual field in early glaucoma and as a screening test for a large population.

**References**

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Herpes Simplex Keratitis

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Herpes Simplex Virus (HSV) is endemic in virtually every human society throughout the world, from urban to remote native tribes. Humans are the only natural reservoirs for HSV and HSV disease is a significant health problem1,2,3,4.

HSV can be detected by polymerase chain reaction (PCR) in the trigeminal ganglia of 18.2% of cadavers of people up to 20 years of age, which increases to reach almost 100% in cadavers of people at least 60 years of age5. Latency with HSV is prevalent, with at least 33% of the world manifesting recurrent HSV infections6. The major portals of entry are the mucous membranes and external skin. Crowding, poor hygiene and age influence HSV-1 prevalence.

Recurrences are typically with the same strain and may be triggered by fever, hormonal changes, ultraviolet exposure, psychological stress, ocular trauma and trigeminal nerve manipulation7. The excimer laser has been shown to trigger reactivation of latent HSV-18.

Pathogenesis

The clinical sequelae of HSV infection are largely a result of recurrent disease and the immunologic response with each episode. After peripheral entry into the host and primary infection with viral replication within the end organ, HSV travels in a retrograde fashion to various ganglia, most commonly, the trigeminal ganglion, and possibly the brain stem9,10,11. Immune defense mechanisms are both beneficial and harmful.

Clinical Manifestations

1) Congenital and Neonatal Ocular Herpes

This is rare. It is usually acquired from genital herpes in the mother, during parturition12. Ocular manifestations include skin lesions, conjunctivitis, epithelial and stromal keratitis and cataracts.

2) Primary Ocular Herpes

By the age of 5 years, 60% population has been infected by HSV13. However, only 6% of those infected actually develop clinical manifestations, which typically affects perioral region rather than the eye.

3) Recurrent Ocular Herpes

Schuster et al14 reported a 33% recurrence within 2 years in patients with two prior infectious epithelial keratitis episodes. A variety of clinical manifestations of infectious keratitis and immunological disease can affect all levels of the cornea. Bilateral disease is noted in 3% cases and is more common in the younger age group and the immunocompromised15.

Classification of HSV Keratitis

1) Infectious epithelial keratitis
   a. Cornea vesicles
   b. Dendritic ulcer
   c. Geographic ulcer
   d. Marginal ulcer

2) Neurotrophic keratopathy

3) Stromal keratitis
   a. Necrotizing stromal keratitis
   b. Immune stromal (interstitial) keratitis

4) Endothelitis
   a. Disciform
   b. Diffuse
   c. Linear

Infectious epithelial keratitis

Dendritic ulcer

This is the most common presentation. It is a branching, linear lesion with terminal bulbs and swollen epithelial borders that contain live virus. It is a true ulcer as it extends up to the basement membrane. It is important to recognise that HSV dendritic ulcer may result in abnormal appearing epithelium for several weeks after the ulcer heals. This
epitheliopathy is dendritic in shape but is not ulcerated and does not require treatment.

**Geographic ulcer**

This is a widened dendritic ulcer and also has swollen epithelial borders that contain live virus. It may be associated with previous use of topical steroids.

**Marginal ulcer**

This lesion results from active virus and is often confused with staphylococcal marginal disease. It has proximity to limbus and is accompanied by a blood vessel. Typically, the patient is more symptomatic.

**Neurotrophic Keratopathy**

Patients who have had epithelial disease are at risk to develop this entity. This is neither immune nor infectious. It arises from impaired corneal innervation. The epithelial defect is oval in shape with smooth borders and eventually leads to stromal ulceration with grey white bed and heaped up borders.

**Stromal Disease**

Stromal disease accounts for 20 to 48% of recurrent ocular disease.

**Necrotising stromal keratitis**

The clinical findings are necrosis, ulceration and dense infiltration of the stroma with an overlying epithelial defect. The combination of replicating virus and severe host inflammatory response leads to destructive intrastromal inflammation. The ulcer resembles microbial keratitis.

**Immune stromal keratitis (interstitial keratitis)**

The role of retained viral antigen as a stimulus for chronic inflammation has been implicated in this entity. The overlying epithelium is usually intact. The stromal infiltration may be focal, multifocal or diffuse. This is accompanied by anterior chamber inflammation and ciliary flush. Stromal neovascularisation at any level of the cornea, may occur.

**Endothelialitis**

Many patients with HSV disease develop stromal oedema without stromal infiltration. They present with KPs, overlying stromal and epithelial oedema and iritis. Disciform keratitis is actually an endothelialitis as the inflammatory reaction is not a reaction of stroma but at the level of the endothelium. The pathogenesis of this entity is unclear but is thought to be immunologic. HSV endothelialitis may present clinically as disciform, diffuse or linear.

**Iridocyclitis**

HSV may develop concomitant or subsequent iridocyclitis. A trabeculitis may occur, which results in severe elevation of IOP.

**Sequelea of infectious epithelial keratitis**

1) Complete resolution
2) Dendritic epitheliopathy
3) Scarring – ghost figures or foot prints
4) Stromal disease (25% patients)

**MANAGEMENT**

**Epithelial keratitis**

The goal is to get rid of the live virus. 3% Acyclovir topical ointment five times a day benefits in reducing patient morbidity, sub-epithelial scarring and risk of immune disease. Topical antiviral therapy should be given for 10 to 14 days. If the keratitis has not healed after 2 weeks, careful inspection of the ulcer should be undertaken to be certain that the lesion is, in fact, an ulcer.

**Neurotrophic Keratitis**

The first step is to stop all unnecessary medications,
Indications for corticosteroids and antivirals in the treatment of different forms of HSV keratitis

No corticosteroids
- HSV conjunctivitis
- Infectious epithelial keratitis
- Mild immune stromal keratitis without prior corticosteroid use
- Mild diffuse endotheliitis without prior corticosteroid use
- Noninflamed neurotrophic keratopathy

Topical corticosteroids
- Marginal keratitis
- Moderate immune stromal keratitis
- Moderate endotheliitis
- Inflamed neurotrophic keratopathy
- Moderate iridocyclitis/trabeculitis

Oral corticosteroids (used in conjunction with topical corticosteroids)
- Severe immune stromal keratitis
- Severe endotheliitis
- All cases of linear endotheliitis
- Severe iridocyclitis/trabeculitis

Topical antivirals
- HSV blepharitis
- HSV conjunctivitis
- Infectious epithelial keratitis
- Prophylaxis for corticosteroid treatment of immune stromal keratitis

Oral antivirals
- Primary HSV infection
- Selected cases of severe diffuse endotheliitis
- Selected cases of severe iridocyclitis/trabeculitis
- Linear endotheliitis
- Immunocompromised patients
- Pediatric patients refractory to topical medications
- Prophylaxis against recurrent infectious epithelial keratitis
- Prophylaxis for post-PK patients with history of HSV keratitis

including antivirals. Frequent use of non-preserved lubrication promotes healing. Low-grade inflammation may require use of topical steroids. A non-healing ulcer would need the assistance of Tarsorraphy for healing.

Immunologic disease

Topical steroids are invaluable in the management of HSV keratitis. The Herpetic Eye Disease Study (HEDS) showed that use of topical steroids in conjunction with antiviral agents resulted in significant reduction of stromal inflammation and duration of immune stromal keratitis. Topical steroids do not increase risk of recurrent epithelial disease. It is important to avoid rapid tapering or abrupt discontinuation of topical corticosteroids to prevent rebound inflammation.

Recommendations of HEDS
- Topical steroids therapy for stromal keratitis leads to faster resolution and fewer treatment failures
- There is no apparent benefit in the addition of oral acyclovir to the treatment regimen of a topical corticosteroid and a topical antiviral for treatment of stromal keratitis
- The study suggests a benefit in adding oral acyclovir to the treatment of HSV iridocyclitis in patients receiving topical corticosteroids and topical antiviral prophylaxis
- In the treatment of acute HSV epithelial keratitis, there was no benefit from the addition of oral acyclovir to treatment with topical antiviral in preventing the development of stromal keratitis or iritis
- Long term use of Oral acyclovir reduces the recurrence incidence of epithelial keratitis and stromal keratitis

References


Cysticercosis refers to human infection with the larval form of the nematode, Taenia solium due to the ingestion of contaminated food especially undercooked pork, contaminated water and vegetables. It is commonly seen in places with poor sanitation.

Life Cycle

Cysticercus cellulosae is the larval form of the pork tapeworm, Taenia solium. Human cysticercosis is acquired by ingestion of tapeworm eggs shed in faeces. The infection is usually acquired by consumption of poorly washed vegetables or fruits and may sometimes be due to auto-infection due to poor hygiene. The eggs mature and the larvae penetrate the intestinal mucosa to enter the portal circulation, from where they are carried to various target organs. The common systemic sites of involvement are subcutaneous tissues, muscles, brain and eyes. The larval form may enter the eye through the choroidal circulation and migrate into the subretinal space or enter the vitreous body. Death of the larvae within the ocular tissues can induce a severe inflammatory reaction, which may lead to blindness. Cysts embedded in the extraocular muscles may cause ocular movement disorders or proptosis.

Clinical Features

Cysticercosis is most prevalent in India, Eastern Europe, Central America, and Mexico. It commonly affects children and young adults. The cyst may lodge in any part of the body, central nervous system being the most common site. It may also lodge in the heart, skeletal muscles and in the eye. In the eye it may be intraocular in location or may be present in the orbit or the adnexa. Extraocular muscles are the commonest structure to be affected in the orbit. Depending on their size and location, orbital cysticercosis may be associated with chemosis, ocular pain, protrusion of the eye, periorbital swelling, drooping of eyelids, double vision and restriction of ocular movements. Extraocular involvement may include involvement of the extraocular muscles, lacrimal gland or optic nerve. The authors have seen five different sets of presentations in over 150 cases seen and treated by them.

a) Proptosis (Fig 1a,b)
b) Ocular motility restriction and diplopia (Figure 2a,b,c,d)
c) Recurrent episodes of redness, swelling and pain that may mimic orbital pseudotumor or even orbital cellulites (Figure 3a,b)
d) Recurrent episodes of ptosis (Figure 8a,b)
e) Subconjunctival cysts with or without abscess formation (Figure 4)

Diagnosis

The diagnosis of myocysticercosis is based on clinical, serologic, and radiological findings. The clinical findings may occasionally be non-specific and hence, non-diagnostic. The serology in myocysticercosis is rarely positive in the experience of the authors. Thus, imaging studies are the most helpful in establishing the diagnosis of cysticercosis.

Diagnosis of infection with adult T. solium is made by stool examination and finding the eggs of proglottids of the worm. One easy method for differentiating the infection with Tania saginata from T. solium is the use of hematoxylin-eosin (HE) staining of proglottids and observing the number of uterine branches. The uterine branches in T. solium infection is about 50 in number while that in T. saginata infection is about 150 in number. The branches are also more convoluted in a T. solium infection than in a T. saginata infection. Though stool examination for the adult worm may be performed in cases of suspected myocysticercosis infections, it is not essential that all patients with myocysticercosis have the adult worm in their intestines except in those cases, which are acquired by auto-infection.
Serological tests used for the specific diagnosis of cysticercosis are indirect hemagglutination, indirect immunofluorescence, and immunoelectrophoresis such as ELISA specific serology. Finding a scolex, hooks, or fragments of the bladder walls in the biopsy material together with clinical symptoms makes the final diagnosis of human T. solium cysticercosis. Blood eosinophilia is usually present.

Imaging modalities of the brain and the orbit combined with neurological evaluation remains the best approach for the diagnosis of neurocysticercosis.

- X-Ray of the orbit and the head is used as a corollary for the diagnosis of calcified cysts.
- Ultra-sonography of the orbit is major diagnostic importance. A-scan ultrasonography shows high amplitude spikes corresponding to scolex and cyst wall. B-scan imaging, shows ring shaped lesion with central or marginal echoes corresponding to scolex. (Figure 5a, b)
- Computed tomography (CT) of the intraorbital cysts may be seen as a small round, well defined, non-enhancing area of low attenuation. The scolex, which is the invaginated head of the larva, may or may not be visualized. When visualized it is seen as an eccentrically placed hyperdense (due to presence of calcareous corpuscles) nodule of pinhead size on the inner aspect of the cyst wall. A cystic lesion with a scolex confirms the diagnosis of cysticercosis. The pericystic inflammation is manifested as thick, irregular enhancing cyst walls, thickening of involved muscle and streaky soft tissue densities in the orbital fat on contrast enhanced CT scans. (Figure 6a, b)
- Magnetic Resonance Imaging (MRI) demonstrates the lesion in the early stage. The cyst in a MRI appears as a small rounded lesion along with surrounding edema. (Figure 7a, b)

Management

Medical therapy is the accepted mode of treatment for myocysticercosis. The combination of oral Albendazole with steroids is the usual regime. The authors were the first to use and describe Albendazole therapy in myocysticercosis (Proceedings of All India Ophthalmological Society, 1975). We have found that a higher dose of Albendazole (30mg/kg/day) for 15 days along with low dose oral corticosteroids (5-10 mg/day) leads to a greater success rate in the therapy. In a small percentage of cases an acute inflammation may occur a few days after starting the medical therapy due to toxins released by a
dying parasite. Subconjunctival cysts may spontaneously extrude following medical management or may require surgical excision in exceptional cases. Patients usually show early clinical improvement after 2 weeks of therapy and may take a couple of months for near complete clinical recovery. Serial ultrasonograms can be performed to assess the size of the cyst. The CT or MRI scan can be repeated after 6 months to 1 year of treatment. Full regression on imaging may take 6-9 months.

Orbital myocysticercosis is a common condition in our part of the country. A high index of suspicion of the condition should be entertained in all cases with proptosis, acquired diplopia or extraocular muscle restriction. Medical therapy in form of oral Albendazole and corticosteroids improves the clinical symptoms significantly and often results in the resolution of the cyst.
Transient Visual Loss

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Transient visual loss refers to temporary visual impairment of variable duration lasting from seconds to hours. Typically, episodes have an abrupt onset, progressing over a few seconds to involve whole or part of one or both visual fields. Within the affected area vision may be dimmed or completely lost. Sight usually returns within seconds or minutes but, exceptionally, attacks may last several hours. We will be discussing the Transient Visual Loss here.

Causes of Transient Visual Loss

Vascular

Thromboembolic:
- Atheromatous disease of internal carotid artery or ophthalmic artery or vertebral artery.
- Carotid occlusions,
- Slow flow retinopathy

Vasculitis:
- Giant cell arteritis,
- Pararteritis nodosa,
- Systemic lupus erythematosus,

Neurological

- Papilloedema,
- Migraine: ocular, classic.
- Epilepsy
- Uhthoff’s phenomenon

Ocular

- Angle closure glaucoma
- Hyphaema
- Optic disc anomalies: drusen, coloboma,
- Retrobulbar tumours,

Haematological

- Hyperviscosity-polycythemia, thrombocythaemia, multiple myeloma
- Coagulopathies, anaemia.

Initial Diagnosis

Thromboembolic disease is the most common cause of transient visual loss and, if an alternative diagnosis cannot be made, the patient should undergo detailed cardiovascular investigations. At presentation there are four important causes:

- Giant cell arteritis.
- Intermittent angle closure glaucoma.
- Slow flow retinopathy.
- Papilloedema

Key features of common or important causes of transient visual loss:

1. Giant cell arteritis: Age > 50, systemic symptoms, raised ESR, disc swelling.
2. Intermediate angle closure glaucoma: Shallow angles, aching pain
3. Slow flow retinopathy: Peripheral haemorrhages, narrow arterioles, central retinal arteriole pulsation with minimal pressure on the globe.
4. Papilloedema: Swollen disc
5. Thromboembolic disease: Normal fundus, peripheral embolus.

1. History

A complete ocular and systemic history is essential in the assessment of transient visual loss because ocular examination is often normal. The following are of particular importance.

Is the visual loss in one or both eyes?

Observant patients will have noticed this but, more often, patients may not be sufficiently aware to be certain. Beware of the error of confusing homonymous hemianopia with unilocular loss. Retinal embolus from carotid artery disease typically produces monocular transient visual loss (amaurosis fugax). The loss is often described as a shutter being lowered or raised.

Duration of each attack

This may vary but typical patterns are-

- Embolic disease- seconds or minutes.
- Migraine- minutes.
- Papilloedema- seconds and related to posture
- Glaucoma- minutes to hours.
Often the causes are variable but usually last over 30 seconds.

Precipitating factors
- Posture - standing up for papilloedema and systemic hypotension.
- Turning the head for carotid artery disease
- Eye movements in some tumours of the orbit
- Eating chocolate as trigger factor for migraine
- Haloes around lights in congestive glaucoma.
- Prolonged dim light as in cinema hall.

Associated symptoms
- Current or previous symptoms include:
  - Other neurological deficits in thrombolic disease
  - Headache in papilloedema and giant cell arteritis
  - Visual aura and other symptoms in migraine
  - Haloes around light in congestive glaucoma

Risk factors for cardiovascular disease - smoking, raised blood pressure, diabetes mellitus and hyperlipidaemia

2. Examination
Full ocular and cardiovascular examinations are required.
- Visual function assessment: This should include visual acuity, visual field, pupil reactions. Most cases will have negative findings but a number of cases of transient visual loss may leave permanent visual loss of which the patient is unaware, e.g. papilloedema causes enlarged blind spots.
- Anterior segment: Depth of anterior chamber for narrow angle glaucoma use a gonioscope, if in doubt.

Measures intraocular pressure (IOP)
Look for causes of transient obstruction of the visual axis, for example, soft lens matter occluding pupil after cataract surgery.

Sources of spontaneous hypaema - e.g. Iris clip lens or Acintra ocular lens.
- Posterior segment
  - Retinal vessels - for patterning and signs of old embolism
  - Disc - for swelling, atrophy or drusen.

Retina - for peripheral haemorrhages: midperipheral haemorrhages in slow flow retinopathy, or scattered punctate haemorrhage in pre retinal vein occlusion
Retinal tear with shifting fluid in posterior pole.

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<td>3. Hypoperfusion (hypotension, Hyperviscosity, hypercoagulability)</td>
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<td>4. Ocular (intermittent angle closure glaucoma, hyphema, optic disc oedema, partial retinal vein occlusion.</td>
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<td>5. Vasculitides (e.g. giant cell arteritis)</td>
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<th>Causes of transient bilateral loss of vision</th>
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<td>1. Migraine</td>
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<tr>
<td>3. Epilepsy</td>
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<tr>
<td>4. Papilloedema</td>
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Cardiovascular system: Pulse and rhythm, BP, carotid auscultation, cardiac auscultation, peripheral pulse when indicated.

3. Investigations

The ESR should be measured for all patients. A high ESR in patients over the age of 50 strongly suggests giant cell arteritis, whereas in younger patients it may be associated with other vasculitic causes of transient visual loss.

Doppler studies are needed for carotid stenosis. Angiography is carried out only if carotid surgery is being considered.

4. Management of Specific Conditions

A) Giant Cell Arteritis

General features: malaise, weight loss, fever. Headache and scalp tenderness- typically painful to put head on pillow. Pain on chewing in severe cases and jaw claudication. Aches and pains from polymyalgia.

Ocular features: non pulsatile temporal late stage arteritis- Ischemic optic neuropathy, central retinal artery occlusion on moving eyes, diplopia from nerve palsy.

Diagnosis: ESR typically more than 80, Temporal artery biopsy may show focal arteritis with giant cells.

Management: Immediate intravenous injection of hydrocortisone 200 mg, oral steroids to be started at the same time, admission of patient for biopsy and control of arteritis.

B) Anterior Ischaemic Optic Neuropathy.

Anterior ischemic neuropathy (AION) is caused by occlusion of the posterior ciliary arteries supplying the preliminary optic nerve.

Signs and symptoms- There is sudden loss of vision and swelling of optic disc. Two forms of AION are recognized: non arteritic and arteritic AION.

- Non arteritic AION: Peak incidence is in the 50-60 year age range but can occur in much younger patients. Field loss is usually altitudinal or arcuate, but may be total. Central vision is usually involved with resultant loss of acuity, but 40% of affected eyes retain an acuity of 6/18 or better. Disc swelling may be subtle and limited to the sector corresponding to the sector involved to the visual field defect. Flame shaped disc haemorrhages are often seen.
Arteritic AION: This is most common beyond the age of 70 and very rare below 50. Patients usually present with profound loss of vision in one or both eyes, but partial field loss may occur. They may have experienced visual loss in the preceding few days. The disc is swollen and milky white in colour.

Non arteritic AION: local arteriosclerosis (embolus is an extremely rare cause).

Arteritic AION: giant cell arteritis

Immediate screening:

Screening for Giant Cell Arteritis (GCA): Systemic features include headache, pain and tenderness of proximal muscle groups (polymyalgia rheumatica), jaw claudication, fever, weight loss, scalp tenderness, and pulseless temporal artery. On immediate ESR measurement, most patients will have an elevated ESR, typically over 80 mm/hr. The age matched upper limit of normal is about half the patient's age in millimeters per hour.

Treatment This should be as though it were giant cell arteritis, the systemic features of which may be absent. Two percent biopsy proven giant cell arteritis have a normal ESR. Giving immediate treatment to a patient with giant cell arteritis may be sight saving, and a short course of steroids (until giant cell arteritis is definitely excluded) is unlikely to harm a patient with non arteritis AION. Therefore, patients should be given hydrocortisone 200 mg intravenously, pending further investigations.

C) Intermittent Angle Closure Glaucoma Symptoms of transient visual loss caused by intermittent angle closure glaucoma are usually accompanied by eye ache and headache, haloes around lights and intermittent blurring of vision. Signs include shallow anterior chamber, positive van Herrick sign where the peripheral cornea is in contact with the iris. Raised intraocular pressure is not always present except during an attack. Narrow or closed angle on gonioscopy will confirm the diagnosis. Management is by medical therapy to lower pressures by Diamox, pilocarpine or by beta blocker eye drops.

D) Slow Flow Retinopathy

Slow flow retinopathy is caused by severe stenosis of the carotid circulation. It may be monocular or binocular.

Symptoms and signs are:

- Intermittent blurring or loss of vision; residual blurred vision may occur because of retinal ischemia
- Photopsia
- Mid peripheral retinal haemorrhage
- Cotton wool spots
- Marked arterial attenuation and mild venous dilatation

- Occasionally new vessels on disc and vitreous haemorrhage.
- Low perfusion pressure in artery results in closure of artery with minimally applied pressure.

Management: This is similar to that for transient visual loss by thromboembolic disease (see below)

E) Thrombo Embolic Disease

Transient thrombosis or embolism associated with atheromatous disease of the internal carotid or ophthalmic arteries accounts for most cases of monocular transient visual loss. Such cases were previously said to have "amaurosis fugax" or "fleeting blindness". Less commonly, may be caused by emboli originating from the heart or proximal vessels. The risk of subsequent stroke, at 3-5% per annum, is five times greater than in an age matched population and 30% of patients will have a myocardial infarction within five years.

Concurrent neurological symptoms are rare but there may be a history of previous transient or permanent neurological deficits within the distribution of the carotid arteries. Retinal emboli, when present are diagnostic.

Symptoms and signs:

There is transient loss of vision which usually lasts for second to minutes-impairment lasts a little longer, up to 20 min. Loss of vision begins as if a curtain was drawn up or down the field and recovery has the reverse effect. An old emboli in peripheral arterial tree may be visible or there may be no signs if the cause is platelet emboli which pass through the circulation.

In central retinal artery occlusion (CRAO), Visual acuity is usually down to counting fingers or less, but some cases (11%) may retain some central vision because of a patent cilioretinal artery.

Management:

The investigation and treatment of transient visual loss resulting from a thromboembolism are ideally coordinated by someone (possibly a neurologist, cardiologist, ophthalmologist, and a vascular surgeon) who has an interest in this field. The aims of treatment are to reduce the risks of subsequent stroke and myocardial infarction.

Carotid duplex ultrasonography is the initial screening investigation, which may be followed by angiography.

Management- Intravenous acetazolamide 500mg.

Ocular massage for 15 mintus by pressing on the eye for 10 second and then suddenly releasing.

Anterior chamber paracentesis under topical anaesthesia using 26 G needle.

Aspirin 300 mg per day has been shown to reduce the
risk of nonfatal stroke by 30% after transient visual loss caused by thromboembolism. There is no definite evidence that anticoagulation with either warfarin or heparin is of benefit. All patients require a cardiac assessment looking for ischemia and sources of emboli.

Risk factors - Cardiovascular risk factors such as smoking, hypertension, diabetes, and hyperlipidemia should be reviewed.

Investigations advised: - Full blood count, urgent ESR, plasma glucose and lipids, and ECG. Carotid duplex ultrasonography and echocardiography can later be advised. Patients should be advised to stop smoking and start on aspirin (unless they have a history of allergy or peptic ulceration).

F) Papilloedema

Transient visual loss associated with papilloedema characteristically lasts for a few seconds and usually affects one eye at a time. Recurrences and repeated episodes are the rule. Visual loss may be precipitated by alteration of posture and can often be reproduced by gentle pressure on globe. Other features of raised intracranial pressure may be elicited, including headache, which is typically worse in the morning and exacerbated by coughing or changes in posture, nausea or vomiting, and horizontal diplopia caused by VI cranial nerve palsy.

Signs: Swollen and hyperaemic disc, peripapillary flame shaped haemorrhages and engorged retinal veins

Management: Urgent investigation is needed to establish the underlying cause. Blood pressure must be measured to exclude malignant hypertension, CT scan is advised and the patient referred for a neurological assessment. Treatment is that of the cause, although if cause is pseudotumour cerebri, then the treatment includes acetazolamide and/or frusemide, repeated lumbar punctures, fenestration of optic nerve or peritoneal shunts.

Other causes of disc swelling:

Papillitis or optic neuritis - visual acuity is usually decreased.

Malignant hypertension: BP raised.

Central retinal vein occlusion (CRVO): rarely bilateral and peripheral retinal haemorrhages

Infiltration of optic nerve head: granuloma, for example sarcoid and neoplasia, for example leukaemia.

Uveitis: signs of inflammation. It commonly affects only one eye. There is no congestion of vessels.

G) Other Causes of Transient Visual Loss

-Transient visual loss is an unusual presentation for a retrobulbar tumour but it should be considered if episodes are precipitated by eye movement.
- Patients with spontaneous hyphaema should be thoroughly screened.
- Optic disc drusen and coloboma may be coincidental findings.
- Vasculitis other than giant cell arteritis may occasionally cause transient visual loss. Arthritis, skin rashes, and Raynaud’s phenomenon, the antinuclear antibody titre and rheumatoid factor should be checked.
- Coagulopathies are an uncommon cause of transient visual loss, but should be considered in young patients and those with unknown malignancy. Screening for lupus anticoagulant and coagulation factor abnormalities may be indicated.
- Hyperviscosity syndromes and anaemia will be detected by a full blood count and ESR.
- Migraine: there are no distinguishing features of monocular transient visual loss resulting from ocular migraine. In particular headache does not always occur with this type of migraine and occasionally accompanies transient visual loss caused by thromboembolic disease. The diagnosis of ocular migraine must therefore be one of exclusion. When the transient visual loss is binocular and is associated with headache, migrating scintillations, and a family history of migraine, the diagnosis of classic migraine is almost certain. If there are any atypical features, other causes of occipital ischaemia should be considered.
- Uhthoff’s phenomenon - temporary decrease in acuity
consequent to exercise or other causes of increased body temperature with demyelinating optic neuropathy (multiple sclerosis)

- Epilepsy
- Functional or psychogenic

**Profound Loss of Vision**

Causes of profound visual loss (which may not recover fully) should also be screened if the patient presents in the early stages. Sudden onset of profound visual loss indicates a vascular aetiology (anterior ischemic optic neuropathy, retinal vein occlusion- BRVO, CRVO, or a Vitreous haemorrhage- Diabetic or due to Eales dis.). Gradually enlarging field defect over hours to a few days indicates a retinal detachment. Progressive dimming of vision over hours to a few days indicates optic neuritis and optic neuropathy. These causes are not discussed here, but should always be kept in mind.
Introduction

Allogeneic rejection is defined as a specific cell-mediated immune reaction directed against the corneal allograft. It is directed against Major Histocompatibility Complex (MHC) allo-antigens present on donor cells.

There are 3 main cell types transplanted at the time of the corneal graft: epithelial cells, stromal keratocytes and endothelial cells. An immune reaction directed against epithelial cells is termed epithelial cell rejection and may manifest as an epithelial rejection (Krachmer) line. Epithelial cells are normally lost from the graft over a matter of months even in the absence of rejection, this does not affect graft clarity.

Stromal keratocyte rejection is uncommonly observed and may manifest as predominantly anterior stromal nummular inflammatory lesions (Krachmer dots) restricted to the graft. Transplanted keratocytes are normally lost over time from the graft, being replaced by invading host keratocytes. This usually does not affect graft clarity unless there is an underlying keratocyte metabolic disorder such as occurs in some of the stromal dystrophies e.g. granular, lattice and macular dystrophy. In these cases this can lead to a recurrence of the disease within the graft.

Endothelial cells maintain a clear and compact cornea in the face of the osmotic load of corneal stromal mucopolysaccharides through two-enzymatic pumps. The most important is ATPase dependent, of less importance is a carbonic anhydrase pump. As such corneal endothelial cells are of prime importance in maintaining normal corneal function. They are non-mitotic and therefore non-replicatory in humans. As such the loss of sufficient endothelial cells as a result of an allogenic immune reaction can lead to irreversible graft edema.

High-risk corneal grafts

The definition of high and low-risk largely relates to outcomes as measured through corneal graft registries and chart reviews. According to the Corneal Collaborative Transplantation Studies, high risk for graft rejection include cases where there is more than two quadrants of stromal vascularization and cases of re-grafts.

The Australian Corneal Graft Registry, one of the largest found the following factors which were responsible for increased chances of rejection:

- Indication for graft other than keratoconus or other corneal dystrophy
- Previous failed ipsilateral graft
- Aphakia
- Inflammation at the time of the graft surgery
- Presence of an anterior chamber or iris clip intraocular lens
- Graft size outside 7.0-7.9mm.
- Post-operative corneal neovascularization

Decreasing graft rejection in high-risk grafts

The mainstay of the success of reducing graft rejection is the liberal use of topical corticosteroids.

The matching of MHC and blood group antigens has also been examined in several major studies including the Collaborative Corneal Transplantation Study (CCTS). This failed to establish any benefit from matching for Class1 or Class 2 antigens for high-risk grafts. CCTS found a significant reduction in the frequency of allograft rejection in high-risk cases when the ABO blood group was matched.

Systemic (oral) cyclosporin A (CsA) has been evaluated in several studies. As with solid organ transplantation dual or triple therapy immunosuppression is probably required to significantly decrease the risk of rejection. As such the substantial risks and cost probably outweigh the small benefit of single therapy oral cyclosporin A.

Prophylactic treatment of graft rejection

Apart from avoiding and identifying high-risk grafts one can reduce the incidence of rejection episodes by identifying and treating high-risk episodes for the graft.

This includes any suture manipulation such as removal or suture manipulation, as is the case in post-operative running suture adjustment to control astigmatism.

Any intraocular surgery such as cataract extraction and intraocular lens implantation or corneal surgery such as LASIK also represents an increased risk to the graft. At such times it is appropriate to prophylactically treat with a short course of a potent topical corticosteroids, such as prednisolone acetate 4 times a day for 1 week.
Other risk factors for graft rejection

Several drugs are thought to affect graft survival either through being proinflammatory or decreasing endothelial cell pump function.

Latanoprost, a topical synthetic prostaglandin analogue, has been implicated in the reactivation and amplification of uveitis and cystoid macular oedema as part of its general proinflammatory nature.

Dorzolamide, a topical synthetic carbonic anhydrase inhibitor, inhibits the endothelial cell enzymatic pump mechanism. This action may jeopardize the graft.

Acute treatment of graft rejection

Prompt reversal of the rejection episode is the primary aim of treatment. It is preferable to achieve reversal of a graft rejection episode quickly with minimal endothelial cell loss than slowly with more marked endothelial cell loss even if both result in a clear and compact corneal graft. For this reason prompt presentation and aggressive treatment is of paramount importance.

Signs and Symptoms

The first step in the management of acute graft rejection is adequate patient education with respect to the symptoms of rejection and the need for prompt presentation. One of the first symptoms is photophobia, usually followed by ache, blur, redness and even tearing.

Graft rejection is uncommon in the first month or two following surgery, presumably because it takes some time for the host immune system to recognize and to become primed to the donor alloantigens. This is not necessarily the case if the donor alloantigens have already been encountered by the host immune system as can occur with prior grafts or blood transfusions.

The signs of rejection can range from minimal anterior chamber reaction with cell and flare up to a gross anterior chamber reaction, even with a hypopyon with associated keratic precipitates and overlying stromal and even microcystic epithelial oedema. The area of affected cornea may be localized. This may be quite marked if there is a progressive line of keratic precipitates, a Khodadoust line.

Usually no investigations are necessary although pachymetry over the affected area may be useful in monitoring the effectiveness of treatment.

Medica Therapy

The mainstay of treatment is the aggressive administration of potent topical corticosteroids with good intraocular penetration. As such prednisolone or dexamethasone conjugated to acetate or sodium phosphate to increase penetration through an intact epithelium is usually chosen. An added benefit is the enhanced absorption provided by the epithelial barrier degradation seen with many preservatives such as benzylkonium chloride.

The added benefit of oral or intravenous corticosteroids is debated and only uncommonly used. Concerns about compliance may also lead to the admission of the patient to hospital for the first few days of treatment. After observing a clinical response to treatment the dosage of steroid is usually tapered over the next several weeks. As the presence of a recent rejection episode indicates an increase in the risk of subsequent rejection it is advisable to keep the patient on some topical steroids for the next year or so.

A commonly used treatment regime is:

- Topical Prednisolone acetate hourly day and night for 1 to 2 days
- Topical prednisolone acetate 2 hourly for several days followed by tapering over 1 month to 3 times a day
- Topical prednisolone acetate three times a day for 1 month then twice a day maintained for 6 months then daily for six months

If the patient does not adequately respond to topical treatment it is important to assess compliance and if necessary admit for inpatient administration of drops and/or add in systemic, usually oral steroids at a dosage of 1 mg/Kg per day for 3 days. Topical 2% eye drops are also given in qid doses for 6 months to 1 year.

Pulse Steroid Therapy

Methylprednisolone 125–250mg intravenously at the time of surgery followed by oral prednisolone 1 mg/kg/day slowly tapered in 3-6 months may be useful in high-risk cases. Severe or refractory rejection may also respond to systemic immunosuppression. The role of pulsed intravenous methylprednisolone for severe rejection is not proven and may only be of benefit if the patient presents early in the rejection episode, some surgeons prefer to use short term high dose oral prednisolone in these cases:

- A single intravenous dose of Methylprednisolone 500mgs 3 or
- Oral prednisolone 80mgs daily 4 for 5-7 days

Immunosuppressants used in graft rejection

Cyclosporine A

**Topical**

Cyclosporin A 2% in castor oil or 1% in artificial tears 4 times daily

Commercial preparations offering better penetration and efficacy should be shortly forthcoming.
**Systemic**

Some success has been achieved with the use of systemic cyclosporin in high-risk keratoplasty:

- 4-5 mg/kg once or two divided doses daily

Blood Cyclosporin A level should be between 100 – 300ng/ml

All patient using Cyclosporin A need close monitoring of blood pressure, renal function including serum creatinine and liver enzymes.

**Azathioprine**

- 50mgs daily increasing to a maintenance dose of 75 - 100mgs daily

Used as a ‘steroid sparing’ agent in rejection for high-risk keratoplasty.

Renal, hepatic and bone marrow function must be monitored.

**Mycophenolate mofetil**

- 2000 - 3000mgs daily

Suppresses lymphocyte proliferation in a similar manner to azathioprine.

Better tolerated than azathioprine.

It may increasingly have a role in the management of rejection in high-risk keratoplasty.

**Tacrolimus**

- This is a macrolide immunosuppressant that is a fungal metabolite and suppresses both humoral and cellular immune responses.

Renal function must be monitored and neurological adverse effects have been documented (more so with intravenous preparations).

It may surpass cyclosporin as the ‘steroid sparing’ agent of choice in the future.

**References**

16. Perry HD, Donnenfeld ED, Acheampong A et al. Topical cyclosporin A in the management of postkeratoplasty glaucoma and corticosteroid-induced ocular hypertension and the penetration of topical 0.5% cyclosporin A into the cornea and anterior chamber. CLAOJ 1998;24:159-165
Subretinal fluid drainage during scleral buckling may not be needed in all cases. It should however be done in case of retinal detachments which are associated with bullae, inferior breaks, PVR of grade B or greater, poor retinal pigment epithelial function (in high myopes, ARMD), glaucoma and chronic detachments.

Site
1. Drainage is safe on either side of the horizontal recti muscles, as these areas have less choroidal vasculature.
2. It is best to drain through sclera that will be buckled-preferably in the posterior third of the bed of the buckle. In case the fluid is posterior to the buckle, the site is chosen posterior to the buckle and closed with preplaced non-absorbable sutures.
3. Drain in an area where the retina appears less mobile, to avoid retinal incarceration
4. Avoid draining through the area of the cryo application, because cryopexy dilates choroidal vessels and increases risk of bleeding.
5. Avoid drainage in the superotemporal quadrant to avoid gravitation of blood under the fovea in case of a subretinal bleed.
6. Do not drain near a large retinal break to prevent vitreous draining out through the break.

Methods
1. The classical method- 3-4 mm sclerotomy is made, its margins diathermized and the choroidal knuckle exposed. The choroid is examined under the microscope to look for large choroidal vessels, and then diathermized. Entry through the choroids can be made with a 26 g needle, 5-0 suture needle, sharp diathermy electrode or even laser.
2. Needle drainage – Using a 26 g needle to pass directly through the sclera and enter the subretinal space. May not help in long standing detachments where the SRF is viscous.
3. Combined method-A partial thickness sclerotomy is made (a thing layer of scleral fibres is retained) and drainage done with 26 g needle.

Technique
1. Complete all essential steps before drainage such as break localization, retinopexy, buckle and suture placement. Also check that there is sufficient SRF to drain and that it has not shifted.
2. Make sure that the IOP is not elevated while perforating the choroids - ask the assistant to relax the traction sutures and loosen all buckle sutures. Drainage of SRF when the IOP is high may cause retinal incarceration. Also make only a small opening in the choroid with a 26g needle or the tip of a 5-0 suture needle to prevent incarceration.
3. Do not allow sudden hypotony during SRF drainage as this could result in a suprachoroidal haemorrhage (especially in eyes with high myopia) or retinal incarceration. A controlled slow drainage has lesser complications, and the assistant has an important role to play at this step. As the SRF drains the assistant should increase the IOP by pulling on the traction sutures. IOP can also be maintained by indenting the sclera at constant pressure using cotton tipped applicators in the quadrant opposite to the drainage site tightening the buckle sutures, and tying the encircling band. Intraocular fluid or sterile air can also be injected to build up the volume in case of extreme hypotony.
4. Pressure over the globe near the ora serrata in the quadrant of drainage helps in moving fluid out of the drainage site. If drainage slows or stops prematurely the sclerotomy can be manipulated with a fine tooth forceps to reestablish flow.
5. Pigment particles in the SRF indicate that drainage is nearing completion. Small amounts of blood may be seen escaping with the SRF and may be innocuous.
6. In case of a larger subretinal haemorrhage, ensure that blood does not pass into the macular area by rotating the globe and turning the patient's head.
7. Total drainage of subretinal fluid is not necessary. Drainage should be enough to allow the scleral buckle to close the retinal breaks effectively. If after drainage the retina follows the contour of the buckle. The drainage is usually adequate even if there is residual SRF. However if the buckling effect is not visible under the retina, additional drainage is usually needed.

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Intraocular pressure (IOP) plays a critical role in ocular health with derangements in IOP causing profound structural alterations in the eye. Measurement of IOP is hence of vital importance in ophthalmic examination. The quantitative assessment of intraocular pressure is known as tonometry; the instruments used for tonometry are known as tonometers. Each technique has inherent advantages and disadvantages, none is ideal.

History

**Schiotz** in 1905 developed the prototype of indentation tonometry. It was the first device that quantified IOP with relative reproducibility along with the added advantage of economy of design and simplicity.

**Maklakov** in 1885 introduced the first applanation tonometer in which IOP was measured by flattening a variable area of cornea by a known weight.

**Friedenwald** (1948 & 1955) identified the role of ‘coefficient of ocular rigidity’ which is a measure of the resistance of the eye to the distending forces of the tonometer. This was applied to improve the accuracy of calculation of IOP using the Schiotz tonometer.

**Kalfa** recognized the concept of ‘elastometric rise’, the equivalent of ocular rigidity in applanation tonometry and used it with the Maklakov tonometer.

**Goldmann** in 1954 introduced the applanation tonometer, the prototype of ‘constant corneal area’ applanation methods. It was an improvement over Schiotz device both in terms of validity and reproducibility.

**Grolmann** in 1972 introduced the prototype non contact tonometer while **Grant** combined the concept of Schiotz tonometry with continuous electronic monitoring to create the Electronic Indentation Tonometer. Hand-held tonometers were designed by **Halberg** in 1967 as refinements of the Maklakov and Posner (1964) tonometers.

**Assessment of IOP**

**Direct Method:**

Manometry is used as a laboratory technique to perform continuous pressure measurements over time in cadaveric eyes of humans or experimental animals. It is presently utilized to evaluate the effect of physiological and pharmacological manipulations on IOP and to study the aqueous humor dynamics in post-mortem eyes.

**Procedure** – A hollow needle is introduced into the anterior chamber and connected to a reservoir of isotonic fluid which is raised just enough to prevent any loss of aqueous from the eye. The height of the fluid column is calibrated in centimeters of water or millimeters of mercury to reflect the IOP.

**Limitations** -
1. It is not practical for routine examination.
2. If utilized in humans, it requires general anesthesia, which itself alters IOP.
3. The needle or cannula introduced into the eye causes breakdown of the blood-aqueous barrier resulting in release of prostaglandins that modify IOP.

**Indirect Methods**

**Classification**

A. **Indentation Tonometers**

B. **Appplanation Tonometers**

(i) Goldmann (Prototype)

(ii) Goldmann – Type Tonometers

   a) Perkins Tonometer
   b) Draeger Tonometer

(iii) Mackay Marg Applanator

(iv) Mackay Marg – Type Tonometers

   a) CAT 100
   b) Challenger Digital
   c) Biotronics
   d) Tono Pen (Hand-held)

(v) Maklakov Applanation Tonometer

(vi) Maklakov Type Tonometers

   a) Planometer
   b) Tonomat
   c) Halberg
   d) Barraquer
   e) Ocular tension Indicator
   f) Glaucotest

(vii) Pneumatic Tonometer (Pneumo-tonometer)
(viii) Non Contact Tonometer
   a) X-Pert Tonometer
   b) Grolman Airblast Tonometer
   c) Keeler Pulsair Tonometer (Hand-held)

C. Miscellaneous Tonometers
   (i) Continuous-IOP Monitoring devices
   (ii) Self Tonometer
   (iii) Impact Tonometer
   (iv) Vibra Tonometer

D. Newer Tonometers
   (i) Trans-palpebral Tonometer (TG Dc-01)
   (ii) Disposable Tonometers
     a) Tonosafe – Acrylic Biprism
     b) Tonosheild – Silicone Shield

E. Other Methods
   (i) Tonography
   (ii) Ocular Blood Flow (OBF) Tonograph

**Indentation/ Impression Tonometry**

**Apparatus: Schiotz Tonometer**

*Principle:* The cornea is indented in the shape of a truncated cone by standard weights (5.5g, 7.5g, 10g, 15g) which are applied via a plunger which moves freely within a shaft in the footplate. The resulting deformation of the globe is measured with a scale reading. Value of these standard weights and the scale record of globe deformation is then used to determine IOP by correlations established in the Friedenwald tables.

*Calculations:* According to Freidenwald, the steady state pressure (Po) of an eye, is raised to a higher pressure (Pt) due to volume displacement caused by corneal indentation. This volume displacement causes some distension of the globe – which itself is regulated by ‘ocular rigidity’ i.e. resistance of the eye to distending force of the tonometer. Thus, calculations must include a constant (k) i.e. “coefficient of ocular rigidity”. Friedenwald simplified these tedious calculations & gave two tables in 1948 (k=0.0245) and 1955 (k=0.0215). The former are supposed to be more accurate.

*Technique:* The patient is laid supine with the cornea anesthetized. The fingers of the examiner spread the eyelids without putting pressure on the globe while the patient is asked to fixate at a distant object. The footplate is applied to the cornea and positioned to keep the tonometer vertical. The needle on the tonometer scale oscillates with the ocular pulse and the mid-point of the excursion is used as the scale reading. If the value of the scale reading is not greater than 4 units, additional weights are added. Conversion tables are used to derive the IOP in millimeters of mercury from the scale reading and plunger weight.

**Errors**

1. Errors inherent to the instrument – due to difference in weights of different parts of tonometers; difference in size, shape and curvature of footplate; friction arising in movement of the plunger and the pointer on the scale.
2. Errors due to contraction of extraocular muscles.
3. Errors due to accommodation – contraction of ciliary muscle increases the aqueous outflow facility by pulling the trabecular meshwork and lowering IOP.
4. Error due to variation of corneal curvature – steep and thick corneas increase the fluid displacement by the tonometer, thus recording a false high IOP.
5. Errors due to high scleral/ocular Rigidity.
6. Observer’s Error or Parallax Error in reading scale.
7. Error due to blood volume alteration - variable
displacement of intraocular blood during indentation.

8. Moses Effect- false high IOP recorded if the cornea gets sucked into the space between the plunger and hole in the footplate.

   Error to the tune of ± 2 mmHg in normal range of IOP, and ± 4mmHg in higher range of IOP has been reported.

Limitations of Indentation Tonometry

1. Tables used to note IOP with reference to weight used and scale reading obtained are based on average ‘k’ values i.e. average “Coefficient of Ocular rigidity”.

   In cases with high ocular rigidity (high k) e.g. extreme myopia, high hyperopia, chronic glaucoma, vasoconstrictor therapy, ARMD, the conversion tables over-estimate IOP. In cases with low ocular rigidity (low k) e.g. high myopia, miotic therapy, retinal detachment surgery using cryopexy, after intravitreal injection of compressible gas; vasodilator therapy, scleral buckling, vitrectomy; the conversion tables underestimate IOP.

2. Corneal Variables: False high IOP is obtained with thick corneas or very steep corneas. Keratoconus is not associated with low ‘k’ – it is only an artifact while measuring IOP due to thin cornea. The finding is not seen after keratoplasty. Measurements are unreliable in significant corneal pathologies.

3. Availability of other accurate applanation tonometers and their ease of application has significantly replaced Schiotz tonometers.

Applanation Tonometry

Prototype: Goldmann Tonometer - Introduced in 1954.

Principle: Imbert-Fick Principle also referred as the Maklakov-Fick Law which says that for an ideal sphere (perfectly spherical, dry, infinitely thin walled and perfectly flexible), the pressure (P) inside sphere is equal to force (F) required to flatten/applanate the surface divided by the area (A) of flattening i.e. \( P = \frac{F}{A} \).

Calculations: Since cornea is not an ideal sphere, two other significant forces should be considered:

1. Force of capillary attraction \( (T) \) between tonometer head and tear film –additive to \( (F) \).

2. Additional force \( (C) \) independent of IOP which is required to flatten the relatively inflexible cornea-opposite to \( (F) \).

   Hence, \( F + T = PA + C \)

   i.e. \( IOP = \frac{(F + T - C)}{A} \)

‘A’ is located on the interior surface of the cornea. Goldmann applanation is designed such that \( A = 7.35 \text{ mm}^2 \) and diameter of flattening of cornea is 3.06 mm. At this value of ‘A’, the opposing forces of capillary attraction and corneal inflexibility cancel out. In addition, at this ‘A’ the IOP (mmHg) = ten times the force applied to the cornea in grams, a convenient conversion. Since only 0.5\( \mu \text{l} \) is displaced from the eye and the pressure induced by the tonometer tip is negligible, applanation tonometry is not significantly affected by ocular rigidity.

Instrument: The applanator tip contains a biprism which it forms the contact point with the cornea. The tip is connected via a rod to the body of the tonometer, which contains an adjustable spring that provides the appropriate applanating force. The force is adjusted by knob with a scale indicating the force applied in grams.

Clinical Measurement: The applanator is attached to slit
lamp aligning the axis of the tip with the oculars and allowing visualization of the semicircles or mires. Maximum illumination with cobalt blue filter is adjusted in the slit lamp. The patient is positioned at the slit lamp, the cornea is anesthetized and tear film is stained with 0.25% sodium flourescein.

The patient is instructed to fixate at distance, relax and breathe normally. Breath holding or valsalva by patient should be avoided. The tip is advanced to approximate the cornea. The biprism splits the circle of contact into two semicircles/mires. When the inner margins of these semicircles touch, a 3.06 mm diameter circle of cornea is applanated. The mires appear green against a blue background. If mires are unequal in size, vertical adjustments are made. 1-gm position is used before each measurement. It is more accurate to increase rather than decrease the force of applanation. The tonometer knob is rotated until the end point is achieved. Ocular pulsations are noted and the internal margin of each mire is aligned.

Sources of Error
1. Wide, blurred mires and vertical misalignment result in false high readings.
2. Corneal Variables: Thin corneas and corneas thickened by edema produce false low IOP readings while thick corneas due to increased collagen result in false high readings. For every 3 diopter increase in corneal power the average IOP is increased by 1mm Hg.
3. Corneal astigmatism results in a 1mm error for every 4 diopters, underestimating for with-the-rule and overestimating for against-the-rule astigmatism. To minimize this error, the biprism is rotated until the dividing line between the prisms is 45º to the major axis of the ellipse.
4. Prolonged contact with cornea gives false low IOP readings, apart from causing corneal injury.
5. Calibration should be done at least monthly.

Other Applanation Tonometers
1. Perkins Applanation Tonometer – It uses the same biprism as the Goldmann tonometer. The light source is powered by battery and a counter balance enables its usage in both horizontal and vertical positions. Readings are consistent and comparable with the Goldmann applanator.
   It is especially useful for infants, children and invalid patients who cannot sit at the slit lamp. It was introduced by Perkins in 1970.
2. Draeger Applanation Tonometer – It is similar to the Goldmann and Perkins applanator except that a different biprism is used. This instrument is also portable and useful in similar situations as the Perkins. It was introduced by J. Draeger (Germany) in 1966.

This hand held tonometer weighs only 700gms.

Mackay Marg Tonometer

Principle: The MacKay-Marg Tonometer applanates the cornea via a plunger that moves within a sleeve, similar in fashion to a Schiotz Tonometer. The excursion of this plunger is electronically coupled to a transducer and graphically records the movement of plunger on a moving paper strip. The plunger indents the cornea, recording on the graph paper the sum of force required to flatten the cornea and the intraocular pressure. As the tonometer advances, the sleeve abuts the cornea transferring the force required to flatten cornea to the sleeve. The pressure tracing then decreases to a level that represents the IOP which occurs when a corneal diameter of 3mm is applanated.

Sources of Error: Greater than 3mm corneal flattening causes false increase in IOP. Since IOP is recorded instantaneously, multiple readings should be averaged to compensate for fluctuation due to ocular pulsation.
Specific Utility: In irregular and edematous corneas.

Mackay-Marg-Type Tonometers
1. Cat 100 Applanation Tonometer
2. Challenger Digital Electronic Applanation tonometer
3. Biotronics

These tonometers have an internal logic program that automatically selects the acceptable measurements while deleting the inappropriate ones.

4. Pneumatic tonometer: Works on a principle similar to the MacKay Marg wherein a central sensing device measures the IOP while the force required to bend the cornea is transferred to a surrounding structure. The plunger is replaced by a column of air and the contact surface is a polymeric silicone (Silastic) membrane. The air column is continually vented via a port and changes in pressure in the column resulting from the applanation are recorded via a transducer on a moving strip of paper. It finds special use in deformed corneas.

5. Tono-Pen: It is a miniature hand-held MacKay-Marg type tonometer, weighing 16grams. A microprocessor analyzes the waveform internally. Four to ten pressure estimations are obtained by briefly touching over the cornea, averaged and digitally displayed as mean of accepted estimations and their coefficient of variance (5%, 10%, 20%, & >20%).

Manometric eye bank studies have indicated that the TonoPen is most accurate between 10-50 mmHg. Various studies have reported no statistical difference between Goldmann & Tono-Pen readings in the range of 10-35mmHg. In another clinical study of 142 eyes, 63% of Tonopen readings were within ±2mmHg of the Goldmann readings and 77% were within ±3mmHg of the Goldmann readings with the best correspondence occurring between
11-20mmHg. The Tonopen overestimated between 4-10mmHg and underestimated between 21-30mmHg.

6. The ProTon tonometer works on the same principle as the MacKay Marg but differs from the Tonopen in that the probe and display units are separated.

Maklakov Applanation Tonometry

**Principle:** The IOP is estimated by measuring the area of cornea that is flattened by a known weight. In this type of tonometry, the volume displacement is large enough to consider the ocular rigidity in calculating IOP. Kalfa utilized different weights to calculate the ocular rigidity and termed it the ‘elastometric rise’.

**Instrument & Technique:** It has a dumble shaped metal cylinder with flat endplates of polished glass on either ends with a diameter of 10mm. A set of 4 such instruments with weights of 5g, 7.5g, 10g & 15g are available. A layer of dye (suspension of argyrol, glycerin and water) is applied over either end-plate which is placed vertically over the anesthetized cornea of supine patient. This produces a circular white imprint over end plate corresponding to the area that was flattened. The diameter of this white area is measured with a transparent measuring scale to 0.1mm and the IOP is read from conversion tables corresponding to the weight used.

Maklakov Type Tonometers

These are applanation tonometers in which variable areas of the cornea are applanated.

1. Maklakov-Kalfa – Prototype
2. Applanometer – Ceramic end plates are used instead of polished glass.
3. Tonomat – It has disposable end plates.
6. Ocular Tension Indicator – Uses Goldmann biprism and standard weights; used only for screening. Detects whether readings are greater or less than 21mmHg
7. GlaucoTest – A screening tonometer with multiple end plates for selecting different ‘cut off’ pressures.

Non-Contact Tonometer

Introduced by Grolman in 1972, it has the unique advantage of not touching the eye of the patient.

**Principle:** A puff of room air directed over the patients’ anaesthetized cornea, momentarily deforms the cornea. The time from an internal reference point to the moment of presumed flattening is measured and converted to IOP based on prior comparisons with readings from the Goldmann applanation tonometer.

The original NCT has 3 components and is mounted on a table

(i) **Alignment system** – Allows the operator to align the patient’s cornea in three dimensions i.e. Axial, vertical & lateral.

(ii) **Optoelectronic applanation monitoring system** which consists of a transmitter which directs a collimated beam of light at the corneal vertex and a receiver and detector which accepts only parallel, coaxial rays reflected from cornea.

(iii) **Pneumatic system** which generates a puff of room air.

Pulsair Tonometer

It is a newer, portable hand-held, non-contact tonometer which has a precision within ± 1mmHg of the Goldmann applanation tonometer.

X-Pert Tonometer

In this instrument, an air puff is automatically triggered when alignment criteria are met. The force of air required to achieve peak light detection is the measured variable.

Limitations of NCT

1. The time interval for an average NCT measurement is 1-3 millisecond which is 1/500th of one cardiac cycle. The measurements are random with respect to the phase of the cardiac cycle so that ocular pulse becomes a significant variable i.e. it can’t be averaged with some tonometers.

2. Glaucomatous eyes have greater momentary fluctuations in IOP. Hence it is recommended that a minimum of three readings with in 3mmHg be taken and averaged as IOP.

Miscellaneous Tonometers

1. **Continuous IOP monitoring devices**
   (i) A strain gauge is placed in a contact lens to measure changes in the meridional angle of the corneo-scleral junction or
   (ii) A strain gauge might be embedded in an encircling scleral band to measure distension of globe or
   (iii) A scleral appplanation device maybe attached to a passive radio telemetry pressure transducer or
   (iv) An instrument with appplanation suction cups to allow bilateral recording of IOP for upto one hour in supine subjects.

2. **Self Tonometer:** An applanation tonometer which can be used by the patient himself without assistance.

3. **Home Tonometry** can be practiced by teaching a family member the technique of Schiotz tonometry.

4. **Impact Tonometry:** Estimates IOP by measuring
duration of contact of spring driven miniature hammer with eye.

5. **Vibra Tonometer**: Measures IOP by frequency of vibrating probe in contact with cornea.

**Comparison of Tonometers**

*For Regular Corneas*

1. **Schiotz Vs Goldmann**: Schiotz reads lower than the Goldmann applanation tonometer even when postural influence is eliminated. Variation is maximum in the 50-60 years age group.

2. **Perkins Vs Goldmann**: Difference of Perkins with the Goldmann when expressed as root mean square difference was 1.4 mm Hg. Perkins is accurate in both horizontal & vertical positions and has special utility in infants & children in the operating theater.

3. **Draeger Vs Perkins**: Draeger has a more complex apparatus and is more difficult to use than Perkins. Also, patient acceptance is worse in Draeger's.

4. **MacKay Marg**: When used without anesthesia mean IOP measured was approximately 2mmHg more than that obtained by same instrument with anesthesia.

7. **Tonopen**: It compares favourably against manometric reading in human autopsy eyes. It underestimates Goldmann in higher ranges and over estimates Goldmann readings in lower range.

8. **Pneumatic Tonometer**: Gives comparable and reproducible readings.

9. **Non Contact Tonometer**: Reliable within normal range of IOP but reliability decreases with high pressure ranges, abnormal corneas and poor fixation.

**Tonometry on Irregular Cornea**

In cases of scarred or edematous corneas, the MacKay Marg Tonometer is considered to be the most accurate. Pneumatic tonometers are also useful in patients with diseased corneas. The Tonopen also compared favorably with MacKay Marg on irregular corneas.

**Tonometry Over Soft Contact Lenses**

The MacKay Marg tonometer, the Pneumatonograph and Tonopen can measure IOP through bandage contact lenses with reasonable accuracy. Applanation measurements are said to be affected by the power of contact lenses with high water content. Correction tables have been developed to compensate for this. Non Contact tonometer readings with and without soft contact lenses indicated that the power of the lens influenced the difference in IOP between paired readings, with hyperopic lenses giving the greatest difference.

**Tonometry with Gas-filled eyes**

Intraocular gas significantly alters scleral rigidity and indentation tonometry is hence unreliable. The Pneumatic tonometer and Tonopen compare favorably with Goldmann applanation readings.

**Other Ocular Conditions**

1. In premature Infants with stage 5 Retinopathy of prematurity, applanation Tonometry was preferable to indentation.

2. In eye bank eyes with flat anterior chamber, none of the tonometric devices correlate well with manometrically-determined pressures.

**Disposable Tonometry Devices**

The risk of cross infection with use of devices that touch the surface of eye has lead to the search for disposable tonometers. Commercially available devices include

1. **Tonosafe**: It has an acrylic biprism and IOP measurements show an accurate correlation with Goldmann applanation readings.

2. **Tonoshield**: Utilizing a silicone shield, this tonometric device tends to overestimate IOP when compared with standard Goldmann application.

**Sterilization of tonometers**

Contaminated tonometers are vectors of infections and have the potential to transmit them from patient to patient. Various agents which have been isolated from tears include Adenovirus 8, HSV I, HBV and HTLV III. Soaking the applanation tip in diluted sodium hypochlorite, 70% isopropyl alcohol or 3% H2O2 can completely disinfect the tonometer. 10 minutes of rinsing in tap water can remove all detectable HBV surface antigens.

**Bibliography**


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Dorzolamide
Sudipta Ghosh, MBBS, DOMS.

Description
DORZOLAMIDE (Dorzolamide hydrochloride ophthalmic solution) is a carbonic anhydrase inhibitor formulated for topical ophthalmic use.

Dorzolamide hydrochloride is described chemically as:
(4S-trans)-4-(ethylamino)-5, 6-dihydro-6-methyl-4H-thieno [2, 3-b] thiopyran-2-sulfonamide 7, 7-dioxide monohydrochloride. Dorzolamide hydrochloride is optically active.

Its empirical formula is C_{10}H_{16}N_{2}O_{4}S_{3}OHCl and its structural formula is shown in Figure 1:

It is a white to off-white, crystalline powder, which is soluble in water and slightly soluble in methanol and ethanol.

The sterile ophthalmic solution is supplied as a sterile, isotonic, buffered, slightly viscous, aqueous solution of Dorzolamide hydrochloride. Each ml of Dorzolamide 2% contains 20 mg Dorzolamide (22.3 mg of dorzolamide hydrochloride). Inactive ingredients added to adjust the pH include hydroxyethyl cellulose, mannitol, sodium citrate dihydrate, sodium hydroxide and water for injection. Benzalkonium chloride 0.0075% is added as a preservative.

Table 1: Physical Properties of Dorzolamide
- Molecular weight: 360.9
- Melting point: 264 Degree centigrade
- pH: 5.6
- Osmolarity: 260 - 330mOsM

Mechanism of Action
Dorzolamide ophthalmic solution contains Dorzolamide hydrochloride, an inhibitor of human carbonic anhydrase II. It catalyzes the reversible reaction involving the hydration of carbon dioxide and the dehydration of carbonic acid. In humans, carbonic anhydrase exists as a number of isoenzymes, the most active being carbonic anhydrase II (CA-II), found primarily in red blood cells (RBCs), but also in other tissues. Inhibition of carbonic anhydrase in the ciliary processes of the eye decreases aqueous humor secretion, presumably by slowing the formation of bicarbonate ions with subsequent reduction in sodium and fluid transport. The result is a reduction in intraocular pressure (IOP).

Pharmacokinetics/Pharmacodynamics
When topically applied, dorzolamide reaches the systemic circulation. Dorzolamide accumulates in RBCs during chronic dosing as a result of binding to CA-II. Dorzolamide binds moderately to plasma proteins (approximately 33%). It is primarily excreted unchanged in the urine; the metabolite also is excreted in urine. After dosing is stopped, dorzolamide washes out of RBCs non-linearly, resulting in a rapid decline of drug concentration initially, followed by a slower elimination phase with a half-life of about four months.

Indications and Usage
- Ocular Hypertension
- Open angle glaucoma
- Pediatric glaucoma

Dosage and Administration
The dose is one drop three times daily.
Dorzolamide may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure.

Storage
Temperature: 15-30° C or 59-86° F.
The drug needs to be protected from light.

Side Effects
More common: Itching, redness, swelling, or other sign...
of eye or eyelid irritation.

Less common: Burning, dry or itching eyes; discharge from the eye; excessive tearing; redness, pain, or swelling of eye, eyelid, or inner lining of eyelid.

Rare
- **Ophthalmic**: Blurred vision; eye pain; tearing; change in vision; flashes of light; floaters in vision; burning, stinging, or discomfort when medicine is applied; feeling of something in eye; sensitivity of eyes to light; dryness of eyes; eyelid reactions;
- **Systemic**: Skin rash; symptoms of kidney stonecough; difficult or labored breathing; hives or welts; itching skin; large, hive-like swelling on face, eyelids, lips, tongue, throat, hands, legs, feet, sex organs; noisy breathing; redness of skin; shortness of breath; tightness in chest; wheezing; bitter taste; headache; nausea; unusual tiredness or weakness.

**Algorithm: Mechanism of Action of Dorzolamide**

**Active Isoenzyme: Carbonic Anhydrase II Anhydrase**

**Inhibition of Carbonic Anhydrase in The Ciliary Processes of the Eye**

**Slow Formation of Bicarbonate and Reduction in Sodium and Fluid Transport**

**Decreased Aqueous Humor Secretion**

**Reduction in Intraocular Pressure**

**Warnings**

Dorzolamide is a sulfonamide and although administered topically is absorbed systemically. The same types of adverse reactions that are attributable to sulfonamides may occur although rarely, including Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias.

**Precautions**

**Pregnancy**

There are no adequate and well-controlled studies of the usage of topical Dorzolamide in pregnant women.

**Lactating Mother**

It is not known whether this drug is excreted in human milk. Therefore, a decision should be made whether to discontinue nursing or to discontinue the drug.

**Pediatric**

Safety and IOP-lowering effects of Dorzolamide have been demonstrated in pediatric patients in a 3-month, multi-center, double masked, active-treatment-controlled trial.

**Geriatric**

No overall differences in safety or effectiveness have been observed between elderly and younger patients.

**Contraindications**

Dorzolamide is contraindicated in patients who are hypersensitive to any component of this product.

**Suggested Reading**

Management Protocol for Chemical Burns

On presentation, treatment should be given, irrespective of previous irrigation or any other form of treatment.

Immediate Treatment
1. Irrigation with NS/water/BSS for atleast 30 mins. or till pH turns neutral.
2. Eyelid immobilization with eyelid speculum or retractor.
3. Instillation of topical anaesthesia.

Evaluation of the extent and depth of burn is done under slitlamp. Fluorescein staining is done. Limbal stem cell ischemia is looked for and graded by the newer classification.

Grade-I Involves little or no loss of limbal stem cells and presents with little or no evidence of ischemia

Grade-II Involves subtotal loss of limbal stem cells and presents with ischemia of less than one half of the limbus.

Grade-III Involves total loss of limbal stem cells with preservation of proximal conjunctival epithelium and presents with ischemia of one half the entire limbus.

Grade-IV Involves total limbal stem cell loss as well as loss of proximal conjunctival epithelium and extensive damage to entire anterior segment.

Aim of treatment is to restore the cornea with normal epithelium and a clear stroma by decreasing the inflammation and enhancing the healing.

Treatment after irrigation is as follows:
1. Topical steroids 2 hourly
   inhibits PMN proliferation and function
2. Topical sodium citrate 10% 2 hourly
   inhibits PMN degranulation by Ca chelation
3. Tetracycline 1% ointment QID
   inhibits collagenase enzyme by chelating with Zn.
4. Oral sodium ascorbate 500mg QID
   promotes collagen synthesis
5. Topical sodium ascorbate 20% 2 hourly
   promotes collagen synthesis
6. Tear substitutes 2 hourly
   promotes epithelial healing
7. Cycloplegics TDS or BD
   relieves pain
8. Topical/oral antiglaucoma therapy, if needed
9. Conjunctival/tenons advancement for grade-IV.
   Improves vascularization

After 1 week, reassess the patient. The severity of injury will show the following healing patterns.

Grade-I Healed cornea with normal epithelium.
Grade-II Epithelial defect, smaller in size.
Grade-III No epithelization, inflammation.
Grade-IV Sterile corneal ulcer + conjunctival defect, inflammation.

Management at this stage would be follows:
1. Taper steroids in the next week.
2. Rest same treatment is continued for 3 weeks.

After 3 weeks to several months

Grade-I/II Healed cornea/healed with pannus.
Grade-III No healing, finally heal as a scarred and vascularized cornea.
Grade IV Sterile corneal ulcer or vascularized cornea after conj. Advancement.

Management Options
For Grade-I/II taper medical treatment
For Grade-III/IV

Impending or actual perforation
1. Tissue adhesives for <1mm perforations
2. Tectonic keratoplasty

Vascularised Cornea
1. Limbal stem cell transplantation followed by
   Penetrating keratoplasty (PK) or
   Lamellar keratoplasty (LK) after 6 months.
2. Large PK or large LK
3. Keratoprosthesis in Bilateral cases.

For symblepharon/cicatrision of conjunctiva
   Amniotic membrane transplant/mucus membrane transplant can be done.