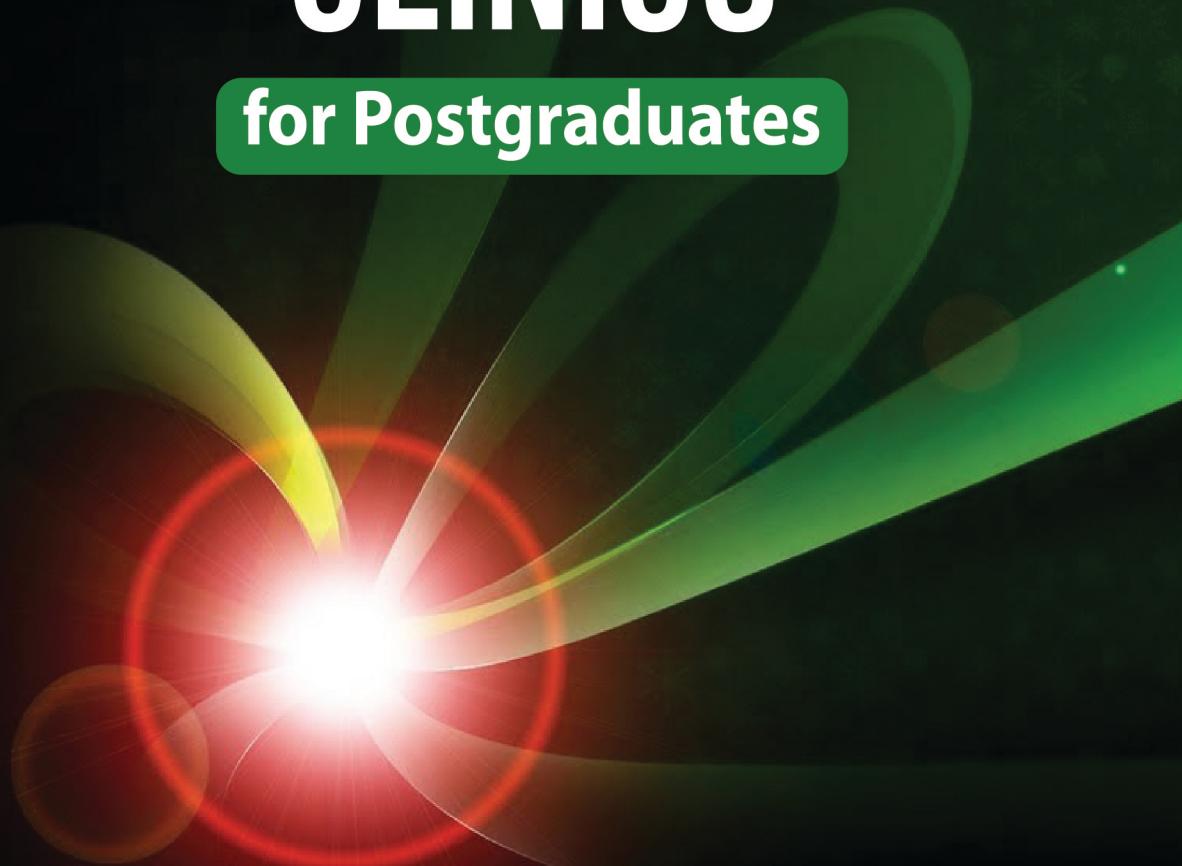


OPHTHALMOLOGY CLINICS

for Postgraduates



**Prafulla Kumar Maharana
Namrata Sharma
Atul Kumar**



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Dedicated to

My parents, Mr Devendra Maharana and Mrs Binadini Maharana

—**Prafulla Kumar Maharana**

*My parents, Dr Ramesh C Sharma and Mrs Maitreyi Pushpa
My husband, Dr Subhash Chandra; and, Daughter, Vasavdatta*

—**Namrata Sharma**

*My late parents, Mr Sanat Kumar and Mrs Swarna Kumar
My wife, Mrs Parul Kumar; and, Children, Aman and Arshi*

—**Atul Kumar**

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Preface

"The whole art of medicine is in observation."

—Sir William Osler

Postgraduate exam is one of the most difficult and stressful milestones in the medical profession. It entails tremendous amount of stress on the candidates who appear for the exam. The never-ending knowledge of ophthalmology makes it quite difficult to revise all the cases from the standard textbooks before the exams. Further, the presentation of cases—long case or short case—is completely in a different format from what is given in the standard textbooks. Most of the time, the candidate fails to present the case properly in spite of good theoretical knowledge. The primary reason for this is that the format in which a topic is discussed in textbooks is completely different from that required for a practical exam.

This book attempts to present the important topics in a format that is exactly same as required in the practical exams. The primary focus is on history taking and proper clinical examination of the cases. Every effort has been made to describe the procedures of clinical examinations in such a way that the candidate can perform these examination techniques accurately in front of the examiner. Special emphasis has been given to the differential diagnosis of the cases, which is often a favorite question amongst the examiner. Clinical photographs of the cases as well as the important signs and investigation findings have been provided that will help the students for better understanding of the cases. The cases are being selected after discussing with experts in this field as well as candidates who have recently appeared in various postgraduate exams. Each chapter ends with a section on viva-voce questions that will help the candidates to mentally prepare for the viva before the final exam. In addition, a chapter on instruments has been included which is invariably a part of all postgraduate practical exams. The editors and all the contributors have made sincere efforts to make things simple and concise and to facilitate quick and thorough revision. However, it must be remembered that this is not a substitute to standard textbooks. The readers are encouraged to read standard textbooks before going through this book. This will make their understanding and application of this book more rewarding.

The editors wish best of luck to the students for their exams!

**Prafulla Kumar Maharan
Namrata Sharma
Atul Kumar**

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CHAPTER

1

Oculoplasty

LONG CASES

PROPTOSIS

Varsha Varshney, Amar Pujari, Mandeep S Bajaj

INTRODUCTION

Proptosis is defined as an abnormal forward protrusion of one or both eyeballs with respect to the orbit. Among adults, the usual distance from the lateral orbital rim to the corneal apex is approximately 16–21 mm.^{1,2} Proptosis is said to be present when following criteria are present.

1. Protrusion more than 22 mm beyond the orbital rim.
2. An asymmetry of more than 2 mm between the eyes.

Proptosis is one of the common topics given as a long case in exams.

HISTORY

Chief Complaint

A case of proptosis usually presents with following complaints:

- Protrusion of one or both the eyes.
- *Loss of vision:* It indicates *optic nerve compression/involvement* [by *intrinsic lesions* of optic nerve such as meningiomas or optic nerve gliomas or *external compression*, e.g. tumors located in the orbital apex, such as a

hemangioma and Graves' disease] or *induced astigmatism* due to globe compression or *exposure keratopathy*.

- Rare presentation includes diplopia, restricted ocular motility, redness/pain/discharge due to associated exposure keratopathy.

History of Present Illness

Following points must be noted while examining a case of proptosis.

- *Age of onset:* Age of onset can point towards the probable diagnosis as shown in **Table 1**.
- *Nature of onset*
 - *Sudden (hours to days):* It suggests inflammatory and infective process, trauma (orbital emphysema, fracture of the medial orbital wall, orbital hemorrhage) or rupture of ethmoidal mucocele.
 - *Gradual (over many months to years):* It suggests tumors, lymphoma—proliferative disorders.
- *Progression*
 - *Slow continuous:* It suggests tumor, however, gradual progression with sudden increase in proptosis can harbor malignant transformation

Table 1 Causes of proptosis based on the age of onset

Newborn	Children	Young adults	Middle age	Senile
<ul style="list-style-type: none"> Orbital cellulitis Orbital neoplasm 	<ul style="list-style-type: none"> Rhabdomyosarcoma Hemangioma Dermoid cyst Orbital cellulitis Optic nerve glioma Craniosynostosis lymphomas 	<ul style="list-style-type: none"> Thyroid ophthalmopathy Pseudotumor Orbital cellulitis Osteomas Infiltrative tumors 	<ul style="list-style-type: none"> Pseudotumor Endocrine Malignant lymphomas/leukemias Optic nerve sheath meningiomas Mucocele 	<ul style="list-style-type: none"> Malignant and metastatic tumor of orbit Pseudotumor Leukemia Lymphomas Sarcomas

- Rapid progression:** It indicates infection/inflammation/hemorrhage/malignant transformation
- Intermittent:** It intermittent proptosis can be due to following causes
 - Periodic orbital edema
 - Recurrent orbital hemorrhage/chocolate cyst and highly vascular tumors
 - Increases during attacks of common cold/upper respiratory infections-lymphangioma
 - Postural (associated with bending forward) or with Valsalva suggests orbital varices.
 - Increases on crying capillary hemangiomas in young children
- Pain:** Depending upon presence of pain proptosis can be
 - Painful:** Infective, acute inflammations, chocolate cyst, orbital hemorrhages
 - Painless:** Tumor, endocrinopathy (Pain can be there in some malignant tumors that show perineural spread, such as adenoid cystic carcinoma of the lacrimal gland).
- Laterality**
Unilateral: Unilateral proptosis is seen in tumors, cysts, and vascular anomalies
Bilateral: The different causes of bilateral proptosis are summarized in **Table 2**.
- Special characteristics:** Rarely, patient can give a history of feeling the *pulsation* within the orbit or periorbital area. An example of such cases include; AV malformation, carotico-cavernous fistula and saccular aneurysm of ophthalmic artery or due to *transmitted cerebral pulsations* in conditions associated

Table 2 Common causes of bilateral proptosis

Pathology	Etiologies
Inflammations	<ul style="list-style-type: none"> Thyroid orbitopathy Wegener's granulomatosis Idiopathic inflammatory pseudotumor Myositis Sarcoidosis Sjögren's syndrome
Neoplasia	<ul style="list-style-type: none"> Lymphoma Leukemia Metastatic carcinoma Optic nerve glioma
Vascular lesions	<ul style="list-style-type: none"> Arteriovenous shunts Varix

with deficient orbital roof such as congenital meningocele or meningoencephalocele, and traumatic or operative hiatus.

History of Past Illness

A careful past history can point towards the provisional diagnosis. Following points must be asked in history of past illness:

- Systemic inflammatory disease such as thyroid disorder, sarcoidosis
- Malignancy—Lungs, breasts, prostate
- Trauma
- Periorbital tumors

Past Surgical History

Prior periorbital surgery or history of surgery for intraocular malignancy such as malignant melanoma might point to the possibility of orbital extension or metastasis.

EXAMINATION

General Examination/Specific Systemic Examination

Look for signs of Graves' disease/Sarcoidosis/Any malignancy/Any infective foci.

Ocular Examination

Following points must be noted in ocular examination:

Visual Acuity

In general, visual acuity is not affected with orbital diseases except in cases with optic nerve compression, refractive changes due to pressure on back of the eyeball or exposure keratopathy.

Eyeball

A case of proptosis should be examined under following headings:

A. Inspection

- Head posture, facial asymmetry, shape of the skull
- *Protrusion of the eye:* In unilateral cases, there will be obvious disparity between the two eyes. In bilateral cases, some difficulty may be there in early cases of proptosis. Following two methods are useful in detection of proptosis:
 1. *Naffziger's method:* Relative proptosis can be observed by simply standing behind a seated patient and gazing downward (tangentially) toward the chin from the forehead to assess protrusion of the eye beyond the orbital rim.
 2. *Worm's eye view:* It is similar to Naffziger's method but the difference is that the examiner examines up from below with the patient's head-tilted back.
- *The direction of proptosis:* The direction of proptosis can indicate the probable etiology. The direction can be following:
 - *Axial:* Thyroid related ophthalmopathy, Glioma of optic nerve (**Fig. 1**), Optic nerve sheath, meningioma, cavernous hemangioma.

- Nonaxial/Eccentric:

- ♦ *Down and out:* Dermoid, dermoli-poma, frontal and ethmoidal mucocele, meningocele
- ♦ *Down and in:* Lacrimal gland tumor, Dermoid
- ♦ *Upwards:* Carcinoma of maxillary sinus, lacrimal sac tumors, Lymphoma, maxillary sinus tumor, metastatic tumors
- ♦ *Outwards:* Lesion of anterior ethmoidal sinus, nasopharyngeal tumor, lymphangioma (**Fig. 2**), lethal midline granuloma, Metastatic tumors, secondary tumor



Fig. 1: Axial proptosis due to optic nerve glioma



Fig. 2: Abaxial proptosis due to medial orbital lymphangioma

- ♦ *Medial displacement:* Dermoid cyst, lacrimal fossa tumors, and cysts, sphenoid wing meningioma
- *Laterality:* Unilateral or bilateral
- *Ocular motility:* Ocular motility disturbance can be due to:
 - Involvement of the rectus or oblique muscles directly
 - Affecting nerve supply of rectus or oblique muscles
 - From restriction of the orbital fascial connective tissue septae
- *Eyelids:* Lids can be affected by direct involvement of the levator muscle or the third cranial nerve, or because of associated proptosis. Examination of lid is especially important in thyroid-associated eye disease. The various lid signs and their terminology has been described in **Table 3**.
- *Periorbital inflammation:* Look for inflammatory signs (erythema, edema, chemosis, dilated vessels) of the periorbital structures that can be associated with infections and acute inflammatory diseases.
- *Nose/roof of mouth* (sinus disease or when intranasal source is suspected) and neck (for goiter)
- *Valsalva:* Orbital varix or highly vascular lesions such as capillary hemangiomas will enlarge with increases in arterial pressure. This can be elicited with the Valsalva maneuver or by asking the patient to bend forward.
- *Lagophthalmos, Bell's phenomena, and exposure keratopathy*
- *Orbital thrill/Pulsation:* Place your index and middle finger over the orbit (with closed lids) and observe following
 - *True pulsation:* Finger will raise and separated
 - *Transmitted pulsation—finger will raise only*
- *Swelling/mass around the eyeball:* If present its size, site, shape, consistency, fixity (skin/bone/muscle), signs of inflammation (*Rubor*—redness; *Color*—raised temperature, check with your back surface of hand; *Dolor*—pain/tenderness; *Tumor*—swelling; *Functionless*—loss of function), and overlying skin changes must be noted carefully.
- *Regional lymph nodes:* Palpate the submandibular and preauricular lymph nodes.
 - Medial and central lower lid (along the facial vein), medial upper lid, central upper lid and medial canthus drains into the submandibular lymph nodes
 - Lateral upper lid and lateral lower lid drain into the preauricular parotid lymph nodes.
- *Orbital rim/margin* with index finger to look for any mass, or erosion (malignancy), irregularity (previous trauma)
- *Reducibility of the mass:* Check for reducibility of the mass lesion. It can provide a clue about the probable etiology, e.g. vascular tumors, schwannoma are reducible masses but lacrimal gland tumor, pseudotumor are not reducible.
- *Infraorbital/supraorbital anesthesia:* Perineural invasion by a tumor can result in pain, numbness, paresthesia in infraorbital or supraorbital area. Adenoid cystic carcinoma (ACC) of the lacrimal glands often presents with orbital pain and paresthesia, since this type of tumor is frequently associated with perineural spreading (Remember, the *lacrimal nerve* is the smallest of the three branches of the ophthalmic division of the trigeminal nerve. It passes through the lacrimal gland then pierces the upper lid and supplies the supraorbital area. It provides sensory innervations for the lacrimal gland, conjunctiva, and the lateral

B. Palpation

It should be carried out to confirm the findings of inspection and also for following:

- *Retropulsion:* In a retropulsion test, thumb/two fingers/palm is used to gently push on the globe through the upper eyelid to know compressibility/resistance of the tumor. While hemangioma, lymphangioma, orbital varices give a soft consistency; optic nerve glioma may give a firm consistency. Resistance to retropulsion suggests retrobulbar tumor or thyroid ophthalmopathy.

Table 3 Lid signs in proptosis

Sign	Description
Abadie's sign	Elevator muscle of upper eyelid is spastic
Ballett's sign	Paralysis of one or more extraocular muscle (EOM)
Beck's sign	Abnormal intense pulsation of retina's arteries
Boston's sign	Jerky movements of upper lid on lower gaze
Cowen's sign	Extensive hippus of consensual pupillary reflex
Dalrymple's sign	Upper eyelid retraction
Enroth's sign	Edema especially of the upper eyelid
Gifford's sign	Difficulty in eversion of upper lid
Goldzieher's sign	Deep injection of conjunctiva, especially temporal
Griffith's sign	Lower lid lag on upward gaze
Hertoghe's sign	Loss of eyebrows laterally
Jellinek's sign	Superior eyelid folds is hyperpigmented
Joffroy's sign	Absent creases in the forehead on upward gaze
Jendrassik's sign	Abduction and rotation of eyeball is limited also
Knies' sign	Uneven pupillary dilatation in dim light
Kocher's sign	Spasmodic retraction of upper lid on fixation
Loewi's sign	Quick mydriasis after instillation of 1:1000 adrenaline
Mann's sign	Eyes seem to be situated at different levels because of tanned skin
Means' sign	Increased scleral show on upgaze (globe lag)
Moebius's sign	Lack of convergence
Payne/Trousseau sign	Dislocation of globe
Pochin's sign	Reduced amplitude of blinking
Rieseman's sign	Bruit over the eyelid
Movement's cap phenomenon	Eyeball movements are performed difficultly, abruptly and incompletely
Rosenbach's sign	Eyelids are animated by thin tremors when closed
Saiton's sign	Frontalis contraction after cessation of levator activity
Snellen-Rieseman's sign	When placing the stethoscope's capsule over closed eyelids' a systolic murmur could be heard
Stellwag's sign	Incomplete and infrequent blinking
Suker's sign	Inability to maintain fixation on extreme lateral gaze
Tellas's sign	Inferior eyelid might be hyperpigmented
Topolanski's sign	Around insertion areas of the four rectus muscles of the eyeball a vascular band network is noticed and this network joins the four insertion points.
von Graefe's sign	Upper lid lag on downgaze
Wilder's sign	Jerking of the eye on movement from abduction to adduction

upper eyelids and adjacent supraorbital area, and partly the zygomaticotemporal area just adjacent to the orbital rim. Hence, in case ACC, these areas must be checked for sensory abnormalities).

C. Auscultation

Auscultation is done with the help of a stethoscope, over eyeball and temporal area, to look for bruit. A bruit can be seen in cases of AV malformation.

D. Transillumination

It is helpful in evaluating anterior orbital lesions. It is usually performed using a penlight. Interpretation is based on the opacity of the mass relative to surrounding tissues as follows:

- *Bright*: The area lights up more than the surrounding tissues, e.g. cyst filled with clear liquid, Dacryops
- *Equal*: The area lights up to the same degree as surrounding tissues, e.g. lipoma.
- *Indeterminate*: The area seems darker than surrounding tissues to a variable degree, e.g. inclusion cyst, dermoid cyst
- *Dark*: The area is clearly opaque, creating a shadow effect. Aneurysm, e.g. solid tumors (lacrimal gland tumors), osteoma.
- Remember some clinicians interpret transillumination test as positive or negative; in that case first two categories can be considered positive while the last two as negative transillumination test

E. Exophthalmometry

The most common type exophthalmometer used in clinical practice is Hertel's exophthalmometer. Other Exophthalmometers used in clinical practice are Luedde scale, Naugle exophthalmometer, and Gormaz exophthalmometer. However, in the absence of any of these an ordinary transparent ruler can be used to measure proptosis. The measurement, in Hertel's exophthalmometer, is done from the lateral orbital rim to the anterior corneal surface. A difference of greater than 2 mm between an individual patient's eyes suggests proptosis. Procedure—following points must be considered while using Hertel's exophthalmometer.

- The patient and the examiner must be at the same level, eye to eye.

- Locate the orbital notch with patients eyes closed (the deepest points on orbital rim) on the temporal side of the orbital rim near the lateral canthus.
- The prisms or the mirrors are slide across the bar to adjust the footplates to fit on the orbital rim. The exophthalmometer is opened so that the grooves are placed in the orbital notch.
- The separation of the exophthalmometer (baseline reading) is very important and must always be noted and the exophthalmometer must always be set at that separation on future or repeated readings.
- The patient is then asked to open the eyes and look straight ahead.
- Look into the exophthalmometer, the red lines should overlap to avoid the parallax. Look into the mirrors located at each end of the exophthalmometer. Now note the millimeter mark corresponding to the corneal apex position on the scale and the readings on the cross bar for baseline reading.

Limitations: There are several limitations to Hertel's exophthalmometer. The readings are unreliable in presence of poor fixation, uncooperative patients with convergence or repeated head movements. In addition, in presence of depressed/fractured lateral orbital rim, it cannot be done.

Luedde's exophthalmometer: It is a transparent plastic ruler which is thicker than the normal ruler. It has several advantages over an ordinary plastic ruler such as, the reading starts from the apex and the apex fits the orbital notch accurately. It is more accurate than Hertel's exophthalmometer in presence of facial asymmetry.

Naugle exophthalmometer: It uses fixation points slightly above and below the superior and inferior orbital rims (cheekbones and forehead). Naugle exophthalmometer measures the difference in proptosis between the two eyes rather than absolute measure with the Hertel method. It is preferred in presence of an orbital fracture or after lateral orbitotomy.

Interpretation: The normal range is 12–21 mm. A difference of > 2 mm between the two eyes is significant. In pediatric age group the readings may vary depending upon the age; <4 years old

(13.2 mm), 5–8 years old (14.4 mm), 9–12 years old (15.2 mm) and 13–17 years old (16.2 mm).

Conjunctiva: Examine carefully (with a slit-lamp) for following:

- Dilated or tortuous blood vessels, chemosis, dilated lymphatics-vascular malformation, inflammation
- Hyperemia over the insertions of the horizontal rectus muscles—one of the earliest sign of thyroid eye disease
- Corkscrew shaped tortuous dilated episcleral vessels-high-flow AV malformations or a carotid cavernous fistula
- Subconjunctival mass—anterior extension of a deeper orbital tumor, such as a lymphoma or intraocular melanoma with extraskeletal orbital extension (a dark subconjunctival mass)

Cornea: Look for signs of exposure keratopathy. Fluorescein staining can reveal early stage of exposure keratopathy showing multiple punctate defects. The corneal sensation must be checked in all cases of proptosis.

Sclera/Iris: Careful examination is carried out to look for signs of inflammation and any nodules

Pupil: Examination of pupil is extremely important since it often provides the first clue of a probable optic nerve involvement. The presence of relative afferent pathway defect (RAPD) must be ruled out in all cases. Any intraconal mass compressing optic nerve or any tumor intrinsic to optic nerve (optic nerve glioma) can lead to RAPD.

Intraocular pressure (IOP): If possible IOP should be recorded in different gaze (ideally in all gazes and at least in primary and superior) especially in cases of suspected thyroid ophthalmopathy (in case of thyroid ophthalmopathy variable IOP in upgaze can be an early sign due to an involvement of inferior rectus muscle). The IOP may vary due to the restricted mobility of extraocular muscles.

Lens: Lens is usually clear except the effect of aging.

Vitreous: Usually normal except in cases of intraocular tumor.

Fundus: Carefully look for signs of globe compression such as venous engorgement, choroidal folds, and papilledema or optic atrophy.

Choroidal folds and opticociliary shunts may be seen in patients with meningiomas. In cases with cavernous sinus thrombosis retinal edema, exudates and engorged retinal veins can be seen due to increased venous pressure.

DIFFERENTIAL DIAGNOSIS

Based upon history and clinical examination the differential diagnosis has to be made. The commonly seen diseases in clinical practice includes:

- Vascular (cavernous fistula, cavernous hemangiomas)
- Endocrine (thyroid eye disease)
- Inflammatory (orbital cellulitis, orbital inflammatory disease, orbital cysticercosis)
- Neoplastic (ON glioma, ON meningiomas, lacrimal gland tumors, frontal sinus mucocele)

INVESTIGATIONS

The line of investigation depends on upon the differential diagnosis arrived. Following tests must be done routinely in a case of proptosis.

- Thyroid function tests,
- Complete blood count (CBC), peripheral smear (leukemia/lymphoma), erythrocyte sedimentation rate (ESR), blood sugar

Specific Tests

Imaging Technique

Noninvasive techniques

- *Plain X-rays:* It is often the initial radiological examination, especially when other modalities are not available. Commonly done exposures are in the Caldwell view, the Water's view, a lateral view and the Rhese view (for optic foramina). The findings of orbital diseases in X-ray include enlargement of orbital cavity, calcification, hyperostosis and enlargement of optic foramina.
- *Ultrasonography:* It is a nonradiational noninvasive, completely safe and extremely valuable initial scanning procedure for orbital lesions. In the diagnosis of orbital lesions, it is superior to computed tomography (CT) scanning in actual tissue diagnosis and can usually differentiate between solid, cystic,

infiltrative and spongy masses. The limitations of USG are; limited ability to evaluate orbital bones, periorbital sinuses, and the orbital apex due to poor distance penetration.

- *Computed tomography scanning:* It is extremely helpful in determining the location and size of an orbital mass. A combination of axial and coronal cuts enables a three-dimensional visualization. In addition to globe, extraocular muscles, and optic nerves visualization it can show areas adjacent to the orbits such as orbital walls, cranial cavity, paranasal sinuses and nasal cavity. Mass lesions in the orbit usually appear as an abnormal density within the typically low-density orbital fat. The lesion may be well defined with sharp borders (e.g. cavernous hemangioma), or infiltrative with diffuse borders (e.g. pseudotumor). CT can give information about adjacent bone erosion (suggestive of malignancy), remolding or fossa formation (encapsulated benign lacrimal gland tumor such as pleomorphic adenoma, encapsulated malignant lacrimal gland tumor, orbital dermoid), or displacement of adjacent bony orbital walls. Its main disadvantage is the inability to distinguish between pathologically soft tissue masses which are radiologically isodense. In addition, the risk of radiation exposure (in contrast to MRI) is always there. Examples of few findings on CT in cases of proptosis includes.
- *Magnetic resonance imaging (MRI):* MRI is very sensitive for detecting differences between normal and abnormal tissues. Advantages of MRI over CT includes:
 - Better soft tissue visualization, especially in the region of the orbital apex, optic canal, and cavernous sinus.
 - Various fat suppression techniques allow the visualization of gadolinium-enhanced lesions that is often difficult to see the normally high signal-generating orbital fat.
 - Better tissue differentiation
 - No radiation exposure.

Invasive procedures

- *Orbital venography:* Useful in orbital varix. It confirms the diagnosis and also outlines

the size and extent of the lesion that helps in proper surgical planning.

- *Carotid angiography:* Useful in cases of pulsatile proptosis and in those associated with a bruit or thrill. It helps to identify the location and extent of ophthalmic artery aneurysms, AV malformations. It is also helpful in identifying the feeding vessels thus, for planning surgery in cases of vascular orbital tumors.

Histopathology

The exact diagnosis of many orbital lesions cannot be made without the help of histopathological studies which can be accomplished by following techniques:

- *Fine-needle aspiration biopsy (FNAB):* Quick, reliable, and relatively accurate. The biopsy aspirate is obtained under direct vision (when there is an obvious mass) or guided by CT/USG using a 23-gauge needle.
- *Incisional biopsy:* The scope of incisional biopsy in the diagnosis of orbital masses is not clearly defined. It is often contraindicated due to the risk of tumor seeding or increased risk of malignant transformation (e.g. benign lacrimal gland tumor).
- *Excisional biopsy:* It is the procedure of choice especially when the mass is well encapsulated or circumscribed. It is performed by orbitotomy.

CLASSIFICATION/STAGING/SCORING

It depends upon the individual disease.

MANAGEMENT

The management depends upon the individual diseases.

VIVA QUESTIONS

Q.1. Explain pseudoproptosis.

Ans. Pseudoproptosis is either the simulation of an abnormal prominence of the eye or a true asymmetry that is not caused by a mass, a vascular abnormality, or an inflammatory process.

Causes are multiple and include:

Enlarged globe

- Myopia
- Trauma
- Glaucoma

Asymmetric orbital size

- Congenital
- Postradiation
- Postsurgical

Asymmetric palpebral fissure

- Contralateral ptosis
- Lid retraction
- Facial nerve paralysis
- Lid scar, ectropion, entropion

Extraocular muscle abnormalities

- Postsurgical muscle recession
- Paralysis or paresis

Contralateral enophthalmos

- Contralateral orbital fracture
- Contralateral small globe
- Contralateral cicatricial tumor

Physiological proptosis: It is proptosis in infants due to the fact that orbital cavities do not attain their full size so rapidly as the eyes.

Q.2. Most common cause of proptosis.

- Ans.** • *Unilateral proptosis:* Thyroid eye disease
• *Bilateral proptosis:* Thyroid eye disease

Q.3. Causes of pulsatile proptosis.

Ans. *True vascular*

- Carotid cavernous fistula
- AV fistula in the orbit between ophthalmic artery and orbital vein, in the neck—Carotid artery and jugular vein
- Highly vascular orbital tumor

- Orbital varix

Transmitted

- Congenital failure in the development of roof of the orbit, e.g. encephalocele/encephalomyelocoele
- Traumatic or operative hiatus in orbit roof resulting in the formation of meningocele

Q.4. The 6 P's of the orbital history and physical examination are

Ans. Useful in the diagnostic process

- Pain
- Proptosis
- Progression
- Palpation
- Pulsation
- Periorbital changes

Q.5. Few facts about orbit dimensions.

- Ans.** • Volume—30 cc
• Horizontal entrance width—40 mm
• Height at orbital rim—35 mm
• Orbital depth (rim to the optic strut)—45–55 mm
• Orbital segment of optic nerve—25 mm

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LID TUMORS

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INTRODUCTION

Lid tumors can arise from the epidermis, dermis, or adnexal structures of the eyelid. Malignant lesions are common around the eyes, because many are induced by sun exposure or develop from sun-related benign lesions. Typically, most of these are small and slowly growing.

The common periocular malignancies are basal cell carcinoma (BCC), squamous cell carcinoma (SCC), sebaceous gland carcinoma (SGC), and malignant melanoma. In western literature, basal cell carcinoma constitute around 85% of the cases because of fair complexion. Whereas in India all three major variants constitute around 33% each.^{1,2}

HISTORY

Demography

Commonly, present in 5th to 6 decade of life with site of involvement:

- Involvement pattern in basal CC (lower eyelid, caruncle, upper eyelid, lateral canthus) (**Fig. 1**)
- Involvement pattern in sebaceous CC (upper eyelid, lower eyelid) (**Fig. 2**)
- Involvement pattern in squamous CC (lower eyelid, caruncle, upper eyelid) (**Fig. 3**).

Chief Complaints

A case of lid tumor can present with presents with following complaints:

- Slow, generally painless growth on lid margins



Fig. 1: Pigmented basal cell carcinoma of the left lower eyelid



Fig. 2: Sebaceous gland carcinoma of the left upper eyelid

- Ulceration of the lid margins
- Loss of eyelashes
- Distortion of eyelid margin
- Ectropion/retraction (secondary due to lid growth or skin contracture)
- Increasing pigmentation of eye lid margins
- Palpebral preauricular lymph nodes
- Dilated blood vessels (telangiectasias).

History of Present Illness

Following points must be noted for a lid tumor:

- *Onset:* Common lid tumors are insidious in onset
- *Progression:* Progression is usually slow
- Any deterioration of vision
- Diplopia or restriction of eye movements (frozen globe)
- Any other swelling around the head and neck region (preauricular and cervical lymph node for metastasis)
- Systemic features of metastasis.

Past History

Predisposing factors: Following are the predisposing factor for lid tumours:

- Ultraviolet exposure (UV-B)
- Ionizing radiation
- Arsenic exposure
- Psoralen plus ultraviolet A (PUVA)
- Human papilloma virus
- Genetic diseases (albinism, xeroderma pigmentosum risk factor for BCC)



Fig. 3: Squamous cell carcinoma of the eyelid with extensive periorbital involvement

- Recurrent Chalazion (could be sebaceous cell carcinoma)
- Previous surgery for eyelid malignancies
- Topical chemotherapy.

Important Examination Findings

- *Eyelid*: Careful examination of the eyelid for signs of lid malignancy
- Eyelid should be examined carefully for depth or plane of involvement, lid margin involvement, and medial and lateral canthal involvement.
- *Bulbar and palpebral conjunctiva*: In cases of sebaceous cell carcinoma to look for "Pagetoid spread" (Intraepithelial spread of tumor cells).
- *Cornea*: Again in case of sebaceous cell carcinoma
- *Look for scleral invasion and globe integrity*: In cases where the tumor is extending beyond the orbital septum.

DIAGNOSIS

The best way to confirm the diagnosis is excision biopsy.

Histopathology

- *BCC*: The tumor cells arise from the basal layer of the epidermis. The cells proliferate downwards thus exhibiting palisading at the periphery.
- *Squamous cell carcinoma*: The tumor arises from the squamous layer of epidermis, well differentiated tumors show characteristic keratin 'pearls'.
- *Sebaceous cell carcinoma*: The tumor shows irregular lobules consisting of sheets of cells with varying degrees of sebaceous differentiation. The malignant cells show foamy, multivacuolated cytoplasm, secondary to intracytoplasmic lipid.

Biopsy Methods

- *Incision biopsy*: Where only a part of the tumor is removed using either blade or biopsy punch.
- *Excision biopsy*: Here the entire tumor is removed.

- *Impression cytology*: After drying the area to be examined, nitrocellulose filter paper is applied, and then firmly presses with Goldmann tonometer head. Peel off paper with forceps and place in appropriate fixative solution for examination.
- *Fine needle aspiration cytology*: In case of large tumor as a preliminary modality or in cases of lymph node involvement.

Imaging

Computed tomography is indicated in cases with postseptal extension to know the extent of orbital spread and bony involvement. PET and SPECT in cases to study the status of sentinel lymph nodes.

STAGING

Staging is required to plan the treatment strategy and prognosis. The most common staging system for carcinoma of the eyelid is the TNM system.

The following information applies for all three common eyelid carcinomas, but melanoma of the eyelid is staged in the manner as skin melanomas. TNM stands for tumor, nodes, and metastasis. This describes the size of the primary tumor, the number and location of any regional lymph nodes metastatic foci anywhere in the body.

MANAGEMENT

Surgical Excision with Standard Frozen Section Control

This technique is performed by noting the clinical boundaries of the tumor edges and excising an additional 3 mm cuff of normal-appearing tissue followed by histopathological assessment of the excised specimen for tumor free margins.

Mohs' Micrographic Surgery

This technique involves removal of the gross mass of the tumor plus a small peripheral margin of normal tissue. A thin layer of tissue, approximately 2 mm thick, is further excised from the entire base and edges of the wound. The initial specimen is divided into 4–7 µm thick portions on glass slides; the edges are marked with different colored dyes to maintain orientation. Frozen sections are

obtained from the under surface and skin edge of each specimen. Locations of residual tumor are marked on a map and only those areas are re-excised. Surgical resection is continued until there is a microscopically proven tumor-free plane. The defect is then reconstructed by the oculoplastic surgeon.

Cryosurgery

It is useful for small lesions, but less effective for larger and deeply invasive tumors.

Contraindications of Cryosurgery

- Involvement of the conjunctival fornix
- Fixation of tumor to periosteum
- Sensory or motor denervation
- Cold intolerance—cryoglobulinemia or cold urticaria
- Deeply pigmented skin
- Indistinct margins
- Diameter of lesion >10 mm
- Sclerosing or multicentric type.

Complications

- Depigmentation
- Hyperpigmentation
- Eyelid notching
- Hypertrophic scar
- Pseudoepithelial hyperplasia
- Ectropion
- Punctal and canalicular stenosis
- Lash loss.

With conjunctival involvement: The adjuvant methods followed are

- Local application of cryotherapy
- Topical mitomycin C application.

Extensive disease: Exenteration for orbital involvement and extended exenteration with radical neck dissection for metastatic disease beyond the orbit with lymph node involvement.

Radiotherapy:

Indication of radiotherapy includes following:

- Inoperable disease
- Multiple medical problems
- Elderly patients unable to tolerate surgical resection

- Patients in whom surgery will result in extensive disfigurement with potential loss of useful ocular function.

Complications of radiotherapy includes:

- Skin atrophy
- Ectropion
- Entropion
- Nasolacrimal duct stenosis
- Keratitis
- Conjunctival keratinization
- Cataract
- Loss of eyelashes
- Globe perforation
- **Chemotherapy:** Used in cases of systemic involvement
- Others like photodynamic therapy and CO₂ LASER treatment are rarely used.

PROGNOSIS

Following are the poor prognostic factor:

- Duration of symptoms >6 months
- Vascular and lymphatic infiltration
- Orbital extension
- Poor tumor differentiation
- Multicentric origin intraepithelial carcinomatous changes of the conjunctiva, cornea, or skin
- Location in the upper eyelid
- Tumor diameter >2 cm
- Location on central face or ears
- Long-standing presence prior to initial treatment
- Incomplete excision
- Aggressive subtype
- Perineural or perivascular involvement

Recurrent tumor:

- Basal cell carcinoma (BCC) of the eyelid rarely spreads to lymph nodes or other organs, so the prognosis for this type of tumor is usually very good.
- Squamous cell carcinoma (SCC) can be more aggressive than BCC and can spread to the orbit, lymph nodes or other organs. However, the prognosis is good if SCC of the eyelid is detected early and can be completely removed.
- The mortality rate (the number of people who die from the disease each year) for

sebaceous gland carcinoma of the eyelid is about 5%–10%. However, sebaceous gland tumors are often not diagnosed early and have a high rate of recurrence and spread (metastasis).

VIVA QUESTIONS

Q.1. Key points of individual malignancies.

Ans. *Basal cell carcinoma:*

- It is the common type of eyelid tumour.
- Usually affects adult population.
- Commonly involve the lower eyelid due to exposure to sunlight.

Inherited conditions predisposing to BCC:

- Albinism
- Xeroderma pigmentosum
- Basal cell nevus syndrome or Gorlin syndrome
- Bazex syndrome
- Rombo syndrome

Sebaceous gland carcinoma (SGC) (Sebaceous gland carcinoma, Meibomian gland carcinoma)[also see short case]:

Important clinical points:

- These arise from the Meibomian glands in the eyelid.
- It is more often in elderly women than men and often present late due to less malignant course.
- These tumors commonly arise from the upper eyelid followed by the lower eyelid the caruncle and bulbar conjunctiva. The upper eyelid is more prone due to more number of Meibomian glands in the upper eyelid (20–25) as compared to (15–20) in lower eyelid.
- SGC can be multifocal due to peculiar pattern of spread called “Pagetoid spread” where there is an intraepithelial spread of the tumor.
- The gross appearance resembles yellowish nodular mass
- May resemble blepharoconjunctivitis.
- Can involve the orbit and regional lymph nodes.

Q.2. Signs of lid malignancy

Ans. Following are the signs:

- Destruction of lid architecture
- Ulceration of the lid margins
- Loss of eyelashes
- Distortion of eyelid margin
- Ectropion/retraction (secondary due to lid growth or skin contracture)
- Increasing pigmentation of eye lid margins
- Palpebral preauricular lymph nodes
- Dilated blood vessels (telangiectasias)

Q.3. Differentiation of three lid malignancies based on clinical findings

Ans. See Text

Q.4. Sentinel lymph node biopsy

Ans. Sentinel lymph node (SLN) biopsy is used for identifying the microscopic nodal metastasis from a malignant tumor. Tumors may preferentially spread to a first draining or “sentinel” lymph node before they spread to distant sites.³

Preoperatively: 99mTc-Sulfur colloid ($t_{1/2}$ 6 hours) will be injected around the tumor followed by hybrid SPECT/CT is performed to locate sentinel lymph nodes (Preauricular, intraparotid and submandibular).

Intraoperatively: In the first setting based on the previous SPECT/CT images maximal radioactive counts were identified by hand held gamma probe, followed by injection of 1% isosulfan blue dye perilesionally followed by gentle massage to augment lymphatic drainage. An incision will be made over the area of highest radioactive count and lymph nodes are dissected. In second setting eyelid tumors are excised and reconstruction done.

Q.5. Map biopsy

Ans. See text

Q.6. Reconstruction of the eyelid defects.

Ans. Lid reconstruction:

Anterior lamella reconstruction:

- Primary closure

- Full thickness skin grafts
- Musculocutaneous flap
- Advancement flap
- Transposition flap
- Rhombic flap.

Posterior lamella reconstruction

- Buccal mucosa (preferred)
- Hard palate mucosa

- Tarsoconjunctival graft.

Full thickness lid defect—See **Table 1**.

Q.7. Different histological types of BCC

Ans. See **Table 2**

Q.8. Different lid manifestation of Malignant Melanoma

Ans. See **Table 3**

Table 1 Full thickness lid reconstruction

Size of the lid defect	Repair
<25%	Direct closure
25–50%	Direct closure with cantholysis
33–66%	Semicircular flap (Tenzel flap) alone or along with the periosteal flap
50–75%	Cutler Beard (Upper eyelid defect) Hughes procedure (Lower eyelid defect)
75–100%	Lower eyelid (Tarsoconjunctival flap with skin grafting) Upper eyelid (Median forehead flap with mucus membrane grafting)

Table 2 Lid manifestation of BCC

Nodular-ulcerative	Pigmented	Morphea or sclerosing	Superficial	Fibroepithelioma
<ul style="list-style-type: none"> • Most common lesion Pink or pearly papule or nodule • Overlying telangiectatic vessels present • Central ulceration with rolled border 'rodent ulcer' 	<ul style="list-style-type: none"> • Similar to the nodoulcerative type in morphology • Brown or black pigmentation • More common in dark complexion persons 	<ul style="list-style-type: none"> • Least common • Flat, indurated, yellow-pink plaque with ill-defined borders • Aggressive and may invade the dermis deeply • Invade into the paranasal sinuses and orbit • Mimic blepharoconjunctivitis 	<ul style="list-style-type: none"> • Scaling patch with a raised pearly border • Arise on the trunk rather than the eyelid 	<ul style="list-style-type: none"> • Pedunculated or sessile smooth, pink nodule. • Arise on the trunk rather than the eyelid

Table 3 Lid manifestation of malignant melanoma

Lentigo maligna melanoma	Superficial spreading melanoma	Nodular melanoma	Acral lentiginous melanoma
Slowly expanding pigmented, flat, nonpalpable, tan to brown macule with irregular borders	Plaque with irregular outline, variable pigmentation	<ul style="list-style-type: none"> • Blue-black nodule with normal surrounding skin • May be non-pigmented 	Occurs on the palms, soles, and distal phalanges as well as on the mucous membranes

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PTOSIS

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INTRODUCTION

Drooping of the eyelid is known as ptosis or blepharoptosis. It is a common pathology seen in all age group. It is given as both long and short case in the examination. The most important part in a case of ptosis is its examination.

HISTORY

Chief Complaints

A case of ptosis can present with following complaints:

- Adult patient commonly complaints of drooping of the upper lid.
- In children, parents often complaints of an affected eye being smaller in comparison to another eye.
- Diminution of vision is not a common complaint and amblyopia is associated only with severe ptosis due to stimulus deprivation. The prevalence of amblyopia is around 12% to 20 % in cases with severe congenital ptosis.¹⁻⁴

History of Present Illness

It is important to note about following points:

- The age of onset and duration (congenital or acquired)
- Progression of ptosis (chronic progressive external ophthalmoplegia)
- Any head position (e.g. chin lift)
- Associated symptoms can often indicate the underlying cause.

For example:

- Associated double vision points towards 3rd cranial nerve palsy/aberrant regeneration.
- Alteration in an amount of ptosis with jaw movements (jaw-winking phenomenon) can be seen in Marcus Gunn syndrome.
- Difficulty in deglutition is seen in oculopharyngeal muscular dystrophy.
- Limitation of ocular motility can be seen in myasthenia gravis and Kearns-Sayre syndrome.
- Worsening of ptosis as the day progresses is seen in myasthenia gravis (Levator palpebrae superioris (LPS) weakness compensated for by Müller's muscle in myasthenia, which fatigues with progression of the day)
- Associated recurrent allergic conjunctivitis can cause mechanical ptosis.

Past History

Following points must be noted in history in a ptosis case:

- Recurrent episodes of ptosis can be seen in recurrent 3rd nerve palsy, e.g. ischemic neuropathy associated with diabetes or hypertension.
- Contact lens wear (ill-fitting contact lens may cause blepharospasm and small palpebral aperture which may be confused with ptosis)
- Drug intake such as neostigmine can point towards the possible diagnosis.

- Trauma (lid or facial trauma may cause scarring or LPS damage) to rule out traumatic ptosis
- Medical conditions, e.g. myasthenia gravis, myotonia, muscular dystrophies, diabetes and hypertension.
- Spectacle use or amblyopia therapy during childhood is important when there is associated vision loss.

Past Medical History

Diabetes mellitus (DM), hypertension, bleeding diathesis (important for surgery), recurrent stye/chalazion/vernal keratoconjunctivitis (mechanical ptosis), any neurological disorder must be ruled out.

Past Surgical History

Peribulbar block for any intraocular surgery, cataract surgery can lead to ptosis. Any previous squint surgery or ptosis surgery must be recorded.

Birth History

Such as pregnancy, delivery, neonatal period, and early development are important in congenital ptosis. Birth history such as instrument/forceps delivery can lead to ptosis point towards the cause of ptosis.

Family History

Positive family history can be present in blepharophimosis syndrome.

- *Pseudoptosis:* Ipsilateral microphthalmos or contralateral lid retraction can lead to pseudoptosis.
- The presence of strabismus must be ruled out by Cover-Uncover test.
- Extraocular muscle function should also be assessed in primary and secondary gazes. The presence of motility abnormalities is seen in congenital conditions such as double elevator palsy (combined superior rectus and LPS muscle maldevelopment), congenital oculomotor palsy and acquired conditions such as ocular or systemic MG, chronic progressive external ophthalmoplegia, oculopharyngeal dystrophy, and oculomotor palsy with or without aberrant regeneration.

Eyelid: Following points must be noted:

- If ptosis is unilateral (**Figs 1 and 2**) or bilateral
- Signs of previous trauma such as eyelid scar
- Mechanical causes of ptosis such as eyelid tumors, multiple chalazia, giant papillae
- Lagophthalmos—important for surgical planning
- Pupillary reaction—pupillary involvement can be seen in cases of 3rd CN palsy and Horner's syndrome
- The position of the lids should be noted in the different position of gaze. Variability of ptosis in the different position of gaze is an indication of aberrant regeneration after third-nerve palsy.
- Note also the speed of saccades: slow saccades are indicative of myopathic muscles.

EXAMINATION

Visual acuity: Visual acuity and refractive error must be assessed in all cases of congenital or childhood ptosis in order to identify and treat the child with concomitant amblyopia. Amblyopia can result from anisometropia, high astigmatism, strabismus or occlusion of a pupil. Amblyopia occurs in approximately 12–20% of patients with congenital ptosis.

Facial symmetry and orbit: Look for following:

- *Head posture:* Chin elevation is seen in cases of bilateral moderate to severe ptosis.
- *Frontalis overaction:* Raised eyebrows to compensate for ptosis.



Fig. 1: Simple severe congenital ptosis before surgery



Fig. 2: Simple severe congenital ptosis after surgery

- Variation in the amount of ptosis with extraocular muscle or jaw muscle movements (synkinesis) should be noted. Synkinesis may be seen in Marcus Gunn jaw-winking ptosis, aberrant regeneration of the 3rd CN or the VII CN, and some types of Duane syndrome.

Measurement of Ptosis

- *Margin-reflex distance 1 (MRD1)*: It is the distance from the upper eyelid margin to the corneal light reflex in the primary position. It is the *single most important measurement* in describing the amount of ptosis. The MRD1 is also checked in the reading position.
- *Margin-reflex distance 2 (MRD2)*: The MRD2 is the distance from the corneal light reflex to the lower eyelid margin. MRD2 is a measure of lower eyelid retraction (or scleral show).
- *Palpebral aperture*: The vertical interpalpebral fissure is measured at the widest point between the lower eyelid and the upper eyelid. This measurement is taken with the patient fixating on a distant object in primary gaze. Normally, the palpebral fissure height in males, is 7–10 mm, and in females, it is 8–12 mm.
Remember the sum of the MRD1 and the MRD2 should equal the vertical interpalpebral fissure height.
- *Margin crease distance (MCD)*: It is the distance from the upper eyelid crease to the eyelid margin. The insertion of fibers from the LPS muscle into the skin contributes to

the formation of the upper eyelid crease. High, duplicated or asymmetric creases may indicate an abnormal position of the levator aponeurosis. The upper eyelid crease is 8–9 mm in males and 9–11 mm in females. The crease is usually elevated in patients with involutional ptosis and is often shallow or absent in patients with congenital ptosis. The height of the crease on the normal side should be measured and compared to the ptotic eyelid in downgaze. In patients, when more than one lid crease is present, *the most prominent one should be considered*.

- *Levator Palpebrae Superioris (LPS) function Berke's Method (lid excursion)*: LPS function is estimated by measuring the upper eyelid excursion from downgaze to upgaze with frontalis muscle function negated. Fixating the brow with digital pressure minimizes contributions from accessory elevators of the eyelids such as the frontalis muscle. Failure to negate the influence of the frontalis muscle results in an overestimation of LPS function. LPS function can be graded according to Beard's classification
 - Normal: >15 mm
 - Good: 12–14 mm
 - Fair: 5–11 mm
 - Poor: <4 mm

Putterman's method: This is carried out by the measurement of the distance between the middle of upper lid margin to the 6'o clock limbus in extreme upgaze. This is also known as the margin limbal distance (MLD). Normal is about 9.0 mm.

Assessment in children:

- Assessment of LPS function in small children is a difficult task, as the child allows no formal evaluation. Following methods may help
- The presence of lid fold and increase or decrease in its size on a movement of the eyelid gives us a clue to the LPS action.
- The presence of anomalous head posture like the child throwing his head back suggests a poor LPS action.
- *Iliff test*: This test can be performed in the first year of life to evaluate the levator function. The upper eyelid of the child is everted as the child looks down. If the levator action is good, lid reverts on its own.

Lagophthalmos: The patient should be assessed for lagophthalmos and if it is present, the degree should be noted, checking head position, chin elevation, brow position, and brow action in attempted upgaze. Lagophthalmos and poor tear film quantity or quality may predispose a patient to complications of ptosis repair such as dryness and exposure keratitis.

Bell's phenomenon: it is an upward and outward movement of the eye when an attempt is made to close the eyes. Bell's phenomenon is a normal defense reflex.

- *Demonstration:* Ask the patient to close the eye forcibly (as if the patient wants to sleep). The examiner then lifts the patient's upper eyelid manually. In a patient with a normal Bell's phenomenon, the globe will rotate upwards and outwards and the eyelid will cover the cornea.
- *Significance:* If a patient does not have a good Bell's phenomenon, a cautious ptosis correction should be undertaken to prevent subsequent corneal exposure, especially when planning for sling surgery.
- Bell's phenomenon is graded into three grades:
 1. *Good:* Less than one-third of cornea visible
 2. *Fair:* One-third to one-half of the cornea visible
 3. *Poor:* More than one-half of cornea visible
- *Inverse Bell's phenomenon:* If the cornea is not in upgaze or if it moves to other position of gaze, such as downgaze on closing the eyes than it is called inverse Bell's.

Cornea

- The corneal sensation must be checked in all cases. A normal corneal sensation is essential for normal blink reflex and prevention of exposure keratitis the following surgery.
- Quantity and quality of the tear film must be documented in the initial examination. Schirmer test, tear break-up time (TBUT) and Tear meniscus must be recorded in all cases of ptosis. Dry eye syndrome is a contraindication for ptosis surgery; especially sling surgeries as it may cause corneal damage postoperatively.

Pupil: Pupillary examination is important in the evaluation of ptosis. Pupil abnormalities

are present in some acquired and congenital conditions associated with ptosis (e.g. Horner syndrome, cranial nerve III palsy). Miosis that is most apparent in dim illumination is seen in Horner syndrome and mydriasis is seen in some cases of 3rd CN palsy.

Fundus: Fundus examination after mydriasis is essential for any concomitant fundus abnormality.

Rest of the findings such as iris, lens, sclera and IOP are usually within normal limits.

DIFFERENTIAL DIAGNOSIS

A case of ptosis must be differentiated from pseudoptosis. Pseudoptosis is apparent eyelid drooping due to ocular or adnexal diseases should be differentiated from true ptosis. On elevating the ptotic lid, the other eyelid droops slightly in true ptosis while remains at the same level in pseudoptosis. Causes of pseudoptosis includes following:

- *Unilateral:*
 - Hypertropia
 - Enophthalmos
 - Microphthalmia
 - Anophthalmia
 - Phthisis bulbi
 - Superior sulcus defect
 - Dermatochalasis
- *Contralateral:*
 - Upper eyelid retraction
 - Proptosis
 - Buphthalmos

INVESTIGATION

A case of ptosis usually does not need any special investigation other than routine tests done before surgery. Investigations like visual field may be required in special situations as discussed under Viva questions.

CLASSIFICATION

Based on the onset

- *Congenital ptosis:* Ptosis present since birth. It can be further categorized into following:
 - Congenital simple ptosis
 - Complicated
 - ♦ With oculomotor abnormalities
 - ♦ With blepharophimosis syndrome

- ♦ Synkinetic ptosis
 - Marcus Gunn Jaw Winking
 - Misdirected third nerve ptosis
- *Acquired ptosis:* True acquired ptosis is the result of some disturbance of the upper lid retractors, the levator or Müller's muscle, or both, and is best classified according to its primary cause, which includes; mechanical (**Fig. 3**), myogenic, neurogenic, and aponeurotic. Differentiating points between congenital and acquired ptosis are given in **Table 1**

Bases on pathogenesis: As shown in **Table 2**.

STAGING/SCORING

The amount of ptosis can be determined by:

- The difference in MRD 1 of the two sides in unilateral cases



Fig. 3: Right upper eyelid mechanical ptosis

Table 1 Differences between congenital and acquired ptosis

Parameters	Congenital ptosis	Acquired ptosis
MRD 1	Mild-to-severe ptosis	Mild-to-severe ptosis
Upper eyelid crease	Weak or absent crease in normal position	Higher than normal crease
LPS function	Reduced	Near normal
Downgaze	Eyelid lag (lid lag sign)	Eyelid drop
Palpebral aperture	Greater in downgaze	Less in downgaze

Abbreviations: MRD, margin-reflex distance; LPS, levator palpebrae superioris

Table 2 Classification of ptosis based on pathogenesis

Type	Mechanism	Example
Myogenic	<ul style="list-style-type: none"> • Maldevelopment of elevators • Myopathic conditions involving the LPS or myoneural junction. • Direct damage to LPS or myoneural junctions 	<ul style="list-style-type: none"> • Congenital simple ptosis • Blepharophimosis syndrome • Double elevator palsy • Congenital ocular fibrosis syndrome • Chronic progressive external ophthalmoplegia • Oculopharyngeal dystrophy • Muscular dystrophy • Traumatic
Neurologic	<ul style="list-style-type: none"> • Dysfunction of the third cranial nerve • Dysfunction of sympathetic innervation to Müller's muscle • Aberrant regeneration after oculomotor nerve palsies 	<ul style="list-style-type: none"> • Oculomotor nerve palsy • Horner's syndrome • Myasthenia gravis • Marcus Gunn jaw-winking phenomenon

Contd...

Contd...

Type	Mechanism	Example
Aponeurotic	<ul style="list-style-type: none"> Dehiscence in the central part of the aponeurosis Disinsertion of the aponeurosis from the tarsus Thinning and stretching, termed attenuation or rarefaction, of the aponeurosis Attenuation or rarefaction, of the aponeurosis 	<ul style="list-style-type: none"> Involutorial (aponeurosis dehiscence) Post-traumatic Post-surgical blepharochalasis Chronic, recurrent edema Pregnancy Chronic ocular inflammation Rigid contact lens wear
Mechanical	<ul style="list-style-type: none"> Excessive weight 	<ul style="list-style-type: none"> Dermatochalasis Eyelid mass Giant papillae/VKC Multiple chalazion Orbital mass Scarring

Grading

- Mild ptosis—2 mm or less
- Moderate ptosis—3 mm
- Severe ptosis—4 mm or more.

MANAGEMENT

The aim of the surgery is to lift the ptotic lid above the pupillary aperture when the eyes are in the primary position. The height of the two lids regardless of whether the ptosis is unilateral or bilateral should be equal. There should also be adequate mobility of the lid when blinking, a normal lid fold and no diplopia. The surgical procedures and their indications are as follows:

- *Fasanella Servat Operation*
 - Mild ptosis (<2 mm or less)
 - Levator action >10 mm
 - Well defined lid fold—no excess skin
- *Levator resection*
 - Mild/moderate ptosis
 - Levator action \geq 4 mm
- *Brow suspension ptosis repair*
 - Severe ptosis
 - Levator action <4 mm
 - Jaw-winking ptosis or blepharophimosis syndrome

The treatment of congenital ptosis has been described in detail in chapter congenital ptosis (short case). The treatment of acquired ptosis depends upon the cause.

VIVA QUESTIONS

Q.1. What are visual problems due to ptosis?

Ans. • Ptosis is a common cause of reversible peripheral visual loss. Although, the superior visual field is most often involved, central vision can also be affected. Patients with ptosis complain of difficulty with reading because the ptosis worsens in downgaze. Ptosis has also been shown to decrease the overall amount of light reaching the macula and, therefore, can reduce visual acuity, especially at night.

- The restricted peripheral visual field is a contraindication for issuing of driving license and jobs requiring broader fields in western countries. Visual fields less than 10 degrees in the better eye with the best correction are considered as legal blindness.

Q.2. What is the normal position of UL?

Ans. The vertical interpalpebral fissure is measured at the widest point between the lower eyelid and the upper eyelid. Normally, the UL should cover 1/6th or 2 mm of the cornea and lower lid should just touch the limbus.

Q.3. Classification of ptosis

Ans. Ptosis can be classified as following:

- *Based on onset:* Congenital or acquired.
- *Based on etiopathogenesis:* Myogenic, aponeurotic, neurogenic, mechanical and traumatic.

The most common type of congenital ptosis results from a poorly developed levator muscle LPS (myogenic). The most common type of acquired ptosis is that caused by stretching or disinsertion of the levator aponeurosis (aponeurotic).

Q.4. Differentiate between congenital and acquired ptosis

Ans. See Table 1

Q.5. What is blepharophimosis epicanthus inversus ptosis syndrome (BPES)?

Ans. Details in short cases.

Q.6. What are Bells phenomenon and its grading?

Ans. See Examination

Q.7. The importance of Hering's law in ptosis

Ans. In cases with bilateral ptosis and with one side having marked ptosis compared to the other side, following surgical correction on the greater ptotic side, the side with minimal ptosis may droop more. This is due to the Hering's law. This is important to predict the postoperative results of ptosis surgery. Patient has to be warned that the contralateral eye may droop following correction of the greater ptotic lid to avoid any postoperative unrealistic expectation by the patient.

Q.8. What should be the sequence of surgery if ptosis and strabismus coexist?

Ans. Since correction of the strabismus may relieve the ptosis, strabismus surgery should be performed before treatment of ptosis. An exception may be made for cosmetically acceptable strabismus for which the only ptosis needs to be treated. If the patient has horizontal strabismus with ptosis, surgery for both strabismus and ptosis can be performed at the same sitting because the result of one is unlikely to influence the result of the other.

Q.9. How to demonstrate and grade Marcus Gunn Jaw winking?

Ans. Synkinesis is best demonstrated by having the patient move the jaw to the opposite side of the ptotic eye, but widely opening the mouth or moving the jaw forward would also elevate the eyelid.

Grading of Marcus Gunn jaw-winking phenomenon is based on the amplitude of lid movement:

- Mild—2 mm or less
- Moderate—3–6 mm
- Severe—7 mm or more

Q.10. What are the other ancillary tests that should be done in ptosis?

Ans. • *Visual field testing* with the eyelids untaped (in the natural, ptotic state) and taped (artificially elevated) helps determine the patient's level of functional visual impairment. Comparison of the taped and untaped visual fields gives an estimate of the superior visual field improvement that can be anticipated following surgery.

- Pharmacologic testing may be helpful in confirming the clinical diagnosis of Horner syndrome, myasthenia gravis. Fluctuating ptosis that seems to worsen with fatigue or prolonged upgaze, especially when accompanied by diplopia or other clinical signs of systemic MG.

• *Phenylephrine test:* One drop of phenylephrine 2.5% is instilled in the upper fornix, stimulates the alpha-receptors in Müller's muscle, causing its contraction and hence lid elevation. It is possible to demonstrate the potential outcome of surgery to a patient with a positive response to phenylephrine. One can also unmask a coexisting ptosis in the so-called normal eye, which appeared normal due to increased LPS stimulation (Hering's law).

Q.11. The significance of pupillary examination in ptosis.

Ans. • A small pupil (miotic) indicates Horner's syndrome

- A large pupil might be a sign of third-nerve palsy.
- In aberrant third-nerve palsy, the size of a pupil may change in different position of gaze.

Q.12. What is MRD3?

Ans. MRD3 is the distance from the ocular light reflex to the central UL margin when the patient looks in extreme upgaze. In unilateral ptosis, the difference between normal and abnormal MRD3 multiplied by 3 approximately shows the amount of LPS that must be resected.

Q.13. What are the bedside tests to rule out myasthenic ptosis?

Ans.

- *Fatigability:* Ask the patient to look up and down for about 1 min to induce fatigue or sustained upgaze for 1 min will achieve the same result. Progressive ptosis will ensue in a myasthenic patient. MRD1 is measured before and after these fatigue tests. Note that myasthenic patients might also develop diplopia with this test.
- *Cogan's twitch sign:* The patient is first asked to look down for 15 s. A small upshoot of the eyelid is noted as a myasthenic patient then moves back to the primary position.
- *Ice-pack test:* Apply an ice-filled glove to the affected eye for 10 min. In a myasthenic patient, the ptosis improves by 2 mm or more.

Tests to confirm Myasthenia:

- *Edrophonium chloride test or Tensilon test:* This test is done in doubtful cases where an acquired ptosis due to Myasthenia Gravis is suspected. In adults, 2 mg of edrophonium is injected slowly in 15–30 seconds. The needle is left in situ and the remaining 8 mg is injected slowly if no untoward incident is observed within 1 minute. The effect occurs in 1–5 minutes and if myasthenia is the cause, ptosis improves after edrophonium injection.
- *Acetylcholine receptor antibody test* when positive has 100% specificity.

- *Single-fiber electromyogram* (EMG: 100% sensitivity) and muscle biopsy are other more invasive tests that are helpful in identifying the site of pathology in myopathic and myasthenic ptosis.

Q.14. Postsurgical ptosis?

Ans. The incidence of ptosis after cataract surgery has been reported to be as high as 13%.³ Although it can be seen following any intraocular surgery, it is often seen following cataract and vitreoretinal surgery. It can be *transient/acute ptosis* that resolves after surgery or *chronic/persistent ptosis* that persists after surgery

Etiopathogenesis: Postsurgical ptosis can be due to the following:

- *Myogenic* due to the process of injecting anesthetic into the muscle or myotoxic effects of the anesthesia
- *Aponeurotic:* Due to use of a bridle suture or rigid lid speculum
- *Neurogenic:* Due to the prolonged effects of anesthetic on the neuromuscular junction, causes transient neurogenic ptosis
- *Mechanical:* May be due to edema or hematoma formation in the eyelid
- *Traumatic:* Due to blunt or sharp trauma to the levator aponeurosis

Prevention: Prevention of postsurgical ptosis is an essential part of the modern ocular surgery.

- Topical anesthesia eliminates all problems with local anesthesia including hematoma and edema of the eyelid and myotoxic effects on the levator.
- Use of ocular massage and compression decreases the amount of eyelid edema and hematoma formation.
- Limit surgical time and thus eyelid complications secondary to ocular inflammation or compressive effects of prolonged use of a lid speculum.
- Disuse of bridle sutures or a rigid speculum
- Superior approach to surgery have a greater risk compared to a temporal approach

Treatment: After a thorough examination in which the etiology is determined, one must decide whether to intervene. In most cases, postsurgical ptosis resolves with time, and therefore observation is the most prudent form of intervention. This form of ptosis typically improves within six months. Ptosis that does not resolve is typically secondary to aponeurotic dehiscence; this is readily repaired surgically.

Q.15. What is traumatic ptosis?

Ans. Trauma to the levator aponeurosis or the LPS muscle may also cause ptosis through myogenic, aponeurotic, neurogenic, or mechanical defects. Eyelid lacerations exposing preaponeurotic fat indicate that the orbital septum has been transected and suggest the possibility of damage to the levator aponeurosis exploration of the LPS muscle or aponeurosis is indicated in these patients if LPS function is diminished or ptosis is present. Orbital and neurosurgical procedures may also lead to traumatic ptosis. The ophthalmologist normally observes the patient for 6 months before considering surgical intervention.

Q.16. What is myogenic ptosis?

Ans. *Congenital myogenic ptosis:* This type of ptosis is due to dysgenesis of the levator palpebrae superioris (LPS) muscle. Congenital ptosis caused by maldevelopment of the LPS muscle is characterized by decreased LPS function, eyelid lag, and sometimes, lagophthalmos. The upper eyelid crease is often absent or poorly formed, especially in cases of more severe ptosis. Congenital myogenic ptosis associated with a poor Bell's phenomenon or with vertical strabismus may indicate concomitant maldevelopment of the superior rectus muscle (double elevator palsy, or monocular elevation deficiency).

Acquired myogenic ptosis: It is uncommon and results from localized or diffuse muscular diseases such as muscular dystrophy, chronic progressive external ophthalmoplegia, MG, or oculopharyngeal dystrophy.

Surgical correction may be difficult, requiring frontalis sling procedures.

Q.17. What is aponeurotic ptosis?

Ans. It is the most common form of acquired ptosis. It results from stretching or dehiscence of the levator aponeurosis or disinsertion from its normal position. Common causes are involutional attenuation or repetitive traction on the eyelid, which may occur with frequent eye rubbing or prolonged use of rigid contact lenses. It can also occur due to intraocular surgery or eyelid surgery. The characteristic sign is a high or an absent upper eyelid crease secondary to upward displacement or loss of the insertion of LPS fibers into the skin. Thinning of the eyelid superior to the upper tarsal plate can also be there. LPS function in aponeurotic ptosis is usually normal (12–15 mm) and worsens in downgaze.

Q.18. Describe neurogenic ptosis.

Ans. *Congenital neurogenic ptosis* is caused by innervational defects during embryonic development. It is rare and commonly associated with congenital 3rd cranial nerve palsy, Horner syndrome or Marcus Gunn Jaw-Winking syndrome. It manifests as ptosis together with an inability to elevate, depress, or adduct the globe. The pupils may also be dilated.

- *Congenital Horner syndrome* is a manifestation of an interrupted sympathetic nervous chain. It is associated with mild ptosis, miosis, anhidrosis, and decreased pigmentation of the iris on the involved side. Decreased sympathetic tone to the inferior tarsal muscle in the lower lid (the analog of the Müller's muscle), results in elevation of the lower eyelid. This phenomenon is called as *lower eyelid reverse ptosis*. The combined upper and lower eyelid ptosis decreases the vertical interpalpebral fissure and may confuse with enophthalmos. The pupillary miosis is most apparent in dim illumination.
- *Marcus Gunn Jaw-Winking syndrome (Figs 4 and 5)* is the most common form



Fig. 4: Right-sided severe complicated ptosis



Fig. 5: Right-sided severe complicated ptosis with improvement in ptosis after chewing movement

of congenital synkinetic neurogenic ptosis.

- Some forms of Duane retraction syndrome also cause elevation of a ptotic eyelid with the movement of the globe.

Acquired neurogenic ptosis results from interruption of normally developed innervation and is most often secondary to an acquired III-N palsy, to an acquired Horner syndrome, or MG. Less common causes of acquired neurogenic ptosis include myotonic dystrophy, chronic progressive external ophthalmoplegia, Guillain-Barré syndrome, and oculopharyngeal dystrophy. Botulinum toxin injection in the forehead or orbital region to ameliorate benign essential blepharospasm can also lead to this form of ptosis.

Q.19. What is mechanical ptosis?

Ans. Mechanical ptosis usually refers to the condition in which an eyelid or orbital mass weighs or pulls down the upper eyelid.

It can be caused by a congenital abnormality, such as a plexiform neurofibroma or hemangioma, or by an acquired neoplasm such as a large chalazion, skin carcinoma, or orbital mass. Postsurgical or post-traumatic edema can also cause temporary mechanical ptosis.

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CONTRACTED SOCKET

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INTRODUCTION

The contracted socket is defined as the shrinkage and shortening of all or a part of orbital tissues causing a decrease in depth of fornices and orbital volume ultimately leading to inability to retain prosthesis. It is characterized by extensive loss of conjunctival surface area, deep cicatrix formation, atrophy of the orbital fat, fornix contraction and volume redistribution leading to post-enucleation syndrome.

In examinations, it can be given as a long or short case.

HISTORY

Chief Complaints

Patient is usually an adult with history previous enucleation or evisceration surgery for any cause with or without prosthesis with complaints of:

- Poor cosmetic appearance
- Repeated extrusion of prosthesis
- Previously fitting prosthesis not fitting now
- The patient sometimes may be a child with a history of the underdeveloped socket.

History of Present Illness

Note about following:

- *Age at onset*: To differentiate between congenital and acquired anophthalmic socket
- *Preceding surgery*: Type of surgery performed and its details from the record if available
- *Progression*: Whether the implant or prosthesis was fitting earlier, and if the implant size has been changed over time.

History of Past Illness

Past history may give a clue about the probable cause, so following points must be noted in past history:

- Ocular insult like chemical or radiation injury may be present
- Panophthalmitis requiring evisceration
- Severe ischemic ocular disease

- Cicatrizing conjunctival diseases may lead to progressive fornical shortening
- Chronic inflammation and infection that might have led to the surgery
- Mutilating trauma to eye in which evisceration might have done to prevent sympathetic ophthalmia.

Surgical History

History of prior surgery; such as enucleation/evisceration, multiple socket reconstruction and the details of the procedure can identify the reason for contracted socket.

History of Systemic Illness

History of hypertension, diabetes mellitus, vascular diseases and any previous cerebrovascular accident must be noted carefully. Any neurological event may indicate the intracranial spread of the disease, for which the surgery have been done, such as infection or malignancy.

EXAMINATION

Systemic Examination

Most of the time the surgery is carried out to remove an intraocular malignancy in an advanced stage, e.g. stage E retinoblastoma. Thus, a detailed systemic examination is carried out to rule out any systemic metastasis, especially the nervous system.

Ocular Examination

Ocular examination includes following:

- *Eyelids*
 - Eyelid notches and abnormalities need to be looked out for. In longstanding cases there may be stretching and lengthening of the lower lid which would need to be tackled simultaneously.
 - Eyelid closure needs to be looked for too.
 - The lower eyelid should be evaluated for laxity. Lash position and lid margin

- position should be noted, as entropion can indicate socket contracture.
- The superior sulcus should be checked for deepening and symmetry with the opposite side. The upper eyelid position should be noted for ptosis, and levator function should be evaluated.
- *Assessment of the socket:* The following parameters are evaluated:
 - General appearance and symmetry compared to the other normal side should be noted carefully.
 - *Area of the socket:* The area is assessed particularly the depth of the fornices. The depth of the fornices can be calculated by inserting a blunt lacrimal probe into each of the fornices and noting down the length to which it can be inserted. The inferior fornix is the most important as it has to support the prosthesis. The other fornices also need to be adequate to ensure the prosthesis fitting.
 - *The volume of the socket:* The volume is assessed by noting the relative depth of the socket compared to the fellow eye. Another practical way of assessing the volume is to inject saline into the socket drop by drop till it overflows. The superior sulcus deformity and presence of ptosis are also indicators of volume loss.
 - *Dry or wet socket:* Look for any discharge from the socket. There should be no active discharge from the socket. Dry fibrotic conjunctiva indicates a poorly vascularized socket.
 - *Movements:* The movements of the muscles are looked for. In a case of dermis fat grafting, suturing the muscles to the graft ensures better survival.
 - The tone of the orbicularis and tarsal sulci.
 - Cicatricial bands and degree of contracture within the socket.
 - Associated any bony contracture must be checked for.
 - Look for signs of inflammation, excessive mucus, giant papillary conjunctivitis under the upper eyelid and pyogenic granulomas.
- Palpation of the socket is done to for the presence or absence of an implant and the position of the implant should be noted.
- *Prosthesis:* With the prosthetic in place the patient should be evaluated for fit, size and its appearance with respect to the fellow eye. The movement of the prosthetic should be evaluated compared to the other eye. The prosthetic can then be removed and evaluated for type, size, smoothness and cleanliness.

INVESTIGATIONS

- *Microbiological investigations* to rule out any infection.
- *Radiological investigation* to look for any fracture in orbit or search of buried implant.

GRADING

- *Gopal Krishna classification*
The soft tissue sockets were divided into five grades for the sake of convenience in the management of contracted sockets.
 - *Grade-0:* Socket is lined with the healthy conjunctiva and has deep and well-formed fornices.
 - *Grade-I:* Socket is characterized by the shallow lower fornix or shelving of the lower fornix. Here the lower fornix is converted into a downwards sloping shelf which pushes the lower lid down and out, preventing retention of an artificial eye. Common causes are physical injuries, endophthalmitis, and retinoblastoma.
 - *Grade-II:* Socket is characterized by the loss of the upper and lower fornices. The common causes are physical injuries, endophthalmitis, panophthalmitis, and retinoblastomas.
 - *Grade-III:* Socket is characterized by the loss of the upper, lower, medial and lateral fornices. Common causes are chemical injuries and panophthalmitis.
 - *Grade-IV:* Socket is characterized by the loss of all the fornices and reduction of a palpebral aperture in horizontal and

vertical dimensions. Common causes are chemical injuries and panophthalmitis.

- *Grade-V:* In some cases, there is the recurrence of contraction of the socket after repeated trial of reconstruction. Common causes are thermal and chemical injuries of the eye.

- *Byron Smith classification*

Socket contraction may also be graded as follows:

- *Mild:* Includes grade I and II where only one fornix is involved and there is a shortening of the posterior lamella of the lids.
- *Moderate:* Includes grade III where both superior and inferior fornices are involved.
- *Severe:* Comprises of cases in which all fornices are involved along with phimosis of palpebral aperture.
- *Malignant contracted socket:* It is the most severe variety of contracted socket and associated bony contraction, resulting from severe trauma or multiple surgeries.

- *Morphological classification:* Guibor has classified clinically contracted socket into 4 morphological types as shown in **Table 1**.

TREATMENT (TABLE 2)

The primary aim of management is to create a socket so as to maintain a prosthesis with a good cosmetic appearance. Before commencing a definitive therapy, it is necessary to identify,

Table 1 Morphological classification of contracted socket

Type	Examples
Anophthalmic contracted socket	Most common seen after enucleation and evisceration surgery
Ophthalmic contracted socket	Following chemical and irradiation injury
Microphthalmic contracted socket	In association with microphthalmos and microcornea
Hypoplastic contracted socket	Congenital under development of bony socket

classify and eliminate any precipitating factors leading to contracture.

General considerations before socket reconstruction:

- Informed consent must be obtained
- The prognosis and aim of surgery must be well explained
- In cases, oral mucosa grafting is planned the patient should have mouthwashes started at least 2 weeks prior to the surgery.
- Ensure that the socket is free of any infection.
- *Mild contracted socket:* This can usually be managed by deepening the inferior fornix with fornix formation sutures.
- *Management of moderate-to-severe contracted socket:* These cases are usually managed with a graft. Grafts that can be used for socket

Table 2 Mechanism of contracted socket

Etiology	Factors
Etiology related	<ul style="list-style-type: none"> • Alkali burns, Radiation therapy leading to severe damage to the socket and fibrosis
Surgery related	<ul style="list-style-type: none"> • Fibrosis from the initial injury • <i>Poor surgical techniques:</i> Extensive dissection of the orbital tissue. • <i>No implant or undersized implant:</i> In children the absence of the stimulus of either eyeball or implant can lead to bony contraction as well. • Excessive sacrifice of the conjunctiva and Tenon's capsule • Traumatic dissection within the socket leading to scar tissue • Multiple socket operations
Site related	<ul style="list-style-type: none"> • Poor vascular supply • Severe ischemic ocular disease in the past • Cicatrizing conjunctival diseases • Chronic inflammation and infection
Implant and prosthesis related	<ul style="list-style-type: none"> • Undersized implant • Implant migration • Implant exposure • <i>Not wearing a conformer/prosthesis:</i> Conformer keeps the fornices stretched and prevents fornacial shallowing • Ill-fitting prosthesis

reconstruction include mucosa, split skin, and dermis—fat grafts. The socket needs to be healthy and vascularized for the grafts to take up. For mucous membrane grafts, mucus can be taken from buccal cavity (lip or cheek), rectum or vagina. The buccal cavity is preferred as it is easy to access.

- **Management severe contracted socket:** These cases usually require both area and volume replacement thus a composite graft is required. The commonly used graft is the dermis fat graft wherein the fat provides the volume and the dermis provides the surface area of the socket. The graft is taken from the hip. Although autogenous dermis fat orbital implantation is an effective means of orbital reconstruction, there is a 30% chance of atrophy of at least half of the graft volume when it is implanted in an avascular socket. Introducing a pedicle flap into the orbit as a vascular bed for an autogenous dermis fat graft may increase the prospect of graft survival, as well as supply additional volume to fill the socket. Temporalis muscle graft is supplied by a superficial temporal artery, a branch of an external carotid artery and it can be used as a pedicle graft.
- **Treatment of moist socket:** Partial-thickness mucous membrane grafts are more susceptible to shrinkage and contracture. Full thickness mucous membrane contracts less and may be obtained with minimal postoperative complications at the donor site. However, mucosal contracture and submucosal scar formation increase with the size of the oral mucous membrane harvested and mucous membrane lacks the rigidity needed for grafting the palpebral surface. A full thickness mucous membrane graft is obtained from oral mucosa of cheeks and lips (Most common), hard palate, preputial skin, the skin of labia. The graft should be 40–50% larger than anticipated to allow for subsequent contracture with healing. It is helpful to harvest the graft at the beginning of the procedure so that it can be soaked in antibiotic solution before use.
- Amniotic membrane can also be used instead of the mucosa. It has less patient morbidity, faster recovery and better fitting of a prosthesis. No contracture is observed with an amniotic

membrane as against mucous membrane. It is cheap and easily available and has no significant complications associated with it.

- **Treatment of dry socket:** The socket is lined with a split-thickness skin graft in these cases. The skin graft is placed around an orbital mould with the epithelial surface towards it and perforations are made in the graft. The mould is sutured into the socket. After the 1-month graft is split open in the area of palpebral fissure. The mould is kept for at least 4 months after which a permanent prosthesis is placed.
- **Management of recalcitrant cases:** A socket that has undergone multiple unsuccessful operations and has excessive scar tissue is unlikely to benefit from further repair. For such sockets exenteration of the eyelid and residual socket material to create a cavity into which a prosthesis is fitted, can be done. Optical methods to improve the appearance includes spectacle prosthesis or smoked lenses, plus or minus lenses to magnify a micro-ophthalmic socket to minimize buphthalmic socket, prisms to change the apparent horizontal or vertical position of malpositioned prosthesis or socket.

VIVA QUESTIONS

Q.1. What are the causes of contracted socket?

Ans. Causes of contracted socket can be congenital or acquired.

- **Congenital:** Conditions such as microphthalmos (**Fig. 1**) or congenital anophthalmos (**Fig. 2**) usually lead to a contracted socket as the stimulus of the eyeball is essential for healthy growth of the orbit.
- **Acquired:** Acquired causes are described here:
 - **Enucleation without implant:** A poorly done enucleation, particularly without implant can lead to a contracted socket. This is more so in children as in the absence of the stimulus of either eyeball or implant, there is a bony contraction as well. The implant needs to be carefully selected, both in terms of size and material.



Fig. 1: Unilateral microphthalmia with contracted socket



Fig. 2: Bilateral anophthalmia with contracted socket

- *Delay in use of conformer:* In both enucleation and evisceration procedures, conformer should be fitted immediately. This keeps the fornices stretched and prevents fornacial shallowing. The conformer should be on the correct side, adequate size and have multiple holes to allow flushing and drainage of secretions.
- *Trauma:* Extensive lacerations of the lids and orbital tissue can lead to tissue loss and fibrosis resulting in socket contraction. Injuries with alkali/acid can also cause fibrosis.
- *Radiotherapy:* Post-operative radiotherapy for retinoblastoma can cause fibrosis and a grossly contracted socket. These sockets are usually poorly vascularized and difficult to reconstruct.
- *Infection:* Socket/implant infection can lead sloughing of the conjunctiva and shortening of the fornices.

Q.2. What precautions should be taken to prevent contracted socket ?

Ans. Socket contraction should be prevented as far as possible by taking some precautions at the primary surgery.

- Proper dissection at the time of initial procedure
- Preserving as much conjunctiva and Tenon's capsule as possible during enucleation

- Secure closure of all layers over the implant without tension or superior displacement of the inferior fornix
- Avoidance of ill-fitting or roughened prosthesis as it may cause a more rapid contracture, symblepharon formation and total abandonment of prosthesis
- Elimination of any source of chronic infection that may arise from lid margin, socket, canaliculi, lacrimal sac, chemical or thermal injury
- Identification of conjunctival cicatrizing diseases like pemphigoid, Stevens-Johnson syndrome
- Avoidance of oversized prosthesis so as to prevent migration of the implant into the inferior fornix and thereby obliteration of inferior cul-de-sac.
- *Conformer:* A conformer should always be placed at the end of the surgery. This is replaced by the prosthetic eye 4-6 weeks later. If the socket has undergone prior irradiation, chemical, or thermal injury, the conformer has to be left for a much longer time.
- Radiotherapy if required, should be used with fractionation of dose.

Q.3. What are the characteristics of an ideal orbital implant?

Ans. Ideal orbital implant should be:

- Lightweight
- Nonantigenic
- Inert

- Biocompatible
- Affordable
- Mimic the motility of the normal globe
- Minimum complications like infection, extrusion and migration.

Q.4. Types of orbital implants

Ans. Presently all implants are broadly classified as:

- *Nonintegrated implants*: Are the ones which are nonporous and are not integrated and have no direct muscle attachment, e.g. silicon and acrylic implants.
- *Semi-integrated implants*: Allow attachment of muscle in tunnels on the anterior surface for better motility. Examples include Allens, Iowa, etc.
- *Biointegrated implants*: These allow fibrovascular ingrowth in the porous channels and result in direct biological integration with orbital contents. Examples include hydroxyapatite, porous polyethylene implants, aluminum oxide, alpha sphere.
- *Biogenic implants*: An autograft or allograft of natural tissue with direct biological integration with orbital structures

but not prosthesis. For example, dermis fat graft, mucous membrane graft.

Porous implants are presently the material of choice as vascularization leads to the integration of implants. But porous implants are significantly more expensive than acrylic and silicon implants.

Q.5. Post-enucleation socket syndrome/volume deficient socket.

Ans. Typically seen the following enucleation and characterized by following:

- Enophthalmos
- An upper eyelid sulcus deformity
- Ptosis or eyelid retraction
- Laxity of the lower eyelid
- A backward tilt of the ocular prosthesis
- Unhappy with cosmetic appearance.

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BLOW OUT FRACTURE OF ORBIT

Aditi Dubey, Amar Pujari

INTRODUCTION

Orbital injury forms an important aspect of ocular trauma. The blowout fracture is the most common type of orbital fracture. The term pure orbital blowout fracture is used to describe fracture of the orbital floor, the medial wall or both, with an intact bony margin. The term impure orbital blowout fracture is used when such fractures occur in conjunction with a fracture of the orbital rim. The most common site for orbital blowout fracture is the posteromedial aspect of the orbital floor medial to the infraorbital neurovascular bundle where the maxillary bone is very thin (0.25–0.50 mm). As the lamina papyracea is also

very thin, the medial orbital wall is also prone to fracture, either in isolation or in association with a fracture of the orbital floor or other facial bones.

In examinations, it can be given as a long case.

HISTORY

Chief complaints: It depends upon the duration following trauma, after which the patient presents. When the patient presents immediately following trauma the complaints, include:

- *Eyelid ecchymosis (Fig. 1)/periorbital hematoma*: Usually present but signs may be absent as seen in the 'white-eyed blowout fracture'.



Fig. 1: Orbital floor fracture

- **Subcutaneous emphysema:** If a blowout fracture communicates with an air-filled sinus it may result in emphysema. Commonly seen in medial orbital wall blowout fractures. It may result in palpable crepitus. Patients should be advised not to blow their nose
- Proptosis of variable degree can also be seen initially due to orbital edema and hemorrhage
- Other complaints such as epistaxis, pain, loss of vision can be there depending on the damage to adjacent structures.
- Diplopia can be there due to muscle entrapment
- Small or inward displacement of an eyeball (enophthalmos) can be there due to soft tissue prolapse into adjacent sinuses.
- In cases, where the presentation is delayed, the complaints are usually of a small or shrunken eyeball, limitation of movements or diplopia.

History of Present Illness

A detailed history regarding mode of injury should be taken to assess the mechanism and extent of an injury. In cases of delayed presentation, progression must be noted carefully. The decision for surgical intervention largely depends upon the course of the symptoms over time.

Past history: Past history of poor vision in the affected eye, repeated trauma should be noted.

Systemic history: Past history of DM, hypertension, bleeding disorders and neurological problems must be noted. This will be helpful while planning surgery, especially under general anesthesia.

EXAMINATION

Systemic examination: General condition of a patient and another nonocular injury should be checked. Life-threatening injuries must be taken care of first before proceeding for ocular examination.

Ocular examination: Following points must be noted in a case of orbital fracture.

Visual acuity: Visual acuity at presentation has medico-legal importance in ocular trauma cases. Uncorrected as well as best corrected visual acuity must be noted in all cases of trauma.

Orbit

- Palpate orbital rim to look for deformity and crepitus. Subcutaneous emphysema with crepitus seen in fractures communicating with air-filled sinuses. The malar eminences should be palpated and any depression noted. The patient should be asked to open and close his mouth to rule out pain or trismus that may be associated with a zygomatic complex fracture.
- Paresthesia or sensory loss over ipsilateral lower lid, cheek and upper lip pathognomonic. Neurosensory loss occurs in the area supplied by the infraorbital nerve. This occurs because the fracture extends along the infraorbital groove or canal injuring the infraorbital nerve. These sensory defects tend to resolve spontaneously with time but may get aggravated by surgery in the area.
- **Ocular motility:** Full orthoptic assessment should be performed in nine positions of gaze. Limitation of ocular motility can occur due to following causes:
 - Entrapment of orbital contents such as connective tissue, septa, extraocular muscle (inferior rectus most commonly) within the fracture.
 - Hematoma/edema in the orbital fat adjacent to the fracture.
 - Hematoma or contusion of the extraocular muscle itself.
 - Palsy of an extraocular muscle due to neuronal damage.
 - Volkmann's ischemic contracture of an entrapped extraocular muscle.

- Inferior rectus muscle leads to motility restriction especially in upgaze (vertical diplopia).

Eyelid: Pseudoptosis occurs due to loss of support. Look for other signs of trauma such as laceration or scar.

Conjunctiva: Subconjunctival hemorrhage and conjunctival chamois may be there.

Cornea: Trauma can lead to corneal abrasion, corneal laceration.

Iris and anterior chamber: Trauma may be associated with iritis, miosis or mydriasis, hyphema.

Pupil: Presence of relative afferent pupillary defect (RAPD) indicates optic nerve injury that needs urgent intervention in the form of pulse steroid therapy.

Lens: Trauma may be associated with subluxation, dislocation of lens.

Fundus: Look for effects of trauma such as dialysis, tear, retinal detachment or vitreous hemorrhage.

Special Tests

- *Hertel exophthalmometer:* Exophthalmometry is done to document enophthalmos.
- *Force duction test (FDT):* FDT is useful in determining whether dysmotility is restrictive or paralytic. In a blow out fracture with inferior rectus entrapment FDT is 'positive' indicating a mechanical cause.
- *Force generation test (FGT):* In testing force generation, the muscle insertion is grasped and the patient is asked to look into the muscle's field of action. A paretic muscle will feel weak when compared with the fellow eye.
- *Diplopia charting:* With red green glass, diplopia charting with streak light shows diplopia worsening in upgaze.
- *Hess screen or Lee screen tests* were done document the muscle involved.

INVESTIGATIONS

- *Plain X-rays:* Easily available and cost-effective imaging modality. *Water's view* is the most useful projection for detecting an orbital floor

fracture. X-ray shows bone discontinuity in the orbital floor with herniation of soft tissue in maxillary antrum seen as '*hanging drop*' sign.

Computerized tomography (CT) scanning: CT gives the detailed visualization of bony and soft tissue injury where entrapment of muscle can be appreciated (**Fig. 2**). Coronal sections are particularly useful and can show antral soft tissue densities, such as prolapsed orbital fat, extraocular muscle or hematoma.

• **Magnetic resonance imaging (MRI):** Can be utilized when there is the need for greater soft tissue evaluation. MRI is insufficient in assessing the bony structures and therefore needs to be combined with CT.

MANAGEMENT

Treatment includes both medical and surgical management:

- *Medical management/Observation:* It consists of oral antibiotics, analgesics and a short course of oral prednisone. Oral steroid benefits the patient by reducing the edema of the orbit and muscle. This also may allow for a more thorough assessment of the relative contribution to enophthalmos or entrapment from the fracture versus that from edema. Medical management is indicated in following conditions:

- No significant enophthalmos (<2 mm)
- Lack of marked hypo-ophthalmos



Fig. 2: Fracture of orbital floor on CT Scan

- Absence of an entrapped muscle or tissue
- Fracture less than 50% of the floor
- No diplopia
- The patient must be advised to avoid nose blowing, to avoid creating or worsening orbital emphysema. Nasal decongestants can be used if not contraindicated. Ice packs may be applied for initial 48 hours to reduce the pain and tissue edema.
- *Surgical treatment*
Surgical intervention is indicated in following cases:
 - *Immediate intervention:*
 - ♦ Diplopia present with CT evidence of an entrapped muscle or periorbital tissue and associated with a non-resolving oculocardiac reflex: bradycardia, heart block, nausea, vomiting or syncope
 - ♦ "White-eyed blow-out fracture." Young patients (<18 years), history of periocular trauma, little ecchymosis or edema (white eye), marked extraocular motility vertical restriction, and CT examination revealing an orbital floor fracture with entrapped muscle or perimuscular soft tissue
 - ♦ Early enophthalmos/hypoglobus causing facial asymmetry.
- *Within 2 weeks:* Patients with diplopia are usually observed for 2 weeks. If the diplopia resolves with a small fracture evident on CT, no surgical intervention is required. It is advisable to wait for 2-3 weeks for resolution of orbital edema/hematoma. However, surgery is indicated in the following scenario:
 - Symptomatic diplopia with positive forced ductions, evidence of an entrapped muscle or perimuscular soft tissue on CT examination, and minimal clinical improvement over time.
 - Large floor fracture causing latent enophthalmos
 - Significant hypo-ophthalmos
 - Progressive infraorbital hypoesthesia

Surgical principle: The basic steps of surgery includes assessing the orbital floor, releasing the soft tissue and muscle entrapment and strengthening the floor with use of implants.

The orbital floor can be approached through following ways:

Subciliary approach: Incision given 2-3 mm below the lash line. It has the advantage of better scar camouflage. The disadvantage is postoperative ectropion and lower lid retraction.

Subtarsal approach: Incision below tarsal plate over orbital rim. The advantage is it gives direct access to the floor with good exposure. The disadvantage is it leads cosmetically unacceptable scar.

Transconjunctival approach: Incision given in lower fornix 3 mm below the tarsal plate and can be combined with a lateral canthotomy for better exposure. The advantage is it gives no visible scar.

Transantral approach: Orbital floor reached via the maxillary sinus using Caldwell-Luc incision. It is a difficult technique and it is not a favored by an ophthalmologist.

Endoscopic approach: Trans-maxillary and trans-nasal endoscopies have been described which eliminate the need for eyelid incisions and gives improved visualization of fractures. However, it is difficult and often clumsy.

The orbital floor is reinforced with either autogenous or synthetic implant (**Table 1**). The surgeon should size the implant to cover the defect adequately and to prevent displacement or extrusion later. While cutting the implant, it should be tapered posteriorly to fit the orbital floor configuration.

VIVA QUESTIONS

Q.1. What is a pure and impure blowout fracture?

Ans. A pure orbital blowout fracture is used to describe fracture of the orbital floor, the medial wall or both, with an intact bony orbital margin. Impure orbital blowout fracture is used when such fractures occur in conjunction with a fracture of the orbital rim.

Q.2. Most common site for the blowout fracture of orbit?

Ans. The posteromedial aspect of the orbital floor medial to the infraorbital neurovascular

Table 1 Examples of implant materials used in orbital floor repair

<i>Implant material</i>	<i>Advantage</i>	<i>Disadvantage</i>
Membranous bone	Autogenous	<ul style="list-style-type: none"> Morbidity at donor site Extended operation time Resorption unpredictable
Cartilage	Autogenous	<ul style="list-style-type: none"> Morbidity at donor site Extended operation time Resorption unpredictable
Titanium mesh	Biocompatible stable	<ul style="list-style-type: none"> Foreign material that remains in the body Combination with bone recommended
Porous polyethylene (Medpor) sheets	Easy to shape and handle, Biocompatible stable	Foreign material that remains in the body
Silicon sheet	Easy-to-handle and cheap	Extrusion rates higher
Silastic sheet (Teflon)	Easy-to-shape and handle	Foreign body reaction and extrusion common

bundle where the maxillary bone is very thin (0.25–0.50 mm) is the most common site.

Q.3. What is the etiopathogenesis of blowout fracture?

Ans. There are two theories to explain the possible mechanism of orbital fracture:

- *Retropulsion theory/hydraulic theory:* States that the backward displacement of the globe caused by a blunt non-penetrating object raises the intraorbital pressure sufficiently to fracture the posteromedial orbital floor and/or the lamina papyracea of the ethmoid.
- *Buckling theory/transmission theory:* A transient deformation of the orbital rim transmits the force of injury directly to the orbital wall. During the course of injury, the force that is transmitted to bony walls of the orbit may also cause concussion ocular trauma leading to angle recession, hyphema, vitreous hemorrhage, commotio retinae, etc.

Q.4. Expanded orbit syndrome

Ans. Multiple fractures in and around the orbit may lead roomy orbit with extensive prolapse of orbital tissues. This expansion can be seen in orbital fracture along

with midfacial fracture as in tripod or Le Fort type III. Clinically patient has gross exophthalmos, inferior displacement of the globe (hypoglobus), deep superior sulcus, eyelid asymmetry and diplopia.

Q.5. What are the features of medial wall fracture?

Ans. Blowout fracture of a medial wall is much less common than a floor and usually seen along with nasoethmoid fractures, rather than as an isolated entity. Horizontal diplopia is usually the primary complaint when medial orbital tissues are involved. However, a vertical or oblique component can also be found in such cases.

Q.6. What is 'white-eyed' blowout fracture?

Ans. The bones of a child's orbit are more elastic than adults. Thus, injury in children causes more anteroposterior buckling creating a fracture with overlapping segments. This leads to 'trapdoor-type' fracture where prolapsed orbital tissue is caught in the fracture site leading to severe motility restriction and diplopia in absence of marked congestion or ecchymosis. The condition is also called the 'white-eyed' blowout fracture. It is seen in orbital blowout fracture in children.

Q.7. Boundaries of the orbital floor and contents

- Ans.**
- The adult orbital floor is formed by the maxillary, zygomatic bones anteriorly and palatine bones posteriorly.
 - Orbital floor measures about 35–40 mm anteroposteriorly and it is the shortest of all the walls. It forms the roof of the maxillary sinus.
 - The floor of the orbit contains infra orbital groove that forms infraorbital foramen. Infraorbital nerve, a branch of the maxillary division of trigeminal nerve passes through the groove, providing sensory innervations to the ipsilateral orbital floor, mid face, and posterior upper gingival area. The infraorbital artery, a branch of the maxillary artery, and the infraorbital vein also are found within the infraorbital groove.

Q.8. What are common complications of floor repair surgery?

- Ans.**
- Intraoperative bleeding
 - Residual or new-onset diplopia
 - Extraocular muscle dysfunction
 - Postoperative neuralgia
 - Residual enophthalmos
 - Implant extrusion
 - Possible loss of vision.

Q.9. How to treat persistent diplopia?

- Ans.** Some patients may have persistent diplopia even after adequate surgical repair of

floor fracture. Diplopias in primary gaze and in downgaze (functional gaze) are more troublesome. Such cases will require muscle surgery. To correct diplopia in down gaze 'Reverse Knapp procedure' performed placing medial and lateral recti behind inferior rectus muscle. Fresnel prisms can be employed in selective cases.

Q.10. How to treat postoperatively cosmetically unacceptable enophthalmos?

- Ans.** A repeat surgery with adequate size orbital implant, if the downward sinking of an eye along with enophthalmos is unacceptable to patient, may have to be done. The pseudo ptosis can be corrected with mullerectomy, which will increase palpebral height.

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THYROID-ASSOCIATED OPHTHALMOPATHY

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INTRODUCTION

Thyroid associated ophthalmopathy (TAO) is the most common cause of proptosis in adults. TAO is a self-limiting autoimmune disease associated mainly with hyperthyroidism, but also with hypothyroid and euthyroid states. Although it can affect any age, most commonly presents during the fourth and fifth decades of life. It is one of the most important long case given in practical

examinations. In TED, it is important to record a proper history and elicit the signs associated with it.

HISTORY

Demography

It can affect any age group. Patients with TAO are more likely to be female by a 2:1 ratio, following the usual predominance of autoimmunity in women.

However, male Graves' disease are at the same, if not higher, risk of TAO development, which is usually of a more severe form and occurs at a more advanced age than in their female counterparts. Asians are having a lower likelihood of developing the disease than Europeans.^{1,2}

Chief Complaints

A case of TAO can present with following complain:

- Excessive lacrimation, a gritty sensation, discomfort, and photophobia are often present in early course of the disease.
- Bilateral upper lid retraction is most common presenting feature of the thyroid eye disease.
- Bilateral proptosis can also be the presenting feature.
- At times it may be detected accidentally or Referred by the endocrinologist.
- Decrease in visual acuity can be a presenting feature when it is associated with Optic nerve compression, exposure keratopathy or induced astigmatism due to globe compression.
- Patients may also complain of general symptoms like weight loss, sweating, heat intolerance, weakness, fatigue and palpitation along with ophthalmic complains.

Approximately 5 to 10% of Graves' orbitopathy patients are euthyroid at presentation and some of them may not have a history of thyroid dysfunction. Around 40% of patients with TAO, the signs of the eye disease occur simultaneously with the first symptoms of hyperthyroidism.

History of Present Illness

The history of present illness must include all the points described in the chapter of proptosis.

- The patient of TED present with the bilateral upper lid retraction and or exophthalmos. A careful history can reveal history of irritation, foreign body sensation, watering and recurrent lid edema in past that is often ignored by the patient. As the disease progresses the full blown picture of TED develops.
- Cigarette smoking has been considered the strongest risk factor for developing TED. Hence, a detailed history of smoking must be asked.

- Females are having more predominance in thyroid eye disease (2:1). However, males presents with more severe disease and usually at a later age.
- Patient may be in hyperthyroid or hypothyroid state, but 5 to 10% cases are euthyroid at the time of presentation.

Past History

- History of diabetes mellitus (DM), hypertension, asthma, thyroid abnormality should be noted.
- In a case of diagnosed TAO, past history of steroid, radiotherapy, orbital decompression or any thyroidectomy must be recorded.

Personal History

Personal history of alcohol intake, smoking, tobacco chewing or any other if present should be noted, because smoking is considered as important risk factor for the TED.

EXAMINATION

Examination of a case of TAO is similar to that of a case of proptosis. Salient features of TAO are described here.

Systemic Examination

General examination may show the signs of hyperthyroidism such as tachycardia, fine hand tremor, warm and sweaty skin, pretibial myxedema, finger clubbing, alopecia and vitiligo. A detailed examination of cardiovascular system, respiratory system, gastrointestinal system and Central nervous system has to be done as these systems gets affected by Graves' disease.

Ophthalmic Examination

The ocular examination is similar to a case of proptosis. Important points to note are described below:

- Proptosis is usually axial.
- Globes are mostly aligned.
- The most characteristic signs are eyelid erythema and swelling, caruncular and conjunctival injection and edema (**Fig. 1**).



Fig. 1: Severe bilateral proptosis due to thyroid eye disease



Fig. 2: Thyroid eye disease with disproportionate proptosis and inferior dystopia in left eye

- Some patients may have restriction of the eye movements leading to squint. The most commonly affected muscle is inferior rectus followed by medial, superior, levator and lateral rectus (**Fig. 2**). The muscles affected results in ocular misalignment, diplopia. Strabismus is also common, and it often presents as hypotropia or esotropia.
- **Eyelid:** Various lid signs which can be seen in thyroid ophthalmopathy (**Table 1**). All signs may not be present in a single patient. Lid retraction, also known as Dalrymple's sign, occurs most commonly as lid sign, in about 37–92% of patients (**Fig. 3**).
- Eyelashes are usually normal.
- Conjunctiva may show mild congestion due the dry eye caused by the excessive evaporation of the tears due to the lid retraction.
- Inflammation along recti muscle (tendonitis) can be an early sign of the disease.
 - Cornea may have exposure keratopathy. Causes of exposure keratopathy include:
 - ♦ Inadequate eyelid closure leading to excessive moisture loss as a consequence of proptosis and eyelid dysfunction.
 - ♦ Diminished tear production resulting from lacrimal gland infiltration.
 - ♦ Lagophthalmos from proptosis.
 - ♦ Loss of Bells phenomenon from inferior rectus infiltration.



Fig. 3: Thyroid eye disease with lid retraction

- Pupillary reaction may or may not be normal. Presence of RAPD or APD suggests optic nerve compression.
- Variable intraocular pressure (IOP) can be there in different gazes due to restrictive myopathy. An IOP rise more than 8 mm Hg on upgaze is significant and warrant treatment. Glaucoma can also result from decreased episcleral venous outflow.
- Lens do not show any specific changes.
- Fundus examination may show signs of globe compression. Compressive optic neuropathy occurs in <5% of patients with thyroid ophthalmopathy resulting in slowly progressive visual loss. It occurs due to compression from the oversized recti and

Table 1 Lid signs in proptosis

Sign	Description
Abadie's sign	Elevator muscle of upper eyelid is spastic
Ballett's sign	Paralysis of one or more extraocular muscle (EOM)
Beck's sign	Abnormal intense pulsation of retina's arteries
Boston's sign	Jerky movements of upper lid on lower gaze
Cowen's sign	Extensive hippus of consensual pupillary reflex
Dalrymple's sign	Upper eyelid retraction
Enroth's sign	Edema especially of the upper eyelid
Gifford's sign	Difficulty in eversion of upper lid
Goldzieher's sign	Deep injection of conjunctiva, especially temporal
Griffith's sign	Lower lid lag on upward gaze
Hertoghe's sign	Loss of eyebrows laterally
Jellinek's sign	Superior eyelid folds is hyperpigmented
Joffroy's sign	Absent creases in the forehead on upward gaze
Jendrassik's sign	Abduction and rotation of eyeball is limited also
Knies' sign	Uneven pupillary dilatation in dim light
Kocher's sign	Spasmodic retraction of upper lid on fixation
Loewi's sign	Quick mydriasis after instillation of 1:1000 adrenaline
Mann's sign	Eyes seem to be situated at different levels because of tanned skin
Means' sign	Increased scleral show on upgaze (globe lag)
Moebius's sign	Lack of convergence
Payne/Trousseau sign	Dislocation of globe
Pochin's sign	Reduced amplitude of blinking
Rieseman's sign	Bruit over the eyelid
Movement's cap phenomenon	Eyeball movements are performed difficultly, abruptly and incompletely
Rosenbach's sign	Eyelids are animated by thin tremors when closed
Saiton's sign	Frontalis contraction after cessation of levator activity
Snellen-Rieseman's sign	When placing the stethoscope's capsule over closed eyelids a systolic murmur could be heard
Stellwag's sign	Incomplete and infrequent blinking
Suker's sign	Inability to maintain fixation on extreme lateral gaze
Tellas's sign	Inferior eyelid might be hyperpigmented
Topolanski's sign	Around insertion areas of the four rectus muscles of the eyeball a vascular band network is noticed and this network joins the four insertion points.
von Graefe's sign	Upper lid lag on downgaze
Wilder's sign	Jerking of the eye on movement from abduction to adduction

orbital fat causing compartment syndrome at the apex of orbit. It is characterized by decrease in vision, color vision, contrast sensitivity and relative afferent papillary defect. Visual loss may progress undetected due to insidious onset and subtlety of neuropathy. Risk factors for optic neuropathy include:

- Older age
- Smoking
- Male gender
- Significant strabismus with mild proptosis.
- **Visual field:** Central and inferior arcuate scotoma and generalized constriction may be seen in advanced cases ophthalmopathy.

DIFFERENTIAL DIAGNOSIS

The diagnosis often straight forward. The characteristic signs and systemic signs are difficult to miss. However, in early course of the disease following diseases may mimic TAO

- Orbital myositis
- Nonspecific orbital inflammatory disease (NSOID)
- Myasthenia gravis
- Chronic progressive external ophthalmoplegia
- Carotid-cavernous fistula
- Specific inflammatory orbitopathy
- Orbital tumors
- Lid retraction, characteristic of TAO can also be seen in number of other diseases as given here.

Upper Lid Retraction

- Congenital
- **Neurologic disorders:** Midbrain disease, Hydrocephalus
- **Post-surgery:** Ptosis surgery, lid reconstruction
- Marcus Gunn phenomenon, Faulty regeneration of cranial nerve III
- Parinaud's syndrome
- Sympathomimetic drugs
- Cirrhosis.

Lower Lid Retraction

- Idiopathic senile flaccidity of lower lid
- Post-traumatic impairment
- Congenital abnormality

- Postsurgical lesion—Recession of the inferior rectus muscle, Repair of a blowout fracture
- Facial nerve lesion.

INVESTIGATIONS

Following investigations are carried out in a case of TAO:

- CBC, Thyroid function test [Tri-iodothyronine (T3), Free thyroxin (T4), Serum thyroid-stimulating hormone (TSH), Thyrotrophic receptor antibodies (TRAB), ESR].
- **Ultrasonography (USG):** On cross-section, there is an increase in thickness of the extraocular muscles. USG of the globe and the orbit can help in visualization of the tendinous intersections. This also helps to differentiate between active and inactive disease. By comparing the muscle thickness, ultrasound may help in confirming the diagnosis in unilateral cases. It also helps in differentiating associated diseases presenting with similar clinical features.
- **Computed tomography (CT) scan:** Typical radiological features seen on CT are muscle belly enlargement that is classically described as 'tendon sparing', an increase in orbital fat volume, and crowding of the optic nerve at the orbital apex in severe cases. It helps in assessing the relationship between the optic nerve and muscles at the apex that helps in planning for the surgical intervention, if needed. CT is more sensitive than MRI in identifying enlarged extraocular muscles. As a standard, 2 mm cuts should be requested for, along with coronal and axial slices. Orbital fat is imaged in CT as a black, low-density area that contrasts with the higher-density image of extraocular muscles and the optic nerve. CT scans allow for better delineation of the bony orbit and therefore are invaluable in planning orbital decompression.
- **Magnetic resonance imaging:** Demonstrates fusiform rectus enlargement and orbital fat expansion. It assesses water content in the muscles that correlates with the active inflammation. In the active phase, the extraocular muscles appear isointense in T1-weighted images and hyperintense in T2 weighted images; where as in the chronic phase, they appear hypointense on T2-images.

- Visual field testing is important for detecting early damage to the optic nerve due to apical crowding around the optic nerve. The changes on visual fields are reversible if the crowding is relieved early, either surgically or medically. Usually, the patterns of visual field loss vary, the most common being central, paracentral and/or inferior.

CLASSIFICATION

Different classification system have been proposed, however there is no consensus on the best way to classify TAO:

- NO-SPECS classification**
 - Proposed by Werner et al. and adopted by the American Thyroid Association (**Table 2**)
 - Based upon clinical presentation
 - Limitation:** Relies on subjective evaluation, does not take into account the severity of manifestations, Patient may fall into more than 1 particular class, may not progress in an orderly fashion from class 1 to class 6 and is relatively insensitive to subtle changes, hence less preferred.
- RELIEF classification of soft tissue signs and symptoms**
 - R – Resistance to retropulsion
 - E – Edema of conjunctiva and caruncle
 - L – Lacrimal gland enlargement
 - I – Injection over the horizontal rectus muscle insertions
 - E – Edema of the eyelids
 - F – Fullness of the eyelids

Staging/Scoring

- Clinical activity score (CAS):**
 - It is one of the widely utilized grading system described by Mourits and colleagues
 - It attempts to identify patients with active disease who are likely to respond to medical therapy.
 - The CAS is generated by the addition of 1 point for the presence of each the following features:* Chemosis, eyelid swelling, eyelid erythema, conjunctival erythema, caruncular swelling, pain in primary gaze,

Table 2 NO-SPECS classification of thyroid associated ophthalmopathy

Class	Grade	Clinical features
0		N – No signs symptoms
1		O – Only signs
2	O A B C	S – Soft-tissue involvement Absent Minimal Moderate Marked
3	O A B C	P – Proptosis <23 mm 23–24 mm 25–27 mm ≥28 mm
4	O A B C	E – Extraocular muscle involvement Absent Limitation of motion in extremes of gaze Evident restriction of movement Fixed eyeball
5	O A B C	C – Corneal involvement Absent Stippling of cornea Ulceration Clouding
6	O A B C	S – Sight loss Absent 20/20 – 20/60 20/70 – 20/200 <20/200

and pain with ocular movement. In addition, if the patient has been examined within the 3 months prior, additional points may be given for decreased visual acuity, worsened diplopia, and increased proptosis compared with that visit.

- TAO is considered active in patients with a CAS of 3 or more out of 7 (if no previous assessment is available), or 4 out of 10 on the complete scale.
- This scale has a specificity of 86%, sensitivity of 55%, positive predictive value of 80%, and negative predictive value of 64% for predicting the activity of the disease.

- **Limitation:** It is subjective (depends on both patient and practitioner) and it fails to account for active improvement or worsening of the disease.
 - **European Group on Graves' orbitopathy (EUGOGO):** It is one of the commonly used scoring systems. It recommends the following classification of patients with thyroid ophthalmopathy.³
- Mild GO:** They usually present with one or more of the following signs:
- Minor lid retraction (< 2 mm)
 - Mild soft tissue involvement
 - Exophthalmos < 3 mm (above the normal range for the race and gender)
 - Transient or no diplopia
 - Corneal exposure responsive to lubricants
- Moderate-to-severe GO:** These patients usually have any one or more of the following:
- Lid retraction >2 mm
 - Moderate or severe soft tissue involvement
 - Exophthalmos >3 mm above normal for race and gender
 - Inconstant or constant diplopia
- Sight-threatening GO:**
- Patients with dysthyroid optic neuropathy and/or corneal breakdown.
 - Other infrequent conditions are ocular globe subluxation, severe forms of frozen eye, choroidal folds, and postural visual darkening.
 - This category warrants immediate intervention.
 - As a rule of thumb, it is considered that all patients who do not have a mild or a sight-threatening ophthalmopathy present a moderate-to-severe disease.
- **VISA scoring:**
 - Developed by Dolman and Rootman and adopted with modifications by the International Thyroid Eye Disease Society (ITEDS).
 - It is based on symptoms (subjective) and signs (objective) inputs.
 - Four severity parameters are analyzed: V (vision); I (inflammation/congestion); S (strabismus/motility restriction); and A (appearance/exposure).
 - Each feature is considered and graded independently
- ♦ **Vision:** 1 point
 - ♦ **Inflammation/congestion:** 10 points
 - ♦ **Strabismus:** 6 points (diplopia: 3 points plus restriction: 3 points)
 - ♦ **Appearance/exposure:** 3 points.
 - ♦ A global severity grade, with maximum score is 20 points, is the sum of each of the involved systems graded independently:
 - **Vision (V):** Evaluates the visual problems, especially due to associated dysthyroid optic neuropathy. It is assessed through visual acuity, pupillary reflexes, color vision, visual fields, optic nerve examination, and visual evoked potentials.
 - Soft tissue **inflammation/congestion (I)** evaluation is graded according to the worst score for the eye or the eyelid with the Inflammatory Index as shown in **Table 3**. Patients with moderate inflammatory index (less than 4 of 10) are managed conservatively. Patients with high scores (above 5 of 10) or with evidence of progression (as documented

Table 3 VISA inflammatory index

Sign or symptom	Score
Caruncular edema	0: Absent 1: Present
Chemosis	0: Absent 1: Conjunctiva lies behind the gray line of the lid 2: Conjunctiva extends anterior to the gray line of the lid
Conjunctival redness	0: Absent 1: Present
Lid redness	0: Absent 1: Present
Lid edema	0: Absent 1: Present but without redundant tissues 2: Present and causing bulging in the palpebral skin, including lower lid festoon
Retrobulbar ache	• At rest • With Gaze 0: Absent; 1: Present 0: Absent; 1: Present
Diurnal variation	0: Absent; 1: Present

on subsequent visits) in the inflammation are offered a more aggressive therapy.

- *Strabismus/motility restriction (S)* is documented by three aspects:

1. Diplopia that is graded from 0 to 3 (0 = no diplopia, 1 = diplopia with horizontal or vertical gaze, 2 = intermittent diplopia in straight gaze, and 3 = constant diplopia in straight gaze).
2. Ocular ductions are measured to the nearest 5° in four directions using the corneal light reflex technique. Any change of ≥ 12° in any direction can be considered progression.
3. Ocular restriction can be graded from 0 to 3 based on the range of ductions (0 = duction > 45°, 1 = 30–45°, 2 = 15–30°, and 3 <15°) quantified by prism cover testing.

- *Appearance/exposure (A)*

- Symptoms include appearance concerns (such as bulging eyes, eyelid retraction, and fat pockets) and those derived from ocular exposure (such as gritting sensation, photophobia, dryness, and secondary tearing).
- Signs include measurements of eyelid retraction (millimeters from the pupillary light reflex to the lid margin); scleral show (millimeters from the limbus to the lid margin); levator palpebrae superioris function; lagophthalmos (incomplete eyelid closure); and proptosis with the Hertel exophthalmometer. Signs of corneal exposure are best assessed with the slit-lamp microscope and may include punctate epithelial erosions, ulcerations, and, in severe cases, corneal thinning and risk of perforation.

The VISA and CAS were designed to determine the clinical *activity*. In comparison, the NO SPECS and EUGOGO classification assess the clinical *severity*. Both VISA (particularly in US) and EUGOGO (European countries) are currently used for deciding upon treatment and also monitoring response to treatment.³⁻⁵

MANAGEMENT

Treatment of Thyroid Gland Dysfunction

It is the most important aspect of treatment of thyroid ophthalmopathy. Frequent monitoring of

thyroid status (every 4–6 weeks) is imperative in the initial phases of treatment when changes in thyroid status are expected.

Treatment of Ophthalmopathy

Treatment should follow the sequence of (V-I-S-A), i.e. 1st take care of visual disturbance then ISA (of VISA scoring).

Treatment Options

- *Supportive measures:*

- *Artificial tears:* Lubricant eye drops during the day and Lubricant ointments at night-time
- *Sunglasses:* To avoid photophobia
- Patients with symptomatic diplopia—Fresnel prisms or occlusion therapy
- Botulinum toxin injection may be considered for upper lid retraction
- Topical adrenergic blocking agents such as 5% guanethidine sulfate drops transiently improve mild eyelid retraction but not of much use
- Cool compresses
- *Head elevation:* To reduce periorbital edema.

- *Medical management:*

Corticosteroids: Systemic steroids are indicated in patients with severe inflammation or compressive optic neuropathy. Intravenous glucocorticoids is required for patients with advanced thyroid-associated orbitopathy. Intravenous glucocorticoids seem to be associated with higher success rate and better tolerability as compared to oral glucocorticoids.

Steroid-sparing immunosuppressive drugs: Cyclosporine and Methotrexate, Intravenous administration of immunoglobulin, Tumor necrosis factor- α blockers and anti-CD20 monoclonal antibodies (rituximab) have been found useful. However, these are inferior to steroids as monotherapy and considered only when steroid is contraindicated.

- *Radiation therapy:*

Acts by a nonspecific anti-inflammatory effect. RT is effective in patients who have active eye disease with recent progression and ineffective in inactive stages of the disease.

The Lymphocytes infiltrating the orbit have high radio sensitivity. Usually a dose of 20 Gy is given per eye fractionated over a 2-week period. However, RT can be associated with transient exacerbations of inflammation, hence simultaneous glucocorticoids must be started. Although, the evidence regarding the efficacy of radiation therapy in the management of TAO is limited, it is still one of the widely used treatment modality.

- **Surgical management**

Orbital decompression: It is indicated in cases with compressive optic neuropathy not improving with medical treatment. It enlarges the existing space of the orbit by partial removal of bony walls and periosteum. The most commonly done decompression involves the posteromedial wall followed by floor and lateral wall.

Treatment

It depends upon the stage and severity:

- **Mild TED:** Only supportive therapy is required. Progression from mild-to-moderate-to-severe TED occurs in about 15%. The side effects of immunosuppressive treatment or radiation do not weigh against the expected beneficial effects.
- **Moderate-to-severe TED:** Moderate-to-severe TED is defined as: no threat to vision but sufficient impact on daily life to justify the risks of immunosuppression. Corticosteroids are the treatment of choice with a response rates up to 80%. Intravenous prednisolone treatment is recommended because it has better results compared with high-dose oral therapy and it is associated with less side effects such as diabetes or weight gain. Prior to starting high dose steroid possible contraindications for high-dose prednisone treatment, such as gastrointestinal ulcer disease, severe osteoporosis, latent tuberculosis or hepatitis B or C positivity, uncontrolled diabetes/hypertension must be ruled out. The cumulative dose of prednisolone should not exceed 8 g in one course of therapy. However, the exact dose of prednisolone that yields satisfactory therapeutic effect without adverse events is not exactly known.

- **Very severe TED:** Very severe TED should be treated with 1 g methylprednisolone IV daily for three consecutive days, repeated after one week, followed by an oral tapering dose. When there is clinical deterioration, urgent orbital decompression should be considered. Indications for surgical decompression includes:
 - Patients with active disease who have refractory or progressing corneal ulcer.
 - A stretched optic nerve
 - Prevention of further corneal damage
 - Cosmetic in acceptability.

In-orbital decompression, part of the bony walls is removed to provide more room for the extraocular muscles and orbital fat. Associated diplopia usually requires surgery of the extraocular muscles. But after the orbital decompression surgery, diplopia surgery should be postponed till effect of the previous if established. Eyelid surgery such as lengthening (in case of upper eye lid retraction) may be a final step in the rehabilitation of the patient with TED.

VIVA QUESTIONS

Q.1. What are the risk factors for TAO?

Ans. *Genetics:* The TED is considered be an autoimmune disease because of its clinical association with Graves disease, an associated condition known to be caused by anti-thyrotropin receptor antibodies (TRAb).

Tobacco smoking: Smoking is the risk factor most consistently linked to either development or deterioration of TAO. Overall, more than 40% of smokers either developed or worsened TAO, which was almost double the rate of non smokers. Cigarette smoke extract increase production by orbital fibroblasts of glycosaminoglycans, hydrophilic macromolecules that accumulate in TAO orbital tissues.

Therapy for TED with RAI: TAO HAS 15% and 39% risk for development or progression after RAI therapy for hyperthyroidism. The majority of patients developing TED after RAI treatment had mild and transient disease requiring no treatment.

Thyroid dysfunction: Both hyper- and hypothyroidism have been shown in multiple reports to be associated with increased risk for development or deterioration of TAO.

Thyroxine and tri-iodothyronine levels: Some studies have suggested that circulating tri-iodothyronine (T3) or thyroxine (T4) may also be associated with GO.

Q.2. What is Rundles curve/natural course of TAO ?

Ans. Rundle conceptualized two distinct phases for TED, which is graphically represented in his famous 'Rundle's curve'. Rundles curve represent the natural course of TED. It helps in understanding and managing TED. It has two stages:

1. An initial *active inflammatory phase* which is associated with periorbital erythema and edema, conjunctival chemosis, orbital inflammation and congestion, associated with upper lid retraction, proptosis, and occasionally diplopia. The inflammatory phase typically lasts for a period between 6 and 24 months
2. This is followed by a quiet, minimally inflammatory chronic fibrotic phase

which is associated with orbital fibrosis, glycosaminoglycan deposition and enlarged extraocular muscles. There are usually no active inflammatory episodes in this phase.

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LACRIMAL GLAND TUMORS

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INTRODUCTION

The lacrimal gland is situated in the superotemporal orbit and it consists of 2 lobes, the orbital lobe, and the much smaller palpebral lobe. The palpebral lobe can be visualized in the superior fornix on lid eversion but not the orbital lobe. Thus, any pathology that affects the orbital lobes only may be missed for a long period of time. Lacrimal gland tumors account for about 10–15% of all orbital tumors.¹ The clinician should consider the axiom: "*Half and a half; then half again.*" Approximately half of all lacrimal fossa masses

are inflammatory, and the other half is neoplastic. Out of the neoplastic group, half are the aggressive adenoid cystic carcinoma (ADCC) variety.^{1,2}

In exams, it can be given as a long case.

HISTORY

Demography

Lacrimal gland tumors are seen more frequently in the third to fourth decade of life (may present from childhood to old age), and the second bimodal peak is in the teenage years.

Chief Complaints

The presentation varies from patients who are asymptomatic but have a slight fullness in the temporal upper lid to those who present with frank proptosis, diplopia, and an encroaching mass lesion.

History of Present Illness

All points as described in section proptosis must be recorded carefully while taking history. In addition following points must be noted:

- History of a long-standing (>1–2 years), non-infiltrating lacrimal gland lesion suggests a benign tumor, such as a pleomorphic adenoma.
- A shorter history suggests either an inflammatory or a malignant process.
- Pain most commonly is seen with inflammatory lesions of the lacrimal gland, but adenoid cystic carcinomas and other malignancies also can present with pain secondary to perineural or bony involvement.
- Malignant lesions characteristically present with a subacute course of proptosis and temporal sensory loss in the distribution of the lacrimal nerve in one-third of patients.
- Limitation of eye movement, diplopia, and diminished visual acuity can be seen with large tumors due to distortion of the globe by the firm tumor mass.
- Benign lesions commonly present with painless inferonasal globe displacement and fullness of the superotemporal lid and orbit. Old photographs may be helpful in establishing the duration of displacement.
- Acute onset of a painful, erythematous, indurated eyelid suggests inflammation.
- Other symptoms that may present include facial asymmetry noted by friends, epiphora, exposure symptoms.

History of Past Illness

Past ocular history may uncover an episode of trauma, prior periorbital surgery, or periocular tumors that could relate to the present illness. A history of intraocular malignancy such as malignant melanoma might point to the possibility of orbital extension or metastasis.

Surgical History

History of surgical removal of similar mass may be there (recurrence is found in pleomorphic adenoma). Incomplete excision of pleomorphic adenoma can lead to relentless recurrences and malignant transformation (**Fig. 1**). Thus the previous history of biopsy (such as incisional or needle) is important in such cases.

History of Systemic Illness

The past general medical history may elicit important diagnostic information. For example, a history of breast cancer might suggest metastasis. A history of systemic inflammatory disease such as sarcoidosis should raise concern for a related orbital inflammatory process.

EXAMINATION

Systemic Examination

A detailed general examination is carried out to rule out any systemic metastasis. Preauricular lymphadenopathy from regional metastasis in malignant lesions must be ruled out. Signs of primary elsewhere in the body must be looked for.

Ocular Examination

Following points must be noted in ocular examination:

- *Visual acuity:* Diminished visual acuity can be seen with rapidly progressive lesions. Patients



Fig. 1: Adenoid cystic carcinoma of lacrimal gland

with induced hyperopia from an orbital mass may show a significant asymmetric refractive error.

- ***Eyeball:*** Displacement of the globe with or without proptosis can occur. The displacement is characteristically nonaxial with *inferomedial globe displacement*.
- ***Ocular balance and ductions:*** Binocular patients should be examined for latent or manifest ocular deviations and the approximate extent of uniocular ductions in the four cardinal positions estimated. A forced duction (traction) test under topical anesthesia will assist differentiation of neurological from mechanical causes of restricted eye movements. Likewise, retraction of the globe during an active duction suggests fibrosis of the ipsilateral antagonist muscle, this being a common sign with chronic orbital myositis.
- ***Lids:*** An *S-shaped contour to the upper lid* (the lateral half of the eyelid lies lower than the medial half) is characteristic for lacrimal gland lesions, but it is relatively nonspecific to the type of tumor. A firm, rubbery, nontender mass can be seen with either benign or lymphoproliferative lesions.
- Complete examination of mass should be done (as discussed in chapter proptosis) which includes size, shape, site, margins, edges, consistency, mobility, adherence to overlying skin and underlying bone, color of skin, temperature of skin, reducibility and compressibility, increase in size with Valsalva maneuver, pulsations, and transillumination.
- ***Conjunctiva, cornea:*** Signs of inflammation such as congestion and chemosis may be present with dacryoadenitis, tumors or infiltration of the lacrimal gland. A "*salmon patch*" subconjunctival lesion may be present and is characteristic of lymphoma. Signs of exposure keratopathy (punctate defects or epithelial defect with infiltrates) may be present. A reduced Schirmer's test may indicate towards an inflammatory lesion (e.g. Sjögren syndrome).
- ***Pupils:*** Usually the pupillary reaction is normal. RAPD may be present if the mass is compressing or infiltrating the optic nerve.
- ***Anterior segment:*** Usually normal. Raised IOP may be present due to globe compression.
- ***Posterior segment:*** (Slit-lamp biomicroscopic examination using a 90D/78D lens and indirect ophthalmoscopy)
 - *Vitreous, optic disc and macula:* Are usually normal.
 - Choroidal folds may be present, resulting from globe indentation by an orbital mass.

INVESTIGATIONS

Following investigating modalities are used in a suspected case of lacrimal gland tumor:

High-resolution Computed Tomography (HR-CT)

- ***Benign tumors:*** Pleomorphic adenomas appear as well-defined, sometimes nodular and non-homogeneous lesions that show moderate enhancement with intravenous contrast. Palpebral lobe tumors lie anterior to the orbital rim, whereas expansion of the lacrimal fossa with preservation of intact cortical bone is seen in most cases of orbital lobe adenoma. Molding of the lacrimal gland fossa on CT scan is a *hallmark* of benign growth. Discrete calcification may also be present in a minority of cases, and indentation of the globe is common with larger tumors.
- ***Malignant tumors:*** These are poorly defined margins, with infiltration into surrounding tissues, and bone. Calcification occurs in about one-third of carcinomas but is diffuse compared to pleomorphic adenomas. In contrast to the hard pleomorphic adenomas that flatten the globe, rapidly growing and softer lesions (such as carcinoma and lymphoma) tend to mold to its surface.

Histologic Findings

Histologic examination of pleomorphic adenomas reveals evidence of both epithelial and mesenchymal differentiation. The proliferation of benign epithelial cells usually is arranged in a double layer to form lumens. Stromal differentiation can be seen in the formation of bone and cartilage.

ADCC are derived from duct cells, and they form spaces into which basement membrane-like material is deposited. This confers a *cryptoid* or "Swiss cheese" appearance to the tissue, which is characteristic of ADCC.

Immunohistochemistry

This may be helpful in distinguishing between inflammatory, benign, and malignant lymphoproliferative lesions. Immunohistochemistry is a laboratory modality that uses special markers to demonstrate the presence of specific antigens in target tissues. Benign inflammatory lesions (pseudotumor) have a polyclonal morphology, whereas the lymphoid lesions tend to be monoclonal.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of a lacrimal gland mass has been described in **Table 1**.

Key features [also See Table 2].

Benign Tumors

- *Pleomorphic adenoma:* It has following important features:
- Most common intrinsic lacrimal gland lesion

Table 1 Differential diagnosis of lacrimal gland mass

<i>Non neoplastic</i>	<i>Neoplastic</i>
Dacryops/ dacryoadenitis	<i>Lymphoproliferative diseases</i> <ul style="list-style-type: none"> • Benign lymphoid hyperplasia • Atypical lymphoid hyperplasia • Malignant lymphoma
Dermoid cysts	<i>Benign tumors</i> <ul style="list-style-type: none"> • Pleomorphic adenoma (benign mixed tumor) • Benign fibrous histiocytoma • Oncocytoma • Myoepithelioma • Cystadenoma
Hemangioma	<i>Malignant tumors</i> <ul style="list-style-type: none"> • Adenoid cystic carcinoma • Malignant mixed tumor (carcinoma expleomorphic adenoma) • Adenocarcinoma • Mucoepidermoid carcinoma • Squamous cell carcinoma • Acinic cell carcinoma • Malignant oncocyctoma • Lung and breast metastases
Amyloid	

- Painless, progressive, slow growing
- Well-circumscribed mass with absence of bony destruction
- Remove with pseudo capsule intact to decrease risk of recurrence or malignant transformation
- *Histopathologically, comprised of two cell components:* Benign epithelial cells arranged in double layer forming ducts stellate spindle cells contained in loose stroma

Myoepithelioma

- Rare tumor with biological behavior similar to that of a pleomorphic adenoma
- *Five subtypes:* Spindle, plasmacytoid, epithelial, clear and mixed.

Oncocytoma

- Rare tumor secondary to metaplasia of ductular cells (epithelial origin).
- Large, eosinophilic cells rich in mitochondria “Warthin Tumor” (Cystadenolymphoma)
- Commonly presents as an epithelial neoplasm of the salivary glands (lacrimal gland is an unusual location).
- Epithelial columnar cells arranged in solid nests or lining cystic spaces.

Malignant Tumors

Adenoid Cystic Carcinoma

- Bimodal distribution with peak incidences in second and fourth decades of life
- Periorbital pain (severe pain due to perineural spread), mild ptosis, proptosis, downward and inward displacement of the globe
- Bony erosion, bone destruction, and soft tissue calcification on CT
- High mortality rate (intra-arterial cytoreductive chemotherapy may improve survival)
- Sheets of epithelial cells arranged in solid or cribriform pattern resembling a glandular structure is characteristic.

Primary Adenocarcinoma

- Rare tumor with clinical findings similar to adenoid cystic carcinoma.
- Pleomorphic, mitotically active cells arranged in sheets and cords.

Table 2 Summary of major lacrimal gland tumors

<i>Types of lesion</i>	<i>Clinical features</i>	<i>Imaging features</i>	<i>Histopathologic features</i>	<i>Treatment</i>
Pleomorphic adenoma (benign mixed tumor) Most common epithelial tumor	Painless, progressive, slow-growing mass on superotemporal area of upper eyelid, Nontender, firm, well-contoured mass. Variable proptosis, Diplopia loss of vision rare	CT—round to oval well circumscribed mass in the lacrimal fossa, with bony expansion and excavation, no bony destruction. USG—round to oval mass with medium to high reflectivity and regular internal structure	Two morphologic cell components: benign epithelial cells arranged in a double forming ducts and stellate spindle cells contained in a loose stroma. Epithelial cells in the stroma can undergo metaplasia with cartilaginous, fibrous or myxoid characteristics	Modified lateral orbitotomy and excision using an extraperiosteal approach for the lateral portion For an anteriorly situated palpebral lobe tumor, isolated dacryoadenectomy via a transcutaneous or transconjunctival approach
Oncocytoma	Rare affects elderly females caruncle most common site		Large, eosinophilic cells rich in mitochondria	Complete surgical excision
Cystadenoma (Warthin's tumor)	Rare Clinical characteristic is similar to pleomorphic adenoma	Similar to those of a pleomorphic adenoma	Epithelial columnar cells arranged in solid nests or lining cystic spaces. Often contains an exudative fluid component and a lymphoid infiltrate with focal follicular organization	Complete excision of the globular cystic mass with preservation of the thin capsule
Adenoid cystic carcinoma	Periorbital pain, mild ptosis, proptosis, brow numbness and diplopia. Rapid progression symptoms are typically present for 6 months, and almost always less than one year	Globular lacrimal gland mass with irregular borders, bony erosion, bone destruction and soft tissue calcification. Contiguous tumor extension to adjacent area	Sheets of epithelial cells arranged in either solid or cribriform patterns with spaces into which basement membrane like material is deposited. (Swiss-Cheese)	<i>En bloc</i> , excision of the orbit and its contents, including the orbital roof, the lateral wall, the lids, and the anterior portion of the temporalis muscle where the zygomatico-frontal and zygomatico-temporal nerves extend. Adjunctive postoperative radiotherapy

Contd...

Contd...

Types of lesion	Clinical features	Imaging features	Histopathologic features	Treatment
Malignant mixed tumor	The average age at diagnosis is 50 years This tumor may arise <i>de novo</i> , because of malignant transformation following an incomplete excision of a benign adenoma, or as malignant transformation years after diagnosis of a presumed benign adenoma	Similar to adenoid cystic carcinoma, may show a bilobed appearance	Histopathologically, the malignant component may be attached to and arise from the benign mixed aspect of the tumor, yielding a bilobed appearance	Complete surgical resection Mortality is high
Mucoepidermoid carcinoma	Rarely Locally aggressive Average age at presentation of 49 years Male: Female 2:3	Similar to adenoid cystic carcinoma	Epidermoid and mucus-secreting cells arranged in a pattern of cords and islands. The mucus-secreting cells and cystoid spaces within the specimen stain positively with mucicarmine, alcian blue stains and Periodic acid-Schiff reaction	Excision with or without adjuvant radiotherapy. Advanced stage has a worse prognosis, require exenteration and radiotherapy
Carcinosarcoma	Carcinosarcoma may arise from a pleomorphic adenoma		Considered in the differential diagnosis of a lacrimal gland mass, if sarcomatous components are encountered on histologic examination	Management requires complete excision of the lesion

Pleomorphic Adenocarcinoma (Malignant Mixed Tumor)

- May arise *de novo*, as consequence of malignant transformation following incomplete excision of benign adenoma or as malignant transformation of a presumed benign adenoma.
- Well circumscribed, pseudo capsulated.

TREATMENT³⁻⁵ (TABLE 3)

Pleomorphic Adenoma

It should be excised intact with a cuff of normal tissue. Palpebral lobe tumors can be resected through an upper lid skin crease incision Stallard-Wright incision (anterior orbitotomy). Orbital lobe tumors can be approached through

Table 3 Difference between pleomorphic adenoma and adenoid cystic carcinoma

Features	Pleomorphic adenoma	Adenoid cystic carcinoma
Pain	Painless	Periorbital pain often severe
Course	Slow-growing mass	Fast growing
Proptosis	Variable	Proptosis with downward and inward displacement of the globe
Associated features	Decreased vision and diplopia rare	Brow numbness is characteristic, diplopia, mild ptosis
Palpation	Non-tender, firm, well contoured mass	Firm irregular bordered mass
Histological features	Benign epithelial cells arranged in a double layer forming ducts and stellate spindle cells contained in a loose stroma	Sheets of epithelial cells arranged in either solid or cribriform patterns (Swiss-Cheese pattern) that mimic glandular structure
Radiological features	<ul style="list-style-type: none"> • Round to oval well-circumscribed mass in the lacrimal fossa • Bony expansion and excavation but no bony destruction • The posterior edge of the lesion typically exhibits a curved contour that molds to the adjacent orbital bone 	<ul style="list-style-type: none"> • Globular lacrimal gland mass with borders that are irregular • Associated with bony erosion, bone destruction and soft tissue calcification • Tumor extension toward the medial orbit, apex and the temporalis fossa

a lateral orbitotomy approach. It is important to avoid any intraoperative spillage during surgery. Thus, a buffer of normal tissue should always be maintained around the tumor mass. If intraoperative spillage of cells occurs through cautery and lavage of the operative field has to be done. If the periosteum is already destroyed, the breach should be treated by strict surgical isolation and Cyanoacrylate glue may be applied to minor capsular breaches during surgery. Excision of the orbital lobe alone, with preservation of palpebral lobe, reduces the incidence of dry eye and secondary corneal disease.

Biopsy (other than excision) *should not be attempted* in any suspected case of pleomorphic adenoma. If it has been inadvertently biopsied, the biopsy tract and the tumor should be meticulously excised since recurrent pleomorphic adenoma is typically infiltrative and may need extensive tissue resection or exenteration.

Adenoid Cystic Carcinoma

It depends upon the extent of the tumor. For tumors that are localized to the orbit excision of the tumor and adjacent tissues should be done. Advanced tumors require surgical resection

followed by external beam radiation therapy (EBRT). ADCC is often extensive and requires orbital exenteration or midfacial resection. EBRT delays the growth or recurrence of the tumor. Brachytherapy (locally implanted radioactive plaques seeds) may also give results similar to EBRT. Chemotherapy does not have a recognized role in the treatment of adenoid cystic carcinoma.

The malignant mixed tumor is treated with local excision followed by irradiation.

Metastatic tumor carries a poor prognosis. The target is to provide palliative therapy through orbital irradiation or chemotherapy.

VIVA QUESTIONS

Q.1. Most common lacrimal gland tumors.

- Ans.**
- Pleomorphic adenomas account for almost all benign tumors of the lacrimal gland.
 - Adenoid cystic carcinoma is the most common (76%) malignant epithelial tumor.
 - Carcinoma arising in pre-existing pleomorphic adenoma (malignant mixed tumor) is the second most common malignancy of the lacrimal gland.

- Lymphoma accounts for about 10–14% of all lacrimal gland masses and may be part of a systemic disease.

Q.2. Where do you find a “salmon patch lesion”?

Ans. Salmon patch subconjunctival lesion is a characteristic non-tender firm reddish fleshy mass of conjunctival lymphoma. It may be an extension of orbital or intraocular lymphoma. Only 25% patients of orbital/adnexal lymphoma have conjunctival involvement. Most commonly, it is confused with chronic follicular conjunctivitis. Histologically, these are non-Hodgkin's lymphoma of low-grade B-cell variety.

Q.3. Differential diagnosis of a lacrimal fossa mass.

Ans. Refer to differential diagnosis.

Q.4. How do you differentiate pleomorphic adenoma from adenoid cystic carcinoma?

Ans. See Table 3.

Q.5. What is “Swiss cheese” pattern of ADCC?

Ans. It refers to the microscopic picture of ADCC. Closely packed small, densely stained cells aggregate around large ovoid spaces containing hyaline or mucin. This resembles the Swiss cheese pattern and hence the description.

Q.6. Prognosis of ADCC.

Ans. The prognosis is poor in cases of ADCC. The overall 5 year survival rate of all adenoid

cystic carcinomas was 47%. This number reduces to 20% after 13 years and 22% after 15 years. Most cases recur within 2 years of treatment. Intracranial spread can occur due to the propensity of perineural invasion that results in the death of the majority of patients.

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SHORT CASES

CONGENITAL PTOSIS

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INTRODUCTION

Drooping of the eyelid is known as ptosis. It may be present at birth, or it may develop later in life. If a droopy eyelid is present at birth or within the first year of life, the condition is called congenital ptosis. In most cases of congenital ptosis, the problem is isolated and does not affect the vision.¹⁻³

Congenital ptosis can be given as a short case in exams.

HISTORY

All pediatric patients presenting with either unilateral droopy eyelid or bilateral droopy eyelids need a thorough history and examination (kindly see the section of ptosis, long case).

Chief Complaint

Parents usually bring the child with the history of drooping of the eyelid (**Fig. 1**) or narrow palpebral fissure since birth.

History of Present Illness

The onset, progression, and other associated abnormalities such as deviation of eyes, nystagmus, face turn and any relation to the amount of ptosis to jaw movement.

Medical History

A careful medical history regarding malignancy should be obtained. Metastatic or primary orbital tumors can result in malpositioning of the eyelid.

Family History

A patient with a strong family history of congenital ptosis may not need an extensive work-up. Family photographs can help determine onset or variability of the ptosis.

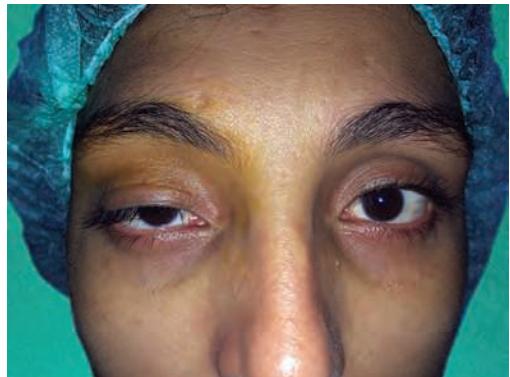


Fig. 1: Simple severe congenital ptosis

History of Drug or Allergic Reactions

A history of drug or allergic reactions may be helpful. Allergic reactions can result in eyelid edema and droopy eyelid.

History of Trauma

Orbital wall fractures (pseudoptosis with enophthalmos) or IIIcranial nerve palsy from trauma may result in ptosis.

EXAMINATION

A case of congenital ptosis must be evaluated in detail as described in the chapter of long case ptosis. In cases of congenital ptosis following should be taken care of:

- **Visual acuity:** Risk of amblyopia is there in case of severe ptosis. The amblyopia can occur due to occlusion amblyopia or rarely due to astigmatism induced by the compression of the droopy eyelid.
- Refractive error and cycloplegic refraction should be recorded in all cases.
- In infants, make sure that the baby can fixate and follow objects with each eye individually.

- The patient should be evaluated for strabismus (misalignment).
- Serial external photographs of the eyes and the face may be included in the patient's record for documentation.
- Tear function should be evaluated.
- Corneal sensitivity should be tested (if possible) may be a difficult test in young pediatric patients.
- The pupillary size and the iris color differences between the eyes should be examined for Horner syndrome.
- Palpebral fissure distance.
- Lid position in downgaze (the ptotic lid appears higher in downgaze).

Levator Function

Measurement of levator function in small children is a difficult task, as the child allows no formal evaluation. The presence of lid fold and increase or decrease its size on the movement of the eyelid gives us a clue to the levator action. The presence of anomalous head posture like the child throwing his head back suggests a poor levator action.

Iliff Test

This test can be performed in the first year of life to evaluate the levator function. The upper eyelid of the child is everted as the child looks down. If the levator action is good lid reverts on its own.

INVESTIGATION

A routine case does not require any specific investigations except those required for general anesthesia if surgery planned (hemoglobin, urea, creatinine, bleeding and clotting time). Neuroimaging (MRI or CT) is indicated in following conditions:

- If history not consistent and onset not clear
- Other neurologic findings along with ptosis are present
- Orbital wall fracture suspected with history of trauma
- Visible or palpable lid mass
- Suspected orbital tumors (e.g. lymphoma, leukemia, rhabdomyosarcoma)
- New onset of Horner syndrome with or without other neurologic findings

- New onset of third cranial nerve palsy with or without other neurologic findings
- Globe displacement with either enophthalmos or proptosis.

Differential diagnosis/classification/management has been covered in detail in the long case, ptosis part.

MANAGEMENT

The following points are considered while performing the surgery.

Timing of Surgery

It is advisable to wait till 4-5 years of age for surgical correction when the tissues are mature enough to withstand the surgical trauma and a better assessment and postoperative care is possible due to improved patient co-operation.^{2,3} *Urgent surgery* is indicated in children with severe ptosis developing amblyopia. In such cases, sling surgery is done.

Surgical Approach

It is based on whether the:

- Ptosis is unilateral or bilateral
- Severity of ptosis
- Levator action
- Presence or absence of abnormal ocular motility, jaw-winking phenomenon or blepharophimosis syndrome.

Aim of Surgery

Target is to lift the ptotic lid above the papillary aperture when the eyes are in the primary position. The height of the two lids regardless of whether the ptosis is unilateral or bilateral should be equal. There should also be adequate mobility of the lid when blinking, a normal lid fold and no diplopia.

Surgical Procedure

The choice of surgery is given below:

- Fasanella-Servat operation
 - Mild ptosis (<2 mm or less)
 - Levator action >10 mm
 - Well-defined lid fold-no excess skin

Table 1 Berke's criteria for levator resection

Degree of ptosis	Levator function	Amount of levator resection	Ideal preoperative correction
1.5–2 mm (mild)	Good (8 or more) Good (8 or more)—usual	Small (10–13) Moderate (14–17)	Under correct by 1–3 mm
3 mm (moderate)	Fair (5–7) Poor (rare, 4 or less)	Large (18–22) Maximal (23 or more)	Match the level of normal lid and correct ptosis fully
4 or more (severe)	Fair (Sometimes, 5–7) Poor (usual, 4 or less)	Super maximal (27 or more) Frontalis sling	Over correct by 1–2 mm

- Levator resection
 - Mild/moderate/severe ptosis
 - Levator action ≥ 4 mm
- Brow suspension ptosis repair
 - Severe ptosis
 - Levator action < 4 mm
 - Jaw-winking ptosis (along with LPS excision) or blepharophimosis syndrome.

In cases with bilateral congenital ptosis, simultaneous bilateral intervention in the two eyes is needed. However, in cases where gross asymmetry exists between the two eyes, the eye with a greater ptosis is operated first and the other eye is operated after 6–8 weeks when the final correction of the operated eye can be assessed.

Levator resection is the most commonly performed procedure, there are different criteria to determine the amount of levator resection required. The two important and widely used guidelines are Berkes (**Table 1**) and Puttermans (**Table 2**) method.

Contraindications to Surgery

Ptosis surgery is relatively contraindicated in presence of following:

- Poor orbicularis muscle function (lagophthalmos and corneal exposure)
- Loss of blink reflex
- Loss of corneal sensitivity
- Significant dry eye
- Poor Bell's phenomena.

VIVA QUESTIONS

Q.1. What are the causes of congenital ptosis?

Ans. Following are important causes of congenital ptosis:

- Idiopathic

Table 2 Puttermans's criteria for amount of levator resection

Levator action	Recommended lid placement
2–4 mm	1 mm above the limbus
5–7 mm	1 mm below the limbus
8 mm or more	2 mm below the limbus

- *Blepharophimosis syndrome (BPES):* Short palpebral fissures, congenital ptosis, epicanthus inversus, and telecanthus.
- Third cranial nerve palsy
- *Horner syndrome: Ipsilateral* findings of mild ptosis, miosis, and anhidrosis characterize this syndrome.
- *Marcus Gunn jaw-winking syndrome:* The motor nerve to the *external pterygoid muscle* is misdirected to the *ipsilateral levator muscle*. Lid elevation occurs with mastication or with the movement of the jaw to the opposite side.
- Birth trauma
- *Periorbital tumor:* Neuroblastoma, plexiform neuromas, lymphomas, leukemias, rhabdomyosarcomas, neuromas, neurofibromas, or other deep orbital tumors may produce ptosis and proptosis.
- *Kearns-Sayre syndrome:* Progressive external ophthalmoplegia, heart block, retinitis pigmentosa, and central nervous system manifestations. This condition begins in childhood but is rarely present at birth.
- Myotonic dystrophy.
- *Blepharochalasis:* Infiltrative processes that thicken the lids and produce ptosis.

- *Myasthenia gravis*: A defect at the neuromuscular junction.
- *Pseudotumor of the orbit*: Ptosis due to inflammation and edema of the eyelid.
- *Pseudoptosis*: Less tissue in the orbit (e.g. unilateral smaller eye, fat atrophy, blow-out fracture) produces the appearance of ptosis secondary to the decreased volume of orbital contents.

Q.2. Describe the pathology in congenital ptosis.

Ans. Histologically, the levator muscles of patients with congenital ptosis are dystrophic. The levator muscle and aponeurosis tissues appear to be infiltrated or replaced by fat and fibrous tissue. In severe cases, little or no striated muscle can be identified at the time of surgery. This suggests that congenital ptosis is secondary to local developmental defects in muscle structure. Congenital ptosis may occur through autosomal dominant inheritance. Common familial occurrences suggest that genetic or chromosomal defects are likely.

Q.3. Complications of the sling surgery.

Ans. Complications associated with the frontalis suspension procedure for congenital ptosis repair include the following:

- Granuloma
- Lid asymmetry
- Overcorrection with exposure keratopathy
- Undercorrection
- Infection.

Q.4. What is the prognosis after surgery?

Ans. The repair of congenital ptosis can produce excellent functional and cosmetic results. Careful observation and treatment, amblyopia ptosis can be treated successfully. Patients who require surgical intervention, 50% or more may require repeat surgery in 8–10 years following the initial surgery.

Q.5. Management of complicated ptosis.

Ans. The management of simple congenital ptosis associated with other anomalies is described below:

- *Ptosis with oculomotor abnormalities*: In cases, with superior rectus involvement

(usually associated with severe ptosis) an inferior rectus recession at times combined with superior rectus resection is carried out on the affected side as the first procedure. To correct the ptosis levator resection with bilateral brow suspension is done later. *Knapp's procedure* may be done for ptosis associated with double elevator palsy where lateral and medial rectus tendons are transplanted to the area of superior rectus insertion. This does not cause significant limitation of adduction or abduction. Ptosis is corrected 3 months later.

- *Blepharophimosis syndrome*: The following sequence is followed:

- Y-V plasty mustard's double "Z" plasty with transnasal wiring is done as a primary procedure. This gives a good surgical result both in terms of correction of telecanthus as well as deep placement of the medial canthus. The results are long lasting.
- Brow suspension is carried out 6 months after the first procedure for correction of ptosis.

- *Marcus Gunn ptosis*: Mild cases of jaw winking where the jaw winking is minimal can be treated satisfactorily by Fasanella-Servat operation while severe cases or cases where jaw winking is prominent, require bilateral resection of levator aponeurosis and terminal levator with fascia lata brow suspension.

- *Misdirected third nerve ptosis*: In cases of misdirected third nerve ptosis where treatment is imperative levator resection with bilateral fascia lata sling is the procedure of choice. Ptosis associated with third nerve palsy is difficult to manage because of poor bell's phenomenon. A crutch glass may be prescribed or a conservative sling surgery may be performed.

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ECTROPION

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INTRODUCTION

Ectropion is characterized by an eversion or outward turning of the eyelid margin away from the globe. It is a commonly encountered eyelid malposition. It is characterized by rotation of lid margin outwards resulting in its fall away from the globe.¹ To make things worse, the constant wiping and rubbing of eyes irritated by the epiphora further aggravates the condition. The underlying factor may vary in each case and an appropriate identification of the type of ectropion and the factor responsible for its occurrence are important in choosing the correct surgical intervention.^{2,3}

In exams, it is usually given as a short case or spot case.

HISTORY

Chief Complaints

Watery, irritation, grittiness, foreign body sensation or chronic red eye. Symptoms are caused by ocular exposure and inadequate lubrication.

Past History

Facial palsy, lid trauma, ocular allergy and previous lid surgery should be taken.

EXAMINATION

The routine examination is carried out and the conjunctiva, cornea, and anterior chamber are examined for any signs of inflammation.

Eyelid: There is outward turning of the lid margin. There may be signs of chronic blepharitis.

Conjunctiva: Keratinization and hypertrophy.

Cornea: Changes secondary to exposure may be present.

Schirmer's test: (to rule out dry eye).

Syringe and Jones test I and II (to rule out lacrimal passage obstruction).

Tests for Ectropion

Pinch Test

To determine the amount of lid laxity. If the lid can be pulled more than 6 mm away from the globe, the lid is lax. If the medial and lateral canthal tendons are lax as well, the lid can be pulled away up to 20–25 mm.

Snap-back Test

Downward traction is applied to the lower lid and then released the lid should revert to its normal position, without the aid of a blink in a normal person. However, when laxity is present, the lid is not opposed to the globe.

Grading of lid laxity according to snap-back test

- *Normal:* The lid returns to its position immediately on release
- *Grade 1:* Approximately 2–3 sec
- *Grade 2:* 4–5 sec
- *Grade 3:* >5 sec but returns to position on blinking
- *Grade 4:* Continues to hang down

Inferior Lid Retractor Laxity

Retractor weakness can be demonstrated by observing the lower lid as the patient looks down. Reduction in inferior movement on down gaze and a deep inferior fornix occurs due to laxity or loss of retractor attachment in this area.

Medial Canthal Tendon (MCT) Laxity

The lateral excursion of the inferior punctum is measured by pulling the lid laterally. The punctum

lies lateral to the caruncle at rest and should not be displaced more than 1–2 mm with lateral lid traction. If pulling on the medial canthus allows the punctum to be stretched, it suggests MCT is lax. Laxity is graded as following:

- *Mild*: Up to the limbus
- *Moderate*: Up to the pupil
- *Severe*: Beyond the temporal pupillary border.

Lateral Canthal Tendon (LCT) Laxity

The lateral canthal angle should be evaluated with the lid at rest. The lateral canthus should have an acute angular contour and should lie 1–2 mm medial to the lateral orbital rim. A rounded appearance of the canthus indicates laxity. The lateral part of the lid if pulled medially should not result in more than 1–2 mm movement of the lateral canthal angle, in absence of laxity.

Position of the Lacrimal Puncta

Punctum alone can be everted or the whole lid may be everted. In a normal lid, the inferior punctum is directed posteriorly against the globe and should not be visible without pulling the lid downward. Direction of the punctum away from the globe is the earliest sign of medial lid ectropion and can be graded as follows:

- *Mild*: Puncta are not opposed to the globe on looking up.
- *Moderate*: Puncta are not opposed to the globe even in primary gaze.
- *Severe*: Palpebral conjunctiva and fornix are exposed.

Cicatricial Skin Changes

Vertical shortening of the anterior lamella—like signs of repair of lid laceration or scar of excision of the tumor should be looked for.

Orbicularis Muscle Weakness

The facial nerve must be examined to rule out ectropion due to paralysis of the seventh nerve. Lagophthalmos and reduced force of contraction on forced eyelid closure demonstrate orbicularis muscle weakness. Other signs of facial palsy such as brow ptosis, loss of forehead wrinkles,

absent nasolabial fold and drooping of the angle of the mouth should also be looked for.

CLASSIFICATION

Ectropion can be classified as following:

- *Congenital ectropion*: Rare, associated with congenital epiblepharon.
- *Acquired ectropion*: Can be further classified as following on the basis of pathogenesis:
 - *Involutorial ectropion*: It is the most common variety. Multiple factors are responsible for its development e.g. horizontal lid laxity, medial canthal tendon laxity, etc. which are all normal aging changes of the lid (**Fig. 1**).
 - *Cicatricial ectropion*: Lid margin is pulled away from the globe due to the shortage of skin e.g. congenital shortage (**Fig. 2**), trauma, burns, cicatrizing skin tumors, allergies, etc. it may be unilateral or bilateral/localized or generalized depending on the cause.



Fig. 1: Senile ectropion



Fig. 2: Paralytic ectropion due to tight skin in a collodion baby

- *Mechanical ectropion:* Tumor or cyst near the lid margin mechanically pulling down the lid.
- *Paralytic ectropion:* VII N palsy resulting in sagging and downward displacement of paralyzed orbicularis muscle.

- *Mild ectropion with an excess of skin:* Modified Kuhnt-Szymanowski procedure: blepharoplasty with a base up lateral triangle and excision of full thickness wedge of lid beneath the blepharoplasty flap.
- *Moderate ectropion—generalized or affecting lateral lid:*

Lateral tarsal strip: In this, a horizontal incision is made and inferior crus of LCT is cut, triangular portion of the temporal lid is resected sparing tarsus and the tarsal strip is sutured with a mattress suture in a superotemporal direction to the periosteum. Smith and Lisman propose an alternative method where after excising the anterior lamella of the lid on temporal aspect the periosteum is exposed in a superotemporal direction and the tarsal strip is sutured to it (**Fig. 3**).

- *Marked ectropion:* Double wedge resection with lateral tarsal strip
- *Extreme ectropion:* Temporalis muscle transfer
Involutional ectropion affecting only the medial aspect
- *Only punctal eversion present and no lid laxity:* Medial conjunctivoplasty
- *Horizontal lid laxity is present but MCT is not lax:* Lazy-T (Excision of tarsoconjunctiva combined with full thickness wedge excision of lid)
- *Horizontal lid laxity which is due to MCT laxity:* MCT plication or resection depending on severity of laxity.

GRADING

Grade of Orbito-lid Apposition

- *Grade 0:* With normal lid-globe apposition
- *Grade 1:* With punctal eversion
- *Grade 2:* With partial lid eversion and scleral show
- *Grade 3:* With conjunctival hyperemia and thickening
- *Grade 4:* As for grade 3 with exposure keratitis.

Grades of Ectropion

- *Grade 1:* Punctal eversion
- *Grade 2:* Eversion of sharp posterior lid margin
- *Grade 3:* Palpebral conjunctival exposure
- *Grade 4:* Exposure of the fornix.

TREATMENT

Factors considered for selection of surgery for ectropion:

- *Basic cause of ectropion*
- Secondary mechanisms coexisting with the basic pathology
- Grade of ectropion
- *Identify the defects in various components of lid lower*
- Excess lid skin
- Laxity of LCT/MCT and its severity
- Shortening of posterior lamella comprising of tarsoconjunctiva
- Any mass lesion in lid causing ectropion
- Any scarring whether localized or generalized
- Systemic disease causing scarring of tarsoconjunctiva.

Surgical Management of Ectropion

Involutional Ectropion

- *Mild-to-moderate ectropion mainly affecting lateral lid:* Full thickness pentagonal wedge resection of the lid.

Management of Cicatricial Ectropion

Correction of a cicatricial ectropion requires lengthening of the cutaneous surface and



Fig. 3: Cicatricial ectropion (Figure 1) after surgery (lateral tarsal strip procedure)

correction of any associated factors-resection of subcutaneous cicatrix or horizontal lid lengthening. Following surgeries have been described:

- *Localized: Z-plasty* (Elschnig's operation)
- V-Y operation
- *Severe or generalized cicatricial ectropion*: Full-thickness skin grafting.

Management of Paralytic Ectropion

Management involves giving support to the lower lid or strengthening of the lower lid. Support can be given medially, laterally or to the lower lid as a whole. In long standing cases associated with cheek ptosis, a cheek lift/mid-face lift may be necessary. Following surgeries have been described:

- *Only medial ectropion*: Medial canthoplasty
- *Generalized lid laxity*: MCT plication + lateral canthal sling
- *Medial with MCT laxity*: MCT resection.

Management of Mechanical Ectropion

Masses near the lid margin causing the ectropion should be excised. Excision should be as vertical as possible and it is important to avoid scar formation/ skin shortening.

VIVA QUESTIONS

Q.1. Pathogenesis of involutional ectropion.

Ans. Ectropion involves the lower lid more commonly than the upper lid. There is decreased resilience and increased laxity of periocular tissues due to age-related microinfarction and secondary atrophy. This inadequate support and effect of gravity cause more pronounced stretching of the lower lid increasing the burden on suspensory canthal tendons and resulting in ectropion. Primary abnormality is laxity of the lateral canthal tendon. Other contributory factors include:

- Horizontal lid laxity
- Medial canthal tendon laxity
- Punctal malposition
- Vertical tightness of the skin

- Lower lid retractors disinsertion or laxity

Q.2. Congenital ectropion.

Ans. Congenital ectropion is a rare entity. It is more often associated with blepharophimosis syndrome (BPES Type 2), Down syndrome or ichthyosis. In rare cases, congenital ectropion occurs as an isolated finding. It is caused by a vertical insufficiency of the anterior lamella of the eyelid. Complications include chronic epiphora and exposure keratitis. Management is as follows:

- Mild congenital ectropion—no treatment.
- Severe and symptomatic—horizontal tightening of the lateral canthal tendon and vertical lengthening of the anterior lamella by means of a full-thickness skin graft.

A complete eversion of the upper eyelids occasionally occurs in premature infants transiently due to orbicularis slippage/lamellar slippage, inclusion conjunctivitis, anterior lamellar inflammation or shortage, or Down syndrome. Treatment includes topical lubrication, short-term patching of eyes, full-thickness sutures or a temporary tarsorrhaphy.

Q.3. What are the disadvantages of lid resection procedures?

Ans. • Does not correct the underlying physiological abnormality
• Causes lid notching
• Causes lid shortening
• Causes loss of meibomian glands.

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ENTROPION

Aditi Dubey, Ritu Nagpal

INTRODUCTION

Entropion is a condition in which eyelid turns inward. This causes the eyelashes or the eyelid margin to rub against the eyeball and results in irritation, watering, redness, keratitis and even corneal perforation. It may occur at any age but occurs primarily because of advancing age. It can be missed easily and thus one should specifically look at the eyelid to diagnose it.¹⁻³

In exam, it can be given as a short case.

HISTORY

Chief Complaints

Patients with entropion commonly complain of:

- Foreign body sensation
- Frequent eye infections
- Red eyes
- Watering.

Past History

History of onset is important to rule out congenital component.

Age of patient: In children, congenital entropion is rare and should be definitely differentiated from epiblepharon.

History of ocular trauma, facial burn, Stevens-Johnson syndrome is important for cicatricial entropion.

History of ocular surface irregularity or any other painful ocular pathology (acute spastic entropion).

EXAMINATION

- Lid margin is found in-turned (**Fig. 1**). Depending upon the degree of in turning it can be divided into three grades.
 - *Grade I:* Only the posterior lid border is in rolled
 - *Grade II:* Entropion includes in turning up to the intermarginal strip
 - *Grade III:* The whole lid margin including the anterior border is in turned.

- *Lid laxity:*

- *The pinch test:* To determine the amount of lid laxity. If the lid can be pulled more than 6 mm away from the globe, the lid is lax. If the medial and lateral canthal tendons are lax as well, the lid can be pulled away up to 20–25 mm.
- There may a hump on lower eyelid due to overriding of preseptal orbicularis over the pretarsal part.
- It is often associated with an absence of the downward excursion of the eyelid in down gaze due to the weakness of the lower lid retractors. Excursion of the lower lid in down gaze usually 3–4 mm—loss of movement indicates retractor weakness/disinsertion.
- *Snap-back test:* Perform this test by pulling the lower lid away and down from the globe for several seconds. If the lid resumes position, note the time required for the lid to return to its original position without the patient blinking. The snap-back test provides a good idea of relative lower lid laxity. Lids with normal laxity immediately spring back to original position; the longer this takes, the more laxity is present.
- *Grades*
 - ♦ *Normal:* Lid returns immediately on release
 - ♦ *Grade 1:* Approximately 2–3 sec
 - ♦ *Grade 2:* 4–5 sec

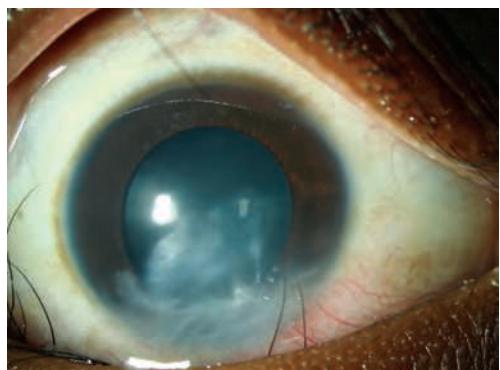


Fig. 1: Entropion causing keratopathy

- ♦ Grade 3: >5 sec but returns to position on blinking
- ♦ Grade 4: Continues to hang down
- *Medial canthal laxity test:* Perform this test by pulling the lower lid laterally from the medial canthus. Measure displacement of the medial punctum. Greater distance equates to more laxity. Normal displacement ranges from only 0–1 mm.
 - Grades
 - ♦ Mild—up to the limbus
 - ♦ Moderate—up to the pupil
 - ♦ Severe—beyond the temporal pupillary border.
- *Lateral canthal laxity test:* Perform this test by pulling the lower lid medially from the lateral canthus. Measure displacement of the lateral canthal corner. Greater distance equates to more laxity. Normal displacement ranges from only 0–2 mm. Assign grades on a scale from 0–4 (0 = normal laxity, 4 = severe laxity).
- *Bell phenomenon:* Instruct patient to attempt eye closure while the examiner holds lids open. If eyes move up, the test indicates a positive result for Bell phenomenon.
- *Orbicularis muscular tone:* Ask the patient to squeeze eyes shut. Note how much worse the entropion is immediately after opening.
 - Grades of orbicularis muscle tone
 - ♦ Grade 0 = no paralysis
 - ♦ 1 = weak
 - ♦ 2 = normal
 - ♦ 3 = overactive
 - ♦ 4 = spastic
- *The digital eversion test can be done to distinguish cicatricial component:* Observe directly by evertting the lids. It can also be ascertained by pulling the lid superiorly if it does not reach 2 mm above lower limbus; lid is vertically deficient.
- *Slit-lamp examination:* To look for corneal status and other evidence of dryness, punctuate keratopathy due to blepharitis, meibomitis, trichiasis, foreign bodies, corneal scarring (**Fig. 2**) and dry eyes.
- *Fluorescein staining:* This test is essential when looking for signs of corneal damage. It can detect damage from lashes or lid skin rubbing on the cornea.
- *Schirmer test:* To rule out other causes of dryness.

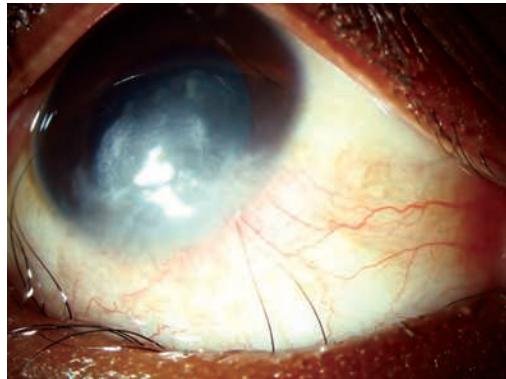


Fig. 2: Entropion with eyelash rubbing cornea causing keratopathy

- *Lacrimal system patency assessment:* Done by syringing, dye disappearance test and jones dye test I & II.

CLASSIFICATION

Entropion can be classified into congenital, involutional, cicatricial and acute spastic.^{1–3}

- *Congenital entropion:* Occurs due to hypertrophy of the anterior lamella. Mostly mild, resolves with time.
- *Involutorial entropion:* An age-related condition caused by the laxity of tarsus, its medial and lateral canthal tendons, lower lid retractors, along with the over-riding of the orbicularis oculi muscle.
- *Cicatricial entropion:* Occurs due to scarring and shortening of the posterior lamella due to chemical injury, infection or Stevens-Johnson syndrome.
- *Acute spastic entropion:* Follows ocular irritation or inflammation.

Most Common Types of Entropion

- Lower lid—involutional entropion
- Upper lid—cicatricial entropion.

MANAGEMENT

Nonsurgical Management

In cases before proceeding to the definitive surgery these medical management plans can be followed.

- Eyelid taping to the malar eminence
- Injecting Botox into the orbicularis muscle.

Surgical Management

Senile Entropion

- Rotational sutures
- Lateral tarsal strip
- Lower eyelid retractor reinsertion.

Spastic Entropion

First treat the underlying condition that might infection or irritation of ocular surface. Followed by either rotational sutures can be passed or Botox can be injected.

Cicatricial Entropion

- Tarsal fracture
- Transverse blepharotomy with marginal rotation
- For severe cases, posterior lamellar lengthening using mucous membrane grafting.

Surgery Names

- Weiss procedure (transverse blepharotomy with evertting sutures)
- Quickert evertting sutures
- Jones retractor plication.

VIVA QUESTIONS

Q.1. Congenital entropion.

- Ans.** • Extremely rare
- Inversion of entire tarsus and lid margin
 - Epiblepharon and horizontal tarsal kink are to be differentiated

- *Surgery (Hotz procedure):* Minimal ellipse of skin and orbicularis is excised from the medial two-thirds of the lower lid. Skin is fixed to the lower edge of the tarsus.

Q.2. Differentiate between congenital entropion and epiblepharon?

Ans. See Table 1.

Q.3. Involutional entropion.

- Ans.**
- Often seen in elderly patients, particularly women.
 - Causes great discomfort as well as problems with clear vision due to constant watering.
 - The appropriate procedure depends on the degree of entropion, keratinization, and distortion of the lid margin and eyelashes and analysis of posterior lamellar shortening and scarring.
 - For cases with mild to moderate degree of cicatrization—tarsal wedge resection or the tarsal fracture procedure.
 - *In severe or recurrent cases:* Posterior lamellar grafting procedure to lengthen the posterior lamella.

Q.4. Causes of cicatricial entropion.

- Ans.**
- Trachoma
 - Acid and alkali burn
 - Ocular pemphigus
 - Leprosy
 - Severe membranous conjunctivitis
 - Stevens-Johnson syndrome

Table 1 Differences between congenital entropion and epiblepharon

Features	Epiblepharon	Congenital entropion
Extrafold of skin	Fold of skin overlapping the lid margin is present medially	Absent
Occurrence	Common	Rare
Lid affected	Lower lid	Both
Lid margin	Not turned inwards	Entire lid margin turned inward
Direction of eye lashes	Straight up and lie flat against the cornea	Turned inward
On pulling down the skin	Lashes turn out but the margin of the lid remains in apposition to the globe	Lid margin also pulls away from the globe
Treatment	Spontaneous resolution	May require surgical correction

Q.5. Causes of spastic entropion.

Ans.

- Senile
- Ocular surface disorder, e.g. dry eye
- Enophthalmos
- Loss of orbital fat
- Tight bandage
- Enucleation socket

Management of acute spastic entropion

- Treatment of the underlying cause-break the irritation-entropion cycle.
- Taping of the inturned eyelid to evert the margin, various suture techniques afford temporary relief for most patients.
- Additional definitive surgical repair to correct the underlying involutional changes.
- In selected cases, botulinum toxin injection can be used to paralyze the overriding preseptal orbicularis muscle.

Q.6. Role of botulinum toxin in management of entropion

Ans.

- Works very well in correcting spastic entropion.
- Also, in selected cases of involutional entropion with significant preseptal muscle override when the patient is not willing for surgery or is bedridden and not fit for surgery.

- *Dose and procedure:* 2.5 units of botulinum toxin are injected at two or three places below the lower lid margin. Injected directly into the muscle by pinching it taking care not to go deep to avoid trauma to extraocular muscles (especially medially as it may cause inferior oblique muscle paresis and lead to diplopia).

- *Disadvantage:* May take around 4–7 days for its effect to appear. Short-term, not a permanent solution.

Q.7. The material of choice for the spacer graft for entropion correction.

Ans.

- Hard palate mucosal graft
- Donor sclera
- Buccal mucous membrane
- Amniotic membrane.

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BLEPHAROPHIMOSIS, PTOSIS, EPICANTHUS INVERSUS SYNDROME

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INTRODUCTION

First described by Komoto in 1921, blepharophimosis-ptosis-epicanthus inversus syndrome (BPES) is a dominantly inherited disorder characterized by the presence of above features (i.e. blepharophimosis, ptosis, and epicanthus) at birth. The main findings of this disorder are eyelids that are abnormally narrow horizontally (blepharophimosis), a vertical fold of skin from the lower eyelid up either side of the nose (epicanthus inversus), and drooping of the upper eyelids (ptosis). It can be given as a short case in the examination.

HISTORY

Chief Complaints

The parents bring the child with anyone or a combination of the following complaints:

- Drooping of eyelid,
- Abnormal head posture, (chin up due to ptosis)
- Small size of eyeball
- Abnormal eyelid
- *Diminution of vision:* Blurring of vision is related to refractive error, astigmatism.
- Absence of eyeball
- Bluish colored swelling (in case of cryptophthalmos)
- Epiphora (due to displaced tear ducts).

Past History

A careful past history should be taken for any:

- Perinatal and pregnancy history
- Family history of congenital eyelid colobomas or other congenital anomalies, especially facial (e.g. cleft lip/palate)
- History of other birth defects
- Pediatric review of systems
- Facial asymmetry
- Hearing loss
- Recurrent infection
- Menstrual history (in case of late presentation).

Past Surgical History

The previous history of ocular surgery (attempts to correct any of the lid deformity or squint) may or may not be present.

EXAMINATION

Systemic Examination

Features frequently observed in both BPES type I and type II are a broad nasal bridge, low-set ears, and a short philtrum.

This condition is sometimes associated with ovarian failure although breast development is often normal. Secondary sexual characteristics are usually normal in both BPES type I and type II. In BPES type I, menarche is usually normal, followed by oligomenorrhea and secondary amenorrhea.

Other malformations that can be seen includes (also known as BPES Plus):

- Contractures
- Low nose bridge, micrognathia, microcephaly
- *Ear abnormalities:* Incomplete ear development/Cupped ears, posteriorly rotated ears
- Infertility in females, premature menopause, primary gonadal failure
- Reduced muscle tone—only early in life
- Mental defects, severe psychomotor retardation, growth retardation
- Genitourinary malformations, Cryptorchidism, syndactyly.

Ocular Examination

Visual acuity: It is variably impaired depending on the severity of ptosis, astigmatism. Cycloplegic

refraction is a must in all such cases since the significant refractive error may be seen in almost 1/3rd of these cases and if untreated can lead to amblyopia. Amblyopia can also occur due to stimulus deprivation (in a case of severe ptosis) but rare.

Head posture: To compensate for the ptosis, affected person assumes a characteristic posture with the head tilted backward, the brow furrowed, and the chin arched upward. Frontalis overaction may be there (eyebrows are increased in their vertical height and they are drawn up into a pronounced convex arch).

Eyeball: The eyeball may show microphthalmos, anophthalmos, cryptophthalmos. The palpebral fissure is reduced in both horizontal and vertical dimension. The normal horizontal fissure length in adults is 25–30 mm whereas in this syndrome it is usually 20–22 mm. Telecanthus is seen in the majority of patients. This refers to a lateral displacement of the inner canthi leading to a widening of the intercanthal distance. The interpupillary distance (IPD) is usually normal. The patient may have esotropia, divergent strabismus or nystagmus.

Eyelids: Eyelids are often covered by the smooth skin without eyelid folds and deficient amounts of skin in both eyelids may be found (**Fig. 1**). Frequently, the upper and lower lacrimal puncta are displaced laterally or duplication of puncta can be seen.



Fig. 1: Blepharophimosis epicanthus inversus syndrome

Blepharoptosis literally means a falling of the lids. The palpebral fissure is abnormally small in the vertical dimension. It is caused by the absence or impairment of the function of the levator palpebrae superioris muscle and is usually bilateral and symmetrical [Kindly see the examination part of ptosis in chapter ptosis for a detailed examination of ptosis].

Dysplastic eyelids: Eyelids are often covered by the smooth skin without eyelid folds and deficient amounts of skin in both eyelids may be found. The upper eyelid margin may show 'S' shaped curve. The lower lid margin usually has an abnormal concavity downwards, particularly laterally where an ectropion might occur. Trichiasis can also occur in BPES.

Epicanthus inversus: A small skin fold that arises from the lower lid and runs inwards and upwards characterizes it. Associated with this are an increased length of the medial canthal ligament and a lack of the normal depression seen at the internal canthus.

Conjunctiva: It is usually normal.

Cornea: It may show micro cornea occasionally. Corneal sensation should be checked.

Lens/Sclera/Iris/Fundus: Usually normal.

INVESTIGATIONS

Diagnosis of the disease is straightforward based on the clinical signs. Molecular genetic testing and specific laboratory studies are indicated in cases of associated syndromes. A pelvic ultrasound examination and measurement of bone mineral density are indicated if ovarian insufficiency is suspected.

CLASSIFICATION

Two types of BPES have been described:

BPES Type I

It is the more common type, in which males transmit the syndrome only and affected females are infertile. It is associated with an early loss of ovarian function (primary ovarian insufficiency) in women, which causes their menstrual periods to become less frequent and eventually stop

before age 40. Primary ovarian insufficiency can lead to difficulty conceiving a child (subfertility) or a complete inability to conceive (infertility).

BPES Type II

Both affected females and males transmit this variant. It is not associated with female infertility.

Both types are inherited as an autosomal dominant trait. There is complete penetrance (100%) in type I and slightly reduced (96.5%) penetrance in type II. Both types I and II include the eyelid malformations and other facial features.¹⁻³

DIFFERENTIAL DIAGNOSIS

Differential diagnosis includes those conditions in which ptosis or blepharophimosis are a major feature (see Table 1 for features of these syndromes)

- Congenital simple ptosis
- Ptosis with external ophthalmoplegia
- Noonan syndrome
- Marden-Walker syndrome
- Schwartz-Jampel syndrome
- Dubowitz syndrome
- Smith-Lemli-Opitz syndrome.

The characteristic combination of signs usually clinches the diagnosis.

MANAGEMENT

Management requires the input of specialists including a clinical geneticist, pediatric ophthalmologist, oculoplastic surgeon, (pediatric or adult) endocrinologist, reproductive endocrinologist, and gynecologist.

Management of BPES is primarily surgical if indicated. However, any refractive error must be corrected to avoid amblyopia. The indication of surgery is moderate to severe ptosis, amblyopia, trichiasis which may cause the corneal lesion, cosmesis, strabismus. Care should be given to treat associated amblyopia.

The timing of eyelid surgery is controversial; it involves weighing the balance of early surgery to prevent deprivation amblyopia and late surgery to allow for more reliable ptosis measurements, the latter of which provides a better surgical outcome. Furthermore, ptosis surgery is hampered by the dysplastic structure of the eyelids. The surgical

Table 1 Syndromes associated with BPES

Association	Inheritance	Features
Hereditary congenital ptosis 1 (PTOS1)	AD	Ptosis
Hereditary congenital ptosis 2 (PTOS2)	XL	Ptosis
Oculo-blepharophimosis syndrome	AD	Blepharophimosis, ptosis, mental retardation, congenital heart defects, teeth abnormality (hypoplastic teeth)
3MC syndrome 1 (Michels syndrome)	AD	Blepharophimosis, ptosis, epicanthus inversus, corneal abnormality, Cleft lip/palate, skeletal abnormalities
Ptosis with external ophthalmoplegia	AR	Ptosis, ophthalmoplegia, miosis. Decreased accommodation
Noonan syndrome	AD	Ptosis, short stature, heart defects, clotting abnormalities
Marden-Walker syndrome	AR	Ptosis, blepharophimosis, growth retardation, mental retardation
Schwartz-Jampel syndrome	AR	Intermittent ptosis, blepharophimosis, telecanthus, cataract, short stature, skeletal anomalies, muscle hypertrophy
Dubowitz syndrome	AR	Ptosis, blepharophimosis, lateral telecanthus, short stature, intellectual disability, immunodeficiencies
Smith-Lemli-Opitz syndrome	AR	Ptosis, epicanthus, cataract, growth retardation, intellectual disability, genitourinary, cardiac, gastrointestinal anomalies
KANSL1-related intellectual disability syndrome	AR	Developmental delay, intellectual disability, long face, high forehead, ptosis, blepharophimosis, large low-set ears, bulbous nasal tip, pear-shaped nose, cardiac septal defects, seizures, cryptorchidism

Abbreviations: AD, autosomal dominant; AR, autosomal recessive; XL, X-linked; BPES, blepharophimosis-ptosis-epicanthus inversus syndrome

management is traditionally performed in two stages and involves a medial canthoplasty for correction of the blepharophimosis, epicanthus inversus, and telecanthus at about the age of 4–5 years and correction of the ptosis about 9–12 months later. Early surgery may be necessary for amblyopia.

Epicanthus fold and telecanthus: The various procedures for correction of epicanthus fold and telecanthus includes: double Z or Y-Z plasties (**Fig. 2**), Transnasal wiring of the medial canthal tendons. If the epicanthal folds are small, a Y-V canthoplasty is traditionally used; if the epicanthal folds are severe, a double Z-plasty is used. An alternate technique for medial canthoplasty has been described recently using the skin redraping method, which has a simple flap design,



Fig. 2: Blepharophimosis, ptosis, epicanthus inversus syndrome (Figure 1 patient) after bilateral Y-V plasty and bilateral sling surgery

less scarring, and the effective repair of epicanthus inversus and telecanthus.³

Ptosis: Generally, it is corrected with brow suspension procedure. Super-maximal resection and frontalis suspension is the preferred method as it leads to a good cosmetic outcome as well as to an improved muscle function.

Although traditional management of blepharophimosis syndrome includes medial canthoplasty between the ages of 3 and 5 years, followed by ptosis correction about 6 months later, patients with severe ptosis may need early surgery to prevent amblyopia. Traditional multiple surgeries may delay the amblyopia management and influence the visual outcome. Thus, many surgeons suggest correction of ptosis first, even at a very early age, to prevent amblyopia. Soft-tissue medial canthal and lateral canthal surgery can wait until the face is grown.³ Treatment of associated abnormalities: It includes management of ovarian failure, hormone replacement therapy, and embryo cryopreservation. Management of amblyopia (i.e. with/without spectacle wear/contact lens must be continued after surgical intervention to obtain optimal results.

Patient education: Genetic consultation is highly recommended, especially for patients with associated syndromes.

VIVA QUESTIONS

Q.1. What is the sequence of surgeries for ptosis and epicanthus in BPES?

Ans. See management part.

Q.2. When should the BPES be repaired?

Ans. See management part.

Q.3. What are the syndromes associated with ptosis?

Ans. See Table 1.

Q.4. Classify BPES.

Ans. Already given in classification.

Q.5. Genetics of BPES.

Ans. Both types are caused by mutations in the *FOXL2* gene. The *FOXL2* gene provides instructions for making a protein that is active in the eyelids and ovaries. The *FOXL2* protein is likely involved in the development of muscles in the eyelids.

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SEBACEOUS GLAND CARCINOMA

Amar Pujari, Sapna Raghuvanshi

INTRODUCTION

Sebaceous gland carcinoma (SGC) is third most common eyelid malignancy of the eyelids. Most sebaceous carcinomas arise from the meibomian glands, Zeiss gland, and Moll gland of the eyelid

usually occurs between fifth and ninth decades of life, women's are more affected than man.¹⁻³ It mostly involves the upper lid (**Fig. 1**).

In exams, it can be given as a long case or short case.



Fig. 1: Sebaceous gland carcinoma

HISTORY

Kindly see the section of lid tumors also.

Chief Complaint

Patient may present with the following complaint:

- Slowly enlarging, firm, and painless mass or nodule at the lid margins (most common presentation)
- Yellowish nodule at eyelid margin or caruncle
- As chronic blepharoconjunctivitis (irritation, redness or foreign body sensation)
- Recurrent chalazion
- Chronic blepharitis with loss of cilia
- Skin or conjunctival ulcer
- Advanced cases may present as eyelid mass with a destruction of marginal cilia and lid architecture
- Proptosis due to local invasion (anterior orbital mass or lacrimal gland tumor).

Past History

A careful history about the onset, progression, association with pain must be recorded (similar to that described under long case section for Lid tumors)

The risk factors of sebaceous cell carcinoma must be ruled out in history such as.

- Recurrent chalazion
- Previous radiotherapy
- Chronic blepharoconjunctivitis
- Immunosuppression
- Asian race

- Prolonged use of thiazide diuretics
- Older age (5th to 9th decade, average age 60–69 years)
- Female sex (55–57% cases are females).

EXAMINATION

Ocular Examination

Eyelids: Eyelid may have a nodule with following features:¹

- Slowly enlarging, firm, and painless mass affecting the tarsal plate or the eyelid margin (Since the meibomian gland is buried deep in the tarsus, initially the tumor will form a firm mass, and may be misdiagnosed as a chalazion. As the tumor invades more superficially, a yellowish cast may be visualized through the skin).
- Location
 - *Upper lid:* 60–70%, most common site, involved two to three times more frequently than the lower lid (**Fig. 1**). This is due to the presence of a greater number of meibomian glands in the upper lid (50 glands in upper eyelids, 25 in lower approximately).
 - *Caruncle:* 5–11%
 - *Eyebrow:* 2%
 - *Simultaneous involvement of both lids:* 6–8%
- Lesions may also exhibit varying degrees of yellow coloration/yellowish cast due to the presence of lipid within the mass.
- Lesions originating from the Zeis glands appear as small, yellowish nodules located at the eyelid margin anterior to the gray line. At times it may form a papilloma or cutaneous horn.
- Tumors arising from sebaceous glands of the caruncle usually appear as a subconjunctival, multilobulated, yellow mass.
- Eyelids are diffusely thickened.
- Skin appears indurated, usually skin is movable on the mass until late stages
- Small telangiectasia's over the mass
- Loss of eyelashes (Disruption of eyelid architecture and lash loss can occur as the tumor destroys lash bulbs)
- Rarely can present as anterior orbital mass or lacrimal gland tumor.

Enlarged lymph nodes: Submandibular, submental, preauricular and cervical.

Conjunctiva: Conjunctival inflammation, superior limbic keratoconjunctivitis can be seen.

Cornea: Superficial keratitis may be present if tumor cells invade corneal epithelium.

Other findings are usually within normal limits.

DIFFERENTIAL DIAGNOSIS

The following disease must be differentiated from the sebaceous cell carcinoma

- Blepharoconjunctivitis
- Blepharitis
- Chalazion
- Superior limbic keratoconjunctivitis
- Basal cell carcinoma
- Squamous cell carcinoma.

The characteristic features of sebaceous cell carcinoma that help in differentiating from these lesions are yellowish discoloration and telangiectatic blood vessels on the surface. At times, it is often difficult to differentiate, especially in early cases and excisional biopsy is the best way to arrive at a conclusion.

INVESTIGATION

A case of SGC needs following investigations.

Routine tests like: Complete blood count, renal and liver function tests.

Metastatic work-up: X-ray chest/USG abdomen/CECT: Brain and orbit.

FNAC: lymph node (lipid stains).

Conjunctival impression biopsy (for pagetoid spread).

Map biopsy: Sebaceous gland carcinoma must be confirmed by a full-thickness wedge biopsy of the affected eyelid. Because of multicentric spread, multiple biopsy specimens should be taken from the adjacent bulbar and palpebral conjunctiva and the other ipsilateral eyelid to form a map of the extent of tumor spread across an ocular surface. After histologic confirmation of sebaceous carcinoma, the surgeon must consider the extent of possible pagetoid involvement of the bulbar

conjunctiva. Map conjunctival biopsies were taken in all four quadrants.¹⁻³

MANAGEMENT

- **Nodular sebaceous carcinoma without pagetoid involvement:** Lesion can be removed by following techniques:
 - Full thickness eyelid resection with frozen section control of margins
 - *Mohs' micrographic technique:* Excision of the visible tumor, with a 5-mm margin of clinically normal tissue on either side.
- Nodular sebaceous carcinoma of one eyelid with evidence of pagetoid spread:
 - Excision of the nodular lesion with conjunctive and superficial keratectomy/cryotherapy of the lesion.
 - Mitomycin C (MMC) can be tried to control conjunctival tumor. MMC 0.4% four times per day for a week and then were medication free for 1 week; this cycle was repeated until resolution of malignancy.
 - *If bulbar conjunctiva is involved extensively by tumor and reconstruction is not possible:* Exenteration is recommended
 - *If both upper and lower eyelids are involved by tumor without an involvement of the conjunctiva:* Remove both eyelids and reconstruct the defect.
 - *Concomitant involvement of eyelids and conjunctiva:* It requires exenteration.
- **Orbital disease with no metastasis:** Orbital exenteration
- **Ocular disease with lymphatic metastasis:** Mass resection/exenteration, radical neck dissection, and postoperative radiation
- Systemic chemotherapy may be required in the management of metastatic disease; however, there is little in the literature on the efficacy of postsurgical chemotherapy for metastatic disease.

PROGNOSIS

- Poor compared to BCC.
- Five year mortality
 - Early disease: 15% (6-30%)¹⁻³
 - Metastatic disease: 50-67%¹⁻³
- Five year recurrence rate: 9-36%¹⁻³

VIVA QUESTIONS

Q.1. Histopathology.

Ans. Dysplasia and anaplasia of the sebaceous lobules in the meibomian glands are seen in SGC, associated with the destruction of tarsal and adnexal tissues. As the neoplastic nodule enlarges, it may erupt toward the eyelid skin to initiate the intraepidermal growth phase, wherein the sebaceous cells spread diffusely throughout the epidermis. This 'pagetoid' epidermal invasion is a distinctive feature of sebaceous carcinomas. Specific characteristics on histopathology

- Stains with oil red O and Sudan IV
- Cytoplasm is frothy and vacuolated
- Cells are larger vesicular and have prominent nucleoli.

Histopathologic subtypes: Lobular (lobules of sebaceous architecture), comedocarcinoma (characterized by a central necrotic core), papillary (papillary projections and areas of sebaceous differentiation), and mixed (features of any subtype). It can also be described as well differentiated, moderately differentiated, and poorly differentiated.

Q.2. Metastasis.

Ans. An invasive, potentially lethal tumor, SGC may cause an extensive local destruction of eyelid tissues. It carries a risk of metastasis to preauricular and submandibular lymph nodes or may spread hematogenous to distant sites. It may invade locally into the globe, the orbit, the sinuses, or the brain. The frequencies of the spreads are:¹⁻³

- *Direct extension:* Orbit, lacrimal glands—6–17%
- *Lymphatic:* Regional nodes—17–28%
- *Hematogenous:* Rare, <1%, lungs, liver, skull, and brain

Pagetoid spread: Intraepithelial or intraepidermal spread of malignant cells similar to that observed in Paget's disease of the nipple or extramammary Paget's disease. Spread along skin or conjunctiva, producing individual cell clusters are characteristic. It is seen in almost 47% of the cases.

Risk factors for subclinical spread include:

- Duration of symptoms >6 months
- Vascular and lymphatic infiltration
- Orbital extension
- Poor tumor differentiation
- Multicentric origin intraepithelial carcinomatous changes of the conjunctiva, cornea, or skin
- Location in the upper eyelid.

Q.3. Prognostic factors.

- Ans.**
- *Site:*
 - Lower lid tumor (better) > Upper lid tumor > Both upper and lower lids (worst)
 - *Conjunctival tumor:* Metastatic disease
 - *Tumor size:* Increased size, worse prognosis >10 mm
 - *Delay in diagnosis:* Delay >6 months, bad prognosis
 - *Histology:*
 - Vascular invasion
 - Lymphatic invasion
 - Highly infiltrative pattern
 - Poor differentiation
 - Pagetoid spread
 - Multicentric origin
 - Orbital invasion.

Q.4. What is Muir-Torre syndrome?

- Ans.**
- It is an autosomal dominant condition in which there are sebaceous (oil gland) skin tumors in association with internal cancer.
 - The most common organ involved is the gastrointestinal tract, with almost one-half of the patients having colorectal cancer. The second most common site is cancer of the genitourinary tract.
 - Following skin lesions are associated with this syndrome
 - Sebaceous adenomas
 - Sebaceous epitheliomas
 - Sebaceous carcinoma
 - Keratoacanthoma
 - Squamous cell carcinoma
 - Multiple follicular cysts
 - It is now thought to be a hereditary non-polyposis colorectal cancer syndrome

due to mutations in the DNA mismatch repair genes *MSH2* or *MLH1*.

Q.5. Sebaceous carcinoma in systemic disease.

Ans. Sebaceous gland carcinoma is seen in association with following:

- Familial retinoblastoma after radiotherapy
- Immunosuppression in HIV disease
- Muir-Torre syndrome.

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PYOGENIC GRANULOMA

Sapna Raghuwanshi, Bijnya Birajita Panda

INTRODUCTION^{1,2}

Pyogenic granuloma is an inflammatory vascular response of the tissue that usually occurs after a previous insult, typically either inflammatory or trauma. It is the most common acquired vascular lesion to involve the eyelids. It also involves the conjunctiva. The name is a misnomer because this lesion is neither pyogenic nor granulomatous.

In exams, it can be given as a short case.

HISTORY

Chief Complaints

The patient may present with following:

- Rapidly growing mass over eyelids and conjunctiva
- Lesion readily bleeds with minor contact
- Pain (associated with superficial ulceration).

Past History

Following points must be noted in history

- Minor trauma
- Surgery (Limbal surgery for pterygium, squamous cell carcinoma, phthisis, squint surgery)
- Chalazion
- Microbial infection
- Pterygium
- Chemical burns.

EXAMINATION

Eyelids: Raised, red, smooth surfaced lesions with a narrow base (**Fig. 1**).

Conjunctiva: If conjunctiva is involved conjunctival inflammation may be present (**Fig. 1**).

Other findings are usually within normal limits.

DIFFERENTIAL DIAGNOSIS

- Kaposi's sarcoma—slow growing, in immunocompromised patient in contrast to fast growing pyogenic granuloma and associated risk factors



Fig. 1: Pyogenic granuloma

- Intravascular papillary endothelial hyperplasia
- Squamous papilloma
- Conjunctival lymphoma
- Ocular lymphangiectasia.
- *Topical or intralesional corticosteroids:* It is better to give a short course of steroid therapy before proceeding with surgery.

HISTOPATHOLOGY

Lesion consists of a mass of granulation tissue, prominent capillaries, and acute and chronic inflammatory cells.

MANAGEMENT

- Surgical excision

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LAGOPHTHALMOS

Varsha Varshney, Ritu Nagpal

INTRODUCTION

Lagophthalmos is a condition in which the eyelids do not close to cover the eye completely. The term lagophthalmos actually comes from the Greek word for hare (lagoos) and derives from a myth that hares sleep with their eyes open.^{1,2} In exams, it can be given as a short or spot case. A normal, healthy eye is covered by a film of tears that protects the surface and washes away dust and particles. Dry eyes that result from lagophthalmos are not only uncomfortable but are also subject to injury or infection from foreign objects landing in and abrading the eye surface. Left untreated, lagophthalmos can lead to permanent loss of vision.

HISTORY

Chief Complaints

Lagophthalmos patients commonly complain of inability to close lids completely (**Figs 1 and 2**).

Associated features are:

- Foreign body sensation
- Increased tearing
- Photophobia
- Pain may be worse in the morning due to increased corneal exposure and dryness during sleep
- Blurry vision, which results from unstable tear film



Fig. 1: Normal lid opening



Fig. 2: Lagophthalmos on lid closure in a case (Figure 1)

- In cases of advanced keratopathy and corneal ulceration, the symptoms and presentation may be severe.

History of Past Illness

- The recent history of trauma or surgery involving the head, face or eyelids should be documented with special attention to fractures to the skull base (a petrous portion of the temporal bone) or mandible that could affect facial nerve.
- Past infections should be reviewed, with particular attention to any history of herpes zoster infection.
- It is also important to document any past symptoms suggestive of thyroid disease or obstructive sleep apnea (*Floppy eyelid syndrome*).

History of Systemic Illness

History of systemic diseases like diabetes (diabetic neuropathy), any neurological disorder (polio, Guillain-Barré syndrome, leprosy), cerebrovascular accidents.

EXAMINATION

Systemic Examination

Complete neurological examination should be performed.

Ocular Examination

Visual acuity: Usually, normal. The blurring of vision may be present due to tearing or dryness.

Eyeball: Usually, normal.

Lids: Ask the patient to look down and gently close both eyes. Lagophthalmos is present when space remains between the upper and lower eyelid margins in extreme downgaze. Document the degree of lagophthalmos by measuring this space, in millimeters, with a ruler. In addition, following points must be recorded carefully.

- Record the blink rate as well as the completeness of the blink.
- Carefully test ocular motility and the strength of the orbicularis oculi muscle. The latter can be assessed by evaluating the force generated on attempted eyelid closure.

- Bell's phenomenon.
- Scar marks of previous trauma or surgery or infections may be present.

Conjunctiva: Diffuse or ciliary congestion may be there in presence of dry eye and exposure keratopathy.

Cornea: Following points must be recorded:

- Corneal sensitivity by applying a wisp soft cotton to the unanesthetized cornea and comparing the blink reaction with that of the fellow eye.
- Fluorescein staining with cobalt blue filter to find out the presence of punctate epithelial erosions or abrasions. Pay particular attention to the inferior cornea where lid excursion ends.
- Tear breakup time.
- Any epithelial defects or corneal ulcers should be carefully documented.
- Schirmer test:** The Schirmer test is used to assess tearing function. The degree of tearing can be compared between the paralyzed and normal sides.

Pupils: Pupillary reflexes are usually normal unless other cranial nerves are involved.

Anterior segment: Normal chamber depth and contents.

Posterior segment: Slit-lamp biomicroscopic examination using a 90D/78D lens and indirect ophthalmoscopy—usually normal.

INVESTIGATIONS

Blood Investigations

To rule out any systemic disease or infection following tests can be performed:

- CBC, blood sugar
- Thyroid function test
- HIV ELISA/western blot
- VDRL/RPR

The tests advised must be based on the history and clinical findings.

Radiological Investigations

Preferrably gadolinium-enhanced MRI: To rule out any neurological causes such as fracture damaging the nerve, mass compressing the nerve, ischemic areas involving facial nerve origin (geniculate ganglion).

Conduction Testing and Electromyography

The tests are most useful when performed 3–10 days after the onset of paralysis. Comparison to the contralateral side helps to demonstrate the extent of nerve injury and has prognostic implications. Nerve conduction responses are abnormal if a difference of 50% in amplitude between the paralyzed and normal side is detected; a difference of 90% between the 2 sides suggests a poorer prognosis.

Electroneurography

It is a physiologic test that objectively measure the difference between potentials generated by the facial musculature on both sides of the face in response to a supramaximal electrical stimulation of the facial nerve.

Electrodiagnostic Testing

Measures the facial nerve degeneration indirectly. If a patient does not reach 90% degeneration within the first 3 weeks of the onset of paralysis, some studies suggest that the prognosis is excellent, with over 80–100% of the patients recovering with excellent function.

Brainstem Auditory Evoked Response (BAER)

It may be obtained in patients with peripheral facial nerve lesions and other neurologic involvement. This test measures the transmission of response through the brainstem and is effective in detecting, notably, retrocochlear lesions.

Blepharokymographic Analysis

A high-speed eyelid motion-analysis system, has been used to evaluate movement of the eyelids. The computer-based analysis may prove helpful in diagnosing Bell palsy, predicting prognosis, and evaluating response to therapeutic measures such as placement of a gold weight in the affected upper eyelid (used in cases in which spontaneous recovery has been limited).

All these investigations must be conducted in consultation with a neurologist.

DIFFERENTIAL DIAGNOSIS

Lagophthalmos can be due to a variety of causes, careful history and neuroimaging often help in

arriving at a diagnosis. Following points must be kept in mind:

- Most common cause is Bell's palsy.
- If another cranial nerve, motor, or sensory symptoms are present, then other neurologic diseases should be considered (e.g. stroke, Guillain-Barré syndrome, basilar meningitis, cerebellar pontine angle tumor).
- Symptoms associated with seventh nerve neoplasm include slowly progressive paralysis, facial hyperkinesis, severe pain, recurrent palsy, and other cranial nerve involvement.
- Cerebellopontine tumors may affect the seventh, eighth, and fifth cranial nerves simultaneously.
- Patients with a progressive paralysis of the facial nerve lasting longer than 3 weeks should be evaluated for neoplasm.
- Recurrent ipsilateral facial paralysis must raise the suspicion of a tumor of the facial nerve or parotid gland. Tumors in the temporal bone, such as facial nerve neuromas, meningiomas, hemangiomas, and malignant primary and metastatic lesions, should be considered as well.
- If a patient reports the sudden onset of hearing loss and severe pain with the onset of facial paralysis, Ramsay Hunt syndrome must be considered. Typically, these patients will also have an erythematous vesicular rash involving the ear canal, auricle, and/or oropharynx.

Bilateral cases: Bilateral simultaneous Bell palsy is a rare (<1% of that of unilateral facial nerve palsy). Examples include Guillain-Barré syndrome, sarcoidosis, Lyme disease, meningitis (neoplastic or infectious), or bilateral neurofibromas (in patients with neurofibromatosis type 2).

TREATMENT

Medical Treatment and Supportive Care for Corneal Exposure

Nonpreserved artificial tears should be administered frequently (at least four times per day) in order to supplement the patient's tear film. Ointments can be applied to the cornea once at bedtime or throughout the day in cases of severe corneal exposure. Prophylactic antibiotics (preferably nonepitheliotoxic such

as chloramphenicol 0.3%) can be added to the regimen. In addition, following measures can be used:

- Moisture goggles also may be used.
- Punctal plugs may be helpful if dryness of the cornea is a persistent problem.
- Infectious corneal ulcers should be treated with appropriate antibiotic therapy.
- Patching the eye in the night time with simple micropore or a Frost suture for temporary protection of the cornea can also be helpful.
- Botulinum toxin can be injected transcutaneously or subconjunctivally at the upper border of the tarsus to paralyze the levator muscle to produce complete ptosis and to protect the cornea.

Tarsorrhaphy

A *temporary tarsorrhaphy* performed if recovery of the eyelid closure is expected within a few weeks. In most cases, the cornea can be protected adequately by suturing the lateral one-third of the eyelids together. Ideally, a small opening remains so that the patient can retain useful vision, the health of the cornea may be assessed and lubrication or antibiotic therapy can be applied to the eye.

A *permanent tarsorrhaphy* performed if a protracted clinical course is expected. If the patient regains useful function of the orbicularis oculi muscle, the adhesions can be lysed. The limitation of tarsorrhaphy is poor cosmetic appearance.

Gold Weight Implantation

Gold weights can be implanted into the upper eyelid to treat paralytic lagophthalmos. It enhances eyelid closure in a gravity-dependent fashion. Gold is considered an ideal substance because it is inert and it is not visible through the thin skin of the eyelid. Gold weights range from 0.6 to 1.6 g (in 0.2-g increments). The appropriate weight is chosen preoperatively by taping weights of varying sizes onto the external lid above the tarsus and observing the closing and opening of the lids. Properly chosen, the ideal weight will allow full closing and the opening of the lids while avoiding ptosis in primary gaze. Gold weight implantation is usually well-tolerated. However, astigmatic shift,

as well as migration and/or extrusion of the gold weight, are its limitations. In cases of allergy to gold, platinum may be used.

Upper Eyelid Retraction and Levator Recession

The recession of the upper eyelid retractors (levator and Müller's muscles) is a useful procedure in patients with lagophthalmos related to upper eyelid retraction from thyroid ophthalmopathy. Also, a combination of full-thickness skin grafts, advancement flaps, tarsal-sharing procedures and release of scar bands can be performed on patients with lagophthalmos from cicatricial or postsurgical lid shortening.

Lower Eyelid Tightening and Elevation

Laxity of the lower eyelid may occur in conditions such as facial nerve palsy and floppy eyelid syndrome. A tightening procedure such as a lateral tarsal strip will improve apposition of the lower eyelid to the globe and decrease tearing. This is also helpful in cases where upper eyelid restructuring procedures fail.

Other Surgical Procedures

In cases of severe lagophthalmos various other procedures have been described such as elevation of the midface using a variety of materials such as autogenous fascia slings, temporalis muscle transposition/transfer, nerve grafts and anastomoses, palpebral springs, soft tissue repositioning and suborbicularis oculi fat lifts.

VIVA QUESTIONS

Q.1. What are the ocular symptoms and signs of Bell's palsy?

Ans. Bell palsy is the most common cause of unilateral facial paralysis. Ocular manifestations have been described in **Table 1**. Two-thirds of patients complain about epiphora which is due to punctal eversion and the reduced function of the orbicularis oculi in transporting the tears (fewer tears arrive at the lacrimal sac, and overflow occurs).

Table 1 Ocular manifestations of Bell's palsy

<i>Early</i>	<i>Late</i>
<ul style="list-style-type: none"> • Lagophthalmos • Paralytic ectropion of the lower lid • Tear overflow • Brow ptosis • Upper eyelid retraction • Dry eye—poor tear distribution • Corneal exposure, erosion, infection, and ulceration (rare) 	<ul style="list-style-type: none"> • Narrow palpebral fissure-generalized mass contracture of the facial muscles(after several months) • Aberrant regeneration of the facial nerve with motor synkinesis • Reversed jaw winking-twitching of the corner of the mouth or dimpling of the chin occurring simultaneously with each blink • Crocodile tears—tearing with chewing

Q.2. Discuss etiology of lagophthalmos.

Ans. Lagophthalmos can occur due to a pathology in the facial nerve or in the lid. The different causes are summarized in **Table 2**.

Q.3. Relevant anatomy of facial nerve and eyelid.

Ans. *Facial nerve:* The facial nerve (seventh cranial nerve) innervates both the frontalis muscle, which raises the eyebrow and the orbicularis oculi muscle, which closes the eyelids. In addition, the 7th nerve innervates the muscles of the facial expression such zygomaticus muscles, which elevate the cheeks as well as the corrugator supercilii and procerus muscles, which depress the eyebrow.

Eyelids: The upper and lower eyelids contain seven structural layers. Beginning anteriorly, these comprise (1) skin and subcutaneous tissue, (2) orbicularis oculi muscle, (3) orbital septum, (4) orbital fat, (5) muscles of retraction, (6) tarsus and (7) conjunctiva. Damage to or degeneration of any of these tissues may inhibit good eyelid closure.

Table 2 Causes of lagophthalmos

<i>Pathology</i>	<i>Etiology</i>	<i>Factors/mechanism</i>
Facial nerve	Trauma	Fractures to the skull base (petrous portion of the temporal bone) or mandible Neurosurgical procedures
	Bell's palsy	Acute viral infection or reactivation of herpes simplex virus
	Tumors	Acoustic neuromas in the cerebellopontine angle Metastatic lesions
	Cerebrovascular accidents	Blockage of anterior inferior cerebellar artery
	Infectious, immune-mediated causes	Lyme disease, chickenpox, mumps, polio, Guillain-Barré syndrome, leprosy, diphtheria and botulism
	Mobius' syndrome	Characterized by cranial nerve palsies (sixth and seventh cranial nerve), motility disturbances, limb anomalies and orofacial defects
Eyelids	Cicatrices	Chemical or thermal burns, ocular cicatricial pemphigoid, Stevens-Johnson syndrome, mechanical trauma
	Eyelid surgery	Excessive removal of eyelid skin or muscle; blepharoplasty, tumor excision Overcorrection in ptosis repair
	Proptosis	Exophthalmos of one or both globes may inhibit eyelid closure
	Enophthalmos	Posterior displacement of the eye may affect eyelid apposition and closure Causes include orbital blowout fractures; orbital fat atrophy (trauma, infection, inflammation, aging, scleroderma, HIV-AIDS); phthisical eye; scirrhous carcinomas
	Floppy eyelid syndrome	Severe laxity and flexibility of the superior and inferior tarsal plates

Q.4. Discuss treatment options for Bell's palsy?

Ans. Treatment options for Bell's palsy includes following:

Pharmacologic therapy: The most widely accepted treatment for Bell palsy is corticosteroid therapy. However, the use of steroids is still controversial because most patients recover without treatment. The recommended dose of prednisone for the treatment of Bell palsy is 1 mg/kg or 60 mg/day for 6 days, followed by a taper, for a total of 10 days.

Antiviral agents: Such as Acyclovir (Zovirax) and Valacyclovir (Valtrex) have shown limited benefit.

Surgical options: Surgical options for Bell palsy include the following: Facial nerve decompression, subocularis oculi fat (SOOF) lift, Implantable devices (e.g. gold weights) placed into the eyelid, tarsorrhaphy, transposition of the temporalis muscle, facial nerve grafting, direct brow lift.

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DERMOID CYST

Shipra Singhi, Deepali Singhal

INTRODUCTION

A dermoid cyst (epidermal dermoid cyst) is an epithelial-lined structure with dermal appendages in its wall and keratin and hair in its lumen. It can be found in any subcutaneous location but more than 80% are located in the region of the head, with the majority in the eyelid and orbital area, usually superotemporally near the zygomaticofrontal suture.

It can be given as a short case or spot case in exam.

HISTORY

Chief Complaint

The presenting feature depends upon the location of dermoid. It can present in following manner:

- Painless fullness of upper eyelid or a mass lesion, most commonly at lateral orbital rim can be the presenting feature in an Anteriorly located dermoid.
- A posteriorly located dermoid can present with Painless, progressive proptosis, and diplopia.
- Rarely there can be associated ptosis and limitation of the movement.

- *Diminution of vision:* Blurring of vision is related to size and nerve compression and the presence of complications. It is usually progressive and painless.
- Sometimes patient may present with Symptoms consist of the rapid onset of unilateral pain, redness and watery discharge due to a ruptured cyst.
- Intermittent increase in size during chewing indicated extension to temporalis muscle of deep dermoid. However this mode of presentation is very rare.

In adults, dermoids may become symptomatic for the first time and grow considerably over a year. Based on this fact, some conclude that these lesions may be dormant for many years or have intermittent growth.

History of Present Illness

The onset, progression, association with pain and any preceding events such as trauma must be noted. Dermoid cyst usually has a insidious onset, painless and progresses slowly over a period of years. Rapid onset of unilateral pain, redness and watery discharge suggests a ruptured cyst.

Past History

A careful past history should be taken of any mass (tumor), nerve paresis, infection, trauma and ocular inflammatory diseases.

Past Surgical History

Previous history of any intraocular surgery should be enquired.

EXAMINATION

Ocular examination: Ocular examination should include following:

Visual acuity: Visual acuity is variably impaired depending on the site of involvement, size and compression of nerve and the presence of complications.

Eyeball

- Proptosis is usually nonaxial. Extension into intracranial fossae is possible if the frontal or sphenoid bones are involved. Temporal fossa involvement is rare but reported; this may result in intermittent proptosis associated with chewing, as positional changes of the temporalis muscle during chewing transmit pressure to the lesion and, hence, to the orbit.
- **Mass:** A mass lesion due to dermoid cysts have following characteristics:
 - Firm in consistency
 - Margins are smooth
 - Non-tender
 - Mobile preseptal masses without fixity to skin or muscle
 - Superotemporal quadrant is the most common site, less commonly, the superonasal quadrant is affected.
 - Many of them have variable periosteal attachment near the underlying frontozygomatic or frontoethmoidal sutures.
 - Occasionally the dermoid will pass into or through defects in the neighboring bone and may communicate intracranially.
 - A dermoid cyst can rupture spontaneously or with trauma, inciting an intense inflammatory response in the orbital soft tissues. This response may be limited to injection of the conjunctiva or may be severe and mimic orbital cellulitis.

- Occasionally, subconjunctival droplets of fat are seen. In some cases, a secondary fistula between the cyst and the skin may allow the contents of the cyst to drain intermittently.

- Rarely the dermoid is incompletely separated from the skin surface and presents as a chronically inflamed and discharging sinus.
- Dermoid cyst can also be associated with motility deficits and diplopia when the extent is large.

Eyelids: When dermoid is located anteriorly it can lead to ptosis.

Anterior segment: Generally normal. Occasionally, subconjunctival droplets of fat are seen in case of rupture of cyst.

Tonometry: IOP is usually unaffected.

Fundus: There may be compressive neuropathy or choroidal folds especially in cases of posterior dermoid.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis depends upon the location of the dermoid:

- Lateral anterior dermoid
 - Lacrimal gland mass
 - Lipodermoid
 - Teratoma
 - Plexiform neurofibroma
- Medial anterior dermoid
 - Mucocele
 - Encephalocele
- Cyst with spontaneous rupture
 - Orbital cellulitis
 - Orbital pseudotumor
- Deep dermoid with mass effect
 - Orbital tumors
 - Thyroid ophthalmopathy.

INVESTIGATION

Classic dermoid cysts located at the frontozygomatic suture whose posterior aspect can be palpated may be diagnosed clinically without imaging. Medial lesions require imaging to rule out an encephalocele or mucocele before surgical excision. Deep orbital lesions also require imaging for diagnostic purposes and to help with surgical planning.

CT Scan

A dermoid cyst typically has a hyperdense wall and a hypodense cavity which remains non-enhancing with contrast. The central cavity may appear heterogeneous as a result of keratin and other cystic debris. CT imaging is especially useful in delineating bony changes such as *smooth pressure erosion (scalloped) near the affected suture, clefts, and full-thickness bony channels*, seen in as much as 85% of cases. A dumbbell cyst have a typical appearance with a component on either side of the bone and a bony communication between them.

MRI

The lesions are generally hypointense on T1-weighted imaging with respect to fat and are best visualized using fat-suppression techniques. It appears as a well defined, round to ovoid structure of variable size. The lesions tend to be hyperintense on T2-weighted imaging. These lesions typically do not enhance with contrast due to lack of blood vessels in the cyst. MRI has the advantage of not exposing the patient to radiation, hence extremely useful in pediatric age group.

Ultrasonography (USG)

Ultrasound characteristics of dermoid cysts include a smooth contour and variable echogenicity.

Color Doppler imaging

Color Doppler imaging of dermoid cysts shows no intraleisional blood flow, which can help differentiate them from hemangioma and rhabdomyosarcoma.

MANAGEMENT

A small, asymptomatic orbital epidermal dermoid cyst requires no immediate treatment. In many cases, however, the cyst slowly enlarges or ruptures, and eventually requires treatment. The treatment of orbital dermoid cysts is surgical excision. The primary goal of excision is to remove the dermoid with the cyst wall intact without causing an

iatrogenic rupture. Leakage of the cystic contents into the orbit can result in significant inflammation and recurrence, while lesions removed in their entirety rarely recur.

The surgical approach depends upon the location of the lesion. An anterior orbital epidermal dermoid cyst can be removed through anterior orbitotomy (superior eyelid crease incision). A posterior orbital epidermal dermoid cyst can be removed through lateral orbitotomy. The use of a cryo-probe can help in the delivery of the cyst intact in these cases. Deeper lesions are approached based upon their location in the orbit and relationship to adjacent structures. Intracranial extension requires a multi-disciplinary surgical approach for complete excision.

Great care should be taken to remove the cyst with the capsule intact, using meticulous dissection at the site of the attachment of the cyst to the bony sutures. If the cyst is accidentally ruptured at the time of surgery, copious irrigation and attempted removal of the cyst remnants should be done.

In the rare case of dermoid cyst at the orbital apex, an orbital deroofing procedure may be necessary. If the cyst is too large to remove intact, its contents can be aspirated in order to facilitate removal. Recurrence can develop after incomplete excision.

In ruptured cyst:

- Systemic steroid therapy
- Systemic NSAID therapy (aspirin, ibuprofen).

CLASSIFICATION

1. Epidermal dermoid cyst—anterior or deep
2. Conjunctival dermoid cyst.

Conjunctival Dermoid Cyst

Occasionally, an otherwise typical dermoid cyst is lined by nonkeratinizing epithelium with features of conjunctival epithelium. This is called a conjunctival dermoid cyst.

Incidence

A conjunctival dermoid cyst is lined by conjunctival epithelium. It accounts for about 5% of dermoid cysts that occur in the orbit, with the other 95% being of epidermal origin.

Clinical Features

Conjunctival dermoid cyst is probably congenital but often it is not evident until childhood or sometimes later in life.

It occurs in the superonasal aspect of the orbit usually and presents as firm or fluctuant subcutaneous mass.

Investigation

With CT or MRI, a conjunctival dermoid cyst has features similar to an epidermal dermoid cyst. However, it is more likely to be situated in the orbital soft tissues in the anterior and nasal aspect of the orbit, usually without contact to bone.

Histopathology

Histopathologically, conjunctival dermoid cyst is lined by nonkeratinizing epithelium which contains goblet cells. Like the epidermoid dermoid cyst, it contains dermal appendages such as hair shafts, sebaceous gland, and occasional sweat glands.

Management

A conjunctival dermoid cyst is usually symptomatic when diagnosed and is best managed by surgical excision.

Either a conjunctival or skin incision superonasally is generally used because it is usually located superonasally in the anterior orbit,

In a skin approach, an eyelid crease incision in the upper eyelid is recommended.

VIVA QUESTIONS

Q.1. What is the epidemiology of dermoid?

Ans. Epidemiology:

- Congenital choriostoma
- Account for 3–8% of orbital tumors in children
- The dermoid cyst becomes the most common noninflammatory space-occupying lesion of the orbit
- In the Wills Eye Hospital pathology series, dermoid cyst accounted for 46% of childhood orbital lesions and for 89% of all cystic lesions.

Q.2. Compare epidermal and conjunctival dermoid cyst?

Ans.

<i>Epidermal dermoid</i>	<i>Conjunctival dermoid</i>
<ul style="list-style-type: none"> • <i>Age of onset:</i> Anterior dermoids typically present in first decade • It accounts for about 95% of dermoid cyst that occur in the orbit 	<ul style="list-style-type: none"> • <i>Age of onset:</i> Deeper dermoids may present in adolescence or adulthood • It accounts for about 5% of dermoid cysts that occur in the orbit
<ul style="list-style-type: none"> • <i>Histopathology:</i> Dermoid cyst is lined by keratinizing stratified epithelium. • It contains dermal appendages such as hair shafts, sebaceous gland, and occasional sweat glands 	<ul style="list-style-type: none"> • <i>Histopathology</i> • Histopathologically, conjunctival dermoid cyst is lined by non-keratinizing epithelium which contains goblet cells. Like the epidermoid dermoid cyst, it contains dermal appendages such as hair shafts, sebaceous gland, and occasional sweat glands
<ul style="list-style-type: none"> • <i>Site:</i> Superotemporal usually 	<ul style="list-style-type: none"> • <i>Site:</i> Superonasal usually
<ul style="list-style-type: none"> • <i>Imaging:</i> On CT, a dermoid typically has a hyperdense wall and a hypodense cavity which remains non-enhancing with contrast. The central cavity may appear heterogeneous as a result of keratin and other cystic debris. An estimated 85% of dermoids are associated with such bony changes as smooth pressure erosion near the affected suture, clefts, and full-thickness bony channels • <i>On MRI:</i> Hypointense on T1-weighted imaging; hyperintense on T2-weighted imaging 	<ul style="list-style-type: none"> • <i>Imaging:</i> With CT or MRI, a conjunctival dermoid cyst has features similar to an epidermal dermoid cyst. However, it is more likely to be situated in the orbital soft tissues in the anterior and nasal aspect of the orbit, usually without contact to bone

Contd...

Contd...

• Treatment: Anterior orbitotomy (superior eyelid crease incision)	• Treatment: Anterior orbitotomy—conjunctival or skin incision superonasally • In a skin approach, an eyelid crease incision in the upper eyelid is recommended
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Q.3. Differentiate between anterior and deep dermoid cyst.

Ans.

Anterior dermoid	Deep dermoid
• Age of onset: Anterior dermoids typically present in first decade	• Age of onset: Deeper dermoids may present in adolescence or adulthood
• Suture involved: - Lateral: Frontozygomatic suture - Medial: Frontoethmoidal or frontolacrimal sutures	• Suture involved: Sphenozygomatic or sphenoethmoidal suture
• Symptoms: Painless fullness of upper eyelid, most commonly at lateral orbital rim	• Symptoms: Painless, progressive proptosis, diplopia
• Signs: Subcutaneous, mobile nodule, most commonly located at frontozygomatic suture	• Signs: Proptosis, motility deficit, inferior or superior displacement of globe
• Treatment: Anterior orbitotomy (superior eyelid crease incision)	• Treatment: Lateral orbitotomy

Q.4. What is choriostoma?

Ans. Choristoma is a mass of histologically normal tissue present at abnormal location.

Q.5. What is difference between choriostoma and teratoma?

Ans. While choristoma is a mass of histologically normal tissue present at abnormal location, teratoma is a mass of neoplastic tissue at abnormal location.

Q.6. What is the most common location?

Ans. Children

- The most common location is in the superior temporal aspect of the orbit. The second most common location is in the superior nasal aspect of the orbit.
- Lesions located superotemporally are generally smooth, firm subcutaneous masses attached to the orbital rim in the region of the zygomaticofrontal suture.
- The mass is generally less than 1 cm in diameter, nontender, and oval in shape. Little displacement of the globe usually occurs.
- Orbital dermoid cysts are not attached to the skin, which helps differentiate them from sebaceous cysts. The cyst usually is tethered to the periosteum of the bone near suture lines, including the sinuses or intracranial cavity.

Adults

- The cysts are palpated less easily and have more vague borders. They are more likely to displace the globe and may erode their way into adjacent structures.
- Dystopia:** A larger dermoid cyst can cause downward and medial displacement of the globe.
- Motility deficits
- Diplopia

Anterior lesions: typically present in the first few years of life as smooth, well-circumscribed, subcutaneous, painless masses.

- Site:** The most common location for the anterior dermoid cyst is at the *superolateral aspect of the orbit at the frontozygomatic suture*, as seen in the case described here. Medial lesions occur less frequently and often arise from tissue sequestered in the frontoethmoidal or frontolacrimal sutures. If there is no orbital extension, the posterior aspect of the mass may be palpable.
- Ptosis:** Because of their anterior location, these lesions do not usually cause globe displacement, but they can cause visually significant ptosis if they grow to a large enough size.

Deep lesions are more insidious, and

- *Site:* often develop at the sphenozygomatic or sphenoethmoidal suture.
- *Proptosis:* Their presence is usually declared by mass effect on surrounding structures: Patients with deep lesions may present in late adolescence or adulthood with painless, progressive proptosis,
- *Dumbbell dermoids:* Dermoids may also straddle the orbital bones (most commonly the lateral orbital wall) such that they have both an anterior lobe and a deeper orbital lobe. These so-called "dumbbell" dermoids must be imaged to assess the extent of the orbital component before excision.

Rupture

- A dermoid cyst can rupture spontaneously or with trauma, inciting an intense

inflammatory response in the orbital soft tissues. This response may be limited to injection of the conjunctiva or may be severe and mimic orbital cellulitis.

- Occasionally, subconjunctival droplets of fat are seen. In some cases, a secondary fistula between the cyst and the skin may allow the contents of the cyst to drain intermittently.
- While this is rarely the first presenting sign for an anterior dermoid, it may be the first presenting sign of a deep dermoid.

Complications

- Rupture of the cyst
- Orbital cellulitis
- Recurrent cyst
- Compressive neuropathy
- Amblyopia
- Strabismus.

ORBITAL HEMANGIOMA

Aditi Dubey, Ritika Mukhija, Rajesh Pattebahadur

INTRODUCTION

Orbital hemangiomas are of two types—capillary hemangioma and cavernous hemangioma. Capillary hemangioma is the most common primary benign tumor of orbit in children (infancy). Cavernous hemangioma is more common in adults (20–30 years), usually women.^{1,2}

CAPILLARY HEMANGIOMA

History

Chief Complaints

Mass over eyelid present since birth or appear in the first few weeks of birth.

History

Usually parents complain of bluish or pink mass over eyelid present since birth with enlarging with age. In addition, there will be a history of increases in size on crying.

Examination

Inspection

Superficial hemangiomas are confined to the dermis, pink-purple mass lesion with mulberry appearance or dimpled texture and increases on crying or Valsalva. Deep orbital lesions may present with axial/non-axial proptosis.

Palpation

Soft, nontender, nonpulsatile, ill-defined mass over the eyelid which may have an orbital extension.

Auscultation

No bruit or pulsation heard.

Deep orbital lesions may present with hyperopia, optic nerve edema (due to compression), retinal striae, raised intraocular pressure and strabismus.

Classification

- *Superficial or simple:* Involves the skin and appear as a bright red, soft mass with a dimpled texture.
- *Preseptal or subcutaneous:* Dark blue/purple soft ill-defined non-tender mass (**Fig. 1**). increases on crying and Valsalva nonpulsatile no bruit.
- *Deep:* Located deeper within the orbit may present merely as a progressively enlarging mass without any overlying skin change (D/D Rhabdomyosarcoma should be ruled out).

Management

Normally the course of capillary hemangioma is as follows:

- Rapid growth up to 6–12 months
- 30% spontaneous resolution by 3 years
- 70% spontaneous resolution by 7 years

Most lesions will regress spontaneously, therefore; observation, refractive correction and amblyopia therapy are the first line of management. Treatment should be deferred until it is clear that the natural course of the lesion will not lead to the desired result.

Indication for Treatment

- Amblyopia secondary to astigmatism, ptosis, and anisometropia.
- Exposure keratopathy
- Optic nerve compression
- Severe disfigurement or cosmetic blemish
- Infection.



Fig. 1: Capillary hemangioma

Modalities of Treatment

- Small lesion < 2 mm thickness—laser
- Superficial or preseptal lesion—intralesional steroid [betamethasone (4 mg/mL) 1–2 mL or triamcinolone (40 mg/mL) 1–2 mL at different site repeat after 2 months]. Adverse effects of steroid injection include skin necrosis, subcutaneous fat atrophy, orbital hemorrhage and rarely central retinal artery occlusion.
- Deep/orbital lesions—systemic steroids
- Systemic beta-blockers (inhibit angiogenesis and acts as vasoconstrictor)
- Surgical excision may be considered for lesions that are smaller, subcutaneous or refractory to steroids
- Interferon- α (however, it has significant systemic adverse effects and poorly tolerated)
- Radiation therapy has also been used, but it has the potential to cause cataract formation, bone hypoplasia, and future malignancy.

CAVERNOUS HEMANGIOMA

Chief Complaints

Cavernous hemangioma—slowly progressive proptosis (growth may accelerate during pregnancy).

History

Cavernous hemangiomas are usually seen in adults presenting as progressive proptosis, sometimes decreased visual acuity may be present due to compressive optic neuropathy.

Examination

Examination is similar to a case of proptosis due to an intraconal tumor. It usually leads to axial proptosis.

Course and Management of Cavernous Hemangioma

- This lesion rarely resolve spontaneously
- *Observation:* If asymptomatic
- *An indication of treatment:* 1. Symptomatic lesion (lesion compromising ocular function); 2. Gradually enlarging
- *Treatment:* Surgical excision.

VIVA QUESTIONS

Q.1. Classify orbital hemangioma.

- Ans.**
- Cutaneous
 - Purely preseptal
 - Preseptal with orbital involvement (extraconal)
 - Preseptal with orbital involvement (extraconal + intraconal).

Q.2. What are the risk factors for capillary hemangioma?

- Ans.** Premature infants and newborns whose mothers had chorionic villus sampling.

Q.3. What is the most common location of hemangioma?

- Ans.** *Capillary hemangioma:* Predilection for the superonasal quadrant of the orbit and the medial upper eyelid, may involve skin over face some patients may have cutaneous and visceral hemangiomas.

Cavernous hemangioma: Extraconal and retrobulbar.

Q.4. Histopathology and imaging in hemangioma?

- Ans.** Shown in Table 1.

Q.5. What are the systemically associated syndromes with capillary hemangioma?

- Ans.**
- *Kasabach Merritt syndrome:* Triad of hemangioma, decrease coagulation factors and thrombocytopenia. Associated with rapidly expanding visceral hemangiomas.

- *Maffucci syndrome:* multiple skin and visceral hemangiomas associated with enchondromas
- High output heart failure associated with fast growing visceral hemangiomas.
- *PHACES syndrome:* Posterior fossa malformations-hemangiomas-arterial anomalies-cardiac defects-eye abnormalities-sternal cleft and supraumbilical raphe syndrome

Q.6. What are the other vascular malformations of the orbit?

- Ans.**
- *Hemangiopericytoma*
 - The uncommon lesion, well encapsulated, hypervascular and hypercellular.
 - Appear in middle age.
 - Resemble cavernous hemangiomas on both CT and MRI, but they appear bluish intraoperatively.
 - Histologically composed of plump pericytes that surround a rich capillary network, microscopically "benign" lesions may recur and metastasize, whereas microscopically "malignant" lesions may remain localized.
 - Treatment—complete excision because they may recur, undergo malignant degeneration, or metastasize.
 - *Lymphatic malformation*
 - Also known as lymphangiomas.
 - Due to vascular dysgenesis.
 - Become apparent in the first decade of life.

Table 1 Differentiating features between capillary and cavernous hemangioma

Parameters	Capillary hemangioma	Cavernous hemangioma
Histopathology	Tumor composed of small anastomosing channels without true encapsulation	Lesions are well encapsulated and composed of large cavernous spaces containing red blood cells with walls of the spaces containing smooth muscle
B scan	For extention of disease and anatomical relations	Well encapsulated mass lesion with cavernous fluid (blood) filled spaces
CT scan	Homogeneous enhancing soft tissue mass ± extraconal extension with fingerlike projections	Homogeneously slowly enhancing, well-encapsulated mass
MRI scan	Fine intralesional vascular channels and high blood flow	Small intralesional vascular channels with slowly flowing blood, i.e. flow voids. Chronic lesions may contain radiodense phleboliths

- Occurs in the orbit, conjunctiva, eyelids, oropharynx, or sinuses.
 - Contain both venous and lymphatic components.
 - May enlarge during URTIs and present with sudden proptosis caused by spontaneous intralesional hemorrhage.
 - *Histology:* Characterized by large, not encapsulated, serum-filled channels that are lined by flat endothelial cells.
 - *MRI:* Pathognomonic features multiple grapes like cystic lesions with a fluid-fluid layering of the serum and red blood cells. Venography shows no arterial or venous connection.
 - *Management:* Surgical intervention should be deferred unless vision is affected, due to the risk of hemorrhage. A subtotal resection is generally needed to avoid sacrificing important structures. Orbital hemorrhage is allowed to resorb spontaneously; but if optic neuropathy or corneal ulceration threatens vision, aspiration of blood through a hollow-bore needle or by open surgical exploration can be attempted.
 - *Venous malformations*
 - Also known as *orbital varices*.
 - Low-flow vascular lesions due to vascular dysgenesis.
 - *Clinical features:* Enophthalmos at rest (when the lesion is not engorged), proptosis when the patient's head is dependent or after a Valsalva maneuver).
- *Diagnosis:* Contrast-enhanced rapid spiral CT during a Valsalva maneuver showing characteristic enlargement of the engorged veins. Phleboliths may be present on imaging.
 - *Treatment:* Conservative
 - *Biopsy:* Avoided because of the risk of hemorrhage.
 - *Surgery:* Reserved for the relief of significant pain or for cases in which the venous malformation causes vision-threatening compressive optic neuropathy. Complete surgical excision is difficult. Intraoperative embolization of the lesion may aid surgical removal.
 - *Arteriovenous malformations*
 - High-flow developmental anomalies due to vascular dysgenesis.
 - Composed of anastomosing arteries and veins without an intervening capillary bed.
 - *Sign:* Dilated corkscrew episcleral vessels.
 - *Treatment:* Selective occlusion of the feeding vessels followed by surgical excision of the malformations (complication -arterial hemorrhage).

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COLOBOMA OF EYELID

Shipra Singh, Amar Pujari

INTRODUCTION

An eyelid coloboma is a full-thickness defect of the eyelid.^{1,2} The word coloboma comes from the Greek word that means, "Curtailed". Lid coloboma occurs due to a delayed fusion of mesodermal components of frontonasal and maxillary processes of the face. It is caused by the failure of fusion of the mesodermal lid folds. Although an eyelid coloboma can occur in many locations, the most common position is at the junction of the medial and middle third of the upper lid.³⁻⁵ In exams, it can be given as a short or spot case.

HISTORY

Chief Complaint

A case of coloboma usually presents with cosmetic issues due to the defect (notching) in the eyelid. It can be associated with following:

- Absence of eyeball
- Bluish colored swelling (in case of cryptophthalmos),
- Small size of eyeball
- Drying of eyes
- Diminution of vision: Blurring of vision is related to corneal opacity, exposure keratoconjunctivitis, cataract and choroidal coloboma. It is usually present since birth which may progress and painless in origin.
- Diplopia due to restriction
- Painless mass (associated limbal dermoid)
- Foreign body sensation/irritation.

Past History

A careful past history should be taken of any—

- Perinatal and pregnancy history
- Family history of congenital eyelid colobomas or other congenital anomalies, especially facial (e.g. cleft lip/palate)
- History of other current birth defects
- Pediatric review of systems, hearing loss, cardiovascular disease, facial asymmetry
- History of progressive corneal problems.

Past Surgical History

Previous history of ocular surgery may or may not be present.

EXAMINATION

Systemic Examination

It may be associated with multiple systemic anomalies.

- Cardiovascular abnormalities, facial hemiatrophy, atresia of the external auditory meatus, accessory auricles, nevus flammeus, neurofibromatosis, preauricular appendages, and pre-tragal fistulas can be there. One-third of cases associated with Goldenhar's syndrome (triad of peribulbar dermoid, preauricular appendages, and pre-tragal fistulas).
- Facial defects that may be associated with eyelid colobomas, include a less prominent supraorbital margin, and a bifid nose.
- Among the syndromes that may include eyelid colobomas are Goldenhar, Treacher Collins, Delleman, Fraser and nano palpebral lipoma coloboma syndrome.

Ocular Examination

Visual acuity: Is variably impaired depending on associated abnormalities such as limbal dermoid.

Eyeball: Microphthalmos, anophthalmos, euryblepharon, cryptophthalmos, lagophthalmos and esotropia can be there.

Extraocular movement: Duane's retraction syndrome may be an associated feature.

Eyebrow: Loss of eyebrow hair may be seen.

Eyelids: Eyelid colobomas have following features

- Most commonly triangular with the base at the eyelid margin.
- It is usually located on the medial half of the upper eyelid or lateral half of the lower eyelid.
- They are usually unilateral, generally located at the medial one-third of the upper eyelids (90%), and may vary from a small notch to complete defects of the eyelid.



Fig. 1: Surgical eyelid coloboma

- Upper eyelid coloboma (**Fig. 1**) is more common than lower lid coloboma and may be associated with Goldenhar syndrome.
- *Lower eyelid coloboma:* Lower lid colobomas are more commonly associated with facial clefts. Treacher Collin syndrome is usually associated with this.

Lacrimal system: Obstruction proximal to the lacrimal sac and lacrimal stenosis can be there.

Conjunctiva: Symblepharon, absence of an upper eyelid fornix and malformation of the caruncle can be seen. Conjunctival traction bands are common (present in a third of eyelid colobomas). These bands are highly amblyogenic owing to strabismus. Forced duction testing (FDT) is often positive in such cases of restriction.

Cornea: Following anomalies can be seen:

- Exposure keratopathy
- Corneal opacities
- *Limbal dermoid:* Yellowish-white, solid, vascularized, elevated nodules straddling the corneal limbus. Size may vary ranging from 2 to 15 mm in diameter. Corneal dermoid occur as single lesions mostly but may be multiple, and they may be unilateral or bilateral, the former being the more common.
- Dellen formation may occur
- Cicatrization.

Lens: Cataract (anterior polar) and subluxation of the lens may be there.

Sclera: Epibulbar dermoid tumor can be there.

Iris: Coloboma (key hole)—may be typical or atypical, complete or incomplete, partial or total.

Intraocular pressure (IOP): It is usually normal

Fundus: There may be choroidal coloboma, retinal detachment due to choroidal coloboma and hypoplastic disc.

CLASSIFICATION

Lid coloboma can be due to following:

- Congenital lid coloboma (isolated or syndromic)
- Acquired lid coloboma (traumatic or post-surgical).

Depending upon the associations, it is classified as following:

Isolated Coloboma

- Coloboma associated with cornea palpebral adhesions
 - *Complete:* No discernable eyelid differentiation and the eyes are completely covered with skin.
 - *Incomplete:* A skin fold devoid of tarsus covers the medial aspect of the palpebral aperture, significant cornea palpebral adhesions, lower fornix, and lateral upper eyelids usually spared.
 - *Abortive type/congenital symblepharon variant:* True coloboma of variable sizes with a diverse range of cornea palpebral adhesions, lower fornix, and lateral upper eyelids usually spared.
- *Simple coloboma:* Coloboma not associated with cornea palpebral adhesions.

Syndromic Variants

- Fraser syndrome
- Goldenhar syndrome
- *Rare syndromes:* Manitoba oculotrichoanal syndrome, Ablepharon-macrostomia syndrome, Nasopalpebral lipoma-coloboma syndrome, Amniotic band sequence, Oculo-ectodermal syndrome, Neurocutaneous syndromes, CHARGE (coloboma, heart defect, atresia choanae, retarded growth and development, genital abnormality, and ear abnormality) syndrome

GRADING

Lid coloboma can be graded as follows (Nouby)³

- *Grade 1:* Coloboma without cryptophthalmos.
- *Grade 2:* Coloboma with abortive cryptophthalmos.
- *Grade 3:* Coloboma with complete cryptophthalmos.
- *Grade 4:* Classic cryptophthalmos (absence of all eyelid structures and complete coverage of eye by skin).
- *Grade 5:* Severe cryptophthalmos (with severe deformity of the nose and ectropion of the upper lip).

INVESTIGATION

The diagnosis of a lid coloboma requires a direct clinical examination. Specific laboratory studies are generally indicated in associated syndromes that may include following:

- X-ray of spine—for hemivertebra or scoliosis
- ECG, echocardiography—for cardiac defect
- MRI of brain
- Complete blood count
- Renal function test
- Audiometry for hearing assessment.

MANAGEMENT

Medical Management

Corneal protection is the primary goal in the medical treatment of eyelid colobomas. Medical therapy includes artificial tears and ointment and Bedtime patching.

Surgical Management

Indication of surgery includes:

- Exposure keratitis
- Trichiasis which may cause corneal lesion.
- Cosmesis
- Amblyopia
- Strabismus.

The initial evaluation of an upper eyelid coloboma consists of measuring the size of the eyelid margin defect and comparing it with the overall length of the horizontal palpebral fissure. The surgical procedure used depends on the size and the location of the defect.

Small defects: If the defect in the upper eyelid involves less than one-third of the margin, and well managed with topical lubrication, then surgery may be delayed until later in childhood. This surgery may require a lateral canthotomy and/or superior cantholysis to rotate or advance adjacent tissue to prevent excessive tension on the wound. The edges of the defect are freshened with sharp incisions, and the precise anastomosis is performed. The lid margin is brought together using a 2-layer approximation of the tarsus and the skin. Lateral cantholysis and placement of near-far, far-near sutures may be necessary to minimize horizontal tension.

Moderately-sized defects: Larger defects, a Tenzel semicircular rotational flap may be used for defects involving approximately one-third of the eyelid margin.

Large defects: If the defect is larger than one-half of the upper eyelid, other surgical procedures should be used. The various surgeries that can be performed include a free transconjunctival graft from the contralateral upper eyelid can be taken, modified Hughes procedure (for lower lid coloboma), modified Cutler-Beard procedure (upper lid coloboma), rotational flap from cheek (Mustard's technique).

Prognosis: Prognosis is excellent to good in eyelid coloboma, depending on the size of the lesion and the speed of therapy.

Patient education: Genetic consultation is highly recommended, especially for patients with associated syndromes, such as Treacher Collins syndrome, which is autosomal dominant with variable penetrance and expressivity.

VIVA QUESTIONS

Q.1. When should the coloboma of eyelid be repaired?

Ans. This depends on the size of the defect and on the presence of corneal exposure. If the defect of the eyelid is small and not associated with corneal exposure, surgery can be delayed until the age of 3–4 years, when there is an increased amount of eyelid tissue is available for repair. In a case of large defect, surgery should be done as soon as possible to avoid corneal lesions.

Q.2. What is the difference between lower and upper eyelid coloboma?

Ans. See Table 1.

Table 1 Difference between upper lid and lower lid coloboma	
<i>Upper eyelid coloboma</i>	<i>Lower eyelid coloboma</i>
More common	Less common
Usually isolated	Usually syndromic association
Occur at the junction of the inner and middle thirds	Occur most frequently at the junction of the middle and lateral thirds
Tend to be full thickness	Tend to be partial thickness involving preferentially the anterior lamella
Have normal adjacent lid margins	Adjacent lid margins may be abnormal
Usually not associated with facial clefts.	Usually associated with facial clefts
Often associated with cryptophthalmos	Usually not

Q.3. What are the clinical findings in Treacher Collins syndrome?

Ans. See Table 2.

Q.4. What are the clinical findings in Goldenhar syndrome?

Ans.

- Limbal dermoid (bilateral in 25% of cases)
- Eyelid coloboma
- Preauricular appendages/skin tags
- Microtia or anotia of external ear can be associated with hearing loss with or without middle ear malformation
- Vertebral abnormalities (butterfly vertebrae or hemivertebrae)
- Congenital heart disease (numerous anomalies have been reported)
- Central nervous system abnormalities (hydrocephalus, intracranial lipomas, cranial nerve dysgenesis and mental retardation have been described).

Q.5. What are the clinical findings in Fraser syndrome?

Ans. *Major characteristics:*

- Cryptophthalmos

Table 2 Treacher Collins syndrome

<i>Structure affected</i>	<i>Clinical features</i>
Eyes	<ul style="list-style-type: none"> • Antimangloid slant of palpebral fissures • Coloboma of lower eyelid • Hypoplasia of lower eyelid • Hypertelorism
Ears	<ul style="list-style-type: none"> • Microtia • Conductive hearing loss • Stenosis or complete atresia • External ear abnormalities
Face	<ul style="list-style-type: none"> • Hypoplasia of facial bones (mandibular or zygomatic arch) or complete absence of zygomatic arch • Dental malocclusion • Microstomia • High arched palate, cleft palate • Clonal atresia • Nasal dorsum parrot like shape
Others	<ul style="list-style-type: none"> • Malformations associated with heart, kidney, vertebral column and extremities • Obstructive sleep apnea.

- Syndactyly
- Genital anomalies
- Sibling with Fraser syndrome.

Minor characteristics:

- Alterations of the nose
- Alterations of the ears
- Alterations of the larynx
- Oral clefts (cleft lip and/or palate)
- Umbilical hernia
- Renal agenesis (unilateral or bilateral)
- Skeletal anomalies.

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CHAPTER

2

Cornea and Conjunctiva

LONG CASES

CORNEAL ULCER

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INTRODUCTION

Any breach in the continuity of an epithelial surface is called an ulcer. However, a corneal ulcer is better defined as an epithelial defect associated with superficial tissue loss along with variable grades of inflammation. Corneal ulcer can be given as a long case in exams. A careful history and examination often clinches the diagnosis.

HISTORY

Chief Complaints

The common presenting symptoms in a case of corneal ulcer are:

- Pain
- Diminution of vision
- Redness, watering, discharge, foreign body sensation
- Photophobia.

History of Present Illness

Following points must be recorded in history:

Onset and Progression

The onset of corneal ulcer depends on the predisposing factor, virulence of the organism and

the host immunity. The predisposing factors are summarized in **Table 1**.

Sudden onset and rapid progression is generally associated with bacterial corneal ulcers such as *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Pseudomonas* species. Gradual onset and an indolent course is commonly seen in ulcers caused by fungi and parasites (*Acanthamoeba*) and few bacteria such as *Moraxella*, *coagulase negative Staphylococcus*, *Nocardia* species and *atypical Mycobacteria*.

In *Acanthamoeba*, keratitis course can be variable (gradual or rapid) and it may be associated with a prolonged course with remissions.

Pain

The occurrence of pain in corneal ulcer can be minimal to excruciating. The type of causative organism and depth of the ulcer influence the severity of the pain.

- Superficial corneal ulcers are more painful than deep corneal ulcers due to rich sensory nerve supply in the superficial cornea.
- *Acanthamoeba* keratitis usually presents with excruciating pain due to associated radial keratoneuritis. The pain is usually out of proportion to the objective clinical findings.

Table 1 Predisposing factors in cases of corneal ulcers

Predisposing factors	Examples
Ocular	<i>Trauma</i> : Mycotic (vegetative) and <i>Acanthamoeba</i> keratitis
	<i>Contact lenses</i> : <i>Pseudomonas</i> and <i>Acanthamoeba</i> keratitis
	<i>Lid and adnexal infections</i> : <i>Pneumococcus</i> keratitis (dacryocystitis) and actinomycetes (canaliculitis)
	Abnormality in lids such as trichiasis, coloboma, ectropion, entropion, lagophthalmos, exophthalmos, proptosis, blepharitis and meibomitis
	Ocular surface disease
	Allergic eye disorders
	Bullous keratopathy
	Topical medications (topical corticosteroids, honey, prolonged use of topical antibiotics)
Systemic	Prior ocular surgery [pterygium surgery, keratoplasty, photorefractive keratectomy and laser <i>in situ</i> keratomileusis (LASIK)]
	Diabetes mellitus
	Sjögren's syndrome
	Steven-Johnson syndrome
	HIV
	Advanced malignancies
	Connective tissue disorders
	Alcoholics
	Extremes of age
Occupational	Measles
	Malnutrition
	Smoking

In contrast reverse is true for fungal ulcers where pain may be completely absent in spite of an advanced corneal ulcer.

- A sudden relief in pain in a case of corneal ulcer may be indicative of perforation of the corneal ulcer.

Redness and Photophobia

Corneal ulcer is usually associated with circumciliary congestion or a combination of conjunctival and circumciliary congestion. Photophobia can be severe due to irritation of the anterior ciliary nerves.

Discharge

Most of the corneal ulcers are associated with discharge, which may be watery (in viral or small bacterial corneal ulcer), mucopurulent or purulent (bacterial ulcer). Corneal ulcers caused by *Pseudomonas* are associated with a greenish-yellowish discharge. A membranous discharge is seen with keratitis caused by *Corynebacterium diphtheriae*.

Decreased Visual Acuity

Loss of vision depends upon the severity and location of the ulcer. Central corneal ulcers (caused by *Pseudomonas* species, *Staphylococcus aureus* and *Fusarium* species) are associated with significant loss of visual acuity. The visual acuity may not be severely affected in small, peripheral ulcers (e.g. early cases of *Acanthamoeba* keratitis where only epithelium is affected).

Other factors that can reduce visual acuity include the presence of an associated pupillary membrane, hypopyon, cataract, glaucoma and endophthalmitis.

History of Past Illness

History of trauma, contact lens use, allergic eye disorders, topical medication use, prior ocular surgery or systemic disease (as mentioned in **Table 1**) has to be noted carefully.

Family History

Family history may be there in cases of connective tissue disorders.

Past Surgical History

Recent surgery can be a predisposing factor for infective keratitis (see **Table 1**).

EXAMINATION

General Examination/Specific Systemic Examination

A thorough general examination must be carried out to look for following:

- Potential source of infection
- Connective tissue disorders
- Immunocompromised states.

Ocular Examination

Visual acuity: Visual acuity may be reduced in cases where the ulcer is located in the center of the cornea or due to presence of corneal edema, massive hypopyon or associated endophthalmitis. The endothelium and associated anterior chamber inflammation (cell, flare, hypopyon, or fibrin) should not be overlooked.

Eyeball: Look for presence of any lagophthalmos, or proptosis/exophthalmos. Blepharophimosis can be there in presence of severe inflammation.

Lid: Look for trichiasis, coloboma, entropion, lid lag, ectropion and blepharitis that may be predisposing factors.

Lacrimal sac: Look for dacryocystitis (can be associated with pneumococcal corneal ulcers) and canaliculitis (associated with *Actinomyces* keratitis). Regurgitation, syringing, and probing must be done in all cases to rule out any potential source of infection.

Conjunctiva: The bulbar conjunctiva and the upper and lower tarsal conjunctiva should be examined for the presence of:

- Any follicles, papillae, for diseases like vernal catarrh and atopic conjunctivitis
- Discharge
- Erythema, cicatrization, keratinization, suggestive of poor ocular surface, severe dry eye and limbal stem cell deficiency
- **Membrane, pseudomembrane formation:** Membranous conjunctivitis is seen with keratitis caused by *Corynebacterium diphtheriae*. Gonococcal, pneumococcal and *Haemophilus*

keratoconjunctivitis may be associated with pseudomembrane formation.

- Foreign bodies can be a cause for non-healing corneal ulcer.

Discharge: Characteristic of discharge can provide a clue about the probable diagnosis such as:

- *Watery*—viral or small bacterial corneal ulcer
- *Mucoid*—bacterial corneal ulcer
- *Mucopurulent*—*Pseudomonas* and *Gonococcus*
- *Frankly purulent*—severe bacterial corneal ulcer
- Corneal ulcers caused by *Pseudomonas* are associated with a greenish-yellowish discharge. A membranous discharge is seen with keratitis caused by *Corynebacterium diphtheriae*.

CORNEA

Ulcer

Following parameters must be noted:

- **Location:** The location of ulcer gives an indication about the probable cause, visual prognosis and the initial choice of antibiotics. The location can be
 - *Central*: *Staphylococcus aureus* (**Fig. 1**), *Pseudomonas*, *Fusarium*
 - *Paracentral*: *Staphylococcus aureus*, *Pseudomonas*, *Fusarium*
 - *Peripheral*: Coagulase -ve *Staphylococcus aureus*, *M. tuberculosis*, Herpes simplex



Fig. 1: Central corneal ulcer

- *Superior*: Ulcer associated with Shield ulcer (VKC) or foreign body (FB) in sulcus subtarsalis [common in children]
- *Inferior*: Ulcers associated with exposure keratopathy.
- *Size*: Record the size of the ulcer along the two largest meridians. (Two axes where the extent is maximum that can be vertical and horizontal or two oblique axes). Micrometer present in slit-lamp can be used to record the size of the corneal ulcer. Recording the baseline size is important as it helps in grading as well as monitoring of therapy.
- The size of the epithelial defect and the size of the infiltration should be measured separately. They should be measured separately as their sizes may not be similar (in corneal abscesses corneal epithelium may be intact). The epithelial defects is best examined using a slit-lamp with cobalt blue light after staining the cornea with fluorescein dye.
- Infiltration may be single or multiple and may be of varying sizes depending on the organism involved, severity and duration of the infection. Look for satellite infiltrates in fungal corneal ulcers.
- *Shape*: Shape of the ulcer can give a clue about the probable cause. Examples include:
 - Dendritic, amoeboid or geographic shape—viral keratitis
 - *Ring shaped ulcer*: *Acanthamoeba* (**Fig. 2**), *Staphylococcus*
 - Oval—neurotrophic ulcer
- *Margins of ulcer*: Margin can be
 - *Well-defined*: Seen in healing infectious ulcer or sterile ulcer
 - *Punched out*: In cases of neurotrophic ulcer
 - *Indistinct*: Seen in cases of progressive ulcer
 - *Hyphae or featheriness*: Characteristic of fungal corneal ulcer
 - *Overhanging*: *Mooren's ulcer*
- *Base*: Usually the base of the ulcer is filled with necrotic slough. A dry looking ulcer suggests fungal corneal ulcer.
- *Depth*: Depth of the ulcer is best measured with the use of a slit-lamp. It helps in grading of the ulcer and deciding the initial treatment protocol. A deep-seated ulcer (>50%) or descemetocoele (**Fig. 3**) may warrant the initiation of systemic antibiotics.
- *Surrounding area*: Look for presence of satellite lesions (characteristic of fungal ulcer), corneal scars (ghost scars, in recurrent viral keratitis).
- *Pigmentation*: Pigment producing fungi such as *curvularia*, *alternaria* can give a distinct color to the ulcer due to pigment production (**Fig. 4**).
- *Vascularization*: Appearance of new vessels (**Fig. 5**) is a sign of healing keratitis. Superficial or deep corneal vascularization of varying extent may be seen in cases of infectious keratitis. A quadrant wise record of corneal vascularization should be made.

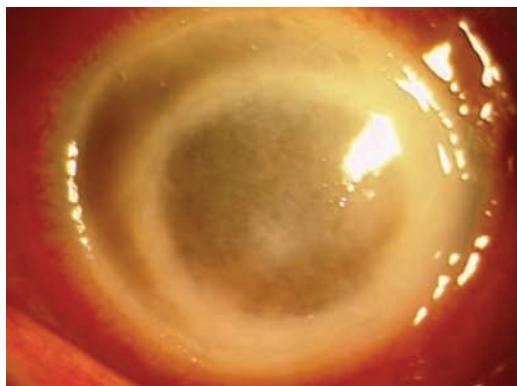


Fig. 2: Ring shaped ulcer in *Acanthamoeba*



Fig. 3: Descemetocoele

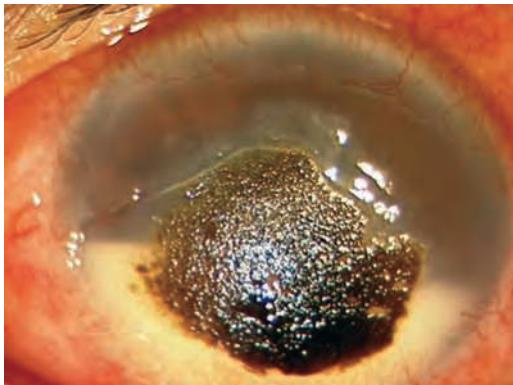


Fig. 4: Corneal ulcer with pigment production



Fig. 6: Perforated corneal ulcer

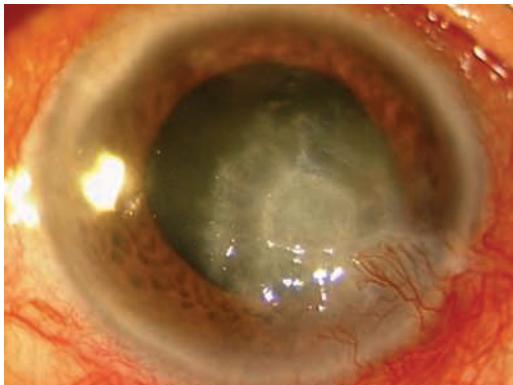


Fig. 5: Appearance of new vessels in a case of healing keratitis

surrounding cornea becomes hazy and grossly edematous appearing like a ground glass. Clearing of surrounding corneal edema after the initiation of medical therapy is an early sign of resolution of the ulcer.

Corneal Thinning/Perforation

The ulcer should be closely monitored for the development of corneal thinning, descemetocoele and perforation (**Fig. 6**). In the presence of shallow anterior chamber and low intraocular pressure, a *Seidel's* test should be performed in all cases. Severe corneal thinning and perforation warrant immediate surgical therapy (glue or tectonic patch graft).

Other Findings

Look for other findings that may give a clue about the possible cause for ulcer, such as foreign bodies, exposed or broken sutures, signs of corneal dystrophies, previous corneal inflammation (thinning, scarring, or neovascularization), and signs of previous corneal or refractive surgery.

Fluorescein or rose Bengal staining may provide additional information, such as the presence of dendrites, pseudodendrites, loose or exposed sutures, and epithelial defects.

Documentation

The documentation of the corneal ulcer may be done using color clinical photographs or using detailed schematic drawings.

Corneal Sensations

Corneal sensations should be measured with the help of a cotton wisp or esthesiometer (Cochet-Bonnet esthesiometer). In cases of herpetic keratitis, neuropathic keratitis and cases with diabetes mellitus, the corneal sensations are decreased.

Surrounding Cornea

The cornea surrounding the lesion may be, clear or hazy due to edema depending on the virulence of the organisms. *Candida* tends to cause localized lesions with distinct borders and minimal surrounding edema. Some organisms like *Pseudomonas* produce ulcers in which the

Color Photographs

In all cases of corneal ulcer a colored photograph of the diffuse as well as the slit section of the cornea should be taken. Measurements should be made of the maximum diameter of the ulcer and the meridian perpendicular to it. Apart from this infiltrate, size should also be measured in same manner.

Schematic Drawings

Following color-coding is used to depict a corneal ulcer:

Black—outline of the corneal limbus, indicates scars resulting from keratitis, degeneration and foreign bodies. *Blue*—designates edema, small dots for epithelial edema or circles for lakes of fluid within the stroma, and wavy lines to depict the folds in Descemet's membrane. *Brown* indicates melanin or iron pigmentation including pupil and iris. *Red*—is used to depict blood vessels and rose Bengal staining. Red wavy lines indicate subepithelial vessels, straight lines indicate deep stromal vessels and dotted lines indicate ghost vessels. The wavy lines of superficial vessels begin outside the limbus circle, whereas straight lines of stromal vessels begin at the margin of the circle. Solid shading depicts hemorrhage and red dots indicate area stained by rose Bengal. *Orange*—denotes inflammation and presence of white blood cells, which may be in the following forms—stromal infiltrate, hypopyon or keratic precipitates. *Green*—indicates fluorescein staining

of the cornea and dots represent punctate epithelial keratopathy, small lines depict filaments and shaded outline demonstrate epithelial defects. Green color is also used to depict the location of lens and vitreous opacities/hemorrhage, etc.

Clinical features of specific keratitis have been described in **Table 2**.

Sclera

One should look for scleral inflammation, ulceration, nodules or ischemia. Any involvement of the sclera should be recorded as this helps in prognosticating the case as well as in the management protocol. Scleral involvement warrants the use of systemic antimicrobial agents. Sclerokeratitis usually occurs in cases of immunologic disorders and *Acanthamoeba* keratitis.

Anterior Chamber

Mild flare to severe hypopyon (**Fig. 7**) formation maybe there. Size of hypopyon should be measured using slit-lamp micrometer. Hypopyon and its characteristics are helpful in establishing the etiological diagnosis (**Table 3**). In order to test the mobility of the hypopyon, following a slit-lamp examination, the patient is asked to lie supine for 10 minutes and a slit-lamp examination is then done. In case of the fixed hypopyon (**Fig. 8**), there is no change in position of hypopyon as demonstrated by the height of hypopyon. In case of the mobile hypopyon, there is actual movement

Table 2 Clinical features of specific keratitis

Disease specific	Clinical features
Bacterial keratitis	Well-defined infiltrate with moderate inflammation in anterior chamber
Fungal keratitis	Dry looking ulcer with feathery margins, satellite lesions, ring ulcer, endothelial plaque, pigmentation in dematiaceous keratitis
<i>Acanthamoeba</i> keratitis	Epithelial haze with pseudodendrites, radial perineuritis, ring ulcer
Microsporidiosis	Multifocal punctate raised epithelial lesions with clear underlying stroma
Viral keratitis	Dendrites, geographic ulcer, annular stromal edema with KPs
<i>Pseudomonas</i> keratitis	Rapidly sloughing ulcer, ring ulcer, with evident corneal edema in the uninvolved cornea, rapid melting with perforation of cornea
Microsporidiosis	Multifocal punctate raised epithelial lesions with clear underlying stroma
Atypical bacteria	Cracked wind shield corneal ulcer, minimal changes in surrounding cornea, minimal reaction in anterior chamber

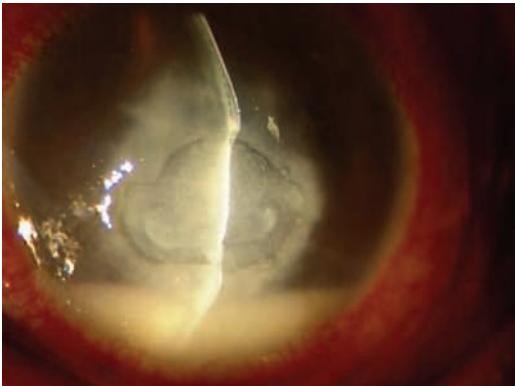


Fig. 7: Hypopyon

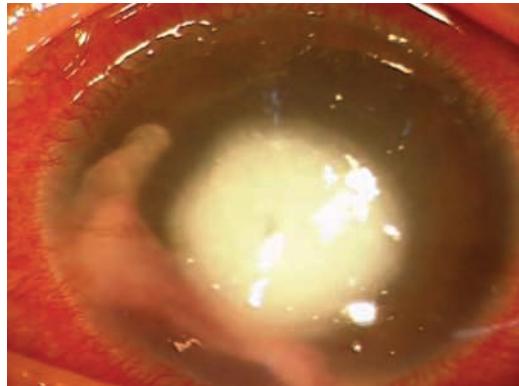


Fig. 8: Fixed hypopyon

Table 3 Characteristics of hypopyon	
<i>Characteristics</i>	<i>Probable diagnosis</i>
Central	Pneumococcal corneal ulcer
Hemorrhagic	Pneumococcal corneal ulcer, herpes simplex viral keratitis
Mobile	Bacterial corneal ulcer
Fixed/immobile	Fungal corneal ulcer
Sterile	Behçet's syndrome

and the upper level or height of the hypopyon decreases.

Iris

Variable degrees of uveal inflammation can occur with infectious keratitis. Synechiae formation maybe there. Presence of new vessels on iris (rubeosis iridis) can also be seen in cases of prolonged inflammation. If the ulcer perforates, uveal prolapse may occur and this may later form a corneoiridic scar.

Pupil

Any abnormality in the pupil size, its shape and location should be recorded. In presence of severe inflammation iris may be atonic.

Intraocular Pressure

Digital tonometry in the experienced hands is the most practical method of assessing intraocular

pressure (IOP) in cases of corneal ulcer. Secondary glaucoma may be present in some cases. Hypotony may be present in case of corneal perforation.

Lens

Cataract formation may be there or pigment deposit may be there.

Posterior Segment

Usually, it is not possible to view the vitreous and retina in case of corneal ulcer due to the presence of hazy cornea. However, if the ulcer is small and peripheral, slit-lamp biomicroscopy may be done to visualize the anterior one-third of the vitreous. Additionally, an indirect ophthalmoscopy may be performed to check for the involvement of the posterior segment.

Fellow Eye

One should also examine the fellow eye as bilateral involvement may be there (usually in immunological cases).

GRADING OF CORNEAL ULCER

Kindly refer to **Table 4**.

DIFFERENTIAL DIAGNOSIS

Based on history and clinical examination a provisional diagnosis can be made. The differentiating features are described in **Table 5**.

INVESTIGATIONS

Microbiological Diagnosis of Infectious Keratitis

Owing to the considerable overlap in the clinical appearances of corneal ulcers due to various microorganisms, a standard basic laboratory

methodology should encompass techniques that allow for the recognition of as large a number of offending organisms as possible.

Collection of samples: The samples should be collected at the initial presentation before the start of antimicrobial therapy. The treatment can be initiated based on the results of smear examination. Samples for diagnosis of corneal ulcer can be following:

- Eyelid swab—not of much use
- Conjunctival swab—not of much use
- Corneal scraping—most important
- Contact lens, contact lens case and solution—must in contact lens user
- Anterior chamber paracentesis (hypopyon)—deep ulceration or when insufficient material is present.

Corneal Scrapings

Instruments

Kimura's spatula is traditionally used to collect scrapings from a corneal ulcer though Bard-Parker blade number 15, 26 gauge needle,

Table 4 Grading of corneal ulcer

Feature	Mild	Moderate	Severe
Size of ulcer (mm)	<2	2–5	>5
Depth of ulcer (%)	<20	20–50	>50
Infiltrate			
• Density	• Dense	• Dense	• Dense
• Extent	• Superficial	• Extension up to mid stroma	• Deeper than mid stroma
Scleral involvement	Not involved	Not involved	May be involved

Table 5 Differential diagnosis of corneal ulcer

Parameters	Bacterial	Fungal	Viral	Acanthamoeba	Atypical bacteria
Risk factors	Blepharitis, dacryocystitis, trichiasis, contact lens use, ocular surface disorder	Trauma with vegetative matter, indiscriminate use of topical antibiotic or steroid	Past history of viral infection	Contact lens use, swimming	Prior corneal surgery
Symptoms	Severe symptoms, rapid progression	Indolent course, signs more than symptoms	Like bacterial, may be associated with recurrences	Waxing and waning course, severe pain	Indolent course, failure to respond to routine antibiotics
Sign	Epithelial defect, infiltration, mobile hypopyon, anterior chamber reaction, mucopurulent discharge	Feathery margins/hyphate edges, rough and dry texture, satellite lesions, gray/brown pigmentation, immune ring of wessely, collar button configuration, fixed hypopyon	Epithelial keratitis (punctate, dendritic, geographic, marginal, neurotrophic), stromal keratitis (immune ring of wessely, stromal neovascularization), endothelitis, uveitis, decreased corneal sensation, periocular lymphadenopathy	Pseudodendrites, radial keratoneuritis, ring shaped infiltrate	Cracked wind shield corneal ulcer, minimal changes in surrounding cornea, minimal reaction in anterior chamber

hypodermic needle, platinum spatula are also used. Cotton swabs are not recommended for collection of corneal material (may interfere with fungal filament interpretation).

Technique

Topical anesthesia drop (0.5% proparacaine) is applied. A lid speculum is applied gently to separate the lids. Any slough or mucus debris must be removed gently. Multiple scraping of the ulcer base and margins is done under topical anesthesia (0.5% proparacaine hydrochloride is proffered since it is the least bactericidal compared to other anesthetic agents like 4% lignocaine hydrochloride or tetracaine) with the aid of a slit-lamp or operating microscope. Streptococci pneumoniae is more readily found at edge of the ulcer whereas *Moraxella* is more likely to be present at the ulcer base hence both base and margin have to be scrapped. Several scrapings are collected and used in a sequence to prepare smears and inoculate culture media. The blade or spatula may be reused when a sterile medium has been streaked. However, a blade must be changed (spatula should be flamed) when a smear has been

made on a slide, which may not be sterile. More recently, calcium alginate swabs moistened with trypticase soy broth provides another method of collecting corneal specimens for yielding higher number of bacteria as well as fungi compared to platinum spatula. However, one limitation is calcium itself may act as an antibacterial agent. Scrapping has to be done with utmost care in cases of severe keratolysis, descemetocoele and deep stromal keratitis.

Inoculation

Solid agar media (**Table 6**) are inoculated on the surface making multiple "C" shaped marks without cutting the agar. In the liquid media, the spatula or blade is swirled to allow the sample to be transferred. In the case of thioglycollate broth and Sabouraud's dextrose agar (SDA) deep inoculation of the medium is ensured by transferring the sample to a swab tip and dropping the swab in the tube allowing it to settle at the bottom.

Routine Smears and Stains

Gram stain (most common), Kinyoun stain (Cold carbol Fuchsin) or Giemsa stain (**Table 7**)

Table 6 Common culture media for various organisms

Culture medium	Growth	Incubation temperature
Blood agar plate	Aerobic bacteria Facultative anaerobic bacteria Fungi	35°C
Chocolate agar plate	Aerobic bacteria Facultative anaerobic bacteria <i>Neisseria</i> <i>Haemophilus</i> <i>Moraxella</i>	35°C
Thioglycollate broth	Aerobic bacteria Anaerobic bacteria	35°C
Sabouraud's dextrose agar plate with antibiotic	Fungi <i>Nocardia</i>	Room temperature
Brain heart infusion broth plate with antibiotic	Fungi <i>Nocardia</i>	Room temperature
Cooked meat broth	Anaerobic bacteria	35°C
Thayer martin blood agar plate	<i>Neisseria</i>	35°C
Lowenstein-Jensen media	<i>Mycobacteria</i> species	35°C with 3–10% CO ₂
Middlebrook-Cohn agar	<i>Mycobacteria</i> species <i>Nocardia</i>	35°C with 3–10% CO ₂

Table 7 Different stains used for smear examination

Type of stain	Organism visualized	Color of the organism
Gram stain	Bacteria	Gram positive-purple Gram negative-pink
Acridine orange	Bacteria, Fungi, <i>Acanthamoeba</i>	Yellow-orange
Calcofluor white	Fungi	Bright green
	<i>Acanthamoeba</i> cysts	Bright green
	<i>Acanthamoeba</i> trophozoites	Reddish orange
Acid fast	Mycobacteria	Pink

are employed to study the corneal material which is spread as a thin layer on several clean glass slides within an area defined with a wax pencil on the reverse. In the preparation of wet mounts such as potassium hydroxide (KOH), lactophenol cotton blue or calcoflour white, the scrapings can be placed on the slide in a demarcated area and covered with a drop of the solution followed by a coverslip. Special stains and media may be included whenever usual procedures have yielded negative results.

Interpretation

Staining methods yield a rapid result and help to determine the initial choice of an antimicrobial agent. *KOH wet preparation*—a 10–20% solution of KOH is used to visualize fungal elements in corneal scrapes. Owing to the chitin in their cell wall, fungal filaments and cysts of *Acanthamoeba* are clearly delineated in a homogeneous background of corneal tissue digested by KOH. Its sensitivity ranges from 90% to 99%. Gram stain is utilized to identify bacteria, fungi as well as *Acanthamoeba*. It has been reported to yield an accuracy of 60–75% in identifying the responsible organisms. Calcofluor white (CFW) is a fluorescent brightener with great affinity for certain polysaccharides such as cellulose and chitin, thus providing the basis for demonstration of fungal cell walls as well as cysts of *Acanthamoeba* species. The preparation is viewed under fluorescence microscope. The cysts of *Acanthamoeba* and fungal filaments appear bright apple green in a corneal scraping stained with CFW. *Acanthamoeba* trophozoites and bacteria such as *Nocardia* and *Actinomyces* do not stain with CFW.

Cultures

Identification of bacteria may be accomplished within 48 hours along with its antibiotic susceptibility pattern. In some cases, the pathogen may be recognized in 12–15 hours. Standardized disk diffusion or dilution techniques should be utilized for antibiotic susceptibility testing of bacteria. The majority of fungi causing keratitis can be detected on SDA within 72 hours. *Aspergillus* and *Fusarium* species grow on blood agar, SDA and brain-heart infusion broth within 48 hours. However, appreciably characteristic colonies develop after 1–2 weeks. Hence, culture media should be observed for at least 2 weeks before they are considered negative. Non-nutrient agar (NNA) is the standard medium used with an overlay of *Escherichia coli* for the growth of *Acanthamoeba*. The specimen is simply touched to the surface of the plate without streaking or breaking the surface. Two plates may be inoculated for incubation at 25°C and 37°C since some species do not grow at the higher temperature and the plates are examined for trophozoites and cysts directly under the microscope (100 X). Trophozoites may be seen in 24–48 hours. They move and cover the entire plate surface on further incubation and turn into cysts. The plates should be observed for at least 7 days.

Special media, selective and non-selective, may be indicated in certain clinical situations. Lowenstein-Jensen medium is used when mycobacterial infection is suspected. *Nocardia* organisms can grow, though slowly, on blood agar as well as other bacterial media.

Remember: Aerobic cultures of the corneal specimens should be held for 7 days, anaerobic

cultures for 7–14 days and Mycobacterial and fungal cultures for 4–6 weeks before being reported as no growth.

Interpretation of Culture Results

Interpretation of the culture results should be made with regard to the clinical situation, the adequacy of the sample and the possibility of contamination by organisms present on the skin, eyelids and conjunctiva. Positive culture rates vary from 40% to 73%.

An isolate is more likely to be considered significant if it is consistent with the clinical signs plus:

- The same organism is grown on more than one media
- Confluent growth of a known ocular pathogen in one solid medium or
- Growth in one medium of an organism with positive smear results or growth of same organism in liquid media.

Jones Criteria for Positive Culture

- Clinical signs of infection plus isolation of bacteria (10 or more colonies) on one solid medium and one additional medium, or
- Isolation of organism (any detectable growth) on any two solid media or
- Isolation of organism in one medium in the presence of a positive smear.

When the culture results are negative, antibiotic treatment can be suspended for 24 hours and rescraping is done, following which repeat cultures are sent and examined.

Corneal Biopsy

Corneal biopsy is indicated if infectious keratitis is suspected clinically and twice repeated microscopic evaluation of smears and culture results are negative and no clinical improvement is noted on the initial broad-spectrum antibiotic therapy. In addition, in certain cases of deep mycotic keratitis and intrastromal abscesses a corneal biopsy is indicated.

A partial-thickness trephination employing a trephine of sufficient size, to guarantee adequate material for the laboratory, is required. Care is taken to avoid the visual axis as far as possible.

Biopsy from below a lamellar flap can be considered for a midstromal lesion such as infectious crystalline keratopathy, or a deep stromal lesion such as fungal keratitis.

Anterior Chamber Paracentesis

This procedure is rarely indicated in the diagnostic evaluation of a patient with a corneal ulcer. However, this procedure may be indicated in the instance where keratomycosis is strongly suspected clinically, yet corneal scrapings and biopsy have been negative, the damage to the cornea is progressive and a hypopyon is present or increasing.

Confocal Microscopy

In vivo confocal microscopy (IVCM) is a non-invasive *in vivo* diagnostic method for microbial keratitis. It has been successfully used to distinguish some unusual pathogens such as *Acanthamoeba* cysts or fungal hyphae. With new generation, IVCM can help in initiating anti-fungal therapy and in monitoring the response to therapy.

Newer Methods

The need for rapid diagnosis has led to modification of various conventional techniques and introduction of new techniques such as immunohistochemistry, fluorescent microscopy, enzyme immunoassays, radioimmunoassay, polymerase chain reaction (PCR) and molecular biology. Most ocular infections can now be diagnosed by these modern techniques within 1–6 hours.

Ultrasonography

It is done in cases of corneal haze for fundus evaluation. In cases of perforated corneal ulcer, endophthalmitis, choroidal and retinal detachment should be excluded.

MANAGEMENT

Management of Bacterial Keratitis

Bacterial keratitis should be treated as an ocular emergency due to its rapid progression and disastrous complications. Initially an empirical antibiotic therapy (combination therapy) is started

to cover for both Gram+ve and Gram-ve organisms. Standard therapy is a combination of:

- Fortified cefazoline 5% or 10% + tobramycin 1.3%
- Fluroquinolone (moxifloxacin 0.5% or gatifloxacin 0.3%) + tobramycin 1.3%.

Monotherapy can be considered in cases where the ulcer is in periphery and is small (<3 mm). For monotherapy, fluoroquinolones are preferred (ofloxacin 0.3%, ciprofloxacin 0.3%, gatifloxacin 0.3% or moxifloxacin 0.5%). Comparison of fluoroquinolones and fortified eye drops is given in **Table 8**.

The frequency of instillation of drops depends upon the severity, but it is usual to start half-hourly drops all through 24 hours for most patients. A loading dose of a drop every 5 minutes for the first 30 minutes is used in severe ulcers. The frequency is reduced based on the clinical response described below.

Favorable signs:

- Stabilization and no progression and improved symptoms
- Reduced activity at infiltrate margins/blunting of ulcer edges
- Resolution of infiltration
- Progressive healing of epithelial defect
- Reduction in adjacent stromal inflammatory reaction and anterior chamber reaction
- Reduction in hypopyon
- Vascularization.

Unfavorable signs: Signs that suggest poor response to therapy includes following:

- Deterioration in symptoms
- Increase in size and density of infiltration

Table 8 Comparison of fluoroquinolones and fortified eye drops

S. No	Fluoroquinolones	Fortified drops
1.	Cheaper	More expensive
2.	Readily available	Need to be prepared
3.	Stable	Preferable to refrigerate
4.	Shelf life of 1 month	Shelf life of 1 week
5.	Less toxic	More toxic
6.	Poor coverage of gram-positive organisms with older generations	Better coverage

- Increase in size of anterior chamber reaction
- Non-healing of epithelial defect
- Progressive stromal thinning

The clinical response should be the first guideline of therapy, although in non-healing ulcer, *in vitro* sensitivity should be given due attention. *In vitro* sensitivity should be correlated with *in vivo* response before considering change in therapy as inadequate frequency, poor penetration, stromal lysis, and necrotic debris covering the site of infection can be the causes of nonresponsiveness of ulcer to therapy.

The aminoglycoside antibiotics used in fortified drops are gentamycin and tobramycin. They give an excellent gram-negative coverage and are active against staphylococci and some streptococci but not against pneumococci. The most commonly used cephalosporin in fortified drops is cefazolin. It gives good coverage for non-penicillinase producing Gram -positive bacteria.

Adjunctive therapy is required to alleviate the symptoms that includes cycloplegic drugs, antiglaucoma drugs, tear supplements and topical corticosteroids. Management in specific bacterial keratitis has been described in **Table 9**.

Indication of systemic antibiotic in bacterial keratitis includes following:

- Perforated/impending perforation in corneal ulcer
- Postperforating injury
- Scleral involvement
- Endophthalmitis
- Highly virulent organisms—*Neisseria, Hemophilus*

The steroid for corneal ulcer trial (SCUT) found no significant difference in 3 month BCVA between patients receiving topical corticosteroid or placebo as adjunctive therapy in the treatment of bacterial corneal ulcers. No apparent increased risk of corneal perforation was observed with the use of corticosteroids.

Management of Fungal Keratitis

The major group of anti-fungal agents available includes the following:

- *Polyenes*: Natamycin, nystatin, amphotericin B
- *Azoles*: Fluconazole, itraconazole, voriconazole, posaconazole, ravuconazole
- *Fluorinated pyrimidines*: Flucytosine
- *Echinocandins*: Caspofungin, micafungin

Table 9 Management of specific bacterial keratitis

<i>Organism</i>	<i>Topical</i>	<i>Systemic</i>
Methicillin resistant <i>Staphylococcus</i>	Vancomycin 50 mg/mL	Vancomycin 2 g/day
Severe <i>Pseudomonas</i> keratitis	Ceftazidime (50 mg/mL)	Ceftazidime (1–2 g/day I/V or I/M)
<i>Mycobacterium fortuitum</i> —cheloneae	Amikacin 40–100 mg/mL	Clarithromycin 500 mg BD
<i>Nocardia</i>	Amikacin 40–100 mg/mL or Trimethoprim (16 mg/mL) sulfamethoxazole (80 mg/mL) injectable	Trimethoprim/sulfamethoxazole (10–20 mg/kg/day) I/V

Table 10 Sensitivity of different anti-fungals (MIC values of different genera in microgram/mL)

<i>Fungus</i>	<i>Voriconazole</i>	<i>AMB</i>	<i>Fluconazole</i>	<i>Natamycin</i>
<i>Candida</i>	0.08–0.016	0.25–0.5	0.12–0.5	3.12–12.5
<i>Aspergillus</i>	0.25–0.5	1–2	>256	3.12–25
<i>Fusarium</i>	1–4	1–2	>256	1.56–6.25

Abbreviations: AMB, amphotericin B; MIC, minimum inhibitory concentration

The standard treatment followed includes the following step wise approach:

- *Topical antifungals*: 5% natamycin (drug of choice) is given hourly at daytime, 2 hourly at bed time
- Taper after 4–7 days interval depending upon clinical response.
- Surface debridement helps to remove slough and reduce load of infection. Benefits are controversial but still preferred by most clinicians.
- If worsening (after 14 days of treatment)—add 0.15% amphotericin B drops or 1% voriconazole. Also review the culture report.
- Therapy duration is 3–4 weeks. Complete resolution often require 4–8 weeks.

Unlike antibacterials, the antifungals suffers from the limitations of poor ocular penetration, poor bioavailability, epithelial toxicity and poor commercial availability. The sensitivity of currently available antifungals are summarized in **Table 10**. The indications of systemic antifungals in fungal keratitis are following:

- Perforated/impending perforation corneal ulcer
- Severe deep ulcer (involving >2/3 stromal depth)

- Large ulcer (>6 mm diameter)
- Post-penetrating keratoplasty
- Scleral involvement
- Endophthalmitis.

Commonly used systemic antifungals include ketoconazole (200 mg bd), fluconazole (200 mg bd), itraconazole (100 mg bd) and voriconazole (200 mg bd). The systemic antifungals can cause a number of adverse reactions, hence monitoring of blood glucose, blood pressure and liver function test has to done regularly.

Targeted Drug Delivery

About 20% of fungal ulcers are refractory to medical therapy. In such cases targeted drug delivery (providing the drug where it is needed the most) is a useful alternative before proceeding for surgery. The different modalities are intracameral, intracorneal or intrastromal drug delivery. The different agents used are amphotericin B (5–7.5 µg/0.1 mL/5% dextrose) and voriconazole 50–100 µg/0.1 mL.

Management of Viral Keratitis

The different antivirals available includes acyclovir 3% ointment, vidarabine 3% ointment,

Table 11 Treatment protocol for viral keratitis

Type of keratitis	Topical acyclovir 3%	Topical corticosteroids	Comments
Epithelial keratitis	5 times for 1 week 3 times for 2–3 weeks	Contraindicated	
Epithelial + stromal	5 times for 1 week 3 times for 2–3 weeks	After 1 week Pred acetate 2–4 hourly	Taper both by 6–8 weeks
Necrotizing and non-necrotizing stromal HSK	5 times for 1 week 3 times for 2–3 weeks	Pred acetate 2–4 hourly	Systemic ACV 400 mg 5 times one week 3 times for 1 week

trifluorothymidine 1% and idoxuridine 1%. The dose and duration of antivirals (acyclovir) has been described in **Table 11**. Remember if a true ulceration persists after 14 days of treatment, one must distinguish between a neurotrophic ulcer and persistent infectious epithelial keratitis. A neurotrophic ulcer has smooth borders and lacks the scalloped edges of infectious epithelial keratitis. If the lesion is persistent infectious epithelial keratitis, resistance to the antiviral medication must be considered, and an alternative medication can be initiated. The readers are advised to refer to a standard textbook for treatment of viral keratitis in detail.

Surgical Management

Surgical treatment is indicated in cases of impending perforation, perforated corneal ulcer and nonhealing corneal ulcer (to reduce microbial load). The decision to surgically intervene in a case of active infectious keratitis should be made after proper evaluation of the clinical progress. Surgery helps to eliminate or reduce the microbial load and in providing tectonic support to the globe where the integrity is threatened as in cases of thinning or perforation of the cornea. The different surgical options and various modalities of treatment available in such cases are:

- Removal of epithelium and anterior lamellar keratectomy
- Conjunctival flaps (Gunderson's flap)
- Patch graft
- Tissue adhesives with bandage contact lens (BCL), therapeutic penetrating keratoplasty
- Deep anterior lamellar keratoplasty
- Collagen crosslinking.

Epithelial Removal and Anterior Lamellar Keratectomy

This is useful in cases of fungal keratitis. Regular debridement of the base of the ulcer helps in elimination of organisms and necrotic material. This procedure facilitates penetration of anti-fungal drugs. This can be done under topical anesthesia leaving a margin of 1–2 mm at the limbus with a number 15 Bard-Parker blade. Anterior lamellar keratectomy helps in removal of the thick mat of fungal filaments on the cornea and facilitates increased drug penetration in cases of dematiaceous fungal filaments. Anterior stromal corneal infiltrates can also be ablated with phototherapeutic keratectomy.

Conjunctival Flaps

Conjunctival flaps help in achieving a stable epithelial surface in cases of persistent or recurrent epithelial defects and progressive ulceration especially in viral keratitis. In advanced cases of corneal ulcer, where the only aim is to save the globe, a Gunderson's flap is done where the entire surface is covered with a conjunctival flap.

Tissue Adhesives

Tissue adhesive (cyanoacrylates) helps in supporting corneal thinning and sealing corneal perforation up to 2 mm. In addition, cyanoacrylate adhesive is bacteriostatic for Gram-positive bacteria. Necrotic stroma or epithelium and other debris must be removed from the base of the ulcer before the adhesive is applied. A BCL is fitted after the application. The adhesive is left in place until

it loosens spontaneously, or the bed becomes vascularized or keratoplasty is performed.

Patch graft: The different types of patch graft that can be done includes following:

- *Tenon's patch graft:* For peripheral ulcers, inexpensive, seals the defect by the fibroblastic response of the tenon's tissue.
- *Multilayered amniotic membrane graft (AMG):* In cases of severe thinning or small perforations.
- *Tectonic patch graft:* A small patch of corneal graft, in perforations 3–5 mm in size.

Therapeutic penetrating keratoplasty: A full thickness graft is performed in perforations ≥ 5 mm. The results of keratoplasty in acutely infected or inflamed eyes are relatively poor, the risk of rejection and glaucoma is greater especially in larger grafts. In all these cases at least 0.5 mm of clear tissue all around the infected area is to be excised to decrease the incidence of recurrence. Postoperative antimicrobial treatment is to be continued. In fungal keratitis, postoperative topical steroids are to be used with caution. Ideally, steroids should be avoided until the culture report (suggesting free margins) is available or at least for 10–14 days. Surgery when performed with 8 mm or smaller diameter donor grafts have better results than larger grafts. Hence, penetrating keratoplasty is to be considered early when fungal ulcers do not respond to antifungal medication. The results of penetrating keratoplasty for *Acanthamoeba* keratitis are poor and surgery is to be considered only in patients with gross corneal thinning or perforation.

Collagen crosslinking (CXL): CXL has direct bactericidal activity (by oxidative damage) to the pathogens and also cross linked corneas become more resistant to degrading enzymes of organisms. Several studies have shown its effectiveness in refractory keratitis.

VIVA QUESTIONS

Q.1. What is the role of hypopyon in etiological diagnosis of corneal ulcer?

Ans. Already discussed in the text.

Q.2. What are the signs of healing and non-healing corneal ulcer?

Ans. Already discussed in the text.

Q.3. What is the interpretation of culture results and describe Jones criteria?

Ans. Already discussed in the text.

Q.4. What are the indications of corneal biopsy in the corneal ulcer?

Ans. • If infectious keratitis is suspected clinically and twice repeated microscopic evaluation of smears and culture results are negative.
• No clinical improvement is noted on the initial broad-spectrum antibiotic therapy.
• Certain cases of deep mycotic keratitis and intrastromal abscesses.

Q.5. What is the grading of corneal ulcer?

Ans. Already discussed in the text.

Q.6. What does the HEDS recommends about viral keratitis?

Ans. • In HSV stromal keratitis—topical anti-virals + steroids are less likely to fail treatment.
• No beneficial effect of systemic acyclovir is there in HSV stromal keratitis
• Oral acyclovir is beneficial in prevention of stromal keratitis/iritis in epithelial HSV keratitis
• Oral acyclovir is beneficial in preventing the blinding sequelae of HSV iridocyclitis
• Prophylaxis is beneficial in recurrent ocular HSV or stromal HSV (400 mg bd)
[Note: Also refer to **Table 12**]

Q.7. What are the indications of systemic therapy in case of corneal ulcer?

Ans. Already discussed in the text.

Q.8. What are the indications of surgical intervention in case of corneal ulcer?

Ans. Already discussed in the text.

Q.9. Different stains used in keratitis.

Ans. • A modification of Gomori methenamine silver stain may be helpful for the identification of fungal elements and

Table 12 Herpetic eye disease (HEDS)

<i>Study group</i>	<i>Intervention</i>	<i>Recommendation</i>
HEDS-1		
Stromal keratitis not on steroids; on trifluridine TFT	Topical prednisolone phosphate	Faster resolution and fewer treatment failures
Stromal keratitis on steroids and TFT	Oral acyclovir 400 mg 5 times a day	No added benefit
HSV iridocyclitis on steroids	Oral acyclovir 400 mg 5 times a day	Fewer patients recruited but potential benefits noted
HEDS-2		
HSV epithelial keratitis trial	Oral acyclovir 400 mg 5 times a day for 3 weeks	No benefit in preventing subsequent stromal keratitis/iridocyclitis
Acyclovir prevention trial	Oral acyclovir 400 mg bd	Reduced the risk of any form of ocular herpes by 41% and stromal keratitis by 50%
Ocular HSV recurrence study	Studied the association between psychological and other forms of stress with HSV recurrence	No association noted

Abbreviation: TFT, trifluridine

Acanthamoeba cysts in corneal scrapings. Fungi and *Acanthamoeba* cysts stain black on a light green background.

- The periodic acid-schiff (PAS) stain may also be used to visualize fungal elements as well as *Acanthamoeba* especially in tissue sections.
- Lactophenol cotton blue stain, which is generally used for the microscopic examination of fungal cultures, has been effectively used for the demonstration of fungal elements and *Acanthamoeba* cysts in corneal scrapings.
- Ziehl-Neelsen stain or its modification (Kinyoun's stain) is indicated for the detection of *Mycobacteria* and *Nocardia* species, respectively.

Q.10. Prophylaxis for postpenetrating keroplasty herpetic keratitis.

Ans. Oral acyclovir 400 mg bd for 1 year is prescribed.

Q.11. Antimicrobials for *acanthamoeba* keratitis.

- Ans.**
- Biguanide*: PHMB 0.02% or chlorhexidine 0.02%
 - Diamidine*: Propamidine 0.1% or hexamidine 0.1%
 - Others*: Miconazole and clotrimazole 1–2% suspension
 - Usually a combination of buguanide and diamidine is used and the treatment has to be continued for at least 6 months.

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KERATOCONUS

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INTRODUCTION

Keratoconus is a disorder characterized by progressive corneal steepening (usually asymmetrical noninflammatory), most typically inferior to the center of the cornea, with eventual corneal thinning, induced myopia, and irregular astigmatism. It is the most common corneal ectatic disorder seen in clinical practice. In postgraduate exam, it can be given as a long case.

HISTORY

Epidemiology/Demography

Prevalence of keratoconus is about 54.5 cases per 100000.¹⁻³ Keratoconus occurs in people of all races. There is no significant gender predilection. Keratoconus usually occurs bilaterally. Unilateral cases can occur but are rare (in the range of 2-4%).¹⁻³ The age at onset is usually around the age of puberty. It is more prevalent in the Asian countries than in the West. Asian patients present at a younger age compared to the western world.

Chief Complaints

A case of keratoconus can present with following:

- Progressive visual blurring and/or distortion due to associated irregular astigmatism. It may be associated with photophobia, glare, monocular diplopia, and ocular irritation.
- Frequent change of glasses—the irregular astigmatism is often difficult to correct with glasses hence the patient keeps on visiting different optometrists.
- Rarely a case may present with symptoms of associated diseases such as recurrent attacks of itching, eye rubbing (vernal keratoconjunctivitis) and keratoconus is discovered during examination.
- Often manifests during the late teens or early twenties, then progresses slowly for the next decade or two as the cornea scars and becomes more elongated.

History of Present Illness

The onset and progression of the disease is characteristic. The onset is usually at puberty. The disease has a rapid progression stage until the age of 30 years. The rate of progression plateaus after this. After the age of 40 years the disease progression usually stops. The onset in Indian eyes may occur earlier especially in cases with associated vernal keratoconjunctivitis (VKC). It is important to know whether the keratoconus is progressive or not. In case of progression, the patient can be advised to undergo corneal collagen crosslinking (CXL). The best way to document progression is serial topography taking into consideration the change in keratometry. However, progressive deterioration of BCVA, progressive decrease in corneal thickness and a previously CL tolerant patient becoming CL intolerant are certain other clinical clues of keratoconus progression.

Past History

Following past history must be recorded carefully.

Contact Lens Wear

If the contact lenses have not been fitted properly, the constant pressure or continual injury can lead to scarring, its role in keratoconus progression is controversial. In addition, a better best-corrected visual acuity (BCVA) with CL indicates good prognosis after keratoplasty.

Eye Rubbing

Mechanical epithelial trauma leads to release of cytokines that have a role in corneal weakening and ectasia. In addition, rubbing can cause mechanical trauma to the keratocytes and increased hydrostatic pressure in the eye. Chronic eye rubbing can lead to orbital fat atrophy that often gives a clue about the cause of keratoconus in cases where a clear cut history of eye rubbing is not there.

Topography

The patient might have been already a case of diagnosed keratoconus and the patient might have undergone corneal topography several times. In that case a serial recording of the keratometry, central corneal thickness (CCT), and thinnest pachymetry must be done. Remember an increase in keratometry by 1 D over a period of one year suggests progression and such cases require CXL (few clinicians consider an increase of 0.5D per 6 months).

Ocular Surgery

Keratoconus can occur secondary to ocular surgeries such as LASIK and radial keratotomy (RK). Hence, any past refractive surgery must be enquired. In few cases, a previous history of CXL maybe there.

Past Medical History

Keratoconus can be associated with certain ocular and systemic disorders. A careful history must be taken to rule out these disorders.

Ocular associations:

- Floppy eyelid syndrome
- Leber's congenital hereditary optic neuropathy
- Cone-rod dystrophy
- Corneal granular dystrophy
- VKC
- Refractive surgery
- Trauma.

Systemic associations:

- Down syndrome
- Atopy-bronchial asthma, angioneurotic edema, Marfan syndrome
- Mitral valve prolapse
- Rosacea.

Family History

A three-generation pedigree chart must be prepared. An autosomal dominant mode of inheritance with variable expression has been suggested for keratoconus. Between 6 and 18% of patients with keratoconus have a positive family history.¹⁻³

EXAMINATION

Visual Acuity

Uncorrected visual acuity and BCVA must be assessed in all cases. Refraction must be attempted in all such cases:

- Scissoring of the red reflex on retinoscopy is one of the earliest sign of keratoconus.
- In presence of irregular astigmatism, visual acuity with rigid gas permeable (RGP) lenses may provide the BCVA. This is important before surgical planning to know the visual potential.

Facial Appearance/Orbit

Look for sign of orbital fat atrophy/oculo-digital sign suggestive of chronic eye rubbing.

Eyelid

Look for signs of allergic conjunctivitis. In advanced keratoconus *Munson's sign*, a V-shape deformation of the lower eyelid when the eye is in downward position, can be elicited.

Conjunctiva

Look for presence of papillae in tarsal conjunctiva. In India, keratoconus is often associated with VKC or allergic conjunctivitis. Signs of VKC include papillae, trantas dots (gelatinous thickening of limbus), limbal nodule, pigmentation andropy discharge.

Cornea

The slit-lamp examination reveals following signs.¹⁻³

- *Corneal thinning*: The thinnest part of the cornea is usually located outside the visual axis, and corneal thinning is a common sign preceding ectasia. Thinning is most commonly seen inferiorly (**Fig. 1**) or inferotemporally.
- *Corneal ectasia*: An eccentrically located ectatic protrusion of the cornea is noted in keratoconus. The apex is usually inferior to a horizontal line through the pupillary axis (**Fig. 1**). Corneal thinning from one-half to

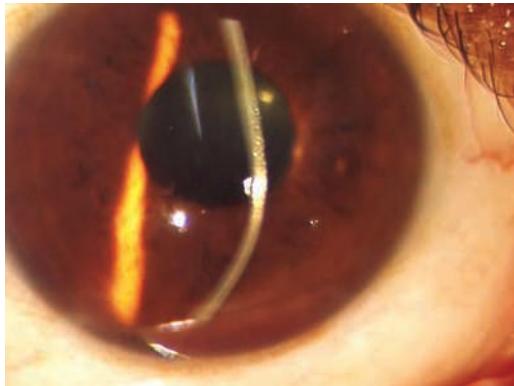


Fig. 1: Ectatic protrusion of the cornea with thinning

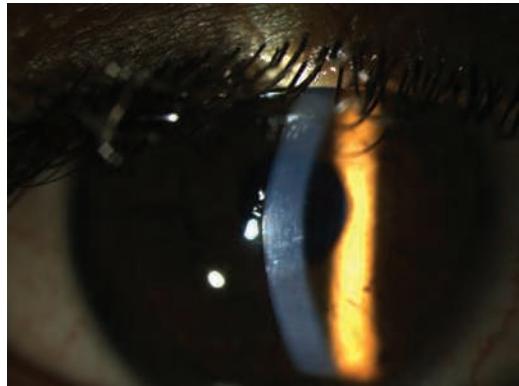


Fig. 3: Vogt's striae

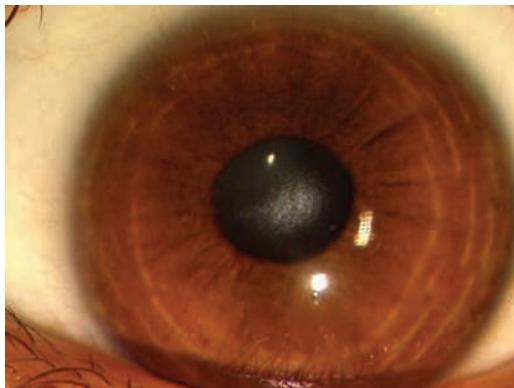


Fig. 2: Corneal scar

one-fifth of normal thickness is observed in the apex of the protrusion. Three types of cones can be seen in advanced keratoconus. The round or nipple-shaped cone is more common. It is of smaller diameter. The center lies mostly inferonasally. These corneas are more easily fit with contact lenses. The oval or sagging cone is larger and lies predominantly inferotemporally. This cone is more often associated with hydrops, scarring, and contact lens fitting problems. When the ectasia involves >75% of the cornea it is termed as a globus type of cone.

- Corneal scarring (**Fig. 2**)
- Fleischer ring—in moderate and advance cases of keratoconus, a Fleischer's ring is a partial or complete annular line commonly seen at the base of the cone. This line is nothing but a

hemosiderin (Iron deposits) arc or circle line seen around the cone base. The ring is formed from hemosiderin pigment deposited deep in the epithelium from the tear film onto the cornea as a result of severe corneal curvature changes induced by the disease and/or due to modification of the normal epithelial slide process. This ring is brown in color and best appreciated with the cobalt blue filter using a broad, oblique beam.¹

- *Vogt's striae:* These are fine vertical lines produced by compression of Descemet's membrane (**Fig. 3**), which tend to disappear when physical pressure is applied on the cornea digitally or by gas permeable contact lens wear. The lines are seen in the deep stroma and Descemet's membrane and are parallel to the axis of the cone.
- *Prominent corneal nerves:* The increased visibility of corneal nerves results from the outward bowing and thinning of the ectatic cornea.
- Superficial and deep corneal opacities.
- *Increased intensity of the corneal endothelial reflex:* An endothelial reflex may appear at the peak of the cone due to the increased concavity of the posterior corneal surface. An annular dark shadow separates the bright reflex of the cone from the reflex of the corneal periphery. This shadow results from total internal light reflection induced by the corneal ectasia. It is best demonstrated using the direct ophthalmoscope in a dilated pupil.

- *Sub-epithelial fibrillary lines:* Bron et al. has described, white subepithelial fibrillary lines in concentric bundles lying just inside the Fleischer's ring.¹ These are best seen under high magnification with a broad, oblique slit beam. The pattern is characteristic of keratoconus and occurs in approximately one-third of patients with this disease.¹
- Corneal hyperesthesia can be detected early in the course of the disease. Later the cone becomes relatively less sensitive.
- *Rizzuti phenomena:* This is demonstrated by a penlight shining on the temporal side of cornea or parallel to the iris plane. Normally, the light rays illuminate the nasal limbal area. In mild keratoconus, the ectatic cornea focuses the light sharply inside the nasal limbus. In more advanced states, the light is focused at the nasal limbus and beyond. It is important to remember that this response can also be elicited in patients with refractive errors.
- Breaks in Descemet's membrane have been described in severe keratoconus, causing acute stromal edema, known as hydrops (**Fig. 4**), sudden vision loss and significant pain.

Fundus Examination

Fundus evaluation after mydriasis is essential for any concomitant fundus abnormality.

Charleux Sign

With a dilated pupil and a lens + 6 D positioned in front of the eye one can appreciate a dark reflex in the area of the cone with a central bright



Fig. 4: Corneal hydrops

reflex resembling a drop of honey or oil (sign of "Charleux"), in the reflection of the red reflex from a direct ophthalmoscope. This is one of the earliest sign of keratoconus.

DIFFERENTIAL DIAGNOSIS

Kindly see **Table 1**.

CLASSIFICATION

Keratoconus is classified based on morphology, disease evolution, ocular signs and index-based systems.

Morphology

Classically, keratoconus has been classified into:

- *Nipple:* The cone has a diameter ≤ 5 mm, round morphology and is located in the central or paracentral cornea, more commonly in the inferonasal corneal quadrant. Correction with contact lenses is normally relatively easy.
- *Oval:* The cone has a diameter >5 mm and a paracentral to peripheral location, more commonly in the inferotemporal corneal quadrant. Contact lens correction is more difficult.
- *Globus:* The cone is located throughout 75% of the cornea. Contact lens correction is a difficult challenge, except in very limited cases.

Disease Progression

Amsler proposed the first keratoconus classification based on the disease evolution.^{2,3} The details of classification is given in **Table 2**.

Curvature

Keratoconus is classified into following:

- *Mild:* <45 D
- *Moderate:* 45–52 D
- *Advanced:* >52 D
- *Severe:* >62 D.

INVESTIGATIONS

Keratometry

Keratometry mires in keratoconus are commonly steep, highly astigmatic, irregular, and often appear egg-shaped (rather than circular or oval).

Table 1 Differential diagnosis of keratoconus

Characteristics	Keratoconus	PMD	Keratoglobus	TMD
Frequency	Most common	Less common	Rare	Rare
Laterality	Usually bilateral	Bilateral	Bilateral	Bilateral
Age at onset	Puberty	20–40 years	Usually at birth	Middle-aged to elderly
Thinning	Inferior paracentral	Inferior band 1–2 mm wide	Maximum in periphery	Superior cornea
CCT	Reduced	Usually normal	May be normal	Usually normal
Protrusion	<i>Thinnest at apex</i>	<i>Superior to band of thinning</i>	Generalized	Superior cornea
Rizutti's phenomenon and Munson's sign	Present	Absent	Present	Absent
Fleischer ring	Present	Sometimes	None	Absent
Scarring	Common	Only after hydrops	Mild	Superior cornea with vascularization, lipid deposition and inflammation
Vogt's striae	Common	Sometimes	Sometimes	Absent

Abbreviations: CCT, central corneal thickness; PMD, pellucid marginal degeneration; TMD, Terrien's marginal degeneration

Table 2 Amsler-Krumeich classification of keratoconus

Stage	Description
1.	Eccentric corneal bulging Myopia and/or astigmatism <5D Corneal radius ≤48D Vogt's striae No central opacity
2.	Myopia and/or astigmatism >5 D but <8 D Corneal radius ≤53 D No central opacity Pachymetry ≥400 μ
3.	Myopia and/or astigmatism >8 D but <10 D Corneal radius >53 D No central corneal opacity Pachymetry 200–400 μ
4.	Refraction not possible Corneal steepening >55.00 D Corneal scarring Pachymetry <200 μ

Inability to superimpose the central keratometric rings suggests irregular corneal astigmatism, a hallmark of keratoconus. In early cases,

keratometry may be normal. Some patients with keratoconus do not exhibit these signs. The disadvantages of keratometry in keratoconus is, it provides information about central 3 mm of cornea only, it is not useful in irregular astigmatism. Few clinicians perform central keratometry, followed by keratometry with the patient in upward gaze, to identify the steepening in the inferior cornea but it is often difficult and inconclusive.

Videokeratography (VKG)

This is based on the Placido disk principle. It provides qualitative contour information. In early cases, there will be an isolated area of smaller ring spacing and distortion. As the keratoconus worsens, the cornea becomes steeper; the ring spacing decreases overall and becomes increasingly irregular. Its disadvantage is it does not give accurate information about posterior curvature (cannot detect early keratoconus) and corneal thickness.

Orbscan

It uses the principle of scanning slit combined with a Placido system. It provides reliable data

on anterior and posterior elevation and best-fit sphere and a corneal pachymetry map. However, the posterior curvature maps are based on assumptions and may not be 100% accurate. In addition, it requires patient fixation for accuracy of data that is difficult at times and data of central cornea (near point of fixation) is not accurate.

Pentacam

This device uses a rotating Scheimpflug camera. It provides reliable measurement of anterior and posterior corneal elevation and accurate measurement of corneal thickness. Pentacam differs fundamentally from the Orbscan by the way in which it takes image slices of the cornea. The Orbscan takes vertical image slices that are separated from one another and have no common point. Thus, the Orbscan cannot re-register for any eye movement that occurs while it is capturing the images. The Pentacam maintains the central point (the thinnest point) of each meridian. Thus, during the examination, the software can re-register these central points and eliminate the eye movement. This single feature makes the Pentacam's measurements 10 times more accurate. Thus, it is largely independent of patient fixation with better repeatability than orbscan. In addition, the central corneal curvature can be measured more accurately compared to orbscan.

Pachymetry

Both ultrasonic and optical based devices (ASOCT) can be used to measure the pachymetry. Measurement of corneal thickness is useful for diagnosis, documenting progression, and planning treatment (see treatment section).

Ocular Response Analyzer

The ocular response analyzer allows keratoconus diagnosis and classification by assessing corneal hysteresis and resistance.

MANAGEMENT

The treatment of keratoconus varies depending on the disease severity. Early cases are managed with spectacles, mild to moderate cases are managed with contact lenses, and severe cases can be

treated with keratoplasty. Other surgical treatment options include intracorneal rings segments, corneal cross-linking, intra-ocular lens implants or a combination of these.⁴⁻⁶

Nonsurgical Management

- *Spectacles:* Spectacles are normally used in early cases of keratoconus only. As the disease progresses, irregular astigmatism develops and adequate visual acuity cannot be achieved with this type of visual correction.
- *Contact lens:* Different contact lenses used for treatment of keratoconus are soft toric lenses, standard bicurved hard lenses, custom-back toric lenses, piggyback systems, hybrid lenses (made of combined hard lens with a soft skirt), scleral lenses, and mini-scleral lenses.
 - *Rigid gas permeable lenses:* Rigid gas permeable (RGP) corneal lenses are the lenses of first choice for correcting the irregular astigmatism. The aim is to provide the best vision possible with the maximum comfort so that the lenses can be worn for a long period. The different fitting strategies of gas permeable contact lenses are as follows:
 - ♦ *Apical clearance:* In apical clearance fitting there is no bearing or touch in the apical area and the lens bearing is in the periphery. Advantages are reduced risk of scarring, whorl keratopathy and erosions; the limitation is that tightening at the periphery can hamper tear exchange and the edge of the lens can come into the visual axis, especially in cases with advanced ectasia. This strategy is very rarely used now-a-days.
 - ♦ Apical touch fitting technique is characterized by providing primary lens support on the apex of the cornea, in which the central optic zone of the lens actually touches or "bears on" the central cornea. The advantage is better quality of vision but the problem is there can be heavy bearing on the cornea resulting in corneal scarring and intolerance over long-term use.

- ♦ The three-point touch fitting technique is the most popular technique. In three-point touch fitting the lens bearing is shared between the apex and the midperipheral cornea that minimizes the risk of apical scarring. These lenses provide good vision, better comfort and prolonged wearing time and are hence the most preferred type of lenses.
- *Piggyback systems:* Consisting of the fitting a rigid gas permeable on top of a soft contact lens. The soft contact lens is used to improve wearing comfort and provide a more regular area for the gas permeable contact lenses to sit, whereas the gas permeable contact lens is primarily used for providing adequate visual acuity.
- *Hybrid contact lenses (such as soft perm, solotica and synergeyes):* Hybrid CL contain a RGP center with a soft skirt. New-generation hybrid CL provides higher oxygen permeability and greater strength of the RGP/hydrogel junction. These lenses are fitted with no or minimal apical touch in the central cornea. The lenses can be fitted on cones of any severity but the problem with these lenses is they can cause hypoxia-related changes such as vascularization and central corneal clouding. However, these lenses have not been widely accepted as the current designs, because they are generally more expensive than gas permeable lenses, do not normally provide improved visual correction and wearing comfort in comparison with gas permeable contact lenses.
- Rose K Lenses (Rose K, Rose K2 XL and Rose K2 IC) are multicurve lenses with a small optical zone that snugly fits over the cone. The Rose-K CL provides greater comfort, better quality of vision and requires less chair time in cases with keratoconus. The Rose K2 IC is a large diameter, intralimbal lens that can be used for large or oval cones.
- *Scleral lenses:* These lenses rest on the sclera and do not touch the cornea and limbus, leaving a clear area between the CL and the cornea. The advantages are good centration, stability and improved VA. The PROSE is a non-fenestrated scleral CL that is filled with fluid before insertion in the eye. Treatment has a high success rate when measured by the ability to achieve satisfactory fit and impact on VA. PROSE treatment can be an alternative to PKP for patients with corneal ectasia who are CL intolerant. The BOSP is a fluid-filled scleral CL. These lenses rest on the sclera and do not touch the cornea. There is a constant pool of tears over the cornea, which acts as a liquid corneal bandage and avoids any friction between the posterior surface of the CL and the corneal apex. In addition, these lenses mask corneal surface astigmatism and improve best-corrected VA. Thus these lenses are extremely useful in patients with advanced ectasia where the patients are intolerant to CL, or immediate surgery is not possible, or when the patient refuses surgery. The limitation of the use of scleral lenses is high cost, reduced tear exchange and difficult insertion-removal, which require considerable practice. Overall, studies have shown a good outcomes with these lenses.^{2,3}

Surgical Management

Current surgical options include:

- *Corneal transplantation:* Penetrating keratoplasty, deep anterior lamellar keratoplasty.
- *Intra-corneal ring segment insert:* Intacs, Ferrara rings.
- UVA/riboflavin corneal cross linkage (C3R).
- Thermokeratoplasty.
- *Lenticular refractive surgery:* Refractive lens exchange with toric intraocular lenses, toric phakic intraocular lenses.

Penetrating keratoplasty (PKP): PKP in keratoconus in comparison to other indications is considered low risk in terms of graft rejection, graft survival and postoperative complications. The success rate is 90–95%. Visual recovery takes several weeks/months, with full stabilization not occurring until a year, after which time the sutures can be removed.

Deep anterior lamellar keratoplasty (DALK): DALK has several advantages over PKP (**Table 3**). In keratoconic eyes, the corneal endothelium is usually intact; with good cell counts even after cases of acute hydrops, hence DALK is the procedure of choice. The major disadvantage is

Table 3 Comparison of deep anterior lamellar keratoplasty (DALK) and penetrating keratoplasty (PKP)

Parameter	DALK	PKP
Indication	Stromal opacification with healthy endothelium	Both endothelial failure and stromal opacification
Visual rehabilitation	Early	Delayed
Quality of vision	Poor than PKP	Best
Interface haze	Affects vision	None
Higher order aberrations	More	Less
Postoperative astigmatism	Less	More
Wound strength	Better	Poor
Open sky procedure	None	Risk of expulsive hemorrhage
Intraocular surgery	None	Complications can occur
Tensile strength	Better	Poor
Steroid use	Early taper	Prolonged
Donor criteria	Not stringent even nonoptical grade can be used	Only optical grade
Single donor multiple use	Possible	Not possible
Graft rejection	Low-risk	High-risk
Technique	Difficult	Easy
Learning curve	Steep	Less steep

corneal stromal rejection and migration of host keratocytes to replace donor keratocytes resulting in recurrence of the disease in graft. However, stromal rejection can never lead to graft failure and recurrence in graft is extremely rare.

The goal of DALK is to achieve a depth of dissection as close as possible to DM. Various agents have been used to create a plane of separation between DM and the deep stromal layers. These include air, fluid, viscoelastic, microkeratome and a femtosecond laser. The common techniques of DALK are described below:

Layer-by-layer Manual Dissection

In this technique, after an initial partial trephination of variable depth ranging from 50% to 70% of corneal thickness, the stroma is removed using either a crescent knife or various types of lamellar dissectors. This is followed by layer-by-layer stromal removal, which is repeated multiple times to reach as close as possible to the DM. The major limitations of this technique are poor visual outcomes due to

residual stroma and interface haze. In addition, it is a very time consuming process.⁷

Air-assisted DALK

Air-assisted lamellar keratoplasty involves injection of air into the corneal stroma that helps to achieve dissection as close as possible to DM. *Archila* first described the technique of air assisted deep lamellar keratoplasty. Over a period of time, many modifications of air-assisted DALK were tried. The big-bubble technique was described by *Anwar and Teichmann* and it is the most widely used technique of DALK.⁷

Big bubble DALK: The basic step of this technique involves injecting air into the corneal stroma deep into a groove, which is created by trephining 60–80% of the stromal thickness. The air infiltrates the potential space between the deep stromal layer and DM. The air anterior to DM creates a dome-shaped detachment of DM, which is then identified by a ring visible with the microscope. Once a plane of separation is achieved, the stromal

tissue can be easily excised. The main advantage of this technique is that the quality of vision achieved is as good as PK. However, the learning curve associated with this technique is very steep. Often its repeatability is uncertain even with the most experienced surgeons. Inadvertent DM perforation can occur at any stage of the surgery.⁷

Viscoelastic-assisted DALK

Melles et al. described a technique that uses a viscoelastic injection rather than air to achieve a cleavage plane between DM from stroma. The depth of stromal dissection is guided by the "air to endothelium" interface which is seen by a specular light reflex localized at the tip of the blade. Once the plane is achieved, the superficial stroma is removed using trephine and lamellar dissection.⁷

Hydrodelamination

This technique was described by Sujita et al. In this technique, saline solution is injected into the cornea, which enhances the identification and removal of the deep stromal fibers. An initial partial thickness corneal trephination is done up to approximately 2/3 of the thickness using vacuum trephines. However, it is difficult to achieve an actual cleavage plane over DM by hydrodelamination.⁷

Femtosecond-assisted DALK

The femtosecond laser (FSL) computer-guided cuts allows precise, accurate and reproducible placement of incisions at desired depths in the corneal stroma. Hence, it can be used to create the initial cut at the desired depth to inject air for the successful formation of big bubbles. In addition, it can be used to create corneal incisions with customized graft edges and lamellar planes for both donor and recipient corneas. Thus, FSL can be utilized for creating customized graft host interfaces, such as mushroom or Zigzag shaped DALK. The greatest advantages are its accuracy of forming the bubble at the desired corneal depth and its positive refractive outcomes due to the successful alignment of the donor and recipient zigzag or mushroom configurations. However, the major limitation is the cost and availability.⁷

Diamond-knife Assisted DALK

Vajpayee et al. have described a new technique of DALK that is easy to perform, provides visual outcomes comparable to those of big-bubble DALK, and can be performed in cases of extreme corneal thinning or corneal scars. The essential steps of this technique involve the use of a diamond knife set at a depth of 30 μ less than the pachymetry reading, to make a 2.0 mm incision at the 11-12 o'clock position. This incision is then extended circumferentially and centripetally to take out the anterior stromal lamella, leaving a thin stromal bed. The authors found comparable outcomes to the big bubble DALK.^{4,7}

Epikeratophakia: It involves removing the corneal epithelium from the host and then sewing onto the corneal stromal bed a previously cryolathed lenticule of donor cornea. The procedure has generally resulted in less favorable outcomes than PKP with reports of failure of re-epithelialization, poor BSCVA, stromal and lenticule inflammation and opacification and interface haze. It is rarely performed now-a-days.

Intracorneal ring segment inserts (intacs and ferrara rings): The technique consist of the implantation of one or two polymethyl methacrylate segments in the corneal stroma to flatten the central cornea and improve visual acuity, contact lens tolerance and delay the need for corneal graft. It acts by its Arc-Shortening effect. It is commonly used to treat mild to moderate cases of keratoconus, as normal corneal transparency and a minimum corneal thickness of 450 μ m at the site of the incision are required.

Three types of rings are available: Intacs which have a hexagonal cross-section and are placed more peripheral than ferrara rings which are triangular/prismatic in shape. Recently, Intacs SK (SK—severe keratoconus) has been introduced for use in more severe forms of corneal ectasia. It has two significant design modifications—a smaller inner diameter of 6.0 mm compared with 6.8 mm of the standard intacs; and an elliptical cross section compared with a hexagonal cross section of the standard Intacs.

The rings are inserted into the posterior stroma (about 75% of corneal depth at the incision site)

in a quick outpatient technique performed under topical anesthesia. The circular intralamellar pockets for the rings are created either using a specially designed vacuum lamellar dissector or with the femtosecond laser. It is assumed that they push out against the ectatic curvature peripherally flattening the peak of the cone centrally and returning the cornea to a more spherical shape. Intracorneal ring technology does not offer a cure for the condition but can very often produce a marked improvement in unaided and best corrected visual acuity and allow eyes to be corrected with spectacles and/or soft rather than rigid lenses.

Corneal collagen crosslinking with riboflavin (C3R) or corneal cross linkage (CXL): CXL using riboflavin(vitamin B2)/ultravioletA(UVA)[370nm] light is a therapeutic modality that can halt and stabilize the keratoconic process. It increases the corneal rigidity and biomechanical stability. The success rate varies between studies but overall 60–70% cases shows some stabilization after CXL.^{2,4} The procedure involves removing the corneal epithelium in a 6–7 mm diameter central zone followed by riboflavin 0.1% solution application and corneal radiation with ultraviolet-A light at 370 nm. Ultraviolet-A light radiation activates riboflavin generating reactive oxygen species that induce covalent bonds between collagen fibrils in the corneal stroma. The irradiation level at the corneal endothelium, lens and retina is significantly smaller than the damage threshold. It has been recommended not to perform this technique in corneas thinner than 400 µm as toxic reactions could take place in the corneal endothelium. In such cases hypotonic CXL have been tried with variable success.

The CXL is largely safe except for the risk of keratitis. No long-term problems in terms of loss of transparency of the cornea or lens have occurred and endothelial counts have been unchanged postoperatively. In addition, this technique has been successfully used in combination with other surgery techniques, such as corneal ring segments.

Refractive lens exchange: Refractive lens exchange and toric phakic intraocular lens insertion may be of some benefit in correcting myopia and astigmatism in selected eyes with early/mild/

stable disease with good spectacle corrected visual acuity.

VIVA QUESTIONS

Q.1. Refractive surgery in keratoconus.

Ans. Keratoconus as a contraindication to corneal surgical procedures such as laser *in situ* keratomileusis (LASIK), photoreactive keratectomy (PRK), laser epithelial keratomileusis (LASEK), excimer laser phototherapeutic keratectomy (PTK).

Q.2. Complications associated with keratoconus.

Ans. Complications of keratoconus include corneal hydrops and corneal perforation. Corneal hydrops is characterized by corneal edema due to seepage of aqueous humor through a tear in the Descemet's membrane (DM). Corneal hydrops has also been reported with PMD, TMD, keratoglobus and post-LASIK ectasia. If not treated, resolution usually takes a long time and occurs by endothelial sliding over a period of 2–4 months. Medical management consists of topical hypertonic drops, topical steroids, prophylactic antibiotic drops and antiglaucoma medications. However, persistent edema can cause complications such as corneal neovascularization, infection and corneal perforation. Surgical intervention is often performed to shorten the duration of the disease. Intracameral injection of air/isoexpansile gases (C3F8/SF6) is the most commonly performed procedure. In the presence of a large DM detachment or stromal clefts, ASOCT guided intrastromal drainage with stab incisions; compressive sutures and even penetrating keratoplasty may have to be performed.

Q.3. What is Munson's sign?

Ans. See text.

Q.4. What is Rizzuti's sign?

Ans. See text.

Q.5. What is posterior keratoconus?

Ans. Posterior keratoconus refers to a congenital corneal anomaly in which the posterior

corneal surface protrudes into the stroma. It usually occurs in a localized area, but may be more diffuse. It is usually sporadic, unilateral, and is nonprogressive. Bilateral and familial cases do occur but are less frequent. The anterior corneal contour is usually unaffected. Frequently, scarring occurs in the stroma anterior to the Descemet's bulge. Scarring at the level of Bowman's membrane and thinning of DM with excrescences has been reported on histopathology. It is considered a variant of corneal mesenchymal dysgenesis. Treatment usually is not necessary, although occasionally keratoplasty is indicated.

Q.6. Forme fruste KC (FFKC).

Ans. The diagnosis of KC is a clinical one that is aided by topography, while the diagnosis of FFKC is topographic. It is a subclinical disease and is not a variant of KC. Cornea specialists define FFKC in two ways:

1. Few consider FFKC is *a normal cornea* with the fellow eye is having keratoconic or there is a family history of KC.
2. Few consider FFKC is *an abnormal cornea*. Corneal topography or corneal hysteresis (ORA) or both are abnormal but there are no obvious clinical signs of keratoconus.

Q.7. Hypotonic CXL.

Ans. It has following features:

- Used for thin corneas <400 µ (320–400 µ)
- Iso-osmolar uses riboflavin 0.1% solution in 20% dextran while hypo-osmolar uses riboflavin 0.1% solution in 0.9% NaCl
- Corneal thickness increases (hypotonic solution) thus allows for safe CXL
- Results variable.

Q.8. Difference between PMD and keratoconus.

Ans. See Table 1.

Q.9. Systemic association and keratoconus.

Ans. See discussion part.

Q.10. Amsler-Krumeich classification.

Ans. See Table 2.

Q.11. Topographic patterns in normal cornea.

Ans. The topographic patterns of both the eyes of an individual often show mirror-image symmetry. This phenomenon is called enantiomorphism. Topographic patterns seen in a normal eye are following; round, oval, superior steepening, inferior steepening, symmetric bow tie, symmetric bow tie with skewed axes, asymmetric bow tie with inferior steepening, asymmetric bow tie with superior steepening, asymmetric bow tie (AB) with skewed radial axes (SRAX) and irregular. Skewing of more than 30° is described as significantly abnormal.

Q.12. What is KISA index?

Ans. Rabinowitz/Rasheed's described KISA% to diagnose keratoconus. KISA% index is usually applied to the axial map. It uses four indices on the topography. It is calculated as:

$$\text{KISA\%} = \frac{(K) \times (I - S) \times (AST) \times (SRAX) \times 100}{300}$$

- K-central keratometric value in excess of 47.2 D (i.e. K-47.2). If value is less then or equal to 47.2, it is replaced by 1.
- I-S or inferior-superior asymmetry
- AST calculated from (Sim K1-Sim K2)
- SRAX is calculated from 180—the angle between two steep axis above and below the horizontal meridian (smaller of the two angles). To amplify any abnormality, the value 1 was substituted in the equation whenever a calculated index has a value of <1

KISA% >100% is considered as highly suggestive of keratoconus.

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CORNEAL STROMAL DYSTROPHY

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INTRODUCTION

The corneal dystrophies are a group of non-inflammatory, inherited, bilateral disorders of the cornea characterized by pathognomonic patterns of corneal deposition and morphological changes which are slowly progressive and not related to environmental or systemic factors. The stromal corneal dystrophies primarily affect the stroma. Over time they often extend into the anterior corneal layers and some may affect Descemet's membrane and the endothelium. In exams, corneal dystrophy can be given as both long and short case.¹⁻³

HISTORY

Demography

Usually the patients are young adults, typically <45 years of age. The disease is usually bilateral, however the presentation may be unilateral.¹⁻³

Chief Complaints

Patient presents with following complaints:

- *Blurring of vision:* Blurring of vision is rare before the 5th decade of life in case of granular corneal dystrophy, (GCD) type 1. It appears as early as 3 years of age in case of granular corneal dystrophy type 2 and between 3 and 9 years of age in case of macular corneal dystrophy (MCD). Lattice dystrophy may present as progressive loss of vision in first decade in LCD1 and in 3rd or 4th decade in LCD2. Schnyder's Crystalline Dystrophy (SCD) is rare before 4th decade.

- *Photophobia:* Photophobia is mild in case of granular corneal dystrophy, type 1 (GCD1). More in case of GCD2 and macular dystrophy.
- *Glare:* Due to diffraction of light by the opacities.
- *Foreign body sensation:* Due to recurrent erosion or lesions extending up to epithelium.
- *Color haloes:* Due to the deposits and corneal edema.
- *Recurrent corneal erosion:* Presents with mild to extreme irritation, and discomfort that is worse in the morning. It may be associated with severe pain due to epithelial defect and fluctuating vision or blurred vision due to irregular astigmatism (uneven surface). These are uncommon with GCD, common with MCD and frequent with LCD.
- *Systemic features:* Rarely, especially in cases with LCD2, the patient may be referred from a physician with systemic symptoms. The various systemic symptoms include dry, itchy skin, laxity of the facial skin, edema over feet, breathlessness, severe mask-like facial paresis with gradual onset of facial drooping, protruding lips and pendulous ears (due to amyloid deposition and secondary muscular dysfunction).
- Usually asymptomatic in early stage and may be detected accidentally.

History of Present Illness

Following points must be noted in present illness:

Age of Onset

- *Blurring of vision* is rare before the 5th decade of life in case of granular corneal dystrophy,

type 1. It appears as early as 3 years of age in case of granular corneal dystrophy, type 2 and between 3 and 9 years of age in case of macular corneal dystrophy. Lattice dystrophy may present as progressive loss of vision in first decade in LCD1 and in 3rd or 4th decade in LCD2. The onset of visual loss is insidious and progressive in all types of stromal dystrophy.

- *Recurrent erosion can occur* in all types of stromal dystrophy but it is most commonly seen in LCD. The onset of recurrent corneal erosions (RCE) is in 1st-2nd decade in cases of LCD, in cases of GCD can occur in early stages but episodes are usually mild and rare (More patients with GCD2 or avellino corneal dystrophy experience recurring erosions than patients with typical GCD1). MCD usually presents with blurring of vision but RCE can occur in 2nd to 3rd decade.
- *Corneal opacities* in MCD usually first appear in adolescence but may become apparent anytime from early infancy to the sixth decade of life. Affected individuals usually experience severe visual impairment before the fifth decade of life, usually in 2nd to 3rd decade, once opacities have coalesced and the entire stroma becomes cloudy. Onset of corneal changes in lattice corneal dystrophy type I usually occurs in the first decade of life, although patients may remain asymptomatic for years. Signs of lattice dystrophy most often appear in early childhood and become more prominent into the 2nd and 3rd decades. In case of GCD the opacities usually appears in 1st to 2nd decade but becomes symptomatic only in 3rd to 4th decade.

Progression: Stromal dystrophies are progressive diseases. To begin with the lesions are localized to stroma. With time the lesions progressively involve the other layers too. The progression is relatively faster in MCD followed by LCD when compared to GCD.

Past History

Similar episodes of recurrent corneal erosions associated with pain and redness in past may be there.

Past Surgical History

History of prior surgery; such as phototherapeutic kerectomy (PTK), penetrating keratoplasty (PKP) or deep anterior lamellar keratoplasty (DALK) must be recorded carefully.

Past Medical History

A careful systemic history is required to rule out hypertension, diabetes and cardiac abnormality, renal failure, skin disease, and neuropathy. Multiple systems may be affected in LCD2.

Family History

Pedigree chart should be drawn to know the hereditary pattern. Autosomal dominant pattern is found in LCD and GCD and autosomal recessive in MCD.

EXAMINATION

Systemic Examination

Systemic features associated with LCD2 are as follows:

- Dry, itchy skin
- Laxity of the facial skin
- Intermittent proteinuria (nephrotic syndromes)
- Severe mask-like facial paresis with gradual onset of facial drooping, protruding lips and pendulous ears (due to amyloid deposition and secondary muscular dysfunction)
- Cranial and peripheral neuropathy
- Peripheral polyneuropathy affects mainly senses of vibration and touch.
- Carpal tunnel syndrome.
- Autonomic disturbance includes orthostatic hypotension, cardiac conduction abnormalities, and dysfunction of perspiration.

Ocular Examination

Visual acuity: Uncorrected as well as corrected visual acuity (VA) must be recorded in all cases. This is important for planning treatment.

Eyeball: Lagophthalmos can be present in LCD2.

Lids: Dermatochalasis can be present in LCD2.

Conjunctiva: Usually normal.

Cornea: On slit-lamp biomicroscopy following signs must be noted:

- *Corneal size:* Usually normal.
- *Corneal shape:* Keratoconus can be found in avellino as well as granular dystrophy otherwise normal.
- *Corneal opacity.*
- *Epithelium/anterior cornea:* Shows atrophy and degeneration of basal epithelial cells and focal thinning or loss of Bowman layer.
- *Stroma.*

GCD1: In early stage of the disease fine dots and radial lines are seen in anterior stroma, these dots are opaque on focal illumination and translucent on retroillumination (**Figs 1 and 2**). Opacities are

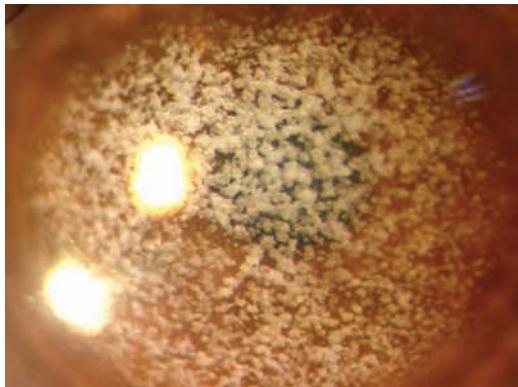


Fig. 1: Multiple opacities resembling popcorn with clear intervening cornea in a case of granular dystrophy



Fig. 2: Multiple opacities resembling crushed breadcrumbs with clear intervening cornea in a case of granular dystrophy

usually grouped into three basic morphologic types: drop-shaped, crumb-shaped, and ring-shaped. The deposits can resemble crushed breadcrumbs or snowflakes or popcorn or Christmas tree. The overall pattern is ray- or disk-shaped. The granules are primarily located in the central cornea. Initially, the stroma between the opacities remains clear (**Fig. 3**). As the disease progresses individual lesions increase in size and number and coalesce. Lesions extend into the deeper and more peripheral stroma but 2–3 mm of the peripheral cornea usually remain free of deposits. In more advanced disease, the intervening cornea develops a diffuse, ground-glass appearance. Corneal sensation is variably affected.

GCD2: The three characteristic clinical signs of avellino corneal dystrophy must be noted:

- Anterior, stromal, discrete gray-white granular deposits
- Mid to posterior stromal lattice lesions
- Anterior stromal haze.

Lattice lesions develop after the granular deposits appear. With increasing age, the granular lesions become larger and more prominent and often coalesce to form linear opacities, especially in the inferior cornea. The lattice lesions also become more prominent with age (**Fig. 4**). Initially, they are found in the mid and deep stroma and later involve the entire stroma. The stromal haze is seen only in patients with advanced granular and lattice opacities and becomes more prominent with age.

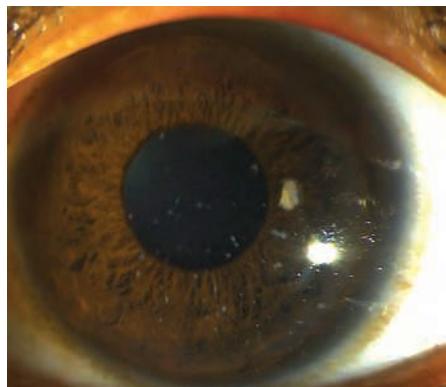


Fig. 3: Multiple scattered opacities with clear intervening cornea in a case of early granular dystrophy

MCD: In the early stages of the disease, ground-glasslike haze in the central and superficial stroma is seen. The epithelium is usually spared. With progression small, multiple, gray-white, pleomorphic opacities with irregular borders are seen (**Fig. 5**). The opacities are more superficial and prominent in the central cornea and are deeper and more discrete in the periphery. The intervening area between the opacities is hazy and gives a ground glass appearance. In later stages, the stroma is diffusely involved, Descemet's membrane takes on a gray appearance and careful slit-lamp examination may show deposits over Descemet's membrane. When the opacities grow anteriorly, the corneal surface becomes irregular

and can lead to RCE, glare and photophobia. There can be associated guttae. This opacification usually involves the entire thickness of the cornea by the second decade of life. The corneal thickness is reduced.

LCD1: In the early stages of the disease discrete ovoid or round subepithelial opacities, anterior stromal white dots, and small refractile filamentary lines may appear (**Fig. 6**). With progression of disease the lesions can appear as small nodules, dots, threadlike spicules, or thicker, radially oriented branching lines. The lines can extend into deep stroma and may opacify. The lattice lines are typically refractile with a double contour and a clear core on retroillumination (**Fig. 7**).



Fig. 4: Pleomorphic opacities with hazy intervening area between the opacities giving a ground glass appearance in a case of macular dystrophy

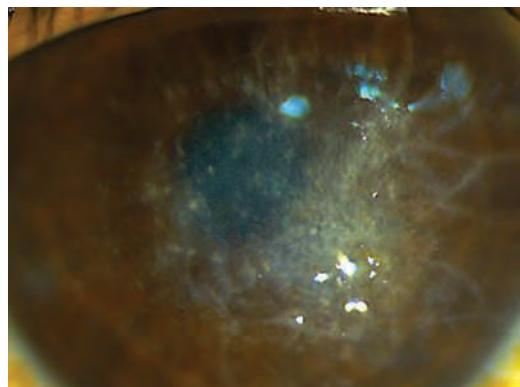


Fig. 6: Lattice lesions along with granular deposits in a case of avellino corneal dystrophy

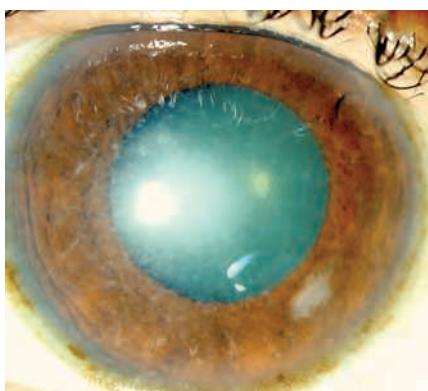


Fig. 5: Multiple anterior stromal white dots and small filamentary lines in a case of Lattice dystrophy

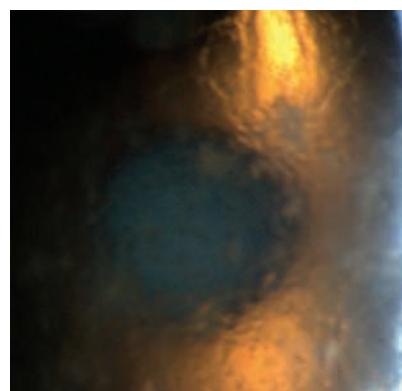


Fig. 7: Lattice lines are typically refractile with a double contour and a clear core on retroillumination

The filaments are opaque with irregular margins. They are radially oriented with dichotomous branching near their central terminations. The lines overlap one another, creating a latticework pattern. The stroma between the lines and dots is clear initially. In extreme cases, vascularization may be present. Central corneal sensitivity also can be decreased. In more advanced stages, the lattice depositions may also exhibit *autofluorescence* with slit-lamp illumination using the cobalt-blue filter. In LCD2 the fine lattice lines extend to the limbus. In LCD3 the lattice lines appear thick, andropy and without any RCE. Lattice dystrophy Type IIIA has been described with similar corneal changes, but with recurrent erosions. A late onset lattice dystrophy, Type IV, with deep stromal opacities has also been described.

- *Descemet membrane/Endothelium:*
 - Unaffected in GCD and LCD.
 - In advanced stage of MCD descemet membrane gets opacified and endothelial guttate changes occur.
 - *Corneal sensations:* Corneal sensations are reduced in LCD and MCD and in advanced cases of GCD
 - *Corneal vascularization:* It can occur in advanced cases of LCD.
 - *Corneal thickness:* It is normal in GCD and LCD. Reduction of corneal thickness occurs in MCD.
- Rest of the anterior segment is usually normal.

Tonometry: Increased IOP can be seen in case of LCD2 which may be associated with POAG.

Posterior segment: Usually normal. In case of media haze due to corneal opacity USG is done to evaluate posterior segment.

Examination of fellow eye is important: Dystrophy is a bilateral disease.

INVESTIGATIONS

- *Axial length, keratometry:* All these cases may undergo keratoplasty and cataract extraction with intraocular lens implantation may be required on a later date. Thus AL and Km must be done in all these cases.
- *CCT (Central corneal thickness):* It is reduced in cases of MCD.

- *ASOCT (Anterior segment OCT):* Depth of the lesions can be determined by ASOCT. This is extremely important for planning of surgery. ASOCT can also provide the details about the anterior segment structure and corneal thickness.
- *Specular microscopy:* It is done to evaluate corneal endothelium in cases of MCD. A healthy endothelium is necessary for any lamellar keratoplasty. Involvement of endothelium requires a full thickness graft.
- *Confocal microscopy:*
 - *GCD1:* Hyper-reflective opacities.
 - *GCD2:* Findings are a combination of GCD1 and LCD. Reflective, breadcrumb-like round deposits with well-delineated borders or highly reflective, irregular trapezoidal deposits are present in the anterior stroma (similar to GCD1). Linear and branching deposits with changing reflectivity are observed (similar to LCD).
 - *MCD:* Blurred limited accumulations of light reflective material are located in the anterior part of the corneal stroma.
 - *LCD1:* Linear and branching structures in the stroma with changing reflectivity and poorly demarcated margins. Lines must be differentiated from other similar images
 - *LCD2:* Prominent deposits, presumably amyloid, are seen contiguous to basal epithelial cells and stromal nerves. In severely affected corneas, sub-basal and stromal nerves are reduced or absent. Anterior stroma shows fibrosis and abnormal extracellular matrix. Thick anterior and mid-stromal filaments corresponding to lattice lines and thin undulating structures are visible.
- *Corneal biopsy:* When a corneal transplant is performed, the specimen is submitted for histopathology evaluation. Corneal biopsy is the gold standard for confirming the diagnosis. Various histochemical stains are specific for stromal dystrophies such as:
 - *LCD:* Congo red-pink to orange staining. Dichromism-alternating red and green color when viewed in green light through

polarized filter. Birefringence-yellow green color against black background viewed through 2 rotating filters.

- **MCD:** Stained with PAS, colloidal iron, and alcian blue. Colloidal iron stain shows abnormal aggregation of *glycosaminoglycan* at sub-epithelial Bowman's and endothelial layer.
- **GCD:** *Amorphous hyaline* deposits stains with Masson trichrome as bright red deposits. Congo red may show some foci of amyloid in GCD2.
- **Genetic analysis:** It is not required routinely [kindly see the Viva section for details].
- Polymorphic amyloid degeneration (LCD2).

DIFFERENTIAL DIAGNOSIS

The differentiating features are summarized in **Table 1**.

CLASSIFICATION OF CORNEAL DYSTROPHY

The corneal dystrophies are classified as following:²⁻⁵

Epithelial and Subepithelial Dystrophies

- Epithelial basement membrane dystrophy (EBMD)—majority degenerative, some C1
- Epithelial recurrent erosion dystrophy (ERED) C4 (Smoldaniensis variant)

Table 1 Differential diagnosis of corneal stromal dystrophy

Feature	Granular dystrophy	Macular dystrophy	Lattice dystrophy
Age of onset of lesions	Ist decade	Ist decade	Ist decade
Age at presentation (years)	30–40	3–9	10–20
Common presentation	Loss of vision in advanced cases (40–50 years)	MC loss of vision (10–30 years), erosion	MC recurrent erosion (10–20 years), loss of vision (20–30 years)
Heredity	Autosomal dominant	Autosomal recessive	Autosomal dominant
Opacity	Breadcrumbs or snowflakes or popcorn opacities with sharp border	Small, multiple, gray-white, pleomorphic opacities with irregular borders	Lattice lines—refractile with a double contour and a clear core on retroillumination Refractile tiny lines and dots, Subepithelial spots in early stages
Intervening stroma	Clear	Hazy	Hazy
Deeper extension	DM, endothelium free	DM, endothelium involved	DM, endothelium free
Extension to limbus	Usually absent	Present	Usually absent
Corneal sensation	Reduced in late stages	Reduced early	Reduced early
Corneal thickness	Normal	Thinned	Normal
Characteristic histochemical stains	Masson trichrome	Periodic acid—schiff, Colloidal iron, alcian blue, metachromatic dyes	Periodic acid—schiff, congo red, thioflavine-T (fluorescence), crystal violet (metachromasia), positive birefringence and dichroism
Material accumulated	Hyaline	Glycosaminoglycans	Amyloid

Abbreviations: DM, Descemets membrane; MC, most common

- Subepithelial mucinous corneal dystrophy (SMCD) C4
- Mutation in keratin genes
- Meesmann corneal dystrophy (MECD) C1
- Lisch epithelial corneal dystrophy (LECD) C2
- Gelatinous drop-like corneal dystrophy (GDLD) C1

Bowman Layer Dystrophies

- Reis-Bücklers corneal dystrophy (RBCD)—granular corneal dystrophy type 3 C1
- Thiel-Behnke corneal dystrophy (TBCD) C1, potential variant C2
- Grayson-Wilbrandt corneal dystrophy (GWCD) C4.

Stromal Dystrophies

- TGFBI corneal dystrophies
 - Lattice corneal dystrophy
 - Lattice corneal dystrophy, TGFBI type (LCD)
 - Classic lattice corneal dystrophy (LCD1) C1, variants (III, IIIA, I/IIIA, IV) are C1 (**Table 2**)
 - Lattice corneal dystrophy, gelsolin type (LCD2) C1, this is not a true corneal dystrophy but is included here for ease of differential diagnosis
 - Granular corneal dystrophy C1
 - Granular corneal dystrophy, type 1 (classic) (GCD1) C1
 - Granular corneal dystrophy, type 2 (granular-lattice) (GCD2) C1

- ♦ Granular corneal dystrophy, type 3 (RBCD) = (Reis-Bücklers) C1
- Macular corneal dystrophy (MCD) C1
- Schnyder corneal dystrophy (SCD) C1
- Congenital stromal corneal dystrophy (CSCD) C1
- Fleck corneal dystrophy (FCD) C1
- Posterior amorphous corneal dystrophy (PACD) C3
- Central cloudy dystrophy of francois (CCDF) C4
- Pre-Descemet's corneal dystrophy (PDCD) C4

Descemet's Membrane and Endothelial Dystrophies

- Fuchs' endothelial corneal dystrophy (FECD) C1, C2 or C3
- Posterior polymorphous corneal dystrophy (PPCD) C1 or C2
- Congenital hereditary endothelial dystrophy 1 (CHED 1) C2
- Congenital hereditary endothelial dystrophy 2 (CHED 2) C1
- X-linked endothelial corneal dystrophy (XECD) C2.

Evidential Categories for IC3D Classification

- Category 1 (C1):* A well-defined corneal dystrophy in which the gene has been mapped and identified and specific mutations are known.

Table 2 Differentiating features between LCD1, LCD2, and LCD3

Features	Type I	Type II (Meretoja)	Type III
Inheritance	AD	AD	AR
Age of onset	<10 years	20–35 years	>40 years
Visual acuity	Poor after age 40	Good until age 65	Impaired after age 60
Recurrent erosions	Frequent	Infrequent	None
Cornea	<ul style="list-style-type: none"> Numerous delicate lines Many amorphous deposits Periphery clear 	<ul style="list-style-type: none"> Few thick lines Few amorphous deposits Extend to periphery 	<ul style="list-style-type: none"> Thick lines
Systemic involvement	None	Systemic amyloidosis (skin, arteries and other organs)	None
Face	Normal	Facial paresis and blepharochalasis after age 40	Normal

Abbreviations: AD, autosomal dominant, AR, autosomal recessive; LCD, lattice corneal dystrophy

- *Category 2 (C2):* A well-defined corneal dystrophy that has been mapped to one or more specific chromosomal loci, but the gene(s) remains to be identified.
- *Category 3 (C3):* A clinically well-defined corneal dystrophy in which the disorder has not yet been mapped to a chromosomal locus.
- *Category 4 (C4):* This category is reserved for a suspected new, or previously documented, corneal dystrophy, where the evidence for it being a distinct entity is not yet convincing.

TREATMENT

Medical Management

Medical management consists of following:

- *Photophobia:* Tinted cosmetic lenses for photophobia
- *Recurrent corneal erosion:* Patching, hypertonic agents, artificial tears, or a therapeutic contact lens.

Surgical Management

It depends on the depth of the opacities (**Table 3**) and described below:

Superficial opacities: For superficial opacity following options are available:

- Epithelial scraping
- Superficial keratectomy
- Lamellar keratoplasty
- Phototherapeutic keratectomy (PTK) with the argon-fluoride excimer laser.

Deep stromal lesions and significant visual loss:

Deep anterior lamellar keratoplasty (DALK) or penetrating keratoplasty. The comparison between the two techniques have been described in **Table 3.**

MCD

- Keratoplasty is required earlier in MCD.
- DALK carries a higher risk of failure due to endothelial involvement (often there is sub-clinical involvement of endothelium without any clinical evidence). Hence, few surgeons prefer PKP to DALK.

Table 3 Comparison of deep anterior lamellar keratoplasty (DALK) and penetrating keratoplasty (PKP)

Parameter	DALK	PKP
Indication	Stromal opacification with healthy endothelium	Both endothelial failure and stromal opacification
Visual rehabilitation	Early	Delayed
Quality of vision	Poor than PKP	Best
Interface haze	Affects vision	None
Higher order aberrations	More	Less
Postoperative astigmatism	Less	More
Wound strength	Better	Poor
Open sky procedure	None	Risk of expulsive hemorrhage
Intraocular surgery	None	Complications can occur
Globe strength	Better	Poor
Steroid use	Early taper	Prolonged
Donor criteria	Not stringent even nonoptical grade can be used	Only optical grade
Single donor multiple use	Possible	Not possible
Graft rejection	Low-risk	High-risk
Technique	Difficult	Easy
Learning curve	Steep	Less steep

Abbreviations: DALK, deep anterior lamellar keratoplasty; PKP, penetrating keratoplasty

- Recurrence less common, appear 1.5–11 years after surgery. The earliest site of recurrence is graft host junction.

GCD

- PTK: Used for superficial lesion and recurrence
- Endothelium is usually uninolved hence; DALK is preferred over PKP in deeper involvement. The success rate for PKP is around 85% at 1 year.
- Recurrence rate is higher than MCD, can recur between 1 and 19 years.

LCD

- Endothelium is usually uninolved hence; DALK is preferred over PKP in deeper involvement.
- Recurrence is very common, usually occurs 2–14 years after surgery.

VIVA QUESTIONS

Q.1. Differentiate between LCD1, LCD2, and LCD3?

Ans. See Table 2.

Q.2. Describe different types of histochemical stains?

Ans. See investigation section.

Q.3. Differentiate between GCD, MCD and, LCD?

Ans. See Table 1.

Q.4. Differentiate between dystrophy and degeneration?

Ans. See Table 4.

Q.5. What is BIGH3 gene?

Ans. Keratoepithelin (Transforming growth factor, beta-induced, 68kDa) is a protein which in humans is encoded by the *TGFBI* gene (initially called BIGH3, BIG-H3), locus 5q31. Keratoepithelin produced in superficial epithelial cells and it has a role in modulating cell adhesion. Mutation of this gene causes accumulation of this product in abnormal deposits. This is associated with several corneal dystrophy such as GCD1, Lattice dystrophy, Avellino, and Reis-Buckler (remember the mnemonic GLARE)

Table 4 Difference between dystrophy and degeneration

Dystrophy	Degeneration
A condition where cells have some inborn defects due to which pathological changes may occur during passage of time	A condition where normal cells of tissue undergo some pathological changes under influence of some abnormal circumstances
Family history positive	Family history absent
Hereditary (except: cogan's)	No heritance pattern
Usually bilateral and symmetrical	Usually unilateral; if bilateral asymmetrical
Onset—early life, slowly progressive	Onset-middle life or later, progressive
Located centrally	Located peripherally or at least eccentrically
To begin with affect a particular layer of cornea	Usually not restricted to a single layer
No vascularization (Except LCD)	May be accompanied by vascularization
No role of environmental factors	Environmental factors have a role in pathogenesis
Usually not associated with any ocular disease	May be secondary to some ocular disease
Not associated with systemic disease	May be associated with systemic disease
Examples—Meesman' dystrophy, lattice dystrophy, Fuch's dystrophy	Examples—BSK, SND, spheroidal deg
<i>Abbreviations:</i> BSK, band shaped keratopathy; LCD, lattice corneal dystrophy; SND, Salzmann nodular degeneration	

Q.6. Classify MCD?

- Ans.** MCD is classified into three phenotypic variants based on the reactivity of the serum and corneal tissue to an antibody that recognizes sulfated epitopes on antigenic keratan sulfate (AgKS).
- Type I has no detectable antigenic keratan sulfate
 - Type IA the serum lacks detectable antigenic keratan sulfate, but the keratocytes react with antibodies to keratan sulfate.
 - Type II: All the abnormal accumulations react positively with AgKS and the serum has normal or lower levels of AgKS.
 - Clinically they are indistinguishable from each other.

Q.7. Associated ocular and systemic findings with LCD2:

Ans. Ocular

- Corneal hypoplasia
- Dermatochalasis (due to amyloid deposition and secondary muscular dysfunction)
- Lagophthalmos
- POAG

Systemic

- Dry, itchy skin
- Laxity of the facial skin
- Intermittent proteinuria (nephrotic syndromes)
- Cardiac conduction abnormalities, orthostatic hypotension, perspiration dysfunctions
- Severe mask-like facial paresis with gradual onset of facial drooping, protruding lips and pendulous ears (due to amyloid deposition and secondary muscular dysfunction).

Q.8. Advantage of lamellar keratoplasty over full thickness penetrating keratoplasty

Ans. See Table 3.

Q.9. Different techniques of DALK?

- Ans.** The goal of DALK is to achieve a depth of dissection as close as possible to DM. Various agents have been used to create a plane of separation between DM and the deep stromal layers. These include air, fluid, viscoelastic, microkeratome

and a femtosecond laser. The common techniques of DALK are described below:⁶

- *Layer-by-layer manual dissection:* In this technique, after an initial partial trephination of variable depth ranging from 50%-70% of corneal thickness, the stroma is removed using either a crescent knife or various types of lamellar dissectors. This is followed by layer-by-layer stromal removal, which is repeated multiple times to reach DM as close as possible. The major limitations of this technique are poor visual outcome due to residual stroma and interface haze. In addition, it is a very time consuming process.
- *Air-assisted DALK:* Air-assisted lamellar keratoplasty involves injection of air into the corneal stroma that helps to achieve dissection as close as possible to DM. *Archila* first described the technique of air assisted deep lamellar keratoplasty. Over a period of time, many modifications of air-assisted DALK were tried. The big-bubble technique was by *Anwar and Teichmann* and it is the most widely used technique of DALK.

Big bubble DALK: The basic step of this technique involves injecting air into the corneal stroma deep into a groove, which is created by trephining 60-80% of the stromal thickness. The air infiltrates the potential space between the deep stromal layer and DM. The air anterior to DM creates a dome-shaped detachment of DM, which is then identified by a ring visible with the microscope. Once a plane of separation is achieved, the stromal tissue can be easily excised. The main advantage of this technique is that the quality of vision achieved is as good as PK. However, the learning curve associated with this technique is very steep. Often its repeatability is uncertain even with the most experienced surgeons. Inadvertent DM perforation can occur at any stage of the surgery.

- *Viscoelastic-assisted DALK:* *Melles et al.* described a technique that uses a

viscoelastic injection rather than air to achieve a cleavage plane between DM from stroma. The depth of stromal dissection is guided by the "air to endothelium" interface which is seen by a specular light reflex localized at the tip of the blade. Once the plane is achieved, the superficial stroma is removed using trephine and lamellar dissection.

- *Hydrodelamination:* This technique was described by Sujita et al. In this technique, saline solution is injected into the cornea, which enhances the identification and removal of the deep stromal fibers. An initial partial thickness corneal trephination is done up to approximately 2/3 of the thickness using vacuum trephines. However, it is difficult to achieve an actual cleavage plane over DM by hydrodelamination.
- *Femtosecond-assisted DALK:* The femtosecond laser (FSL) computer-guided cuts allows precise, accurate and reproducible placement of incisions at desired depths in the corneal stroma. Hence, it can be used to create the initial cut at the desired depth to inject air for the successful formation of big bubbles. In addition, it can be used to create corneal incisions with customized graft edges and lamellar planes for both donor and recipient corneas. Thus, FSL can be utilized for creating customized graft host interfaces, such as mushroom or Zigzag shaped DALK. The greatest advantages are its accuracy of forming the bubble at the desired corneal depth and its positive refractive outcomes due to the successful alignment of the donor and recipient zigzag or mushroom configurations. However, the major limitation is the cost and availability.
- *Diamond-knife assisted DALK:* Vajpayee et al. have described a new technique of DALK that is easy to perform, provides visual outcomes comparable to those of big-bubble DALK, and can be performed in cases of extreme corneal thinning or corneal scars. The essential steps of this

technique involve the use of a diamond knife set at a depth of 30 μ less than the pachymetry reading, to make a 2.0 mm incision at the 11-12 o'clock position. This incision is then extended circumferentially and centripetally to take out the anterior stromal lamella, leaving a thin stromal bed. The authors found comparable outcomes to the big bubble DALK.

Q.10. Genetics of stromal dystrophies.

- Ans.**
- *Granular dystrophy-AD TGFBI* (5q31) corneal dystrophy.
 - *Macular dystrophy (MCD):* Autosomal recessive, chromosome 16 (16q22.1), a mutation in a new carbohydrate sulfotransferase gene (*CHST6*) has been identified as the cause of macular dystrophy.
 - *Lattice dystrophy:* *TGFBI* gene-related dystrophy with two different types, both representing *Category I* (C1).

Lattice corneal dystrophy type II is not a true corneal dystrophy. It part of the systemic disorder *familial amyloid polyneuropathy Type IV (Finnish type)*, also known as *Meretoja's syndrome*. Nearly all cases are bilateral, progressive and usually inherited as an autosomal dominant trait and it is due to single amino acid substitution in the plasma protein *gelsolin*, the consequence of a single nucleotide guanine to adenine change on chromosome 9q 32-34. *Lattice corneal dystrophy type III* is an autosomal recessive disorder. The gene has not yet been mapped. *Lattice corneal dystrophy type IIIA*—has an autosomal dominant pattern, and the clinical findings are due to a mutation at 5q31(Pro501Thr; Ala622His; His626Ala). *The lattice corneal dystrophy type IV* is associated with a Leu527Arg mutation in the *big-h3* and is a dominant form of late-onset, deep lattice dystrophy.³⁻⁵

Q.11. Dystrophies associated with keratoconus.

- Ans.** Keratoconus associated with other corneal dystrophies.
- In a study by Cremona et al. 51 patients manifested typical signs and topographic

evidence of keratoconus associated with another corneal dystrophy.⁷ These dystrophies were

- Fuchs dystrophy (most common)—52.9%
- Anterior basement membrane dystrophy—25.5%
- Posterior polymorphous dystrophy—13.8%
- Combination of Fuchs dystrophy and anterior basement membrane dystrophy—5.8%
- Granular dystrophy—2%

Few case reports have reported keratoconus in association with macular dystrophy and avellino dystrophy also.

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FUCHS' ENDOTHELIAL CORNEAL DYSTROPHY

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INTRODUCTION

Fuchs' endothelial corneal dystrophy (FECD) is the most common corneal endothelial dystrophy seen in clinical practice. It is characterized by bilateral, noninflammatory, progressive loss of corneal endothelium that ultimately results in corneal decompensation and loss of vision. In exams, it is given as a long case. Most of the time it may be a case of corneal decompensation following cataract surgery with evidence of FECD in the other eye or it may be a case of operated corneal graft in one eye for corneal decompensation with evidence of FECD in the other eye.

Asian countries compared to the western world. Females are affected more than males (corneal guttae 2.5 times and corneal edema 5.7 times more than males; overall 4:1 ratio).¹

Chief Complaints

Presenting features may depend upon the stage of the disease. Patient may presents with following complaints:

- *Early stage:* Blurring of vision (initially in morning gradually improving as the day passes)
- *As the disease progresses:* Mild blurring due to stromal edema, glare, and colored halos around lights (due to corneal edema) can occur.
- *Late stages:* Loss of vision, recurrent attacks of redness and pain due to epithelial edema and bullae rupture.
- *Advanced stages:* Loss of vision but without any pain or photophobia due to corneal scarring.

HISTORY

Demography

The FECD is a slowly progressive disease affecting persons between 5th and 7th decade. The onset of the disease occurs around one decade earlier in

History of Present Illness

The natural course of the disease is quite characteristic. The onset is gradual. In early stages there is blurring of vision in morning that gradually improving as the day passes. As the disease progresses the blurring of vision becomes persistent and symptoms of pain, photophobia, watering may appear due to epithelial edema. There may be repeated exacerbations of the symptoms associated with episodes of epithelial bullae formation-rupture-healing cycle. In advanced cases a pannus or fibrosis forms that leads to resolution of symptoms.

Past History

Past medical history must include diseases such as diabetes mellitus, hypertension, tuberculosis, bronchial asthma. These diseases may not be related directly to FECD but are important for surgical planning.

Past Surgical History

Quite often a case may present with persistent corneal edema following cataract surgery and a careful examination of the other eye reveals signs of FECD. Thus history of any recent intraocular surgery must be noted. In addition, the postoperative best corrected visual acuity is an important parameter while considering for keratoplasty and its visual prognosis.

EXAMINATION

General Examination

A thorough general examination must be carried out to look for any systemic condition that may need attention before surgical planning.

Ocular Examination

Visual acuity: It depends on the stage of the disease and severity of corneal edema (see chief complaint).

Eyeball: Usually normal.

Eyelid: Usually normal. There may be blepharospasm in presence of corneal epithelial defect as a consequence of ruptured bullae.

Conjunctiva: Conjunctival congestion and watery discharge can be there in presence of epithelial defect.

Cornea: The findings in cornea depends upon the stage of the disease.

- **Stage 1 (stage of corneal guttae)**
 - **Central corneal guttae:** It appears as tiny dark spots (**Fig. 1**) on the posterior corneal surface on direct illumination. Specular reflection also reveals dark spots and disruption of regular endothelial mosaic. In retroillumination the guttae appears as dewdrops.
 - As the disease progresses, guttae spread peripherally and coalesce centrally along with pigment dusting on the endothelium. This characteristically gives the appearance of “beaten metal appearance”.
 - As the disease progresses the Descemet's membrane becomes thickened and irregular.
- **Stage 2 (stage of corneal stromal edema)**
 - Corneal edema initially appears in the posterior stroma, which is best seen with sclerotic scatter as a fine gray haze.
 - Vertical wrinkles or striae in Descemet's membrane appear due to swelling of the corneal stroma.
 - Progressive stromal edema results in a ground-glass opacification with marked thickening of the central cornea (**Fig. 2**).
- **Stage 3 (stage of corneal epithelial edema)**
 - Multiple epithelial microcysts that may coalesce to form bullae (**Fig. 3**).
 - Rupture of bullae leads to epithelial erosions and fingerprint lines following healing of such lesions.



Fig. 1: Central corneal guttae in stage 1 of FECD

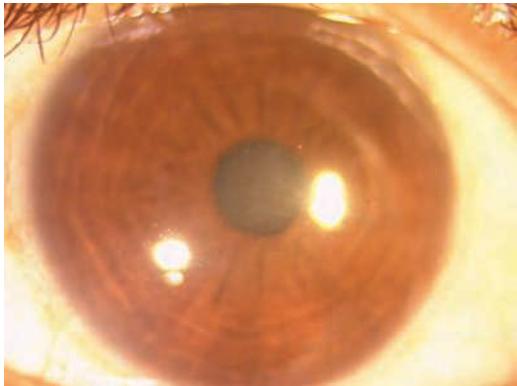


Fig. 2: Progressive stromal edema with ground-glass opacification in FECD stage 2

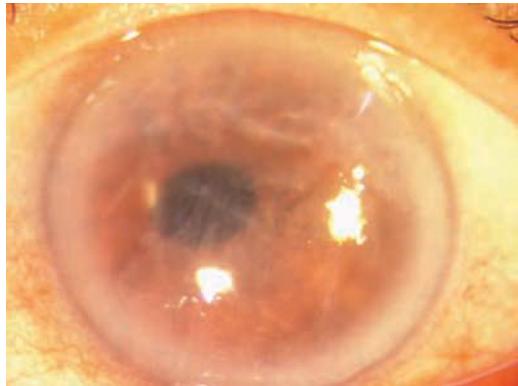


Fig. 4: Stromal scarring in stage 4 FECD

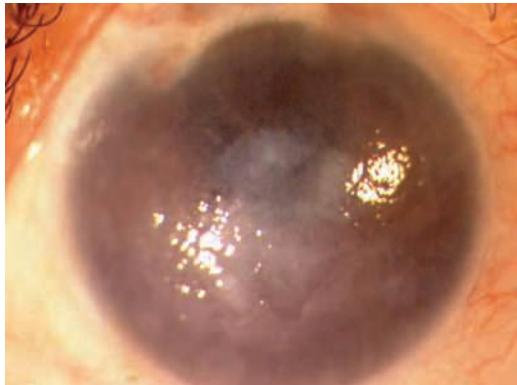


Fig. 3: Bullae formation and progressive stromal edema in stage 3 FECD

- **Stage 4 (stage of scarring)**
 - Avascular subepithelial fibrous scarring occurs between the epithelium and Bowman's membrane. Scarring leads to resolution of symptoms but visual acuity further deteriorates due to irregularity of corneal surface (**Fig. 4**).
 - Peripheral superficial corneal neovascularization.

Anterior chamber/sclera/iris/pupil/fundus are usually within normal limit. Shallow AC with angle closure glaucoma have been reported in few cases.

Lens: Carefully examine the lens for presence of cataract. Detection of cataract is important for management of FECD.

DIFFERENTIAL DIAGNOSIS

A case of FECD must be differentiated from following:

- Hassall-Henle bodies
- Central herpetic disciform keratitis-KP present
- Aphakic or pseudophakic bullous keratopathy
- Congenital hereditary endothelial dystrophy (CHED)
- Iridocorneal endothelial syndrome (Chandler's syndrome) (ICE)
- Posterior polymorphous corneal dystrophy (PPCD).

Hassall-Henle Bodies

They are present in 70% of the population over 40 years old. Resembles guttae of FECD but are located only in the peripheral cornea and are not associated with progressive visual loss or corneal edema.

Central Herpetic Disciform Keratitis

Differentiating features are:

- Presence of keratic precipitates (KP's)
- Respond to steroids
- Presence of scarring (herpetic footprints).

Aphakic or Pseudophakic Bullous Keratopathy

Following are the differential features:

- History of cataract surgery often with signs of complicated surgery
- Other eye will be normal.

CHED/ICE/PPCD

See Table 1.

INVESTIGATION

- Specular microscopy:** Specular microscopy can reveal following changes:
 - Qualitative parameters—pleomorphism (variation in shape, indicates disruption in the regular hexagonal pattern of the endothelium), polymegathism (variation in size, indicates injury to endothelium)
 - Quantitative parameters:
 - ♦ Reduced endothelial cell density in mm^2
 - ♦ Increased coefficient of variation (CV)—CV represents the degree of variation in the sizes of the endothelial
- Percentage of hexagonal cells (HEX)—in a normal endothelium, more than 60% of the endothelial cells are hexagonal. In FECD it is <60%
- Corneal pachymetry:** Measurement of central corneal thickness is important for diagnosis (in doubtful and early cases) and planning of treatment.
- Confocal microscopy:** In presence of corneal edema, confocal microscopy is the best technique for evaluation of corneal endothelium
- Anterior segment optical coherence tomography (ASOCT):** It can provide the details of anterior

Table 1 Differential diagnosis of FECD

Parameters	FECD	PPMD	CHED (type 1)	ICE
Age of onset	40s to 50s	Teens to 20s	Birth to 10 years	Young adult
Laterality	Bilateral	Bilateral	Bilateral	Unilateral
Sex predilection	F > M	F = M	F = M	F > M
Heredity	AD	AD	AD	No
Basic defect	Attenuation and reduced number of endothelial cells	Epithelialization of endothelium	Mutation of solute carrier family 4, sodium borate transporter member 11—SLC4A11	Abnormal proliferation of endothelium
Corneal findings	Guttae, stromal thickening, epithelial edema, sub-epithelial fibrosis	Vesicles, bands, diffuse opacities, plaques at Descemet's membrane	Marked corneal thickening and opacification, endothelium rarely visible	Fine, guttae-like changes, 'hammered silver'
Other ocular abnormalities	Increased intraocular pressure, narrow angles	Iris atrophy/ corectopia, broad peripheral synechiae, glaucoma 25%	Usually none	Iris atrophy, iris nodules, glaucoma in 80–100%
Progression	Progressive	Minimal	Progressive	Relentless
Specular microscopy	Polymorphism Polymegathism Decreased endothelial cell count	Focal change, endothelial cells usually enlarged but count is usually normal	Not possible	Diffuse changes, ICE cell

Abbreviations: CHED, congenital hereditary endothelial dystrophy; FECD, Fuch's endothelial corneal dystrophy; ICE, irido-corneal endothelial dystrophy; PPCD, posterior polymorphous corneal dystrophy

chamber in presence of an edematous cornea. In addition corneal thickness and level of scarring can also be detected.

- **Ultrasonography (USG):** USG is done to rule out any posterior segment pathology before proceeding for keratoplasty.

MANAGEMENT

The management of FECD includes following.^{2,3}

Medical Management

- **Corneal edema**
 - *Topical hypertonic saline solutions and ointments:* It artificially raises the osmolality of the tear film and dehydrates the cornea by drawing fluid from the epithelium and anterior stroma.
 - Dehydration of the cornea by a blow dryer in the morning or throughout the day can decrease the symptoms in early stages.
 - Cycloplegics and nonsteroidal anti-inflammatory agents are useful in diminishing corneal pain from bullous keratopathy.
 - *Reduction of intraocular pressure:* Use of intraocular pressure-lowering medications may reduce corneal edema in patients with elevated or even normal intraocular pressure.
- **Recurrent erosion**
 - *Bandage contact lenses:* Use of therapeutic so contact lenses help in relieving the pain from recurrent epithelial erosions, while decreasing irregular astigmatism in cases that have progressed to bullous keratopathy
 - Anterior stromal puncture/amniotic membrane graft/phototherapeutic keratectomy/anterior stromal puncture/conjunctival flaps have been described for symptomatic relief of bullous keratopathy when the visual prognosis is poor. However, these procedures are rarely required in FECD, where the visual potential is often good.

Surgical Management

The different surgical options in a case of FECD are described below:

Endothelial Keratoplasty

Currently the treatment of choice. The different techniques of endothelial keratoplasty are as follows:

- *Descemet's stripping endothelial keratoplasty (DSEK):* The donor tissue (consisting of DM-endothelium complex and some stroma) is prepared using manual technique.
- *Descemet's stripping automated endothelial keratoplasty (DSAEK):* Similar to DSEK except the donor tissue is prepared using a microkeratome.
- *Descemet's membrane endothelial keratoplasty (DMEK):* Donor tissue is consist of only DM-endothelium complex and no stroma. Technically difficult than DSAEK but visual results are better than DSAEK.

Penetrating Keratoplasty

A full thickness graft is indicated in presence of corneal scar or the surgeon lacks the expertise.

FECD with Cataract

Senile cataract is commonly seen in cases of FECD due to the common age group affected. It is often a dilemma to decide if only cataract surgery is enough or the patient needs a triple procedure. Although there are no universal guidelines, most corneal surgeons follow following approach:

- Only Cataract with IOL
 - Specular count >1000 cells/mm²
 - CCT <600 μm
 - Good corneal clarity to allow cataract surgery
- Triple procedure
 - Specular count <800 cells/mm²
 - CCT >640 μm
 - Corneal clarity is not enough to allow cataract surgery

In cases where the values of CCT and endothelial counts are in between, the decision is individualized and based on surgeons experience.

VIVA QUESTIONS

Q.1. Association of FECD: FECD has been associated with following:

- Ans.** • Axial hypermetropia, shallow anterior chamber and angle closure glaucoma

Table 2 Early and late onset FECD

	<i>Early FECD</i>	<i>Late FECD</i>
<i>ICD category</i>	<i>Category 1</i>	<i>Category 2/3</i>
Genetics	Mutation in the gene for the alpha 2 chain of collagen VIII (COL8A2-Q455K) on chromosome 1 p34.3-p32	AD, many with no inheritance pattern 13pTel-13q12.13/18q21.2-q21.32/ possible SLC4A11
Onset	First decade	4th-5th
Retroillumination	Fine, patchy distribution of corneal guttae	Coarse and distinct corneal guttae
Specular microscopy	Small, shallow guttae	Larger guttae
DM	Considerably thicker than late	—
Sex distribution	F = M	F > M

Abbreviations: AD, autosomal dominant; DM, descemets membrane; F, female; FECD, Fuchs' endothelial corneal dystrophy; M, male

- Keratoconus
- Increased prevalence of age-related macular degeneration (controversial)
- Increased rate of cardiovascular disease (controversial)

Q.2. Causes of corneal guttae.

Ans. Corneal guttae may be seen in the following cases:

- *Interstitial keratitis:* Focal gutta formation without corneal edema
- Macular dystrophy
- Posterior polymorphous dystrophy
- Pseudo-guttae (appears as gutta but these are transient, due to edema of the endothelial cells, and disappear with resolution of the underlying condition)
 - trauma, intraocular inflammation, infection, toxins and thermokeratoplasty.

Q.3. What is difference between early and late onset FECD?

Ans. Kindly see Table 2.

Q.4. Normal endothelial cell count and rate of endothelial loss.

Ans. The normal endothelial cell count as per age is as follows:

- At birth: 4000–5000
- 10–19 years: 2,900–3,500 cells/mm²
- 20–29 years: 2,600–3,400 cells/mm²
- 30–39 years: 2,400–3,200 cells/mm²
- 40–49 years: 2,300–3,100 cells/mm²
- 50–59 years: 2,100–2,900 cells/mm²
- 60–69 years: 2,000–2,800 cells/mm²
- 70–79 years: 1,800–2,600 cells/mm²
- 80–89 years: 1,500–2,300 cells/mm²

The normal rate of endothelial loss is approximately 0.6% per year.

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ACUTE GRAFT REJECTION

Ritu Nagpal, Vaishali Ghanshyam Rai, Prafulla Kumar Maharana, Manpreet Kaur

INTRODUCTION

Corneal graft rejection can be defined as development of graft edema in conjunction with inflammatory signs in a graft that has been clear for at least 2 weeks in a primary graft and one week in a regraft. It is an immunological response of the host to the donor corneal tissue without regard to the effect of the response on graft survival. Immune rejection of the transplanted cornea is the major cause of graft failure in the intermediate and late postoperative period. It is primarily of three types; epithelial, stromal and endothelial rejection. Endothelial rejection is the most common and clinically important type of rejection. Approximately 30% of eyes with penetrating keratoplasty experience at least one episode of graft rejection and about 5–7% lead to eventual graft failure. Around 12% of graft rejection cases in patients with good prognostic keratoplasty and 40% in complicated cases have been reported to lead to subsequent graft failure.¹⁻³

HISTORY

Demography

Several clinical series have shown that a younger recipient conferred a higher risk of rejection probably due to a robust immune system. Recipients younger than 40 years are at a higher risk for graft rejection.

Chief Complaints

A case of acute graft rejection presents with following symptoms:

- Redness
- Sensitivity to light
- Vision loss
- Pain.

These characteristic symptoms are present in approximately 70% of the cases while 30% cases are asymptomatic and diagnosed during routine follow-up.

History of Present Illness

- The onset is usually acute and progresses if not treated. Graft rejection after PKP usually occurs after an average period of 8 months. Most cases occur within one year. If the symptoms are there from day one, it may be a case of primary graft failure.
- It is important to enquire about the best vision gained after the corneal graft. This helps in deciding for a re-graft on a later date.

Past History

A careful past history must be taken to rule out the risk factors responsible for graft rejection. Following history is important in a case of graft rejection

- History of ocular surface diseases and treatment should be asked to the patient, e.g. Ocular surface diseases, such as severe dry eye, severe chemical burns, radiation burns, ocular pemphigoid, Steven-Johnson syndrome, neuroparalytic disease etc.
- Past history of herpes simplex keratitis and recurrent episodes should be asked.
- Past history of any ocular surgery, e.g. penetrating keratoplasty, excimer laser phototherapeutic keratectomy (can also trigger a corneal graft rejection episode).
- Past history of glaucoma and antiglaucoma medications taken.
- History of a previous graft failure, especially if the failure was a result of an allograft rejection. One study demonstrated that the rate of graft failure secondary to allograft rejection increased from 8% in patients with no history of previous transplantation to 40% in patients with two or more previous grafts.
- *Details of the surgery:* Look for following if the detailed record of the surgery is available:
 - Presence of corneal vascularization at the time of surgery—puts the graft at high risk for graft failure

- Concomitant vitrectomy with PKP—a twofold increased risk of graft failure
- Concurrent intraocular inflammation
- Donor endothelial count
- Presence of anterior synechiae in host.

All these factors are risk factors for graft rejection and subsequent graft failure.

Past Medical History

A case of acute graft rejection needs aggressive steroid therapy. Hence any systemic history that is a contraindication for systemic therapy must be rule out. A careful history of diabetes mellitus, hypertension, peptic ulcer disease, tuberculosis, osteoporosis and any neuropsychiatric disorder must be ruled out.

EXAMINATION

General/Systemic Examination

Carefully look for any systemic contraindication for steroid therapy.

Ocular Examination

- **Visual acuity:** Best corrected visual acuity (BCVA) must be recorded at the base line. Monitoring BCVA on a daily basis can indicate the response to pulse steroid therapy.
- **Eyeball/Eyelids:** Looks normal. However, lid edema can be there in an acutely inflamed eye. Also look for any findings such as ectropion, entropion, meibomian disease, trichiasis that may put the graft at risk.
- **Conjunctiva:** Circumciliary congestion is characteristically seen in corneal graft rejection. Often, it is the earliest sign of rejection reaction and can occur before clinical appearance of cellular infiltrates in the cornea or the anterior chamber.
- **Cornea:**
 - Cellular infiltration of the cornea as discrete subepithelial infiltrates reminiscent of those seen in epidemic keratoconjunctivitis. These small (0.2–0.5 mm), hazy infiltrates are usually scattered in the central cornea and occur exclusively in the donor tissue but not the peripheral recipient tissue.

- An epithelial rejection line, also known as Krachmer's line, in the graft from the host graft junction without edema and keratic precipitates/infiltrate can be seen. It is usually seen in epithelial rejection. An epithelial line stains with fluorescein or Rose Bengal. The epithelium behind the rejection line may appear hazy, irregular and is replaced by recipient epithelium. Superficial epithelial infiltrates appear near the suture lines which progress centrally. These are known as Kaye's dots. It usually subsides in 6–10 days but may last several weeks. Both Krachmer's line and Kaye's dots are seen in epithelial rejection commonly. However, they can be present in endothelial rejection also.
- **Keratic precipitates:** They can appear as scattered deposits or can form a distinct line known as the Khodadoust line (**Fig. 1**). This line tends to migrate from the peripheral cornea to the central cornea and many a times its origin can be traced to a loose suture or donor corneal vessel. *Khodadoust line* is the hallmark of graft rejection.

- **Differential edema:** Endothelial rejection is often associated with stromal edema overlying the areas that have been traversed by the endothelial rejection line while the areas ahead of the line are clear (**Figs 2 and 3**).

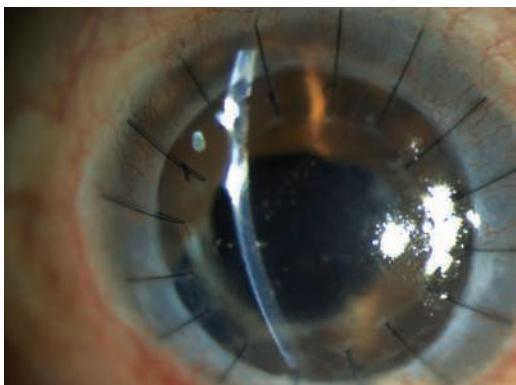


Fig. 1: Khodadoust line on the endothelium in a case of acute graft rejection following penetrating keratoplasty

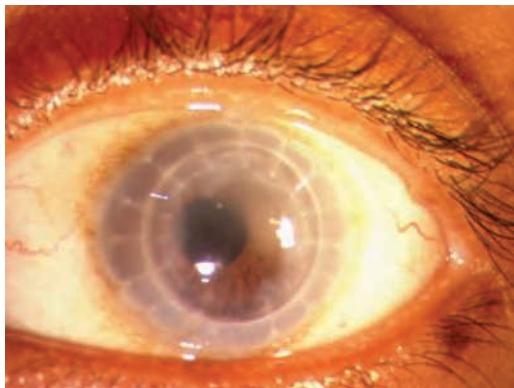


Fig. 2: Differential stromal edema in a case of acute graft rejection

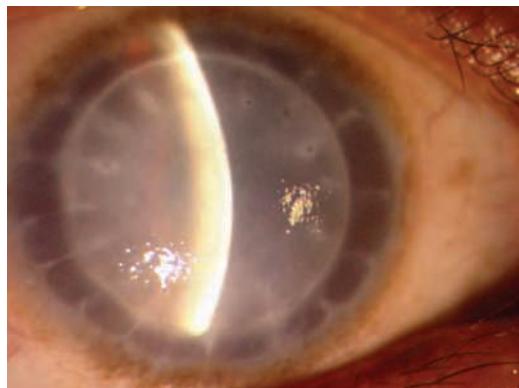


Fig. 4: Failed graft after an episode of acute graft rejection

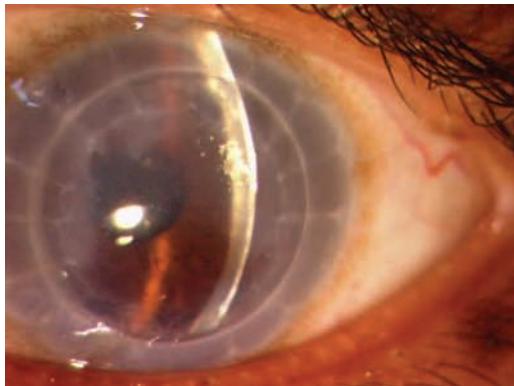


Fig. 3: Acute graft rejection with stromal thickening and edema

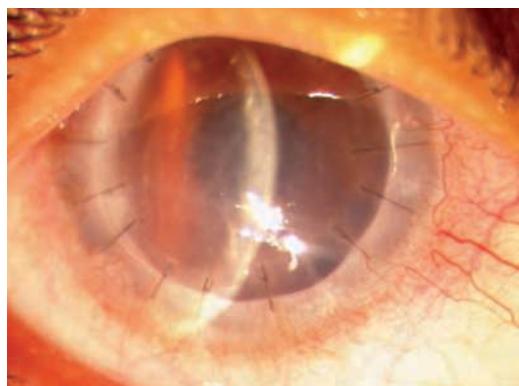


Fig. 5: Decompensated corneal graft with stromal thickening after acute graft rejection

- Deep corneal vascularization should be noted.
- *Staining:* Cornea must be stained to look for presence of epithelial defect or recurrence of a herpetic keratitis.
- In delayed presentation the entire graft becomes edematous (**Fig. 4**) with significantly increased graft thickness (**Fig. 5**).
- *Anterior chamber (AC):* AC flare and cells can be noted which indicates elevated levels of protein in the aqueous humor due to leakage from the uveal vasculature.
- *Intraocular pressure (IOP)* raised IOP can both be a consequence or cause for corneal graft rejection. In edematous cornea IOP may be falsely low with Goldmann's applanation

tonometry. A Mackay-Marg principle based tonometer (Tonopen) can give more reliable values.

DIFFERENTIAL DIAGNOSIS

A case of acute corneal graft rejection must be differentiated from graft failure, sterile/infectious endophthalmitis, epithelial down growth and recurrent herpetic keratitis. The differentiating points are summarized in **Table 1**.

INVESTIGATIONS

Pachymetry

Increased central corneal thickness (CCT) is often the first indicator of endothelial dysfunction.

Table 1 Differential diagnosis of acute corneal graft rejection

Condition	Features
Late graft failure	<ul style="list-style-type: none"> Gradual onset of graft edema Not associated with signs of inflammation such as AC cells/flare or keratic precipitates No Khodadoust line or differential edema
Sterile/infectious endophthalmitis	<ul style="list-style-type: none"> Inflammatory signs are severe Presence of hypopyon Presence of infiltrates in vitreous
Epithelial down growth	<ul style="list-style-type: none"> Clumps of cells like material in the anterior chamber Cells larger than that of cells of inflammation These cells does not respond to corticosteroid therapy Presence of white membrane over anterior surface of iris Associated increased intraocular pressure that is unresponsive to medical therapy
Recurrent herpetic keratitis	<ul style="list-style-type: none"> KP's are restricted to host cornea only History of previous herpetic keratitis Absence of Khodadoust line Characteristic shape Response to topical antiviral therapy

CCT can be measured with the help of ultrasonic pachymeter, orbscan, pentacam or anterior segment OCT (ASOCT). Serial monitoring of CCT is important for monitoring the response to steroid therapy.

Specular Microscopy

It can reveal the reduced endothelial cell count that further reduces each episode of graft rejection.

Confocal Microscopy

In presence of severe graft edema, where specular microscopy is not possible, confocal microscopy can reveal the endothelial changes.

Ultrasonography (USG)

In presence of severe corneal edema USG is helpful in ruling out sterile endophthalmitis.

MANAGEMENT

Most episodes of allograft rejection can be reversed if prompt and aggressive treatment is initiated. The treatment of choice is steroids.

Steroids

Topical Steroids

A case of acute graft rejection can be managed on outpatient basis but admission to hospital for the first few days of treatment is helpful monitoring compliance. Aggressive administration of potent topical corticosteroids with good intraocular penetration (such as prednisolone acetate 1% or prednisolone phosphate 1% eye drop) aborts most attacks of acute graft rejection. Commonly used treatment regime is:

- 1 hourly–3 days
- 2nd hourly–15 days
- 4 times–2 months
- 3 times–2 months
- 2 times–3 months
- Once–4 months

Topical steroids are effective in epithelial rejection, stromal rejection and mild-moderate endothelial rejection.

Systemic Steroids

- Severe episodes of endothelial rejection needs systemic steroid therapy.

- Pulse steroid therapy is more effective than oral steroids for the treatment of a rejection episode. A single pulse (500 mg intravenous methylprednisolone) in a single dose is more effective and better tolerated than daily oral prednisolone. Repeating the dose at 24 or 48 hours after the initial dose does not add any advantage.
- Intravenous dexamethasone (100–200 mg) single dose has been found to be equally efficacious as methylprednisolone and thus may be used as an alternative in patients who are nonaffording.
- In severe cases of rejection, topical prednisolone acetate 1% hourly, one dose of pulsed intravenous methylprednisolone (500 mg), and oral prednisone at 1 mg/kg/day for 5 days is recommended.
- The IV steroid therapy beyond 8 days of the onset of symptoms may not add any benefit to intense topical steroid therapy. In a study by Hills et al. when patients were treated within 8 days of the onset of symptoms, the survival rate of grafts was 92% versus 55%.

Supportive Therapy

Anti-glaucoma medications have to be given when IOP is raised. Cycloplegics can reduce pain by relieving ciliary spasm. Topical lubricating drops are useful in presence of sutures and associated epithelial defect.

Immunosuppressive Therapy

Immunosuppressive therapy is not required routinely. Probable indications includes high risk graft and cases where long-term steroid use is contraindicated or causing complications. Following immunosuppressive therapy have been tried with variable success.

- **Cyclosporine A:** CsA is a powerful immunosuppressive agent which binds to an intracellular protein called cyclophilin and inactivates calcineurin. The inactivation of calcineurin inhibits IL-2 and lymphokine production, thus limiting the activity of CD4+ and CD8+ lymphocytes.

- *Topical* cyclosporine A is available as 2% in castor oil or 1% in artificial tears 4 times daily
- *Systemic*
 - ♦ Recommended dosage is 15 mg/kg/day for 2 days followed by 7.5 mg/kg/day for 2 days then adjusted to maintain trough blood levels of 100–200 mg/L for 6 months after reversal of acute rejection episode
 - ♦ Close monitoring of blood pressure, renal function including serum creatinine and liver function test

Recently studies suggest topical cyclosporin A (CsA) as well as oral CsA have not been found to reduce the risk of allograft rejection.

Mycophenolate mofetil

- MMF acts by inhibiting inosine monophosphate dehydrogenase required for proliferation of T- and B-lymphocytes
- Dose 750 mg bd
- Renal, hepatic and bone marrow function must be monitored
- Recent studies suggest that oral MMF is effective in the prevention of allograft rejection in high risk keratoplasties.
- Unlike CsA, therapeutic drug monitoring is not required which significantly reduces the cost of treatment.

Azathioprine

- 1–2 mg/kg/day orally
- It reduces the need of systemic corticosteroids, and, thus, reduces the systemic complications expected by high-dose corticosteroids.
- Renal, hepatic and bone marrow function must be monitored

Tacrolimus (FK-506)

- Macrolide immunosuppressant with a mechanism of action similar to CsA, but 10–100 times more potent than the latter. It inhibits calcineurin by binding to immunophilin or FK-506 binding protein (FKBP). Topical (ointment 67 or drops) as well as systemic tacrolimus has shown to be promising as a prophylactic agent against corneal graft rejection.
- A dose of 0.16 mg/kg/day.
- Renal function must be monitored.

- *Other agents:* Rapamycin/Sirolimus, anti-lymphocyte monoclonal antibodies have been tried with variable success.

VIVA QUESTIONS

Q.1. What are the risk factors for acute corneal graft rejection?

Ans.

- *Donor factor*
 - The method and duration of storage of the donor cornea and nature of donor button cutting.
 - Pretreatment of donor tissue with ultraviolet radiation may reduce the chances of development of rejection.
- *Host factor*
 - *Vascularization of the host cornea:* Deep stromal vascularization of the host cornea of two or more quadrants classifies as a high-risk cornea. CCTS has defined vascularization of the host bed in 2 or more quadrants extending at least 2 mm into the stroma as a risk factor associated highly with the rejection of the corneal grafts.
 - *Regraft:* A cornea with a previously failed graft due to any cause is considered to be at high risk.
 - *Herpes simplex virus keratitis:* Active or healed HSV keratitis considered as high risk for graft rejection. The increases risk is due to the vascularization associated with HSV keratitis.
 - Ocular surface diseases, such as severe dry eye, severe chemical burns, radiation burns, ocular pemphigoid, Steven-Johnson syndrome, and neuroparalytic disease, are also associated with poor prognosis for the corneal graft.
 - Young patients and bilateral graft have more chances of graft rejection due to active immune system.
 - *Pediatric patients:* The immune system of children is more active than that of adults and due to rapid wound healing suture becomes loose early, both these factors along with the inability of the child to communicate timely leads to an increases risk of

rejection. These eyes are more prone for rejection.

- *Intraoperative factors:*

- *Large graft:* Graft is nearer to limbal vessels
- *Eccentric graft:* Proximity to limbal vessels
- *Small graft:* Less endothelial cell transferred
- *Iris adhesion at graft host junction:* Immune cells through iris vasculature get exposed to antigens
- *Recent anterior segment surgery:* Associated inflammation brings more immune cells
- Anterior vitrectomy
- Full thickness graft > lamellar graft

- *Postoperative factors*

- Corneal epithelial breach
- *Exposed suture knots, loose suture:* By inciting vascularization
- Postoperative uveitis
- Postoperative glaucoma
- Synechiae between iris and graft host junction.

Q.2. What are the measures you can take to prevent graft rejection?

Ans.

- *Preoperative measures:* Reducing the antigenic load of donor tissue.
 - Use the central corneal graft
 - Removal of the donor epithelium
 - Exposure to ultraviolet light
 - Depletion of local macrophages—subconjunctival injection of clodronate liposomes which alters delayed type hypersensitivity
 - Pretreatment of the graft with hyperbaric oxygen and use of heterologous antibody treated corneal button.
- *Intra-operative factors:* Meticulous surgical technique, including of avoiding decentration of the recipients bed cut, optimal suturing, and good graft-host apposition
- *Postoperative measures:* Controlling or alleviating the host immune response to the foreign donor tissue. Steroids are the best option for prophylaxis against graft rejection. Long-term (12-18 months) of

topical steroids have a better rejection free graft survival.

Q.3. What is a relation between corneal vascularity and graft rejection?

- Ans.**
- Low-risk—avascular
 - *Medium risk:* Vascularization 1–2 quadrants.
 - *High-risk:* Vascularization 3 or more quadrants.

Q.4. Graft rejection following endothelial keratoplasty.

- Ans.** Graft rejection in EK differs from rejection following PKP in following ways:
- Lower rates of rejection compared to cases with PKP probably due to the lower antigenic load.
 - The incidence of graft rejection is around 7.5%.
 - Rejection episodes are less severe with high rates of reversibility and low rates of graft failure
 - One-third of patients with graft rejection after endothelial keratoplasty are asymptomatic

- Presenting symptoms are minimal such as mild irritation, photophobia and rarely mild blurring of vision.

Q.5. Unusual manifestations of graft rejection.

- Ans.** Rarely acute graft rejection can present with following (without the characteristic presentation described in history section).
- Raised IOP due to engorgement and/or edema of TM
 - Acute epithelial defect along with ocular inflammation. This type of unusual presentation is usually seen in young patients.

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SHORT CASES

KERATOGLOBUS

Prafulla Kumar Maharana, Sapna Raghuvanshi, Namrata Sharma

INTRODUCTION

Keratoglobus is a rare noninflammatory corneal thinning disorder characterized by generalized thinning and globular protrusion of the cornea (**Fig. 1**). Nearly all cases are bilateral. The onset is often at birth with minimal or no progression. However, both congenital and acquired forms have been reported, and may be associated with various other ocular and systemic syndromes including the connective tissue disorders. In exams, it is given as a short case.

HISTORY

Chief Complaints

Patient may present with following complaints:

- Blurring of vision due to irregular astigmatism (most common presentation)
- Itching, watering (if associated with atopy, VKC)
- Corneal perforation, either spontaneous or following minimal trauma
- At times diagnosed incidentally and may be completely asymptomatic.



Fig. 1: Globular corneal protrusion and corneal thinning in a case of keratoglobus

Rarely a case may present with sudden loss of vision, pain, conjunctival injection, photophobia and glare, typically in cases of acute hydrops.

EXAMINATION

Systemic Examination

Keratoglobus can be associated with connective tissue disorders; hence, a thorough systemic examination must be carried out (especially look for blue sclera, joint hypermobility, skeletal abnormalities, hearing loss, abnormal dentition, high-arched palate). The diseases that have been reported to be associated with keratoglobus are described in **Table 1**.

Ocular Examination

The ocular examination includes following:

- *Eyeball:* Usually normal.
- *Eyelid:* Usually normal.
- *Conjunctiva:* Usually normal, however signs of VKC can be there.
- *Cornea:* Corneal thinning is characterized by the presence of limbus-to-limbus corneal thinning (**Fig. 2**) with globular corneal

Table 1 Associations of keratoglobus

Connective tissue disorders	<ul style="list-style-type: none"> • Ehlers-Danlos syndrome type VI • Marfan syndrome • Rubinstein-Taybi syndrome • Osteogenesis imperfecta
Hereditary ocular disorders	<ul style="list-style-type: none"> • Leber's congenital amaurosis • Posterior polymorphous dystrophy
Acquired ocular disorders	<ul style="list-style-type: none"> • Vernal keratoconjunctivitis • Chronic marginal blepharitis • Idiopathic orbital inflammation • Post-traumatic

protrusion (**Fig. 3**). Usually the thinning is greatest in the corneal periphery or mid-periphery initially but with progression, limbus-to-limbus thinning occurs.

Prominent folds and areas of thickening may be present in Descemet's membrane. Other corneal parameters, however, are normal, including a normal corneal diameter that is an important criterion in differentiating it from conditions such as buphthalmos.

Sclera: Usually scleral thinning or "blue sclera" is present, especially in association with connective tissue disorders and is most apparent over the ciliary body. It creates a "blue halo" around the limbus.

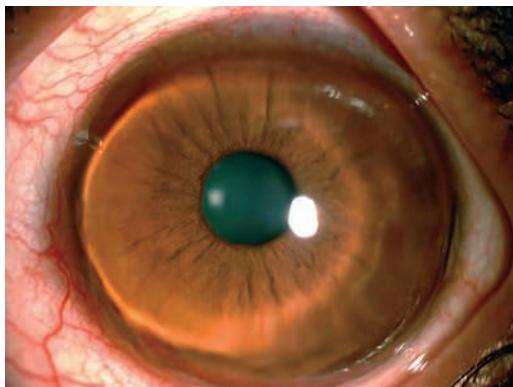


Fig. 2: Limbus-to-limbus corneal thinning

Anterior chamber: It is usually deep.

Iris/pupil/lens/fundus/IOP: All these findings are usually within normal limits. However, retinal changes of associated diseases such as Leber's congenital amaurosis may be there.

DIFFERENTIAL DIAGNOSIS

The differentiating features from other corneal ectatic disorders are summarized in **Table 2**. In addition, it must be differentiated from following:

Megalocornea

It is nonprogressive symmetric enlargement of the cornea (greater than 12 mm in horizontal diameter)

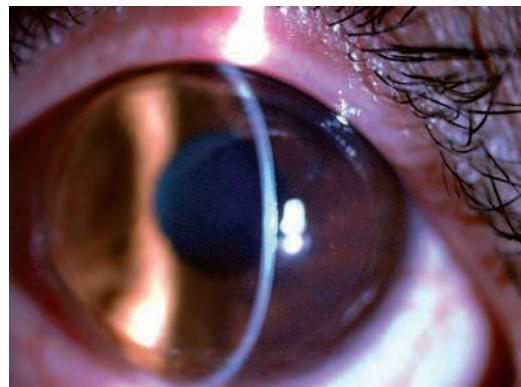


Fig. 3: Globular corneal protrusion with normal corneal diameter

Table 2 Differential diagnosis

Parameters	Keratoconus	Pellucid marginal degeneration	Keratoglobus	Terrien's marginal degeneration
Frequency	Most common	Less common	Rare	Less common
Laterality	Usually bilateral	Bilateral	Bilateral	Bilateral
Age at onset	Puberty	20–40 years	Usually at birth	20–40 years
Thinning	Inferior	Paracentral	Inferior band 1–2 mm wide, greatest in periphery	Usually starts superiorly then progress circumferentially
Protrusion	Thinning at apex	Superior to band of thinning	Generalized	
Iron line	Fleischer ring	Sometimes	None	None
Scarring	Common	Only after hydrops	Mild	Only after hydrops
Striae	Common	Sometimes	Sometimes	Sometimes

without a significant change in corneal thickness or contour unlike keratoglobus where corneal diameter is normal but thickness is reduced.

Congenital Glaucoma

It is associated with elevated intraocular pressure, a cloudy cornea, changes in the optic disc or generalized enlargement of the eye that are absent in keratoglobus.

INVESTIGATIONS

The diagnosis of keratoglobus is essentially a clinical one owing to the characteristic clinical findings. Following investigations are done in a case of keratoglobus if the diagnosis is doubtful and while planning treatment.

Ultrasonic Pachymetry

It would show reduced corneal thickness.

Corneal Topography (Orbscan/Videokeratography/Pentacam)

It shows diffuse thinning and irregular astigmatism with irregular power distribution. In advanced cases, it is often difficult to perform corneal topography.

MANAGEMENT

The management consists of following:

Conservative Management

Often the patient maintains a good visual acuity till late. Thus observation is the rule in early cases. These patients are advised to use protective eye wear (e.g. polycarbonate glasses), and avoidance of contact sports owing to the high risk of perforation. Visual rehabilitation is achieved through refractive correction for high myopia. Spectacles are normally used in early cases of keratoglobus only.

Table 3 Treatment options for keratoglobus

<i>Surgical procedure</i>	<i>Advantage</i>	<i>Disadvantage</i>
Large diameter (limbus-to-limbus) PKP	Covers the thinned part and suturing is easy	<ul style="list-style-type: none"> Increased rejection due to proximity of limbal vasculature Limbal stem cell damage Damage to Angle structure
Epikeratoplasty	<ul style="list-style-type: none"> Good tectonic stability Corneal flattening effect 	<ul style="list-style-type: none"> Limbal stem cell disruption Persistent epithelial defect
Epikeratoplasty with 360 host peripheral intrastromal tucking	<ul style="list-style-type: none"> No limbal stem cell disruption, No angle structure disruption 	Poor visual outcome due to interface opacities and intraepithelial cysts
Tuck-in lamellar keratoplasty	<ul style="list-style-type: none"> Good tectonic stability No limbal stem cell disruption No angle structure disruption 	<ul style="list-style-type: none"> Technically difficult Interface haze
Pentacam-based deep anterior LK	Advantages of lamellar graft	Technically demanding
Corneoscleral rim (Buttress over thinned corneal periphery for tectonic stability)	<ul style="list-style-type: none"> Technically easy Allows for delay in further surgical intervention 	Temporary measure
Epikeratoplasty/tectonic LK followed by 2nd stage PKP	Better visual outcome	<ul style="list-style-type: none"> Two stage procedure Two donor corneas required

Abbreviations: PKP, penetrating keratoplasty; LK, lamellar keratoplasty

As the disease progresses, irregular astigmatism develops and adequate visual acuity cannot be achieved with this type of visual correction.

Contact Lens

Various types of contact lenses (CL) are available for treatment of keratoglobus such as scleral lenses, rigid gas permeable (RGP) lenses, reverse geometry hydrogel lenses and large diameter inverse geometry RGP lenses.

Surgical Management

Surgery in keratoglobus is difficult because of following:

- Large graft is required to include the thinned periphery and large graft as such is a risk factor for graft rejection.
- Owing to the fragility of the thinned cornea at periphery placement of sutures is difficult and often leads to cut through or 'cheese-wire'.
- Proximity of the graft to limbus can lead to increased chance of graft rejection.

- Higher chance of perforation while performing lamellar graft due to limbus-to-limbus thinning. The various treatment options for keratoglobus are summarized in **Table 3.¹**

VIVA QUESTIONS

Q.1. Difference between congenital and acquired keratoglobus

Ans. Remember keratoglobus is almost always a congenital disease. Recently, it has been reported to be associated with few acquired diseases (**Table 1**). The acquired types are more severe with a higher chance of perforation from trivial trauma. Few authors consider these acquired forms as nothing but severe variants of keratoconus only.

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PELLUCID MARGINAL DEGENERATION

Sapna Raghuwanshi, Manpreet Kaur, Namrata Sharma

INTRODUCTION

Pellucid marginal corneal degeneration (PMCD) is a bilateral, peripheral corneal ectatic disorder characterized by a band of thinning 1–2 mm in diameter extending from 4 o'clock to 8 o'clock position in the inferior cornea. The area of thinning is separated from limbus by a 1–2 mm width of normal thickness cornea. Atypical cases can present with superior thinning or thinning beyond 4 o'clock to 8 o'clock hour, but these cases are rare. In exams, PMCD can be given as a short case.

HISTORY

Demography

The disease is almost always bilateral without any gender predilection. The onset is often between second to fifth decade of life.

Chief Complaints

Patient may present with following symptoms:

- Blurring of vision due to marked against-the-rule astigmatism (most common presentation)
- Frequent changes of glasses
- Rarely a case may present with sudden loss of vision, pain, conjunctival injection, photophobia and glare typically in cases of acute hydrops.

Past History

Past history of spectacle or contact lens (CL) use must be noted carefully.

EXAMINATION

Ocular Examination

Eyeball/eyelid/conjunctiva is usually within normal limits.

Cornea: On slit lamp biomicroscopy following signs may be present.

- **Corneal thinning:** A band of thinning 1–2 mm in width, typically in the inferior cornea, extending from the 4 o'clock to 8 o'clock position is present (**Figs 1 and 2**). Between the area of thinning and limbus there is usually a 1–2 mm width of cornea with normal thickness. Unlike Terrien's marginal degeneration, there is no scarring, lipid deposition, or vascularization.
- **Corneal protrusion:** The area of ectasia is just superior to the area of thinning (**Fig. 3**).

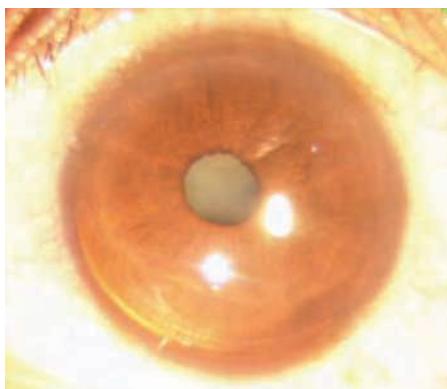


Fig. 1: Inferior corneal thinning extending from the 4 o'clock to 8 o'clock position

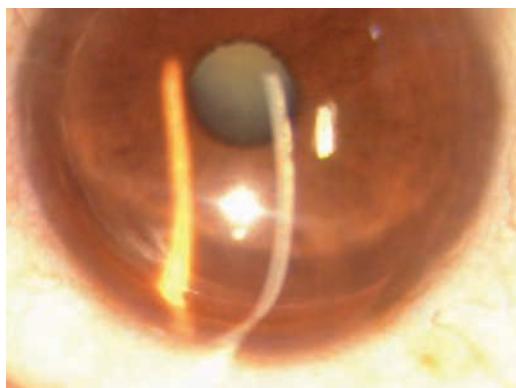


Fig. 2: Inferior corneal thinning extending from the 4 o'clock to 8 o'clock position with a 1–2 mm width of cornea with normal thickness between the area of thinning and limbus

Unlike keratoconus the protruding cornea is of normal thickness. When viewed from the side, the inferior-central cornea in PMD typically shows the side-profile contour of a "beer-belly".

- **Stromal scars:** Scarring can be present at the superior aspect of the thinned area and can extend into the mid stroma.
 - **Descemet's folds:** These are occasionally seen concentric to the inferior limbus, may disappear with external pressure.
 - **Bowman's layer:** It may be normal or focal disruption within the area of corneal thinning can be there.
 - In case of previous attack of hydrops, corneal scarring and vascularization of the inferior cornea can be seen.
- Other ocular findings are usually within normal limits.

DIFFERENTIAL DIAGNOSIS

A case of PMCD must be differentiated from peripheral corneal thinning disorders such as Terrien's marginal degeneration, Mooren's ulcer and Furrow degeneration. The differentiating features are summarized in **Table 1**. Advanced keratoconus and rarely keratoglobus can also be confused with PMCD. The differentiating features are summarized in **Table 2**.



Fig. 3: Corneal ectasia superior to area of thinning in PMD

Table 1 Differential diagnosis of pellucid marginal corneal degeneration

Features	<i>Pellucid marginal corneal degeneration</i>	<i>Terrien's marginal corneal degeneration</i>	<i>Mooren's ulcer</i>	<i>Senile Furrow degeneration</i>
Age at onset	Second to fifth decade	Middle-aged to elderly	Adult to elderly	Elderly
Laterality	Bilateral	Bilateral	Either	Bilateral
Gender	M = F	M > F	M > F	M = F
Astigmatism	Common	Common	Sometimes	Absent
Thinning	Inferior band 1–2 mm wide	Superior cornea	Starts within lid fissure	Occurs within arcus
Inflammation	Absent	May be present	Present	Absent
Epithelial defect	Absent	Usually absent	Present	Absent
Vascularization	Absent	Crosses area of thinning	Peripheral edge of thinning	Absent
Lipid deposition	Absent	Common; central to thinning	Rarely	Absent
Perforation	Can occur	Can occur	Can occur	Never

Abbreviations: M, male; F, female

Table 2 Differential diagnosis of pellucid marginal degeneration

Characteristics	<i>Keratoconus</i>	<i>PMD</i>	<i>Keratoglobus</i>
Frequency	Most common	Less common	Rare
Laterality	Usually bilateral	Bilateral	Bilateral
Age at onset	Puberty	20–40 years	Usually at birth
Thinning	Inferior paracentral	Inferior band 1–2 mm wide	Maximum in periphery
CCT	Reduced	Usually normal	May be normal
Protrusion	Thinnest at apex	Superior to band of thinning	Generalized
Rizzuti's phenomenon and Munson's sign	Present	Absent	Present
Fleischer ring	Present	Sometimes	None
Scarring	Common	Only after hydrops	Mild
Striae	Common	Sometimes	Sometimes

Abbreviations: PMD, pellucid marginal degeneration; TMD, Terrien's marginal degeneration

INVESTIGATIONS

Corneal Topography

Topography characteristically shows inferior peripheral steepening extending into the

mid-periphery, inferior oblique corneal meridians in a classic “crab-claw”, “butterfly” or “kissing doves” appearance. It shows the presence of superior flattening with against-the-rule astigmatism superiorly and with-the-rule astigmatism inferiorly.

MANAGEMENT

Spectacles: Spectacles are normally used in early cases of PMD only. As the disease progresses, irregular astigmatism develops and adequate visual acuity cannot be achieved with this type of visual correction.

Contact lens: Newer generation CL such as ROSE K, scleral lenses [Prosthetic Replacement of the Ocular Surface Ecosystem (PROSE) and Boston ocular surface prosthesis (BOSP)] and hybrid lenses (such as the Soft Perm-gas-permeable lens center and a hydrogel skirt) have shown promise in PMCD in early studies. These lenses offer improvements in the VA and good stability so they could be an option for patients who have failed conventional treatments before considering surgery.

Surgical Treatment

- **Large-diameter or eccentric penetrating keratoplasty:** A large diameter PKP is done so as to include the thinned out periphery. The problems with such grafts are an increased risk of rejection due to proximity to the limbus and severe postoperative astigmatism associated with a decentered graft.
- **Combined lamellar keratoplasty (LK) with penetrating keratoplasty (PKP):** LK with PKP can be done in the same setting or as a two-stage procedure (LK followed by PKP 6 months later). The large diameter lamellar graft provides the tectonic support to the weakened peripheral host cornea while a central small diameter full thickness graft can provide excellent visual outcome.
- **Crescentic lamellar keratoplasty:** A 'match and patch' lamellar graft procedure is done. Precise lamellar dissection of the recipient bed is done to achieve vertical margins and an even stromal bed depth. A lamellar donor undersized by 0.25–0.5 mm is then sutured to the recipient bed that results in flattening and reduction of ectasia.
- **Crescentic or wedge excision:** This technique is useful when the ectasia is confined to a small sector of periphery. It has several advantages over a corneal graft such as; preservation of

normal central cornea, no risk of rejection or interface haze, better wound strength, and shorter visual rehabilitation period. However, postoperative unstable astigmatism is an issue due to persistent tension at the sutured wound. Various modifications have been described to improve the outcome of wedge resection, such as wedge resection followed by complete (limbus-to-limbus) or partial host lamellar dissection and corneal wedge resection combined with paired, opposed clear corneal penetrating relaxing incisions. The relaxing incisions prevent the astigmatic drift seen following wedge resection.

VIVA QUESTIONS

Q.1. How to differentiate between keratoconus and PMCD

Ans. Kindly see Table 1.

Q.2. How to differentiate between PMCD and TMCD

Ans. Kindly see Table 2.

Q.3. What are the difficulties in performing PKP in PMCD?

Ans. There challenges in performing PKP cases of PMCD are as follows:

- Due to involvement of paracentral and peripheral cornea a large graft with increased proximity to limbus is required that increases the chances of graft rejection.
- Extreme corneal thinning makes suturing difficult and increases the chances of intraoperative DM perforation.

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BAND-SHAPED KERATOPATHY

Manpreet Kaur, Sapna Raghuvanshi, Ritu Nagpal

INTRODUCTION

Band shaped keratopathy (BSK) is a slowly progressive, usually painless, corneal degeneration characterized by deposition of calcium across the cornea at the level of Bowman's membrane, epithelial basement membrane and stroma. BSK is divided into two forms calcific and non-calcific form.

Its examination is especially important as it is given as short case in examination.

CHIEF COMPLAINT

Patients present with following complaints:

Early stage: Usually asymptomatic

Late stage: May present with the following symptoms:

- Blurring of vision
- Foreign body sensation
- Tearing
- Photophobia.

PAST HISTORY

BSK may be associated with several diseases, (**Table 1**) hence a thorough history must be taken to rule out these disorders.

EXAMINATION

Systemic Examination

A careful systemic examination is carried out to rule out any systemic association (*see Table 1*).

Ocular Examination

Eye ball: It is usually normal. Blepharophimosis may be present in cases of epithelial erosion or elevated nodules associated with inflammation.

Eyelid: Lid edema may be present if BSK is associated with ocular inflammation.

Conjunctiva: It may be normal or signs of previous disease may be present. Ciliary as well as conjunctival congestion can be there in presence of epithelial defect.

Cornea: On slit lamp examination following signs must be noted.

- Most of the times the opacity begins in the form of peripheral interpalpebral calcification at the 3 and 9 o'clock positions (**Fig. 1**).
- In the peripheral form, sharply demarcated peripheral edge of the opacities separated from the limbus by a lucent zone is seen. This zone is either due to the lack of Bowman's

Table 1 Associations of band shaped keratopathy

Ocular disease	Hypercalcemia	Systemic diseases	Chemicals	Familial
<ul style="list-style-type: none"> • Chronic uveitis • Phthisis bulbi • Long-standing glaucoma • Interstitial keratitis • Dry eye and corneal exposure syndromes • Spheroidal keratopathy • Keratoprosthesis • Trachoma • Viscoelastics 	<ul style="list-style-type: none"> • Hyperparathyroidism • Hypophosphatasia • Sarcoidosis • Renal failure (e.g. Fanconi's syndrome) • Excessive vitamin D (e.g. oral intake, sarcoidosis, and osteoporosis) • Multiple myeloma • Milk alkali syndrome • Metastatic carcinoma to bone • Idiopathic • Paget's disease 	<ul style="list-style-type: none"> • Discoid lupus • Gout • Tuberous sclerosis • Norrie's disease • Congenital band keratopathy • Still's disease • Uremia 	<ul style="list-style-type: none"> • Mercury fumes • Phosphate containing drops • Intraocular silicone oil • Viscoelastic • Thiazides • Lithium • Vitamin D toxicity 	<ul style="list-style-type: none"> • Fanconi's disease • Ichthyosis • CHED

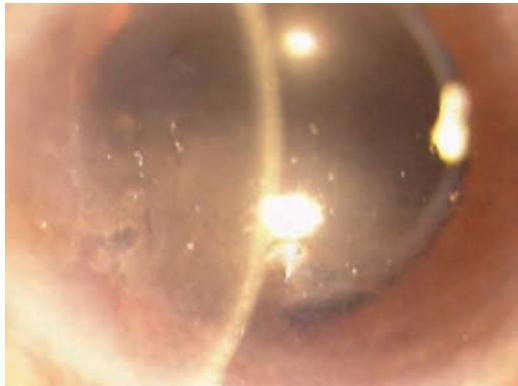


Fig. 1: Interpelbral calcification

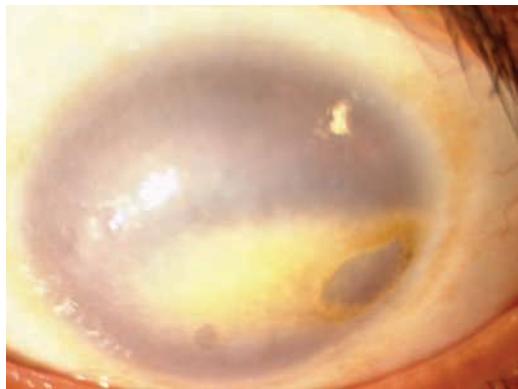


Fig. 2: BSK in CHED

layer at the periphery or from the buffering capacity of the limbal vessels, which prevent precipitation of calcium.

- In chronic ocular inflammation, the band may start centrally.
- Gradual central spread to form a complete limbus-to-limbus band like chalky plaque containing the small lucent holes representing penetrating corneal nerves is seen in late stage.
- Advanced lesion may become nodular and elevated which may lead to epithelial breakdown (**Fig. 2**).

Iris: Festooned pupil, muddy iris, and posterior synechiae may be present in case of uveitis.

Anterior chamber: Emulsified silicon oil may be present in anterior chamber.

Lens: Complicated cataract may be present in case of uveitis.

Other findings are usually within normal limits.

INVESTIGATION

Following investigations should be done in BSK to rule out underlying systemic disorders that affect the calcium homeostasis:

- Serum calcium
- Serum phosphorus
- Serum uric acid
- Renal function measurements
- Parathyroid hormone (PTH)
- Angiotensin-converting enzyme (ACE) levels.

MANAGEMENT

The most important part is to recognize and treat the underlying causes. The indications for corneal intervention in a case of BSK are:

- Central band keratopathy contributing to reduced vision
- Mechanical irritation because of calcific deposits causing discomfort and foreign-body sensation.

Following are the surgical options for BSK:

- Mechanical debridement:* If calcium plaque is thick, it is scraped off the cornea with forceps.
- Superficial keratectomy:* Superficial calcium is scraped off the corneal surface with a no. 15 scalpel blade until a sufficiently clear cornea can be observed.
- Chelation:* After application of topical anesthesia and placement of an eyelid speculum, all the epithelium overlying the calcium deposits is removed with a sponge or a no. 15 blade to allow penetration of the EDTA. EDTA (0.05 mol/L) is applied to the subepithelial calcification by surgical sponges or directly using a corneal trephine as a well. The chemical reaction takes several minutes to occur (5–30 minutes depending on the severity). Then all of the calcium can be removed using blunt dissection with cellulose sponges or with gentle scraping using a blunt spatula.
- Phototherapeutic keratectomy (PTK):* The basic steps of PTK include removal of corneal epithelium with hockey stick spatula; ablation

of superficial corneal tissue with excimer laser and placement of bandage contact lens. The complications of PTK include hyperopic shift, corneal haze, glare and myopic shift.

- *Anterior lamellar keratoplasty (ALK)*: When the opacities extend into deeper stroma and the visual potential is good, ALK is performed. Visual prognosis is generally good after ALK.
- *Amniotic membrane transplantation (AMT)*: AMT is used as an adjunct to augment conventional surgical and chemical removal of band keratopathy by replacing the damaged basement membrane. It facilitates healing and provides long-term stability to the corneal epithelium.

VIVA QUESTIONS

Q.1 What is Still's syndrome?

Ans. Still's disease is also known as systemic-onset juvenile idiopathic arthritis. Still's triad consists of complicated cataract, glaucoma and BSK. It is characterized by high spiking fevers, salmon-colored rash that comes and goes, and arthritis and hepatosplenomegaly.

Q.2 Pathogenesis of BSK.

Ans. Following mechanism are involved in the deposition of calcium in cornea:

- Corneal exposure-calcium deposition occurs primarily in the exposed part of cornea due to precipitation left as tears evaporate.
- Alteration of tear film osmolarity.
- Elevation of pH due to corneal tissue metabolism.
- Increase in concentration of calcium and phosphate.

Q.3 Histopathology of BSK.

Ans. Calcium is deposited as the hydroxyapatite salt in the epithelial basement membrane, basal epithelium, and Bowman's membrane. The deposits are usually extracellular, although hypercalcemia may cause intracellular epithelial accumulation.

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SPHEROIDAL DEGENERATION

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INTRODUCTION

Spheroidal degeneration (SD) is a corneal degeneration characterized by the appearance in the cornea, and sometimes in the conjunctiva, of translucent, golden brown, spheroid deposits in the superficial stroma. It is known by many different names including Bietti's nodular corneal degeneration, Labrador keratopathy, climatic droplet keratopathy, degeneratio cornea sphae-rularis elaioides, corneal elastosis, fisherman's keratitis, keratinoid corneal degeneration, and chronic actinic keratopathy. Spheroidal degeneration and climatic droplet keratopathy (CDK) are the most commonly used terms.

HISTORY

Epidemiology/Demography

SD is commonly seen in cases associated with high UV exposure and/or reflected light such as observed in desert, ocean and snow-covered regions. Thus, it is more common in males and persons involved in outdoor activities. It is a disease of elderly and the incidence rises with age.

Chief Complaints

The presenting feature depends upon the severity of the disease:

- *Grade 1 (nodules in periphery)*: Usually asymptomatic (diagnosed incidentally during routine corneal examination)

- *Grade 2 (nodules encroaching pupillary axis):* Blurring of vision (6/30)
- *Grade 3 (involvement of visual axis):* Blurring of vision (<6/60)
- *Grade 4 (raised elevated nodules):* Pain, photophobia, redness, foreign body sensation. CDK is slowly progressive, painless, asymmetric, may be unilateral or bilateral and is more common in males.

Past History

A careful past history can identify the predisposing factor. Most cases are idiopathic and following are the risk factors for secondary spheroidal degeneration.

- Ultraviolet light exposure
- Drying of the cornea and repeated corneal trauma
- Corneal scars after keratitis, trachomatous keratopathy or trauma
- Lattice corneal dystrophy
- Glaucoma
- Microtrauma including sand, dust, wind, and drying
- Herpes keratopathy.

EXAMINATION

Systemic Examination

One must look for chronic signs of sun damage on the skin in addition to routine systemic examination.

Ocular Examination

Eye ball: It is usually normal.

Eyelid: If it is associated with inflammation, lid edema may be present. Features of associated disease such as trichiasis (trachoma) may also be there.

Conjunctiva: Signs of chronic sun exposure such as keratinization, pigmentation, pinguecula, or pterygium can be there. In addition, findings of related disease such as conjunctival scar, herbert's pits must be looked for. If the nodules involve the conjunctiva (type 3), clear to yellow-gold spherules are seen interpalpebrally in the 3 o'clock and 9 o'clock positions. The spherules are generally smaller and less numerous. They may be found in

association with pinguecula. The spherules darken with age, progressing from a lighter yellow to a brownish-yellow color.

Cornea: On slit lamp biomicroscopy following signs must be noted.

- Clear to yellow-gold spherules seen in the subepithelium, within Bowman's, or in the superficial corneal stroma. The droplets appear oily (**Fig. 1**).
- Initially the spherules appear at the limbus in the interpalpebral zone at 3 o'clock and 9 o'clock. Following grades of the primary form have been noted:
 - *Grade I:* Initially SD begins as a gray haze in the superficial cornea, close to the nasal and temporal margins of the cornea but usually separated from them by a clear zone. On retroillumination, the haze can be resolved into small gray deposits, which look like 'droplets' immediately beneath the epithelium. The deposits are restricted to a nasal and temporal strip in each cornea but must be present at both margins of the corneas.
 - *Grade II:* As the disease progresses, the deposits extend towards central cornea into the optical axis. The disease is restricted to the interpalpebral area of cornea.
 - *Grade III:* Characterized by central involvement over the pupil, sufficiently dense to reduce vision to any degree. In this stage, exposed band of the cornea appears as ground glass.

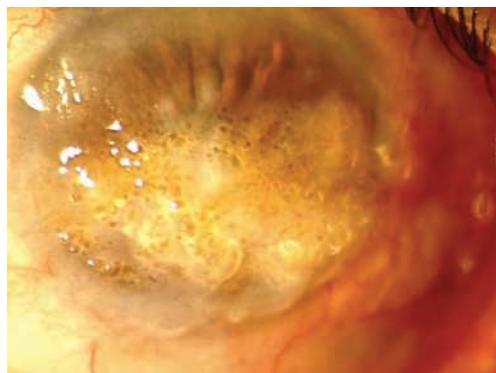


Fig. 1: Yellow-gold spherules in spheroidal degeneration



Fig. 2: Coalescence of droplets to form corneal nodules

- **Grade IV:** In this stage, the droplets coalesce to form large corneal nodules (**Fig. 2**). These nodules may cause corneal epithelial defect.
- In type 2, the spherules may be diffuse or begin centrally. There can be associated corneal scarring and neovascularization. A clear interval is observed between the spherules and neovascularization.

Sclera/Anterior chamber/Iris: All these structures are usually within normal limits.

Lens: Since the age groups as well as the risk factors are similar to that of senile cataract, these cases are often associated with cataract.

Fundus: The fundus may be normal or signs of age related macular degeneration may be seen.

In addition, careful examination must be done to rule out any complication such as:

- Sterile ulceration, descemetocoele or perforation
- Corneal scar, macular or leucomatous
- Recurrent corneal epithelial defect.

CLASSIFICATION

CDK is classified into three basic types:

1. **Type 1 or primary form:** It is usually bilateral, not associated with other ocular pathology.
2. **Type 2 or secondary spheroidal degeneration:** it may be unilateral or bilateral and is associated with other ocular pathology.

3. **Type 3:** It is usually bilateral, involves the conjunctiva too and may be associated with types 1.

MANAGEMENT

The management of CDK includes following:

Medical Management

It consists of artificial tear substitute, both in the form of drops and ointments. In presence of inflammation, topical steroid can be added. Central nodules with recurrent erosion can benefit from application of bandaged contact lens (BCL).

Surgical Management

The surgical management consists of following options:

Conjunctival lesions: These nodules can be directly excised.

Central corneal lesions: These lesions can be managed in following ways:

- **Superficial keratectomy with or without amniotic membrane grafting (AMG):** Superficial keratectomy can be done using a simple no. 15 blade or a crescent knife. After keratectomy, a BCL is placed until the epithelium heals. Application of AMG improves healing, decreases scarring and vascularization.
- **Excimer laser phototherapeutic keratectomy (PTK):** If the nodules cannot be removed completely by superficial keratectomy or surface irregularity persists after keratectomy than PTK has to be done. PTK is useful only for lesions extending up to 100 µm depth. Preoperative corneal thickness must be done before proceeding with PTK. Postoperative corneal haze and hyperopic shift are the major complications associated with PTK.
- **Lamellar keratoplasty (LK)/anterior lamellar therapeutic keratoplasty (ALTK):** LK is done in cases where there is corneal scar and visual potential is good.
- **Penetrating keratoplasty:** Penetrating keratoplasty is rarely required in cases of CDK.

VIVA QUESTIONS

Q.1. Histopathology of spheroidal degeneration.

Ans. In spheroidal degeneration deposits appear as extracellular mauve colored amorphous globules, which may coalesce to form larger masses in Bowman's membrane. The globules are often confluent. These globules are made up of a protein material with elastotic features. Histopathology—It is very easy to confuse these globules with calcification especially when they are in the cornea near Bowman's layer. However,

careful examination shows that they lack the granular quality and deep purple color of calcium crystals but rather are amorphous centrally homogeneous deposits.

Q.2. What are the other names of spheroidal degeneration?

Ans. Already given in introduction section.

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CONGENITAL HEREDITARY ENDOTHELIAL DYSTROPHY

Prafulla Kumar Maharana, Vaishali Ghanshyam Rai, Manpreet Kaur

INTRODUCTION

Congenital hereditary endothelial dystrophy (CHED) is a corneal endothelial dystrophy. CHED is a disorder characterized by bilateral, symmetric, noninflammatory corneal clouding that is usually present at birth. There are two main forms, CHED 1 and CHED2, the latter being more severe.

It is given as short case in postgraduate/DNB/Diploma examination.

HISTORY

Chief Complaints

Presenting complaints depend on the type of CHED.

Child's parents present with the following complaints.

CHED 1

- Corneal clouding
- Photophobia
- Tearing
- Blurring of vision.

CHED 2

- Nystagmus
- Blurring of vision.

Age at onset is extremely important. Both types are usually bilateral, symmetric, slowly progressive, but they differ in their age at onset. While CHED 1 is usually evident in the 1st decade (*first year or in the second year of life*) CHED 2 is usually evident *at birth or within the early postnatal period*. Also presence of nystagmus almost always suggests CHED 2.

EXAMINATION

Systemic Examination

A complete examination is a must, preferably by a pediatrician.

Ocular Examination

Visual acuity: Often difficult to record, preferential looking test should be performed whenever possible.

Eye ball: Usually the size of eyeball is normal but if it is associated with glaucoma then size of eyeball is increased.

Eyelid: Usually normal. In presence of corneal edema blepharophimosis may be there.

Conjunctiva: Usually normal but if it is associated with glaucoma then congestion may be present.

Cornea: On slit lamp biomicroscopy following signs may be present.

- Initially corneal clouding is seen (**Fig. 1**)
 - Diffuse gray-blue ground-glass appearance of cornea (**Fig. 2**). The corneal opacification extends to the limbus without any clear zones.
 - Corneal thickness is increased *two to three times than normal* and often greater than 1 mm centrally (**Fig. 3**).
 - Epithelial surface is irregular.
 - Discrete white dots may also be seen in the stroma.
 - In some areas where stromal opacification is less dense, Descemet's membrane appears gray and on specular reflection may have a *peau d'orange* texture.
 - A fine corneal pannus may be seen.
- Other ocular findings are usually within normal limits.



Fig. 1: Corneal clouding in CHED



Fig. 2: Diffuse gray-blue ground-glass appearance of cornea in CHED

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of both types of CHED are summarized below:

CHED1

- PPCD
- FECD
- Iridocorneal endothelial syndrome.

CHED2

- Congenital glaucoma
- Congenital rubella
- Forceps injury
- Peters' anomaly
- Mucopolysaccharidoses
- Congenital rubella.

Mucopolysaccharidoses: Following features differentiate it from CHED.

- Corneal clouding is not present at birth and usually develops within the first few years of life
- Cornea is not thickened
- Systemic stigmata of MPS are typically present. A urinalysis or corneal biopsy will usually identify the abnormal metabolic product to confirm the diagnosis.

Congenital glaucoma:

- Increased intraocular pressure in glaucoma
 - Increase in corneal diameter
 - Haab's striae
 - Buphthalmos
- All these features are absent in CHED.

Congenital rubella: In contrast to CHED, there is episcleral injection, nuclear cataract, raised IOP, posterior synechiae, miosis, chorioretinopathy.

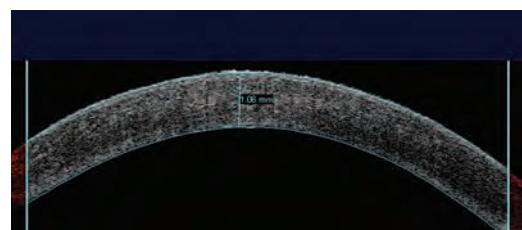


Fig. 3: Increased corneal thickness (>1 mm) in CHED

Forceps injury: Edema is transient, localized, overlying the break in Descemet's membrane and unilateral in contrast to CHED. A double linear scar in Descemet's membrane at the rupture edges can be seen once the edema resolves.

Peters anomaly: Other associated anterior segment abnormalities would be there.

Congenital hereditary stromal dystrophy (CHSD):

- Normal corneal thickness
- No edema but opacity that is full-thickness with feathery clouding of the stroma.

PPCD, ICE and early-onset FECD: Especially when the patient presents late; the differentiating features are summarized in **Table 1**.

INVESTIGATIONS

- *VER:* For visual potential assessment.
- *Pachymetry:* Corneal thickness increases 2–3 times.
- *Ultrasonography:* For posterior segment evaluation.
- *Specular/Confocal:* Difficult to perform.

MANAGEMENT

• **Penetrating keratoplasty (Fig. 4):**

- Success rate 40–75%

- Later the onset better the prognosis
- Most commonly done procedure.

- *Descemet-stripping automated endothelial keratoplasty (DSAEK) (Fig. 5):*

Compared to PK, DSEK offers the advantage of:

- Faster visual recovery
- No risk of complications of open globe surgery such as expulsive hemorrhage
- Less corneal astigmatism, less aberration
- Relatively less chance of graft rejection (although controversial)
- Preservation of corneal tectonic stability.

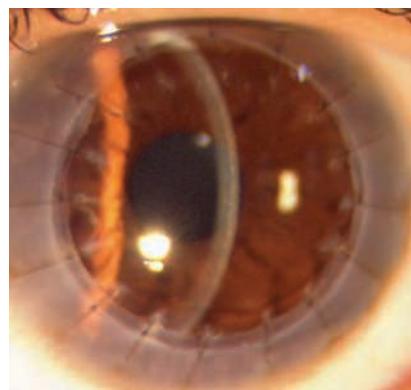


Fig. 4: Penetrating keratoplasty in CHED

Table 1 Differences between PPCD, ICE, FECD and CHED

Parameters	PPCD	FECD	CHED 1	ICE
Onset	Teens to 20s	40–50, early onset in 1st–3rd decade	1st decade	Young adults
Hereditary	AD	AD	AD	No
Corneal findings	Vesicles bands Diffuse opacities Corneal steepening (rare)	Guttae Stromal thickening Epithelial edema Subepithelial fibrosis	Marked corneal thickening and opacification	Fine, guttae-like changes, hammered silver appearance
Other ocular abnormalities	Broad peripheral synechiae	Narrow angles	–	Glaucoma Iris atrophy/corectopia
Specular microscopy	Vesicles, bands, mosaic Endothelial cells usually enlarged but count may be normal	Polymorphism Polymegathism Decreased endothelial cell count	Often not possible	Diffuse changes, ICE cell

Abbreviations: PPCD, posterior polymorphous corneal dystrophy; FECD, Fuchs endothelial corneal dystrophy; CHED 1, congenital hereditary endothelial dystrophy; ICE, iridocorneal endothelial dystrophy; AD, autosomal dominant.

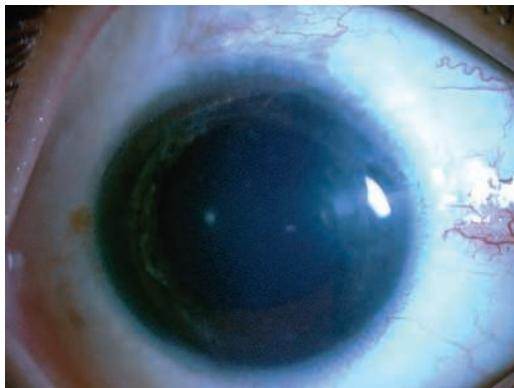


Fig. 5: Descemet Stripping Automated Endothelial Keratoplasty (DSAEK) in CHED

Disadvantage:

- Poor visibility
- Risk of clear lens damage in phakic eye
- DM scoring is difficult.

If patients maintain good fixation with normal alignment, surgery may be delayed; loss of fixation or development of nystagmus should lead to prompt intervention.

- *CHED associated with glaucoma:*

- Trabeculotomy
- Combined trabeculectomy with trabeculectomy
- Combined trabeculectomy with trabeculectomy with subconjunctival collagen matrix.

VIVA QUESTIONS

Q.1. Pathogenesis

Ans. Mutations in the SLC4A11 (solute carrier family 4, sodium borate transporter, member 11) gene is seen in CHED2 which encodes a membrane-bound sodium borate cotransporter. The transporter regulates intracellular boron concentration regulate the growth and terminal differentiation of neural crest cells. Loss of function of this transporter may affect the normal restrictive pattern of corneal endothelial synthesis and secretion that leads to failure of growth regulation during the terminal differentiation and reorganization of the

Table 2 Difference between CHED type-1 and 2

Parameters	CHED1	CHED2
Inheritance	AD	AR
Gene	20p11.2-q11.2	20p13-12, SLC4A11 gene
Corneal clouding	First decade (Initial few years of life)	At birth (First week to 6 months)
Nystagmus	Absent	Present
Amblyopia	Absent	Present
Photophobia and tearing	More common	Less common
Subepithelial fibrosis with some calcification	More common	Less common
Spheroidal degeneration	More common	Less common

Abbreviations: CHED, congenital hereditary endothelial dystrophy; AD, autosomal dominant; AR, autosomal recessive.

endothelium. Subsequent endothelial cell death may lead to loss of barrier function and progressive corneal edema.

Q.2. Complication of CHED.

Ans. • Subepithelial fibrosis/corneal pannus
• Amblyopia
• Glaucoma
• BSK

Q.3. What is Harboyan syndrome?

Ans. It is an autosomal recessive disease with CHED 2 and sensorineural deafness (CDPD).

Q.4. What is the difference between CHED 1 and CHED 2?

Ans. See Table 2.

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IRIDOCORNEAL ENDOTHELIAL SYNDROME

Vaishali Ghanshyam Rai, Neelima Aron, Prafulla Kumar Maharana

INTRODUCTION

The iridocorneal endothelial (ICE) syndrome describes a group of disorders characterized by abnormal corneal endothelium that is responsible for variable degrees of iris atrophy, secondary angle-closure glaucoma in association with characteristic peripheral anterior synechiae (PAS), and corneal edema. It can be given as a short case in postgraduate exams.

The following three clinical variations within the ICE syndrome have been distinguished primarily on the basis of changes in the iris (**Table 1**).

1. Progressive essential iris atrophy.
2. Chandler syndrome.
3. Cogan-Reese syndrome.

HISTORY

Epidemiology/Demography

The syndrome affects individuals between 20 and 50 years of age. It occurs more often in women and is almost always unilateral. Glaucoma is present in approximately half of all cases.

Chief Complaints

ICE can present in following ways:

- Most common presentation is unilateral pain and DOV which may be worse in the morning and improves later in the day.

- In the advanced stages of the syndrome, symptoms of blurred vision and pain may persist throughout the day.
- Patients also may present with a chief complaint of an irregular shape or position of the pupil (corectopia), or they may describe a dark spot in the eye.

EXAMINATION

Cornea

- Corneal edema (**Fig. 1**) with abnormal corneal endothelium may be seen on specular reflection.



Fig. 1: Corneal edema in ICE

Table 1 Iridocorneal endothelial syndrome: Variants¹

Parameters	Progressive (essential) iris atrophy	Chandler's syndrome	Cogan-Reese syndrome
Corneal endothelium abnormal (slit lamp or specular microscopy)	Yes, may be subclinical	Yes	Yes
Corneal edema	Variable–late	Present–early	Present
Peripheral anterior synechiae beyond Schwalbe's line	Present	Present	Present
Iris surface change	Present	Present	Present
Iris atrophy	Marked	Minimal	Variable
Iris nodules	Appears late	Appears late	Appears early
Ectropion uveae	Present	Rare	Present
Glaucoma	Present	Present	Present

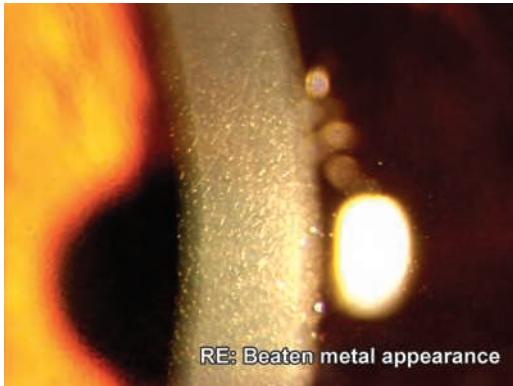


Fig. 2: Hammered-silver appearance on posterior surface of cornea

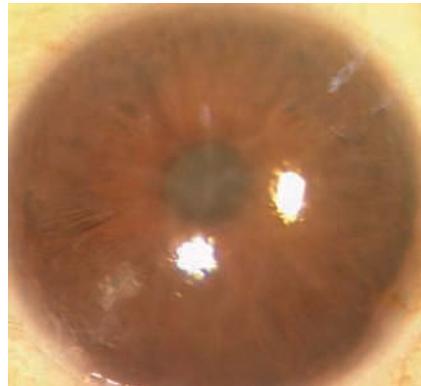


Fig. 3: Iris atrophy in ICE

- A fine hammered-silver or beaten metal appearance on posterior surface of cornea (Fig. 2) can be seen, similar to that of Fuchs' dystrophy.

Iris

- *Chandler syndrome* usually presents with corneal edema and minimal iris alterations like iris stromal atrophy (Fig. 3) and corectopia.
- *Progressive iris atrophy* is characterized by marked atrophy of the iris, associated with variable degrees of corectopia and ectropion uveae. The hallmark of progressive iris atrophy is hole formation in the iris, which occurs in two forms: stretch holes and melting holes.
- *Cogan-Reese syndrome* is characterized by any degree of iris atrophy, but the predominant feature is the presence of multiple, pigmented, pedunculated *iris nodules*.

IOP

In early stage, IOP may be in normal range with minimal corneal edema. But in late stage, high IOP with marked corneal edema can be noted.

Gonioscopy

Peripheral anterior synechia (PAS) on gonioscopy, usually extending to or beyond Schwalbe's line, is another clinical feature common to all variations of the ICE syndrome.

Other ocular structures are usually within normal limits.

DIFFERENTIAL DIAGNOSIS

Corneal Disorders

The two main differential diagnoses for corneal endothelial disorders are posterior polymorphous dystrophy (PPMD) and Fuchs endothelial dystrophy (Refer **Table 1**).

- *PPMD* is a bilateral disorder with autosomal dominant inheritance. Specular microscopic findings are different in two entities.
- *Fuchs endothelial dystrophy* does not have the anterior chamber angle or iris features seen in ICE syndrome. Specular microscopic findings are similar in both conditions.

Iris Disorders

Iris disorders that could be confused with ICE syndrome include Axenfeld-Rieger syndrome, aniridia and iris melanosis.

- *Axenfeld-Rieger syndrome* has clinical and histopathologic similarities to ICE syndrome but differs in being *bilateral* and *congenital*. The iris and angle alterations in Axenfeld-Rieger syndrome are due to retention and contraction of a primordial endothelial layer, whereas changes in ICE syndrome are secondary to migration and subsequent contraction of abnormal corneal endothelial cells.
- *Aniridia* is usually bilateral and congenital absence of the iris tissue.

- Iris melanosis* should be differentiated from Cogan-Reese syndrome. Iris melanosis is typically bilateral and familial. Glaucoma is uncommon.

INVESTIGATIONS

Specular Biomicroscopy

- Specular microscopic appearance of corneal endothelial cells in the ICE syndrome demonstrates the pleomorphism in size and shape, dark areas within the cells, and loss of clear hexagonal margins.
- Endothelial changes studied by specular microscopy are typical: in early stages, a rounding off of cell angles and intracellular blackout areas can be seen; in former stages, black out areas increase and there is a disruption of the regular mosaic.
- Fellow eye specular microscopy is important, which is normal in ICE syndrome whereas abnormal or similar to other eye in Fuchs dystrophy.
- Less role in ICE syndrome with marked corneal edema.
- ICE cells—in which the hexagonal borders are lost, a light or dark area is seen within, and reversal of the usual normal light/dark pattern occurs. Although it is characteristic but not necessary for the diagnosis.

Pachymetry

Increased central corneal thickness (CCT) in involved eye due to corneal edema whereas normal in fellow eye.

Confocal Microscopy

- Important diagnostic tool in case of corneal edema to study corneal endothelium morphology.
- Confocal microscopy may be used to diagnose the ICE syndrome by demonstrating epithelial-like endothelial cells with hyperreflective nuclei. Normal in fellow eye.

TREATMENT

- Medical treatment:* Aqueous suppressant medications are effective in controlling the IOP. Corneal edema may often be controlled using hypertonic saline solutions.
- Surgical treatment:* If the IOP level remains uncontrolled despite medical treatment, filtration surgery is indicated.

VIVA QUESTIONS

Q.1. Clinical variants of ICE.

Ans. See Table 1

Q.2. What is an ICE cell?

Ans. The endothelial mosaic, on specular microscopy, may contain a typical ICE cell in which the hexagonal borders are lost, a light or dark area is seen within, and reversal of the usual normal light/dark pattern occurs. Oval dark and light bodies within cell boundaries and smaller round structures with either a bright or dark appearance near cell centers are thought to be endothelial cell nuclei and blebs of the apical cell membrane. Epithelialization of the endothelial cells are thought to be the histological correlate of the ICE cell seen on specular microscopy. These cells are usually seen in Chandler's syndrome.

Q.3. What is Iris nevus syndrome?

Ans. It is considered to be a variant of Cogan-Reese syndrome. It is characterized by loss of surface architecture of the iris resulting in a matted appearance, ectropion uvea, heterochromia, PAS, corneal edema, and unilateral glaucoma.

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PETERS' ANOMALY

Shipra Singh, Neelima Aron, Manpreet Kaur

INTRODUCTION

Peters' anomaly is a developmental abnormality of the cornea, usually present at birth and is characterized by a central white opacity (leukoma) with a lucent periphery. Most cases are sporadic and bilateral in 80% of cases. It is associated with glaucoma, presumably due to abnormal development of aqueous humor drainage structures. Approximately 50–70% of the patients with Peters' anomaly will develop glaucoma, which is frequently present at birth.

In exams, it can be given as a short case.

HISTORY

Chief Complaints

- Parents may complain of unilateral or bilateral white opacity or hazy eyes of the child since birth.
- Photosensitivity or lacrimation since birth may be there.
- Infant with cardiac disease or neurological anomaly may be referred by Pediatrician to ophthalmologist to rule out Peters' anomaly (Peters' plus syndrome).

Perinatal History

A detailed antenatal history, history of delayed development milestones and history of cardiac disease, central nervous system anomalies or deafness should be asked as there are many systemic associations with Peters' anomaly.

History of Present Illness

Corneal edema may be present early in the course of the disease and may persist or recur in the face of elevated intraocular pressure. The edema may progressively resolve as peripheral endothelial cells migrate over the posterior defect, leaving an overlying corneal scar. Corneal edema may recur later in life secondary to the natural attrition of already compromised endothelial cells. Glaucoma develops in approximately 50–70% of patients and

can present at any time. However, most commonly it develops soon after birth.

EXAMINATION

General Examination

Detailed systemic examination of a child is required to rule out any cardiac disease, central nervous system anomaly, deafness or delayed development. Peters' plus syndrome refers to patients with Peters' anomaly associated with cleft lip and palate, short stature, abnormal ears, and mental retardation. General examination must be done carefully to rule out all these associations.

Ocular Examination

Most of the time the examination has to be done under general anesthesia.

Visual acuity: Child may have poor fixation to light and may resist occlusion of better eye.

Eye ball: Microphthalmos is common with Peters' anomaly.

Cornea: Following findings can be there:

- Bilateral central leukomatous corneal opacity with lucent periphery is characteristic. Look for central or paracentral corneal edema or central or paracentral corneal opacity with a lucent periphery. The size and density of the central defect is variable. It can range from a small, faint opacity to a dense leukoma precluding visualization of the anterior chamber.
- Anterior chamber:** AC depth may be shallow or irregular.
- Iris:** Iris strands arising from collarette attached to periphery of corneal opacity is an important sign. Iris coloboma can be seen.
- Lens:** Look for lenticular adhesion to posterior corneal surface which is a sign of type II Peters' anomaly. Look for presence of cataract that is frequently seen in cases of Peters' anomaly. Cataract can be from a primary lens anomaly or due to a secondary change as the lens is

pushed forward against the cornea. The lens may touch or be adherent to the cornea, but can also be in its normal position and yet be cataractous.

Gonioscopy: Using direct gonioscopy look for peripheral anterior synechiae or angle anomalies which is the main cause of glaucoma in Peters' anomaly.

IOP: Raised IOP may be there when associated glaucoma is there. Glaucoma is seen in 50–70% of the cases. Glaucoma in PA can appear at any age but it is most commonly seen soon after birth.

Posterior segment: Look for choroidal coloboma, persistent hyperplastic primary vitreous, and optic nerve hypoplasia which can be seen in cases of PA, although rarely.

DIFFERENTIAL DIAGNOSIS

Other causes of central corneal opacities in infants (**Table 1**) and the differentiating points (**Table 2**) are summarized below:

- **Congenital glaucoma:** Breaks in Descemet's membrane (Haab's striae) as well as buphthalmos are common.
- **Birth trauma:** Birth trauma is usually unilateral and should demonstrate breaks in Descemet's membrane. Only corneal edema will be there without any opacity characteristic of PA.
- **Mucopolysaccharidoses:** The cornea is usually diffusely hazy with no stromal thickening as opposed to centrally hazy with stromal edema and clear periphery in case of PA.

The urinalysis shows the abnormal metabolic product. Systemic features of the underlying cause will be there.

- **Congenital hereditary endothelial dystrophy (CHED):** The cornea is usually diffusely hazy as opposed to centrally hazy in Peters' anomaly. Corneal thickness is 2–3 times increased as compared to PA.

Table 1 Causes of congenital corneal opacities—STUMPED classification

Category	Disease	Subcategories
S	Sclerocornea	
T	Tears in Descemet's membrane	<ul style="list-style-type: none"> • Congenital glaucoma • Birth trauma
U	Ulcer	<ul style="list-style-type: none"> • Herpes simplex virus • Bacterial • Neurotropic
M	Metabolic (Rarely present at birth)	<ul style="list-style-type: none"> • Mucopolysaccharidoses • Mucolipidoses • Tyrosinosis
P	Posterior corneal defect	<ul style="list-style-type: none"> • Peters' anomaly • Posterior keratoconus • Staphylooma
E	Endothelial dystrophy	<ul style="list-style-type: none"> • Congenital hereditary • Posterior polymorphous corneal dystrophy • Congenital stromal corneal dystrophy

Table 2 Differential diagnosis of congenital corneal opacity

Peters' anomaly	Sclerocornea	Dermoids	CHED	PPCD
Central leukomatous opacity with normal peripheral cornea	Diffuse full-thickness corneal opacity, encroaching from periphery. Center relatively clear	Yellowish-white vascularized elevated nodules that may contain hair follicles, sebaceous and sweat glands, smooth and skeletal muscle, nerves, blood vessels, bone, cartilage, and teeth	Diffuse corneal edema	Diffuse corneal edema (less than CHED)
Lens normal or abnormal	Usually normal	Usually normal	Usually normal	Usually normal
Bilateral	Bilateral but asymmetric	Unilateral	Bilateral	Bilateral

CLASSIFICATION

- **Type I:** Consists of a central or paracentral corneal opacity with iris strands that arise from the collarette and attach to the periphery of the opacity.
- **Type II:** It has lens adherence to the posterior cornea. Type I usually is unilateral, while type II frequently is bilateral.
- **Peters plus syndrome:** Characterized by Peters' anomaly in association with cleft lip/palate, short stature, abnormal ears, and mental retardation.

MANAGEMENT

Treatment of Corneal Opacity

It depends upon the location and size of corneal opacity. In addition the presence of glaucoma also need to be considered.

- **Small central opacity and a clear lens:** A large peripheral iridectomy (Optical iridectomy) may permit a formed retinal image. Mydriatic therapy in cases where the opacity is not large can be considered in an effort to reduce the likelihood of amblyopia, while awaiting a more definitive procedure.
- **Large central corneal opacity and a clear lens:** Penetrating keratoplasty may be required to clear the visual axis.
- **Corneal opacity with cataract:** A triple procedure or a cataract surgery with IOL with pupilloplasty (when CO is small) can be done in such cases. The success rate of penetrating keratoplasty in PA is between 22% and 83%. Prognosis is poor in presence of glaucoma and in type 2 PA.

Treatment of Glaucoma

- Topical antiglaucoma medications and oral carbonic anhydrase inhibitors are effective in few cases. Most cases require surgery for IOP control.
- Surgical treatment such as trabeculectomy, tube-shunt procedures, or cyclodestructive procedures are done in cases of glaucoma refractory to medical management.

VIVA QUESTIONS

Q.1. Ocular anomalies associated with Peters' anomaly.

Ans. Chorioretinal coloboma, iris coloboma, persistent hyperplastic primary vitreous, microphthalmos, and optic nerve hypoplasia.

Q.2. Systemic associations with Peters' anomaly.

Ans.

- *Krause-Kivlin syndrome (inheritance is autosomal recessive):* The systemic associations of Peters' anomaly include short stature, facial dysmorphism, developmental delay, and delayed skeletal maturation.
- *The Peters'-plus syndrome* consists of Peters' anomaly cleft lip and palate, short stature, abnormal ears, and mental retardation.

Q.3. Histopathological findings of cornea in Peters' anomaly.

Ans. There are abnormalities in all layers of the cornea which include:

- Disorganized epithelium
- Loss of Bowman's layer
- Stromal edema at the affected area
- An abrupt absence or marked attenuation of the endothelium and Descemet's membrane underlying the corneal opacity. Peripheral to the opacity, the endothelium is normal.

Q.4. What are the risk factors for graft rejection in penetrating keratoplastomy in cases of Peters' anomaly?

Ans. Anterior synechiae, co-existing glaucoma, large corneal grafts and central nervous system abnormalities.

Q.5. Genetics of PA

Ans. Most cases are sporadic; however, autosomal recessive and autosomal dominant pedigrees have also been reported rarely. Genetic mutations in four genes have been described in PA. These are

1. PAX6 gene associated with aniridia.

2. PITX2 genes associated with Axenfeld-Rieger syndrome.
3. FOXC1 genes associated with Axenfeld-Rieger syndrome.
4. CYP1B1 gene associated with primary congenital glaucoma.

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LIMBAL DERMOID

Shipra Singhi, Deepali Singhal, Neelima Aron

INTRODUCTION

Limbal dermoids are benign congenital tumors that contain choristomatous tissue (tissue not found normally at that site). They appear most frequently at the inferior temporal quadrant of the corneal limbus. However, they may occasionally present entirely within the cornea or may be confined to the conjunctiva. They may contain a variety of histologically aberrant tissues, including epidermal appendages (Fig. 1), connective tissue, skin, fat, sweat gland, lacrimal gland, muscle, teeth, cartilage, bone, vascular structures, and neurologic tissue, including the brain. Malignant degeneration is extremely rare. It can be given as a short case or spot case in exam.

Chief Complaints

In adults, dermoids may become symptomatic for the first time and grow considerably over a year. Based on this fact, some conclude that these

lesions may be dormant for many years or have intermittent growth.

- Painless mass (cosmetic deformity)
- Foreign body sensation/irritation
- Drying of eyes
- *Diminution of vision:* Blurring of vision is related to size, astigmatism and involvement of visual axis. It is usually progressive and painless.
- Diplopia due to mechanical restriction of ocular movements.

Past History

A careful past history should be taken of:

- Mass
- Facial asymmetry
- Hearing loss
- Cardiovascular disease
- Infection
- Trauma
- Ocular inflammatory diseases.

Past Surgical History

Previous history of intraocular surgery may or may not be present.

EXAMINATION

Systemic Examination

Cardiovascular abnormalities, facial hemiatrophy, atresia of the external auditory meatus, accessory auricles, nevus flammeus, neurofibromatosis, preauricular appendages, and pretragal fistulas should be examined if present.

One-third of cases associated with Goldenhar's syndrome. It is a non-familial syndrome that

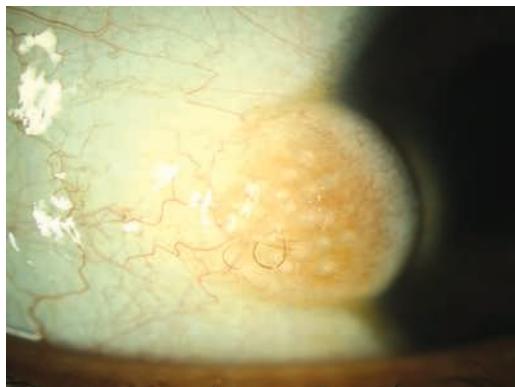


Fig. 1: Limbal dermoid with epidermal appendages such as hair

presents with a classic triad of epibulbar dermoids, preauricular appendages, and pretragal fistulas.

Ocular Examination

Visual acuity: It is variably impaired depending on the site of involvement, pupil encroachment size and astigmatism.

Cycloplegic refraction: Irregular astigmatism-compound hypermetropic.

Amblyopia

- Anisometropic or strabismic amblyopia
- Stimulation deprivation amblyopia.

Eye ball

- Microphthalmos
- Anophthalmos
- Upper eyelid coloboma
- Lower eyelid coloboma.

Lacrimal system: Lacrimal stenosis

Extraocular movement: Duane's retraction syndrome.

Slit Lamp Biomicroscopy

Anterior Segment

- **Limbal dermoid:** Yellowish-white, solid, vascularized, elevated nodules straddling the corneal limbus (**Fig. 2**). Size may vary ranging from 2 mm to 15 mm in diameter. Corneal dermoids occur as single lesions mostly but may be multiple, and they may be unilateral or

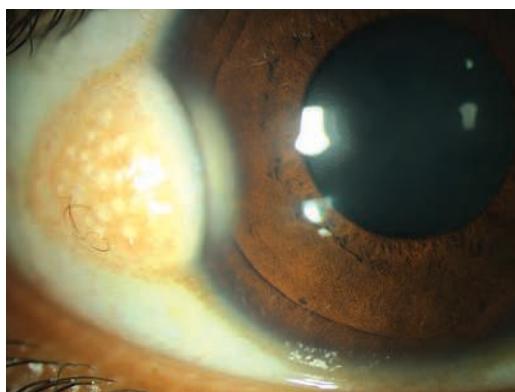


Fig. 2: Limbal dermoid

bilateral, the former being the more common. Dermoids can be central and often appear to have satellite lesions.

- Dellen formation may occur.
- Anterior staphyloma can be present.
- Aniridia may be present.
- Anterior segment dysgenesis—may be present in severe cases.
- Lens involvement can occur. Congenital cataract or aphakia may be there.
- Neuroparalytic keratitis can occur.

Tonometry

IOP usually normal.

Gonioscopy

Posterior corneal protrusion, synechiae or pigmentation, dermoid involving ciliary body.

Fundus: There may be:

- Irido fundal coloboma
- Hypoplastic disc.

Complications

- Recurrent dermoid
- Dellen formation
- Amblyopia
- Strabismus.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis of dermoids (**Table 1**).

Others

- Ectopic lacrimal gland
- Lymphoma
- Dermolipoma
- Corneal scar (infection or trauma)
- Pterygium, atypical
- Foreign body granuloma
- Epibulbar dermoid
- Episcleral osteoma
- Juvenile xanthogranuloma.

INVESTIGATIONS

The diagnosis of a limbal dermoid requires a direct clinical examination. Specific laboratory studies are generally not necessary.

Table 1 Differential diagnosis of dermoids

Dermoids	Corneal keloids	CHED	Peters' anomaly	Sclerocornea
Yellowish-white vascularized elevated nodules	Chalky white solid masses with glistening gelatinous texture	Diffuse corneal edema bilaterally; cornea is not vascularized; there are never hair follicles present	Corneal opacity + iridocorneal adhesions with or without lens abnormality (position or transparency)	Loss of transition between cornea and sclera
Inferotemporal at the limbus junction		Inheritance may be recessive or dominant	Denser corneal opacity	Cornea plana commonly associated
May contain hair follicles, sebaceous and sweat glands, smooth and skeletal muscle, nerves, blood vessels, bone, cartilage, and teeth			Most frequently bilateral	Peripheral cornea more opacified than central cornea
Usually unilateral				Surface vascularization
Can be central but do not involve the most peripheral cornea (leaving a definite sclerocorneal junction) and often appear to have satellite lesions				

Imaging Studies

- **MRI:**
 - Some dermoids may appear to extend into the conjunctival fornix or lateral canthus.
 - These lesions may contain connective tissue that entangles with the orbital fat and muscle tissue belonging to the extraocular muscles.
 - Radiologic imaging with an MRI can be useful in identifying such lesions, especially if surgical management is being considered.
 - Biopsy is not necessary except in rare instances when the diagnosis is doubtful.
- **UBM:** To determine the depth of the corneal tissue involvement.
 - Ultrasound biomicroscopy may serve as a useful diagnostic adjunct for limbal dermoids. Additionally, it may be helpful in delineating the extent of these lesions.
 - Clinical examination may be done under general anesthesia in pediatric along
- with an anterior segment high resolution B-scan (ultrasound biomicroscopy) to assess for involvement of Descemet's membrane. These steps are necessary in order to plan for the appropriate surgical approach. Meticulous biomicroscopic ultrasound examination is needed to improve the depth of corneal penetration for sound waves, since studies have demonstrated that dermoids produce strong sound attenuation, reducing the visibility of deep corneal structures and in particular Descemet's membrane.
- **Anterior segment OCT:**
 - Anterior segment OCT is done to determine the depth and posterior extension of the lesion.
- **Histologic findings:**
 - Limbal dermoids contain choristomatous tissue, including epidermal appendages, adipose and lacrimal gland tissue, smooth and striated muscle, cartilage, brain, teeth,

and bone. Lymphoid nodules and vascular elements also have been reported. The surface of the dermoids consists of corneal or conjunctival epithelium. The lesion may be cystic or solid.

Systemic Work-up

- X-ray of spine—for hemivertebra or scoliosis
- ECG
- Echocardiography—for cardiac defect
- MRI of brain
- Complete blood count
- Renal function test
- Audiometry for hearing assessment.

MANAGEMENT

Indications for Surgery

- Cosmetic deformity
- Involvement of the visual axis
- Regular or irregular astigmatism
- Amblyopia
- Strabismus
- Dellen formation
- When the lesion becomes progressive and starts to increase in size or cause irritative symptoms.

In a small, asymptomatic orbital epidermal dermoid cyst no immediate treatment is required.

Medical Management

- Medical management is generally reserved for grade I dermoids which are smaller lesions in terms of diameter and height
- Inducing only mild astigmatism of <1 D with minimal surface irregularity
- Parents report relatively good compliance with spectacle correction. Essentially small asymptomatic grade I limbal dermoids should not be removed because they may lead to postoperative scarring and development of pseudopterygium. It is recommended that these children undergo close clinical observation with serial examinations in the office, not only to monitor stability but also to provide reassurance for parents.
- Occlusion therapy.

Surgical Management

- Shave and excision
- Shave and excision with lamellar keratoplasty (LK)
- Shave and excision with patch graft
- Shave and excision penetrating keratoplasty with relaxing corneal incisions
- Shave and excision with corneal-limbal scleral donor graft transplantation
- Shave and excision with amniotic membrane graft/limbal stem cell allograft/ pericardial graft—improves postoperative reepithelialization, prevents postoperative scarring, and protects the limbal stem cells.
- Use of mitomycin C may improve the results.
- It can reduce recurrences by the inhibition of fibroblast proliferation at the level of the episclera. Therefore, the use of mitomycin C can be beneficial in the treatment of limbal dermoids in matters of postoperative complications like formation of pseudopterygium.
- *Management of amblyopia:* Occlusion treatment, chemical penalization with/without spectacle wear/contact lens (in unilateral cases) must be continued after surgical excision to obtain optimal results if the surgery is done at a younger age.

Prognosis of Surgical Outcome

Grade	Depth of involvement %	Extent of corneal involvement from limbus (mm)	Surgery to be planned	Prognosis
I	<50	<3	Excision (Ex)	Excellent
II	<50 >50	3–5 <3	Excision Excision + lamellar keratoplasty (LK)	Good
III	<50 >50	5.1–7 3–5	Excision Ex/Ex+LK	Fair

Contd...

Contd...

<i>Grade</i>	<i>Depth of involvement %</i>	<i>Extent of corneal involvement from limbus (mm)</i>	<i>Surgery to be planned</i>	<i>Prognosis</i>
IV	<50 >50	>7 5.1–7	Excision +LK Excision +LK	Guarded
V	>50	>7	Excision +LK	Poor

Complications of Surgery

- Residual vascularization
- Corneal scar
- Persistent epithelial defect
- Pseudopterygium formation
- Ocular perforation
- Recurrent dermoid.

Corneal Choristoma Classification

Stargardt Scheme

Grade I	Microphtalmos, no involvement of lens
Grade II	Lens involvement
Grade III	Cornea only
Grade IV	Limbal dermoid

Corneal Choristoma Classification

Mann's Scheme

Grade I	Limbal or epibulbar dermoid
Grade II	Superficial
Grade III	Anterior segment involvement with or without microphtalmos

Classification

Grading of Dermoids

<i>Grade 1 (limbal or epibulbar)</i>	<i>Grade 2</i>	<i>Grade 3</i>
Most frequent type	Much larger	Most severe type
Small (5 mm in diameter)	Covers part or entire central corneal surface	Very rare

Contd...

<i>Grade 1 (limbal or epibulbar)</i>	<i>Grade 2</i>	<i>Grade 3</i>
Single	Variable depth of stromal extension	Entire anterior segment is involved
Inferotemporal limbus	Does not involve Descemet's membrane or the corneal endothelium	Associated abnormalities: Microphthalmos, posterior segment abnormalities
It may enlarge (especially at puberty)		
Superficial		
One-third of cases associated with Goldenhar's syndrome: Nonfamilial; triad of epibulbar dermoids, preauricular appendages, and pretragal fistulas		
Other abnormalities: Coloboma of the lids, aniridia, microphthalmos, anophthalmos, neuroparalytic keratitis, lacrimal stenosis, Duane's syndrome, cardiovascular abnormalities, facial hemiatrophy, atresia of the external auditory meatus, accessory auricles, nevus flammeus, and neurofibromatosis		

VIVA QUESTIONS

Q.1. What is the epidemiology of dermoid?

Ans. Epidemiology:

- Congenital choristoma
- Account for 3–8% of orbital tumors in children

Contd...

- The dermoid cyst becomes the most common noninflammatory space-occupying lesion of the orbit.
- In the Wills Eye Hospital pathology series, dermoid cyst accounted for 46% of childhood orbital lesions and for 89% of all cystic lesions.

Q.2. What are the common variants of ocular dermoids?

Ans. There are two main dermoid types that occur on or around the eyes. First, an orbital dermoid is typically found in association with the bones of the eye socket (closure of embryonic sutures). Second, an epibulbar dermoid is found on the surface of the eye. There are two typical locations for an epibulbar dermoid. One of the locations is at the junction of the cornea and sclera (limbal dermoid). The second location of an epibulbar dermoid is on the surface of the eye where the lids meet in the temporal corner (towards the ear).

Q.3. What is the inheritance pattern and site of involvement of ocular epibulbar dermoids?

Ans. A study by Nevares et al. indicates that the majority (76%) of ocular dermoids occur at the inferotemporal bulbar location of the eye, with the other 22% reported to occur superotemporally. In a study by the Armed Forces Institute of Pathology,

75 of 1016 such lesions were documented to be epibulbar choristomas, with more than 80% of lesions noted to be located temporally and inferiorly. In another study at the Wilmer Eye Institute of Pathology, choristomas comprised 33% of all epibulbar lesions in individuals younger than 16 years of age. This study showed that these lesions may sometimes be associated with other ocular findings, including scleral/corneal staphyloma, aniridia, congenital aphakia, cataract, and microphthalmia.

The pattern of inheritance is quite variable in epibulbar choristomas. They can be autosomal dominant, recessive, X-linked, or multifactorial.

Q.4. What is Goldenhar syndrome?

Ans. The characteristic features of Goldenhar syndrome (also known as Oculo-Auriculo-Vertebral spectrum, craniofacial dysostosis, or first and second branchial arch syndrome) are summarized in **Table 2** (**Figs 3 and 4**)

Differential diagnoses for Goldenhar syndrome (especially the facial abnormalities):

- Treacher Collins syndrome
- Romberg disease (hemifacial atrophy) seen later in life could have a similar appearance to hemifacial microsomia
- Craniosynostosis
- Hemifacial microsomia.

Table 2 Goldenhar syndrome

Epidemiology	Signs
<ul style="list-style-type: none"> Sporadic, no documented inheritance pattern No proven environmental insult during pregnancy (medication, infection, or otherwise) Males affected 2:1 compared to females Incidence between 1 in 3,000 and 5,600 live births 	<ul style="list-style-type: none"> Limbal dermoids (bilateral in 25% of cases) Eyelid colobomas Preauricular appendages/skin tags Microtia or anotia of external ear, can be associated with hearing loss with or without middle ear malformation Vertebral abnormalities (butterfly vertebrae or hemivertebrae) Congenital heart disease (numerous anomalies have been reported) Central nervous system abnormalities (hydrocephalus, intracranial lipomas, cranial nerve dysgenesis and mental retardation have been described)

Contd...

Contd...

Symptoms	Treatment
<p>The syndrome is almost always diagnosed early in life, before there is any complaint of symptoms by the infant patient. Symptoms could include:</p> <ul style="list-style-type: none"> • Double vision (motility restriction or strabismus) • Dry eye (exposure due to coloboma or large dermoid) 	<ul style="list-style-type: none"> • Large eyelid colobomas resulting in exposure keratopathy may require surgical repair • Spectacle • Superficial keratectomy may be required to excise large limbal dermoids causing occlusive or astigmatic amblyopia or exposure • Cleft lip and palate will require surgical repair, if present • Severe underdevelopment of the mandible may require reconstruction, perhaps with the aide of a bone graft (i.e. from the rib) • In cases of microtia or other ear defect, external ear reconstruction is generally done between 6 and 8 years of age and is a multistage process • Further facial reconstruction may be required • Cardiac defects (ventricular or atrial septal defect, other) are treated accordingly • If the facial or tongue malformation is severe, speech therapy may be indicated



Fig. 3: Limbal dermoid with preauricular tags



Fig. 4: Goldenhar syndrome with limbal dermoid and ear anomalies

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CHAPTER

3

Glaucoma

LONG CASES

PRIMARY OPEN ANGLE GLAUCOMA

Dewang Angmo, Vaishali Ghanshyam Rai, Ritika Mukhija

INTRODUCTION

Glaucoma is a chronic, degenerative optic neuropathy which may or may not be associated with raised intraocular pressure (IOP). The glaucomas are classified by the appearance of the iridocorneal angle into two broad categories open angle (**Fig. 1**) and closed angle. In open-angle glaucoma (OAG) the iridocorneal angle is open (unobstructed) and normal in appearance but aqueous outflow is diminished.¹ It may be of primary or secondary type. Primary (no other associated disease) open-angle glaucoma (POAG) includes both adult-onset disease (occurring after 40 years of age) and juvenile-onset disease (occurring between the ages of 3 and 40 years of age). Secondary (secondary to some other disease in eye) OAG include those associated with pseudoexfoliation or pigment dispersion syndrome.¹ Primary open angle glaucoma case is commonly kept in practical examination as long case.²

HISTORY

Epidemiology

Primary open angle glaucoma (POAG) primarily affects persons >40 years of age, which is the second

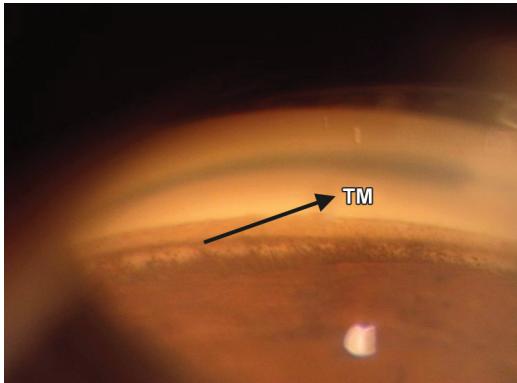


Fig. 1: Open angles on gonioscopy
Abbreviation: TM, trabecular meshwork

leading cause of blindness in the United States and the leading cause of blindness among black Americans. In India it accounts for almost half of the cases (5.8% of blindness in India is attributable to glaucoma). Gender predilection is controversial, most study reports no predilection.^{1,2}

Chief complaints: POAG can present in following ways:

- Commonly an incidental finding on ocular examination.

- POAG has no associated symptoms or other warning signs before the development of advanced visual field loss.
- Patient may present with eye pain and redness and gradually diminishing vision for distance.
- Other complaints can be blurred vision with or without color halos, frequent change of glasses or early morning or afternoon blurred vision with or without heaviness in eyes depending on IOP peak.

History of Present Illness

History must include the onset and progression of vision loss. In addition, following points must be noted:

- Brief history of patient's previous records to get baseline IOP.
- Patient who is already on treatment for glaucoma, it is important to know how many medications he/she is using and whether this treatment has sufficiently controlled IOP and visual field loss.
- Patient's previous visual fields record should be checked to know the progression of glaucoma.
- Any other record such as OCT, GDx.

History of Past Illness

Past history of ocular trauma is important to rule angle recession glaucoma.

Surgical History

History of previous ocular surgery like cataract surgery, retinal surgery, trabeculectomy, penetrating keratoplasty or any laser procedure such as peripheral iridotomy (PI) must be recorded.

History of Systemic Illness

- Hypertensive, thyroid diseases and diabetic patients are at increased risk of developing POAG.
- *Cardiovascular disease:* Systemic hypertensive (HTN) has weak association with glaucoma. Beta-blockers given for systemic HTN can reduce IOP and so a patient who is on systemic beta blockers, topical ones should be avoided as the first line therapy. Thyroid diseases

and diabetic patients usually show more association with POAG.

- *Vasospastic diseases:* Migraine, Raynaud's syndrome may be associated with increased incidence of glaucoma.
- *Hemodynamic crisis:* Acute blood loss (post-partum hemorrhage, ruptured abdominal aneurysm, severe trauma, stroke) can cause severe systemic hypotension, destabilizing the ocular blood flow and increase the optic nerve damage.
- *Endocrine:* Diabetes and thyroid may have an increased risk of glaucoma. Cushing's syndrome cause endogenous release of corticosteroids.
- It is very important to ask about cardiovascular disease, renal diseases and bronchial asthma before deciding on antiglaucoma treatment.
- History of disorders which cause endogenous release of corticosteroids, e.g. Cushing's syndrome must be enquired.

Drug History

- History of use of ocular and systemic medications, especially if patient is already on systemic beta-blockers (topical beta-blockers would work sub-optimally) must be enquired.
- Known local or systemic intolerance to ocular or systemic medications.
- History of long-term use of corticosteroid in any form like eye drop, nasal spray, systemic is important to rule out steroid induced glaucoma.
- Long-term systemic use of steroids following any major organ transplantation surgery, e.g liver or kidney transplant surgery.
- long-term topical use of steroids following keratoplasty or chronic allergic keratitis, e.g. vernal keratoconjunctivitis.
- History of systemic use of topiramate needs to rule out.
- Any hypersensitivity reaction to anti-glaucoma medications both topical and sulpha allergy.

Family History

Relatives of POAG patients are at higher risk for developing glaucoma. The severity and outcome of glaucoma in family members, including history of visual loss from glaucoma is also important.

EXAMINATION

General Examination/Specific Systemic Examination

Detailed systemic examination to rule out neurofibromatosis, Sturge-Weber syndrome, carotid cavernous fistula, thyrotoxicosis exophthalmus which cause elevated episcleral venous pressure and secondary open angle glaucoma must be done.

Ocular Examination

Eyeball: Usually looks normal.

Lids: Usually normal. In patient who is already on anti-glaucoma medications like Prostaglandin analogues look for hyperpigmentation of lid margin and long eyelashes.

Conjunctiva: All anti-glaucoma medications can cause some form of conjunctival toxicity so always look for conjunctival congestion. This congestion is more in inferior quadrant.

Cornea: The cornea is typically normal in POAG. Ocular hypertension has a higher incidence of increased central corneal thickness (CCT) hence CCT measurement is important. Thinner CCT corneas are at higher risk for POAG. IOP is also affected by CCT. Fluorescein (Na fluorescein 1%) staining with cobalt blue light examination of cornea is advisable to look for corneal surface toxicity caused by some antiglaucoma medications.

Pupils: The pupils are examined for direct and consensual light reflex. Relative afferent pupillary defect indicates advanced glaucoma.

Anterior segment: A slit-lamp biomicroscopic examination of the anterior segment can provide evidence of physical findings associated with narrow angles, corneal pathology, or a secondary mechanism for elevated IOP such as pseudoexfoliation, pigment dispersion, iris and angle neovascularization, or inflammation.

IOP: IOP is measured in each eye, preferably using a Goldmann applanation tonometer before gonioscopy or dilation of the pupil. Time of day should be recorded because of diurnal variation.

Gonioscopy: The diagnosis of POAG requires careful evaluation of the anterior-chamber angle to exclude angle closure or secondary causes of

IOP elevation, such as angle recession, pigment dispersion, peripheral anterior synechiae, angle neovascularisation (**Fig. 1**).

Optic disc and retinal nerve fiber layer: It is best done using +90D or +78D lens with slit lamp under dilated pupils. Following points must be remembered:

- Early findings include enlargement of the optic disc cup, deep cup, thinning or saucerizing of the neural rim (**Fig. 2**), disc hemorrhages, and peripapillary atrophy (common at beta zone) (**Fig. 3**).
- The diagnosis of glaucoma should be strongly considered if vertical CD ratio ≥ 0.7 or asymmetric cupping between two eyes is > 0.2 .
- Changes at lamina cribrosa—laminar dot sign.



Fig. 2: Enlargement of the optic disc cup, thinning or saucerizing of the neural rim and peripapillary atrophy



Fig. 3: Advanced glaucoma with near total cupping, thinned neural rim and peripapillary atrophy

- Changes at neuroretinal rim—look for focal or diffuse defect in neuroretinal rim which does not obey ISNT rule.
- Vascular changes—nasalization of retinal vessels, bayonetting of vessels, baring of circumlinear vessels.
- Changes in retinal nerve fiber layer (RNFL)—look for focal or diffuse defect in RNFL using red-free illumination (green filter).

Look for other abnormalities of fundus that might account for visual field defects, e.g. optic nerve pallor, tilted disc, disc drusen, optic disc pits, optic nerve hypoplasia, neurological disease, macular degeneration, and other retinal disease.

DIFFERENTIAL DIAGNOSIS

Ocular hypertension: Following points help in differentiation:

- High IOP > 21 mm Hg on 2 consecutive occasions with applanation tonometry
- Normal optic disc and neuro-retinal rim (NRR)
- Normal visual field
- Open angles on gonioscopy
- Absence of any other ocular disease causing raised IOP.

Pigmentary glaucoma: Following points helps in differentiation:

- Younger age group 20–30 years
- Pigments dispersion on corneal endothelium, lens surface
- Mid-peripheral iris transillumination defect
- Wide open angles with dark broad pigmentation of trabecular meshwork on gonioscopy.

Pseudoexfoliation glaucoma: Following points helps in differentiation:

- Higher IOP and greater 24 hours IOP fluctuation
- Exfoliation material deposits on corneal endothelium, at pupillary margin, on lens surface, upon trabecular meshwork on gonioscopy.
- Diffuse loss of NRR
- Greater visual field loss
- Steroid induced glaucoma—following points helps in differentiation
- History of corticosteroid intake in any form
- History of endogenous disease causing increased blood corticosteroid levels
- Usually bilateral but can be unilateral also

- Other ocular side effects due to steroid use, e.g. posterior subcapsular cataract.

Angle recession glaucoma: Following points helps in differentiation:

- Past history of ocular trauma
- Angle recession on gonioscopy
- Other signs may be seen as phacodonesis, iridodonesis, traumatic cataract or retinal tear
- Usually unilateral.

INVESTIGATIONS

Following investigations are done in a case of POAG:

Diurnal variation in IOP: IOP needs to be recorded every 3 hourly for 24 hours, important for

- Diagnose early cases of glaucoma
- Assess pre-treatment baseline IOP (highest recorded IOP before the diagnosis of glaucoma without any medication)
- Pick up nocturnal rise of IOP
- Helpful in timing of anti-glaucoma medications
- Assess maximum-minimum variation of IOP—IOP difference of 8 mm Hg or more between any two reading is significant.

Pachymetry: To estimate central corneal thickness and correction of IOP accordingly.

Perimetry: Usually automated perimetry to document visual field loss.

Retinal nerve fiber layer thickness: Retinal nerve fiber layer (RNFL) assessment by optical coherence tomography (OCT), GDx and heidelberg retinal tomogram (HRT).

Fundus photography: For documentation of optic nerve head changes.

MANAGEMENT

Medical Treatment

- Target IOP:** In every diagnosed case of glaucoma, target IOP should be calculated to halt or prevent further glaucomatous damage to optic nerve and visual field loss progression.
- Start with one or two medication based on target IOP (see viva section). Beta-blockers and prostaglandin (PG) analogues are often the first choice (See **Table 1**).²

Table 1 Commonly used antiglaucoma medications

Class	Mechanism	Drugs	Dose	Ocular side effects	Systemic side effects
Prostaglandin analogues (prostamide)	Increase in uveoscleral outflow of aqueous humor	Latanoprost (Xalatan)—0.005%, travoprost (Travatan)—0.004%, tafluprost (Zioptan)—0.0015%, bimatoprost (Lumigan)—0.01%, 0.03% Unoprostone (Rescula)—0.15%	HS	Conjunctival hyperemia, lengthening and darkening of eyelashes, brown discoloration of the iris, uveitis, macular edema	Minimal; may be related to headaches
β-adrenergic blockers	Reduction of aqueous humor production	Timolol (0.5/0.25%), levobunolol, carteolol, metipranolol, betaxolol	OD or BD	Irritation and dry eyes	Contraindicated in patients with asthma, chronic pulmonary obstructive disease, and cardiac failure, bradycardia
α-adrenergic agonists	Initial reduction of aqueous humor with subsequent effect of increase in outflow	Brimonidine (0.1/0.15%), Apraclonidine	TID sometimes BD	Irritation, dry eyes, allergic reaction	CNS effects and respiratory arrest in young children (contraindicated <2 years); caution in patients with cerebral or coronary insufficiency, postural hypotension, renal or hepatic failure
Carbonic anhydrase inhibitors	Reduction of aqueous humor production	Dorzolamide (2%), brinzolamide (1%), acetazolamide (oral)	TID sometimes BD	Irritation, dry eyes, burning sensation with topical agents	Oral form may be associated with paresthesia, nausea, diarrhea, loss of appetite and taste, lassitude, or renal stones
Cholinergic agonists	Increase in aqueous humor outflow	Pilocarpine (0.5/1.0/2.0 %), carbachol	Usually QID, but may vary	Irritation, induced myopia and decreased vision due to ciliary spasm	Ciliary spasm leading to headaches in young patients

- Adjuvant treatment with neuroprotectives like N-methyl D-aspartate (NMDA) receptors like memantine; Alpha 2 adrenergic agonists like brimonidine; Calcium channel blocking agents, e.g. Flunarizine, nimodipine, anti-oxidants or nitric oxide synthetase inhibitors can be considered.
- Follow every 3 months in mild to moderate visual field loss cases and 1 monthly in advanced cases. Every patient should be checked for compliance and tolerance to anti glaucoma medications. IOP with Goldmann applanation tonometry should be recorded at each follow-up to monitor IOP control and target IOP with medication.
- Visual fields with standard automated perimetry should be done every year in ocular hypertension with high-risk cases, every 6 monthly in mild to moderate cases while every 3 monthly in advanced cases to monitor progression of disease and modification in treatment accordingly.

Laser trabeculoplasty: In patients who cannot or will not use medications reliably due to cost, memory problems, difficulty with instillation, or intolerance to the medication.

Filtration Surgery: Trabeculectomy

Indication

- Patients from rural areas where follow up is likely to be difficult
- Patients with baseline IOP of more than 40 mm Hg where even maximal medical therapy will be unsuccessful
- Patients who have lost one eye due to glaucoma at presentation
- Failure to control IOP after maximal tolerated medical therapy
- Patient develops side-effects of antiglaucoma treatment
- IOP not at target on 3 topical medications or progression of visual fields despite maximum medical therapy
- Poor compliance to medical therapy.

Glaucoma Drainage Devices

Indication

- Patients who have failed filtering surgery with antimetabolites

- Patients whose conjunctiva is so scarred from previous surgery that filtering surgery with antimetabolites is at high risk for failure.

Newer Nonpenetrating Glaucoma Surgery

- Viscocanalostomy
- Nonpenetrating deep sclerectomy
- Sinusotomy
- Canaloplasty.

VIVA QUESTIONS

Q.1. What are the most important parameters on clinical examination that lead you to investigate the patient for open angle glaucoma?

- Ans.**
- Raised intraocular pressure (IOP)
 - Optic disc cupping:
 - A suspicious disc with increased vertical cup-to-disc (CD) ratio more than or equal to 0.7
 - Asymmetric cupping between two eyes >0.2
 - A diffuse or focal thinning of the neuroretinal rim which does not obey the ISNT rule (normally the inferior rim is thickest followed by superior, nasal and temporal), and a retinal nerve fiber layer defect in red free light.
 - Field changes suggestive of glaucoma
 - Additional risk factors, e.g. age, myope, diabetes mellitus, hypertension, thyroid disease, family history of glaucoma.

Q.2. What is the importance of DVT in POAG management?

- Ans.** Diurnal variation is very important in a glaucoma patient both for
- Diagnosis—to establish baseline IOP, determine magnitude of IOP fluctuation and the timing of peak IOP.
 - Management—to establish diurnal control with ocular hypotensive drugs and maintain IOP below target with a fluctuation of less than 5 mm Hg, instill medicines at a time to cover peak IOP spikes.

Q.3. Define target IOP and how you will calculate target IOP?

- Ans.** Target IOP may be defined as a pressure, rather a range of intraocular pressure levels

within which the progression of glaucoma and visual field loss will be delayed or halted. It is calculated depending on severity of glaucomatous optic damage. The severity of glaucoma damage can be estimated using the following scale:

- *Mild*: Characteristic optic nerve abnormalities consistent with glaucoma and a normal visual field as tested with standard automated perimetry.
- *Moderate*: Characteristic optic nerve abnormalities consistent with glaucoma and visual field abnormalities in one hemifield and not within 5° of fixation.
- *Severe*: Characteristic optic nerve abnormalities consistent with glaucoma and visual field abnormalities in both hemifields and loss within 5° of fixation in at least one hemifield.

Depending on severity of glaucomatous optic disc damage, American Association Ophthalmology has given guidelines to estimate target IOP as follow:

- In Mild damage cases—30% reduction of IOP from baseline IOP
- In advanced damage cases—40% reduction of IOP from baseline IOP
- In ocular hypertension cases—20% reduction of IOP from baseline IOP
- In normal tension glaucoma (NTG) cases—30% reduction of IOP from baseline IOP.

Q.4. What are the qualitative evaluation and quantitative evaluation of optic nerve head in case of glaucoma?

Ans. Qualitative evaluation

- Contour of the neuroretinal rim
 - Optic disc hemorrhage
 - Parapapillary atrophy
 - Bared circumciliary vessels
 - Appearance of retinal nerve fiber layer.
- Quantitative evaluation
- Optic disc size (vertical disc diameter)
 - Cup disc ratio
 - Rim disc ratio.

Q.5. Which cup disc ratio is important horizontal or vertical and why?

Ans. The vertical cup disc ratio is more important since early neuroretinal rim loss occurs

preferentially in upper and lower poles of disc.

Q.6. Why Goldmann's applanation tonometry should be done before gonioscopy and before dilatation of pupils?

- Ans.**
- During gonioscopy angle of anterior chamber opens up due to pressure over cornea, which results in reduction of IOP and applanation tonometry performed after gonioscopy gives low IOP than correct IOP.
 - By dilatation of pupil there is transient rise in IOP 4–5 mm Hg that also gives high IOP than actual IOP on applanation tonometry if performed on dilated pupils.

Q.7. Which are pre-perimetric diagnostic tools of glaucoma?

Ans. Pre-perimetric diagnostic tools can detect early glaucomatous damage in RNFL even before that damage can be located on perimetry. These are GDxVCC, HRT, OCT and SWAP.

Q.8. What is the pathogenesis of primary open angle glaucoma?

Ans. Genetics

- *MYOC*: Myocilin (GLYC1A, chromosome 1), associated with juvenile open angle glaucoma and ≈4% of adults with POAG
- *OPTN*: Optineurin (GLYC1E, chromosome 10)
- *Other loci*: GLYC1B, GLYC1C

- Pressure dependent (mechanical factors)
 - Increased IOP → compression and backward bowing of lamina cribrosa → obstruction of axoplasmic transport → ganglion cell death
- Ischemic factors/pressure independent (esp significant for NTG)
 - Vascular perfusion compromise (DM, HTN, migraine, Raynaud's phenomenon)
 - Abnormal coagulability
 - Nocturnal hypertension, significant blood loss
- Neurodegenerative factors
 - Primary ON damage leads to glutamate release, which interacts with cell receptors that leads to an increase in intracellular calcium levels

- This triggers cell death via apoptosis and leads to further release of glutamate and a vicious cycle occurs.

Q.9. What is the role of central corneal textbook (CCT) in ocular hypertension (OHT)/open angle glaucoma (OAG)?

Ans. CCT measurement is important before diagnosing glaucoma and deciding the management, while it is not helpful in predicting risk of progression of existing glaucoma. CCT influences IOP measurement by applanation tonometry and therefore it is important to note CCT in every patient being evaluated for glaucoma. CCT can be broadly categorised as: Thin (<500 µm), Normal and Thick (>570 µm).

Refractive surgeries reduce the CCT and therefore the IOP measurements in such patients would be falsely low.

Q.10. Classify antiglaucoma drugs, their common side effects.

Ans. Refer to any Standard Textbook (see Table 1).

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PRIMARY ANGLE CLOSURE GLAUCOMA

Vaishali Ghanshyam Rai, Talvir Sidhu, Dewang Angmo

INTRODUCTION

Primary angle closure glaucoma (PACG) is usually allotted in practical examination as a long case. Primary angle closure (PAC) is appositional or synechial closure of the anterior-chamber angle caused by pupillary block. The angle closure may or may not be associated with elevated intraocular pressure (IOP) or glaucomatous optic neuropathy, and may occur in either an acute or chronic form. This entity does not include secondary forms of angle closure induced by other causes, e.g. subluxed lens.

HISTORY

Chief Complaints

A case of PACG can present in following ways:

- Majority of patients with angle closure glaucoma are asymptomatic.
- Blurred vision or smoke filled room
- Some patient present acutely with color halos around lights due to corneal edema, aching eye or brow pain and/or eye redness.
- Patient with acute angle closure attack presents usually with unilateral diminution

of vision with redness in eye with severe eye pain associated with ipsilateral headache with nausea and vomiting.

History of Present Illness

Following must be enquired:

- History of symptoms precipitated by watching television, darkened room, reading, pharmacological mydriasis.
- Brief history of patient's previous records to get baseline IOP.
- Patient who is already on treatment for glaucoma is important to know how many medications he/she is using and whether these treatment has sufficiently controlled IOP and visual field loss.
- Patient's previous visual fields record should be checked to know the progression of glaucoma.

History of Past Illness

Ask for previous use of glasses. Hypermetropic patients are at higher risk to develop PACG.

History of Systemic Illness

- Diabetic or hypertensive patients who need frequent dilated fundus examination, need special attention to rule out PAC or PACG since shallow anterior chamber depth may develop acute angle closer attack on dilation of pupil.
- It is very important to ask about cardiovascular disease, renal diseases and bronchial asthma before deciding on antiglaucoma treatment.

Family History

Relatives of PACG patients are at higher risk for developing glaucoma. The severity and outcome of glaucoma in family members, including history of visual loss from glaucoma is also important.

Drug History

- History of use of ocular and systemic medications.
- Known local or systemic intolerance to ocular or systemic medications.
- History of drugs which induce angle closure attack needs to be asked. Such drugs include:
 - Anticholinergic agents (topical, e.g. atropine, cyclopentolate, and tropicamide, or systemic, e.g. antihistamine, antipsychotic (especially antidepressants), anti-parkinsonian, atropine, and gastrointestinal spasmolytic drugs).
 - Adrenergic agents (topical, e.g. epinephrine and phenylephrine, or systemic, e.g. vasoconstrictors, central nervous system stimulants, bronchodilators, appetite depressants, and hallucinogenic agents).
- Specific questioning includes asking about the use of topical or systemic medication (e.g. sulfonamides, topiramate, phenothiazines) that may induce angle narrowing and subsequent symptoms that suggest intermittent angle-closure attacks should be enquired.

Surgical History

History of previous ocular surgery like trabeculectomy or any eye laser like iridotomies must be asked for.

EXAMINATION

General examination/specific systemic examination is carried out to look for any contraindication to antiglaucoma medications.

Ocular Examination

- *Eye ball:* Usually looks normal. Small eye ball in case of hypermetropia.
- *Lids:* Usually normal. In patient who is already on anti-glaucoma medications like prostaglandin analogues look for hyperpigmentation of lid margin and long eyelashes.
- *Conjunctiva:*
 - In case of acute angle closure attack, marked circumciliary congestion can be noted.
 - Patients of chronic angle closure glaucoma who already on anti-glaucoma treatment, always look for conjunctival congestion as all antiglaucoma medications can cause some form of conjunctival toxicity. This congestion is more in inferior quadrant.
- *Cornea:* Following signs can be seen.
 - In acute angle closure attack, unilateral epithelial and stromal cornea edema due to raised IOP.
 - In chronic cases, Krukenberg spindle (pigment distribution over the inferior corneal endothelium).
- *Anterior chamber:*
 - Anterior chamber is shallow (**Fig. 1**). The Van Herick technique is useful for estimating the peripheral anterior

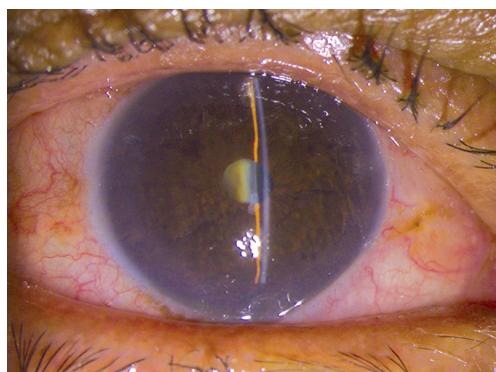


Fig. 1: Shallow anterior chamber



Fig. 2: Patchy iris stromal atrophy

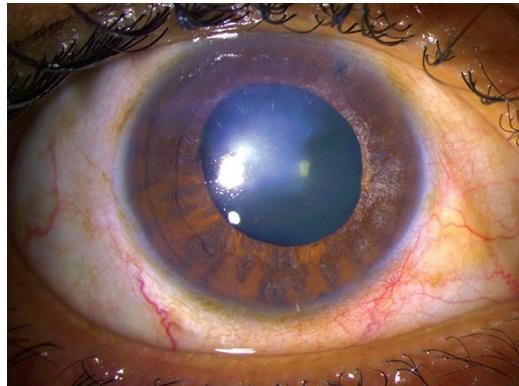


Fig. 3: Segmental iris atrophy

chamber depth. In PACG cases, peripheral anterior chamber is shallow that can be graded by Van Herick technique (discussed later in viva questions). When the peripheral anterior chamber depth is less than one fourth of the corneal thickness, the anterior chamber angle may be potentially occludable.

- Anterior-chamber inflammation suggestive of a recent or current attack.
- **Iris:** Following points must be looked for
 - In acute attack, iris bombe is usually present due to pupillary block.
 - In recent PACG attack, iris whorling (sectoral infarction of the iris sphincter) or patchy iris stromal atrophy is usually present (**Fig. 2**).
 - Mid-dilated pupil is common in acute or recent PACG attack.
 - Signs of previous angle-closure attacks are PAS, segmental iris atrophy (**Fig. 3**), posterior synechiae, irregular pupil.
- **Lens:** In previous angle closure attack, look for glaukomflecken (small gray-white anterior subcapsular or capsular opacities (**Fig. 4**) in the pupillary zone, due to infarction of lens fibers). Lens thickness might be increased. An intumescent lens can be there in angle closure attack. Vogt's Triad: Sectoral iris atrophy, Krukenberg spindle and glaukomflecken is characteristic of PACG.
- **Intraocular pressure (IOP):**
 - IOP is measured in each eye, preferably using a contact applanation method

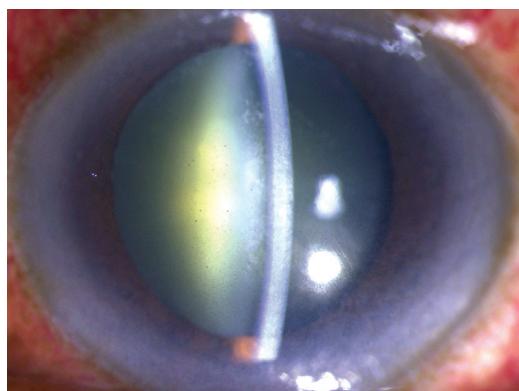


Fig. 4: Glaukomflecken

(typically a Goldmann tonometer) before gonioscopy. Measuring central corneal thickness should be postponed until resolution of an acute attack.

- In acute attack, IOP is usually very high (50–100 mm Hg).
- In chronic PACG, IOP elevation may be intermittent.
- **Gonioscopy:**
 - Gonioscopy of both eyes should be performed on all patients in whom angle closure is suspected.
 - This is best performed using first a two-mirror Gonio lens (e.g. Goldmann) to avoid artifactual distortion of the angle caused by inadvertent pressure on the cornea.

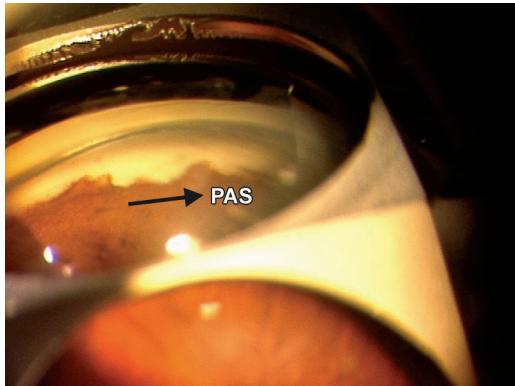


Fig. 5: Gonioscopy shows presence of PAS

- This is required to evaluate the angle anatomy, appositional closure, and presence of primary angle closure (PAS) (**Fig. 5**).
- Compression (indentation) gonioscopy with a four-mirror or similar lens is particularly helpful to evaluate for appositional closure versus synechial angle closure and for extent of PAS.
- Various grading systems including Scheie, Shaffer, and Spaeth have been proposed for the recording of gonioscopic findings. These gonioscopic grades provide an index of the likelihood of angle closure.
- **Fundus examination:**
 - For patients with PAC or narrow angle who are not in an acute attack, pupil dilation is contraindicated until iridotomies have been performed.
 - Although a dilated examination may not be advisable in patients with anatomic narrow angles or angle closure, an attempt should be made to evaluate the fundus and optic nerve using the direct ophthalmoscope or biomicroscope with +78D or +90D.
 - In acute attack, optic nerve head may look hyperemic and edematous in early stage, the disc then became pale and glaucomatous cupping can be observed after 9 to 10 days.

DIFFERENTIAL DIAGNOSIS

Since primary narrow angles and PAC tend to be bilateral, the observation of a wide-open angle in the fellow eye suggests a diagnosis other than PAC.

- **Plateau iris syndrome:**
 - The peripheral iris is forced into the angle by anterior rotation of the ciliary body or anteriorly positioned ciliary processes.
 - Angle closure attack may be precipitated after dilatation of pupil even in presence of patent peripheral iridotomy.
- **Neovascular glaucoma:**
 - Neovascularisation of iris or angles hallmark sign
- Inflammatory causes of angle closure (e.g. posterior synechiae, iris bombe).
- Iridocorneal endothelial syndrome.
- Ciliary body engorgement or suprachoroidal effusion caused by systemic medications (e.g. topiramate, sulfonamides, phenothiazines).
- Ciliary body engorgement associated with retinal vascular occlusion or scatter (panretinal) photocoagulation.
- Anterior suprachoroidal effusions (e.g. congestion, edema, displacement).
- Aqueous misdirection (ciliary block) syndrome after incisional or laser surgery (e.g. following peripheral iridectomy).
- Lens-induced angle closure (e.g. phacomorphic or subluxed).
- Developmental disorders (e.g. nanophthalmos, retinopathy of prematurity, persistent hyperplastic primary vitreous).
- Iris or ciliary body mass lesions or cysts.

CLASSIFICATION

Recently angle closure glaucoma has been classified into three categories (**Table 1**). (1) Primary angle closure (PAC); (2) Primary angle closure glaucoma (PACG); (3) Primary angle closure suspect (PACS); depending upon the presence of following:

- Iridotrabecular contact (>180°)
- Elevated IOP
- PAS
- Glaucomatous optic neuropathy.

Table 1 Classification and management of angle closure glaucoma

Characteristics	PACS	PAC*	PACG**
Iridotrabecular contact (>180°)	+	+	+
Elevated IOP	-	+/-	+/-
PAS	-	+/-	+/-
Glaucomatous optic neuropathy	-	-	+
Treatment	Close observation with serial gonioscopy or LPI***	LPI+ medical or surgical therapies to control IOP	LPI+ medical or surgical therapies to control IOP

Abbreviations: IOP, intraocular pressure; PAC, primary angle closure; PACG, primary angle closure glaucoma; PACS, primary angle closure suspect; PAS, peripheral anterior synechiae, LPI, laser peripheral iridotomy.

*For a diagnosis PAC either elevated IOP or PAS, one of them must be positive, along with Iridotrabecular contact (>180°).

**For a diagnosis of PACG either elevated IOP or PAS, one of them must be positive, along with Iridotrabecular contact (>180°) and optic nerve damage.

***LPI should be considered taking into consideration of symptoms suggestive of intermittent angle closure, systemic medications that may predispose to pupillary block, need for frequent pupillary dilation or lack of reliable access to healthcare.

INVESTIGATION

- Visual field analysis by automated perimetry to document visual field loss.
- Ultrasound biomicroscopy (UBM):* It can help to elucidate the underlying mechanism of angle closure in most cases, including plateau iris syndrome and iridociliary cysts, thereby allowing the appropriate treatment to be given.
- Anterior segment optical coherence tomography (AS-OCT):* A comparison with gonioscopy has found that it may be superior in its ability to detect angle occludability.

MANAGEMENT

Medical Management

Management of acute angle closure attack:

- Acetazolamide (250–500 mg) oral stat, then 125 to 250 mg tid/qid until symptoms subside or IV Mannitol 1.5g/kg of body weight of 20% 200 mL over 30 minutes then oral Acetazolamide 250 mg qid.
- Topical pilocarpine 2% stat, then qid can be given but after inflammation control.
- Analgesics and antiemetic as required.
- Topical beta-blockers eye drop BD.

- Topical steroids qid.
- Preventive laser peripheral iridotomy (LPI) should be done in fellow eye as early as possible.
- Once IOP is controlled and corneal edema clears a LPI should be performed.

Management of Primary Angle Closure Suspect

Management options include LPI or close observations with regular follow for IOP checking, gonioscopy and disc evaluation. Indication for LPI in PACS includes:

- Patient who needs frequent dilatation, e.g. diabetic, hypertensive age-related macular degeneration (ARMD)
- Patient who had previous angle closure attack in one eye, prophylactic peripheral iridotomy (PI) for fellow eye
- Hyperopic patient
- Patient who is unlikely to come for regular follow-up.

Surgical Treatment

A patient whose IOP does not come under control with PI and medications, and those with fairly

advanced disease will require filtering surgery. The application of antifibrotic agents such as 5-Fluorouracil (5-FU) and Mitomycin C (MMC) results in greater success and lowers IOP following trabeculectomy.

VIVA QUESTIONS

Q.1. How do you grade peripheral anterior chamber depth (PACD) on slit lamp?

Ans. By Van Herick's method

- Grade 0: Iridocorneal contact
- Grade 1: PACD < 1/4 corneal thickness
- Grade 2: PACD = 1/4 corneal thickness
- Grade 3: PACD = 1/4–1/2 corneal thickness
- Grade 4: PACD ≥ 1 corneal thickness
Grade 0, 1 and 2—suspicious of angle closure

Q.2. Which are the risk factors for developing PACG?

Ans. Following are risk factors for PACG

- Patient factors:
 - Advancing age
 - Female gender
 - Asian or Inuit descent
 - Family history of angle closure
- Ocular factors:
 - Shallow anterior chamber
 - Narrow angle
 - Relative anterior location of iris-lens diaphragm
 - Hyperopia [increased lens thickness, small corneal diameters and short axial length (AL)]

Q.3. What are the mechanisms of angle closure?

Ans. • Pupil block (most common)

- Abnormalities anterior to iris:
 - PAS
 - ICE syndrome
 - Neovascular glaucoma
- Abnormalities of iris and ciliary body:
 - Cysts thick peripheral iris
 - Peripheral iris roll
- Abnormalities of lens:
 - Thick intumescent lens
 - Subluxated lens
- Abnormalities posterior to lens: Malignant glaucoma.

Q.4 What are the indications for laser peripheral iridotomy in PACS?

- Patient who needs frequent dilatation, e.g. diabetic, hypertensive, ARMD
- Patient who had previous angle closure attack in one eye, prophylactic PI for fellow-eye
- Hyperopic patient
- Patient who is unlikely to come for regular follow-up.

Q.5 Explain technique to perform laser peripheral iridotomy (LPI)?

Ans. The procedure of LPI involves following

- *Before LPI:* Pilocarpine eye with 1% pilocarpine then anesthetize eye with 0.5% proparacaine.
- *LPI:* Abraham's type of contact lens is applied. This lens has a +55 D, peripheral button over a routine contact lens. This lens helps in the following way:
 - It stabilizes the eye and prevents undue movements.
 - It helps to open the eye and keep the lids retracted during the procedure.
 - It smoothens out the corneal surface.
 - It provides peripheral view, which is highly magnified.
 - It helps to reduce the axial expansion of plasma, which reduces the unnecessary spread of the damage.
 - It increases the power density of the spot.
 - Gives pressure to prevent the bleed from increasing.
- *Site of LPI:* The iridotomy site should be in the peripheral third of the iris, just anterior to the arcus. A crypt or a thinned area of the iris is recommended. Most ophthalmologists place the iridotomy between 11 o'clock and 1 o'clock, where the lids superiorly cover it.
- *Size of LPI:* Iridotomy be at least 200 µm in size. The preferable size is 500 µm in diameter.
- *End point:* Once the iridotomy is complete one can notice a sudden gush of aqueous or outflowing of the pigment from the posterior to the anterior chamber along with sudden deepening

of the anterior chamber. The presence of retro-illumination may be looked for after a few weeks of laser iridotomy, however it is not a sure sign of total penetration. Visualization of the anterior lens capsule confirms LPI.

- *Parameters for LPI:* In Indian patients brown irides, LPI can be performed with a neodymium: yttrium-aluminum-garnet (Nd:YAG) laser, using the following settings:
 - Power—4–8 mJ
 - Pulses/burst—1–3
 - Spot size—fixed
- *Monitoring and follow-up post LPI:* At 1 hour after completion of LPI, the IOP should be checked to make sure that it did not increase significantly (i.e. IOP has not increased by 8 mm Hg or more and that IOP does not exceed 30 mm Hg). Topical prednisolone acetate 1% is given 4 times a day for 5–7 days. Topical beta-blocker is added in cases of PACS or continue antiglaucoma medications if patient is already on anti-glaucoma medications. At 1 week, the patient is seen to monitor IOP, to confirm the patency of the iridotomies site, and to check for any significant intraocular inflammation.

Q.6. What are the complications of LPI?

Ans. Common complications are:

- Postoperative intraocular pressure spike
- Anterior uveitis
- Iris bleeding and hyphema
- Focal cataract
- Posterior synechiae

- Visual symptoms
- Corneal decompensation.

Rare complications of LPI are:

- Aqueous misdirection
- Recurrent herpetic keratouveitis
- Retinal and subhyaloid hemorrhage
- Choroidal and retinal detachment after argon LPI
- Stage I macular hole.

Q.7. Risk of progression of PACS to PAC/PACG.

Ans. The reported rates of developing AACC range from 6 to 10%, and rates of PAC or PACG are 17–35%.

Q.8. The International Society of Geography and Epidemiology of Ophthalmology classification of angle closure glaucoma.

Ans. Classified PAC disease into PAC suspect (PACS), closure (PAC) and glaucoma (PACG) based on intraocular pressure (IOP), gonioscopy findings, disc, and visual field examination.

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SHORT CASES

STURGE-WEBER SYNDROME

Vaishali Ghanshyam Rai, Ritika Mukhija, Dewang Angmo

INTRODUCTION

Sturge-Weber syndrome (SWS) is a rare congenital neuro-oculocutaneous disorder present at birth. It is also known as encephalotrigeminal angiomas. The ocular component manifests as glaucoma and vascular malformations of the conjunctiva, episclera, choroid, and retina. The hamartoma occurring in SWS arises from vascular tissue and produces a characteristic ipsilateral port-wine hemangioma of the skin along the trigeminal distribution. Classic SWS comprises the triad of Port-wine facial telangiectasia (nevus flammeus) in the distribution of the trigeminal nerve that respects the vertical midline, ipsilateral glaucoma, and intracranial angiomas.¹⁻³ Glaucoma occurs in approximately one half of the cases (30–70%) in which the Port-wine stain involves the ophthalmic and maxillary divisions of the trigeminal nerve.⁴⁻⁶

HISTORY

Chief Complaints

A case of SWS can present with following:

- Commonly referred to ophthalmologist from general practitioner or neurologist to rule out ocular manifestation of SWS.
- Heaviness and dull aching pain around eye
- Progressive peripheral visual field loss.

History

Parents usually give history of presence of unilateral port wine hemangioma of skin along the trigeminal distribution since birth. The angiomas are present at birth and are usually unilateral, although bilateral cases also occur. History of seizures generally in infancy is usually present.

EXAMINATION

Systemic Examination

Sturge-weber syndrome (SWS) can involve central nervous system (CNS) as well skin hence; a thorough examination of both the system is required. SWS is called tri-symptomatic when the skin, eye, and CNS involvement is there. Similarly, it is called bisymptomatic when the skin and CNS or the skin and eye are affected; and monosymptomatic when the skin or the CNS is affected.⁴

Specific examination to rule out nervous system involvement such as hemispheric motor or sensory defects, and intellectual deficiency has to be done. Dermatological examination may reveal a characteristic Port-wine hemangioma (dilated, telangiectatic cutaneous capillaries) of the skin along the trigeminal distribution (**Fig. 1**).

Ocular Examination

Eyeball: Usually normal.



Fig. 1: Bilateral facial angiomas

Eyelids: A unilateral port-wine hemangiomas of the lid skin long the trigeminal distribution (maxillary and/or ophthalmic division) can be seen.

Conjunctiva: A dense episcleral vascular plexus and occasional ampulliform dilatations of conjunctival vessels is common on the site of cutaneous lesion.

Cornea: Usually normal. Corneal edema can be there in presence of high IOP.

Anterior chamber: When the glaucoma is congenital *abnormalities of the chamber angle* similar to other forms of congenital glaucoma can be there. When glaucoma occurs later in life; at that time, it is associated with a more normally appearing anterior chamber angle.

Fundus: Good indirect ophthalmoscopy should be performed to look for choroidal hemangiomas. Also, look for retinal edema and retinal detachment, which are usually associated with choroidal hemangiomas. A 90 D stereoscopic disc evaluation should be performed to document cup-disc ratio, neuroretinal rim status and any retinal nerve fiber layer defect.

IOP: In unilateral cases, IOP is >21 mm Hg in ipsilateral eye in around 50% of patients with facial port-wine stain and normal in contralateral eye.¹⁻³ While in bilateral facial port-wine stain, IOP is >21 mm Hg in both eyes.

Gonioscopy: In infants, look for developmental anomalies or neovascularization of angles of anterior chamber. In adults, usually angles of anterior chamber look normal.

INVESTIGATIONS

Visual fields: A standard automated perimetry to document visual field defect should be performed.

Pre-perimetric test: OCT, GDxVCC or HRT to document any early glaucomatous damage of RNFL is advisable in cases of SWS with borderline IOP and no evidence of glaucoma.

MRI brain/CT head: To look for cortical calcifications, which can be appreciated as *double densities or railroad tracks*.

MANAGEMENT

The treatment includes following:

Medical Treatment

Antiglaucoma agents may suffice to control the glaucoma that occurs in later life, whereas the infantile form usually requires surgical intervention. Beta-blockers, alpha-adrenergic agonists or carbonic anhydrase inhibitors can be used as mono therapy or in combination to achieve target IOP. One should *avoid prostaglandin analogues* in cases of SWS (where episcleral venous pressure is already raised) since it can cause anterior uveal effusion.

Surgical Treatment

The surgical options include following:

Goniotomy: It is first choice, as chance of intraoperative choroidal effusion is not associated with goniotomy.

Combined trabeculotomy: Trabeculectomy may improve the chances of success, by treating both possible sources of elevated IOP that anterior chamber angle anomaly as well as elevated episcleral venous pressure.

Trabeculectomy: Chances of intraoperative choroidal effusion and expulsive choroidal hemorrhage are more with trabeculectomy. It is preferable to perform one or more sclerotomy before trabeculectomy to reduce chances of intraoperative complications.

Glaucoma drainage device: Another surgical approach to reduce pressure in these patients while minimizing intraocular complications.

Cyclophotocoagulation: Performed in patients with refractory glaucoma or in patients with high risk of intraoperative or postoperative complications (choroidal expulsive hemorrhage or choroidal detachment) after glaucoma filtration surgery and when the visual potential is poor.

VIVA QUESTIONS

Q.1. What is the cause of glaucoma in SWS?

Ans. The cause differs according to the onset.

Table 1 Differentiating feature between congenital glaucoma and glaucoma due to Sturge-Weber syndrome (SWS)

Congenital glaucoma	Glaucoma due to SWS
Bilateral	Usually unilateral, rarely bilateral
Absence of port-wine stain	Ipsilateral port-wine stain
Other systemic involvement rare	Neurological involvement common

- In infants or children (approximately 60% of the cases) cause of raised IOP is anomalies of anterior chamber angles.
- In late-onset glaucoma (approximately 40% of the cases), raised IOP is due to increased episcleral venous pressure.
- Remember the incidence of glaucoma increases when the port-wine stain involves the eyelid. It is usually ipsilateral to the lesion but can also manifest bilaterally.^{5,6}

Q.2. How would you differentiate secondary glaucoma due to SWS and congenital glaucoma?

Ans. Differentiating feature between congenital glaucoma and glaucoma due to SWS are given in **Table 1**.

Q.3. Explain port-wine stain (PWS).

Following points must be remembered about PWS:

- It is a well delineated red macule present at birth
- With increasing age, it gets darker and thicker and many small and large dark nodules can grow on the surface, resembling pyogenic granulomas.
- It typically presents in the V1 and V2 distributions of the trigeminal nerve.
- The upper eyelid is more frequently affected than the lower.
- In cases where PWS is present bilaterally, the likelihood of having SWS is higher than unilateral cases.
- Rarely ipsilateral nasal and buccal mucosa may also be involved on the side of PWS.
- The severity of associated neurological deficits and glaucoma is often correlated

with the distribution of PWS along various branches of the trigeminal nerve. Involvement of both V1 and V2 carries the highest risk of glaucoma while involvement of only V2 distribution carries the lowest risk.

- The treatment of PWS is pulsed dye laser photocoagulation, which causes irreversible damage to blood vessels but spares other components of the skin. Multiple treatment session is required. The side effects are minimal. However, 100% clearance of the skin discolouration is not possible.

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BUPHTHALMOS

Vaishali Ghanshyam Rai, Dewang Angmo

INTRODUCTION

Buphtalmos is a term that is applied to congenital glaucomas with enlargement of globe that appear during the first 3 years of life. The incidence of buphtalmos is 1:3300 in India and 1:10, 000–1:20, 000 in western world.^{1,2} It is bilateral in up to 65–80% of cases. Around 90% of cases appear to be sporadic, 10% of cases appear to be a strong familial component.^{1,2}

HISTORY

Chief Complaints

- Infant is usually referred to an ophthalmologist from pediatrician due to corneal cloudiness.
- Parents of infant may complaint of large eye ball, lacrimation and or blepharospasm.
- Triad of epiphora, photophobia and blepharospasm is the most common presentation.

Family History

Similar complaint in other offspring is important due to familial inheritance. The chance of a second child having the disease is approximately 3%, and it may be as high as 25% if two children have the disease.

OCULAR EXAMINATION

- *Visual acuity:* Child may have severe photophobia due to corneal edema and breaks in Descemet's membrane with torch light while checking fixating and following light. The enlargement of the globe with elevated IOP during the first 3 years of life creates a myopic shift in the refractive error.
- *Eyeball:* Enlarged eyeball is common (**Fig. 1**), which occurs because the immature and growing collagen that constitutes the cornea and sclera in the young eye still responds to increased intraocular pressure (IOP) by stretching.
- *Sclera:* Bluish discoloration of sclera due to stretching can be seen.

- *Cornea:* Increase in corneal diameter (**Fig. 2**). A horizontal corneal diameter >12 mm gives a high index of suspicion for the disease. Corneal edema with horizontal breaks in Descemet's membrane, i.e. Haab's striae should be noted. In severe cases, acute hydrops may be seen.
- *Anterior chamber:* Usually deep.
- *Iris:* Usually normal, although it may have stromal hypoplasia with loss of the crypts.
- *Posterior segment:* Examination of optic nerve head is important to look for asymmetric cupping between two eyes or >0.3 CDR.



Fig. 1: Clinical photograph of a case of congenital glaucoma showing bilateral buphtalmos



Fig. 2: Clinical photograph of a case showing right eye buphtalmos

INVESTIGATIONS

- **IOP:** The IOP in normal infants is in the range of 11–14 mm Hg using Tonopen or handheld Goldmann tonometer, IOP >14 mm Hg in bilateral cases or >5 mm Hg difference between two eyes in unilateral or asymmetric case should be considered for diagnosis of Buphthalmos.
- **Gonioscopy:** Evaluation of the anterior chamber angle is essential for the accurate diagnosis of congenital glaucoma. It is done under anesthesia using an infant Koeppen goniolens. The iris inserts anteriorly compared to the normal infant angle. The stroma of the peripheral iris is hypoplastic, unpigmented, and has a scalloped appearance.
- **Barkan's membrane:** It refers to a membrane formed due to incomplete resorption of mesodermal tissue across the anterior chamber angle, referred to as the Barkan's membrane. Although its existence is controversial it forms the basis of the surgical procedure of goniotomy which results in cleaving of the membrane to increase aqueous flow.^{1,2}
- **Monster vessels:** Normally, the angle is usually devoid of blood vessels. In congenital glaucoma loops of blood vessels from the major arterial circle may be seen above the iris surface and referred as monster vessels and this phenomena is called Loch Ness Monster phenomenon.^{1,2}

TREATMENT

Treatment of buphthalmos is mainly surgical.

- **Goniotomy:** It is surgical choice where cornea is clear so that angle of anterior chamber can be visualized clearly.
- **Trabeculotomy:** Where cornea is hazy, trabeculotomy is the surgical procedure of choice.
- **Filtration surgery:** Cases where goniotomy and trabeculotomy failed, filtration surgery trabeculectomy or drainage implant is an option. It is usually combined with trabeculotomy (Trab+Trab).
- **Cycloablative procedures:** Cases in which conventional glaucoma surgery has failed to control IOP cycloablative procedures, e.g.

cryocryotherapy or laser cyclophotocoagulation may lower the IOP profoundly.

- **Penetrating keratoplasty:** Permanent corneal scarring may persist after normalization of the IOP, in those cases penetrating keratoplasty can be indicated.
- **Endothelial keratoplasty:** Recently Descemet stripping automated endothelial keratoplasty has gained popularity for treatment of endothelial dysfunction associated with buphthalmos.
- **Tube surgery:** Initial results are encouraging.
- **Non penetrating Sx:** Rarely done.

VIVA QUESTIONS

- Q.1. What is normal corneal diameter in infants and when would you suspect buphthalmos?**

Ans. Normal horizontal corneal diameter in infants is 10–10.5 mm, increases from 0.5 to 1.0 mm during the first year of life. A horizontal corneal diameter >12 mm gives a high index of suspicion for the disease.

- Q.2. What is differential diagnosis of buphthalmos?**

Ans. Differential diagnosis of buphthalmos depending on ocular signs are:

- Corneal edema or clouding
 - Congenital hereditary endothelial dystrophy—cornea thickness increased two/three times normal, corneal enlargement is typically absent. Corneal clouding is often symmetrical with no descemet breaks or corneal scarring.¹
 - Mucopolysaccharidoses—absence of elevation of IOP and corneal enlargement.
 - Sclerocornea—the opaque corneal tissue extends onto the cornea.
 - Obstetric birth trauma (“forceps injury”)—See Table 1.
- Epiphora and/or red eye
 - Nasolacrimal duct obstruction
 - Ophthalmia neonatorum/Conjunctivitis (viral, Chlamydial, bacterial)
 - Corneal epithelial defect, abrasion

Table 1 Differentiation of birth trauma and congenital glaucoma

Features	<i>Birth trauma</i>	<i>Congenital glaucoma</i>
Corneal diameter	Normal	Large (buphthalmos)
IOP	Normal	High
Photophobia	No	Yes
Onset of corneal edema after birth	Immediate	Weeks to months later
Clearing of edema	Spontaneous	After reducing IOP
Tears in Descemet's membrane	Vertical or oblique	Horizontal or concentric to the limbus
Eye affected	Left more	Equal
Soft tissue injuries	May be there	Absent

- Photophobia
 - Conjunctivitis
 - Uveitis
- Corneal enlargement
 - Axial myopia
 - Megalocornea (X-linked or sporadic)
 - Microphthalmic fellow eye.

Q.3. How to differentiate between Haab's striae and force injury?

Ans. In case of forcep injury, Descemet's membrane tears are usually vertical or oblique but these tears are horizontal in congenital glaucoma (i.e. Haab's striae). [also See **Table 1**]

Q.4. Is buphthalmos reversible?

Ans. Cupping of the optic nerve head proceeds more rapidly in infants than in adults and is more likely to be reversible if the pressure is lowered early enough. The cupping appears to be caused by incomplete development of connective tissue in the lamina cribrosa, which allows compression or posterior movement of the optic disc tissue in response to elevated IOP, with an elastic return to normal when the pressure is lowered.

Q.5. Write about classification of congenital glaucoma.

Ans.

- Primary
 - Congenital
 - Infantile
 - Juvenile

- Secondary
 - Systemic disorders
 - ◆ Chromosomal abnormalities
 - ◆ Metabolic disorders (Lowe's syndrome, Zellweger's syndrome)
 - ◆ Phakomatoses (Sturge-Weber syndrome)
 - Ocular developmental disorders
 - ◆ Anterior segment dysgenesis
 - ◆ Aniridia
 - ◆ Congenital ectropion uvea
 - ◆ Nanophthalmos
 - Ocular diseases—retinoblastoma, retinopathy of prematurity (ROP), persistent hyperplastic primary vitreous (PHPV), trauma, uveitis.

Q.6. What are the issues in management of congenital glaucoma?

Ans. Following are the issues in management of congenital glaucoma:

- Assessing etiology and inheritance of congenital glaucoma
- Managing systemic problems of secondary congenital glaucoma
- Deciding type of surgery
 - Goniotomy-clear cornea
 - Trabeculotomy or Trabeculotomy + Trabeculectomy
 - Valve implant
- Managing associated ocular problems—refractive errors, corneal opacity, cataract, squint, amblyopia
- Counselling of parents.

Table 2 Hoskins' anatomic classification of the developmental glaucomas

Group	Major category	Sub-category	Variants	Examples
I	<i>Isolated trabeculodysgenesis</i> Malformation of trabecular meshwork in absence of iris or corneal anomalies	Flat iris insertion	<ul style="list-style-type: none"> • Anterior insertion • Posterior insertion • Mixed insertion 	
		Concave (wraparound) iris insertion		
		Unclassified		
II	<i>Iridotrabeculodysgenesis</i> Trabeculodysgenesis with iris anomalies	Anterior stromal defects of the iris	Hypoplasia	Can be seen in Axenfeld's, Rieger's, and Peters' anomalies
			Hyperplasia	Sturge-Weber syndrome with glaucoma
		Anomalous iris vessels	<ul style="list-style-type: none"> • Persistence of tunica vasculosa lentis • Anomalous superficial vessels 	
		Structural anomalies	<ul style="list-style-type: none"> • Holes • Colobomas • Aniridia 	
III	<i>Corneotrabeculodysgenesis</i> Trabeculodysgenesis with congenital corneal defects. Usually associated with iris anomalies	Peripheral corneal defects		Axenfeld's anomaly
		Midperipheral corneal defects		Rieger's anomaly
		Central corneal defects		Peters' anomaly
		Abnormalities of corneal size		Microcornea or megalocornea and their associations

Q.7. Give details of Hoskin's anatomic classification of the developmental glaucomas.

Ans. See Table 2. Developmental anomalies of anterior segment is the hallmark of congenital glaucoma. It may involve one or more of the angle structures such as the trabecular meshwork, the iris, and/or the cornea. Hoskin's classification is based on this. It is very useful for planning the treatment as well as prognostication of the cases.³

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NEOVASCULAR GLAUCOMA

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INTRODUCTION

Neovascular glaucoma (NVG) is a severe form of secondary glaucoma characterized by proliferation of fibrovascular tissue in the anterior chamber such as iris and angles. It is a potentially blinding clinical condition, where delayed diagnosis or poor management can result in the treatment involves management of both the elevated intraocular pressure (IOP) and the underlying cause of disease.^{1,2}

HISTORY

Chief complaints: A case of NVG usually presents with:

- Pain, redness and decrease of vision in the affected eye.
- Depending on the cause of the neovascularization patient may give a history of dimness of vision preceding pain and redness for few weeks or months.

History of Present Illness

Dimness of vision may precede the history of pain and redness by few weeks to months depending on the cause of the neovascularization. Usually the loss of vision in the affected eye is of sudden onset but may be of gradual onset as well depending on the underlying cause. At the time of presentation patient may or may not have regained the lost vision.

History of Past Illness

Neovascular glaucoma (NVG) can be associated with recurrent attacks of angle closure glaucoma hence; similar episodes of dimness of vision in the past may be present.

Past Surgical History

- Patients may have history of cataract surgery. More often, it is associated with complicated cataract surgeries resulting in posterior capsular dehiscence or leaving the patient aphakic.

- Common in post vitrectomized eyes of proliferative diabetic retinopathy especially if the eye is having untreated retinal detachment.

EXAMINATION

Systemic Examination

The underlying cause of retinal ischemia is associated with several systemic diseases such as diabetes, hypertension. A thorough systemic examination is carried out to look for complications of these diseases.

Ocular Examination

Lid: Normal or edematous if there is acute rise of IOP in the affected eye as in angle closure glaucoma stage.

Conjunctiva: May be congested if IOP is grossly raised.

Cornea: Clear or hazy due to epithelial edema depending on the IOP.

Iris: Presence of neovascularization can be seen (**Fig. 1**). A careful examination of the iris and angle of the anterior chamber is essential, before the pupil is dilated and any drops put in the eye. Once the pupil is dilated, it may not be easy to find the NV.¹ During the early stages, neovascularization of the iris (NVI) is essentially at the pupil margin and is very fine and delicate in character (**Fig. 1**). At times new vessels may be seen in angles (NVA) on gonioscopy, while NVI is yet to appear (**Fig. 2**).

Anterior chamber (AC): The AC often shows the presence of flare and sometime a few cells. There may be presence of hyphema also.

Pupil: Following signs can be seen:

- Fine randomly oriented superficial vessels near pupillary margin.
- Presence of ectropion uveae.
- Pupillary reaction may be sluggish or absent or there may be relative afferent pathway defect (RAPD) depending upon the extent of optic nerve damage.

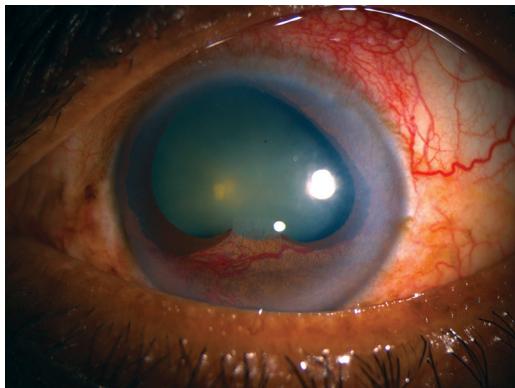


Fig. 1: Neovascularization of iris

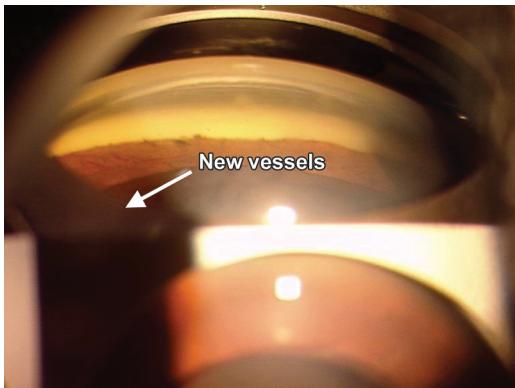


Fig. 2: Neovascularization of angle

Table 1 Stages of neovascular glaucoma

Stage	Characteristic	NVI/NVA	Symptoms	Other signs	IOP	Gonioscopy
Prerubeosis stage	Predisposing ocular/extraocular condition is present	Absent	Absent	Laser photometry or fluorescein iris angiography is helpful in detecting early leakage of iris vessels	Normal	Open angle
Pre-glucoma stage	Rubeosis iridis stage	Present	Absent	Usually none	Normal	Open angle with early NVA
Open angle glaucoma stage	Florid rubeosis with leaky vessels	Florid	Present	Cells, flare, hyphema	Elevated	Open angle with florid NVA
Angle closure glaucoma stage	Contraction of fibrovascular membrane in the angle	New vessels become less apparent	Present	Loss of visual acuity Ectropion uvae, flat smooth, glistening appearance of the iris. Conjunctival congestion Corneal edema Cells, flare, hyphae Optic disc changes	Persistently high (> 60 mm)	Variable PAS Sometime complete angle closure

Abbreviations: IOP, intraocular pressure; NVI, neovascularization iris; NVA, neovascularization of angles; PAS, peripheral anterior synechiae

IOP: Markedly raised in angle closure stage.

Lens: Pseudophakia with or without posterior capsular dehiscence or aphakia are risk factors for NVI.

Fundus: Evidence of retinal ischemia in the form of central retinal vein occlusion (CRVO), proliferative diabetic retinopathy (PDR), central retinal artery occlusion (CRAO), etc. maybe there.

Optic nerve hypoplasia (ONH) damage depends upon the duration and severity of raised IOP.

It is important to remember that the disease process progresses through four stages and the symptoms and signs depend upon the stage at which the patient presents. The stages and the associated symptoms and signs have been described in **Table 1**.

DIFFERENTIAL DIAGNOSIS

Normal iris vessels: In some eyes normal iris vessels are seen easily, particularly in blue eyes that may be mistaken for NVI or even angle NV when the vessels are seen near the root of the iris.¹

Following points may help in differentiating:

- Iris vessels are present in stroma but new vessels are superficial.
- Iris vessels are radial in arrangement, unlike irregularly arranged new vessels.
- Sizes of iris vessels are uniform, new vessels are of varying sizes.
- Branching of new vessels is absent in iris vessels.
- New vessels are leaky as is found in fluorescein angiography or fluorophotometry.

In the *open angle stage*, neovascular glaucoma may have to be differentiated from other glaucoma of acute onset such as angle closure glaucoma and glaucoma with uveitis. NVG can be differentiated easily by the presence of rubeosis iridis in spite of the fact that eyes with uveitis may have dilated iris vessels.

In *angle closure stage*, when new vessels are less apparent the condition has to be differentiated from other causes of iris distortion and peripheral anterior synechia, e.g. old trauma or iridocorneal endothelial (ICE) syndrome.

MANAGEMENT

The treatment of NVG includes identifying the underlying etiology and its timely and adequate treatment to prevent the development and progression of NVG. Once NVG develops and IOP is high, the target is to control high IOP and prevent optic nerve damage in addition to treatment of underlying etiology.

Prophylactic Treatment

Panretinal photocoagulation: Mechanism is uncertain, but probably it acts by reducing oxygen demand. PRP is able to reverse IOP elevation in the open angle glaucoma stage and in early angle closure stage where synechial angle closure is not more than 270° yet.

Trans-scleral panretinal cryotherapy or anterior retinal cryopexy (ARC): When cloudy media preclude PRP.

Anti-VEGF agents: As an adjunctive treatment with PRP.

Medical Management

Medical management consists of following:

Antiglaucoma drugs: Mainstay of medical treatment is to reduce aqueous production with topical beta-blockers, alpha-2 agonists and with topical and/or oral carbonic anhydrase inhibitors. Mannitol (hyperosmotic agents) may also be required in cases of acute rise in IOP. Topical prostaglandin analogues and Miotics are better avoided as they may increase ocular inflammation.

Anti-inflammatory drugs: Topical steroids and cycloplegics are recommended to reduce the inflammation that is often present.

Antiangiogenic drugs: Several studies propose the usefulness of anti-VEGF agents as an adjunct to traditional treatments such as PRP and additional surgery. Anti-VEGF (intracameral or intravitreal, or both simultaneously) have been used in following circumstances.

- As an adjunct to panretinal photocoagulation (PRP) or bevacizumab alone when visibility of the posterior segment is difficult due to opacities of the media (e.g. hemorrhage).
- Intracameral injection of bevacizumab may provide additional strategy for treating rubeosis iridis in NVG. Bevacizumab is well tolerated, effectively stabilizes NVI, and controls IOP when used alone and at an early open angle stage of NVG.
- In advanced cases of NVG, it can be used as a therapeutic window before PRP or surgical intervention (usually 1 week before but can be within 14–48 hour also). It decreases the risk of failure, hemorrhage and inflammation.
- In cases where PRP is not possible due to poor retinal view, intravitreal bevacizumab can be given followed by Trabeculectomy with Mitomycin C.

Remember

- Bevacizumab (most reported anti-VEGF in NVG) cause regression of the NVI within 24 to 48 hours following intravitreal injection whereas NVI starts regressing post PRP by 2 weeks and is complete by 4–6 weeks.³

- Most studies report similar dose for intravitreal and intracameral use (1.25 mg/0.05 mL).
- Medical management with anti-VEGF along with retinal ablation can control the IOP in the open angle stage of NVG only; in advanced stage with synechial, angle closure surgical intervention for IOP lowering is often required.

Surgical Management

The type of surgery depends upon level of IOP, presence of active or regressed NVI, prior laser or anti-VEGF treatment, prior intraocular surgeries, degree of inflammation, stage of disease, degree of angle closure, severity of glaucomatous optic neuropathy and visual potential.³ Following options are available:

- *Filtration surgery:* Success rate of trabeculectomy are poor if performed alone. It is usually combined with use of intra-operative mitomycin C (MMC). Chance of success increases significantly when combined with preoperative bevacizumab and/or PRP (success rate may improve up to 95%).³
- *Glaucoma drainage device surgery:* Glaucoma drainage devices (GDDs) are often considered as a primary surgical procedure in the management of NVG where there is a high risk for failure of conventional filtering surgery. Various drainage devices like Molteno implant; Baerveldt implant and Ahmed glaucoma valve have been used in management of NVG and shown comparable results to trabeculectomy.
- *Cyclodestructive procedure:* These procedures are indicated in cases with refractory NVG with poor visual prognosis. Trans-scleral cyclophotocoagulation (TSCPC) with non-contact neodymium:yttrium-aluminum-garnet (Nd:YAG) (TSCPC) or semiconductor diode laser cyclophotocoagulation (DLCP) have proven useful in treatment of such cases. Repeat treatment may be required to maintain good control of IOP.³
- *Other surgeries:* Endoscopic cyclophotocoagulation, intravitreal injection crystalline triamcinolone acetonide, injection of silicon oil during revision of vitrectomy after unsuccessful vitreous surgery in diabetics.

VIVA QUESTIONS

- Q.1. Name important causes of neovascular glaucoma.**

- Ans.**
- *Diabetic retinopathy:* Most common cause of NVI. In fact 1/3rd of rubeotic cases have diabetic retinopathy.
 - *Retinal vascular occlusive diseases:* Second commonest cause—ischemic central retinal vein occlusion (CRVO), central retinal artery occlusion (CRAO), branch retinal vein occlusion (BRVO), branch retinal artery occlusion (BRAO), sickle cell retinopathy.
 - *Extraocular diseases:* Carotid artery disease, ocular ischemia, giant cell arteritis, pulseless disease, and carotid-cavernous fistula.
 - *Assorted retinal diseases:* Retinopathy of prematurity (ROP), retinal detachment (RD), Eale's disease, Coat's disease, persistent hyperplastic primary vitreous (PHPV), Norrie's disease.
 - Trauma
 - *Ocular neoplasms:* Malignant melanoma, retinoblastoma, and optic nerve glioma.
 - *Ocular inflammatory diseases:* Chronic uveitis, endophthalmitis, sympathetic ophthalmia and Vogt Kayanagi Harada's disease (VKH).
 - *Ocular surgery:* Cataract extraction especially in diabetics, vitrectomy, retinal detachment surgery.

Note: Of all these causes three most common causes are diabetic retinopathy, ischemic CRVO and ocular ischemic syndrome. In Indian set-up, chronic angle closure glaucoma is also an important cause of NVG.

- Q.2. Where does neovascularization start?**

- Ans.** At pupillary margin, from capillaries of minor arterial circle.

- Q.3. In what percentage of cases of neovascular glaucoma neovascularization at the angle (NVA) may be found in absence of NVI at pupillary margin?**

- Ans.** In approximately 12%.^{1,3}

- Q.4. How can we differentiate between normal iris vessels and new vessels?**

- Ans.** Following points helps:

- Iris vessels are present in stromal but new vessels are superficial.
- Iris vessels are radial in arrangement, unlike irregularly arranged new vessels.
- Sizes of iris vessels are uniform, new vessels are of varying sizes.
- Branching of new vessels is absent in iris vessels.
- New vessels are leaky as is found in fluorescein angiography or fluorophotometry.

Q.5. How do you identify NVA on gonioscopy?

Ans. New vessels extend from iris root across the ciliary body and sclera spur; arborize over the trabecular meshwork.

Q.6. What is hundred-day glaucoma?

Ans. NVG occurring after 3 months following CRVO.

Q.7. Describe the stages of NVG.

Ans. Stages of NVG are as follows (See Table 1)

- Pre-rubeotic stage—In patients with proliferative diabetic retinopathy and ischemic CRVO, neovascularization must be looked for carefully under high magnification on the iris and in the angle of the anterior chamber (neovascularization of angle—NVA) at every visit. The iris should be examined before dilatation of the pupil and pupillary margins and margins of iridotomy should be carefully looked for new vessels.
- *Pre-glaucoma stage/rubeosis iridis:* Variable amounts of neovascularization (rubeosis) can be found at pupillary margin, iris surface and in the angle. Characteristic features of this stage are normal IOP, unless pre-existing concomitant POAG/PACG is present. Patients are usually asymptomatic at this stage unless the underlying condition produces symptoms like field loss due to CRVO or decreased vision due to vitreous hemorrhage or macular ischemia in diabetic retinopathy (DR).
- *Open angle glaucoma stage:* New vessels spreading and fibrovascular tissue covering angle. At this stage, IOP begins to rise and stays elevated. In some cases, the IOP may rise suddenly resulting

in acute-onset glaucoma. Rubeosis iridis in this stage is more florid and is often associated with anterior chamber inflammatory reaction. Due to fragile nature of the new vessels, a hyphema can also present at this stage sometimes. Gonioscopy shows an open angle but with more intense neovascularization.

- *Angle-closure glaucoma stage:* Heavy neovascularization and extensive peripheral anterior synechia. Most patients present or are detected at this stage. In this stage, the contraction of fibrovascular membrane in the angle leads to progressive synechial angle closure, ectropion uveae and flat, smooth, glistening appearance of the iris. Gonioscopy reveals varying degrees of peripheral anterior synechiae or complete angle closure may be present at this stage. The IOP is usually very high and can go up to 60 mm Hg. Conjunctival congestion and corneal edema are frequently present. Glaucomatous optic nerve damage is often moderate to advance. Visual acuity may also be severely affected.

Few authors include a regression stage characterized by total synechial angle closure and less visible vessels.

Q.8. How does surgery influence the occurrence of neovascularization?

Ans. Crystalline lens, posterior capsule, vitreous all act as mechanical barriers for angiogenic factors liberated by ischemic retina to reach anterior chamber. Vitrectomy, cataract surgery especially with disruption of posterior capsule removes this mechanical barrier and an increased risk of NVG.

Q.9. What are the theories behind neovascularogenesis in NVG?

Ans. Following factors play an important role in NVG:

- *Retinal hypoxia:* Stimulus for release of angiogenic factors.
- *Angiogenesis factors:* VEGF with its several isoforms, angiogenin, and platelet derived endothelial growth factor, TGF beta, TNF alfa, vascular endothelial growth factor.

- *Vaso-inhibitory factors:* Vitreous and lens may be potential source of these factors; explains why NVG is more common following lensectomy and vitrectomy.
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ANGLE-REcession GLAUCOMA

Prakhar Goyal, Divya Agarwal, Talvir Sidhu

INTRODUCTION

Angle recession glaucoma is a secondary open angle glaucoma that is associated with blunt trauma to eye. Angle recession is a tear between the longitudinal and circular muscles of the ciliary body. It is a gonioscopy diagnosis. Post-traumatic hyphema is strongly associated with angle recession (60–90%).^{1,2}

HISTORY

Chief Complaints

The patient may present with following:

- Deep set pain, redness and gradually diminishing vision for distance (when associated with glaucoma).
- Onset can be immediately after injury or months to years after blunt trauma.
- May be completely asymptomatic.

History of Past Illness

Patients presenting late with complaints of deep seated ocular pain or other symptoms of raised intraocular pressure will give past history of trauma weeks or months back. The case may present years after the trauma, when glaucoma occurs. Although eye trauma invariably occurs before angle recession, it is common to have forgotten details of the injury or even the entire episode after a number of years have passed.

EXAMINATION

General Examination/Specific Systemic Examination

Look for any signs of trauma especially scars around the eye.

Ocular Examination

Examination will show features of trauma along with angle recession which is diagnosed on gonioscopy.

Eyeball: Look for any associated signs of trauma such as orbital fracture, enophthalmos, periocular scars.

Lid: In case of early presentation lid edema or lid laceration may be present due to blunt trauma. Those presenting late may show scar of eyelid repair.

Conjunctiva: May be normal in delayed presentation. Presence of subconjunctival hemorrhage can be seen in acute cases.

Cornea: Following points must be noted:

- Stromal edema and pigment deposition on endothelium, blood staining of the endothelium may be there in early onset cases.
- Longstanding cases, no abnormality can be seen.

Sclera: Partial or complete scleral tear may be associated in early presentation.

Anterior chamber (AC): Following points must be noted.

- Deep and irregular AC depth may be seen
- Hyphema in early onset.

Iris: Look for other manifestations of blunt trauma such as:

- Iridodialysis (D shaped pupil)/cyclodialysis
- Iris sphincter tears
- Iridoschisis.

Pupil: Signs of trauma such as corectopia and traumatic mydriasis can be there.

IOP: IOP is raised when presents with glaucoma. A reduced IOP may be seen in early cases due to ciliary shock/ciliary shutdown.

Lens: Look for previous signs of trauma such as:

- Subluxated or dislocated lens.
- Cataract may be present in some cases due to associated trauma.
- Vossius ring.

Vitreous: Vitreous hemorrhage may be present as a consequence of trauma.

Fundus: Following signs of trauma must be looked for:

- Retinal dialysis, retinal detachment, sub-retinal hemorrhages.
- Patients will long-standing raised IOP will show glaucomatous optic nerve changes and other features as seen in POAG.

Gonioscopy: In acute cases gonioscopy examination should be deferred for at least 4–6 weeks post acute injury. Gonioscopy signs:

- Gonioscopy examination using 4-mirror Gonio lens shows asymmetry of angle recess if compared to nontraumatized eye or to other quadrants of same eye. Simultaneous, bilateral Koeppe gonioscopy is the most useful technique to detect subtle angle recession.
- Widening of the ciliary body band due to retro displacement of iris root is the most important gonioscopic findings of angle recession (**Fig. 1**).
- Prominent scleral spur.
- Irregular and darker pigmentation of angle.
- Peripheral anterior synechiae.

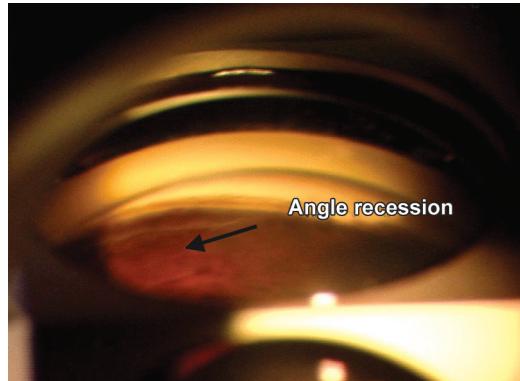


Fig. 1: Widening of the ciliary body band due to retrodisplacement of iris root

DIFFERENTIAL DIAGNOSIS

Although diagnosis of angle recession glaucoma is evident on gonioscopy and optic disc examination other differential diagnosis of *unilateral glaucoma* should be considered like:

- Pseudoexfoliation glaucoma
- Neovascular glaucoma
- Lens particle and phacolytic glaucoma should be considered and differentiated from angle recession.

MANAGEMENT

The treatment of angle recession glaucoma can be divided into following:

Medical Management

In acute cases treatment should be directed at lowering IOP and reducing inflammation by use of aqueous suppressants like topical B-blockers-Timolol (0.5%) BD or/and alpha 2 agonists like apraclonidine or brimonidine (0.2%). Topical cycloplegics like atropine and steroids should be given for relief of pain and to reduce inflammation and possibly risk of secondary hemorrhage.

Laser Trabeculoplasty

It has found to be *ineffective* in angle in most cases due to distortion of angle anatomy and

TM scarring. Nd:YAG laser trabeculopuncture has found to be effective in some cases as shown in some studies where TM was intact on gonioscopy.

Filtration Surgeries

Trabeculectomy is effective in controlling IOP when used with antimetabolites however success rate is lower as compared to POAG. Use of glaucoma drainage devices has also limited benefits in angle recession glaucoma.

VIVA QUESTIONS

Q.1. What is the incidence of angle recession after blunt trauma?

Ans. Angle recession is reported to occur in 20 to 94% of eyes after blunt trauma. It is often masked initially due to the presence of concomitant hyphema, which results from shearing of the anterior ciliary arteries.¹

Q.2. What are the chances of getting angle recession in a case of traumatic hyphema?

Ans. Angle recession may occur in 85% (range 71 to 100% of eyes) of patients with traumatic hyphema.^{1,2}

Q.3. What is the mechanism of angle recession?

Ans. Close globe injury causes anteroposterior globe compression with equatorial scleral expansion, limbal stretching, and posterior displacement of the lens/iris diaphragm. This may lead to the angle recession.

Q.4 What is the mechanism of glaucoma in angle recession?

Ans. Mainly due to trabecular damage and not the recession itself.

Q.5. What are the sources of traumatic hyphema?

Ans.

- Major arterial circle and branches of the ciliary body (MC >90% cases)
- Choroidal arteries (rare)
- Ciliary body veins (very rare)
- Iris vessels at the pupillary margin or in the angle (very rare).

Q.6. What are the 7 rings of trauma?

Ans. This often refers to the seven commonly injured intraocular structures following contusion injury:

- Iris sphincter tear
- Iridodialysis
- Angle recession
- Cyclodialysis
- Tear in trabecular meshwork
- Zonular dialysis, subluxation or dislocation of lens
- Retinal dialysis or tears.

Q.7. What is the risk of glaucoma in angle recession?

Ans.

- Glaucoma is seen in only 5.5% (7 to 10%) of patients with angle recession.¹⁻³
- An increased risk of glaucoma development was found if the angle recession exceeded 180°.
- Two peaks in incidences of glaucoma is seen, less than 1 year and at least 10 years after trauma. A 3.4% incidence of glaucoma after ocular contusion has been reported during a 6-month follow-up and up to 10% during the 10 years after trauma.^{1,2}

Q.8. How to differentiate angle recession from cyclodialysis?

Ans. Ciliary muscle is torn between the longitudinal and circular layers in angle recession. The longitudinal or meridional ciliary muscle remains attached. This distinguishes recession from cyclodialysis, where the entire ciliary body including the longitudinal muscle is detached.

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STEROID-INDUCED GLAUCOMA

Vaishali Ghanshyam Rai, Talvir Sidhu

INTRODUCTION

A certain percentage of the general population responds to repeated instillation of topical corticosteroids with a variable increase in the intraocular pressure (IOP). Certain people do manifest this response to chronic steroid therapy, whether given by the topical, systemic, or periocular route, and the IOP elevation can lead to glaucomatous optic atrophy and loss of vision. Such a condition is referred to as steroid induced glaucoma. Following 4–6 weeks of topical steroid administration, about 5% of the population will demonstrate a rise in IOP of more than 16 mm Hg and 30% a rise of 6–15 mm Hg.¹

HISTORY

Chief Complaints

The clinical presentation and onset is highly variable. Patient may present with pain and gradually diminishing vision for distance or may be completely asymptomatic.

Past History

Patient may give history of long-term use of corticosteroids in any form like topical, systemic or local applications in past. History of intravitreal triamcinolone acetonide (IVTA) or slow release intravitreal implant of dexamethasone like ozurdex is also important.

Risk factors for steroid induced glaucoma include:

- Patients with primary open angle glaucoma (POAG)
- Family history of POAG
- Children below 10 years
- High myopia
- Diabetes mellitus
- Connective tissue disorder, e.g. rheumatoid arthritis.

EXAMINATION

Ocular examination:

- Eyeball—normal
- Eyelids—usually normal, or may show eyelid skin atrophy or ptosis with topical steroids

- Conjunctiva and sclera—usually normal
- Cornea—long-term topical steroid may cause increased corneal thickness or corneal ulcers.
- Angle of anterior chamber—normal depth and contents.
- Pupil—topical steroids use can cause mydriasis.
- Lens—usually appears normal or may show posterior sub capsular cataract that is also a side effect long-term use corticosteroid.
- Vitreous—normal
- Fundus—glaucomatous cupping of optic nerve.
- IOP—with Goldmann's applanation tonometer may be normal due to discontinuation of steroid therapy in past. IOP may be high in cases of intravitreal steroid implants or patient currently on any steroid medication.
- Gonioscopy with four mirror Gonio lens reveals open angles in all quadrants.

DIFFERENTIAL DIAGNOSIS

Primary Open Angle Glaucoma

- Usually bilateral with high IOP. Steroid induced glaucoma can be unilateral or bilateral depending upon steroids used with normal or high IOP.
- History of steroid intake
 - Uveitic glaucoma
 - Normal tension glaucoma—usually bilateral with thin cornea with normal IOP
 - Glaucomatocyclitic crisis—usually unilateral with other uveitis signs like circumciliary congestion, keratic precipitates on corneal endothelium, anterior chamber reaction with raised IOP.
 - Primary juvenile open angle glaucoma.

MANAGEMENT

- Stop the responsible steroid medication, in majority of cases raised IOP comes to normal levels within few weeks to months.
- In refractory cases with advanced glaucomatous optic nerve, damage management would

- be cessation steroid and start antiglaucoma medication to reduce IOP.
- Glaucoma following IVTA needs to be managed with antiglaucoma medication till the intravitreal steroid crystals resolve, i.e. 6 months
 - Intractable glaucoma following intravitreal steroid depot may be treated by removal of depot through pars plana vitrectomy combined with trabeculectomy.
 - Substitute potent steroid with lower potency steroid where complete cessation of steroid for medical condition is not possible. Lower potency steroids like phosphate forms prednisolone and dexamethasone, rimexolone, loteprednol etabonate or fluorometholone can be used to substitute potent steroids.
 - Steroids can also be substituted with non-steroidal anti-inflammatory drugs like diclofenac, nepafenac or ketorolac.
 - Other steroid sparing agents are immunosuppressant like tacrolimus ointment or cyclosporine for vernal keratoconjunctivitis or methotrexate can be used in uveitis or systemic conditions.
 - *Laser trabeculoplasty:* Argon laser trabeculoplasty or selective laser trabeculoplasty can be considered where medical treatment failed to control the IOP or patient is intolerant to medical treatment or in cases where filtering surgery is precluded due to systemic condition.
 - *Trabeculectomy:* With or without antimetabolites is indicated in patients whom both medical or laser treatment fail to control IOP.
- Prevention of steroid induced glaucoma
- By regular monitoring of patients on steroids for IOP, check every 2 weeks
 - Avoid topical steroids wherever possible by using alternatives
 - Use of lower potent steroids like fluorometholone or loteprednol.

VIVA QUESTIONS

Q.1. Define steroid induced glaucoma.

Ans. Steroid induced glaucoma is a form of open angle glaucoma occurring as an adverse effect exogenous corticosteroid therapy or excess endogenous production of glucocorticoids.

Q.2. What is an average time taken for IOP rise in different routes of steroid administration?

Ans. See Table 1.

Q.3. Explain the mechanism of steroid induced glaucoma.

Ans. Corticosteroids cause IOP elevation by increasing the outflow resistance and thereby decreasing the facility of aqueous outflow. The main mechanisms of steroid induced glaucoma are as follow:

- Stabilization of lysosomal membranes and leading to accumulation of polymerized glycosaminoglycan (GAG).
- Alteration of the composition of the extracellular matrix through which aqueous flows, thereby increasing resistance to outflow.

Table 1 Average time taken for IOP rise in different routes of steroid administration

Route	Average dose	Average time taken for IOP rise
Oral	25 mg hydrocortisone/day 50 mg prednisolone /day	1 year 2–15 months
Inhalational	Most of steroid inhalers	3 months
Pulse steroids	140 mg repeated 4 weekly	6 months
Dermatological	Betamethasone cream 0.1%	3 months
Topical	QID doses of potent steroid	2–6 weeks
IVTA	4 mg	4–8 week
Posterior sub tenon	40 mg of triamcinolone acetonide	5–9 weeks

- Increased production of collagen, elastin, laminin and fibronectin within trabecular meshwork and resulting in increased in trabecular meshwork resistance.
- Inhibition of phagocytosis activity of endothelial cells lining the trabecular meshwork and leading to accumulation of debris in the trabecular meshwork.
- Decreased production of extracellular proteinase like fibrinolytic enzymes, stromolysin and matrix metalloproteinases.
- Inhibition of the production of outflow enhancing prostaglandins such as PGF 2 α .

Q.4. Name gene associated with steroid induced glaucoma.

Ans. Many genes associated with steroid induced glaucoma are myocin, optineurin, antichymotrypsin, pigment epithelium-derived factor, cornea-derived transcript 6, prostaglandin D2 synthase, decorin, insulin-like growth factor binding protein 2, ferritin light chain and fibulin-1C. Myocilin gene (previously known as the trabecular meshwork inducible glucocorticoid response or *TIGR* gene) is the most studied amongst these.^{1,2}

Q.5. Name two landmark studies done on steroid induced glaucoma. What findings were demonstrated in those studies?

Ans. Becker and Armaly studies. The findings have been described in Table 2.

Q.6. Lowpotency steroid and risk of glaucoma.

Ans. Different low potency steroids are phosphate forms prednisolone 0.1% and rimexolone 1%, loteprednol etabonate 0.5% or fluorometholone 0.1%. Risk of glaucoma after use of low potency steroid has not been studied in detail. However, the general agreement is it is very less.

Table 2 Becker and Armaly studies

Parameters	Becker	Armaly
Frequency	QID	TDS
Duration	6 weeks	4 weeks
Parameter	Final IOP	IOP change
Type of responder		
Low	<20 mm Hg	<6 mm Hg
Intermediate	20–30 mm Hg	6–15 mm Hg
High	>31 mm Hg	>15 mm Hg

Table 3 Intraocular pressure elevation in different type of steroid

Type of steroid	Mean intraocular pressure rise (in mm Hg)
Dexamethasone 0.1%	22
Prednisolone 1.0%	10
Dexamethasone 0.005%	8
Fluoromethalone 0.1%	6
Hydrocortisone 0.5%	3
Tetrahydrotriamcinolone 0.25%	2

Q.7. Intraocular pressure elevation in different type of steroid

Ans. See Table 3.²

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PSEUDOEXFOLIATION GLAUCOMA

Vaishali Ghanshyam Rai, Dewang Angmo

INTRODUCTION

Pseudoexfoliative syndrome (PXF) is a systemic condition characterized by the deposition of white powdery or fluffy material within the anterior segment of the eye including lens, angle, pupil and cornea. The deposits most notable on the anterior lens capsule. PXF can cause secondary open angle glaucoma which is more aggressive in its clinical course with high IOP at onset, progresses at a faster rate and responds poorly to medical therapy, compared to primary open angle glaucoma (POAG). Pseudoexfoliative glaucoma is seen in up to 50% of eyes with PXF.^{1,2}

HISTORY

Epidemiology

Pseudoexfoliative syndrome (PXF) is seen worldwide with a high prevalence in Scandinavian countries. Incidence varies between 1.5% to 27%. Incidence increases with age. Commonly seen after the age of 40 years. Few studies suggest a female preponderance however it is still debated.^{1,2}

Chief Complaints

Patient may present with following:

- Pain and redness usually unilateral
 - Gradually diminishing vision for distance
 - Patient may be completely asymptomatic.
- The majority of patients are asymptomatic, and PXF is often an incidental finding.

EXAMINATION

Ocular Examination

- Eyeball—usually normal or may be deep seated as patients with pseudoexfoliation are usually present in 7–8th decade. Relative anterior microphthalmos (normal axial length but anterior segment is smaller) may also be there.
- Eye lid—normal.

- Conjunctiva—may be normal or ciliary congestion can be there in presence of raised IOP.
- Cornea—small whitish powdery flakes or clumps may be found on corneal endothelium. Early corneal endothelial decompensation is common with PXF syndrome (*Fuchs like keratopathy*). Corneal guttata may also be found the exact cause of which is not known. Pigment can be observed dispersed on the endothelium. The pigment is believed to arise from disruption of iris pigment epithelium secondary to frictional interaction with PXF material on the lens capsule.²
- *Anterior chamber (AC)*: AC may be shallow in pseudoexfoliation syndrome. Small pigments can be appreciated floating in anterior chamber. PXF syndrome has been associated with a disrupted blood-aqueous barrier. Testing with a flare meter demonstrated markedly increased flare in comparison with primary open angle glaucoma.² The zonulopathy can also lead to anterior displacement of the lens, that is, a phacomorphic narrowing, with intermittent pupillary block.
- *Iris and pupil*: Iris and pupil examination can reveal following signs:
 - Small flecks of PXF material deposits can be seen on pupillary margin which is hallmark of PXF syndrome.
 - There may be flakes deposits on iris crypts and folds.
 - Trans-illumination defect can be appreciated in pupillary margin resulting from atrophic and/or fibrotic changes in the iris sphincter muscle. The pupillary margin of the iris is also affected with loss of the pupillary ruff. These changes collectively result in what is described as a “moth eaten” pupil margin.²
 - Look for iridodonesis which is common in PXF syndrome.
 - Sphincter muscle degeneration and posterior synechiae are also seen.

- **Pupil:** Usually poor mydriasis (atrophic and/or fibrotic changes in the iris sphincter muscle) and asymmetric pupil is seen in PXF.
- **Lens:** Following signs can be seen:
 - Whitish powdery ring deposit on anterior lens capsule is more consistent and diagnostic sign of PXF (**Fig. 1**).
 - *Target sign:* The deposition is observed in 3 distinct zones; a central zone of material deposition; clear intermediate zone (secondary to iris excursion rubbing the PXF material off); a peripheral zone of PXF material (**Figs 2 and 3**) outside of this intermediate zone. The central zone may be absent in 20% of cases of PXF and the peripheral granular zone can only be observed with dilation.² Clinically three distinct zones can be found on anterior lens capsule on dilated pupil, two concentric rings of powdery deposits with central translucent zone.
 - Cataractous lens, nuclear sclerosis is more common with PXF. Asymmetric nuclear cataract formation can be there.
 - Look for phacodonesis.
 - In advanced stage there can be subluxated or dislocated cataractous lens due to weak zonules.
- **Fundus:** Unilateral glaucomatous cupping of optic disc with diffuse neuroretinal rim damage if media is clear. In cases of mature cataract needs to get B-scan biometry to see optic nerve head and retina status.

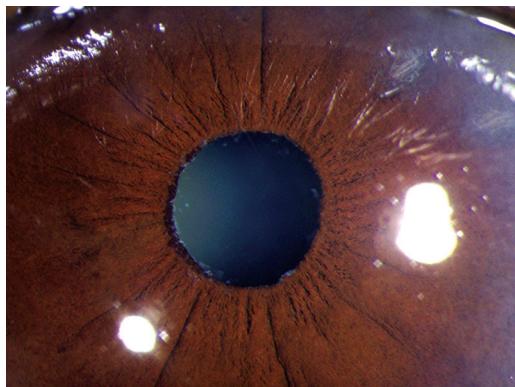


Fig. 1: Whitish powdery ring deposit on anterior lens capsule and pupillary margin

- **IOP:** Measured with Goldmann applanation tonometer shows >21 mm Hg. Usually mean IOP in PXF patient is more than that of POAG cases. 40% of pseudoexfoliation syndrome patients will develop glaucoma or ocular hypertension.
- **Gonioscopy:** Shows characteristic increased pigmentation of trabecular meshwork, more prominent in superior quadrant and usually unilateral. Dark, dense and uneven wavy pigmentation along the Schwalbe's line (*Sampaoli's line*) is also seen in PXF. This finding is not exclusive to PXF (also seen in pigment dispersion syndrome and chronic inflammation).² In 9–18% angle is occludable in pseudoexfoliation syndrome.²



Fig. 2: Peripheral zone of PXF material over lens capsule

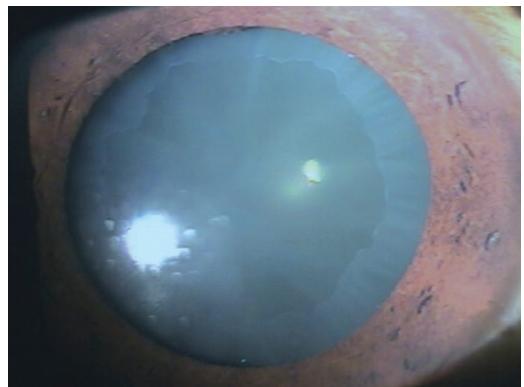


Fig. 3: Peripheral ring of target sign

DIFFERENTIAL DIAGNOSIS

A case of PXF has to be differentiated from following:

Pigmentary Glaucoma

- Common in young age group.
- Usually bilateral.
- Transpupillary defect is common in mid-peripheral area of iris.
- Prominent uniform dark pigmentation band of trabecular meshwork is characteristic feature of pigmentary glaucoma.

True Exfoliation

- Characterized by thin clear membrane like material separating from anterior lens capsule.
- Glaucoma is infrequent associated with true exfoliation.
- Underlying pathology can be anterior uveitis or exposure to UV rays.

Primary Amyloidosis

- Generalized systemic disorder with numerous ocular manifestation along with glaucoma.
- Bilateral ocular involvement is common.
- Fine whitish powdery deposits throughout eye is characteristic.

POAG: Differentiation table in viva questions.

PACG: Can be differentiated by characteristic clinical signs.

Uveitic glaucoma: AC reaction, and other signs of uveitis are absent.

INVESTIGATIONS

- Diurnal variation of IOP is valuable in evaluating the true magnitude of IOP reduction
- Baseline perimetry
- RNFL imaging
- Specular biomicroscopy shows reduced endothelial cells count
- A-scan biometry for axial length and keratometry
- B-scan ultrasonography in case of hazy media to evaluate retina.

MANAGEMENT

The medical management – similar to that of POAG like beta-blockers, alpha adrenergic agonists, carbonic anhydrase inhibitors or prostaglandin analogs. Mono therapy is usually insufficient to control IOP in PXG so combination therapy is advisable.

Argon/selective laser trabeculotomy is successful and well-established procedure for reducing IOP in PXG associated with open angles.

Trabeculectomy is indicated when medical or laser therapy has failed to obtain target IOP or when there is progressive glaucoma.

Combined trabeculectomy and cataract surgery is indicated in PXG with intractable IOP with cataract. Common complications anticipated during combined surgery in PXG are (also See **Table 1**).

- Poor dilation of pupil
- Zonular dialysis and vitreous loss
- Dislocation or decentration IOL
- Corneal decompensation
- Postoperative ocular inflammation.

VIVA QUESTIONS

Q.1. What is Sampaolesi's line?

Ans. In PXG cases on gonioscopy a dark, dense and uneven wavy pigmentation along the Schwalbe's line is known as Sampaolesi's line.

Q.2. What are the complications anticipated during cataract surgery in PXG cases?

- Ans.**
- Poor dilation of pupil
 - Zonular dialysis and vitreous loss
 - Dislocation or decentration IOL
 - Corneal decompensation
 - Heightened postoperative inflammation
 - Postoperative IOP elevation
 - Late intraocular lens implant decentration and prolapse into the posterior segment.

Q.3. How do you differentiate between PXG and primary open angle glaucoma?

Ans. See **Table 2**.

Table 1 Difficulties and precaution during cataract surgery

<i>Difficulty</i>	<i>Precaution</i>
Poorly dilating pupil	<ul style="list-style-type: none"> • Atropine • Stretch the pupil with instruments • Iris hooks • Pupil expansion rings
Endotheliopathy	<ul style="list-style-type: none"> • Visco-adaptive (Healon 5 or Visco-dispersive viscoelastic (Viscoat) • Ashrinoff's soft-shell technique
Weak zonules	<ul style="list-style-type: none"> • Chopping techniques or prolapse the lens nucleus out of the capsular bag during phaco • Traditional extracapsular surgery • Capsular tension ring (CTR) • 3-piece intraocular lens implant (IOL)
Postoperative inflammation	<ul style="list-style-type: none"> • Aggressively with postoperative steroids and perhaps for a longer duration
Postoperative pressure spikes	<ul style="list-style-type: none"> • Postoperative Diamox
Capsular phimosis	<ul style="list-style-type: none"> • Nd-YAG laser, placing relaxing incisions in the anterior lens capsule at the 4 cardinal positions

Table 2 Differentiation between PXG and POAG

	<i>POAG</i>	<i>PXG</i>
Age of onset	40–50 years	>60 years
Vision loss	Less marked	Marked due to presence of nuclear sclerosis
IOP	> 21 mm Hg	High IOP >40 mm Hg
Laterality	Bilateral	Usually unilateral
Anterior segment	Usually normal	White powdery deposits on pupillary margin, on lens capsule with weak zonules. Subluxated or dislocated lens can be seen
Anterior chamber	Normal	May be normal or shallow Flare may be present
Gonioscopy	Open angle	Marked blotchy pigmentation of trabecular meshwork. Sampaolesi's line is characteristic
Disc	Focal or diffuse RNFL defect depending on early or late presentation	Usually diffuse RNFL defect
Severity of glaucoma	Less	More
Response to therapy	Good	Poor
Surgery	May be required	Often required

Q.4. Cause of zonular weakness in PXF.

Ans. The exact cause is not known, however, the possible mechanisms include following:²

- PXF material directly induce zonular damage

- Accumulation of PXF material at the origin of the zonules on pre-equatorial regions of the lens disrupts zonular architecture.

Table 3 Differential diagnosis

Parameters	Pigment dispersion	Pseudoexfoliation
Demographics	30–50 years Men Related to myopia White race	60 years Men and women Related to aortic aneurysms (abnormal basement membrane) Scandinavian countries
Pathomechanism	Posterior bowing of the iris Constant rubbing of posterior iris and zonules <i>Release of pigments</i> Trabecular block	Systemic disease of <i>abnormal basement membrane</i> (skin, viscera, eyes) Secretion of amyloid like material (oxytalon) in AC Deposit in trabeculum and zonules Trabecular block
Clinical features	Krukenberg's spindle Deep AC with posterior bowing of iris (<i>reverse pupillary block</i>) Iris atrophy in periphery of iris Pigment deposit on lens (<i>Zentmayer's line</i>)	White powdery deposits on pupillary margin (pseudoexfoliative material), on lens capsule (<i>Target sign</i>) with weak zonules. Subluxated or dislocated lens can be seen Poorly dilating pupil Iris atrophy at edge of pupil margin
Gonioscopy	Heavily pigmented angle Queer iris pigmentation	Marked blotchy pigmentation of trabecular meshwork. <i>Sampaoli's line</i> is characteristic Pseudoexfoliative material

- Intrinsic differences between normal and PXF zonules because PXF zonules are composed of modified forms of zonular fibers.

Q.5. How do you differentiate between PXG and pigment dispersion syndrome (PDS)?

Ans. See Table 3.

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CHAPTER

4

Retina

LONG CASES

VITREOUS HEMORRHAGE

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INTRODUCTION

Vitreous hemorrhage (VH) is defined as the presence of extravasated blood within the space outlined by the internal limiting membrane of the retina posteriorly and laterally, the nonpigmented epithelium of the ciliary body laterally and the lens zonular fibers and posterior lens capsule anteriorly.¹ The incidence of VH is seven cases per 100,000, which makes it one of the most common causes of acutely or subacutely decreased vision. Such cases are a common reason for surgery and a favorite for long case. During work-up, focus should be on identifying the cause of VH.

HISTORY

Chief Complaint

The symptoms of VH are varied but usually include:

- Early or mild hemorrhage cases presents with floaters, which patient describes as cobwebs, ring shadow, multiple insects moving in front of eye, smoke signals, dark clouds or even a red hue.
- In severe cases, sudden onset painless unilateral visual loss is the usual complain (MC presentation). Patients often say vision is

worse in the morning as blood has settled to the back of the eye, covering the macula.

- Hemorrhage that is more significant can cause visual fields defect or scotomas.

History of Present Illness

Presentation can be unilateral or bilateral. It may be rapidly progressive. Preceding events such as trauma, Valsalva maneuver, recent surgery or recent retinal laser therapy must be recorded. Many a times the patients would give history suggestive of the cause of VH, e.g. recurrent pain and redness s/o uveitis or VF loss s/o RVO/ glaucoma or central scotoma in age-related macular degeneration (ARMD). Scotomas remain fixed in the field whereas generally floaters move with eye movement.¹

History of Past Illness

History of trauma, diabetes, hypertension, tumor (hemangioma, retinoblastoma, melanoma, retinal angioma), valsava maneuver, shaken baby syndrome, venous occlusion, bleeding disorder, leukemia, ocular surgery (glaucoma surgery, RD surgery, cataract surgery), laser (panretinal photocoagulation), vasculitis, chest compression,

pseudotumor cerebri must be asked as it may provide a clue to the underlying cause.

Recurrent VH may point towards Eales' disease, proliferative diabetic retinopathy (PDR), or bleeding diathesis. History from the fellow eye may also be suggestive of ocular predisposition to VH. In cases of trauma it is necessary to classify as per BETTS, to prognosticate as such cases can often be medico legal.

Family History

Family history of diabetes, hypertension, bleeding disorder, leukemia, tumor, and vacuities must be recorded.

Past Surgical History

A detailed past ocular surgery must be noted.

Medical History

Medical history of diabetes mellitus, systemic hypertension, drug intake, sickle cell disease, anemia, bleeding diathesis and cerebral stroke can give a valuable clue even before ocular examination.

EXAMINATION

Systemic Examination

Systemic examination is important in a case of VH to rule out the above-mentioned causes. It is especially important in cases of vascular occlusion since there may be some cardiology or associated intracranial events that need immediate attention by a general physician. Similarly, it is not uncommon to discover signs of hematological disorder in patients with unexplained VH. It becomes more important when the disease or causation cannot be localized to the eye.

Ocular Examination

Visual Acuity

Recording of VA of either eye is necessary. The status of the other eye often guides the management plan.

Eyeball

Usually normal. May be large in case of high myopia. Proptosis may be in cases of tumor (axial in cavernous hemangioma).

Lid

Usually normal.

Conjunctiva

Multiple hemorrhages in conjunctiva may be there. Conjunctival microvascular abnormality in sickle cell disease "*the comma sign*" is pathognomonic but its pathogenesis remains obscure. In such cases, corkscrew vessels are seen. Similarly, in heart disease conjunctiva may reveal vascular tortuosity or in rare cases bulbar telangiectasia.

Cornea

May be large and corneal thinning may be there in myopes.

Sclera

Scleral thinning may be there (blue sclera in collagen vascular disease).

Anterior Chamber

Keratic precipitates, cell and flare may be present in the inflammatory diseases. Deep AC is seen in high myopic eyes. There may be signs of angle closure glaucoma (ACG).

Iris

Iridodialysis, neovascularisation of iris (NVI) or angle (NVA) may be there. This is extremely important, as it is prognostic and diagnostic.

Pupil

Presence of relative afferent pupillary defect points unequivocally to an underlying retinal detachment, retinal vascular occlusion, and large macular lesion or optic nerve disease.

Intraocular Pressure

An intraocular pressure (IOP) less than 9 mm Hg or more than 22 mm Hg needs to be investigated and explained. Hypotonic globe would suggest retinal detachment, wound leak, or an open globe injury (occult or obvious). Raised IOP could be due to neovascular glaucoma, hemolytic glaucoma, corticosteroid usage, or tumor invasion under conditions of VH.

Gonioscopy

Neovascularization of angle (NVA) can be seen in cases of PDR, angle recession or cyclodialysis may be there in case of blunt trauma.

Lens

Following points must be noted subluxation, dislocation, zonular dialysis, phacodonesis and traumatic cataract presence of all this points towards trauma as the underlying cause of VH.

Anterior Vitreous

Presence of vitreous pigments or *Shaffer's sign* commonly seen in presence of retinal detachment (RD) but rarely also in cases of trauma. Presence of RBC's or hemosiderin pigments can be typically there. Importantly, retro Lenten cells may also be seen, their presence however is not specific for uveitis.

Fundus

Posterior vitreous detachment (PWD) can cause VH. If PVD is there scleral depression is mandatory to rule out a peripheral retinal break. It is important to remember that an acute PVD with VH has an up to 70% incidence of retinal tears, compared to low incidence in acute PVD without VH. Other findings to look for includes NVE, NVD, wet ARMD, DR, familial exudative vitreoretinopathy (FEVR), retinopathy of prematurity (ROP), Retinal vasculitis, signs of trauma proliferative sickle cell retinopathy, venous occlusion, retinal macroaneurysm, choroidal melanoma, and angioma. Presence of fresh red hemorrhage mixed with old bleed is suggestive of recurrent bleeding, and indicates retinal neovasculopathy. In old hemorrhage, one should look for presence of fibrotic clots. Presence of diffuse whitish opacity should indicate possibility of other causes of media opacity, other than blood. Specific fundus features of individual diseases may be there (see viva section).

Different Forms of Vitreous Hemorrhage

Hemorrhage into the Berger's space (retrolental space of Erggelet) and the Canal of Petit (except for the Canal of Hannover) or in a space generated

by a posterior vitreous detachment (retrohyaloid or subhyaloid hemorrhage) are also considered VH.¹ *Blood within Berger's space* settles down and forms a crescent-shaped pool with the hyaloideo-capsular ligament as its inferior border. *Hemorrhage into the Canal of Petit-* also has a crescent-shaped superior border, which is also formed by the hyaloideo-capsular ligament. *Blood in Cloquet's canal*-outlines its inferior border and, *Blood in the retrohyaloid space*—generated by a vitreous detachment (retro- or subhyaloid hemorrhage) can collect as a meniscus at the inferior vitreoretinal demarcation. A clinically similar appearance is caused by hemorrhage into the space between the internal limiting membrane and the nerve fiber layer (subinternal limiting membrane hemorrhage). In the latter type of hemorrhage, the blood is under tension and does not shift with changes in the position of the patient's head, as observed in subhyaloid hemorrhage. Subinternal limiting membrane hemorrhage has been described in penetrating ocular injury, Terson's syndrome, anemia, valsalva maneuver-induced retinopathy, shaken baby syndrome, retinal macroaneurysm, diabetic retinopathy, and branch retinal vein occlusion.¹

In contrast to the above-mentioned types of hemorrhage into defined vitreous spaces, bleeding into the vitreous gel (intravitreal hemorrhage) shows no characteristic borders and rapidly clots.

Visual acuity with vitreous VH and retained macular function is primarily determined by the location and density of the hemorrhage. Only small amounts of blood are necessary to cause a substantial reduction in visual acuity. Around 12.5 pL of diffuse blood in a 5 mL aphakic or 10 pL of diffuse blood in a 4 mL phakic vitreous cavity may decrease the visual acuity to hand motions.¹

Natural Course of Vitreous Hemorrhage

There are certain unique biochemical features of the vitreous in catabolism of bloodlike—rapid clot formation, slow lysis of fibrin, persistence of intact red blood cells for months and lack of early polymorphonuclear response, extracellular lysis of red blood cells, spontaneous clearance is more common in diseases, which have no recurrent bleeding, syneresis of vitreous gel, and in elderly and aphakic patients. The VH does not clear as

spontaneously in patients with diabetic retinopathy, longstanding VH, with *an ochre membrane* (the accumulated red cells and red cell debris suspended in and mixed with vitreous collagen). Complications that can occur must be looked for such as hemosiderosis bulbi, retinal detachment, glial and fibrovascular proliferation and glaucoma (ghost cell/hemolytic/hemosiderotic), hyphema, and staining of ocular structures.

Fellow Eye

Evaluation of the fellow eye can often help in diagnosis of VH. Common conditions of the fellow eye that help speculate cause of VH in the affected eye include diabetic retinopathy, hypertensive retinopathy, ARMD, myopic changes, lattice, vitreous condensation, retinal white without pressure (WWOP) changes, retinal tear, retinal hole, giant retinal tear, peripheral retina breaks/retinal detachment, retinal vasculitis (including Eales' disease), ocular ischemic syndrome, venous occlusions, familial exudative vitreoretinopathy (FEVR), and retinoschisis. We should also look for any retinal detachment in fellow eye.

Fundus Findings in Eales' Disease

Retinal phlebitis—characterized by mid-peripheral venous dilation, perivascular exudates along the peripheral veins, and superficial retinal hemorrhages. Vascular sheathing ranges from thin white lines limiting the blood column on both sides to segmental heavy exudative sheathing. **Peripheral nonperfusion**—Fine solid white lines retaining configuration of normal retinal vasculature as a remnant of obliterated large vessels, sharply demarcated junction between the anterior peripheral nonperfusion and the posterior perfused retina, vascular abnormalities at the junction between the perfused and nonperfused zones such as microaneurysm, venovenous shunts, venous beading, and occasionally hard exudates and cotton-wool spots can be seen. **Neovascularization**: NVE, NVD, recurrent VH, proliferative changes, tractional retinal detachment (TRD). The macula is usually not involved, but when it does, it is termed as central Eales' disease. In this variant, all mid-peripheral lesions appear in the posterior pole and cause loss of vision in the early stage of the disease (**Fig. 1**). Sea fan new vessels may be there.^{1,2}

Differential Diagnosis

These are causes of media opacity and true for old white VH:

- Vitritis
- Amyloidosis
- Lymphoma
- Asteroid hyalosis
- Vitreous degeneration
- Leukemic vitreous infiltration.

INVESTIGATIONS

Systemic

Based on the disorder suspected.

Lab Tests

Blood sugar, complete hemogram, coagulation profile, erythrocyte sedimentation rate (ESR), C-reactive (CRP), peripheral blood smear, enzyme-linked immunosorbent assay (ELISA), venereal disease research laboratory (VDRL), Mantoux carotid Doppler scan, ECG, chest X-ray, echocardiography.

FFA/ICG

Once media is partially or totally clear angiography can be done for deciding on management or diagnoses.



Fig. 1: Central Eales disease. Note sheathing of the major vascular arcade with macular edema

USG

Extremely important in management of media haze related cases. Multiple scans must be taken including transverse and longitudinal just like in a screening USG. If the whole or a part of the underlying retina is obscured due to VH, ultrasound B scans with corresponding A-scan is mandatory to detect any associated retinal detachment/mass lesion. During the scan, emphasis should be on three sites: the vitreous cavity, vitreoretinal interface and retinochoroidal layer. With ultrasound, it is possible to differentiate between fresh and clotted hemorrhage. Unclotted hemorrhage with no cellular clumps may not be visible ultrasonically. Asteroid hyalosis is one condition that may appear similar to clotted VH on B-scan. It allows determination of the location and density of the VH, the location and extent of traction membranes and retinal detachment (**Fig. 2**), and the vitreoretinal relationship, all of which may help to predict the visual outcome after vitreous surgery. Status of PVD and its differentiation from RD is necessary. Rarely retinal breaks may also be picked up.

Some patients may need repeated retinal evaluation and serial ultrasonography in 7–10 days to reaffirm the cause and again rule out any retinal detachment/retinal break that would warrant an early surgery. Typically, patients with acute PVD need repeat USG.

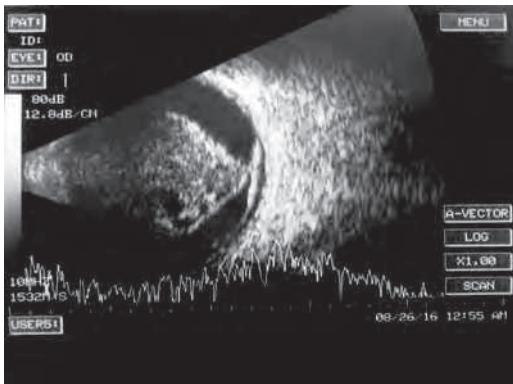


Fig. 2: USG showing VH with TRD in a case of PDR. The membrane persisted on low gain and had poor after movements. Ruling out RD is necessary as it affects visual prognoses severely

X-ray, CT and MRI

Occasionally, computed tomography (CT) and magnetic resonance (MR) imaging are performed on patients with VH, for example, in Terson's syndrome to evaluate for intracranial hemorrhage. Computed tomography does not easily differentiate hemorrhage from the surrounding vitreous. May also be useful in cases of trauma.

VER

It may be useful in cases where visual prognoses is doubtful.

MANAGEMENT

As discussed earlier, first part is determining the possible cause of VH, as management involves systemic consultations accordingly. A case of uveitis may need prior treatment with steroids; whereas a case of RD may need urgent surgery.

After establishing the etiology, management of VH should be individualized. Management is done in form of observation, laser photocoagulation, cryotherapy and pars plana vitrectomy.

The choice depends on several factors. It include patient's age, the duration of disease, visual acuity, intraocular pressure, presence or absence of neovascularization of iris, amount of hemorrhage, retinal status, adequacy of photocoagulation if done before the onset of hemorrhage, lens status (phakic or aphakic/pseudophakic) and presence or absence of posterior vitreous detachment (PVD).¹

Principles of Management

Observation: Fresh VH often clears in days to weeks to allow evaluation of retina. Serial USGs are of paramount importance in such cases.

In case of retina attached—In unknown etiology: In these patients, the patient is asked to rest with the head in an elevated position and we should reevaluate after 3–7 days to ascertain the possible source of hemorrhage. Oral ascorbic acid (Vitamin C) may be given for faster clearance (though not clinically proven), as there is more liquefaction and loss of gel structure in eyes with ascorbic acid. **In known etiology—**In these patients re-evaluation is done after 3–4 weeks. This group includes

post laser or postvitrectomy recurrent VHs, VH in Tersons' syndrome or after acute PVD and hemorrhage associated with bleeding diathesis.

In retinal detachment: Early surgery is recommended in VH associated with retinal detachment. In eyes with attached macula, one may wait for some days for PVD to occur, as this will enhance the technical ease and improve the outcomes of surgery. This includes penetrating trauma without retained intraocular foreign body (and not associated with infection), fresh retinal detachment with VH and no PVD, Eales' disease without PVD and rhegmatogenous retinal detachment, VH in closed globe injury without retinal detachment. In macula-off retinal detachment with VH, we should do immediate surgery.

Laser photocoagulation: Laser photocoagulation in proliferative vasculopathies should start as soon as any part of retina is visible. In some cases, one may start laser therapy using an indirect ophthalmoscope delivery system in dense VH and later on one can shift to slit lamp delivery. After partial clearing of hemorrhage, one may visualize a retinal break or avulsed vessel that can be treated with barrage laser. In media haze due to VH, cataract, corneal edema (as in neovascular glaucoma) or poorly dilating pupil, transconjunctival cryopexy mode of laser can be used for pan retinal photocoagulation or treatment of retinal breaks. Role of preoperative anti-VEGF has been discussed in the chapter on PDR.

Anterior retinal cryotherapy (ARC): Has limited use. Generally not applied.

Vitrectomy: Early vitrectomy is indicated in situations where the underlying pathology is likely to progress fast if left untreated.¹ Surgery can be delayed in eyes with well-lasered proliferative retinopathy with retina attached. Vitrectomy can be deferred till good PVD occurs in eyes with Tersons' syndrome, closed globe-injuries, postcataract surgery VH (if not due to peribulbar anesthesia related globe perforation), VH in bleeding diathesis, etc.

Indications of Vitrectomy

- Severe nonclearing VH over 2-3 months.

- Advanced proliferative retinopathy where the VH does not resolve in 6-8 weeks after adequate laser therapy
- VH with retinal detachment
- VH with giant retinal tear
- Tractional retinal detachment involving the macula
- Combined tractional and rhegmatogenous retinal detachments
- Severe progressive fibrovascular proliferation
- Anterior segment neovascularization with posterior segment opacities
- Dense premacular hemorrhage
- Ghost cell glaucoma
- Macula edema associated with premacular traction
- Anterior hyaloid fibrovascular proliferations
- Fibrinoid syndrome with associated retinal detachment
- VH with retained intraocular foreign body
- VH due to AMD and idiopathic polypoidal choroidal vasculopathy (IPCV).

Management of Specific Conditions

Proliferative Diabetic Retinopathy

(See Long Case for PDR)

Eales' disease: Eales' disease usually presents with VH at the time of onset. Sixty-two percent patients have VH at the time of initial presentation. It can occur due to severe retinal vasculitis or in the proliferative stage due to new vessels and traction. It can be treated with retinal photocoagulation initially. Early vitrectomy has been advocated, with 87% eyes showing improvement in visual acuity.

Macroaneurysm: VH develops in as many as 30% of macroaneurysm. Mostly occurs in women over 60 years of age with systemic hypertension. These may resolve spontaneously or may require laser treatment.

Uveitis: Pars planitis can result in retinal neovascularization and cause VH. Sarcoidosis, Behçets' syndrome and toxoplasmosis may cause VH due to retinal neovascularization whereas ocular histoplasmosis syndrome causes VH from choroidal neovascularization.

IRVAN (idiopathic retinal vasculitis, aneurysms and neuroretinitis) can also present with VH.

Retinal vascular anomalies and tumors: Cavernous hemangioma of the retina and optic disc, capillary hemangiomatosis or juxtapapillary vascular hamartomas of the retina, and congenital arteriovenous anastomoses can lead to VH. Parafoveal telangiectasia and Coats' disease cause VH rarely. A choroidal melanoma does not cause VH until it reaches a considerable size.

Sickle cell disease and leukemia: With peripheral scatter photocoagulation reduces the risk of VH in Sickle cell hemoglobinopathies. Retinal neovascularization may also develop in chronic cases of chronic myelocytic leukemia and can cause VH.

Posterior vitreous detachment: Spontaneous VH can occur with posterior vitreous detachment. An early diagnosis is crucial because a retinal tear is a common cause of VH. A detailed peripheral retinal evaluation with scleral depression is mandatory to screen for any retinal tears, obscured by VH. B-Scan (sometimes dynamic USG) and A-scan may be helpful to detect the retinal tear and the traction site. Surgery is indicated in case of retinal detachment.

Age-related macular degeneration: VH secondary to age-related macular degeneration results from a subretinal bleeding due to choroidal neovascularization. Ultrasonography shows a highly echogenic subretinal mass temporal to the optic disc typically, without any choroidal shadowing. In these patients, the hemorrhage usually resolves spontaneously. If surgery is planned, antivascular endothelial growth factor (VEGF) may be given at the end of surgery.

Miscellaneous: VH may occur in eyes undergoing intracapsular or extracapsular cataract extraction. Most VHs are mild and clear spontaneously, the possibility of needle perforation due to local anesthesia should be excluded. VH in Terson's syndrome occurs due break through bleeding from the internal limiting membrane of the retina and extends into the vitreous cavity. In a Valsalva maneuver, increased intravascular pressure causes VH due to retinal vein rupture. VH can also occur in warfarin or aspirin users.

VH in children: One of the most common causes of VH in children is trauma. Other causes are shaken-baby syndrome (in otherwise unexplained

VH in a child), retinoblastoma and leukemia. In infants, disseminated intravascular coagulopathy or Terson's syndrome are causes of VH. Pediatric retinal diseases that can present with VH include familial exudative vitreoretinopathy retinoschisis, high myopia with retinal tears/detachment, retinopathy of prematurity, toxocariasis. Early surgery is advocated in these eyes to avoid amblyopia and anisometropia.

VIVA QUESTIONS

Q.1. Describe causes of VH on the basis of age of the patient

Ans. The age of the patient can provide clues about etiology of VH. For example:

- *Newborn babies*—trauma after spontaneous vaginal delivery (but not after cesarean delivery), shaken baby syndrome and retinopathy of prematurity.
- *Young boys*—X-linked retinoschisis. Children—trauma, retinoblastoma, leukemia and other coagulopathies.
- *Young healthy adults*—Eales' disease in the Indian subcontinent is an important cause of VH. Retinal tears with or without associated retinal detachment.
- *In elderly*—choroidal neovascular membrane (CNVM) secondary to age-related macular degeneration (AMD), proliferative retinopathy associated with diabetes or retinal vein occlusion, and rarely due to retinal tears, posterior vitreous detachment, melanoma, IPCV, or systemic anticoagulants.

Q.2. What are the causes of VH?

Ans. See Table 1. Depending upon the source, following categories can be seen.

A. Bleeding from abnormal vessels

- i. Retinal vascular disorders that cause retinal ischemia (due to VEGF, FGF, IGF-NVD, NVE)
 - Proliferative diabetic retinopathy
 - Ischemic retinal vein occlusion (RVO), more commonly branch retinal vein occlusion (BRVO)
 - Eales' vasculitis
 - FEVR

Table 1 Causes of vitreous hemorrhage

Ocular causes Vascular	Coat's disease, retinal branch artery malformation, retinopathy of prematurity, ocular ischemic syndrome, branch retinal artery occlusion, central retinal artery occlusion, choroidal vascular aneurysm, retinal vein rupture, retinal neovascularization after retinectomy, hypertensive uveitis, persistent hyaloid artery, venous stasis retinopathy, arteriovenous communications of the retina
Inflammatory	Retinal vasculitis, Behcet's disease, sarcoid posterior uveitis, multiple sclerosis with retinal vasculitis, pars planitis, syphilitic retinitis, dermatomyositis. Systemic lupus erythematosus, toxocara
Iatrogenic	Retinal laser photocoagulation, after scleral buckling, molteno implant surgery, trabeculectomy, ocular perforation, during peribulbar injection, secondary IOL, cataract wound neovascularization, penetrating keratoplasty
Tumor	Retinoblastoma, cavernous hemangioma of the optic disc, combined retinal-retinal pigment epithelial hamartoma, vasoproliferative tumors, retinal angioma, retinal astrocytic hamartoma, choroidal malignant melanoma
Others	Senile bullous retinoschisis, juvenile retinoschisis, tearing of retinal pigment epithelium, Talc retinopathy, Retinitis pigmentosa, extracorporeal membrane oxygenation, trauma
Indirect causes	Pseudotumor cerebri, Valsalva retinopathy, chest compression, newborn after vaginal delivery
Blood disorders	Thrombocytopenia, idiopathic thrombocytopenic purpura, hemophilia, pernicious anemia, disseminated intravascular coagulation disorder, von-Willebrand's syndrome, Protein C deficiency, anticoagulant therapy

- Proliferative sickle cell retinopathy
 - Hematological disorders
 - ii. Retinal vascular disorders that is not associated with retinal ischemia-
 - Retinal artery macroaneurysm
 - Retinal angioma
 - Severe early vasculitis in absence of ischemia
- B. Rupture of a normal retinal vessel**
- Posterior vitreous detachment
 - Blunt trauma
 - Terson syndrome
 - Valsava retinopathy
 - Hematological disorder (anemia, leukemia, coagulation disorder).
- C. Breakthrough bleeding**
- Choroidal neovascular membrane (CNVM)
 - Choroidal melanoma
 - Idiopathic polypoidal choroidal vasculopathy (IPCV)
- Peripheral exudative hemorrhagic chorioretinopathy (PEHCR).
- Q.3. What is the role of fellow eye?**
Ans. See chapter.
- Q.4. USG differentiation of PVR/RD.**
Ans. For RD: Persistence at low gain, poor after movements, attached to disc, quantitative method.
- Q.5. Reasons for early surgery.**
Ans. Unlasered PDR, RD, IOFB, one-eyed patient, other eye lost to VH, Zone 3 injuries.

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CENTRAL RETINAL VEIN OCCLUSION

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INTRODUCTION

Retinal vein occlusion (RVO) is an obstruction of the retinal venous system may involve the central, hemicentral or branch retinal vein. The most common etiological factor is compression by adjacent atherosclerotic retinal arteries travelling through the same adventitial sheath. Other possible causes are external compression or inflammation of the vein wall. Central retinal vein occlusion (CRVO) may result from thrombosis of the central retinal vein when the vein passes through the lamina cribrosa. The prevalence of CRVO is reported to be around <0.1% to 0.4%.^{1,2} CRVO is usually a unilateral disease, the risk of developing any type of vascular occlusion in fellow eye is approximately 1% per year, and about 7% of persons with CRVO may develop CRVO in the fellow eye within 5 years of onset in the first eye.^{3,4}

HISTORY

The CRVO occurs predominantly in elderly population (>65 years), and affects male and female equally. These patients may often have ocular or systemic risk factors.

Chief Complaints

- Sudden painless loss of vision
- Rarely pain, redness due to neovascular glaucoma (NVG) or accompanying high intraocular pressure (IOP).

History of Present Illness

Patients usually present with sudden painless loss of vision in one eye. Some patients may also present with gradual decline of vision in cases of less severe occlusion. Marked deterioration of visual acuity especially on waking in morning can be seen in ischemic CRVO. Patients with non-ischemic CRVO may have no symptoms and it may be detected as an incidental finding on a routine ophthalmic examination. It is not rare to find some of these patients complain of episodes of amaurosis fugax before the constant blur.

Patients with partially recovered CRVO may give history of visual field loss or constriction. Floaters can rarely occur due to accompanying vitreous hemorrhage.

Decrease in contrast sensitivity, micropsia, macropsia, metamorphopsia, scotoma can also be there due to associated macular edema. Vision recovery is dependent on onset and duration of occlusion.

History of Past Illness

Ocular disorders predisposing to crowding/compression at the level of optic disc, and systemic disorders predisposing to thromboembolic disease or disease of the vascular wall are the most commonly identified risk factors. For example, there may be history of open angle glaucoma or angle closure glaucoma, ischemic optic neuropathy, pseudotumor cerebri, tilted optic nerve head, optic nerve head drusen, hypermetropia, hypertension, cardiovascular diseases, carotid insufficiency, diabetes, bleeding/thrombotic disorder, leukemia, multiple myeloma, sickle cell disease, SLE, HIV, herpes zoster, syphilis, sarcoidosis. It may also be presented after retrobulbar block, dehydration and pregnancy.

There is small risk of past CRVO in the fellow eye, ~7% in 5 years.

Family History

Family history of risk factors may be there.

Past Surgical History

History of ocular surgery, cardiovascular surgery maybe there.

Personal History

History of smoking, alcohol intake, tobacco use.

Drug History

History of intake of oral contraceptive, diuretics, and hepatitis-B vaccine must be enquired.

EXAMINATION

General examination/specific systemic examination should be aimed at ruling out the systemic risk factors.

Ocular Examination

Visual acuity: Visual acuity at the time of presentation is variable (ischemic vs nonischemic **Table 1**), and is an important prognostic indicator

of final visual outcome. Generally, visual acuity better than 20/200 is believed to be a sign of good final prognoses.

External and anterior segment evaluation can reveal signs of systemic risk factors.

Eyeball: Proptosis in case of tumor (abaxial in sarcoid)

Lid: Signs of other systemic risk factors may be present.

Table 1 Types of central retinal vein occlusion (CRVO)

Parameters	Nonischemic CRVO	Ischemic CRVO
Incidence	80%	20%
Age	Young adults and past middle age	Past middle age
Symptoms—vision	Vague blurring of vision Normal/>6/60	Marked deterioration of vision especially on waking in morning <6/60
Pupil	Normal	RAPD present >0.7 log units (on neutral density filter)
Site of occlusion	Further back in retrolaminar region	At or near retrolaminar region
Early stages	Mild to moderate dilatation of all branches of central retinal vein	Marked tortuosity and engorgement of retinal vein
Retinal hemorrhages	Mild to moderate, more in periphery	Extensive hemorrhages involving Periphery and posterior pole
Cotton wool spots	Rare	Common
Optic disc	Hyperemic and may be edematous	Marked optic disc edema
Macula	Normal or may show edema	Gross hemorrhages and edema
Late ophthalmoscopic finding	Veins—mild to moderately engorged Sheathing +/- No neovascularization Macula—normal/CME	Veins—mild to moderately engorged Sheathing—frequently seen Hemorrhages—none or few Retina has—aneurysms, neovascularization, preretinal/vitreous hemorrhages Optic disc—pale Macula—degenerative/pigmentary disturbances
FFA	<10 disc area of capillary non-perfusion	>10 disc areas of capillary nonperfusion
ERG	Minimal or no change	Marked reduction of b-wave amplitude <60%
Goldmann perimetry	No or minimal defects	Marked peripheral visual field defects
Complications	Macular edema, macular degeneration	Macular edema, macular degeneration, preretinal hemorrhages, vitreous hemorrhage, NVE, NVD, NVG
Prognosis	Good	Poor
Abbreviations: ERG, electroretinogram; FFA, fundus fluorescein angiography; NVE, neovascularization elsewhere; NVD, neovascularization of the disk; NVG, neovascular glaucoma		

Conjunctiva: Multiple hemorrhages in conjunctiva may be seen (bleeding disorders).

Cornea: Peripheral ulcerative keratitis (PUK) in case of SLE, PAN.

Sclera: Nodular scleritis.

Anterior chamber: It may be shallow in patients with angle closure glaucoma or short axial length. Keratic precipitates, cells and flare may be present in the inflammatory diseases (vasculitis, sarcoidosis, HIV). Flair may be noted in patients with NVI and presence of hyphema is uncommon.

Gonioscopy: Undilated gonioscopy is essential to determine the presence of NVA or evidence of angle closure. NVA may be present without neovascularization of the iris (NVI) in 12% of eyes.⁵

Iris: NVI or NVA may be there. Pupillary margin should be carefully examined for the presence of NVI. As later discussed, it is an important sign deciding on management.

Pupil: Presence of relative afferent pupillary defect is an ominous sign. It is important to look for RAPD before pupil dilation whenever one is suspecting vascular occlusion.

Lens: Generally normal or age-related nuclear sclerosis. Complicated cataract can be seen in inflammatory conditions.

IOP: An IOP more than 22 mm Hg needs to be investigated and explained. Raised IOP could be due to neovascular glaucoma, underlying open angle glaucoma. ACG attack around the time of CRVO is not uncommon. It may be both causative as well as the effect of CRVO.

Posterior segment (Figs 1 to 3): The typical clinical constellation in CRVO includes retinal hemorrhages (both superficial flame shaped and deep blot type) in all four quadrants with dilated, tortuous retinal veins (classic “blood and thunder appearance”). Optic nerve head swelling, cotton wool spots, splinter hemorrhages, and macular edema are present to varying degrees. Macular edema may be accompanied accumulation of sub-retinal fluid. In severe cases, the retinal thickening may be 4–5 times the normal. With time, retinal hemorrhages may decrease or resolve completely with secondary retinal pigment epithelium alteration. An epiretinal membrane may form.

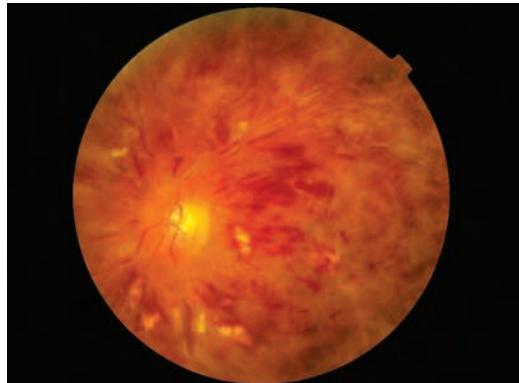


Fig. 1: Fundus picture of ischemic CRVO with macular edema. Four quadrant retinal hemorrhages can be seen along with soft exudates and retinal edema

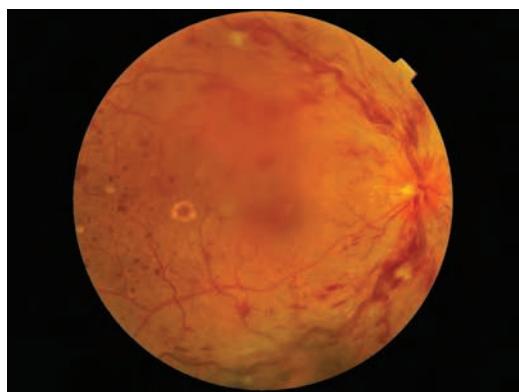


Fig. 2: Fundus picture of CRVO showing venous tortuosity

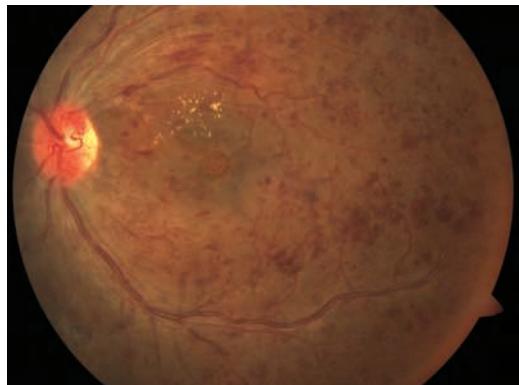


Fig. 3: Fundus picture of old CRVO with macular edema. Collaterals have developed over the optic disc

Optociliary shunt vessels (disc collaterals) can develop on optic nerve head and are very important clue to an old RVO. With time disc pallor ensues. NVD or NVE may develop. Careful 90 D examination should be done to differentiate disc collaterals from NVD. The vessels that comprise NVD are typically of smaller caliber than optociliary shunt vessels and branch into a vascular network. Fibrovascular proliferation from NVD or NVE may result in vitreous hemorrhage or traction retinal detachment.

Gross signs of vascular sclerosis may be present as well as clues to systemic disorders discussed before. One should always look for presence of atherosclerosis in the retinal arteries.

Fellow eye should be examined carefully to look for signs of hypertensive retinopathy, diabetic retinopathy, vasculitis or signs of vascular occlusion. Gonioscopy should be performed to rule out occludable angle (vascular occlusion may be secondary to angle closure glaucoma).

Complications associated with CRVO: A careful examination must be done to rule out any of these complications of CRVO.

- Macular edema
- Macular ischemia
- Neovascular glaucoma
- Vitreous hemorrhage
- Tractional retinal detachment
- Optic atrophy.

DIFFERENTIAL DIAGNOSIS

A case of CRVO may have to be differentiated from following:

- Ocular ischemic syndrome
- Diabetic retinopathy
- Papilledema
- Radiation retinopathy
- Retinopathy due to anemia
- CRAO with CRVO
- Venous stasis retinopathy.

INVESTIGATIONS

One important part of work-up includes identifying appropriate risk factors, ocular or systemic. Ocular risk factors enlisted before should be ruled out as appropriate.

Systemic Work-up

It is generally not indicated in elderly patient with known systemic vascular risk factor for CRVO. However, routine blood pressure, fasting blood glucose and lipid profile should be checked. A cardiac consultation should be done when possible.

Younger patients, patients with bilateral simultaneous vascular occlusion, prior occlusion in the fellow eye, prior systemic thrombotic disease, family history of thrombosis require detail evaluation for hypercoagulable condition as these persons may be at risk for future, nonocular thrombotic events. These investigation include:

- Complete hemogram with peripheral smear
- Erythrocyte sedimentation rate
- Plasma homocysteine level
- Chest X-ray—to rule out TB, sarcoidosis and left ventricular hypertrophy.
- C-reactive protein
- Thrombophilia screen—PT, TT, activated partial thromboplastin time (aPTT), protein C, protein S, activated protein C resistance, factor V Leiden mutation, lupus anticoagulant, anticardiolipin antibody.
- Autoantibodies—ANA, ANCA, anti-DNA antibody, rheumatoid factor.
- Serum angiotensin converting enzyme
- Treponemal serology
- Carotid Doppler scan.

Ocular Investigation

- *Fundus fluorescein angiography (FFA):* Fluorescein angiography in CRVO (**Fig. 4**)

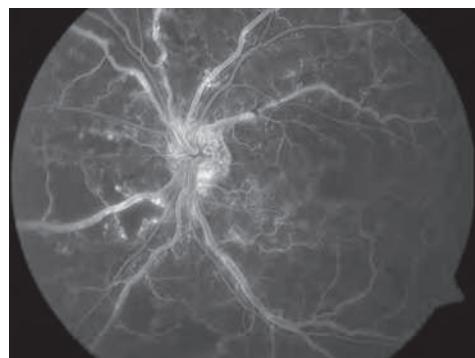


Fig. 4: Fluorescein angiography picture of CRVO showing collateral vessels, severe retinal ischemia and microaneurysms

shows marked delay in arteriovenous transit time, blocked fluorescence due to retinal hemorrhages, vessel wall staining, areas of nonperfusion, collaterals, NVD, NVE and macular edema. Blocked fluorescence of the underlying retinal circulation occur if extensive intraretinal hemorrhages are present especially in the early part of the disease and therefore FFA may not reveal useful information. So, best to wait for resolution of hemorrhages.

FFA is indicated to rule out macular ischemia, to determine the type of CRVO (ischemic vs. nonischemic), and to detect NVD and NVE. CRVO is said to be nonischemic if capillary nonperfusion is less than 10 disc areas and ischemic if capillary nonperfusion is more than 10 disc areas (definition of CVOS).

- *Optical coherence tomography (OCT):* Optical coherence tomography is useful in the assessment of macular edema, and particularly in monitoring its course, especially with treatment of the edema. It can readily detect cystic spaces, retinal thickening and serous retinal detachments, all of which are rather frequent in CRVO. In long-standing cases, helps to detect ERM and VMA.
- *Ultrasonography:* If the whole or a part of the underlying retina is obscured due to vitreous hemorrhage, ultrasound B-scan with corresponding A-scan is mandatory to detect any associated retinal detachment/mass lesion. Also useful in detecting hypermetropia and disc drusens.
- *Electroretinogram (ERG):* This is an objective functional test, very useful in the differentiation of ischemic from nonischemic CRVO. In ischemic CRVO, there is reduced b-wave amplitude (<60% of normal), reduced b: a ratio and prolonged b-wave implicit time on the electroretinogram.
- *Perimetry:* Visual field (VF) plotting with a Goldmann perimeter, helps in the differentiation of ischemic (defective V4e target) from nonischemic CRVO.

MANAGEMENT

Goals of treatment in CRVO are to identify and treat predisposing medical condition, to maintain

central visual acuity by minimizing macular edema, reducing the risk of bleeding into the vitreous cavity by producing regression of retinal neovascularization, and preventing neovascular glaucoma. Previously there has been lot of interest in relieving the obstruction or bypassing it, but none of therapies have proven to be of benefit (discussed later).

Macular Edema

Before the advent of intravitreal pharmacotherapy, observation was the standard of treatment for macular edema associated with CRVO as recommended by CVOS. In CVOS group M, no significant improvement in visual acuity was seen with grid laser as compared to untreated group, though macular edema was decreased angiographically. Hence macular grid is not routinely recommended.

Intravitreal steroids by reducing vascular permeability and inhibiting the expression of the VEGF gene and the metabolic pathway of VEGF plays an important role in the treatment of macular edema due to CRVO (SCORE trial, GENEVA trial). Ozurdex (sustained release intravitreal dexamethasone delivery system) is also now FDA approved for treatment of macular edema secondary to CRVO, but it has complications like cataract and increased IOP. Intravitreal antivascular endothelial growth factor (VEGF) agents are currently the first-line therapy for macular edema. Various trials have shown their efficacy Ranibizumab in CRUISE trial, VEGF trap (Aflibercept) in Galileo and Copernicus, and they have now replaced observation established by CVOS as the standard of care for the treatment of macular edema associated with CRVO. Anti-VEGF drugs are also FDA approved for treatment of macular edema due to CRVO. A common dosing would be 3 or 6 monthly injections of ranibizumab followed by as required dosage as the shunt vessels develop and the RVO relieves itself with time, the need for injections decreases. It is less needed in nonischemic CRVO.

Ocular Neovascularization

Panretinal photocoagulation (PRP) should be promptly delivered after the development of

NVI/NVA to prevent secondary complications. CVOS did not recommend prophylactic PRP in ischemic CRVO. PRP in patient without NVI has the risk of making future NVI refractory and is not indicated. Laser should be delivered as anterior as possible and supplementary cryo may be added as per need.

Prophylactic PRP can however be considered in cases of ischemic CRVO where follow-up is not possible in high risk cases.

Anti-VEGF agents results in rapid regression of neovascularization, but these should be used as temporizing adjunctive measure with subsequent PRP as definitive treatment.

Role of Vitrectomy

It is indicated in cases of nonresolving vitreous hemorrhage or tractional retinal detachment secondary to retinal neovascularization.

Pars plana vitrectomy with ILM peeling has also been investigated for macular edema secondary to CRVO and has shown variable results.

Other Modalities

- Role of *systemic anticoagulants* in management of CRVO is unclear, though it does not alter the natural course of CRVO it may help to prevent nonocular thrombotic events.
- Role of *oral pentoxifylline (vasodilator)/hemodilution* in management of CRVO is still controversial.
- *Recombinant tissue plasminogen activator (r-tPA)* has been administered by several routes systemic, intravitreal and by endovascular cannulation of retinal vessels for treatment of CRVO and has shown variable results.
- *Chorioretinal venous anastomosis* between nasal branch retinal vein and the choroidal circulation have been created using Nd: YAG laser in nonischemic CRVO. It may allow transretinal retrograde flow of the venous blood from the eye and may prevent retinal ischemia. Studies have shown limited visual recovery even after successful anastomosis due to thrombosis of the treated retinal vein.
- *Radial optic neurotomy* involves transvitreal incision of the nasal scleral ring to release pressure on the central retinal vein at the level of the scleral outlet. Some studies have shown improvement in visual acuity but its use has been abandoned owing to significant risks.

VIVA QUESTIONS

Q.1. What are the various risk factors for CRVO?

Ans. Refer text.

Q.2. What is the pathogenesis of CRVO?

- The site of occlusion in CRVO is at or just proximal to the lamina cribrosa.
- The central retinal artery and vein are aligned parallel to each other in a common tissue sheath within the retro-laminar portion of the optic nerve and they are naturally compressed as they pass through rigid sieve like openings in the lamina cribrosa but they typically give off branching collateral vessels just before piercing the lamina. These vessels may be subject to compression from increase in intraocular pressure which causes posterior bowing of lamina cribrosa due to mechanical stretch or occlusion of central retinal vein can be due to compression by an atherosclerotic central retinal artery or it can be primary due to inflammation of the central retinal vein. Hemodynamic alterations may lead to thrombus formation in the central retinal vein by Virchow's triad (diminished blood flow, increased blood viscosity, altered lumen wall).
- Occlusion of both the retro-laminar central retinal artery and central retinal vein posterior to lamina cribrosa and prior to the branching of collateral channels from the main trunk is required to produce ischemic CRVO while non-ischemic CRVO is due to occlusion of the central retinal vein at a site further posterior, allowing normal collateral channels to provide alternative routes of venous drainage.
- Resistance to venous flow, blood stagnation and ischemia stimulates production of VEGF resulting in neovascularization and macular edema.

Q.3. What are the types of CRVO and how to differentiate between them?

Ans. Refer to Table 1.

Q.4. What is the risk of nonischemic CRVO converting to ischemic CRVO?

Ans. About 1/3rd cases of nonischemic CRVO convert to ischemic CRVO over a period of one year.

Q.5. What is the common site of neovascularization in CRVO?

Ans. Following are the sites:

- Iris
- NVI develops in about 50% of eyes, usually in 2–4 months (100 days glaucoma).
- NVG develops in 1/3rd of cases with NVI.
- Retinal neovascularization is seen in 5% of cases.

Q.6. What is ischemic index and what is its importance?

Ans. Ischemic index⁶ = $\frac{\text{Non-perfusion area}}{\text{Total area of retina}}$

An ischemic index of 50% corresponding to about 10 disc areas of retinal capillary nonperfusion was considered the threshold for a significant risk of neovascular complications.

Q.7. When will you call anterior segment neovascularization significant?

Ans. When there is NVI of more than 2 clock hours or there is presence of NVA.

Q.8. What are the objectives and conclusion of CVOS?

Ans. The main objectives of CVOS study are:

- To assess whether grid-pattern photocoagulation therapy will reduce loss of central visual acuity due to macular edema secondary to CVO.
- To determine whether photocoagulation therapy can help prevent iris neovascularization in eyes with central vein occlusion (CVO) and evidence of ischemic retina.

Its conclusion are:

- There is no visual benefit to treating macular edema from a CRVO with grid laser photocoagulation.
- There is no benefit of treating ischemic CRVO with early (prophylactic) PRP.

Interpretations: Delaying treatment with PRP until the development of NV resulted in significant regression of neovascularization and no additional risk of neovascular glaucoma compared to patients treated with prophylactic PRP.

The study also suggested a follow-up schedule, which basically advised regular monthly follow-up for first 6 months and then tapered follow-up. However, in the day of anti-VEGF treatment, the discussion is rather arbitrary.

Q.9. What are the indications for FFA in CRVO?

Ans. Refer text.

Q.10. When is PRP indicated in CRVO?

Ans. Refer text.

Q.11. What is the treatment of choice for macular edema in CRVO?

Ans. Refer text.

Q.12. What are the causes for CRVO of the young?

Ans. Refer to risk factors and work-up.

Q.13. What are the risk factors for development of NVI in CRVO cases?

Ans. Risk factors of NVI includes:

- >10 DD of nonperfusion in the posterior pole (greater risk with greater nonperfusion)
- RAPD
- Decreased visual acuity
- ERG: decreased b: a ratio if <1 (normal 2:1)
- Elevated central retinal venous pressure
- Duration <1 month.

Q.14. What is CRAO with CRVO?

Ans. In this case, the retinal hemorrhages are scattered and less due to the accompanying RAO. These cases are at very high risk of developing NVI, some figures as high as 80%.

Q.15. Why does CRVO cause more of NVI and BRVO cause more of retinal new vessels?

Ans. In CRVO, particularly, ischemic variant, the ischemia is so severe that the retinal tissue may not be able to respond to VEGF load to develop new vessels. Hence, retinal

new vessels are much less frequent than in BRVO.

Q.16. What is the current role of Laser in CRVO macular edema?

Ans. As discussed above macular laser has no or poor role in treating macular edema. Recent studies, RELATE study for CRVO, are indicating role of peripheral laser for treating edema refractory to injections. The earlier the laser done, the more chance of it being effective. With availability of wide field FA, targeted laser may be attempted to knock off the VEGF producing CNP areas.

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BRANCH RETINAL VEIN OCCLUSION

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INTRODUCTION

Retinal vein occlusion is the second most common retinal vascular disease. Amongst vascular occlusions, branch retinal vein occlusion (BRVO) is commoner (78%). Most patients are in the 6th decade of life. However, it can occur in younger population. In such cases, systemic investigation becomes imperative for finding the underlying cause. Risk factors for BRVO are: (**see Table 1**) BRVO patient is usually given as long case or spotter.

HISTORY

Chief Complaint

BRVO most commonly present in an elderly patient with complaints of:

- Sudden, painless diminution of vision/blurred vision/onset of field defect.
- Patient may also have metamorphopsia, which will indicate towards macular edema.
- Occasionally, patient old occult RVO may present with sudden onset of floaters, leading

to complete loss of vision. In such cases patient may have vitreous hemorrhage.

- Lastly, in certain cases patient may entirely be asymptomatic and a peripheral BRVO may be detected on routine clinical examination.

History of Present Illness

It includes complete documentation of onset duration and progress of visual complaints. Associated ocular and systemic symptoms (discussed above) should also be enquired. There may be history of similar episodes in the same or the other eye, for which patient might have sought medical attention.

Medical/Treatment History and Past History

It should include following:

- Detailed history of patient's systemic status like hypertension, diabetes, hyperlipidemia, hypercholesterolemia, cardiovascular disease and any other drug intake.

- Young people should be specifically asked about previous history of hypercoagulability (bruises elsewhere in body, blood transfusions etc.), HIV or other infectious diseases, use of OCPs.
- Personal history should include smoking, chewing tobacco, and alcohol consumption.
- Patient may have received some form of laser or intravitreal therapy, which need careful documentation.
- Careful documentation of past ocular disorders and therapies, e.g. for glaucoma/retinal vasculitis, must be obtained.

EXAMINATION

Systemic Examination

Detailed systemic examination should be carried out (*See Table 1*). In patients with VH, other eye may reveal the predisposition to BRVO.

Ocular Examination

Visual Acuity

It is paramount to note the best-corrected vision with correction, as it would decide the need to treat. In treated cases, it is important, as it would

Table 1 Risk factors for BRVO

Risk factors	What to look
Systemic	
Age	>60 years
Hypertension	Blood pressure
Diabetes mellitus	RBS, PPBS, HbA _{1C}
Coagulopathies	<ul style="list-style-type: none"> Serum homocysteine Screening blood test: Activated protein C resistance Antiphospholipid antibodies (<i>aPL</i>): Anticardiolipin antibodies (aCL) Lupus anticoagulant (LA) Anti-beta 2-glycoprotein-1 (anti-B2GP1) Free protein C/S antigen.
Inflammatory	<ul style="list-style-type: none"> HLA B51, Pathergy Test Serum ACE, Chest X-ray, Chest CT C-ANCA, Chest X-ray
Infections	<ul style="list-style-type: none"> Mantoux test, Chest X-ray VDRL ELISA and Western Blot ELISA
Chronic renal failure	RFT
Others	<ul style="list-style-type: none"> Smoking Oral Contraceptive Dehydration
Ocular	
Glaucoma	Intraocular pressure
Short-axial length	Axial length

Abbreviations: VDRL, venereal disease research laboratory; ELISA, enzyme-linked-immunosorbent assay; RBS, random blood sugar; PPBS, post prandial blood sugar; RFT, renal function test

help in monitoring the response to therapy. In addition, initial visual acuity could be a prognostic factor for post intervention success.

Ocular Adnexa and Globe

Ocular adnexal skin can be examined for signs of coagulopathy, collagen vascular disorders and infections. There is no significant examination regarding ocular alignment or movements. Lids, eyebrows and eyelashes are in their limits for the age.

Conjunctiva

Patients with glaucoma may have conjunctival blebs. Conjunctival hemorrhages may be present in coagulopathies.

Cornea

Involvement is rare, except in collagen vascular disorders.

Anterior Chamber

It may be shallow if the patient has a preexisting glaucoma or short axial length. AC should be inspected for signs of uveitis. Similarly, gonioscopy may reveal NVA in selected cases.

Pupil

Rarely neovascularization may be present at pupillary border. Presence of RAPD may indicate CRVO or HRVO or AION rather than BRVO. Even major BRVOs will not have RAPD.

Lens

As patients are elderly, there may be cataractous changes present in the lens.

Posterior Segment

It requires +90D/78D and +20D examination after pupillary dilatation.

- Vitreous is mostly clear except when there maybe vitreous haze present posthemorrhage with red blood cells floating in the vitreous.
- The next important structure for assessment is the optic disc and the peri-papillary area to rule out signs of glaucoma and NVD and AION.

- As most of the patients are hypertensive, signs of hypertensive retinopathy should be noted. Splashed tomato and blood and thunder appearance must be kept in mind in cases of RVO.
- Macular assessment on slit lamp biomicroscopy with +90D lens may reveal macular edema seen as elevation of retina with loss of foveal reflex. Long standing cases may have intraretinal hard exudates and cystic type of edema.
- Meticulous inspection of vitreoretinal interface may show area of vitreomacular adhesion or an epiretinal membrane in recalcitrant cases.
- Mostly BRVO occurs in superotemporal quadrant (**Fig. 1**), as more arteriovenous (AV) crossings are present in this area. AV crossing should be carefully evaluated as it may reveal the site of occlusion.
- In contrast, a nasal BRVO or a peripheral BRVO may even go unnoticed. There will be dilated, tortuous vessels proximal to the occlusion. Intraretinal flame shaped hemorrhages; microaneurysms can be present along the occluded vessel. Cotton wool spots are also seen.
- Old cases may have collaterals, telangiectatic vessels and neovascularization.
- Neovascularization can be present on the disc or at the junction of perfused and



Fig. 1: Clinical photograph of fresh superior-temporal BRVO depicting scattered hemorrhages in the area of drainage of the major vein and macular hemorrhages

non-perfused retina. After 6–12 months, the acute findings will resolve and there will be venous sheathing and sclerosis. Macular edema can also be seen with +90D or +78D.

Amsler grid testing: It is important to monitor the response of the patient. Patients at their home itself can do it. It can provide objective evidence to the patient if there is sudden increase in metamorphopsia or blurring of vision, so that patient can seek medical attention in time. This is more important for patients who present with vision of more than 6/12 and hence a follow-up is recommended for monitoring any deterioration in vision.

Major Complications Associated with BRVO

- Macular edema—main cause of low vision
- Macular ischemia
- Neovascularization leading to vitreous hemorrhage. NVE develops in 40% of cases.
- NVI develops rarely (1%).

DIFFERENTIAL DIAGNOSIS

In patients with NVs or VH or Macular edema, differentials are essentially of the same (*See relevant chapters*). For intraretinal hemorrhages, differentials include DR, CRVO, AION, CNVM, PEHCR, Coats, Homocysteine disorders, retinitis, vasculitis, etc. Usually the typical sectoral or quadrantic appearance in a predisposed patient is the clincher for BRVO.

INVESTIGATIONS

Systemic Investigation

In a person aged more than 60 years, BRVO may occur as an age related vasculopathy even in the absence of hypertension. However, routine blood pressure, fasting blood glucose and lipid profile should be checked.

In a young person the investigations that should be done are:

- Plasma homocysteine level
- Chest X-ray- to rule out TB, sarcoidosis and left ventricular hypertrophy.
- C-reactive protein
- Thrombophilia screen—PT, TT, aPTT, protein C, protein S, activated protein C resistance,

factor V leiden mutation, lupus anticoagulant, anticardiolipin antibody.

- Autoantibodies—ANA, ANCA, Anti DNA antibody, Rheumatoid factor.
- Serum angiotensin converting enzyme
- Treponemal serology
- Carotid duplex imaging
- Full blood count.

Ocular investigation: It includes following:

Fluorescein angiography (FA): Although the diagnosis of BRVO is purely clinical, FA does reveal additional findings that help in treatment and prognostication. FA may not be useful in acute onset BRVO due to extensive areas of hemorrhage resulting in block fluorescence and masking of underlying features. Therefore, the best time to do FA would be when substantial clearing of hemorrhage is seen. The characteristic findings on FA is delayed filling of the occluded retinal vein, block fluorescence due to intraretinal hemorrhages, microaneurysms, dye extravasation secondary to macular edema, telangiectatic collateral vessels, capillary non perfusion and retinal neovascularization (**Fig. 2**).

The two most important features to note on FA are the type macular edema and BRVO. Macular edema may be perfused or nonperfused (ischemic). In perfused, FA would reveal areas of macular leakage with a normal foveal avascular zone (FAZ), whereas an ischemic edema may have



Fig. 2: Late FA picture showing blocked fluorescence in the area of the hemorrhages along with minimal leakage of the capillary bed

a distorted and enlarged FAZ apart from leakage. Type of edema will help guide our treatment, as ischemic cases have shown not to benefit from any intervention. Secondly, it helps us assess whether BRVO is Ischemic, marked by presence of >5 disc area of capillary non-perfusion. These cases have more chances of developing neovascularization and may need to be laserized. Another recent concept is to map peripheral ischemic areas, which may be responsible for constant production of VEGF leading to chronic macular edema. These areas may need targeted laser ablation to decrease VEGF load. FA is also essential for follow-up.

Wide-field Angiography (UWA)

UWA gives 200 degrees field of vision. A single image helps in delineating the extent of peripheral capillary non-perfusion and can help in targeted laser. In addition, it can pick up any neovascularization, as dynamic FA may lead to skip areas.

Optical Coherence Tomography (OCT)

It is a noninvasive and highly informative investigation. Even in acute BRVO where FA might not be helpful, OCT is minimally affected by extensive intraretinal hemorrhages. Characteristic findings may include intraretinal edema, cystoid macular edema, intraretinal hyper-reflectivity from hemorrhages, shadowing from edema and occasional neurosensory detachment. Some studies have also assessed IS-OS junction abnormalities in chronic cases. Chronic cases may also show ERM or VMA.

It is the most preferred investigation for following up cases of macular edema and response to therapy.

MANAGEMENT

Systemic condition should be taken care of properly. Anticoagulants are not of much benefit. OCPs and HRTs may be avoided if possible. Treatment for BRVO is usually done for its complications.

The treatment of BRVO macular edema (See Table, also See Chapter on CRVO) until recently was guided by the Branch Vein Occlusion

Study (BVOS), which recommended grid laser for perfused macular edema of more than 3 months' duration with best corrected vision <6/12. They showed 63% of these patients recovered more than two Snellen's lines at 3 years follow-up following laser treatment in comparison to shams 36%. However, the visual gain was delayed and somewhat incomplete, and hence treatment options hastening recovery were explored. Although various forms of steroids (SCORE trial, GENEVA trial) have been used, their efficacy is less than anti-VEGF agents, along with increased risk of glaucoma and cataract. The second most important trial was the BRAVO study, which evaluated efficacy of intra-vitreal ranibizumab in macular edema. They concluded that ranibizumab treated patients gained more than 3 line improvement in nearly 60% of patients and maintained it at 2 year follow-up (HORIZON trial, not to be confused with the ARMD Horizon trial). Thus, the first line of treatment is anti-VEGF. Single monthly injection for first 3 months followed by PRN dosing is preferred, though the trials gave continuous monthly injections for 6 months. Laser can be used as second line of treatment. Recalcitrant cases should be assessed for cause—chronic breakdown of blood-retinal barrier, peripheral ischemia or epiretinal membrane (ERM). Most of cases respond well to steroids, others may need targeted laser to peripheral ischemic areas or vitrectomy for significant ERM. Later, neovascularisation may occur and complicate further by vitreous hemorrhage, which may require vitrectomy in nonresolving cases. Recently another anti-VEGF Aflibercept has also shown equal efficacy with longer duration of action (VIBRANT trial). Combination treatment of anti-VEGF with laser are ongoing has shown no additional benefit of laser with anti-VEGF (RELATE and BRIGHTER trial).

These case scenarios may be encountered.

Condition 1: Patient having BRVO with no macular edema or neovascularization. FFA shows <5DD of capillary nonperfusion.

Rx: Follow up.

Condition 2: Patient having macular edema but no neovascularization. FFA shows <5DD of capillary nonperfusion.

Rx: Determine the cause of macular edema by fluorescein angiography. If the cause is leaking capillaries, but the vision is 6/9 or better, observation can be employed with serial follow-up. If the vision is worse than 6/12 or hampers patients activities, Anti-VEGF injection can be given. In chronic cases or in recalcitrant edema steroid in the form of Triamcinolone (SCORE trial) or dexamethasone (GENEVA trial) can be given with the risk of side effects like IOP elevation and cataract. In cases of macular ischemia, only observation can be done and the macular edema usually resolves within one year with gain of visual acuity. BVOS had suggested a wait period of 3 months, though current studies do not suggest the same.

Condition 3: Patient having BRVO with no macular edema or neovascularization. FFA shows >5DD of capillary nonperfusion.

Rx: More stringent follow-up, as the chances of developing neovascularization are more in these cases.

Condition 4: Patient having BRVO with no macular edema but with neovascularization present, either NVE or NVD.

Rx: According to Branch retinal vein occlusion study, sectoral retinal photocoagulation. Now with wide field angiography available trend has shifted towards targeted laser photocoagulation with repeat fluorescein angiography after 6 months to look for any new areas of capillary nonperfusion or neovascularization and repeat laser.

Condition 5: Patient having BRVO with macular edema and neovascularization.

Rx: Determine the cause of macular edema as to ischemia or leakage. Laser of peripheral capillary nonperfusion areas has to be done. However, prior to that an anti-VEGF intravitreal injection may be considered to reduce macular edema in cases of leaking capillaries as laser photocoagulation increases macular edema. OCT should be done to document macular edema. This is a current gray zone. In patients with NVs, though BRVO is likely to be long standing and so the chronic edema, it may be prudent to treat the NVs first followed by sequential/simultaneous and rapid management of edema.

VIVA QUESTIONS

Q.1. What are common causes of BRVO? What are risk factors in young patients and how will you work up such patient?

Ans. Refer text.

Q.2. What is the pathogenesis of BRVO?

Ans. The obstruction occurs at the A/V crossing. Most of times the artery is above the vein and can lead to compression of the other as they share the common adventitial sheath. Vitreous has also been implicated, with greater vitreomacular attachments at greater risk for the developing BRVO. Thus turbulent flow may lead to endothelial swelling, increase in vessel wall size and obstruction. The resulting venous obstruction leads to elevation of venous pressure that may overload the collateral drainage capacity and lead to macular edema and ischemia. Increase in venous pressure can also result in rupture of the vessel wall with intraretinal hemorrhage. Recently increased VEGF load has shown to lead to lessening of endothelial cells and increase in permeability of capillaries, thereby validating the use anti-VEGF.

Q.3. What is the classification of BRVO?

Ans. It is classified based on anatomical location—Major and macular. Major is when the vessel supplying the entire quadrant gets affected. Macular is when a macular branch gets affected.

It can also be classified based on area of capillary nonperfusion—Ischemic or Non-ischemic. Ischemic having more than 5 disc diameter area of CNP. These cases are more likely to develop neovascularization.

Q.4. Which is the most common quadrant for BRVO and why?

Ans. Superotemporal quadrant is the most commonly involved quadrant as superior hemi retina has the most number A/V crossing changes and superonasal BRVO do not present due to lack of symptoms.

Q.5. What is the most common cause of defective vision due to BRVO?

Ans. The most common cause is macular edema. However, it is imperative to rule out on FA

whether it is perfused or nonperfused as it guide the further course of treatment.

Q.6. What are the common complications of BRVO? What are chances of a non-ischemic BRVO to convert into ischemic BRVO?

Ans. The most important complications are macular edema, macular ischemia and neovascularization sequelae. Neovascularization may progress to vitreous hemorrhage, tractional retinal detachment and neovascular glaucoma. Patients with macular edema with vision < 6/12 are treated with above mentioned therapeutic options. Macular ischemia has not been shown to benefit from treatment. Neovascularization sequelae are expected in 11% of nonischemic and 40% of ischemic BRVO. It can occur up until 3 years of BRVO, although in most cases it occurs between 6–12 months. Laser is recommended only after development of new vessels. There is no additional benefit of prophylactic laser in ischemic cases without new vessel formation.

Q.7. What investigations would you do in a case of BRVO and what would they reveal?

Ans. Refer text.

Q.8. When do you treat a patient of BRVO and what are the treatment options?

Ans. Refer text.

Q.9. Name two landmark clinical trials.

Ans. BVOS and BRAVO. Refer text.

Q.10. What is the first line of treatment for macular edema?

Ans. Refer text.

Q.11. What are the treatment options in recalcitrant macular edema?

Ans. Refer text.

Q.12. What is the role of laser in management of macular edema? Recent trials for the same?

Ans. Refer text. RELATE and BRIGHTER (ongoing).

Q.13. Compare modalities for managing macular edema in BRVO.

Ans. See discussion.

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PROLIFERATIVE DIABETIC RETINOPATHY

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INTRODUCTION

Diabetic retinopathy is leading cause for vision loss in middle-aged population. Worldwide prevalence of DR is 34.6% and that of vision threatening DR is 10.2%.¹ Broadly, diabetic retinopathy is classified into nonproliferative diabetic retinopathy (NPDR), proliferative diabetic retinopathy (PDR) and diabetic maculopathy. It is important that students undergoing examination should be able to examine and identify the changes of DR and PDR, which is harbinger of severe visual loss.

HISTORY

Chief Complaint

Proliferative diabetic retinopathy (PDR) generally presents in a known case of diabetes mellitus (DM) along with established diagnosis of DR under follow-up. Nevertheless, it is not uncommon to see a patient with presentation of PDR on first ophthalmic visit. The different presenting symptoms depend on the stage and complications of PDR and are as follows:

- *Gradual loss of vision:* Due to deterioration of DR, macular edema or associated progression of cataract or tractional papillopathy/retinopathy
- *Acute loss of vision:* When associated with vitreous hemorrhage (VH) or tractional retinal detachment (TRD) involving macula or Diabetic macular edema (DME)
- *History of floaters:* Due to VH (mild) or vitreous degeneration associated with PDR
- *Acute pain, redness and loss of vision:* Due to associated neovascular glaucoma (NVG).

History of Present Illness

While taking history of such case the onset and progression of decrease of vision (DOV) is important, because the sudden onset implies the causes like vitreous hemorrhage, retinal detachment (secondary rhegmatogenous retinal detachment) whereas the slow onset DOV can be caused by the complication like diabetic macular edema, clinically significant macular edema, etc.

History of Past Illness

See chapters on NPDR and DME for history.

Past Surgical History

See chapter on NPDR/DME.

Family History

Family history of DM, hypertension and other risk factors for DR.

Personal History

History of smoking, alcohol intake, tobacco chewing.

EXAMINATION

General Examination/Specific Systemic Examination

Diabetes is multisystem disorder involving causing vasculopathy and neuropathy. So detailed systemic evaluation of cardiovascular system, respiratory system, central and peripheral nervous system, renal system should be done to rule out the co-morbidity associated with DM.

Ocular Examination

The examination findings are similar to a case of NPDR. Few important points for PDR are summarized below:

Visual Acuity

Uncorrected visual acuity (UCVA) and best corrected visual acuity (BCVA) must be noted. This is important for decision-making.

Eyeball

Usually normal in such case. In few cases squint can be seen due to associated ischemic mononeuropathy involving cranial nerve 3rd, 4th or 6th (classically pupil sparing III CN palsy or VIth CN palsy).

Cornea

Following points must be noted:

- Corneal hypoesthesia (risk of neurotrophic keratitis)
- Decrease corneal healing (risk of recurrent corneal erosion and persistent epithelial defect)
- Tear film abnormalities (Dry eye due to autonomic neuropathy affecting sensory nerves associated with tear secretion)
- Corneal endothelium is usually normal in clinical examination. However, specular microscopy significantly higher coefficient of variation, a decrease in the percentage of hexagonal cells, and a low figure coefficient.

Iris

Check for neovascularization of iris (NVI). Pupillary margin are the earliest sites where neovascularization the NVI. (See chapter on NPDR and DME)

Pupil

Following points must be noted

- Ectropion uvea (the fibrous tissue accompanying neovascularization contracts which caused eversion of posterior pigmented layer at pupillary margin).
- Increase pigment at angles.

- Difficulty in dilating pupils (manifestation of diabetic neuropathy resulting in reduced functional innervation of the dilator muscle). The maximum pupillary dilatation should always be noted. In DM the pupils dilates poorly. This is important because every surgery including cataract and retinal surgery will need the maximum papillary dilatation. Diabetic pupil dilates poorly in response to standard anticholinergic eye drops (Tropicamide, Homatropine and Cyclopentolate that act by paralyzing the iris sphincter muscle). This failure of dilatation is due, atleast in part, to a sympathetic dysfunction related to the autonomic neuropathy of these patients. The addition of phenylephrine (which acts directly by stimulating α -adrenergic receptors on iris dilator muscle, producing contraction of the dilator muscle of the pupil), which utilizes the denervation super sensitivity (sharp increase of sensitivity of postsynaptic membranes to a chemical transmitter after denervation) of the small diabetic pupil, greatly improving the mydriatic drug response in diabetic patients.
- Argyll Robertson pupils (bilateral small pupils that reduce in size on a near object (they "accommodate"), but do *not* constrict when exposed to bright light (they do not "react" to light)- an useful mnemonic **Accommodation Reflex Present**).

Intraocular Pressure (IOP)

Raised IOP can be there due to POAG (6% to 11%), neovascular glaucoma or ghost cell glaucoma (in long standing cases of VH) can be seen in DM.

Lens

See chapter on NPDR.

Vitreous following findings can be there:

- The vitreous in diabetic patients undergoes abnormal collagen crosslinking and non-enzymatic glycation, which lead to precocious liquefaction and posterior vitreous detachment (PVD).
- Asteroid hyalosis
- In cases with secondary RRD along with TRD will show the tobacco dust (Schaffer's sign) is seen.

Fundus

Following signs must be noted.

- *Early PDR:* New vessels at disc or within 1 DD of disc (NVD) or New vessels elsewhere (NVE).
- *High risk PDR:* The presence of any three of the following four features characterizes DRS.
 1. Neovascularization (at any location)
 2. Neovascularization at the optic disc (NVD)
 3. Severe neovascularization:
 - New vessels within one disc diameter of the optic nerve head (NVD) that are $>1/4\text{--}1/3$ disc area in size
 - NVE at least 1/2 disc area in size
 4. *Vitreous or preretinal hemorrhage:* To simplify presence of the following indicates need for treatment
 - NVD $>1/3$ to 1/4 of disc area
 - Any NVD with associated VH
 - NVE greater than 1/2 with vitreous or preretinal hemorrhage.

Tractional retinal detachment: It is important to note if TRD is involving macula and TRD is threatening macula (**Figs 1 and 2**).

TRD threatening macula: Retinal elevation at least 4 DD area whose at least some part is within 30° of center of macula or retinal elevation of less than 4DD, along with one or more vitreo-retinal adhesion causing elevation of retina within 30° of center of macula in presence of new vessel or fresh bleed vitreous hemorrhage.

TRD involving macula: Vitreo-retinal traction along the arcade or disc or retinal traction lines

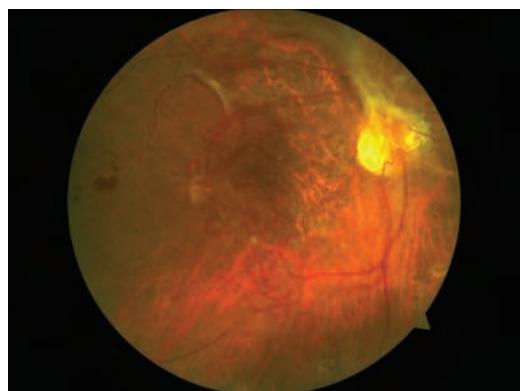


Fig. 1: Fibrovascular proliferation on disc and along arcades can be seen in the fundus photograph

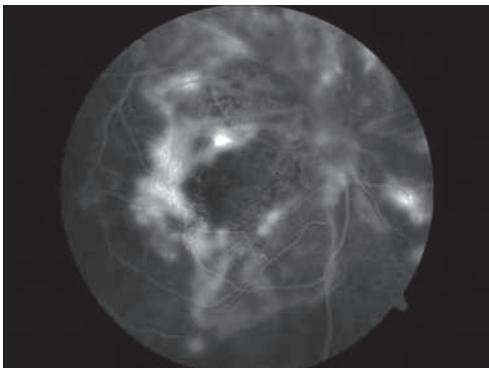


Fig. 2: FA picture is suggestive of NVD and NVEs. Severe peripheral ischemia and macular ischemia are also visible

extending through fovea and causing progressive vision loss.

Presence of TTPH, VMT and CSME should always be noted as it affects treatment management. Very commonly these attachments are around the arcades.

Advanced DR: Also known as end stage DR or burnt out DR. The retina becomes feature less with sclerosed vessels and loss of sheen. There may be massive TRD and accompanying absolute NVG.

DIFFERENTIAL DIAGNOSIS

See chapter on DME and NPDR.

INVESTIGATION

(See chapter on DME and NPDR)

- UWFA may be very helpful in picking up peripheral anterior ischemia with peripheral new vessels
- USG should be done in VH. It also helps in prognostication.

MANAGEMENT

[Also See Chapter on VH, NPDR and DME (**Table 1**)].

Non-high-risk PDR

These cases are treated with careful follow-up (at 2–4 month intervals) and prompt pan-retinal photocoagulation (PRP) if progression to high-risk

PDR occurred. However, PRP can be done under following circumstances:

- Patient has poor DM control with associated DM complications (nephropathy).
- The patient will not or cannot be followed closely
- Access to health care is difficult
- Fellow eye is blind from DR
- Poor patient compliance to follow-up
- Prior to cataract operation or pregnancy (controversial)
- Whenever iris or angle neovascularization is seen, early PRP should be done irrespective of presence or absence of retinal HRC.

High-risk PDR

- High-risk PDR requires immediate *pan retinal photocoagulation* (PRP) or scatter photocoagulation
- Patients with HRC treated with PRP have a 50% reduction in risk of severe visual loss. The rate of severe visual loss (visual acuity <5/200) was reduced by treatment from 16% in non-treated eyes over 2 years to 6% in treated eyes, a reduction of 57% in DRS.^{1,2}
- Following points must be remembered, PRP:
 - Does not improve visual acuity
 - May cause worsening macular edema, and loss of peripheral vision and night vision
 - Indications for supplementation are uncertain
 - Does not always cause regression of NVD/NVE: Regression of neovascularization occurs in 30–55% of eyes after laser photocoagulation. Complete regression of NVD was found in 29.8% and partial regression in 24.5% of eyes at 12 months after treatment in DRS.^{1,2} Regression is marked by fibrotic changes.
 - Is also indicated in patients with NVI from PDR even in the absence of NVD/NVE or in presence widespread retinal ischemia and capillary drop-out on fluorescein angiography
 - Protocols of Diabetic Retinopathy Clinical Research Network (DCRNet) have attempted management of NVs with monthly intravitreal Ranibizumab alone,

Table 1 Comparison of anti-VEGF

	<i>Pegaptinib</i>	<i>Bevacizumab</i>	<i>Ranibizumab</i>	<i>Aflibercept</i>
Composition	Aptamer (single stand of RNA or DNA)	Full length antibody	Antibody fragment	Recombinant protein combined with Fc portion of IgG
Molecular weight	50 kD	149 kD	48 kD	115 kD
	VEGF-165 isoform	All isoforms of VEGF-A	All isoforms of VEGF-A	All isoforms of VEGF-A, VEGF-B, PLGF-1 and 2
Half-life	2 days	5 days	3 days	7 days
Doses	0.3 mcg/0.9 mL	1.25 mg/0.05 mL	0.5 mg or 0.3 mg/0.05 mL	2 mg/0.05 mg
Systemic side effect	Bronchitis Plural effusion Diarrhea Nausea Vomiting Carotid artery occlusion CVA TIA Contact dermatitis HS reaction/ anaphylactic reaction	Arterial thromboembolic events CHF Dizziness Confusion CVA	Acute HTN CVA MI Facial skin redness Itchy skin rash	CVA HT

Abbreviations: RNA, Ribonucleic acid; DNA, Deoxyribonucleic acid; VEGF, Vascular endothelial growth factor; PLGF, Placental growth factor; CVA, Cerebrovascular accident; TIA, Transient ischemic attacks; HS, Hypersensitivity; CHF, Congestive heart failure; MI, Myocardial infarction.

but up to 2 years, though there is no benefit in terms on vision in comparison to laser PRP, which is an economically easier therapy.

- If CSME is also present in addition to high-risk PDR, combined anti-VEGF therapy and PRP at the first treatment session should be considered. In the days of LASER and early treatment diabetic retinopathy study (ETDRS), it was suggested that diabetic macular edema (DME) should be managed prior to PDR to prevent its worsening. However, now intravitreals are preferred which act on NVs also, making decisions easier.
- Complications of PRP
- Transient side effects:* Blurring of vision, Macular edema, CD, Headache, iritis
- Medium term side effects:* Macular edema may persist for more than 3 months

- Long-term:* Foveal burn, Macular edema, Choroidal neovascularization, PVD, Retinal, subretinal or choroidal hemorrhage due to excessive power of laser, Exudative RD, VH, Increased IOP, Mydriasis and paresis of accommodation, Loss of visual field, Loss of dark adaptation/Nyctalopia, Lens opacities, Increase in traction detachments.

High-risk PDR—not Amenable to Photocoagulation

In presence of severe vitreous or pre-retinal hemorrhage, it may not be possible to deliver laser photocoagulation adequately. In such cases, retinal cryopexy or vitrectomy has to be considered.³ Reported benefits of peripheral retinal cryotherapy include resorption of vitreous hemorrhages and regression of NVD, NVE,

and NVI. The main complication is the development or acceleration of traction retinal detachment in 25–38% of eyes.¹ Therefore, this treatment should be avoided in patients with known traction retinal detachment, and all patients must be monitored carefully. Now days, generally surgery is preferred.

Vitrectomy in diabetic patients: Following are the Indications of vitrectomy in PDR:

- Non-clearing Hemorrhage-Vitreous/Subhyaloid/Premacular
 - The Diabetic Retinopathy Vitrectomy Study (DRVS) was the landmark randomized controlled trial to evaluate indications and timing of pars plana vitrectomy for the management of advanced DR.
 - Early vitrectomy (within 3 months) for treatment of vitreous hemorrhage secondary to DR was highly cost-effective in a cost-utility analysis using DRVS results.
 - ♦ The benefits of early vitrectomy for nonresolving severe VH are greater for patients with T1DM and lower for T2DM.
 - ♦ With diffuse or chronic DME, or a thickened or taut posterior hyaloid, early vitrectomy reduces DME.
 - ♦ If retinal detachment is present, an early vitrectomy is usually suggested.
 - ♦ Patients with bilateral severe vitreous hemorrhage generally should undergo vitrectomy in one eye when they are medically stable.
- Tractional retinal detachment not involving the macula may remain stable for many years. When the macula becomes involved, immediate vitrectomy is generally recommended.
- Combined tractional and rhegmatogenous RD may progress rapidly, and early surgery should be considered in these patients.
- Anterior segment neovascularization with post segment opacity
- Tractional RD threatening/involving macula
- Ghost cell/hemolytic glaucoma
- Anterior hyaloid fibrovascular proliferation
- Epiretinal membrane
- Concurrent internal limiting membrane (ILM) peeling may be done for cases with DME.

VIVA QUESTIONS

Q.1. Define NVD and NVE.

Ans. When neovascularization arise on or within 1 disc diameter of the optic disc they are referred to as neovascularization of the disc (NVD). When they arise further than 1 disc diameter away, they are called neovascularization elsewhere (NVE).

Q.2. What is the prevalence of retinopathy in diabetes?

Ans. The overall prevalence is about 25%. It is 40% in insulin-dependent diabetes mellitus (IDDM) and 20% in non-insulin-dependent diabetes mellitus (NIDDM).

Q.3. What associated systemic conditions worsen diabetic retinopathy?

Ans. These are—Pregnancy, Hypertension, Anemia and Renal failure.

Q.4. What do you know about the pathogenesis of retinal new vessel formation?

Ans. It is not completely understood and current theories emphasize the production of angiogenic factors by areas of ischemic and hypoxic retina. More recently, vascular endothelial growth factor (VEGF) has been isolated from ocular fluid and is an endothelial cell-specific angiogenic factor whose production is increased by hypoxia: it has been implicated in the neovascularization seen in diabetic retinopathy and retinal vein occlusion.^{2,4}

Q.5. Enlist non-DR causes of visual loss in diabetic subjects.

Ans. These are as follows:

- Trauma and injury
- Amblyopia
- Age-related macular degeneration
- Retinal vein and artery occlusion, ischemic optic neuropathy
- Cataract
- Glaucoma
- Hypertension (and macroaneurysms)
- Retinal detachment
- Optic atrophy
- Retinal dystrophies and myopic degeneration.

Q.6. PASCAL (Pattern-scanning retinal laser)

Ans. PASCAL technology is a semi-automated pattern generation method using short laser pulse durations of typically 20 ms (five times shorter than conventional systems). These laser pulses are delivered in a rapid pre-determined sequence resulting in precise even burn patterns as well as improved safety, patient comfort, and a significant reduction in treatment time when compared to single-shot photocoagulation. Multiple spot lasers are similar technology.

Q.7. What is the role of anti VEGF injections in surgical management of PDR.

Ans. It is helpful in managing unlasered cases posted for surgery to prevent bleeding. It should be given 1–3 days before surgery. In patients with TRS, however, caution should be exercised for risks of conversion to secondary rhegmatogenous RD. Some surgeons also leave it at the end of surgery as it may help in managing concurrent DME and prevent rebleed to some extent.

Q.8. What is Rebleed?

Ans. Up to 20% of patients may have recurrent VH following PPV. Early causes include dispersed hemorrhage, hypotony and port site bleeds. Late causes include inadequate laser, poor hyaloidal dissection with retinal breaks, poor systemic status and port site new vessels.

Q.9. How is diabetic PPV different from other surgeries?

Ans. After core vitrectomy, the surgeon should cauterize all possible bleeders first and then identify VR adhesions. Vitreoschisis is frequent in such cases. PVD should not be induced before clearing all adhesions to retina or new vessels. Intraoperative bleeding is very common and the surgeon should be prepared for it. Keep suction and other parameters low. An old protocol would involve segmentation, delamination

and en bloc methods of dissection. These days the role of MIVS cutter as multi-purpose instrument has made surgery much easier. Meticulous PRP should be done and ILM peeling as needed. At the end of surgery, again all bleeders must be cauterized.

Q.10. Management of NVG.

Ans. See glaucoma chapters.

Q.11. What are the specifications for PRP

Ans.

- 300–500 µm laser spot size depending on type of lens used (for magnification adjustment)
- Laser power starts at 100 mW and increase
- Spot distance half-one spot size apart
- Total spots around 2000–2500
- To be done in 2–3 sittings to avoid exudative RD, angle closure and CD
- Mark boundary and start inferiorly first
- Stay 500 µm a far nasal to disc, just outside/within arcades and always atleast 2 DD away from fovea
- Augmentation may be done as needed.

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NONPROLIFERATIVE DIABETIC RETINOPATHY

Dhaval Patel, Brijesh Takkar, Rajesh Pattebahadur

INTRODUCTION

Broadly, diabetic retinopathy (DR) is classified into nonproliferative diabetic retinopathy (NPDR), proliferative diabetic retinopathy (PDR) and diabetic maculopathy. The previous concept of background retinopathy generally falls under NPDR. DR is a very common disorder in wards and retina clinics. Hence, the chances of getting DR as short or long cases are very high. Particularly the viva revolves around the landmark studies done for DR. In India, most of the results seen in western trials have been echoed by the Sankara Nethralaya-Diabetic Retinopathy Epidemiology and Molecular Genetic (SN-DREAMS) study conducted in southern India.

HISTORY

Chief Complaints

It primarily depends upon whether associated maculopathy is present or not. The various modes of presentation can be

- Gradual or acute loss of vision (macular edema)
- History of floaters
- Paracentral scotomata
- Some patients may be asymptomatic if macula is spared
- Detection during DR screening.

History of Present Illness

Typically, the patient is a known case of diabetes mellitus (DM) often referred by general physician for screening. In India, it is not uncommon for the Ophthalmologists to see a case of DR without a previous diagnosis of DM.

History of Past Illness

Unlike many ocular disorders, this is very important in a case of diabetic retinopathy.

Following points must be noted in history:

- *History of DM:* It is very important to note down the following:

- *Type of DM:* Screening of DR is done immediately after diagnosis in Type 2 and within 5 years of diagnosis in cases of Type 1 DM. Typically diabetic macular edema (DME) is more common presentation of Type 2 DM and PDR is more common in Type 1.¹
- *Duration of DM:* Duration of DM is directly proportional to the risk of DR. After 5 years, approximately 25% of Type 1 patients will have retinopathy.¹ After 10 years, almost 60% have retinopathy, and after 15 years, 80% have retinopathy. In the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), most vision-threatening complications were present in approximately 50% of Type 1 patients who had the disease for 20 years.¹ In the Los Angeles Latino Eye Study (LALES) and in Proyecto VER (Vision, Evaluation and Research), 18% of participants with diabetes of more than 15 years' duration had PDR, with no difference in the percentage with PDR between those with Type 1 versus Type 2 diabetes.^{1,2} Type 2 patients with duration of diabetes of less than 5 years, 40% of those patients taking insulin and 24% of those not taking insulin have DR.¹ These rates increased to 84% and 53%, respectively, when the duration of diabetes was 19 years.^{1,2} It is generally believed that almost all diabetics develop some forms of DR overtime, whether treatable or not.
- *DM control:* Poorly controlled DM is highly likely to be associated with DR. *Duration of diabetes and severity of hyperglycemia* is the major risk factor for developing retinopathy. Remember HbA1c is the most important parameter to evaluate control of (DM) over a period of 3 months. As per guidelines, HbA1c of 7% or lower is the target for glycemic control in most patients with DM.

As per the Diabetes Control and Complications Trial (DCCT) for each 10% decrease in the HbA1c the risk of progression of retinopathy decreases by 39%.^{1,2}

- ***Insulin use:*** Recent change from oral hypoglycemic agents to insulin can be associated with a high risk of having DR. Among the Type 2 patients a higher proportion of cases on insulin develops DR compared to those not taking insulin (40% vs 24% at 5 years and 84% vs 53% at 19 years).¹ Certain oral hypoglycemic agents (OHAs) may in fact precipitate DME.
- ***Associated nephropathy:*** The development of PDR parallels an increased risk of nephropathy, myocardial infarction, and/or cerebral vascular accidents.¹ However, the same cannot be said for DME as nearly all the studies on the topic have failed to find an association between nephropathy and DME.
- ***History of retinal laser for DR*** may be present, type, number of settings must be noted.
- ***History of prior treatment with intravitreal injections*** should always be asked for as leading questions.
- ***Hypertension:*** Intensive management of hypertension may slow retinopathy progression.
- ***Hyperlipidemia:*** Management of serum lipids may reduce retinopathy progression and the need for treatment. This has been noted both in Action to Control Cardiovascular Risk in Diabetes (ACCORD) and Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) Trials.¹
- ***Anemia/use of angiotensin-converting enzyme inhibitor/clotting factors*** have been described to influence the onset of DR, although the evidence is inconclusive. Overall, ACE inhibitors were not found to have any conclusive effect on DR progression.^{1,2}
- ***Pregnancy:*** DR can worsen during pregnancy. This is due to the physiologic changes of pregnancy as well as the changes in overall metabolic control. During the first trimester, an eye examination should be performed and subsequent follow-up visits must be scheduled depending on the severity of retinopathy.

If no DR, then at least one examination should be done in every trimester. FA, intravitreal injections and lasers should be avoided if possible. The retinopathy can eventually subside on its own following delivery.

- Cardiac disease and neurological disease

Past Surgical History

Previous history of any cataract surgery must be enquired. Effects of cataract surgery on the acceleration of the progression of DR are controversial. Some reports suggest that eyes that had phacoemulsification had a two-fold increased risk of developing retinopathy compared with eyes that were not subjected to cataract surgery and cataract surgery may deteriorate the progression of diabetic macular edema.^{1,2} But the Early Treatment Diabetic Retinopathy Study (ETDRS) did not find an association between clinically significant macular edema and cataract extraction.

EXAMINATION

General Examination/Specific Systemic Examination

- A detailed general examination must be done to rule out other complications of DM such as neuropathy, nephropathy, and diabetic foot.
- Other medical problems (often coexisting with DM) must be looked for such as:
 - Hypertension
 - Smoking
 - Obesity
 - Hyperlipidemia
 - Anemia.

Ocular Examination

Visual acuity: Reversible refractive errors with changes in glycemic levels even during a day should be kept in mind while performing vision testing. Best-corrected visual acuity (BCVA) is often helpful in deciding the treatment modality in presence of macular edema.

Eyeball: Cranial nerve (CN) palsies (classically pupil sparing III CN palsy or VIth CN palsy as a sign of reversible ischemic mono neuropathy).

Lid: Xanthelasma (suggestive of hyperlipidemia), recurrent hordeola and blepharitis in uncontrolled diabetes can be seen.

Conjunctiva: There is an increased risk of developing conjunctival bacterial infections. In addition, microaneurysms can be seen in the bulbar conjunctiva.

Cornea: Look for following:

- Corneal hypoesthesia (due to associated neuropathy; risk of neurotrophic keratitis)
- Decrease corneal healing (risk of recurrent corneal erosion)
- Tear film abnormalities (a manifestation of autonomic neuropathy).

Iris: Check for neovascularization of iris (NVI) that indicates presence of PDR.

Pupil: Look for following:

- Ectropion uvea (the fibrous tissue accompanying neovascularization contracts which caused eversion of posterior pigmented layer at pupillary margin)
- Increase pigment at angles
- Difficulty in dilating pupils (manifestation of diabetic neuropathy resulting in reduced functional innervation of the dilator muscle)
- Argyll Robertson pupils (bilateral small pupils that reduce in size on a near object (they “accommodate”), but do *not* constrict when exposed to bright light (they do not “react” to light)—an useful mnemonic Accommodation Reflex Present).

Intraocular pressure (IOP): DR can be associated with primary open angle glaucoma (POAG) and neovascular glaucoma (NVG).

Lens: Look for following:

- Reduction in accommodative ability.
- DM can produce following forms of cataract:
 - Typically nuclear and cortical cataract formation is chronic and progressive cases.
 - Acute cortical cataract formation with profound elevations in blood glucose.
 - Snowflake cataracts, which are white subcapsular opacifications, have been described in young Type 1 diabetic patients. This type of cataract is less commonly seen today because it is usually associated with long-term untreated hyperglycemia.
 - Rapid progression of senile cataract occurs in DR.

Vitreous: The vitreous in diabetic patients undergoes abnormal collagen cross-linking and nonenzymatic glycation, which lead to precocious liquefaction and posterior vitreous detachment (PVD). Asteroid hyalosis can also occur.

Fundus: The different changes that can be seen in DR are summarized in **Tables 1 and 2**.

Stages of NPDR

- *Mild NPDR:* Microaneurysm (one or more) (**Fig. 1**)
- *Moderate NPDR:* Microaneurysm, retinal hemorrhages (dot and blot), hard exudates, cotton wool spots (CWS), venous beading,

Table 1 Fundus changes in diabetic retinopathy

Clinical sign	Pathogenesis	Layer of retina affected	Effect of treatment
Cotton wool spot	Nerve fiber layer ischemic necrosis	Nerve fiber layer	Persists
Microaneurysms	Secondary to capillary wall outpouching due to pericyte loss	Superficial retinal layers	Resolves if controlled
Dot and blot hemorrhages	Microaneurysms rupture in the deeper layers of the retina	Inner nuclear and outer plexiform layers	Resolves gradually
Flame-shaped hemorrhage	Splinter hemorrhages that occur in the more superficial nerve fiber layer	Superficial layers	Resolves gradually
Retinal edema and hard exudates	Breakdown of the blood-retina barrier, allowing leakage of serum proteins and lipids from the vessels	Deeper layers	Resolves but complete resolution unlikely

Table 2 International diabetic retinopathy severity scale

Disease Severity level	<i>Dilated ophthalmoscopy findings</i>
No apparent DR	No abnormalities
Mild nonproliferative DR	Microaneurysms only
Moderate nonproliferative DR	More than "mild" but less than "severe"
Severe nonproliferative DR	Any of the following: 20 or more intraretinal hemorrhages in 4 quadrants Definite venous beading in 2 or more quadrants Prominent IRMA in 1 or more quadrants and no neovascularization
Proliferative DR	One or more of the following: Definite neovascularization Preretinal or vitreous hemorrhage

**Fig. 1:** Mild NPDR with microaneurysm and hemorrhage**Fig. 2:** Moderate NPDR with retinal hemorrhages and venous beading

- arteriolar narrowing, intraretinal microvascular abnormalities (IRMA) (**Figs 2 and 3**).
 - **Severe NPDR:** All of above plus anyone of the following three (the famous 4:2:1 rule in ETDRS) (**Fig. 4**):
 1. Blot hemorrhages in 4 quadrants
 2. Venous beading in 2 quadrants
 3. IRMA in 1 quadrant.
 - **Very severe NPDR:** More than one of the above mentioned rules.

Clinically Significant Macular Edema (CSME)

- Retinal thickening or edema at or within 500 micron of the center of the macula
- Hard exudates at or within 500 micron of the center of the macula associated with retinal thickening of the adjacent retina

**Fig. 3:** Very severe NPDR with retinal hemorrhages, hard exudates, cotton wool spots (CWS) and venous beading

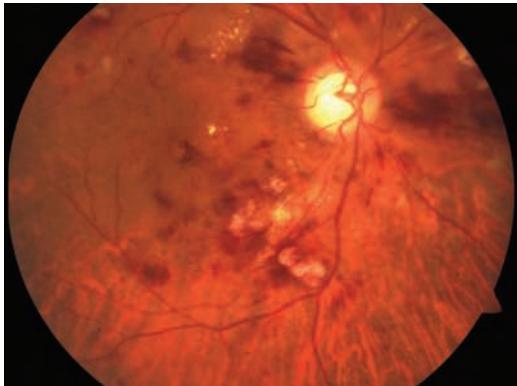


Fig. 4: Severe CWS and arterial attenuation along with features of NPDR in a case of combined retinopathy

- An area or areas of retinal thickening at least one disk area in size at least part of which is within 1 disk diameter of the center of the macula.

Retinovascular Disease

- Retinal vein and artery occlusion
- Ischemic optic neuropathy.

Diabetic Papillopathy

- It is a rare cause of bilateral (or sometimes unilateral) disc swelling in patients with type-1 DM.
- Disc edema is often associated with capillary telangiectasia's overlying the disc surface.
- It differs from anterior ischemic optic neuropathy (AION) in that there is often bilateral, simultaneous optic nerve involvement.
- Visual acuity is often normal.
- The pathogenesis is impaired of blood flow causing disc swelling, but not have sufficient to significantly affect optic nerve function.
- Most cases, the optic disc edema resolves without residual visual deficit.

DIFFERENTIAL DIAGNOSIS

The characteristic clinical findings and history of DM often differentiates DR from other disorders. However, following disorders must be kept in mind that can mimic NPDR, especially in unilateral cases:

- Hypertensive retinopathy

- Retinal vein occlusion (branch or central)
- Hemoglobinopathies
- Anemia or leukemia
- Ocular ischemic syndrome
- Radiation retinopathy
- Idiopathic juxtapapillary telangiectasis
- Coats' disease
- Vasculitis (e.g. sarcoidosis, lupus).

INVESTIGATION

Systemic investigations: Following are specific for DR:

- Fasting and postprandial blood sugar test
- Glucose tolerance test
- Hemoglobin A1c
- Renal function test
- Others for the systemic entities listed before.

Fundus photography: Color fundus photography is commonly used to document retinal disease and its evolution in diabetic patients. It is used for tracking disease progression and is accepted as the best screening method for DR especially in teleophthalmology.

Optical Coherence Tomography

- Noninvasive imaging technique
- It is important in managing diabetic macular edema (see the short case on DME).

Following are uses of optical coherence tomography (OCT) in DR:

- To investigate cases with unexplained visual acuity loss
- To detect areas of vitreomacular traction (VMT)
- To evaluate patients with difficult and/or questionable examinations for DME
- To rule out other causes of macular edema
- To screen a patient with no or minimal diabetic retinopathy.

Fundus fluorescein angiography (FFA): Following are uses of FFA in DR.

Diagnosis

- Ischemic maculopathy
- Areas of capillary nonperfusion
- To rule out other causes of macular swelling
- Differentiate between new vessels from IRMA

- To identify suspected but clinically obscure retinal neovascularization
- To evaluate unexplained visual loss.

Aid in Treatment

- To guide laser treatment of CSME
- Delineate fovea and fovea avascular zone
- Delineate area of leakage
- To detect areas of untreated retinal capillary nonperfusion that may be the cause for persistent retinal or disc neovascularization after previous scatter laser photocoagulation.

Ultra wide imaging: Instead of the previously used 7 field fundus imaging, now the focus is shifting towards ultra wide field imaging for monitoring NPDR.

Red-free imaging: This is helpful in identifying new vessels, which may not be visible to the clinician.

Electroretinogram (ERG): Full field and multifocal ERG are helpful in diagnosing what has been called as diabetic neuroretinopathy. This entity particularly can cause mild/minimal/functional/ qualitative visual loss in patients without maculopathy.

OCT angiography: Role is under evaluation, and current concept involves imaging microaneurysms and FAZ changes.

MANAGEMENT

Following points are important in management of NPDR:

- Joint management with family physician or endocrinologists
- Stress should always be on systemic control first, and ocular management later
- Ensure good DM control (good glycosylated hemoglobin levels)
- Treat associated systemic disease most important among them is maintaining, serum lipids, and blood pressure.
- Worsening DR is an indicator of poor systemic control.

Normal or minimal NPDR (with rare microaneurysms): Follow-up patient and watch for progression and macular edema. Remember within 1 year 5–10% of such patients can progress to advanced stages of DR.¹

Mild to moderate NPDR without macular edema:

Re-examine within 6 to 12 months. Approximately 16% in cases of mild and 23% in cases of moderate NPDR of patients may progress to proliferative stages within 4 years.

Mild to moderate NPDR with CSME: If it is center-involving (ci-CSME) anti-VEGF is the treatment of choice. If it is *non-center-involving (nci-CSME)* then focal/grid laser surgery guided by the ETDRS is the treatment of choice. (Refer to the chapter short case diabetic macular edema for detail on management of macular edema).

Severe and very severe NPDR: Follow-up patient very closely (2–4 months). Half of patients with in case of severe NPDR 50% of the cases progresses PDR within 1 year, and 15% will develop high-risk PDR. Similarly in cases very severe NPDR 75% of the cases develop PDR within 1 year while 45% will develop high-risk PDR. Therefore, a close follow-up of such cases is required.

Classic indication of PRP is high risk PDR, however it may be done even without CSME in special situations such as:

- Patient is a young insulin-dependent diabetic (IDDM)
- Patient has poor DM control with associated DM complications (nephropathy)
- Fellow eye is blind from DR
- Family history of blindness from DR
- Poor patient compliance to follow-up
- Prior to cataract operation or pregnancy.

VIVA QUESTIONS

Q.1. Describe pathophysiology of microaneurysm development.

Ans. Normally there is one pericyte per endothelial cell. Pericytes are contractile cells that play an important role in microvascular autoregulation and maintaining the blood retinal barrier. In people with diabetes, the pericytes die off and are decreased in number (SORBITOL accumulation). Their absence weakens the capillaries and permits thin-walled dilatations, which are known as microaneurysms. Naturally, these microaneurysms tend to collapse upon themselves but may leak causing disease.³

Q.2. Describe pathophysiology of macular edema development.

Ans. Breakdown of the blood-retina barrier is an important pathophysiologic feature of diabetic retinopathy that leads to the development of macular edema.

Q.3. How would you differentiate between microaneurysm and small dot hemorrhage?

Ans. It is often difficult to distinguish a small dot hemorrhage from a microaneurysm by ophthalmoscopy alone. On fluorescein angiography patent microaneurysms will fill with dye quickly and then leak, unlike a small dot hemorrhage that will block fluorescence.

Q.4. Describe pathophysiology of dot-blot and flame-shaped hemorrhage.

Ans. If the hemorrhage is deep (i.e., in the inner nuclear layer or outer plexiform layer), it usually has a round or oval shape (dot or blot hemorrhage). Superficial (nerve fiber layer) hemorrhages, on the other hand, become flame or splinter-shaped. This is due to the peculiar arrangement of nerve fibers in respective layers. Superficial hemorrhages may be associated with CWS, which represent blocked axoplasmic flow in the RNFL following focal ischemia.³

Q.5. Intraretinal microvascular abnormalities (IRMAs)

Ans. These are shunt vessels and appear as abnormal branching or dilation of existing blood vessels (capillaries) within the retina that appears to supply the areas of non-perfusion. These vessels represent either new vessel growth within the retina or remodeling of pre-existing vessels through endothelial cell proliferation stimulated by hypoxia bordering areas of capillary non-perfusion. When compared to neovascularization (NV) in PDR, IRMAs are slightly larger in caliber with a more broad arrangement and are always contained to the intraretinal layers. Conversely, NV tends to be much finer and delicate in caliber, and is sometimes more focal in location depending on its severity. In severe

cases, NV tends to grow along the posterior hyaloid interface especially around the optic nerve (NVD) and periphery (NVE). On fluorescein angiography, NV will often show late leakage whereas IRMAs traditionally do not leak.³

Q.6. How often would you screen diabetic patients for retinopathy?

Ans. *Type-1 (Insulin-dependent diabetics):* 5 years after diagnosis then annually. Type 1 diabetes, substantial retinopathy becomes apparent as early as 6–7 years after onset of the disease. In addition, the disease is diagnosed early because of its severity, hence screening is recommended beginning 5 years after the diagnosis of Type 1 diabetes.

Type-2 (Non-insulin-dependent diabetics): Screening is done at diagnosis and then annually. The diagnosis of DM may be delayed in these cases and when the diagnosis is made, it is assumed that the disease might have already been present for last 4–5 years. About 30% of patients will have some manifestations of DR at diagnosis hence screening has to be done immediately after diagnosis.

Pregnancy (Type 1 or Type 2):

- First examination—soon after conception and early in the first trimester.
- Follow-up—no retinopathy to mild or moderate NPDR: every 3–12 months. If severe NPDR or worse is present than follow-up: every 1–3 months.

Q.7. What is the earliest sign of retinal change in diabetes?

Ans. Microaneurysms at posterior pole are the first clinical signs. An increase in capillary permeability, evidenced by the leakage of dye into the vitreous humor after fluorescein injection, is the earliest sign of retinal change in diabetes mellitus.

Q.8. What are the three questions that ETDRS addressed and what are the inferences?

Ans. • What is the role of aspirin in diabetic retinopathy?
Answer: It neither improves nor worsens retinopathy.

- What is the role of initiating early laser (as compared to DRS high-risk criteria) in the management of severe non-proliferative and early proliferative retinopathy?

Answer: Inconclusive. No strong benefit to early scatter panretinal photocoagulation (PRP) was found. Certain clinical circumstances (e.g. poor compliance with follow-up examinations, rapid progression in fellow eye, very poor cardiorenal status) may justify early initiation of PRP.

- What is the role of laser (PRP or focal macular laser, or both) in the management of macular edema?

Answer: Traditionally, there is no role for PRP in treatment of macular edema. Macular laser is of benefit, reducing the risk of moderate visual loss by 50%. Patients with CSME should be treated. However, now research focus is towards targeted laser for peripheral ischemic areas detected upon wide FA.

Q.9. What is international DR severity scale?

Ans. A workshop was held in April 2002 in conjunction with the International Congress of Ophthalmology to develop and build broad-based consensus around a *clinically relevant and simplified DR disease severity scale* that is summarized in **Table 2**.

Q.10. What is subthreshold micropulse diode laser photoagulation?

- A. *Subthreshold:* The intent of treatment is to lightly affect the retinal pigment epithelium alone, restricting the lateral spread of heat and thus, sparing damage to the overlying photoreceptors and mid-retinal interneurons

Micropulse: Employs repetitive trains (50–500) of laser pulses of short duration (0.8–5.0 ms) and extending the “off-time” between micropulses.

Diode laser: Using a longer wavelength near-infrared 810 nm diode laser.

Q.11. How does laser act in macular edema?

Ans. It acts by following mechanism:

- Reduces metabolic need.

- Direct diffusion of oxygen from chorio-capillaries through scar to inner retina.
- Stimulates endothelial repair process.

Q.12. How will you differentiate between Diabetic papillopathy and AION?

Ans. See fundus changes above in the chapter.

Q.13. Preoperative/intraoperative/postoperative precautions for cataract surgery in presence of NPDR with CSME.

Ans. Following are the precautions:

Preoperative care

- In patients with existing rubeosis, this should be treated preoperatively with panretinal photocoagulation.
- Laser of macular edema or anti-VEGF injection should be given.
- Topical nonsteroidal anti-inflammatory drugs (NSAIDs) can prevent intraoperative miosis.

Intraoperative care

- It is advisable to perform a large capsulorrhesis with a 6 mm optic lens, thus allowing the better visualization of the fundus for PRP if required.
- Multifocals are contraindicated as they reduce the contrast and fundus evaluation is difficult.

Postoperative care

- Patients with diabetes are at slightly greater risk of cystoid macular edema which may be difficult to differentiate from true diabetic maculopathy (see DME chapter).
- Incidence of capsular opacification is greater in diabetics than in nondiabetics. Therefore, a large yttrium aluminum garnet (YAG) capsulotomy to improve vision or improve visualization of the retina may become necessary.

Q.14. Role of NSAIDS.

Ans. DM induces inflammatory reactions by many mechanisms including, oxidative stress NF- κ B activation, NOS dysregulation, AGEs formation, hypertension, dyslipidemia and impaired anti-inflammatory pathways. Topical nonsteroidal anti-inflammatory medications are common treatment for DME. These agents are

directed at decreasing intraocular prostaglandin levels, which have been implicated in the pathogenesis of DME. Bromfenac perhaps has the highest vitreal penetration.

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RETINITIS PIGMENTOSA

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INTRODUCTION

Retinitis pigmentosa (RP) is a retinal dystrophy affecting the rod photoreceptors, to begin with, and subsequently cones resulting in severe visual loss. The prevalence is 1:3500 to 1:4000. The inheritance pattern is complex. It usually presents clinically in the second or third decade. Central vision is preserved late in the course of the disease. However, earlier loss of central vision may be attributed to cystoid macular edema occurring in 10–50% of individuals.^{1–3} Typically X-linked variants present very early in childhood whereas autosomal recessive (AR) variants present around 10–12 years of age. Autosomal dominant (AD) linked and spontaneous variants present later. In exams, it is usually given as a long case.

HISTORY

Chief Complaint

The usual presenting complaints are following:

- Dark adaptation difficulty (earliest, but patient often fail to recognize)
- Night blindness (most common presentation)
- Progressive loss of peripheral visual field—rarely the patient can present with tunnel vision when the central field is the only vision left.
- Gradual decrease in visual acuity—central visual acuity is usually preserved until the end stages of retinitis pigmentosa (RP). Early central acuity loss can occur from cystoid

macular edema (CME), complicated cataract or in atypical form of RP.

- Acquired tritan color vision defect
- Noted during sibling screening
- Noted during fundus evaluation after medical advise.

History of Present Illness

- The disease usually begins in childhood or adolescence. The initial symptom is difficulty in dark adaptation. The earlier the onset of defective dark adaptation, the more severe is the course of RP.
- The loss of red cell functioning in the retina of RP patients leads to many glare-related problems. In low light, these patients have night blindness. However, in bright light they can experience “white out” glare. Parents may note an affected child to bump into objects at night.
- Subsequently there occurs constriction of visual field with preserved central vision until late in the disease. A careful history can often reveal frequent bumping or frequent accidents while driving vehicle in cases unaware of their constricted field of vision.

History of Past Illness

Past medical and surgical history must include careful history to rule out the systemic associations of RP. This is more important in X-linked and AR variants. There may be past history of associations of RP as well.

Family History

Meticulous family history should be taken and a pedigree should be prepared. A three generations pedigree chart must be prepared in all such cases. Effort should be made to identify the inheritance pattern if present.

EXAMINATION

General Examination

Detail systemic examination is done to know any associated sensory neural hearing loss, vestibular nerve function, ataxia, and speech disorder. RP can be associated with multiple syndromes; some of them and their systemic features are summarized in **Table 1**. Associated sleep disturbance and headache are common in RP patients.¹⁻³

Ocular Examination

Visual acuity: The visual acuity is normal in early cases. Early central acuity loss can occur from cystoid macular edema (CME), epiretinal membrane (ERM), and complicated cataract or in atypical form of RP.

Eyeball: Myopia is a common association of RP (22–75% of people with RP have myopia of about -2 D).

Lid/Conjunctiva/Cornea/Sclera: These are usually within normal limits (WNL). There may be fat atrophy of the orbits due to frequent rubbing, typically seen in LCA. Keratoconus may be noted as an association of RP.

Iris: Forward shifting of iris lens diaphragm may occur due to zonular weakness.

Table 1 Common forms of syndromic retinitis pigmentosa

Syndrome/disease	Characteristic features	Etiology
Usher syndrome	Bilateral sensory neural hearing loss Lack of development of speech Vestibular nerve dysfunction Ataxia	Most commonly due to a mutations in the <i>MYO7A</i> gene on chromosome 11q
Laurence-Moon-Bardet-Biedl syndrome (BBS)	Obesity Mental retardation or mild psychomotor delay Post-axial polydactyly Hypogenitalism Renal abnormalities/renal failure	Mutation involving at least six distinct loci
Refsum disease	Neuropathy Ataxia Deafness Arrhythmia	Recessively inherited condition in which the patient accumulates exogenous phytanic acid
Bassen-Kornzweig syndrome (abetalipoproteinemia)	Acanthocytosis Malabsorption Ataxia	A malabsorption syndrome associated with absence of low-density plasma lipoproteins or so-called β -lipoproteins
Friedreich-like ataxia with retinitis pigmentosa	Friedreich-like ataxia, dysarthria, hyporeflexia, and decreased proprioceptive and vibratory sensation, as well as markedly decreased serum vitamin E levels	Recessively inherited, mutation in the α -tocopherol-transfer protein (α -TTP) gene
Kearns-Sayre syndrome	Conduction defects of heart External ophthalmoplegia RP	Mitochondrial DNA disorder

Pupil: As per traditional teaching, afferent papillary defect (APD) does not occur in normal room luminance, as light reflex pathway dependent on melanopsin RPE cells is still functional. Relative afferent pupillary defect (RAPD) suggests underlying optic atrophy. However, RAPD can be absent in spite of optic atrophy as RP is a bilateral disorder.

IOP: Increase in IOP may occur in cases with RP with glaucoma, open angle glaucoma (OAG) is an association.

Lens: Posterior subcapsular cataract (PSC) may occur in some cases (41–53%). Zonular weakness, although rare, can also occur in RP.

Vitreous: Vitreous degeneration and early posterior vitreous detachment can occur. Dust-like particles can be seen in the vitreous. These particles are fine, colorless consisting of free melanin pigment granules, pigment epithelium, uveal melanocytes, and macrophage-like cells. They are found evenly distributed throughout the vitreous cavity. Observation of these particles can be helpful in the diagnosis of early RP before fundus changes are apparent. Retrolental cells may also be noted, as pars planitis is known to be associated with RP.

Fundus: Following signs can be seen in a case of typical RP:

- Arteriolar narrowing (most common but not earliest, seen in 90–95% of cases)
- *Pigmentary changes:* (Some authors list this as the first and most prevalent sign)
 - Earliest changes include fine dust-like intraretinal pigmentation, and loss of pigment from the pigment epithelium.
 - The pathognomonic pigment clumps in a characteristic “bone spicule” configuration appears subsequently as the photoreceptor deterioration progresses, and there is increasing loss of pigment from the pigment epithelium with intraretinal clumping of melanin (**Fig. 1**).
 - The term bone spicules are used to refer to the type of small cells that are laid down in the formation of new bone matrix. These spicules in bone have a similar shape to the classic pigment finding in RP, thus the name.

– The bony spicules are characteristically perivasculär. Remember the spicules are initially more around the venules. They appear first in the mid periphery.

- In advanced cases waxy pallor of the optic disc is seen (50–55%) (**Fig. 2**).⁴
- Associated cystoid macular edema (CME) is seen in 19–70% of cases (**Fig. 3**).^{1,4}
- Macula may show atrophy or epiretinal membrane (ERM) formation.
- Optic disc drusen can be seen in cases of RP.
- There may be the golden ring around the optic disc sign.

Atypical RP

In 20–30% of cases of RP the classical triad of attenuated vessels, bone spicules and waxy pallor



Fig. 1: Fundus photograph showing bony spicules with waxy disc pallor

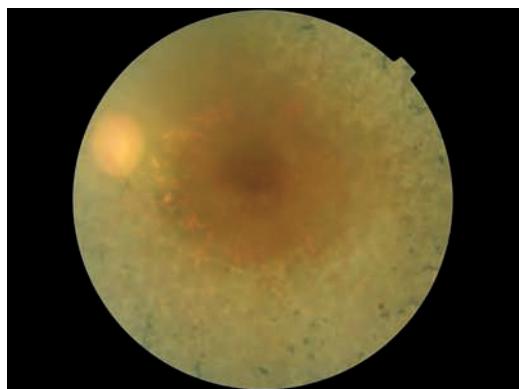


Fig. 2: Fundus photograph in case of RP showing severe vascular attenuation



Fig. 3: Macular scarring in a case of RP with CME

may not be seen. These forms of RP are known as atypical forms.

- *Retinitis pigmentosa sine pigmento*: Fundus appears normal but there is evidence of photoreceptor dysfunction in electroretinogram (ERG).
- *Retinitis punctata albescens*: Retinal pigment epithelial degeneration appears as presence of deep white dots at the level of RPE.
- *Sectoral RP*: Only one quadrant or one-half of the fundus has degenerative changes of retinitis pigmentosa. Most commonly, the inferior and nasal quadrants are involved and the involvement is often symmetrical.
- *Retinitis pigmentosa inversus or pericentric RP*: Changes of RP primarily affects macula and posterior pole. Thus, it can mimic hereditary fundus dystrophies. Visual acuity and color vision are affected early in the course of the disease. It progresses at a slower rate than typical RP and in advanced cases, the central vision is severely affected but the peripheral vision is retained. The visual field defect is near mid-peripheral scotoma extending from the 5 to 30° isopter in contrast to the 20–40° isopter seen in cases of typical RP.
- *Unilateral RP*: It is characterized by fundus changes of RP in one eye and no evidence of RP in the fellow eye. ERG findings are substantially reduced in the affected eye but normal in the fellow eye. The RP progresses in the affected eye while the other eye remain unaffected. DDs of pseudo RP must be evaluated.

- *Paravenous RP*: In this form the ERG changes and intraretinal pigment and atrophy of the pigment epithelium remains confined to the distribution of the retinal veins in each eye. Patients may lose central vision but, like pericentral RP, they retain peripheral vision into later life.

Syndromic RP

- RP associated with systemic disorder
- Usually AR or mitochondrial inheritance
- Usher syndrome, Kearns-Sayre syndrome, Bassen-Kornzweig syndrome, rafsum disease, Bardet-Biedl Syndrome (**Table 1**).

DIFFERENTIAL DIAGNOSIS

Pseudo-RP

This term refers to the conditions that mimic the fundal appearances of retinitis pigmentosa.¹⁻³ This can occurs in following conditions:

- Syphilis (leopard skin retinopathy)
- Congenital rubella
- *Drug induced*: Thioridazine streaks, chloroquine, quinine and phenothiazine
- Laser scars
- Old retinal detachment
- Trauma
- Chronic uveitis
- Cancer-associated retinopathy.

Choroideremia

- X-linked disease
- *Early stage*: Fine pigmentary stippling and atrophy of fundus
- *Later stage*: Patchy RPE and choroidal atrophy which gradually coalesce.

Gyrate Atrophy of Retina and Choroid

An AR disorder. Discrete round patches of choroidal and retinal atrophy occur in midperipheral fundus. Gradual coalescence of the lesions occurs leading to sharply defined scalloped defects. There are 10 to 20-fold increase in plasma ornithine level due to ornithine ketoacid aminotransferase deficiency.¹

Cone and Rod Dystrophy

In contrast to typical retinitis pigmentosa (known as the rod-cone dystrophies), cone rod dystrophies reflect the opposite sequence of events, where cone cells are primarily first affected with later loss of rods. Thus, the presenting features are difficulty with the clarity of vision, color vision problems and light sensitivity. It can occur in association with Alstrom syndrome, Bardet-Biedl syndrome, neuronal ceroid lipofuscinosis, Joubert syndrome and related disorder. Remember few clinicians term this as inverse RP; but this is better termed as inverse retinal pigmentary dystrophy; in inverse RP although the lesion starts around macula or posterior pole the pathogenesis is same unlike cone rod dystrophy where cones are primarily affected.¹

Leber's Congenital Amaurosis

Following points helps in differentiating from RP:¹⁻³

- AR inheritance with onset in 1st year life.
- Severely reduced visual function with nystagmus/nystagmoid movements, sluggish pupillary response, photophobia, and hyperopia.
- *Oculodigital sign:* Characterized by orbital fat atrophy (apparent by the deep sockets with a prominent eyeball), and development of keratoconus if the child survives into later decades. This is because the child repeatedly rubs, pokes and presses the eyes to elicit retinal stimulation.
- Initially fundus appears normal but later in childhood pigmentary retinopathy changes develop. *Toxoplasma* like scars can occur.
- ERG is nondetectable and severely abnormal quite in early stage of the disease.
- *SECORD (Severe childhood onset retinal dystrophy):* Similar to LCA but with better visual acuity than LCA later in life.

INVESTIGATION

- *ERG:* It shows early and severe reduced rod response, decreased a and b wave amplitude, prolonged implicit time, reduction in cone response in advanced cases.

- *Visual field:* In early RP, there is presence of ring scotoma in midperiphery (20–25° from fixation). It usually starts as a group of isolated scotomas around 20–25° from fixation, and gradually coalesces to form a partial followed by a complete ring. The outer edge of the scotoma expands relatively rapidly, while the inner edge constricts slowly toward fixation. In advanced cases, the inner edge progresses to center giving rise to tunnel vision. (It must be remembered that when visual acuity is low only Goldman's visual field is possible and this is the preferred modality in RP).
- *Optical coherence tomography (OCT):* It is done to rule out any macular pathology. This must be done in any case presenting with early loss of central vision or acute loss of vision during the course of RP. Choroidal changes have also been studied in RP, but have been found to not relate to visual acuity in these patients.
- *Fluorescein angiogram:* It shows diffuse hyperfluorescence due to RPE window defects.
- *Ultra wide imaging* helps in documenting peripheral changes.
- *Color vision and contrast sensitivity* may also be done for evaluation.

CLASSIFICATION

- *Non-syndromic or simple:* It does not affect other systems of body. It may occur as AD, AR, X-linked, and digenic forms.
- *Syndromic:* Affects other neurosensory systems of body such as hearing [see Table 1]
- *Systemic:* Affects multiple organs of the body.

STAGING

Typical form of RP has been divided into following three stages:¹⁻³

Early Stage

- Involvement occurs in first years of life
- Night blindness
- Very early minimal visual field defect
- Normal fundus appearance
- ERG shows decreased b wave amplitude particularly in scotopic conditions.

Mid Stage

- Peripheral visual field defect in day light
- Fundus changes like bony spicule like pigmentary changes, attenuated vessels and optic disc pallor.
- *ERG*: Unrecordable in scotopic conditions and hypovolted cone response

End Stage

- Tunnel vision
- Decreased visual acuity due to cone involvement
- Unmasking of choroidal vessels giving the fundus tessellated appearance
- Unrecordable ERG.

COMPLICATIONS

- Keratoconus
- Posterior subcapsular cataract
- Open angle glaucoma (3%)
- Occasional intermediate uveitis
- Exudative vasculopathy often called coats like disease.

MANAGEMENT

Currently there is no definitive treatment for retinitis pigmentosa. The visual prognosis in advanced cases is usually poor. Various treatment modalities are under trial to slow down the disease progression, treatment of complications and improve the visual rehabilitation of RP patients.¹⁻⁴

- Smoking should be avoided
- *Optical aids and light protection*:
 - *UV A and UV B blocking sunglasses*: It reduces the retinal degeneration by reducing short wave length light exposure. Use of CPF 550 lenses filters out 97–99% spectral and UV ray.
 - Low vision aids, e.g. magnifiers, closed circuit television are given to people with decreased central vision.
 - Wide field bright intensity flashlight improves night vision by producing bright wide beam of light.
- *Vitamin A palmitate*: It is prescribed in a dose of 15000 IU/day. However, the use is highly controversial. Pregnancy is a contraindication

as there is risk of teratogenicity. It should not be given to children <18 years and persons with ABCA4 deficiency due to risk of accumulation of toxic product A2E. Vitamin E in high dose has been shown to adversely affect the course of RP and should therefore be avoided.

- Increased intake of docosahexaenoic acid and lutein-zeaxanthin has shown promising results in decreasing progression.
- Systemic carbonic anhydrase inhibitors in a dose of 500 mg daily have been shown to reduce the cystoid macular edema associated with RP. However, the CME is chronic and often difficult to treat. Topical carbonic anhydrase inhibitor not very effective in treating CME.
- Intravitreal triamcinolone and anti-VEGF injections have shown to reduce CME.
- Cataract extraction is often indicated for decreased vision due to posterior subcapsular cataract especially in cases with less than 10° of visual field.
- Hyperbaric oxygen therapy to promote photoreceptor survival, retinal cell transplantation, calcium channel blockers, neurotrophic growth factors (CTNE, GDNF, cardiotrophin 1, b FGF, BDNE, topical brimonidine tartrate 0.2%) are various treatment modalities which are under trial.
- Gene therapy with surgical administration of AAV vectors having RPE65C DNA to subretinal space was found to save vision in LCA in an animal model. This is an upcoming treatment under advanced phases of studies in humans. This is likely to benefit LCA/SECORD.
- Retinal prosthesis like microphotodiode that capture light and stimulate retina, optic nerve and visual cortex are being developed.
- Psychological and visual rehabilitation is often necessary and patients should be trained to develop new professional skill.
- *Follow-up*: Goldmann visual perimetry and dilated fundus examination by ophthalmoscopy should be done on annually and biannually. In cases with RP associated with CME, more frequent follow-ups are necessary.
- Examination of other family members of the affected person is recommended. People who are undergoing family planning should have proper genetic counseling regarding the

mode of inheritance and possible affection of the offspring's and manifestations of RP to help them taking proper decision.

VIVA QUESTIONS

Q.1. Mechanism of glaucoma in RP.

Ans. RP can be associated with both angle closure and open angle glaucoma.

- *Angle closure glaucoma:* There is increased zonular instability with anterior shifting of iris lens diaphragm resulting in angle narrowing and angle closure glaucoma.
- *POAG, NTG and JOAG:* attributed to the mutation of gene for retinitis pigmentosa GTPase regulator-interacting protein 1 (RPGRIP1) on chromosome 14q11.

Q.2. Differential diagnosis of tunnel vision.

Ans. The loss of peripheral vision with retention of central vision gives rise to tunnel vision. Tunnel vision can be caused by:

Common: Glaucoma, retinitis pigmentosa
*Rare:*¹⁻⁴

- Blood loss (hypovolemia)
- Alcohol consumption
- Sustained, i.e. 1 second or more high accelerations, (typically, flying an airplane with a centripetal acceleration of up to or over 39 m/s^2 with the head towards the center of curvature, common in aerobatic or fighter pilots)
- Hallucinogenic drugs (dissociative)/ extreme fear or distress/intense physical fight/excitement or extreme pleasure (causing a surge of adrenaline in the body)
- Altitude sickness/hypoxia in passenger aircraft/exposure to oxygen at a partial pressure above 1.5-2 atmospheres (producing central nervous system oxygen toxicity, called narcosis)
- Pituitary tumors (or other brain tumors that compress the optic chiasm)
- Advanced cataract, during the aura phase of a migraine, intense anger (due to the body being rapidly flooded with adrenaline and oxygen)

- A bite from a Black Mamba and other snakes
- Mercury poisoning (especially Methyl mercury).

Q.3. Why does bony spicules occur in perivascular region? Why there is thinning of blood vessel in RP?

Ans. *Bony spicules:* It is referred to the type of small cells that are formed during the formation of new bone matrix. In RP, the appearance of pigment has similar shape as spicules in bone.

Attenuation of vessels: Due to progressive damage of outer retina the vascular demand of retina on choriocapillaries and inner retinal arteries decrease.

Perivascular distribution: In RP due to progressive outer photoreceptor and outer retinal damage the inner retina and the inner retinal blood vessels lie in contact with RPE. This blood vessel-RPE contact sends a trigger signal for bony spicule like pigment formation. Progressive attenuation of inner retinal arteries leads to gradual hypoxia and subsequent damage to the cells forming inner blood retinal barrier. The bony spicule like pigment (along with RPE cells) migrates along the vessels in order to reform the inner blood retinal barrier. The RPE cells seal the vessels with tight junction linkage, deposit perivasculär extracellular matrix and induce fenestrations in the vascular endothelium of the cuffed vessels that leads to the characteristic "spicule" pattern.¹⁻⁴

Q.4. Bionic eye in RP.

Ans. In RP patients who are blind several prosthesis prototypes have been tested that electrically stimulate the inner retina. These devices can induce phosphenes and can improve performance on some tests of visual function. However, it needs a functional optic nerve and its role in RP with optic atrophy is unclear.

Q.5. Stem cell transplant.

Ans. Several studies have demonstrated *in vitro* differentiation of embryonic and adult stem cell into retinal cell types. The *in vivo*

transplantation of these cells as well as fetal retinal cells to animal models has given promising results. Some studies of stem cell transplantation on individuals with RP have shown improvement of visual function.

Q.6. Can an RP patient be legally blind inspite of having good central vision?

Ans. Yes, visual field of <10° is considered as blind even when the visual acuity is 6/6.

Q.7. Role of multifocal ERG.

Ans. Records local response from the macula and is able to detect residual macular functions in advanced cases. Thus, in cases with advanced RP, long-term follow-up and monitoring of visual function can be done with multifocal ERG.

Q.8. Full field ERG.

Ans. It stimulates the full visual field and records response from the entire retina. It is used traditionally to follow the disease progression in RP.

Q.9. Genetics and RP.

The different genes associated with RP are described below.¹⁻⁴

AD RP: These are mildest forms with some cases occurring after age 50. RHO (most common), PRPF 31, PRPH2, RP1, IMPDH1, PRPF8, KLHL7, NR2E3, CRX, PRPF3, TOPORS, CA4, NRL, ROM1, RP9, RDH12, SNRNP200, AIPL1, BEST1, PRPF6, RPE 65, GUCA1B, FSCN2, SEMA4A.

Sporadic: May have favorable prognosis. Retention of central vision until 6th decade or later.

AR RP: Usually start in the first decade. USHA2A (most common), ABCA4, PDE6A, PDE6B, RPE65, CNGA1, BEST1, C20orf71, C8orf37, CLRN1, CNGB1, DHDDS, FAM161A, IDH3B, IMPG2, LRAT, MAK, MERTK, NRL, PDE6G, PRCD, PROM1, RBP3, RGR, RHO, RLBP1, RP1, SPATA7, TTC8, TULP1, ZNF513, ARL6, NR2E3, EYS, CRB1, CERKL, SAG.

X-linked: Early onset and frequently associated with myopia. Least common, but most severe, usually complete blindness by 3rd or 4th decade. In most of the cases, transmission is recessive. RPGR, RP2.

Digenic (very rare): Inherited in pseudo-dominant pattern. Simultaneous presence of PRPH2 and ROM1.

Prognosis:

- Best prognosis: AD.
- Worst prognosis: XR.
- AD>Sporadic>AR>XR

MC mode of inheritance:

- Sporadic/simplex (40–50%)
- AD (15–25%)
- AR (5–20%)
- X-linked (5–15%)
- Digenic (very rare).

Q.10. Type of Sunglasses preferred in RP

Ans. Some clinicians prefer orange photochromic sunglasses with tinted side shields or dark amber sunglasses with tinted side shields. However, no particular type of sunglasses has been shown to delay the progression of the disease. Sunglasses should be selected for outdoor use that provide maximal comfort to the vision without compromising vision.

Q.11. Causes of completely extinguished ERG.

Ans.

- Leber's congenital amaurosis
- Severe retinitis pigmentosa
- Retinal aplasia
- Total detachment of retina
- Ophthalmic artery occlusion
- Advanced siderosis.

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MACULAR HOLE

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INTRODUCTION

A macular hole (MH) is an anatomic discontinuity of the neurosensory retina that develops in the center of the macula or fovea. Idiopathic macular hole is the most common type seen in clinical practice. Typically, the patient presents with metamorphopsia and decreased visual acuity. In examinations, MH can be given as a long case and needs elaborate work up. Most discussion is around full thickness idiopathic MH.

HISTORY

Epidemiology/Demography

The incidence of MH ranges between 7 and 9 eyes per 100,000 people per year.¹⁻⁴ Females are affected more than males (approximately 2:1). Most cases occur in 6th to 7th decade. However, young myopes can present in 3rd decades of life, as do patients with traumatic MH. The 5-year risk of a patient with a full-thickness macular hole (FTMH) of developing an FTMH in the fellow eye is approximately 10–15%.¹⁻⁴ Rarely, they are with simultaneous presentation.

Chief Complaints

A case of MH can present in following manners:

- Asymptomatic-early stages of MH are asymptomatic, especially if the other eye is normal. Such cases may be detected during fundus examination for other causes, most commonly cataract due to the age group affected.
- Late-stages of MH can present with significantly reduced visual acuity (VA), metamorphopsia, and loss of central vision with a central scotoma. VA is inversely correlated with the size of the MH.
- Symptoms of vitreo-macular tension (VMT) and vitreous traction—may precede or be the only presentation in early cases of MH. These symptoms include metamorphopsia (distorted VA), micropsia (a diminution of objects within the visual field), and photopsia (flashes of light).

History of Present Illness

The formation of a MH typically evolves over a period of weeks to months. However, it is frequently detected when the patient's symptoms change relatively abruptly. Thus, the onset can be subacute or acute and the visual acuity progressively deteriorates. Typically, metamorphopsia would precede significant visual loss.

History of Past Illness

Any preceding history of trauma, ocular surgery, sun or eclipse gazing or use of myopic glasses must be recorded. This will help in identifying the cause of MH. Other eye history may be pertinent in indicating interface anomalies. There may be history of diabetic retinopathy (DR), retinal vein occlusion (RVO), or radiation exposure in secondary cases. History of similar complaint in the fellow eye must be enquired, as MH is bilateral in 10–15% of the cases. Medication use that may be related to macular cystoid edema (e.g. systemic niacin, topical prostaglandin analogs) should be asked. Lastly, history of glaucoma, cataract or ARMD must be ruled out as these may coexist with MH and may account for the poor visual acuity.

Systemic History

Since most of the cases occur in 60–70 years of life coexisting systemic diseases such as Diabetes mellitus (DM), hypertension, bronchial asthma or any posture-related issues (cervical spondylitis, kypho-scoliosis) must be checked. Following MH surgery the patient may be advised certain posture for few days, hence posture-related problems must be enquired carefully.

EXAMINATION

Systemic Examination

As discussed earlier coexisting systemic diseases, due to the age factor, must be ruled out. In addition, any posture-related issues must be looked for.

Ocular Examination

Visual acuity (VA): VA measurement, especially best corrected (BCVA) is extremely important in cases of MH. A BCVA <6/60 or 20/200 is rare in MH and in presence of such low acuity other causes of loss of VA (such as ARMD, cataract or glaucoma) must be ruled out. Poor BCVA is also an indicator of poor prognoses.

Examination should cover all the aspects of the external eye and intraocular structures should be done to look for secondary causes of MH. Pupil dilation is of essence for further management.

Lens: MH surgery invariably leads to cataract formation (almost 100%) hence many surgeons prefer to perform the cataract surgery during vitrectomy itself. Presence of PSC is especially hampering during the macular surgery. In addition, cataract and MH may coexist and few cases may benefit from only cataract surgery and observation.

Posterior segment: Slit-lamp biomicroscopy is the best technique to evaluate the MH (**Fig. 1**). The MH progresses characteristically through four stages (Gass classification).¹⁻⁴ The clinical findings of these stages are described below:

Stage 1: Impending macular holes

- **Stage 1A:** Loss of the foveal depression associated with a small yellow spot (foveal pseudocyst)
- **Stage 1B:** Loss of the foveal depression associated with a small yellow ring



Fig. 1: Fundus photograph showing old macular hole of the left eye. Large diameter along with pigment changes at the base and disc pallor are noticeable

- Typically include central vision loss (with visual acuity typically measuring 20/25 to 20/60) and metamorphopsia.

Stage 2:

- Macular hole represents the progression of a foveal pseudocyst to a full thickness dehiscence
- Small opening in the inner layer (<400 µm diameter) may be either centrally or eccentrically located
- Visual acuity 20/25 to 20/80
- May have partially detached operculum.

Stage 3:

- Macular hole is a fully developed hole (>400 µm diameter), typically accompanied by a rim of thickened and slightly elevated retina.
- Visual acuity may range from 20/100 to 20/400.
- Posterior hyaloid is detached from the macula but remains attached to optic disc.
- A detached operculum is present on the posterior hyaloid over the hole and is visible clinically or by means of optical coherence tomography.
- A cuff of subretinal fluid may be detected along with intraretinal edema and cysts.
- Drusen-like or yellow deposits may be occasionally seen in the base of the hole. These deposits represent macrophage activity at the level of the retinal pigment epithelium, suggesting chronicity of disease. These typically have poor outcomes.
- A rim of retinal pigment epithelium hyper/hypopigmentation is often present at the junction between edematous or detached retina and normal-appearing attached retina in long-standing cases.
- Epiretinal membranes may be present.

Stage 4

- A full-thickness hole with a diameter usually larger than stage 3 (>400 µm in diameter).
- A complete posterior vitreous detachment with a Weiss ring.
- A cuff of subretinal fluid, intraretinal edema, and cystoid changes are usually present.
- Drusen-like deposits may be occasionally seen in the base of the hole.
- Epiretinal membranes are more frequent.
- Visual acuity is more profoundly decreased to 20/100 to 20/400.

Following macular examination, periphery must be examined for presence or squeal of anomalous PVD. These patients commonly have VR problems as pathogenesis revolves around anomalous vitreous traction. In addition, peripheral lesions would need attention during the surgery, as these patients are especially prone to peripheral iatrogenic breaks as well. Signs of trauma or other secondary causes may also be picked up.

Traumatic hole: Apart from other history and signs of trauma, these holes typically have irregular/ragged borders secondary to contusion necroses, irregular margins and shape, larger (usually $>1000\text{ }\mu\text{m}$) with underlying pigmentary changes, and PVD may be absent. Surrounding retina may appear atrophic.

Diagnostic Tests (Help in Differentiating Lamellar Holes)

Watzke-Allen Test

This test is performed at the slit-lamp biomicroscope by using a fundus/macular lens and placing a narrow vertical slit beam through the center of macula. In a FTMH a positive test is noted, that is the patient detects a break in the bar of light.

The Laser Aiming-beam Test

This is similar to Watzke-Allen test. It is performed similarly using a macular/fundal lens and placing a $50\text{-}\mu\text{m}$ laser (Helium Neon) aiming beam through the center of macula. In presence of FTMH, a positive test is observed when the patient cannot detect the aiming beam within the hole area but is able to detect it in surrounding intact tissue. This test is possibly *more sensitive* and *more specific* for FTMH.

Amsler Charting

It is useful in early stages of holes to document clinical progression also to document metamorphopsia.

DIFFERENTIAL DIAGNOSIS

Pseudomacular Holes

Pseudomacular holes associated with epiretinal membranes can be differentiated by the presence

of retinal vascular tortuosity and compression and absence of rim of subretinal fluid. Watzke-Allen test and red beam tests are negative in pseudomacular hole.

Lamellar Macular Holes

These are sharply circumscribed, partial-thickness defects of the macula usually seen following chronic cystoid macular edema or an aborted FTMH. In contrast, in FTMH a "well" is noted depicting boundaries of the hole. A flat, reddish hue-type lesion with intact outer retinal tissue characterizes a lamellar macular holes (LMH). Unlike true FTMH, they do not have subretinal fluid, drusen-like yellowish deposits in the base of the hole or operculum. Watzke-Allen and laser aiming beam tests are negative. LMH do not progress to full-thickness lesions.

Other lesions that may confuse with MH includes following:

- Vitreomacular traction syndrome
- Foveal drusen
- Choroidal neovascular membrane
- Solar retinopathy
- Central serous chorioretinopathy
- Macular atrophy
- Macular hemorrhage.

All these lesions can be easily differentiated, as the characteristic findings of FTMH are absent. In doubtful case, OCT often confirms the diagnosis.

INVESTIGATION

Optical Coherence Tomography

Gold standard tool for diagnosing, staging, prognosticating, planning for macular hole surgery and following up later (**Fig. 2**). Several indices have been described based on OCT that often helps in predicting the prognosis of surgery. These are described below:¹⁻⁵

- **MH minimum diameter** also known as the minimum linear dimension of MH—a smaller minimum diameter is associated with better postoperative visual acuity, irrespective of the presence/absence of a statistical significance, eyes with MHs smaller than $400\text{ }\mu\text{m}$ tended to have greater visual acuity improvement.
- The **basal hole diameter** is a linear dimension of MH at the level of the retinal pigment

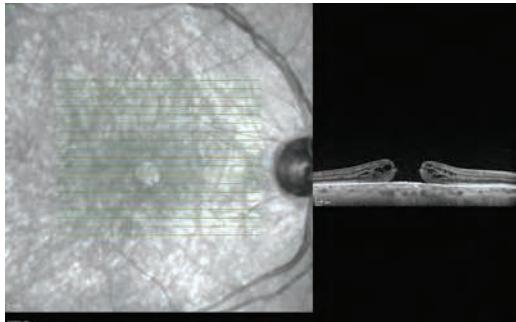


Fig. 2: EDI OCT of a right eye macular hole showing a large full thickness hole with cystoid spaces

epithelium layer. The smaller the basal hole diameter becomes, the better the postoperative visual acuity.

- **Hole form factor (HFF)** is the first calculated OCT index used as a prognostic factor. The HFF is the quotient of the summation of the left and right arm lengths divided by the basal hole diameter. The HFF is reported to be positively correlated with the postoperative visual acuity. $HFF > 0.9$ indicates better prognoses.
- **MH height:** The hole height is another preoperative OCT parameter, defined as the greatest distance between the retinal pigment epithelium layer and the vitreoretinal interface. Previous studies concluded that there is no significant relationship between the hole height and postoperative visual outcomes, with the exception of one retrospective study showing a negative correlation between the hole height and visual acuity more than 5 years after MH surgery.
- The photoreceptor *inner segment/outer segment (IS/OS) junction* line (now termed the EZ): It is recognized as a hyper-reflective band by spectral domain OCT imaging. There are studies reporting that the preoperative IS/OS junction defect length is associated with the postoperative macular sensitivity and visual acuity.
- Similarly ELM and COST have also been used as markers for visual prognostication in MH.
- **Macular Hole Index (MHI):** The MHI is defined as the ratio of the hole height to the basal hole diameter and is reported to be positively correlated to the postoperative visual acuity in

several studies. The visual outcomes is better in patients with MHI value ≥ 0.5 compared to a value of <0.5 .

- **Diameter Hole Index (DHI):** It is calculated by the ratio of minimum hole diameter and basal hole diameter. It indicates *tangential traction strength*.
- **Fractional Hole Index (THI):** It is defined as the ratio of the hole height to the minimum diameter. It is another OCT index useful as a predictor for visual outcome. It indicates anteroposterior VMT. Larger THI indicates stronger AP VMT & weaker tangential traction and hence a better outcome.

Remember Min hole Diam of $<310 \mu$ and THI >1.4 are associated with good visual outcome following MH surgery.^{1,5}

Fluorescein Angiography

Fluorescein angiography (FFA) may be a useful test in differentiating macular holes from masquerading lesions, such as CME and choroidal neovascularization (CNV). Full-thickness stage 3 holes typically produce a window defect early in the angiogram and do not expand with time. No leakage or accumulation of dye is observed as opposed to other lesions.

TREATMENT

The treatment depends upon the stage of the disease (**Table 1**).¹⁻⁵

- Stage 1 can be followed up regularly. Only about 50% of early stages progress to an FTMH. In a small number of cases, VMT resolves spontaneously without intervention (reported incidences are 10–11%).
- Stages 2, 3 and 4 require surgical intervention.
- Patients with very good visual acuity may be followed up.
- **MIVI-TRUST trials:** These have found up to 40% success with ocriplasmin for MH closure. However, results are still in initial phase of study.

Surgery for Macular Hole

Indication

Life style hampering metamorphopsia or significant visual acuity loss, usually taken as less than

Table 1 Management of macular hole

Stage	Management	Follow-up
1-A and 1-B	Observation	2–4 months with prompt return if new symptoms develop Monitoring with Amsler grid
2	Vitreoretinal surgery	Depending on the outcome of surgery and the patient's clinical course
	Vitreo-pharmacolysis	Follow-up at 1 week and 4 weeks, or with new symptoms (i.e. retinal detachment symptoms)
3 and 4	Vitreoretinal surgery	Depending on the outcome of surgery and the patient's clinical course

6/12 is considered to be the criteria for surgery by most clinicians. Cautious decisions has to be taken in one eyed patients measuring the risk benefit ratio. Stage 1 holes are usually kept under observation.

Aim

Surgical repair of macular holes include relief of all tangential traction and AP traction, to use vitreous substitute or reverse ILM flap for allowing the repair process to heal the hole.

Technique

A standard pars plana vitrectomy (PPV) with ILM peeling with gas injection is the most commonly procedure done. Three sclerotomies are created 3.5 mm from the limbus for infusion cannula, illumination pipe and vitreous cutter. Using active aspiration (150–250 mm Hg), a silicone-tipped suction cannula/vitreous cutter, using suction only is used very effectively for PVD induction—“fish strike sign” or “diving rod sign”. Once the vitreous is completely detached, vitrectomy is completed.

Internal Limiting Membrane Peeling

Several studies have reported excellent macular hole closure rates (87–96%) using internal limiting membrane (ILM) peeling techniques.¹ The ILM act as a scaffold for cellular proliferation or attachment of contractile tissue elements that may cause persistent traction. Thus, failure of the original surgery or late reopening of initially successfully closed holes may occur without removal of the ILM. However, the limitation of ILM peeling is loss of its structural role or secondary collateral nerve

fiber layer loss during removal. ILM peeling can be done using indocyanine green (ICG), trypan blue (TP), brilliant blue (BB), and triamcinolone acetonide (TA), to optimize visualization of the ILM during surgery. ICG was used initially, reports of visual field defects and retinal pigment epithelium abnormalities in the foveal center raised concerns for possible toxicity. Importantly, when the surgeon prefers ICG to stain the ILM, the lowest possible concentration with correct osmolarity of ICG should be used. Currently ICG and infracyanine green have fallen out of favor due to toxicity and stringent use conditions. Trypan blue was commonly advocated, it being a “real vital dye” staining the ERM more than an ILM. However, it required injection under air and a wait period of 5–8 mins for proper staining. Next BBG was introduced which is more active in staining ILM, though it may also stain ERMs. Steroid crystals typically attach to hyaloids/ERM, rather than actual staining. Combination of Trypan Blue and BBG have been used, and pegylated BBG is heavier than BBG and may offer better staining. Blood has also been used in combination with another dye or as sole agent for this purpose. “Negative staining” is useful in cases where both ERM and ILM are planned to be removed.

Peeling is carried out using the ILM forceps. *Pinch and peel technique* is commonly applied. Peel the ILM across the hole to relieve all traction at the edge of the hole. Few surgeons prefer peeling from arcade to arcade. Adequate sized peel is debated, for usual stage 2–3 holes, 1 disc diameter (DD) peel usually suffices. For larger holes, up to 2 DD peel may be done. Total fluid-air exchange is performed, nonexpansile concentration of gas is exchanged for air.

Postoperatively, prone position is advised for 3–5 days. There is no clear consensus regarding duration of facedown positioning to seal macular holes following vitrectomy surgery, but longer positioning may be required for holes larger than 400 µm or those with inadequate tamponade.

Post-ILM peeling OCT features: These may be early or late. Early features include dimpling of inner retina, double or split in nerve fiber layer. Late changes include thinning of retina, ganglion cell layer and nasalization of fovea.

Common Complications

- *Nuclear sclerotic cataracts:* Almost all cases (80–98%) develop cataract within few years of surgery.^{1–5} In addition, a closed macular holes may reopen after cataract surgery and cystoid macular edema after surgery further increases the risk by seven-fold. Thus, some surgeons advocate combining macular hole surgery with phacoemulsification and placement of an intraocular lens.
- *Peripheral retinal breaks:* Occurs in 3–17% of macular hole surgeries and most occur inferiorly.^{1–4}
- *Rhegmatogenous retinal detachment:* Most series report an incidence of 1–5%. The detachment is typically located inferiorly and caused by tears at the posterior vitreous base.^{1–5}
- *Visual field defects:* The reported incidence is 10–20% of patients. Most believe that this field loss is caused by either mechanical injury (such as trauma to the peripapillary retinal vasculature or nerve fiber layer) or dehydration damage to the retina as a result of air streaming from the temporally placed infusion cannula during the air–fluid exchange.
- Enlargement of the hole and late reopening of the hole occurs in 2–10% of the cases.^{1,2,5}
- *Endophthalmitis:* Endophthalmitis has been reported rarely.

Success rate: Recent reports on acute (less than 6 months) idiopathic macular holes are showing anatomic success rates from 89% to 100% and improvement in visual acuity of two or more lines in 72–95% of patients.^{1,3,5}

VIVA QUESTIONS AND ANSWERS

Q.1. What is stage 0 macular hole?

Ans. An abnormal vitreofoveal traction observed on OCT in the contralateral eye of a patient with a macular hole is associated with an elevated risk of macular hole formation in the contralateral eye. May be present in extremely high number of contralateral eyes.

Q.2. What is a lamellar macular hole?

Ans. A hole in the macular region that is not full thickness. It may be outer or inner. It may also be an early stage towards full thickness hole, or an aborted full thickness hole that may spontaneously close. Inner holes usually occur secondary to rupture following CME, like in uveitis or DR. Outer holes are seen typically after solar retinopathy, macular dystrophy, PFT etc. ERMs typically accompany inner holes, surgery is controversial and usually reserved for few cases.

Q.3. Prognosis factor for macular hole.

Ans. Following are prognostic factors for macular hole surgery:

- Better closure rates and better final visual acuities have been reported when the duration of symptoms is less than 6 months.
- Patients whose macular holes fail to seal after the first surgery usually have a less favorable visual acuity outcome when compared with primary closure.
- Hole size >400 µm is associated with poor prognosis.
- *Presenting visual acuity:* <6/60 is associated with poor prognosis.
- *OCT indices:* Smaller base diameter, smaller inner opening size, shorter minimum linear dimension and larger THI are associated with good visual outcome and hole closure.
- Traumatic holes and those related to secondary pathologies have usually poor outcomes.

Q.4. Controversies of macular hole.

Ans. *ILM peeling:* The role of internal limiting membrane (ILM) peeling its necessity,

preferred technique, and potential complications, including toxicity of adjuvant agents are far from definitively established. Removal of the ILM increase the rate of macular hole closure and perhaps improve the final visual acuity. Closure rates as high as 88–100% have been reported.^{1–3} There is controversy, however, as to whether all sizes of macular holes require ILM peeling. IMH of <400 µm in diameter may close equally with and without ILM peeling. In addition, ILM peeling can lead to reduced retinal sensitivity and microscotomas. Lastly various dyes used to facilitate ILM peeling (especially ICG) can lead to retinal toxicity.

Duration of face-down positioning: The ideal duration of positioning (short vs prolonged) is not well defined. Most vitreoretinal surgeons recommend strict face-down positioning for at least 1 week postoperatively. However prolonged positioning may be required especially in large diameter holes. Most holes close by 1 day, up to 80% by 3 days, as proved with face down positioned OCT.

Surgical adjuvants: The effect of adjuvants on MH closure rate is controversial. Most surgeons do not currently use adjuvant agents in the surgical repair of macular holes.

Role of silicone oil: Few surgeon advocates silicone oil tamponade instead of gas tamponae for a prolonged effect. However, the visual acuity and closure rates are better among eyes undergoing surgery with gas tamponade compared with silicone oil. The use of silicone oil for postoperative tamponade can be considered for patients unable to position or when prolonged positioning is required.

Combined phacovitrectomy or sequential vitrectomy and phacoemulsification (during the first year following vitrectomy): Since almost all the patient develop cataract following VR surgery in MH few surgeons advocate phacovitrectomy. However, There is no clear evidence that combined phacovitrectomy affects the long-term

results of PPV for IMH but visual recovery is quicker.

Role of vitreous substitute: The major function of vitreous substitutes (air/SF6/ C3F8/silicone oil) is to segregate the hole from fluid filled vitreous cavity, allowing the healing process to occur. Typically, short acting substitute like SF6 is preferred.

Other techniques (adjunctive or sole): These include ILM flap techniques (pedunculated/detached/multilayered, etc.), MH tapping, temporal arcuate retinectomy, fluid injection at MH base, blood in MH well and others. Such techniques are usually reserved for holes with poor chances of postoperative closure or those undergoing second surgeries.

Q.5. Types of hole closure.

Ans. As per postoperative OCT, U, V and W types of closures have been seen. U closure has the best outcomes. Closure, as proved on OCT, would typically occur by 3 days, though visual acuity increases slowly. Type 1 closure includes U and V. Type 2 closure (W types) indicates poor visual outcome, seen in advanced stages and traumatic holes.

Q.6. ILM peeling.

Ans. • Techniques for removal of the ILM involve establishing an elevated edge of the ILM and then peeling the ILM from around the macular hole. Establishing an initial edge may be accomplished with the use of a barbed microvitreoretinal blade or with Tano diamond dusted scraper or with the use of fine intraocular end-grasping forceps to 'pinch' and elevate the ILM. Peeling is generally carried out using a pinch-peel technique with fine-tipped forceps.

- The ILM peel is most often performed in a circular motion around the hole ('maculorhexis'). The ILM is usually peeled to a radius of approximately one disc diameter around the hole.

- *It work by:* Removing residual adherent vitreous cortex remnants on the ILM surface; removing associated fibro-cellular

Table 2 International Vitreomacular Traction Study Group optical coherence tomography (OCT)-based anatomic classification system for diseases of the vitreomacular interface (VMI)

<i>Anatomic state</i>	<i>Definition</i>	<i>Classification</i>		
VMA	<ul style="list-style-type: none"> Evidence of perifoveal vitreous cortex detachment from the retinal surface. Macular attachment of the vitreous cortex within a 3-mm radius of the fovea. No detectable change in foveal contour or underlying retinal tissues 	<ul style="list-style-type: none"> By size of attachment area Focal ($\leq 1500 \mu\text{m}$) Broad ($> 1500 \mu\text{m}$, parallel to RPE and may include areas of dehiscence) 	<ul style="list-style-type: none"> By presence of concurrent retinal conditions (other associated macular abnormalities, including ARMD, RVO and DME) Isolated Concurrent 	
VMT	<ul style="list-style-type: none"> Evidence of perifoveal vitreous cortex detachment from the retinal surface Macular attachment of the vitreous cortex within a 3-mm radius of the fovea Association of attachment with distortion of the foveal surface, intraretinal structural changes, and/or elevation of the fovea above the RPE, but no full-thickness interruption of all retinal layers 	<ul style="list-style-type: none"> By size of attachment area Focal ($\leq 1500 \mu\text{m}$) Broad ($> 1500 \mu\text{m}$, parallel to RPE and may include areas of dehiscence) 	<ul style="list-style-type: none"> By presence of concurrent retinal conditions Isolated Concurrent 	
FTMH	Full-thickness foveal lesion that interrupts all macular layers from the ILM to the RPE	<ul style="list-style-type: none"> By size (horizontally measured linear width across hole at narrowest point, not ILM) Small ($250 \mu\text{m}$) Medium ($> 250 \mu\text{m}$ and $400 \mu\text{m}$) Large ($> 400 \mu\text{m}$) 	<ul style="list-style-type: none"> By presence or absence of VMT 	<ul style="list-style-type: none"> By cause Primary (initiated by VMT) Secondary (directly due to associated disease or trauma known to cause macular hole in the absence of prior VMT)
LMH	<ul style="list-style-type: none"> Irregular foveal contour Defect in the inner fovea (may not have actual loss of tissue) Intraretinal splitting (schisis), typically between the outer plexiform and outer nuclear layers Maintenance of an intact photoreceptor layer 			
Macular Pseudo-hole	<ul style="list-style-type: none"> Invaginated or heaped foveal edges Concomitant ERM with central opening Steep macular contour to the central fovea with near-normal central foveal thickness No loss of retinal tissue 			

Abbreviations: ERM, epiretinal membrane; FTMH, full-thickness macular hole; ILM, internal limiting membrane; IVTS, International Vitreomacular Traction Study; LMH, lamellar macular hole; RPE, retinal pigment epithelium; VMA, vitreomacular adhesion; VMT, vitreomacular traction; ARMD, age-related macular degeneration; RVO, retinal vein occlusion; DME, diabetic macular edema

collections; removing the rigid and less compliant ILM (relative to the retina itself); and causing a retinal glial cell proliferation that may help macular hole contraction and repair.

Q.7. Macular hole formation, pathogenesis, tangential traction.

Ans. Gass hypothesised that IMHs begin with tangential traction of the prefoveal vitreous cortex, which results in a foveal dehiscence that progresses from foveolar detachment to a full-thickness IMH. However, more recent research (using ultrasound and OCT) has elucidated that IMHs are initiated during perifoveal PVD as a consequence of anteroposterior and dynamic VMT.^{1,2} The anterior tractional forces acting at the foveola firstly produce an intrafoveal split, which evolves into a foveal pseudocyst. Dehiscence of the foveal cyst creates a full-thickness defect. Complete detachment of the cyst roof is observed by the appearance of an operculum within the vitreous gel.^{1,2}

Q.8. Adjunctive therapy in macular hole repair

Ans. The role of adjunctive therapy in macular hole repair is controversial. The adjuvants

are applied to the site of the macular hole in hopes of stimulating a cellular reparative response and hole closure. Examples includes autologous serum, autologous platelet concentrate, thrombin-activated fibrinogen, thrombin, transforming growth factor beta-2 (TGF β 2), and tissue glue.

Q.9. IVMTS Classification.

Ans. See Table 2.

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RETINAL DETACHMENT

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INTRODUCTION

Retinal detachment refers to separation of the neuro-sensory layers of the retina from the underlying retinal pigment epithelium (RPE).

Retinal detachment occurs by 3 basic mechanisms and thus is classified into the following 3 main types (**Table 1**):

- Rhegmatogenous retinal detachment (RRD)** (*the most common type*): This results when a hole, tear, or break in the neuronal layer allows fluid from the vitreous to seep between and separate sensory and RPE layers (**Fig. 1**).
- Traction retinal detachment:** This results from adhesions between the vitreous gel/ fibrovascular proliferation and the retina (**Fig. 2**).

- Exudative (serous) retinal detachment:** This results from exudation of material into the subretinal space (**Fig. 3**) from retinal vessels (as in hypertension, central retinal venous occlusion, vasculitis, or uveitis, tumors, infective disorders, chronic rhinosinusitis etc.) The RRDs are usually kept as long cases and the subsequent discussion particularly revolves around it.

HISTORY

Chief Complaints

A case of RRD may present with following:

- Flashing lights
- Floaters

Table 1 Types of retinal detachment

	<i>Rhegmatogenous</i>	<i>Tractional</i>	<i>Exudative</i>
History	Photopsia, visual field defects	Diabetes, penetrating trauma, sickle cell disease	Malignant hypertension, eclampsia and renal failure, uveitis, tumor
Retinal break	Present	No primary break. May develop secondary break	No break or coincidental
Extent of detachment	Extends to ora early	Does not extend to ora.	Gravity dependant
Retinal shape	Convex	Elevated till level of traction, concave	Extremely high convex
Motility	Undulating	Taut. Peaks to traction point	Smoothly elevated bullae
Subretinal fluid	Clear	Clear. No shift	May be turbid. Shift rapidly to dependant location.
Choroidal mass	None	None	May be present
PVR	+	-	-

Abbreviation: PVR, proliferative vitreoretinopathy

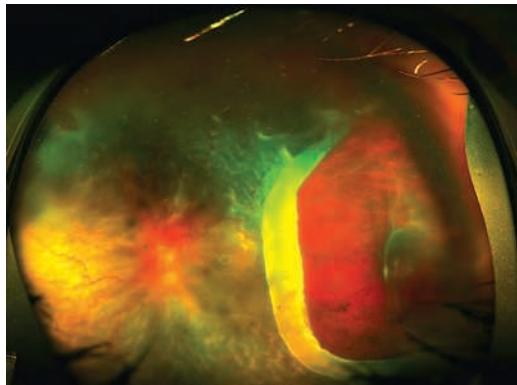


Fig. 1: Ultrawide field pseudocolor image of rhegmatogenous retinal detachment with large tear

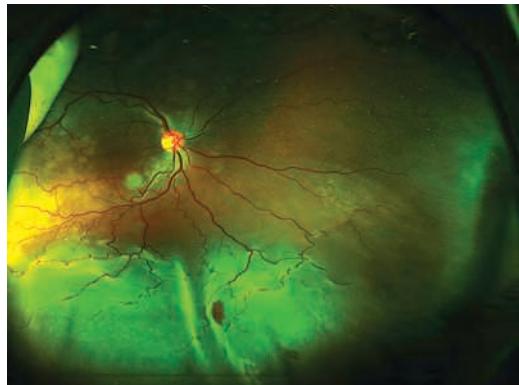


Fig. 2: Ultrawide field pseudocolor image of choroiditis with inferior exudative retinal detachment

- Visual field defect
- Visual loss.

History of Present Illness

Photopsia: It includes the sensation of a flashing light related to retinal traction. Typically described as sensation of falling stars, even when the eyes are closed or in a dark room. A shower of floaters and vision loss often accompanies it.

Floater: Floaters are a very common visual symptom in the population; thus, distinguishing their etiology requires eliciting a detailed history.

The sudden onset of large floaters in the center of the visual axis may indicate posterior vitreous detachment (PVD). The patient observes a circular floater when the vitreous detaches from its annular ring surrounding the optic nerve (Weiss ring). More serious is the description of hundreds of tiny black specks or multiple small insects floating in front of the eye, as this is suggestive of a vitreous hemorrhage, resulting from tear of a retinal blood vessel caused by a retinal tear or mechanical traction of a vitreoretinal adhesion. A few hours after the initial shower of black spots, the patient can note cobwebs that result from

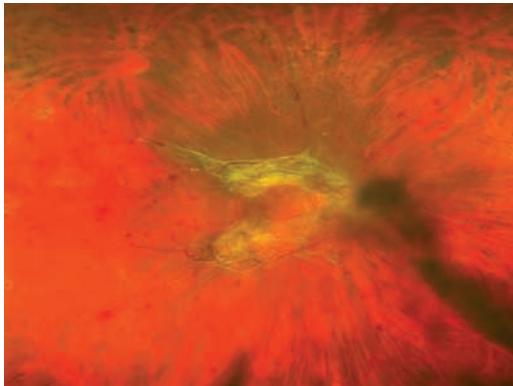


Fig. 3: Ultrawide field pseudocolor image of fractional retinal detachment

blood forming irregular clots. Generally, the new onset of floaters associated with flashing lights is highly suggestive of a retinal tear, full thickness or otherwise.

Field defect: Patient may report a black curtain or shadow in the peripheral visual field, which, over a period of few days, may spread to involve the entire visual field. Bullous (i.e. large ballooning) detachments produce dense visual field defects (i.e. blackness), and flat detachments produce relative field defects (i.e. grayness). The visual field defect can be helpful in guessing the probable quadrant of detachment.

Visual loss: If the retinal detachment (RD) involves the central visual area or the macula, the complaint is sudden onset painless visual loss. Patient may describe this as cloudy vision. The intensity of the same depends on height and duration of the macular detachment.

History of Past Illness

For RRD, one should inquire regarding family history of retinal disorders or degenerations, myopia or prior retinal therapies. History of past intraocular surgeries should always be identified in detail (see further), history of trauma should be asked on leading questions, especially if suggestive by signs.

Systemic history is very essential for tractional retinal detachment (TRD) and exudative RD. One may find history of DM, hypertension,

Table 2 Disorders associated with retinal detachment

Familial vitreoretinal disorders

- Familial exudative vitreoretinopathy
- Goldmann-Favre vitreoretinal degeneration
- Familial retinal dialysis
- Stickler syndrome (types I and II)
- Knobloch syndrome
- Enhanced S-cone syndrome
- Autosomal dominant vitreoretinochoroidopathy
- Wagner disease
- Snowflake vitreoretinal degeneration

Hereditary systemic disorders

- Marfan syndrome
- Homocystinuria
- Ehler-Danlos syndrome
- Sickling hemoglobinopathies

Other causes of RD

- Infections
- Inflammatory conditions
- Toxoplasma
- Toxocara
- Pars planitis
- ROP

Abbreviations: RD, retinal detachment; ROP, retinopathy of prematurity

tuberculosis, tumors and other syndromes (**Table 2**) as applicable in the case.

Past Surgical History

Following points should be noted:

- History of vitreous loss during cataract surgery.
- Previous laser capsulotomy.
- Intraocular foreign body removal.

Family History

It may be helpful in certain cases of familial RD, where retinal degenerations are hereditary. Such cases may also be syndromic, e.g. Stickler's, Marfan's, Wagner's etc. (**Table 2**).

CLINICAL EXAMINATION

Visual acuity: Check visual acuity at near and distance, correcting for refractive error should be noted. Always look for myopia in the fellow eye.

External examination: For signs of trauma (see chapter on traumatic RD).

Anterior segment: Look for signs of trauma, stability of lens barrier/status, and media clarity etc. Uveitis, neovascularization of the iris (NVI) may be seen in TRD/exudative RD.

Pupil Reaction: A fixed dilated pupil may indicate previous trauma; a positive Marcus-Gunn pupil can occur with any disturbance of the afferent pupillomotor pathway, including retinal detachment. Relative afferent pupillary defect (RAPD) is more likely to be seen clinically if the RD is bullous, >2 quadrants and especially if the macula is off.

Intraocular pressure: A relative hypotony of >4–5 mm Hg less than the fellow eye is common. If intraocular pressure (IOP) is extremely low, choroidal detachment may be present. It may be raised in Schwartz-Matsuo syndrome in which RRD is associated with a mild anterior uveitis and due to blockage of the angles by parts of photoreceptors. This is also seen due to retinal dialysis due to prior blunt trauma in a young man.

Vitreous: Look for signs of pigment or tobacco dust (i.e. Shaffer sign), which is suggestive for retinal tears in 70% of cases with no previous eye disease or surgery, hence a sign of RRD. Other findings that must be looked for includes VH in TRD, RL cells in exudative RD and vitreous degeneration in RRD.

Fundus examination: Indirect ophthalmoscopy is the definitive means of diagnosing retinal detachment. Direct funduscopy may detect vitreous hemorrhage and large detachment of the posterior pole, but it is inadequate for complete examination because of the lower illumination, lack of stereopsis, and limited view of the peripheral retina. However, following IO, either 90 D assisted biomicroscopy or direct fundoscopy must be done to assess the macular status. All the findings must be recorded in a modified Amsler-Dubois chart (**Fig. 4**).

Obvious detachment is observed as marked elevation of the retina, which appears gray due to loss of transparency with dark blood vessels that may lie in folds. The detached retina may undulate and appear out of focus. Shallow detachments are much more difficult to detect; thus, comparing the suspected area with an adjacent normal quadrant is helpful to detect any change in retinal

transparency. A pigmented or nonpigmented line may demarcate the limit of a detachment.

Specifically for RRD:

- Identify the extent of RD, identify fresh or old, identify location, types-numbers of retinal breaks, grade of PVR, macular status, presence of risk factors. See viva questions for detailed discussion.
- For exudative RD and TRD, see the differentiating features **Table 1**.
- Remember the triad of cardinal signs: RAPD, gray reflex and hypotony for presumptive diagnosis of RRD.
- A thorough fellow eye examination must be done for risk factors of RD, or for signs of causative etiology of TRD and exudative RD.

DIFFERENTIAL DIAGNOSIS

- Posterior uveitis/scleritis
- Posterior vitreous detachment
- Vitreous Hemorrhage
- Vitreous syneresis
- Thick hyaloid
- Vitreous membranes
- Retinoschisis
- Retinal cyst
- Sub retinal exudates
- Other differentials of TRD/Exudation
- Retinal mass
- CD.

INVESTIGATION

- **USG B-SCAN:** In presence of media haze USG helps in differentiating the type of membrane, rule out IOFB, sub retinal mass, CD etc.
- Systemic investigations as needed
- Other eye investigations may depend depending on complete diagnoses

MANAGEMENT

The management for RRD is usually surgical. In certain poor prognoses cases, surgery may be deferred, while in certain other like subclinical RD medical management may be opted for. Broadly for RRD, the surgical options include: Vitrectomy, scleral buckling and pneumatic retinopexy (**Table 3**). See viva questions as to how to choose

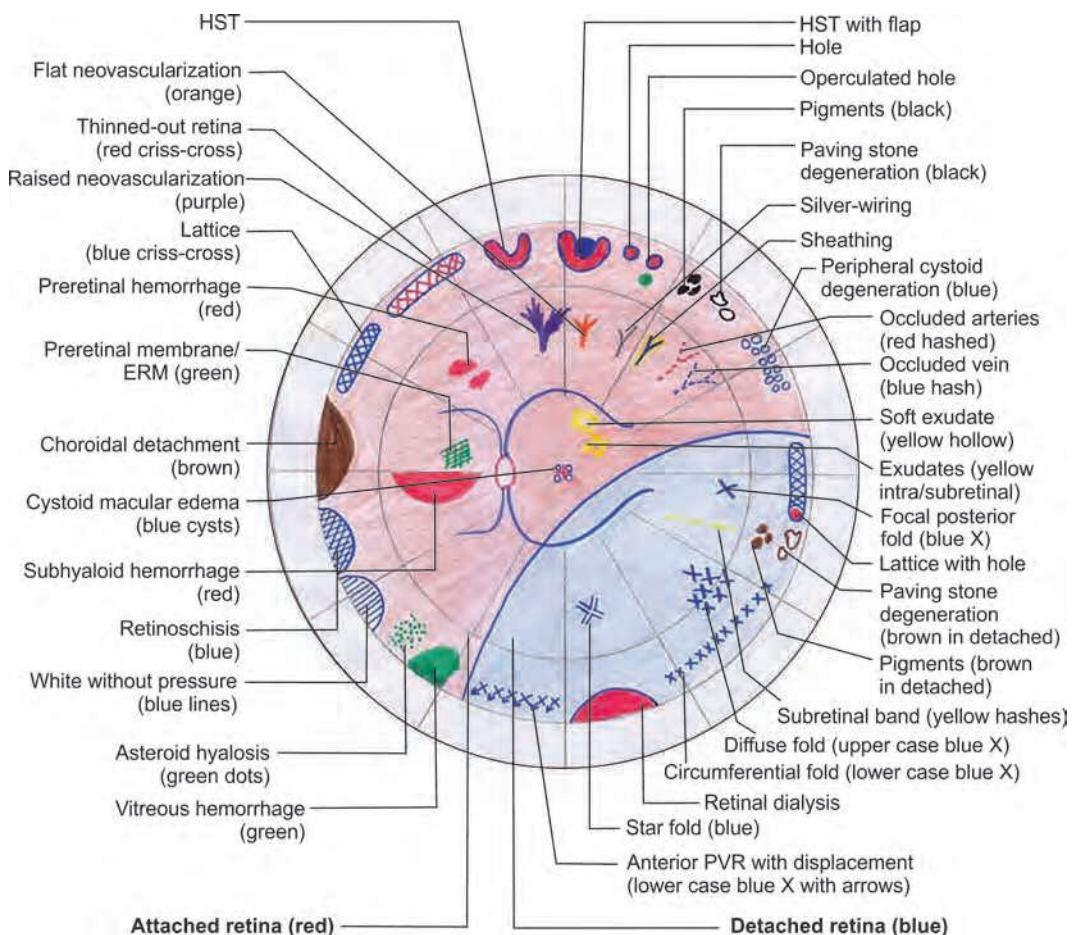


Fig. 4: Modified Amsler-Dubois retinal detachment chart with color coding

for best plan. In all cases, fellow eye treatment must be considered as optimum.

The management for TRD may be observation or vitrectomy depending on macular status. In all cases, efforts should be made for identification of the cause of TRD. For exudative RD, either observation or management with steroids is done. Like TRD, efforts should be made to discern the cause and initiate treatment accordingly. See relevant chapters for further discussion.

VIVA QUESTIONS

Q.1. What keeps the retina attached?

Ans. Embryologically, RPE and the neurosensory retina arise from different neuroectodermal

layers, hence the potential space. Normally, the hydrostatic pressure of the fluid dynamics, mechanical vitreous pressure and glycoprotein matrix between these layers keeps the retina in position.

Q.2. How to identify Ora serrata on examination?

Ans. Ora is the anterior most limit of the retina. Dentate process, oral bays, meridional folds, oral bays are present. The choroid also ends there with beginning of the pars plana.

Q.3. Define vitreous base.

Ans. This is a 3–4 mm wide zone of condensed and firmly adherent vitreous cortex

Table 3 Surgery for retinal detachment

	Scleral buckling	VR surgery	Pneumatic retinopexy
Indications	<ul style="list-style-type: none"> • RRD (PVR less than C1) • Inferior retinal breaks • Retinal dialysis • Pediatric RD 	<ul style="list-style-type: none"> • RD with PVR changes • RD with GRT • RD with vitreous hemorrhage • RD with intraocular FB 	<ul style="list-style-type: none"> • A detachment caused by a single break, in superior 8 clock hours • The break should not be more than 1 clock hour • Multiple breaks but in 1–2 clock hours of each other
Contra-indications	<ul style="list-style-type: none"> • Posterior breaks • Opaque media • Vaso-occlusive diseases like sickle cell anemia • PVR more than C2 	<ul style="list-style-type: none"> • Bleeding disorders • Suspected tumors like RB, melanoma 	<ul style="list-style-type: none"> • Break larger than 1 clock hour or multiple breaks in more than one clock hour • Break in inferior 4 clock hours • PVR grade C or D • Patient not able to maintain the head position • Severely uncontrolled glaucoma or recent cataract surgery • Hazy media preventing adequate visualization of retina
Complications	<ul style="list-style-type: none"> • Perforation • Rise in IOP • Extrusion • Infection • Diplopia • Anterior segment ischemia • Extrusion of explants • Epiretinal membrane (ERM) • Recurrent retinal detachment 	<ul style="list-style-type: none"> • Iatrogenic breaks • Lens trauma • Re detachment • Secondary glaucoma • PVR • Cataract progression 	<ul style="list-style-type: none"> • Incarceration of vitreous • Subconjunctival gas • New or missed breaks • PVR • Re-detachment • Persistent sub retinal fluid • Re-opening of original break • Vitreous haze • Sudden rise in IOP
Benefits	Excellent anatomic results, longevity, good visual outcomes	Visualization of the all tears/breaks, removal of opacities/synechiae, anatomic success in complicated detachments	In-office procedure, minimally invasive, reduced recovery time, better postoperative visual acuity

Abbreviations: RD, retinal detachment; RRD, rhegmatogenous retinal detachment; PVR, proliferative vitreoretinopathy; IOP, intraocular pressure; GRT, giant retinal tear; RB, retinoblastoma

straddling either side of ora. It starts around 5 mm from limbus.

Q.4. Enumerate some retinal degenerations not leading to RD.

Ans. Microcystoid (most common), paving stone, reticular, WWOP. WWOP is considered by some as an optic illusion.

Q.5. What are the normally strong adhesions of vitreous?

Ans. Fovea, vascular arcades, optic disc and vitreous base (strongest).

Q.6. What is retinal break?

Ans. Retinal break is full thickness deficiency in neural retina. Holes, Horseshoe tears

and retinal dialysis are the types. Scleral depression may be needed to identify peripheral breaks.

Q.7. Which retinal degenerations are associated with RD?

Ans. *Lattice:* It is the most important degeneration. Though it may be seen in up to 8% of the normal population, it is present in up to 50% of RD, and cause of up to 20%. It is bilateral in 50%. It can develop HSTs at posterior border or atrophic holes. Clinically it is seen as cigar shaped, pigmented or nonpigmented peripheral circumferential lesion, though it may be radial also like in Stickler syndrome. It has hyalinized criss cross-vessels, thin retina with overlying liquefied vitreous, strongly adherent on its posterior border.

Retinoschisis: This is split in retinal layers. It may be typical (split in OPL) and reticular (split in NFL layer). Reticular is seen in congenital schisis as the X linked retinoschisis syndrome. It is characterized by bicycle maculopathy, vitreous veils, pockmarks, snowflakes and is seen hypermetropes. Some children may develop RD or VH rarely. In contrast, degenerative schisis is seen elderly, in inferior temporal region and may or may not be bilateral. This develops due to coalescence of cystoids degeneration. The retinal breaks may develop in inner layer or outer layer of schisis. While inner breaks do not lead on to RD, outer layer breaks singularly, or in combination can lead on to RD and should be treated. Retinoschisis has an absolute scotoma in contrast to RD, and diagnostic differentiation is the laser uptake test in schisis.

Snailtrack degeneration: White frost like peripheral degeneration, HSTs are uncommon due to less traction. Some believe it to be lesser form of lattice.

Q.8. What are flashes due to?

Ans. The perception of flashes or photopsia is due to the production of phosphenes by pathophysiologic stimulation of retina. During PVD, as the vitreous separates from the retinal surface, the retina is disturbed

mechanically stimulating a sensation of light. Ocular migraine is a differential diagnosis.

Q.9. What is the significance of floaters?

- Ans.**
- Sudden appearance of one large floater near the visual axis is mostly due to PVD (Weiss ring)
 - Appearance of numerous curvilinear opacities within the visual field indicates vitreous degeneration
 - Floaters due to vitreous hemorrhage are characterized by numerous tiny black dots, followed by cobwebs as the blood forms clots. While single floater has low (~15%) risk of having a retinal tear, multiple floaters have higher risk (70%). PVD with VH is particularly ominous.

Q.10. Why is the intraocular pressure (IOP) decreased in RRDs?

Ans. An eye with rhegmatogenous RD typically has decreased IOP and it is due to the following factors:

- *Early transient pressure drop* may result from inflammation and reduced aqueous production. A vicious cycle sets up between CD and inflammation.
- *Prolonged hypotony* may be caused by posterior flow, presumably through a break in the RPE and even anterior PVR and CD.

Q.11. What is Schwartz-Matsuо syndrome?

Ans. RRD is typically associated with decreased IOP. Schwartz described a condition in which patient presents with unilateral intraocular pressure elevation, retinal detachment and open anterior chamber angle with 'cells' in the anterior chamber. Elevated intraocular pressure is often seen in the evening. The detachment is typically caused by a dialysis at the ora serrata or a break in the nonpigmented epithelium of the pars plana or pars plicata of the ciliary body. The elevated intraocular pressure is usually discovered incidentally at the time of diagnosis of the retinal detachment, and resolves without specific treatment when the retina is reattached.

The proposed hypothesis for raised IOP: The cells in the aqueous were infact

photoreceptor outer segments rather than inflammatory cells. These fragments are derived from the rods. The peripheral retinal break allows free communication between the subretinal space and aqueous humor. Outer segments then flow into the aqueous and obstruct the trabecular meshwork.

Q.12. Why is IOP raised in certain RD's?

- Ans.**
- Chronic low grade uveitis in RDs damage the trabecular meshwork
 - In long standing RDs, Rubeosis iridis (NVI) followed by increased IOP due to NVG.

Q.13. What is "tobacco dusting"?

- Ans.**
- Pathognomonic of RRD
 - Present in the anterior vitreous phase
 - The cells represent macrophages containing shed RPE.

Q.14. What is the incidence of retinal detachment in myopes?

- Ans.** 40% of all RDs occur in myopes. The reasons for high myopes to have RRD includes following:
- Increased stretch of the retina over the bigger eye ball
 - Incidence of lattice generation is higher
 - Incidence of PVD is higher
 - Macular hole
 - Vitreous loss during cataract surgery
 - Diffuse chorioretinal atrophy.

Q.15. What is high myopia, pathological myopia? What are the signs of myopia?

- Ans.** A refractive error greater than 6D, or axial length >26 mm are typical of high myopia.
- Pathological myopia refers to occurrence of pathological changes in a high myope, the most typical being a posterior staphyloma.
 - Other signs of myopia includes disc changes like large, pale disc, high CDR, temporal crescent, disc pit, disc tilt, disc coloboma; macular changes like MH, foveoschisis, subretinal hemorrhage, lacquer cracks, foster fuchs spots, CNVM, focal atrophy; peripheral changes like retinal degeneration, lattice, paving stone, atrophic retinal holes, WWOP,

HSTs, tessellated or tigeroid fundus, diffuse chorio retinal atrophy etc. None of these however is specific for myopia.

Q.16. Which are the systemic conditions associated with rhegmatogenous RD?

Ans. See Table 2.

Q.17. Why is configuration of SRF important?

Ans. Because SRF spreads in gravitational fashion and its shape is governed by anatomic limits (ora and optic nerve), it can be used to locate primary break. Knowledge of Lincoff's rules is imminent as these rules indicate the location of retinal break.

Q.18. What are the factors promoting SRF into the break?

- Ans.**
- Ocular movements
 - Gravity
 - Vitreous traction, at the edge of the break
 - PVD.

Q.19. What is Lincoff's rule?

Ans. SRF usually spreads in gravitational fashion and its shape is governed by anatomical limits and location of the primary retinal break. If the primary break is located superiorly, SRF first spreads inferiorly on the same side of the break and then spreads superiorly on the opposite side of the fundus.

- A shallow inferior RD in which SRF is slightly higher on the temporal side points to a primary break on that side.
- A primary break at 6 o'clock will cause inferior RD with equal fluid levels.
- In a bullous inferior RD, the primary break usually lies above the horizontal meridian.
- If a primary break is in the upper nasal quadrant, the SRF will revolve around the optic disk and then rise on the temporal side until it is level with the primary break.
- A subtotal RD with a superior wedge of attached retina points to a 1° break located in the periphery nearest its highest borders.
- When the SRF crosses the vertical midline above the primary break is near

to 12 o'clock the lower edge of the RD corresponding to the side of the break.

Q.20. What is vitreoretinal traction?

Ans. It is the force exerted on the retina by structures originating in the vitreous.

Types:

- *Dynamic:* It is induced by rapid eye movement, where there is a centripetal force towards the vitreous cavity. Responsible for retinal tears and rhegmatogenous RD.
- *Static:* Independent of ocular movements and plays an important role in pathogenesis of tractional RD and proliferative vitreoretinopathy.

It may be:

- *Tangential:* Epiretinal fibrovascular membranes
- *Anteroposterior traction:* Contraction of fibrovascular membranes
- *Bridging (trampoline) traction:* Contraction of fibrovascular membranes, which stretch from one part of the posterior retina to another or between vascular arcades, which tends to pull the 2 involved points together.

Q.21. How do you differentiate between the three types of RD?

Ans. See Table 1.

Q.22. Differentiate clinically between CD and RD

Ans.

- RD is gray, CD is brown.
- RD has undulating motions, while CD may have "jiggly" movements.
- USG shows the typical double peaked sign of a membrane arising from equator till ora.

Q.23. What are the factors governing visual function following surgical reattachment?

Ans.

- *Macular involvement:* If the macula has been involved the prognosis is poorer.
- *Duration:* Typically a macular detachment <7 days is believed to have good visual prognoses. The patient may achieve the pre-RD visual acuity. Detachment beyond 10 days usually had poor outcomes.

- Height of macular detachment.
- Age >60 years negatively affect visual restoration.

Q.24. What are the indications for segmental circumferential buckling?

Ans.

- Multiple breaks located in one or 2 quadrants and varying distance
- From ora serrata
- Anterior breaks
- Wide breaks, dialysis and giant tears.

Q.25. What are the indications for encircling buckle (360°)?

Ans.

- Break involving 3 or more quadrants
- Extensive RD without detectable breaks particularly in eyes with hazy media
- Lattice degeneration, snail track degeneration involving 3 or more quadrants
- Along with vitrectomy
- Multiple breaks
- Pseudophakia, aphakia.

Q.26. What are the steps in scleral buckling surgery?

Ans.

- Preliminary examination
- 360° peritomy
- Traction (bridle) sutures around the recti
- Inspection of sclera
- Localization and marking of the break
- Cryotherapy
- Scleral buckling
- Drainage of SRF
- Intravitreal air or BSS injection followed by reinspection
- Closure of the peritomy.

Q.27. What are the indications for subretinal fluid (SRF) drainage?

Ans.

- Difficulty in localization of retinal breaks in bullous detachments
- Long standing RD as SRF is viscous
- Bullous RD
- As part of DACE procedure
- Glaucomatous cyclitis
- Resurgeries.

Q.28. What are the methods of SRF drainage?

Ans. *Prang:* Here digital pressure is applied till central retinal artery is occluded and choroidal vasculature is blanched. Then full thickness perforation is made with

27-gauge hypodermic needle to drain SRF. Air is injected to form the globe.

Cut down: Radial sclerotomy is made beneath the area of deepest SRF. Mattress suture may be placed across the lips of the sclerotomy. Prolapsed choroidal knuckle is examined with +20D lens for large choroidal vessels. After ruling this out, light cautery is applied to knuckle to avoid bleeding and knuckle is perforated with 25-gauge hypodermic needle.

Q.29. What are the advantages of SRF drainage?

Ans. It provides immediate contact between sensory retina and RPE with flattening of the fovea. If this contact is delayed, the stickiness of RPE wears off and adequate adhesion may not occur, resulting in nonattachment of retina.

Q.30. What are the precautions taken before drainage of SRF?

Ans.

- Examine the fundus to make sure, SRF has not shifted
- Avoid vortex vein
- IOP should not be elevated (it may cause retinal incarceration).

Q.31. How to choose site for drainage?

Ans. Most dependent retinal area, horizontal median as it is generally devoid of vortex vessels, just behind muscle insertions, preferably nasal site to avoid macular complications. Superior site should be avoided for the risk of macular bleeds. Cryo sites and break sites to be avoided, draining under planned buckle area is suitable.

Q.32. How do you know that SRF drainage is completed?

Ans. By the presence of pigments.

Q.33. What are the complications of SRF drainage?

Ans.

- Choroidal hemorrhage
- Ocular hypotony
- Iatrogenic break
- Retinal incarceration
- Vitreous prolapse
- Damage to long posterior ciliary arteries and nerves
- Endophthalmitis

- Sub retinal bleed. Just after drainage, IO must be done to rule this out. If present, immediate build of IOP with head tilt must be done. If still bleed reaches beneath macula, gas injection with positioning or immediate vitrectomy should be considered.

Q.34. What are the indications for internal tamponade in scleral buckling?

Ans.

- Superior break
- Hypotony
- Retinal folds
- Fish mouthing
- Posterior breaks
- Sub retinal bleed
- DACE procedure.

Q.35. Who are the best candidates for pneumatic retinopexy?

Ans.

- A detachment caused by a single break, in superior 8 clock hours
- The break should not be more than 1 clock hour
- Multiple breaks but in 1-2 clock hours of each other
- Free of systemic disease (rheumatoid arthritis) (who can maintain position)
- Phakic patients
- Total PVD.

Q.36. What are the principles of pneumoretinopexy?

Ans. Intraocular gases keep the retinal break closed by the following properties:

- Mechanical closure and thus RPE pump removes excessive SRF
- Surface tension
- Buoyancy.

Q.37. What are the substances used as vitreous substitutes in RD surgery?

Ans.

- *Intraocular gases:*
 - *Nonexpansile:* Air, SF6: Air mixture, C3F8: Air mixture
 - *Expansile:* SF6, C3F8 (**Table 4**)
- SILICON OIL
- Perfluorocarbon liquids (PFCL)

Q.38. What are different surgical option for RRD and compare them?

Ans. See Table 1.

Table 4 Commonly used vitreous substitute

Gas	Expansion	Non-expansile conc.	Average duration	Volume used for PR
SF6	2x	20%	10–14 days	0.5 mL
C3F8	4x	12%	30–45 days	0.35 mL
Air	Non-expansile	–	5–7 days	0.8 mL

Q.39. What is the difference between fresh and old RD?

Ans. See Table 5.

Q.40. What is the pathogenesis of traumatic RD?

Ans. See chapter on traumatic RD.

Q.41. How to draw an RD chart?

Ans. See Figure 1.

Q.42. What are disadvantages of silicone oil?

Ans. The major disadvantage is need for a second surgery for removal. Complications include emulsification of oil causing media opacification, glaucoma, corneal edema, BSK, cataract amongst others. It has been noted that aphakic patients do not do well with long-term silicone oil. The silicone oil study suggested use of oil in children and other patients non-compliant to positioning and in eyes with large breaks and hypotony. Otherwise, results with C3F8 were comparable.

Q.43. What is PVR?

Ans. *Proliferative vitreoretinopathy:* This is de-differentiation followed by proliferation, migration and then fibrotic metaplasia of progenitor cells like RPE cell, glial cells or muller cells. The most common theory states that RPE cells exposed to vitreous as in an open break are responsible for the same. They migrate to form epiretinal membranes and sub retinal bands. RD is not a prerequisite of PVR and it may form in attached retinas as well.

Q.44. What are classification systems for PVR?

Ans. Three important classification systems include retina society classification, silicone oil study classification and then the updated retina society classification system. See Tables 6 to 9.

Table 5 Features of fresh and old RD

Fresh RD	Old RD
<ul style="list-style-type: none"> Loss of choroidal pattern <i>Retina:</i> Convex configuration, corrugations Fluid extending up to ora serrata Slightly opaque with dark blood vessels Moves freely with eye movements 	<ul style="list-style-type: none"> Demarcation lines Immobile retina Very thin atrophic retina Secondary intra-retinal cysts Tobacco dust Advanced PVR

Abbreviations: PVR, proliferative vitreoretinopathy; RD, retinal detachment

Table 6 Retinal society proliferative vitreoretinopathy classification

Grade (Stage)	Characteristics
A	Vitreous haze, vitreous pigment clumps
B	Wrinkling of the inner retinal surface, rolled edge of retinal break, retinal stiffness, vessel tortuosity
C	Full-thickness retinal folds in
C-1	One quadrant
C-2	Two quadrants
C-3	Three quadrants
D	Fixed retinal folds in four quadrants
D-1	Wide funnel shape
D-2	Narrow funnel shape (anterior end of funnel visible by indirect ophthalmoscopy)
D-3	Closed funnel (optic nerve not visible)

Q.45. How can PVR be managed?

Ans. Medical management for prevention includes use of steroids, antineoplastic drugs like daunorubicin, use of heparin and other drugs like tetracyclines. These have not proven to be beneficial.

Table 7 Silicone study classification system to proliferative vitreoretinopathy	
<i>Grade</i>	<i>Features</i>
A	Vitreous haze, vitreous pigment clumps
B	Inner retinal wrinkling, rolled edge of retinal breaks
CP	
P1: 1 quadrant (1–3 clock hours)	Starfolds and/or diffuse contraction in posterior retinal and/or subretinal membrane in posterior retina
P2: 2 quadrants (4–6 clock hours)	
P3: 3 quadrants (7–9 clock hours)	
P4: 4 quadrants (10–12 clock hours)	
CA	Circumferential and/or perpendicular and/or anterior traction in anterior retina
A1: 1 quadrant (1–3 clock hours)	
A2: 2 quadrants (4–6 clock hours)	
A3: 3 quadrants (7–9 clock hours)	
A4: 4 quadrants (10–12 clock hours)	

Surgical management peeling of mature membranes, removal of sub-retinal membranes, using PFCLs and performing relaxing procedures like retinotomies and retinectomies.

Q.46. Discuss prophylactic management of RD.

Ans. Normally, HSTs should always be treated. As per theory holes, other lattice degenerations need to be treated only if there is symptomatic PVD or it is fellow eye of a patient. Patients with family history, high myopia, undergoing cataract surgery or any other predilection need to be

Table 8 Updated proliferative vitreoretinopathy grade classification by machemer	
<i>Grade</i>	<i>Features</i>
A	Vitreous haze, vitreous pigment clumps, pigment clusters on inferior retina
B	Wrinkling of inner retinal surface, retinal stiffness, vessel tortuosity, rolled and irregular edge of retinal break, decreased mobility
CP 1–12	Posterior to equator, focal, diffuse, or circumferential full-thickness folds, subretinal strands
CA 1–12	Anterior to equator, focal, diffuse, or circumferential full-thickness folds, subretinal strands, anterior displacement

Table 9 Silicone study classification of contraction type in proliferative vitreoretinopathy

<i>Type number</i>	<i>Contraction type</i>	<i>Location of PVR</i>	<i>Summary of clinical signs</i>
1	Focal	Posterior	Star fold
2	Diffuse	Posterior	Confluent irregular retinal folds in posterior retina; remainder of retina drawn posterior; optic disc may not be visible
3	Subretinal	Posterior	"Napkin ring" around disc, or "Clothesline" elevation of retina
4	Circumferential	Anterior	Irregular retinal folds in the anterior retina; series of radial folds more posteriorly; peripheral retina within vitreous base stretched inward
5	Perpendicular	Anterior	Smooth circumferential fold of retina at insertion of posterior hyaloid
6	Anterior	Anterior	Circumferential fold of retina at insertion of posterior hyaloid pulled forward; trough of peripheral retina anteriorly; ciliary processes stretched with possible hypotony; iris retracted

informed regarding the same, before opting for treatment. Methods of prophylaxis may be laser delimitation or cryotherapy.

Q.47. What is subclinical RD?

Ans. It is a break surrounded by minimal SRF. Different definitions may be found. One definition says SRF <1 DD around a break no part of which is posterior to equator. While another definition says SRF <2 DD, no part of which is >1 DD posterior to equator. Such patients can be managed by walling off the RD till ora or by laser delimitation around the SRF. Cryo may be done in selected cases.

Q.48. What are basic principles of vitrectomy for RD?

Ans. These include performing a central vitrectomy, inducing PVD and complete peripheral vitreous dissection followed by SRF drainage. This is followed by retinopexy around all retinal breaks and finally a vitreous substitute is inserted.

All membrane removal is done before fluid air exchange and SRF drainage.

Q.49. What are causes of pediatric RD?

Ans. Trauma, ROP, FEVR, hereditary syndromes, high myopia, coloboma, coats disease, IOFB, previous surgery etc.

Q.50. What are causes of failed surgery?

Ans. Major causes include missed/new retinal breaks and PVR. Additionally in buckling optimum break buckle relationship and in vitrectomy optimum tamponade and positioning is required. Poor drainage and poor retinopexy are other causes of failure or relapses.

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AGE-RELATED MACULAR DEGENERATION

Shipra Singhi, Raghav Ravani, Brijesh Takkar

INTRODUCTION

Age related macular degeneration (ARMD or AMD), a degenerative disease of persons above the age of 50 years that is characterized by the following abnormalities in the macula:¹

- Presence of at least intermediate-size drusen (63 µm or larger in diameter)
- Retinal pigment epithelium (RPE) abnormalities such as hypopigmentation or hyperpigmentation
- Reticular pseudodrusen
- *Presence of any of the following features:* Geographic atrophy of the RPE, choroidal neovascularization (exudative, wet), polypoidal choroidal vasculopathy, or retinal angiomatic proliferation.

Visual acuity is not a factor in the disease definition or classification scheme. In postgraduate exam, it can be given as a long case.

HISTORY

Chief Complaint

ARMD can present with

- Gradual painless loss of vision in eye (dry ARMD)
- Sudden loss of vision (wet ARMD)
- Shadows, distorted vision, difficulty for discerning colors, decreased contrast, slow recovery of visual function after exposure to bright light, and slow reading may accompany the loss of vision.
- Central scotomas—shadows or missing areas of vision may be present (positive scotoma).

History of Present Illness

Those with non-exudative macular degeneration may be asymptomatic or notice a gradual loss of central vision, whereas those with exudative

macular degeneration often notice a rapid onset of vision loss.

History of Past Illness

History of previous anti VEGF injections, laser, PDT, low vision aid may be there. AMD is multi-factorial in etiology, and is thought to involve a complex interaction between polygenic, lifestyle and environmental factors. The various risk factors should be identified on history and includes following:

- Age is the major risk factor.
- *Race:* Late AMD is more common in white individuals than those of other races.
- *Heredity:* Family history is important; the risk of AMD is up to three times as high if a first-degree relative has the disease.
- Variants in many genes have been implicated in AMD risk and protection such as the complement factor H gene *CFH*, which helps to protect cells from complement-mediated damage and the *ARMS2* gene on chromosome 10. Genes related to lipid metabolism are also thought to be important.
- Smoking roughly doubles the risk of AMD.
- Hypertension and other cardiovascular risk factors.
- *Dietary factors:* High fat intake and obesity may promote.
- Aspirin may increase the risk of neovascular AMD. Though the evidence is limited, if an individual at high risk requires an antiplatelet agent it may be sensible to consider an alternative to aspirin.
- *Other factors:* Such as cataract surgery, blue iris color, high sunlight exposure and female gender are suspected, but their influence remains less certain.

Family History

Family history may be there.

Past Surgical History

Rule out any past intravitreal surgery.

EXAMINATION

General examination/specific systemic examination should be carried out to rule out any systemic risk factors as described above.

Ocular Examination

Eyebrow: Brow-ptosis may occur due to aging.

Eyeball: Generally normal.

Lid: Senile ptosis, dermatochalasis may be present (due to aging).

Conjunctiva: Generally normal.

Cornea: Arcus senilis may be present (due to aging).

Sclera: Usually normal.

Anterior chamber: Usually normal.

Iris: Increased risk of AMD in people with blue or light iris color compared with those with darker iris pigmentation.

Pupil: Usually normal.

IOP: Usually normal.

Gonioscopy: Usually normal.

Lens: Senile cataract, another comorbidity is found due to aging factor.

Anterior Vitreous: Liquefied vitreous, mostly age related and may be present.

Fundus: Stereoscopic fundus examination is the best method for examining a patient with suspected choroidal neovascularization (CNV). A fundus contact or non-contact lens in conjunction with slit lamp biomicroscopy should be utilized for the exam. For those less comfortable with the non-contact fundus macular lenses, a fundus contact lens is easiest to use. Following findings should be looked for.

Dry ARMD:

- *Drusen:* Age-related drusen are rare prior to the age of 40, but are common by the sixth decade. Numerous intermediate—large soft drusen; may become confluent. Drusen is positively associated with the size of lesions and the presence or absence of associated pigmentary abnormalities. The distribution is highly variable, and they may be confined to the fovea, may encircle it or form a band around the macular periphery (**Fig. 1**). They may also be seen in the peripheral and mid-peripheral fundus.
- *Pigment epithelial abnormalities:* Focal hyper- and/or hypopigmentation of the



Fig. 1: Clinical photograph of dry AMD. Both soft and hard drusens are present



Fig. 2: Clinical photograph of geographic atrophy

RPE is associated with a significantly higher likelihood of progression to late AMD with visual loss.

- Sharply circumscribed areas of *RPE atrophy* associated with variable loss of the retina and choriocapillaris atrophy.
- *Geographic atrophy*, enlargement of atrophic areas, within which larger choroidal vessels may become visible and pre-existing drusen disappear (**Figs 2 and 3**). Visual acuity may be severely impaired if the fovea is involved. Rarely, CNV may develop in an area of GA.
- *Dystrophic calcification* may develop in all types of drusen.
- *Drusenoid RPE detachment* may occur. Drusenoid PED develops from confluent large soft drusen, and is often bilateral. Shallow elevated pale areas with irregular scalloped edges.

High-risk characteristics of drusen for development of CNV include: Soft type, large size, greater than five in number, confluent, and presence of RPE stippling, family history of wet AMD or other eye wet AMD. These risk factors have been used by the AREDS to formulate a 5 year risk of developing wet AMD.

Wet ARMD Neovascular

CNV: It can be occult or classic CNV (see **Table 1**).

- It appears as a gray—green or pinkish-yellow lesion. Associated medium-large drusen are a typical finding in the same or fellow eye.

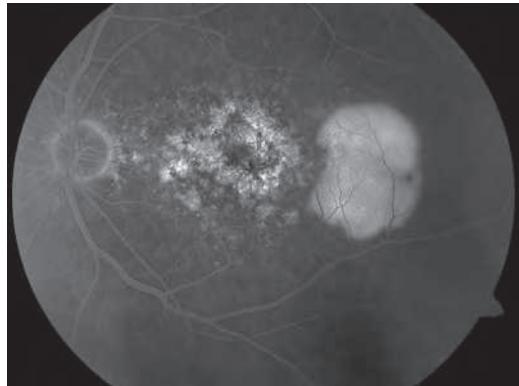


Fig. 3: FFA of geographic atrophy with large temporal PED

- Signs of CNV include subretinal fluid, hard exudates, subretinal hemorrhage or intraretinal hemorrhage, pigmented subretinal lesions, and subRPE fluid.
- Localized subretinal fluid, sometimes with cystoid macular edema may be present.
- Intra- and subretinal lipid deposition, sometimes extensive.
- Hemorrhage is common, e.g. subretinal, pre-retinal/retrohyaloid, or vitreous (breakthrough bleed can occur in to vitreous).
- Serous and/or hemorrhagic detachment of the sensory retina or RPE may occur.
- *Serous PED:* An orange dome-shaped elevation with sharply delineated edges, often with a paler margin of subretinal fluid. Multiple lesions may occur. An associated pigment

Table 1 FFA and ICG findings in ARMD

<i>Clinical condition</i>	<i>FFA</i>	<i>ICG</i>
Classic CNV	Well demarcated boundaries, discerned during transit, late leakage often obscuring boundaries	Similar to FFA but less well delineated. ICGA demonstrates CNV as a focal hyperfluorescent "hot spot" or "plaque"
Occult CNV: Fibrovascular PED (FVPED)	<i>Stippled hyperfluorescence</i> Irregular elevation of RPE, Boundaries may or may not be well demarcated, Persistent staining or leakage of fluorescein at 10 minutes	<i>Stippled hyperfluorescence</i>
Serous PED	A well demarcated oval area of hyperfluorescent pooling that increases in intensity but not in area with time; an indentation (notch) may signify CNV	An oval hypofluorescent area with a surrounding hyperfluorescent ring
Drusenoid PED	Early diffuse hypofluorescence with patchy relatively faint early hyperfluorescence, progressing to moderate irregular late staining	Hypofluorescence predominates
Hemorrhagic PED	Dense masking of background fluorescence, but overlying vessels are visible	Similar to ICG
Basal laminar drusen	Hyperfluorescence early and give an appearance of "starry night"	
Hard exudates	Window defects with early hyperfluorescence and fading of fluorescence in late frames	
Soft exudates	Early hypofluorescence or hyperfluorescence with no late leakage	
RPE tear/rip	The fluorescein angiogram shows blocked fluorescence in the area of scrolled RPE and hyperfluorescence in the area without RPE	
Idiopathic polypoidal choroidopathy (IPC)	Hyperfluorescent dilated complexes of choroidal vessels (branching vascular networks) that leak in the later phases of the angiograms. These dilated complexes look like polyps or grapes	Hyperfluorescent nodules and a network of large choroidal vessels with surrounding hypofluorescence appear in the early phase. The polyp-like swellings rapidly begin to leak. The previously darker surrounding region becomes hyperfluorescent by the late phase
Geographical atrophy	Autofluorescent hyperfluorescent on angiography due to transmission defect and staining	
RAP	FFA is usually similar to occult or minimally classic CNV, but may show focal intraretinal hyperfluorescence	ICGA is diagnostic in most cases, showing a hot spot in mid and/or late frames, and frequently a perfusing retinal arteriole and draining venule ('hairpin loop' when linked)

Abbreviations: ARMD, age-related macular degeneration; ICG, indocyanine green; PED, pigment epithelial detachment; CNV, choroidal neovascularization; IGGA, indocyanine green angiography; FFA, fundus fluorescein angiograms

band may indicate chronicity. Associated blood, lipid exudation, chorioretinal folds or irregular subretinal fluid may indicate underlying CNV.

- **Fibrovascular PED** is much more irregular in outline and elevation than serous PED. This is regarded as a form of wet AMD and should not be confused with serous/drusenoid PEDs.
- **Hemorrhagic PED**: Sub RPE or subretinal blood is found (**Fig. 4**).
- Fibrovascular disciform scar.
- **Retinal pigment epithelial tear/rip**: An RPE tear may occur at the junction of attached and detached RPE. Tears may occur spontaneously, following laser (including PDT), or after intravitreal injection. Older patients and large irregular PEDs associated with CNV are at higher risk. A crescent-shaped pale area of RPE dehiscence is seen, next to a darker area corresponding to the retracted and folded flap. An RPE tear is readily identifiable as a sharply-demarcated area of bare choroid with a straight, linear edge. This straight, linear edge corresponds to the location of the associated retracted, scrolled RPE.
- **Retinal angiomatic proliferation (RAP)**: It is an atypical form of neovascular AMD. The presence of small central macular hemorrhages, sometimes punctiform, associated with edema in an eye with soft drusen, is highly suggestive of RAP in its initial stages. The following lesions suggest RAP in AMD:
 - Small multiple hemorrhages, pre, intra or subretinal, normally not observed in macular neurosensory detachments with choroidal neovascularization.
 - Tortuous, dilated retinal vessels, sometimes showing retino-retinal anastomoses.
 - Telangiectasias.
 - Microaneurysms.
 - Sudden disappearance of a retinal vessel that appears to have moved deeper.
 - Hard exudates around the retinal lesion.

Earlier CNV was classified into Type 1—sub RPE, Type 2—sub-retinal with sub RPE. RAP now has been labelled as type 3 CNV.

Idiopathic polypoidal choroidopathy (IPC): This is another atypical form of neovascular AMD in



Fig. 4: Clinical photograph of wet AMD showing disciform scar with subretinal bleed

which highly exudative lesions with steep walled hemorrhagic pigment epithelial detachments are seen most typically adjacent to the optic disc, but can occur anywhere within the macula and even outside the macula.

DIFFERENTIAL DIAGNOSIS

Non-exudative macular lesions mimicking AMD: A number of conditions feature lesions similar to age-related drusen

- **Doyne honeycomb retinal dystrophy** (malattia leventinese, autosomal dominant radial drusen) is an uncommon condition in which fairly characteristic drusen appear during the second or third decades.
- **Pattern dystrophy (PD)**: It affects the macula and can be mistaken for nonexudative AMD. The most common types of PD seen are adult vitelliform macular dystrophy (AVMD) and less commonly butterfly shaped pattern dystrophy. Differentiating AVMD from AMD can be difficult. Fundus autofluorescence imaging especially when combined with optical coherence tomography is helpful in distinguishing PD from AMD. Fluorescein angiography can show a typical '*corona sign*' in AVMD, and the branching lines seen in butterfly shaped PD are associated with a hyperfluorescence distributed in the area of the deposits, which does not show leakage throughout the phases of the angiogram.

- *Cuticular drusen*, also known as grouped early adult-onset or basal laminar drusen tend to be seen in relatively young adults. The lesions consist of small (25–75 µm) yellowish nodules that tend to cluster and increase in number with time and can progress to serous PED. FA characteristically gives a ‘stars in the sky’ appearance. The condition has been linked to a variant of the *CFH* gene.
- *Type 2 membranoproliferative glomerulonephritis* is a chronic renal disease that occurs in older children and adults. A minority of patients develop bilateral diffuse drusen-like lesions. The *CFH* gene has again been implicated.

Exudative macular lesions mimicking AMD

- Diabetic maculopathy
- High myopia
- Inflammatory CNV
- Angioid streaks, and chorio retinal inflammatory conditions such as presumed ocular histoplasmosis.

INVESTIGATIONS

- *Ultrasonography*: USG is useful in cases of media haze for fundus evaluation.
- *Fluorescein angiography (FA)*: This is central to diagnoses and management. See **Table 1** for various findings. FA is used to diagnose CNV (**Figs 5 and 6**) and to plan and monitor the

response to laser photocoagulation or PDT. Current indications include:

- Diagnosis of CNV prior to committing to anti-VEGF treatment; FA should usually be performed urgently on the basis of clinical suspicion. To detect the presence of and determine the extent, type, size, and location of CNV. If verteporfin PDT or laser photocoagulation surgery is being considered, the angiogram is also used as a guide to direct treatment.
- To detect persistent or recurrent CNV following treatment.
- To assist in determining the cause of visual loss that is not explained by the clinical examination.
- As an adjunct to diagnosis of an alternative form of neovascular AMD such as PCV and RAP.
- Localization for extrafoveal photocoagulation, or guidance for PDT.
- Monitoring response to therapy.

CNVs can be detected and categorized either as classic or occult, or a combination of the two, depending on the leakage patterns they present at various time points on the angiogram. This differentiation was imperative for laser treatments where well defined margins for treatment decision were necessary.

Classic CNVM—present as discrete, early hyperfluorescence with late leakage of dye into the overlying neurosensory retinal detachment. A lacy pattern within the CNVM

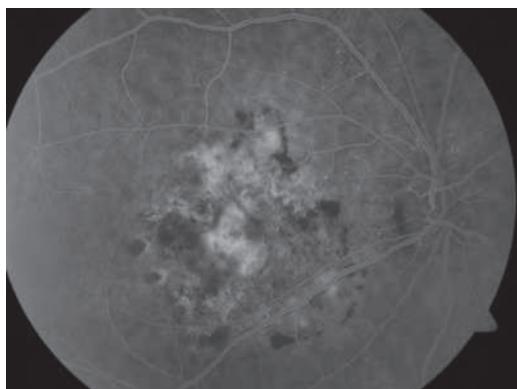


Fig. 5: FFA of wet AMD with disciform scar with subretinal bleed

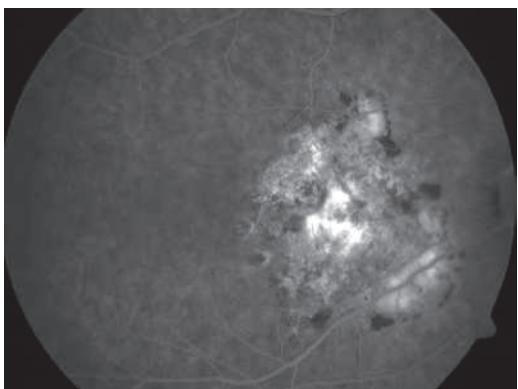


Fig. 6: Late phase FFA of wet AMD of Figure 5, confirms presence of leakage

is most often not observed in exudative AMD. Only 12% of newly diagnosed patients with exudative AMD present with classic CNV.

Occult CNVM—are categorized into 2 basic forms, late leakage of undetermined source and fibrovascular PEDs.

Late leakage of undetermined source (LLUS) manifests as regions of stippled or ill-defined leakage into an overlying neurosensory retinal detachment without a distinct source focus that can be identified on the early frames of the angiogram.

Fibrovascular PEDs present as irregular elevation of RPE, which is associated with stippled leakage into an overlying neurosensory retinal detachment in the early and late frames of the angiograms. Fibrovascular PEDs can be differentiated from serous PEDs, which show more rapid homogenous filling of the lesion in the early frames without leakage in the late frames of the angiogram. Serous PEDs typically show smooth and sharp hyperfluorescent contours.

Stereoscopic fluorescein angiography is indicated to determine the extent, type, size and location of CNV. ICG is useful when assessing patients with macular hemorrhage or suspected of having retinal angiomatous proliferative lesions, idiopathic polypoidal choroidopathy, or nonvascularized versus vascularized PEDs.

- *Optical coherence tomography (OCT):* High resolution OCT, such as spectral domain OCT, is mandatory for diagnosis and monitoring response to therapy (**Fig. 7**). With enhanced depth imaging OCT (EDI OCT) and swept source OCT choroidal evaluation has opened up new windows as has OCT angiography. The CNVM can be charted out and response to therapy measured. On OCTA, various types of CNVMS have been seen Sea fan like, spider like, medusa head pattern, poorly defined etc. for different findings see **Table 2** and **Figures 8 and 9**.
- *Amsler grid:* The Amsler grid is a useful test for detecting the early visual symptoms of

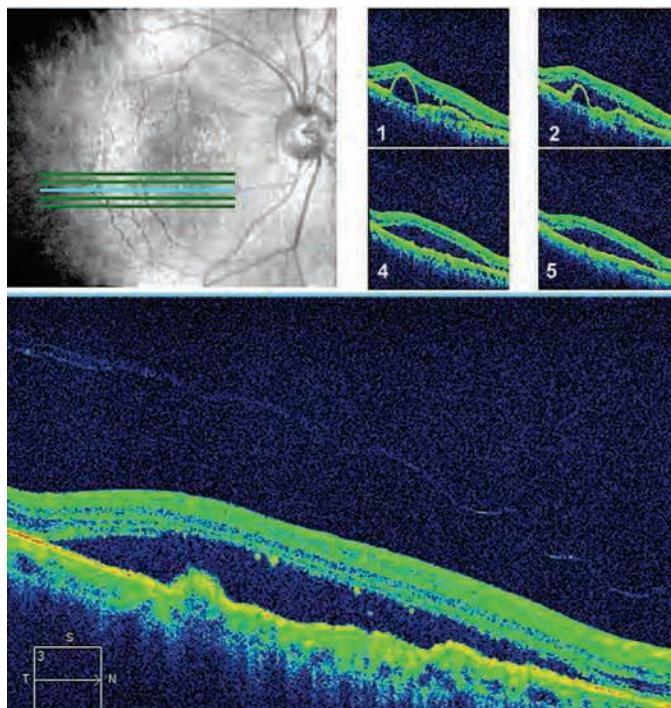


Fig. 7: OCT collage of a patient with PED, CNVM complex and subretinal fluid

Table 2 OCT in ARMD

<i>Clinical condition</i>	<i>OCT findings</i>
Classic CNV	Classic CNV presents on OCT as a fusiform thickening and disruption of RPE-BM-CC complex. Some CNV is anterior to it but in contact with it
Occult CNV	Occult is characterized by a focal, irregular poorly defined enhanced reflectivity anterior to choroid. Hyperreflectivity extends from above to below the RPE with no separation line
CME	On OCT images is seen as hyporeflective, dark spaces within retinal tissue
RPE detachments	Highly reflective tissue beneath the dome of the RPE detachment (OCT shows separation of the RPE from the Bruch membrane by an optically empty area. CNV may be indicated by a notch between the main elevation and a second small mound)
Double RPE detachments	Separated by notch rest similar to RPE detachments
Fibrovascular PED	Less uniform than a serous PED; both fluid and fibrous proliferation are shown, the latter as irregular scattered reflections
Drusenoid PED	OCT shows homogeneous hyper-reflectivity within the PED, in contrast to optically empty serous PED. There is commonly no subretinal fluid
RPE tears	Loss of the normal dome shape of the RPE layer in the PED, with hyper-reflectivity of the folded RPE
PCV	Cup-shaped RPE elevations and choroidal angiomatic lesions. Hemorrhagic and serous detachments of the retina and the RPE also can be seen
RAP	Initial signs that correspond to stage 1 (intranetinal vascularization) consist of a focal area, usually extrafoveal, with increased retinal reflectivity that are not associated with epiretinal, intraretinal, or subretinal changes or changes in the retinal thickness. When RAP reaches the subretinal space and merges with the RPE, a serous detachment of the RPE usually develops (stage 2 or CNV). In well-developed cases, there may be retinal choroidal anastomoses (stage 3 or CNV)
Drusen	<ul style="list-style-type: none"> • RPE excrescences overlying reflective material consistent with drusen • Saw-toothed configuration or bunching of the RPE • Discrete nodular drusen which actually disrupt as opposed to distort the RPE
Outer retinal tubulations	Roundish hyporeflective spaces, often around the margin of GA
Outer retinal corrugations	Basal <i>laminar</i> deposit Basal <i>linear</i> deposit

Abbreviations: ARMD, age-related macular degeneration; OCT, optical coherence tomography; PED, pigment epithelial detachment

exudative AMD in patients with high risk AMD. Each box on the grid represents one degree of visual field. Thus, the *Amsler grid tests the central 10°* of visual field beyond fixation. The patient is asked to fixate on the central black dot and to note whether surrounding lines are wavy, missing or obscured by scotomas (dark areas). If these findings are present, the patient should be instructed to seek attention urgently with his or her ophthalmologist as it is likely that the

cause is neovascular AMD. There are limits to Amsler grid testing which includes the cortical completion phenomenon, crowding phenomenon and lack of forced fixation.

- *Preferential hyperacuity perimeter (PHP):* A newly developed computer-automated, three dimensional, threshold, Amsler grid visual field test has been shown to be useful in earlier detection of AMD. The central 14° are tested in about five minutes.

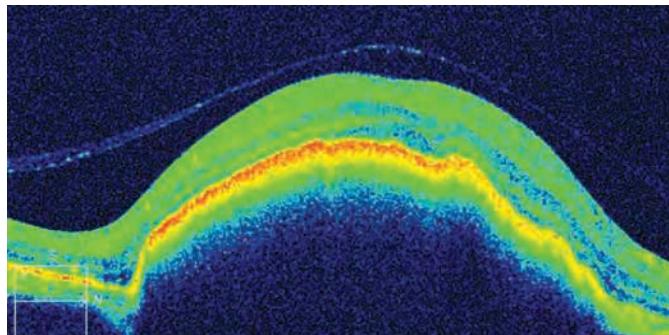


Fig. 8: OCT of a large PED. Note the notches in the PED

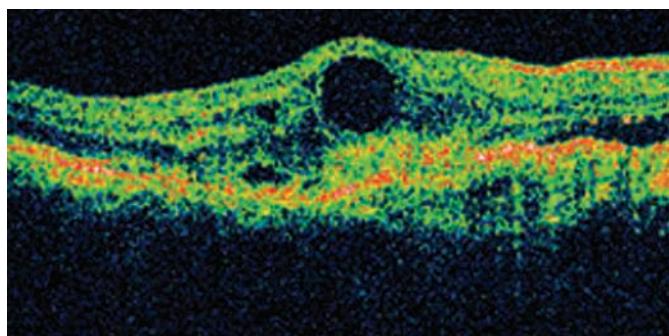


Fig. 9: A time domain OCT of a patient with disciform scar and cystoids retinal spaces

- *SLO microperimetry:* SLO microperimetry have found impaired rod photoreceptor function and photopic sensitivity respectively in areas of increased FAF in the junction zone, which underscores abnormalities associated with increased fundus autofluorescence.
- *Fundus autofluorescence:* FAF imaging in patients with GA is characterized by a decreased signal with sharp borders corresponding to the area of atrophy on conventional retinography.

CLASSIFICATION

See **Tables 3 to 5.**

Classification of CNVM

Angiographic

Terminology used to describe CNV on FA is derived from the Macular Photocoagulation Study (MPS):

- *Classic CNV* (20%) fills with dye in a well-defined 'lacy' pattern during early transit

Table 3 Clinical classification of age-related macular degeneration

Category	Definition, based on presence of lesions within two disc diameters of the fovea in either eye
No apparent aging changes	<ul style="list-style-type: none"> • No drusen • No AMD pigmentary abnormalities
Normal aging changes	<ul style="list-style-type: none"> • Only drupelets • No AMD pigmentary abnormalities
Early age-related macular degeneration (AMD)	<ul style="list-style-type: none"> • Medium drusen ($>63 \mu\text{m}$ but $<125 \mu\text{m}$) • No AMD pigmentary abnormalities
Intermediate AMD	<ul style="list-style-type: none"> • Large drusen ($>125 \mu\text{m}$) • Any AMD pigmentary abnormalities
Late AMD	Neovascular AMD and/or any geographic atrophy

subsequently leaking into the subretinal space over 1–2 minutes, with late staining of fibrous tissue. Most CNV is subfoveal, extrafoveal being defined as ≥200 µm from the center of the foveal avascular zone on FA.

- *Occult CNV* (80%) is used to describe CNV when its limits cannot be fully defined on FA. Variants are fibrovascular PED and 'late leakage of an undetermined source' (LLUS).
- *Predominantly or minimally classic* CNV is present when the classic element is greater or less than 50% of the total lesion respectively.

Topographic

The location of well-demarcated CNVs was broken into three categories:

1. *Extrafoveal*: CNV is 200 microns or more from the foveal center.

Table 4 Classification of age-related macular degeneration

Non-neovascular (DRY)	Neovascular (WET)
<ul style="list-style-type: none"> • Drusen • Focal hyperpigmentation • Nongeographic atrophy • Geographic atrophy 	<ul style="list-style-type: none"> • Choroidal neovascularization • Disciform scarring

2. *Juxtafoveal*: CNV is between 1 micron and 199 microns from the foveal center.
3. *Subfoveal*: CNV is under the foveal center.

MANAGEMENT

The management guidelines have been described in **Table 6**.

Management of Dry AMD

Most vases need observation only. Prophylaxis for prevention of complications includes following:

- *Antioxidant supplementation*: Age-related eye disease study (AREDS), now known as AREDS1 and AREDS2 has proven the efficacy of such therapy.

Indications

- *Extensive intermediate*: ($\geq 63-125 \mu\text{m}$) drusen
- Atleast one large ($\geq 125 \mu\text{m}$) drusen
- GA in one or both eyes
- Late AMD in one eye (greatest benefit in AREDS1)

AREDS 1 formulation included antioxidant vitamins—500 mg of vitamin C; 400 IU of vitamin E; 15 mg of beta-carotene; 80 mg of zinc oxide and 2 mg of cupric oxide. This formulation

Table 5 AREDS classification

Class	AREDS category	Features
No AMD	1	No or few small drusen (<63 µm in diameter). Represented the control group of (AREDS)
Early AMD	2	Combination of multiple small drusen, few intermediate drusen (63–124 µm in diameter), or mild RPE abnormalities
Intermediate AMD	3	Any of the following features: <ul style="list-style-type: none"> • Numerous intermediate drusen • At least one large druse ($\geq 125 \mu\text{m}$ in diameter) • Geographic atrophy not involving the center of the fovea
Advanced AMD	4	One or more of the following (in the absence of other causes) in one eye: <ul style="list-style-type: none"> • Geographic atrophy of the RPE involving the foveal center. • Neovascular maculopathy that includes the following: <ul style="list-style-type: none"> – CNV – Serous and/or hemorrhagic detachment of the neurosensory retina or RPE – Retinal hard exudates (a secondary phenomenon resulting from chronic intravascular leakage) – Subretinal and sub-RPE fibrovascular proliferation – Disciform scar (subretinal fibrosis)

Abbreviations: AREDS, age-related eye disease study; CNV, choroidal neovascularization

Table 6 Management of ARMD¹

<i>Major category</i>	<i>Recommended treatment</i>	<i>Diagnoses eligible for treatment</i>
Non-neovascular AMD	Observation	<ul style="list-style-type: none"> • Early AMD (AREDS category 2) • Advanced AMD with bilateral subfoveal geographic atrophy or disciform scars
	Antioxidant supplements as recommended in AREDS2 reports	<ul style="list-style-type: none"> • Intermediate AMD (AREDS category 3) • Advanced AMD in one eye (AREDS category 4)
Neovascular AMD	Aflibercept intravitreal injection 2.0 mg	Macular CNV
	Bevacizumab intravitreal injection 1.25 mg	Macular CNV
	Ranibizumab intravitreal injection 0.5 mg	Macular CNV
• Less commonly • Used treatments for neovascular AMD	PDT with verteporfin as recommended in the TAP and VIP reports	<ul style="list-style-type: none"> • Macular CNV, new or recurrent, where the classic component is >50% of the lesion and the entire lesion is ≤5400 µm in greatest linear diameter • Occult CNV may be considered for PDT with vision <20/50 or if the CNV is <4 MPS disc areas in size when the vision is >20/50 • Juxtafoveal CNV in select cases
	Laser photocoagulation as recommended in the MPS reports	<ul style="list-style-type: none"> • May be considered for extrafoveal classic CNV, new or recurrent • May be considered for juxtapapillary CNV

Abbreviations: AMD, age-related macular degeneration; AREDS, age-related eye disease study; CNV, choroidal neovascularization; MPS, macular photocoagulation study; OCT, optical coherence tomography; PDT, photodynamic therapy; TAP, treatment of age-related macular degeneration with photodynamic therapy; VIP, verteporfin in photodynamic therapy

has been shown to reduce the risk of developing advanced AMD and the associated visual loss by as much as 25%, over 5 years, in individuals with moderate to high risk of age-related macular degeneration (AREDS categories 3 and 4). These findings were accompanied by a 19% reduction in the risk of moderate vision loss (loss of three or more lines on the visual acuity chart), at 5 years.

However, high zinc doses are potentially associated with genitourinary tract problems. Beta-carotene can increase the incidence of lung cancer in current and former smokers. AREDS2 looked at adjusting the beta-carotene and zinc components, and also whether additional or alternative supplements could enhance outcomes.²

Recommended daily supplementation based on AREDS2 includes:

- Vitamin E (400 IU)
- Vitamin C (500 mg)
- Lutein (10 mg)

- Zeaxanthin (2 mg)
- Zinc (25–80 mg; the lower dose may be equally effective)
- Copper (2 mg; this may not be required with the lower zinc dose).

Risk factors modification should be addressed, e.g. smoking, ocular sun protection, cardiovascular, dietary.

An Amsler grid should be provided for home use, with advice to self-test on a regular basis, perhaps weekly, and to seek professional advice urgently in the event of any change, when imaging (e.g. OCT, FA) should be performed to rule out progression to neovascular AMD. This might be of increased importance following cataract surgery.

Provision of low vision aids for patients with significant visual loss and certification as visually impaired if available as this may facilitate access to social and financial support.

Management of Wet AMD

Anti-VEGF

Indications of anti-VEGF includes following:

- All CNV subtypes respond to anti-VEGF therapy, but benefit is only likely in the presence of active disease.
- Active disease includes fluid or hemorrhage, leakage on FA, an enlarging CNV membrane, or deteriorating vision judged likely to be due to CNV activity.
- An eye with almost any level of vision may benefit, although better VA at presentation is associated with a better visual outcome.

Anti-VEGF agents: See **Table 1** in chapter on proliferative diabetic retinopathy (PDR).

Aflibercept (Eylea) is a recombinant fusion protein that binds to VEGF-A, VEGF-B and placental growth factor (PIGF). The advantage is the maintenance regimen consists of one injection every 2 months in contrast to the monthly injections recommended with ranibizumab and bevacizumab. In addition, it is more efficacious than Lucentis due to its increased affinity to bind the receptors. The standard dose is 2 mg in 0.05 mL; an induction course of three injections is given at monthly intervals.

Ranibizumab (Lucentis): Ranibizumab is a humanized monoclonal antibody fragment developed specifically for use in the eye, though is derived from the same parent mouse antibody as bevacizumab (see next). It non-selectively binds and inhibits all isoforms of VEGF-A. The usual dose is 0.5 mg in 0.05 mL.

Bevacizumab (Avastin): In contrast to ranibizumab, bevacizumab is a complete antibody originally developed to target blood vessel growth in metastatic cancer deposits. Its use for AMD and other indications is 'off label'; it is very much cheaper than ranibizumab and aflibercept. Clinical trial suggest comparable results to ranibizumab in efficacy and safety. The dose of bevacizumab is usually 1.25 mg/0.05 mL.

Pegaptanib (Macugen): Pegaptanib sodium was the first anti-VEGF agent approved by regulatory authorities for ocular treatment; the results are similar to outcomes with PDT, and its use is now extremely limited.

Photodynamic Therapy (PDT)

Photodynamic therapy (PDT) is useful for eyes with subfoveal CNV (see **Table 6**). Verteporfin is a light-activated compound preferentially taken up by dividing cells including neovascular tissue. It binds to LDL receptors and upon reaction to light produces singlet oxygen residues. It is infused intravenously followed by the delivery of laser light of a wavelength of 689 nm to the CNV lesion as a single spot with a diameter 1000 µm larger than the greatest linear diameter of the lesion. When activated by diode laser it cause thrombosis.

Laser

Thermal argon or diode laser ablation of CNV is now rarely used, though may still be suitable for the treatment of small classic extrafoveal membranes well away from the macular center, and possibly some cases of PCV and RAP.¹

Other Therapies

Various treatment modalities have been tried with variable success. These are—Transpupillary Thermotherapy (TTT), Teletherapy (EBRT), Brachytherapy (Plaque Radiotherapy), Anecortave Acetate (an angiostatic steroid), small interfering RNA (siRNA), Vatalanib (inhibitor of all known VEGF receptor tyrosine kinases), Squalamine Lactate (an anti-angiogenic amino sterol derived from cartilage of the dogfish shark, action includes blockade of cell membrane ion transporters that regulate cell function by controlling pH and metabolism. Sphingomab (monoclonal antibody targeted against sphingosine-1-phosphate, which has been implicated in angiogenesis, scar formation, and inflammation), Volociximab (a chimeric monoclonal antibody that inhibits the functional activity of a5β1 integrin, a protein found on activated endothelial cells, and prevent angiogenesis), Designed ankyrin repeat proteins (DARPins) [genetically engineered antibody mimetic proteins that is a potent VEGF inhibitor], Sirolimus (Rapamycin), Infliximab (a monoclonal antibody that binds and neutralizes tumor necrosis factor alpha), Eculizumab (Complement Inhibitors), Pigment epithelial-derived growth factor (PEDF), Brimonidine, antioxidant eye drops, Alprostadil (Choroidal Blood Perfusion

Enhancers), Maculoplasty (overall tissue engineering attempt to reestablish the normal subretinal anatomy), Macular translocation (moving the neurosensory retina of the fovea in one eye with recent-onset subfoveal CNV to a new location before the occurrence of permanent retinal damage, may allow it to recover or to maintain its visual function over a healthier bed of RPE-Bruch's membrane-choriocapillaris complex), gene therapy, stem cells.

Management of Poor Vision

Low vision aid refers to an optical device that improves or enhances residual vision by magnifying the image of the object at the retinal level. Non-optical aids also work as LVAs as they may help in enhancing the visual performance.³

VIVA QUESTIONS

Q.1. What is the rate of progression of CNV?

- Ans.**
- Progress rapidly irrespective of its initial location and extent at a mean rate of 18 µm/day.
 - Disciform scars with fibrous tissue or geographic atrophy represent the end stages of both types of CNV.

Q.2. What is Drusen?

- Ans.** *Drusen* (singular: druse) are extracellular deposits located at the interface between the RPE and Bruch membrane. The material of which they are composed has a broad range of constituents, and is thought to be derived from immune-mediated and metabolic processes in the RPE. Their precise role in the pathogenesis of AMD is unclear, but is positively associated with size. The earliest pathological changes are the appearance of basal laminar deposits (BlamD) and basal linear deposits (BlinD). BlamD consist of membrano-granular material and foci of wide spaced collagen between the plasma membrane and basal lamina of the RPE. BlinD consist of vesicular material located in the inner collagenous zone of Bruch's membrane.

Q.3. High-risk characteristics of drusen for development of CNV.

- Ans.** High-risk characteristics of drusen for development of CNV include: soft type,

large size, greater than five in number, confluent, and presence of RPE stippling.

Q.4. High-risk characteristics for development of CNV.

- Ans.** Systemic risk factors associated with CNV include increased age, Caucasian race, smoking. Ocular risk factors associated with increased risk of CNV include large drusen, confluent drusen, hyperpigmentation and hypertension.

Q.5. Median rate of enlargement of GA?

- Ans.** GA continues to enlarge over time with a median rate of enlargement over a two-year period of 1.8 MPS disc areas. The prevalence of GA increases with age, being half as common as CNV at age 75, and more common than CNV in older age groups. GA is bilateral in more than half of the people with this condition.

Q.6. What is BIONIC EYE/ARGUS II?

- Ans.** Designed for patients who are blind due to diseases like retinitis pigmentosa or AMD. Relies on patient having a healthy optic nerve and a developed visual cortex. The prosthesis consists of—a digital camera built into a pair of glasses—a video processing microchip built into a hand held unit—a radio transmitter on the glasses—a receiver implanted above the ear—a retinal implant with electrodes on a chip behind the retina. Camera captures an image Send image to microchip convert image to electrical impulse of light and dark pixels—Send image to radiotransmitter—Transmits pulses wirelessly to the receiver sends impulses to the retinal implant by a hair thin implanted wire—The stimulated electrodes generate electrical signals that travel to the visual cortex.¹

Q.7. What is implantable miniature telescope?

- Ans.** Implantable miniature telescope is implanted into one eye only (typically the non-dominant or poorer seeing eye). It generates a 20°-24° field of vision. The FDA approved the implantable miniature telescope (IMT) in 2010 for patient 75 years and older with stable severe-to-profound vision impairment (20/160 to 20/800) caused by bilateral end-stage AMD.

Q.8. Name some low vision aids.

- Ans.** *Optical devices:* Hand held telescopes, mounted telescopes, intra-ocular LVA (IO-LVA) NEAR, spectacles—prismatic ½ eyes—bifocals, magnifiers,
Absorptive lenses: Tinted lenses, photochromatic lenses, polarization glasses, Filters—corning CPF, younger PLS—visual field enhancement devices, fresnel prisms, gottlieb field expanders, reverse telescopes, hemianopic mirrors.
Non-optical: Lighting, contrast enhancement, increasing size of object, auditory aids.
Electronic magnifiers: CCTV, large print computers.
Orientation and mobility LVA: Canes, guide dog, electronic orientation devices, GPS
Newer technology LVA: E-readers, smart phones, tablets.

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INTERMEDIATE UVEITIS

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INTRODUCTION

As per its anatomical definition, intermediate uveitis (IU) is defined as an inflammation involving the anterior vitreous (hyalitis), ciliary body (posterior part of ciliary body), and peripheral retina.¹

NOMENCLATURE

Various names were used to describe the condition including chronic cyclitis, vitritis, cyclochorioretinitis, pars planitis, intermediate uveitis, peripheral uveoretinitis, etc.¹ Recently, as per the SUN (Standardization of Uveitis Nomenclature, IUSG*) working group's guidelines,² IU refers to the subset of uveitis wherein the major site of inflammation is vitreous and there is an associated infection or systemic disease. The term, pars planitis refers to the "idiopathic" subset of intermediate uveitis occurring in absence of any associated infection or systemic disease.

Pars planitis forms the majority subset of intermediate uveitis, as high as 70–80%.

Also note that involvement of vessels in form of peripheral vascular sheathing and cystoid macular edema (CME) does not change the nomenclature or classification.

Intermediate uveitis is usually given as a long case or a short case in the exams.

HISTORY

Chief Complaint

The condition may have minimal symptoms. Unlike anterior uveitis, the symptoms are bilateral more than unilateral, and often asymmetrical. Also the disease may present with its complications like CME, vitreous membranes, glaucoma and cataract. The usual presenting complaints are:

- *Floater:* The most common (due to snow balls, membranes, vitreous opacification)
- Blurring of vision (chronic, painless—due to CME, cataract)

*International Uveitis Study Group

- Loss of vision [sudden, painless due to glaucoma, spill over uveitis, secondary rhegmatogenous retinal detachment (RD)]—rarely
- Noted during routine fundus evaluation.

History of Present Illness

- Intermediate uveitis tends to affect young individuals with a bimodal distribution, i.e. affecting two age groups, 5–15 years and 20–40 years, equally affecting males and females. Some reports from India put it as the most common subtype of uveitis in children, whereas others report it as the least common.
- Unlike anterior uveitis, it has an insidious onset.
- The most common presenting symptoms are floaters.
- Associated pain, redness, watering is usually absent or may be present in children with associated anterior uveitis. These are usually minimal when present and often seen as spill over anterior uveitis.
- Patient may have history of similar episodes in the past with remissions or may have a chronic history without remissions.
- Patient may complain of chronic worsening of vision or a sudden worsening of vision in a background of long standing history.

History of Past Illness

Past medical and surgical history must include careful history to rule out the systemic associations or etiological causes of intermediate uveitis. There may be past history of associations of intermediate uveitis as well (i.e. sarcoidosis,

tuberculosis, multiple sclerosis, etc.) Even on absence of symptoms, leading questions must be asked for commonly associated disorders as IU may be the primary presentation (**Flow chart 1**).

Family History

Intermediate uveitis though not hereditary has been seen reported in families. It is associated with HLA DR-15 and HLA DR-51 alleles. IU is seen in families with common HLA haplotypes. Also note that HLA DR-15 is associated with multiple sclerosis and thus may suggest a predisposition of it in patients with IU with HLA DR-15 positivity.

EXAMINATION

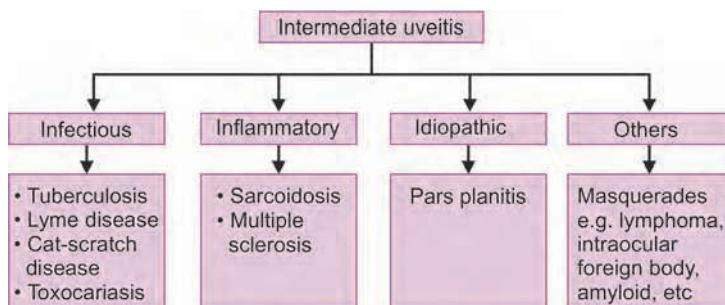
General Examination

Detailed systemic examination is warranted to know any associated conditions like sarcoidosis, tuberculosis, multiple sclerosis, signs of tick bite or Lyme disease. The following condition are associated with IU (**Flow chart 1**).

Ocular Examination

Visual acuity: The visual acuity is usually normal in early cases. Patient may have vision acuity of 6/6 with floaters being the only complains. Main cause of decreased visual acuity in IU is development of cystoid macular edema (CME). Other causes of dimness of vision include development of cataract, dense vitreous membranes/opacities, epiretinal membrane (ERM), vitreous hemorrhage from neovascularization, tractional or rhegmatogenous retinal detachment.

Flow chart 1: Flowchart depicting common causes of intermediate uveitis



Eyeball: Squint may be present, but is a consequence of complications of disease due to loss of fusion.

Lid/conjunctiva/cornea/sclera are usually within normal limits (WNL). There may be aponeurotic ptosis or in rare cases enophthalmos as a side effect of previous treatment in form of periocular steroid injections. Scleritis may be present, the disease is then called sclerouveitis. Keratic precipitates (KPs) may be present, in fact IU is characterized by KPs that may be central rather than the typically inferior Arlt's triangle KPs of anterior uveitis.

Anterior chamber: It may show variable number of spill-over anterior chamber cells/flair. These should be carefully documented as per SUN classification (**Table 1**).

Pupil: Pupil is circular as there is no or minimal anterior chamber reaction, and usually no synechiae. Pupillary reflexes are usually within normal limit, unless complicated by retinal detachment, which is rare.

Intraocular pressure (IOP): A rise in IOP may occur, especially as a complication in IU due to steroid use or secondary glaucoma. A rise in IOP in uveitis is also associated with increasing age, duration since diagnosis and active inflammation. IOP may be low in case of severe reaction and formation of cyclitic membrane.

Lens: Cataract may occur in 50–60% of cases and is one of the causes of decreased vision in IU. Posterior subcapsular cataract is the most common cataract associated, however even anterior subcapsular cataract may be found. Cataract in IU may be due to chronic inflammation or long-term

steroid treatment or glaucoma medications (esp. cholinergic agents) used in treatment of uveitis and uveitic glaucoma. Retrobulbar space should be carefully examined for cells, which is pathognomonic for present/past anterior vitreous inflammation. However, presence of these cells does not indicate active disease. Vitreous haze should be noted and graded (**Table 2**). Increasing vitreous haze is a sign of activity and decreasing vitreous haze is a sign of response.

Vitreous: Vitreous is the major site of inflammation in intermediate uveitis. Thus inflammatory cells mainly accumulate in the vitreous cavity in form of retrobulbar cells, vitreous membranes, may condense as 'snow-balls' or may settle down inferiorly over retina or pars plana as 'snow-banking' leading to variable degrees of vitreous haze. 'Snow-balls' appear as yellow-white condensations in mid-vitreous, especially inferiorly.

Table 1 Grading of anterior chamber cells as per standardization of uveitis nomenclature (SUN) workshop (2004) consensus.
The cells are counted in a dark background of an undilated pupil in a slit of 1 mm × 1 mm

Grade	Number of cells/field
0	<1 cells
0.5+	1–5 cells
1+	6–15
2+	16–25
3+	26–50
4+	>50

Table 2 NEI grading of vitreous haze as adapted by the standardization of uveitis nomenclature (SUN) working group

Grade	Description
4+	Optic nerve head not visualized
3+	Optic nerve head hazily visualized
2+	Retinal vessels visualized better. Optic nerve head hazy
1+	Vitreous cells and haze present but optic nerve head and retinal vessels clearly visualized
0.5+	Some media haze present, nerve fiber layer striations not able to be visualized. But disc and retinal vessels are seen distinctly
0	No inflammation, normal fundus view

'Snow-banking' depicts more severe inflammation. 'Snow-banking' appears like exudates over the pars plana, especially inferiorly, but may be seen all around. Scleral indentation or use of Goldmann three-mirror contact lens may be required to view peripheral retina and pars plana. Sometimes vitreous haze may be severe enough to obscure view of the fundus preventing further examination. Early posterior vitreous detachment may be seen.

Fundus: If media clarity permits, examination of retina must be done carefully in all cases of intermediate uveitis. The fundus findings in IU includes:

- Tortuosity of vessels
- Involvement of peripheral retinal vasculature in form of sheathing (e.g. periphlebitis)
- Neovascularization, which is usually peripheral near the area of snow-banking
- Peripheral vitreous traction and hole formation due to contraction of inflammatory membranes may be seen
- Retinal detachment has also been reported as a complication of intermediate uveitis
- Peripheral choroiditis may also be seen, though severe chroidal involvement indicates review of clinical diagnosis.

DIFFERENTIAL DIAGNOSIS

- Vitreous membranes
- Vitreous degeneration
- Leukemia
- Lymphoma
- Endophthalmitis
- Panuveitis
- Amyloidosis
- Old vitreous hemorrhage.

INVESTIGATION

Systemic Evaluation

As previously mentioned, many infections and systemic conditions are associated with intermediate uveitis (IU). A careful history, ocular examination and ancillary/laboratory tests should be carried out to search for the etiology or associated condition. The test may include:

- Complete blood count with differential count and erythrocyte sedimentation rate (ESR).

- Purified protein derivative skin test (PPD) (Mantoux test)
- Chest X-ray (to look for evidence of pulmonary TB or sarcoidosis)
- Serum angiotensin-converting enzyme levels
- Gallium scan
- MRI brain
- Lyme titers and western blot—if high suspicion and in endemic areas.

The list is very large and should be based on a tailored work up. Refer to **Flow chart 1**. In Indian subcontinent, TB should be ruled out in all the cases. Masquerades should be considered when ever applicable.

Ocular Investigation

- *Ultrasonography (USG) B-scan:* To be done to rule out complications like retinal detachment in cases where intense inflammation leads to severe media haze preventing fundus evaluation. It may also help to rule out conditions masquerading as intermediate uveitis like intraocular tumors.
- *Ultrasound biomicroscopy (UBM):* To demonstrate pars plana exudates when clinical examination is difficult in presence of media opacities.
- *Optical coherence tomography (OCT):* To document presence of cystoid macular edema, especially in patients with complain of dimness of central vision (**Fig 1**). It can be used as a guide to therapy. Choroidal thickness should also be monitored once treating concomitant choroiditis. Later on, epiretinal membranes (ERMs) and tractional changes can also be seen up on studying the virtual reality (VR) interface.
- *Fluorescein angiogram* shows presence of peripheral capillary non-perfusion, peripheral neovascularization, presence of retinal vasculitis and petaloid (**Fig 2**) and honeycomb leakage suggestive of cystoid macular edema (CME). Fluorescein angiography may also be helpful for follow-up after cryotherapy or laser photocoagulation treatment.
- *Ultrawide imaging* helps in documenting peripheral changes. Ultrawide field fluorescein angiography may also help in documenting peripheral CNP areas and presence of peripheral neovascularization.

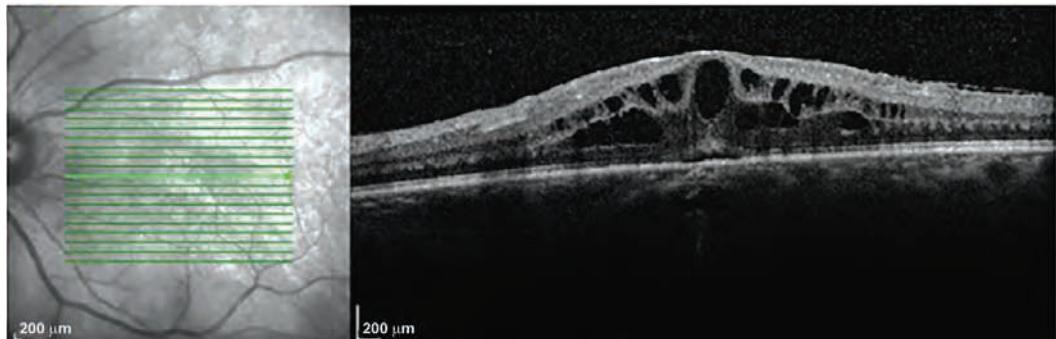


Fig 1: OCT image depicting cystoids macular edema

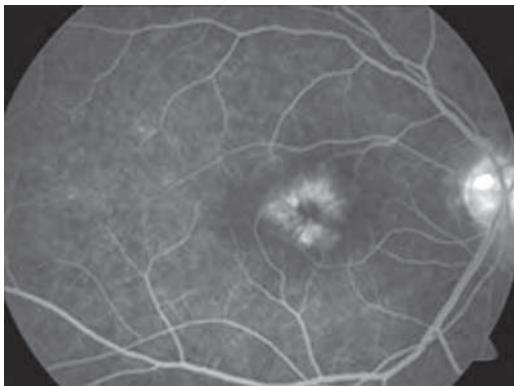


Fig 2: FA image showing macular leakage of dye in CME. Note the petaloid configuration

COMPLICATIONS

- Cataract
- Glaucoma
- Cystoid macular edema
- Epiretinal membrane
- Vitreous hemorrhage
- Retinal detachment
- Rarely, optic disc edema.

MANAGEMENT

If an etiology has been identified on investigation, treatment depends on the cause. In cases where no specific etiology has been identified, following are the management options. Mild cases without CME may be managed conservatively by observation. A four-step approach for the treatment of intermediate uveitis was proposed by Kaplan.³ It should be remembered that every case

may not need treatment. In absence of media haze (less than grade 1), in cases with only few inferior snow balls and absence of complications like CME, just meticulous frequent observations may suffice.

Following are the management options:

- *Step 1:* Infections should always be ruled out if planning for steroids. Periocular steroids may be considered as initial treatment modality especially in uniocular conditions. Sub-tenon injection is the most common route for depot corticosteroids. Other route for local therapy includes intravitreal corticosteroid injection. In case of failure of depot steroids and in bilateral cases, systemic corticosteroids could be considered. In cases with CME, periocular steroids help by maintaining a constant influx of steroids. Presence of CME should indicate an alerting sign warranting aggressive therapy as it may lead on to permanent visual loss. Throughout therapy patient should be monitored for ocular and systemic side effects of steroids, which can be debilitating at times. Dietary supplementation for calcium should also be considered.

A more recent advancement is use of sustained release steroid implants like ozurdex and retisert. These have now been approved for ocular use in noninfectious uveitis. They work well in isolated ocular disease, but complications should be monitored. The recently conducted multicenter uveitis steroid treatment (MUST) study has shown good results with flucinolone implant when compared to systemic therapy.

- **Step 2:** Peripheral retinal ablation over snowbank near pars plana region may be considered in case of nonresponse to peribulbar steroids. This may be done either using cryopexy (double-freeze thaw technique) or peripheral scatter photocoagulation, especially in cases with peripheral neovascularization. This may help decrease the risk of bleeding and regression of neovascularization. Recent studies indicate primary role of cryotherapy as a first measure also. However, this treatment may lead on to temporary worsening of disease as well.
- **Step 3:** Pars plana vitrectomy with induction of posterior vitreous detachment and peripheral laser is helpful in cases resistant to previous modalities and in whom immunosuppressive therapy may be contraindicated. This is particularly helpful in cases with decreased vision due to severe media haze with vitreous membrane, in cases with vitreous hemorrhage, in cases with nonresponding CME or cases complicated with retinal detachment/ERMs.
- **Step 4:** Systemic immunomodulatory therapy is of special benefit in bilateral disease. Chronic or frequently relapsing cases may benefit due to lesser steroid dependence. Further, volcosporin [Lux Uveitis Multicenter Investigation of a New Approach to Treatment (LUMINATE study)] is showing promise as a steroid sparing agent.

Note: The treatment plan may not necessarily follow the step wise approach and a combination of one or more modalities may be considered as per individual cases and to achieve early remission or decrease the duration of corticosteroids.

VIVA QUESTIONS

Q.1. What is the most common presenting symptom in case of intermediate uveitis?

Ans. The patients most commonly present with symptoms of floaters in a case of intermediate uveitis.

Q.2. What are the causes of vision loss in a case of intermediate uveitis?

Ans. Cystoid macular edema (CME) is the most common cause of dimness of vision. Other causes include:

- **Cataract:** Especially posterior subcapsular cataract
- **Epiretinal membrane:** May lead to distortion of vision and if severe, dimness of vision.
- Media haze due to intense vitritis leading to vitreous veils/membranes.
- **Vitreous hemorrhage:** Secondary to peripheral neovascularization.
- **Retinal detachment:** Tractional or rhegmatogenous retinal detachment.

Q.3. Other causes of ocular inflammation with 'white' eye?

Ans. Apart from intermediate uveitis, other causes include:

- Fuch's heterochromic iridocyclitis
- Juvenile rheumatoid arthritis
- Posner-Schlossman syndrome
- Kawasaki disease.

Q.4. Causes of intermediate uveitis?

Ans. • Infectious conditions

- Tuberculosis (*Mycobacterium tuberculosis*) (especially in endemic countries like India)
- Syphilis (*Treponema pallidum*)
- Toxoplasmosis (*Toxoplasma gondii*)
- Toxocariasis (*Toxocara canis*)
- Lyme's disease (*Borrelia burgdorferi*) (in endemic areas)
- Cat-scratch diseases (*Bartonella henselae*, *B. quintana*)
- Human T-lymphotropic virus type 1 (HTLV-1)

• Noninfectious conditions

- Sarcoidosis
- Multiple sclerosis
- Intraocular lymphoma

• Idiopathic/pars planitis.

Q.5. Describe Kaplan's four-step management for intermediate uveitis?

Ans. It is as described above in the text.

Q.6. Differential diagnoses of IU

Ans. *Causes of media haze:* Old vitreous haze (VH), ocular lymphoma, amyloidosis, endophthalmitis, *Candida* infections, *Propionibacterium acnes* endophthalmitis, leukemia, acute retinal necrosis (ARN), intense vitritis due to other causes such as toxoplasmosis.

Q.7. Discuss steroid implants.

Ans. See above and chapter on DME.

Q.8. What are the side effects of steroids?

Ans. *Ocular side effects:* Cataract, glaucoma, activation of viral keratitis (topical), fungal corneal ulcer, central serous chorioretinopathy.

Systemic side effects: Cushingoid state, diabetes, hypertension, osteoporosis, peptic ulcer disease, sodium and water retention, worsening of psychosis, menstrual irregularities, weight gain, thromboembolism, muscle weakness, aseptic necrosis of femoral head, pancreatitis, easy bruising, convulsions, etc.

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CHOROIDAL MELANOMA

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INTRODUCTION

Uveal melanoma is a rare form of melanoma accounting for <3% of the primary malignant melanomas in the body. This includes anterior uveal melanoma (which includes iris melanoma) and posterior uveal melanomas (which include ciliary body melanoma and choroidal melanoma). In this chapter, we will focus only on choroidal melanoma. Choroidal melanoma is the most common uveal melanoma (90%) and also the most common primary intraocular tumor in an adult. It has an incidence of about 5 cases per million population per year in the west. Like other melanomas, it is much less commonly seen in India as compared to the west. In the west, it is seen 150 times more frequently in Caucasians as compared to the blacks.

HISTORY

The presenting clinical features of a case of choroidal melanoma are highly variable.^{1,2}

Chief Complaint

Patients with choroidal melanoma are usually picked up incidentally. Symptoms are often absent, with the tumor detected by chance on routine

fundus examination. When symptoms do occur, they can be variable depending on the tumor characteristics such as location, size, proximity to macula, proximity to optic nerve and presence or absence of overlying retinal changes. Anteriorly located masses present later and are usually larger in size and more advanced at the time of diagnosis while posteriorly located tumors present early due to visual symptoms. Gradual painless diminution of vision is the most common presentation and is usually due to the presence of an exudative retinal detachment or a cystoid macular edema. An intelligent patient can also report a scotoma or a field loss. A subfoveal growth can cause a central scotoma or can cause refractive error. Very rarely, patients may present with severe eye pain due to involvement of the posterior ciliary nerves or sudden onset of loss of vision due to vitreous hemorrhage subsequent to the tumor involving a large retinal or choroidal vessel. Photopsias can occur due to the subretinal location of the tumor. Presentation with loss of weight and appetite, bony pain, head ache may suggest an advanced disease with metastasis.

History of Present Illness

Choroidal melanoma usually presents in patients over 60 years of age in the west. But in Asian

population it is noted to occur early at around 45 years. Males are affected slightly more frequently than females. Note the duration and progression of symptoms. Rapidly changing symptoms in a patient with exudative RD may be a uveitic entity. Eliciting a history of pain, redness and photophobia is also important for the same reason. Symptoms in the contralateral eye are also less likely to occur—choroidal melanoma is only rarely multicentric and extremely rarely bilateral.

History of Past Illness

History of previous medical and surgical illnesses are important to document and rule out other differentials of a choroidal mass or exudative RD such as tuberculoma, hypertension, metastases, Vogt-Koyanagi and Harada's disease and other posterior uveitic entities. History of mass lesion anywhere else in the body should be specifically sought for to rule out a metastases to the eye of a primary elsewhere or a metastases of the choroidal melanoma. Choroidal melanoma is rarely inherited or familial—it is a sporadic malignancy. Relevant systemic history should be elicited when deciding for other differential diagnoses (**Table 1**).

EXAMINATION

General Examination

Should include examination of the general condition of the patient—to look for pallor, icterus, lymphadenopathy, cachexia, other palpable masses in the neck or abdomen, pathological fractures etc. which may indicate distant metastases. In the skin examination, look for nevi, atypical nevi, cutaneous melanocytosis and freckles—all of which are risk factors for the development of uveal melanoma.

Ocular Examination

Visual acuity: As discussed above, visual acuity may be decreased in certain presentations of melanoma.

Eyeball and lids: Look for proptosis, chemosis and restriction of movements—all of which suggests an extraocular extension of the melanoma.

Conjunctiva: A sentinel vessel might be observed in cases of ciliary body melanoma or an anteriorly

located choroidal melanoma. It is a dilated tortuous anterior ciliary artery in the quadrant of the tumor which supplies the tumor of its blood supply.

Cornea: Corneal edema may be present if there is a co-existing glaucoma.

Sclera: Nevus of Ota (Oculo cutaneous melanocytosis) is a risk factor for choroidal melanoma. It presents as unilateral slate-gray pigmentation of the sclera, uvea, orbit, periocular skin, meninges etc. Also, look for any scleral thinning/uveal show which may indicate a scleral extension of the tumor.

Iris/Pupil: Iris nevus is a risk factor for uveal melanoma (Iris melanoma > choroidal melanoma). Choroidal melanoma with extension into ciliary body or primary ciliary body melanoma causes variety of abnormality in the angle and anterior chamber—irregular anterior chamber depth, localized peripheral anterior synechiae etc. Rarely choroidal melanoma with extensive exudative RD can cause neovascular glaucoma. Also note iris color—light iris is a risk factor for choroidal melanoma.

IOP: Choroidal melanoma can cause neovascular glaucoma. Ciliary body extension can cause glaucoma by destruction/infiltration of the trabecular meshwork.

Lens: Localized cataract can occur in anteriorly placed tumors which impinge upon the lens or tumors with ciliary body extension.

Vitreous: Look for cellular infiltration of the anterior vitreous—if present indicates an inflammatory pathology.

Fundus: A distant direct ophthalmoscopy examination may reveal a dark shadow in the area of the mass, a ciliary body mass on the other hand may obliterate the red reflex all together. Choroidal melanomas are usually seen as dome shaped masses smoothly arising from the underlying choroid varying in size from <3 mm to large tumors over 15 mm in base diameter. The height of the tumor is more important as a differentiating feature from benign nevus (**Tables 2 and 3**). When they break through the bruch's membrane they take the classically described collar-stud appearance or mushroom appearance. They can arise anywhere

Table 1 Differentiating choroidal melanoma from other mass-like choroidal pathologies

Character- istic	Choroidal melanoma	Choroidal nevus	Circumscribed choroidal hemangioma	Choroidal metastasis	Choroidal osteoma	Congenital hypertrophy of RPE	Optic disc melano- toma	Posterior scleritis
Age/Sex	5th decade and above	Adolescence	Elderly	30–50 years	10–30 years, 90% female	Congenital	30–40 years	30–50 years, female
Laterality	Unilateral	Unilateral	20% bilateral	Unilateral	20% bilateral	Mostly unilateral	Unilateral	Unilateral
Location	Posterior pole or periphery	Posterior to equator	Posterior pole	Within 2DD from ONH	Juxtapapillary/ circumpapillary	Peripheral	ONH	Peripheral/ posterior pole
Symptoms	Occasional visual loss	Asymptomatic	Occasional visual loss	Occasional visual loss	Occasional visual loss	Asymptomatic	Enlarged blind spot	Pain
Clinical appearance	<ul style="list-style-type: none"> Amelanotic to darkly pigmented Dome/mushroom shaped Shifting SRF + Overlying orange pigment 	<ul style="list-style-type: none"> Amelanotic or pale Flat, <5 DD, Overlying drusen (50–80%), Rare: Orange pigment/SRF/CNV 	<ul style="list-style-type: none"> Broad based with variable thickness Overlying RPE changes Often extensive SRF 	<ul style="list-style-type: none"> Orange-red, <5 DD, RPE changes and SRF + • Overlying RPE changes 	<ul style="list-style-type: none"> Yellow-white to orange, well demarcated, pseudopod margins, RPE changes, vascular spider, occasional CNV 	<ul style="list-style-type: none"> Jet black, rarely melanotic, well defined, flat to ovoid, overlying melanotic lacunae 	<ul style="list-style-type: none"> Jet black to brown, fibrillated margin, choroidal nevus can be associated 	<ul style="list-style-type: none"> Yellowish or same color as adjacent RPE, concentric choroidal folds
Fluorescein Angio- graphy	Early hyperfluorescence with late leakage and stippling	Hypofluorescence unless drusen/RPE changes	Diffuse late leak	Early prearterial hyperfluorescence of large choroidal vessels, late staining/leakage	Irregular fluorescence with late staining	Hypofluorescence with hyperfluorescence of lacunae	Hypofluorescence, late ON hyperfluorescence is possible	Hyperfluorescent mottling with multiple pinpoint areas of leakage
Ultrasono- graphy	<ul style="list-style-type: none"> Low-medium reflectivity, Kappa sign Regular internal structure Choroidal excavation, “hollowing”, subjacent shadowing 	<2 mm thick variable reflectivity	<ul style="list-style-type: none"> Flat/multi-nodular High irregular internal reflectivity 	<ul style="list-style-type: none"> Homogenous medium-high internal reflectivity 	<ul style="list-style-type: none"> High initial spike (low gain) Acoustic shadowing 	Flat	<ul style="list-style-type: none"> Slight elevation, irregular height 	<ul style="list-style-type: none"> High internal reflectivity, thickened sclera and choroid, fluid in subtenon space (T-sign)

Table 2 Differentiating a choroidal melanoma from a choroidal nevus

<i>Characteristic</i>	<i>Choroidal nevus</i>	<i>Choroidal melanoma</i>
Age	Any age, discovered on screening	6th or 7th decade
Symptom	More likely to be asymptomatic. But can cause vision loss due to SRF, CME or CNVM	More likely to be symptomatic. Symptoms described above
Margins	Well defined	Poorly defined or abruptly elevated edges
Elevation	Tends to be flat (<2 mm)	>2 mm
Drusen	More likely	Less likely
Depigmented halo	Characteristic	Absent
Orange pigment	Less likely	More likely
Subretinal fluid	Less likely	More likely
Overlying RPE changes	Likely	Likely
Growth	Very slow (0.5 mm in a decade)	Rapid (Over 1–2 years)

Table 3 Showing the definitions used in COMS

<i>COMS</i>	<i>Apical height</i>	<i>Largest basal diameter</i>
Small tumor	1.5–2.4 mm	5–16 mm
Medium sized tumor	2.5–10 mm	≤16 mm
Large sized tumor	>10 mm	>16 mm

in the fundus either de-novo or from a pre-existing choroidal nevus. They are usually pigmented in most of the cases (about 85% of the cases) but about 15% are amelanotic—which means they do not show any melanin clinically. The color per-se could vary from dark brown to tan (**Fig. 1**). About 5% of the tumors are diffusely infiltrative without any nodular mass. About 60% of the tumors are located within 3 mm of the optic disc or fovea. They could be bilobular or multilobular and could even be multicentric.

The retinal pigment epithelium (RPE) overlying the tumor often show stress changes such as drusen, mottling, areas of atrophy, pigment epithelial detachment etc. owing to the deprivation of normal choroidal circulation to the RPE due to the presence of the tumor. Orange pigment on the melanoma is an important sign to differentiate it from the benign choroidal nevus and represents the accumulated melanin and lipofuscin in the RPE cells after phagocytosis of the cellular debris of the melanocytes. The overlying

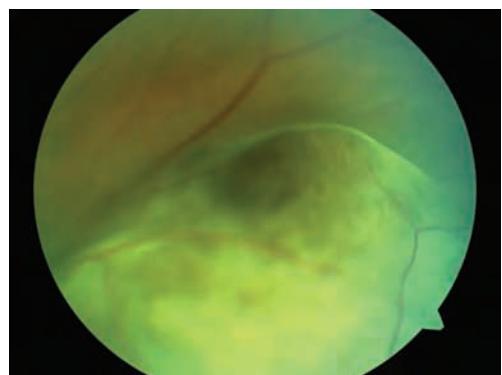


Fig. 1: A pigmented choroidal melanoma with surrounding subretinal fluid and orange pigmentation over it

neurosensory retina may also show chronic degenerative changes such as cystoid spaces, schitic cavity and CME.

Exudative RD is commonly associated with choroidal melanoma and is again an important

differentiating feature from choroidal nevus (**Table 2**). The exudative RD may be so bullous it can sometimes hide the tumor under it and appear like an RRD. Typically the sub retinal fluid is seen surrounding the mass, and largely spread fluid indicates a possibility of choroidal metastasis. Associated intra and subretinal hemorrhage is generally a sign of development of choroidal neovascular membrane in a long standing dormant melanoma. Vitreous hemorrhage and massive subretinal hemorrhage can occur in melanoma owing to erosion of a large retinal/choroidal vessel by the tumor or due to necrosis of a part of the tumor.

INVESTIGATION

Choroidal melanoma is a clinical diagnosis that is aided by ancillary diagnostic testing. Collaborative ocular melanoma trial showed that clinical evaluation along with fundus photography, ultrasonography and fluorescein angiography is 99% accurate in diagnosing a choroidal melanoma.

Ultrasonography

Ultrasonography (**Fig. 2**) is the most useful investigative modality in the diagnosis of choroidal melanoma.³ A standardized ultrasonography has a diagnostic accuracy of >95%. On A scan, Ossining

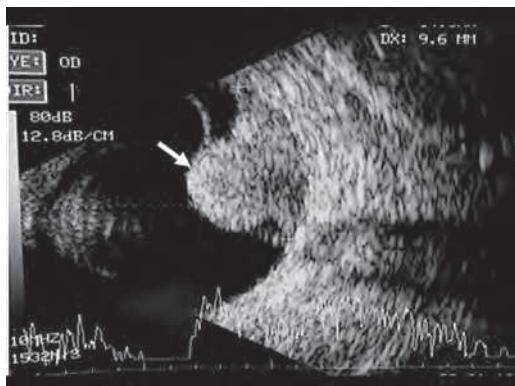


Fig. 2: Combined ultrasonography A- and B-scan showing a mushroom shaped mass arising from the choroid with surrounding subretinal fluid and homogenous internal reflectivity. A-scan shows moderate spikes. There is acoustic hollowing towards the base of the tumor

described four cardinal acoustic hallmarks of malignant melanoma: (1) A regular internal structure with similar height of the inner tumor spikes or regular decrease in height (positive angle kappa sign); (2) low to medium reflectivity; (3) solid consistency; and (4) echographic sign of vascularization with a fast, spontaneous, continuous, flickering vertical motion of single tumor spikes.

B-mode ultrasonography can help detect tumors and detail the internal characteristics in cases of exudative detachment and hazy media. It can help in measuring the size, extent, spread and in ruling out differentials. The characteristic findings are: (1) homogenous internal structure with low to medium reflectivity; (2) choroidal excavation; (3) shadowing of the subjacent choroidal structures; (4) an acoustically empty zone at the base (acoustic hollowing). A 'collar stud' appearance is highly suggestive of choroidal melanoma. It will also define the area of RD.

Fluorescein Angiography

Fluorescein angiography (FA) is not diagnostic and adds limited information to the diagnosis. It helps in ruling out hemorrhagic lesion such as a ruptured retinal arterial macroaneurysm or peripheral choroidal neovascularization, which generally blocks fluorescence. Choroidal melanomas on fluorescein angiography show their intrinsic vasculature different from the overlying retinal vasculature and this is called "dual circulation". There may be early stippling and late leakage and staining. There are no pathognomonic signs on angiography for choroidal melanoma.

Indocyanine Green Angiography

Indocyanine green angiography (ICG) angiography better delineates the extent of mass since the infrared red waves used penetrate the RPE well. They can also pick up choroidal neovascularization. It helps in differentiating a melanoma from a choroidal hemangioma, the latter shows a wash out of dye.

Fundus Autofluorescence

Intense diffuse or confluent hyperautofluorescence is seen in melanoma.

Optical Coherence Tomography

The OCT (EDI) may be useful in detecting tumors <3 mm in size which are difficult to pick up on clinical examination and ultrasonography. It is also helpful in confirming the presence of subretinal fluid in small doubtful lesions. Presence of subretinal fluid shifts the diagnosis more towards melanoma than towards choroidal nevus. Secondary retinal changes like CME, atrophic changes are often evident overlying the lesion. Recently, due to the enhanced choroidal imaging, OCT characteristics of melanoma and other choroidal tumors have been defined, the focus being on shape and edge of the tumor, as well as the internal vascularity. Still like FA, these features are not conclusive of a differential diagnoses.

CT Scan

Melanomas appear hyperdense on CT scanning with moderate contrast enhancement. It is useful for evaluation of metastasis.

Magnetic Resonance Imaging

For ocular diagnoses, MRI is more useful than CT scan. On MRI, melanomas (like retinoblastoma) are hyperintense to vitreous on T1 and hypointense to vitreous on T2. It is also useful in assessing extraocular spread and in ruling out some of the differentials.

Tissue Diagnosis

When clinical methods and non-invasive investigative modalities fail to conclusively prove or rule out the diagnosis of a melanoma, tissue diagnosis by a fine needle aspiration or a transscleral biopsy or a bimanual biopsy with chandelier assisted 25-G vitrectomy system may be useful. One should be careful of port/aspiration site spread, and cryotherapy should be considered at the entry sites. Also if diagnosis is proven to be melanoma, earliest possible further management (like enucleation should) be done to avoid tumor spread. A lymph node biopsy or that of other site of spread may also be done if appropriate.

Systemic Investigations

It is directed principally towards detecting metastatic spread. Hepatic transaminases and alkaline

phosphatase are the basic screening test since liver is the most common site of metastasis. If these enzymes are elevated CT scan of the abdomen or ultrasonography can be considered. PET-CT scan should be considered if available as metastasis was believed to be the rule (Zimmermans hypothesis), even after successful excision of the tumor. Other sites of systemic spread include bone marrow, skin, brain and lungs.

DIFFERENTIAL DIAGNOSIS

Since the clinical manifestation and appearance of the tumor are highly variable, numerous differentials need to be considered in a case of choroidal mass. **Table 1** summarizes the differentials in a tabular form.

MANAGEMENT

Treatment in a case of choroidal melanoma depends on the size and extension of the tumor, life expectancy of the patient and visual potential of the eye. Treatment is tailor made for each patient.

Observation

Increasingly the trend in ocular oncology is to treat smaller melanomas to reduce the risk of metastasis. But observation still has a role especially in tumors <2.5 or 3 mm in height and <10 mm in diameter which are very slow growing or in tumors in whom an unequivocal diagnosis of choroidal melanoma could not be reached. Also in patients with limited life expectancy or untreatable conditions, observation might be a prudent choice.

Enucleation

Enucleation is the classic treatment modality for large melanomas or melanomas with poor visual potential or extensive spread within and outside the globe. The COMS also suggested enucleation for "large" tumors (see below). Additional precautions must be taken in the form of performing an indirect ophthalmoscopy after draping the parts to confirm the correct eye is enucleated. In large tumors pre-enucleation radiotherapy may not provide additional mortality benefit. If there is extrascleral extension, the entire

tumor should be removed en bloc to reduce the risk of residual disease. All treatment modalities developed subsequently to preserve globe and salvage some useful vision are compared against enucleation in terms of mortality and metastasis.

Episcleral Plaque Brachytherapy

Brachytherapy is done by suturing an Iodine-125 or Ruthenium-106 plaque to the sclera over the area of the tumor. This may be used for medium sized tumors with some potential for salvaging vision and <15 mm in basal diameter and up to 10 mm in height. Survival is similar to that following enucleation. Complications include cataract, papillopathy (with or without disc neovascularization) and radiation retinopathy. About 25% of the patients develop iris neovascularization.

External Beam Radiotherapy

Melanomas are radio resistant. To radiate them using conventional external-beam radiotherapy techniques would require high radiation dose and this subsequently leads to severe complications. Modern techniques of delivering precise high dose radiation like proton beam irradiation and stereotactic radiotherapy can be used for tumors that are unsuitable for brachytherapy due to their large size or posterior location. These techniques cause minimal damage to the adjacent tissues. Their efficacy is similar to brachytherapy.

Transpupillary Thermotherapy and Photodynamic Therapy

These modalities can be used to treat smaller lesions. In some reports, double fluence (100 J/cm^2) and double duration (166s) of PDT have been used. While TTT is more useful in pigmented tumors, PDT is useful in amelanotic tumors.

Surgical Management

Melanomas can be removed through the scleral approach or through pars plana vitrectomy. In the scleral approach, the tumor is removed en-bloc with surrounding choroid and overlying sclera if involved. In the pars-plana approach the tumor is removed in piece meal through a vitreous cutter (Endoresection). These procedures are technically

difficult and are indicated in carefully selected tumors that are too thick for radiotherapy but less than about 16 mm in diameter. The results are difficult to compare as long term follow-up is needed to disprove systemic spread. Orbital exenteration is rarely done for melanoma with orbital extension because the disease has generally reached an advanced stage with extensive metastasis by this time. Nonconventional approach should be considered where visual/eye ball salvation is possible.

Systemic Chemotherapy

Systemic chemotherapy is used only in cases with metastatic disease.

VIVA QUESTIONS

Q.1. What are the risk factors for choroidal melanoma?

Ans. Risk factors include fair skin, lighter iris color, blonde hair, chronic sun light exposure, choroidal or iris nevus, nevus of Ota, atypical nevus syndrome, multiple nevi, exposure to arc welding, uveal melanocytoma and BRCA-1 associated protein 1 (BAP1) mutation. The exposure to sunlight is although hypothesized and believed widely, it has not been proven by epidemiological studies.

Q.2. What is the diagnostic accuracy of ultrasonography in diagnosing choroidal melanoma?

Ans. Combined A- and B-scans have a diagnostic accuracy of over 95% in diagnosing choroidal melanoma. (COMS showed that clinical diagnosis which included clinical examination, fundus photography and ultrasonography was 99% accurate in diagnosing choroidal melanoma).

Q.3. What are the histopathological features of choroidal melanoma?

Ans. Calender in 1931 developed a histopathological classification system for uveal melanomas depending on the most prominent cell type in a tumor. This included tumors classified as:

- Spindle cell subtype A
- Spindle cell subtype B

- Epithelioid type
- Fascicular type and
- Mixed type.

There were inherent limitations in this system and therefore this classification was revised in 1983 by McLean and he classified uveal melanomas as follows:

- Spindle cell melanoma (composed of spindle B cells)
- Epithelioid cell melanoma and
- Mixed types melanoma.

McLean did not classify Spindle A cells as malignant. They are fusiform cohesive cells which form choroidal nevus. Spindle B cells are also fusiform but are plumper and have poorly defined margins. Epithelioid cells are round or pleomorphic, non-cohesive cells with large nucleus, prominent mitotic figures and defined borders. There are also intermediate cells—intermediate between spindle and epithelioid. These cell types and other histopathological features can only be detected on enucleation or block resection specimens. Needle biopsy and tumor removed in piece meal are difficult to type.

Choroidal melanomas arise *de novo* from the melanocytes in the uveal tissue. They can also arise from a choroidal nevus (in which case histopathology may show spindle A cells) or a melanocytoma. Immunohistochemical markers of melanoma are S-100 and HMB-45.

Q.4. What are the prognostic factors of choroidal melanoma?

Ans. Tumor size is the most important prognostic factor.^{4,5} Several studies have shown that large tumors have the highest 5 year mortality rate—53% while small and medium-size tumors has a mortality of 16% and 32% respectively. Tumor histology is another important prognostic factor. Epithelioid tumors had a 10-year mortality of 72–100% while the spindle A tumors has a 10 year mortality of 11–19%. Modern histopathological prognostic markers are indices such as number of epithelioid cells per hpf and inverse standard deviation of nucleolar area. Extrascleral extension is

another important prognostic marker—5 year survival is poor if there is extrascleral extension. Anteriorly located tumors present much later and therefore has poorer prognosis. Among medium sized tumors, posteriorly located tumors have poorer prognosis since it is difficult to provide brachytherapy to more posterior sites. Ciliary body invasion of choroidal tumors indicate a poor prognosis. Tumors recurrent after brachytherapy or external radiotherapy also behave poorly. Tumor genetic characteristics such as somatic mutations in the BAP1 gene are also linked to greater chance of metastasis.

Liver, bone and lung are the common sites of metastasis. At presentation only about 1–2% of patients have detectable metastases but mortality is up to 50% at 10 years.

Q.5. What is a diffuse infiltrating choroidal melanoma?

Ans. It is a variant of choroidal melanoma which does not present as a tumorous mass but shows lateral growth in the choroid and presents with exudative RD. It has been defined as a tumor <5 mm in height and occupying >25% of the uveal tract. It accounts for about 5% of all the choroidal melanomas. It is difficult to diagnose because of the absence of the tumor and presence of an exudative RD. It generally has poor prognosis.

Q.6. What is collaborative ocular melanoma study?

Ans. Collaborative ocular melanoma study (COMS) is a National Eye Institute sponsored multicentric three armed study started in 1985. The first arm studied the natural history of small choroidal melanoma. The other two arms were randomized control trials evaluating treatment options of medium and large sized tumors. Iodine-125 brachytherapy was compared against enucleation for medium sized tumors and enucleation alone was compared to enucleation preceded by external beam radiotherapy in large tumors. The definitions of small,

medium and large tumors are summarized in **Table 3**.

The natural history arm recruited 204 patients. 6 deaths occurred due to metastatic melanoma. The 5-year tumor specific mortality rate was 1%. The medium sized tumor trial showed that there was no statistically significant difference in the mortality rates of patients treated with enucleation and iodine-125 brachytherapy. The risk of treatment failure in case of brachytherapy was 10% and was increased in patients with thicker tumors and in patients with posterior tumors. In the large sized tumor trial, pre-enucleation brachytherapy was not found to significantly affect survival.

Q.7. What is Zimmerman's hypothesis?

Ans. Zimmerman, McLean, and Foster in 1978 hypothesized in their paper that enucleation may accelerate metastases. This was based on their observation of a peak in the mortality rates 2 years postenucleation which after 6 years stabilized to the pre-enucleation rates. They hypothesized that tumor manipulation during surgery caused dissemination of the tumor causing a spike in metastasis and mortality. Based on this they also suggested high vigilance during enucleation for uveal melanoma and pre-enucleation radiotherapy.⁶

Subsequent epidemiological studies have also shown a post-therapeutic spike (spike after any form of treatment to the melanoma—enucleation, brachytherapy or proton beam radiotherapy) in the mortality rates in accordance with the observation made by Zimmerman et al. The current understanding of this phenomenon is that it involves host-tumor interaction and host immune mechanisms. Also there could be a role played by antiangiogenic mediators such as angiostatin produced by the primary melanoma which may have growth inhibitory effects on the micrometastases. Removal/treatment of the primary tumor alters the host immune response and the antiangiogenic signals from the primary tumor and causes micrometastases to progressively grow and cause mortality.

Therefore, the surgery *per se* is not the cause of the increased postenucleation mortality but the treatment of the tumor is.

Q.8. What are the pros and cons of endoresection of tumors, and how are the results?

Ans. Endovitreal resection of medium to large sized choroidal melanomas (limited to the globe) have been reported by multiple authors. The advantages of this procedure are globe preservation, preservation of some visual function, removal of the tumor in its entirety, abundant sample for histopathology and genetic studies, avoiding radiation complications and photocoagulation of microscopic elements under direct observation. The disadvantages of this procedure are the theoretical risk of tumor seeding and metastasis (although the MIVS systems with the trocar and cannula entry have been shown to be safe), need for hypotensive anesthesia, demands more skill, need for multiple surgeries. The reported results are good, comparable to other globe salvaging procedures in terms of metastasis. Survival data is as yet limited.⁷

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SHORT CASES

CHERRY-RED SPOT

Rajesh Pattebahadur, Brijesh Takkar

INTRODUCTION

Cherry-red spot (CRS) is an important finding suggestive of a large group of diseases. Among these diseases, diagnosis of metabolic disorders helps in prognosticating the condition, while early diagnosis of conditions like central retinal artery occlusion (CRAO) help in early management and salvaging the permanent loss of vision.¹

HISTORY

Chief Complaint

As stated earlier CRS is not a disease, a patient with history of metabolic disorder may show CRS on fundus examination. Also a case of sudden diminution of vision (CRAO) or ocular contusion will have CRS on fundus examination.

History on Present Illness

The patients age of presentation will have different set of complaints and different sets of diagnosis. In pediatric age group patient may show hepatosplenomegaly, bone changes, neurological changes, ascites, myoclonic jerk, mental retardation. Whereas in adults, history of trauma to eye can be present or sudden diminution of vision (CRAO) may be there.

Medical History

Past medical history of hypertension, dysostosis multiplex (DM), hypercoagulable states, sickle cell, atherosclerosis, cardiac valvular disease, sepsis, intravenous drug abuse may be there.

Family History

Family history is important in cases with metabolic disorders associated with the CRS.

EXAMINATION

Systemic Examination

Detailed examination may reveal systemic findings of the underlying cause, in a case of CRS.

- *Cardiovascular system:* Patient may be having hypertension along with valvular heart disease.
- *Abdominal system:* Hepatosplenomegaly is important finding suggestive of severe metabolic abnormalities. Along with this ascites can also be seen.
- *Neurological system:* Delayed response, mental retardation, myoclonic jerks, hypotonia are important findings.
- *Respiratory system:* Interstitial pneumonia can be present.
- Along with these other features includes coarse facies, bone changes.

Ophthalmic Examination

Following points must be recorded:

- Uncorrected and best corrected visual acuity
- Globes are generally aligned
- Eyelids are generally within normal limit
- Conjunctiva do not show any specific finding but in cases of ocular trauma may show bleeding or tear in conjunctiva.
- Corneal clouding can be seen, typical of underlying systemic diseases.
- Anterior chamber is usually within normal limit. Angle recession can be seen in cases of severe ocular trauma. Iridodialysis, lens subluxation, post-traumatic cataract are few finding which suggest the ocular trauma as cause for the CRS.
- Distant direct ophthalmoscopy may not reveal any specific finding unless there is cataract.



Fig. 1: Fundus photograph of cherry-red spot in a case of central retinal artery occlusion (CRAO)

Indirect Ophthalmoscopy

- Detailed examination should include cup disc ratio, neuroretinal rim, arteriovenous ratio and foveal reflex.
- The CRS is visualized as a bright to dull red spot at the center of macula, surrounded and bordered by a grayish white or yellowish halo (**Fig. 1**).

DIFFERENTIAL DIAGNOSIS

As said earlier the underlying cause has to be identified. The common causes are:

- Bilateral CRS:* Metabolic disorders, quinine and other drug toxicity and Leber's congenital amaurosis.
- Unilateral CRS:* CRAO, orbital contusions, macular hole with retinal detachment or macular hemorrhage.

The CRS is more commonly associated with CRAO in adults. The age, health of patient, history of trauma or vascular disease and unilaterality of lesion may help to distinguish it from the metabolic disorders. In such instances providing emergency management and treating the underlying disorders or risk factors constitute vital therapeutic interventions.^{1,2}

In children with CRAO hemoglobinopathies like sickle cell disease, hypercoagulable states like antiphospholipid antibodies and vasculitis due to systemic lupus erythematosus are more common causes, whereas in adults two-thirds of all patients with CRAO have associated

hypertension, one-fourth have carotid occlusive disease, diabetes or cardiac valvular disease or a combination. Bilateral involvement is rare and suggestive of arteritic disease.^{1,2}

MANAGEMENT

Treatment involves treating the underlying cause. CRAO, an ophthalmic emergency should be treated within 24 hours. Medical and surgical lowering of intraocular pressure, carbon dioxide rebreathing, steroids (in vasculitis), vasodilator drugs, hyperbaric oxygen, antifibrinolytic drugs, barbiturate coma, free radical scavengers and antioxidants have been tried with variable results. The CRS resolves in due course with resolution of edema, however, optic atrophy ensues.^{1,2}

VIVA QUESTIONS

Q.1. What is cherry-red spot (CRS)?

Ans. It is a clinical sign seen in the context of thickening and loss of transparency of posterior pole of the retina. The CRS is visualized as a bright to dull red spot at the center of macula, surrounded and accentuated by a grayish white or yellowish halo. Its color is due to the pigment epithelium and choroid, and therefore may demonstrate color variability according to the race.¹

Q.2. What is differential diagnosis for CRS?

Ans. See Table 1.

Q.3. What are causes of CRS—like lesions and pseudo CRS?

Ans. Certain illnesses are associated with macular lesions resembling a CRS. These include:

- Adult Niemann-Pick disease (ring of perifoveal crystalloid deposits)
- Gaucher's disease (atypical macular CRS)
- Lactosyl ceramidosis (increasing redness of macula)
- Sea blue histiocyte syndrome (perifoveal yellowish white scintillating granules in doughnut shaped pattern)

Conditions like macular hemorrhage or macular hole with retinal detachment could

Table 1 Differential diagnosis of cherry-red spot

- Central retinal artery occlusion (CRAO)
- Orbital contusion
- Orbital ischemia
- Tay-Sachs disease
- Sandhoff's disease
- Sialidosis
- Infantile Niemann-Pick disease type IA
- GM1 gangliosidosis
- Metachromatic leukodystrophy
- Goldberg's disease
- Gaucher's disease (infantile form), Hurler's syndrome
- Mucopolysaccharidosis VII
- Hallervorden Spatz syndrome
- Batten-Mayou; Vogt-Spielmeyer syndrome
- Spranger's disease
- Cryoglobulinemia
- Leber's congenital amaurosis
- Drugs—Quinine, carbon monoxide, methanol and dapsone toxicity

be considered as pseudo-CRS, because the abnormality is in the foveola rather than parafoveal area.

Q.4. What is pathophysiology of CRS?

- Ans.**
- The retina has around 1 million ganglion cells.
 - However, macular region (foveola, in particular) is almost devoid of these cells.
 - Diseases associated with accumulation of storage material (such as glycolipids or sphingolipids) in the retinal cellular layers result in swelling and loss of transparency of the multilayered ganglion cells giving it a "white" appearance.
 - The foveola, the thinnest part of the retina being devoid of ganglion cells, retains its relative transparency allowing the normal choroidal vasculature to be seen through it.
 - These histological features result in the appearance of the central red area (normal foveola) that is surrounded by dull halo resulting from attenuation of transparency of the surrounding area.
 - Later in the course of the disease, ganglion cell death makes the spot less

prominent. Atrophy of retinal nerve fiber layer and optic atrophy may also follow.

- In *CRAO* the fundoscopy reveals a diffuse retinal arteriole constriction often with visible emboli or blood flow segmentation. The fovea retains its blood supply via the choroidal circulation while the surrounding retina appears milky white due to infarction, intracellular edema, cellular necrosis and cellular debris accumulation.
- The CRS seen in *methanol poisoning* is due to macular cystoid edema and in *quinine poisoning* due to retinal edema.
- In *macular hemorrhage*, blood which is darker red than the retina contributes to the CRS appearance.

Q.5. Which are predisposing conditions for the CRAO?

- Ans.** Conditions that predispose to CRAO include retinal emboli due to endogenous or exogenous source; hypertension, diabetes mellitus, carotid occlusive disease, cardiac valvular disease, atheromatous vascular disease, arteriosclerotic vascular disease, vasculitic syndromes (temporal arteritis, SLE, etc.), blood dyscrasias (e.g. sickle hemoglobinopathy), hypercoagulable states (e.g. antiphospholipid antibodies), sepsis and DIC, vasospasm, vascular compression, cervical trauma with carotid artery dissection, intravenous drug use and migraine.

Q.6. How to diagnose and manage the CRS?

- Ans.** *In pediatric age group:* Metabolic diseases constitute the most common cause for CRS. The exact metabolic or storage disease can be diagnosed on the basis of age of onset, associated manifestations, inheritance pattern.

In newborns:

- Hepatosplenomegaly with vacuolated lymphocytes would suggest GM1 gangliosidosis, Niemann-Pick disease type IA or early infantile galactosialidosis.
- An additional finding of coarse facies, bone changes, edema with ascites would favor GM1 gangliosidosis or early infantile galactosialidosis; Interstitial

pneumonia and neurologic deterioration would suggest Niemann-Pick disease type IA disease.

In infancy:

- Exaggerated neuronal response, hepatosplenomegaly, myoclonic jerks, hypotonia and neuroregression would suggest a diagnosis of GM2 Gangliosidosis type 1 (Tay-Sachs disease) or type 2 (Sandhoff's disease).
- Whereas hepatosplenomegaly with bone changes would favor a diagnosis of late infantile galactosialidosis.
- In late childhood, blindness and progressive myoclonic jerks suggest Sialidosis (CRS Myoclonus syndrome) whereas bone changes, dysmorphism, angiokeratoma, corneal opacities and psychomotor

retardation would suggest juvenile galactosialidosis.

Several inherited metabolic diseases have no definitive treatment. However, early diagnosis allows for appropriate counseling and prenatal diagnosis (For example, determination of levels of hexosaminidase A and B levels in Sandhoff's disease).

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CENTRAL SEROUS CHORIORETINOPATHY

Vaishali Ghanshyam Rai, Raghav Ravani

INTRODUCTION

Central serous chorioretinopathy (CSCR) is a maculopathy characterized by idiopathic circumscribed serous retinal detachment, usually confined to the central macula. It is a favorite short case for PG exams.

HISTORY

Demography

Central serous chorioretinopathy (CSCR) typically affects individuals in the 20–50 years age range.^{1,2} Males are much more commonly affected than females. The incidence in men was approximately six times higher than in women. Younger patients usually have unilateral involvement, while older patients are more likely to have bilateral involvement in CSCR.

Chief Complaint

The patient can present with following:

- Recent unilateral painless diminution of vision is the most common symptom. Often the patient's complaint is one of transiently seeing a dark spot in the center of the visual field in one eye, with or without metamorphopsia.

- Unilateral metamorphopsia is the classic symptom.
- Patients may also present with unilateral blurred vision, micropsia, impaired dark adaptation, color desaturation and a relative scotoma.

Past History

Following points must be noted:

- History of any emotional stress.
- History of *type A personality* is important.
- History *long-term steroid* use in any form, e.g. oral, inhaler or topical.
- History of pregnancy in female patients.
- History of any organ transplant in past should be taken.
- History of similar complaint in past is important to rule out recurrent CSCR.

EXAMINATION

General Examination

Look for presence of any disease requiring chronic steroid intake. Also, look for signs of steroid toxicity.

Ocular Examination

Visual Acuity

- Visual acuity ranges from 20/15 (6/5) to 20/200 (6/60) but averages 20/30 (6/9).
- The visual acuity may *improve with hyperopic correction.*

Anterior Segment

It is usually normal.

Posterior Segment

- *Acute form of CSCR*

- Oval yellow-gray elevations at parafoveal or macular area may be seen (**Fig. 1**). These are generally less than one-fourth of a disc diameter in size and are surrounded by a faint grayish halo.
- Absence of the normal foveal light reflex.
- The subretinal fluid is usually clear, but granular or fibrinous deposits may be present in the subretinal space. The accumulation of granular/fibrinous material between the RPE and the neurosensory retina increases with the duration of symptoms.
- Abnormalities of the RPE presents as one or more yellow spots or a small pigment epithelial detachment (PED).
- The fellow eye may show evidence of either concurrent or previously resolved CSCR, manifested as focal areas of retinal



Fig. 1: Fundus photograph of a case of CSCR

pigment epithelium rarefaction or small asymptomatic retinal pigment epithelium detachments. Bilateral involvement occurs in approximately 20% of patients.

- Recurrence of CSCR can be seen in 40-50% of patients in long course. A patient can have recurrent focal leaks or progress inexorably to the more visually threatening chronic CSCR.

- *Chronic CSCR*

- It is characterized by a diffuse or multifocal, irregular retinal pigment epitheliopathy that progresses in conjunction with persistent or intermittent subretinal fluid. It is also known as diffuse retinal pigment epitheliopathy (DRPE). Recently, multifocal posterior pigment epitheliopathy (MPPE) has also been described with multiple leaks with large amounts of SRF. Subretinal fibrosis and choroidal neovascular membranes (CNVMs) may ensue as complications.
- The retinal detachments tend to be shallow and more diffuse than in the classic form and with amorphous subretinal deposits. Subretinal lipid that typically appears as discrete, hard-edged, subretinal accumulations at the borders of a neurosensory detachment can be seen.
- More often bilateral and may occasionally present with gravitational tracts a term used for oblong, vertical patches of RPE hypopigmentation that extend inferiorly. These tracts are produced by subretinal fluid of high specific gravity sinking toward the inferior fundus and dissecting its way through the subretinal space.

- *Rare forms*

- *Bullous form of CSCR:*

- Rarely CSCR can present as a bullous, inferior nonrhegmatogenous peripheral retinal detachment. Atrophic tracts of the RPE extending inferiorly to the serous retinal detachment can be seen in such cases.
- It is often associated with subretinal fibrinous exudates and shows the phenomenon of subretinal fluid shifting position with changes in posture.

- More common in Japan, and patients with history of organ transplant

Neovascular CSCR: Rarely as a complication of chronic CSCR.

DIFFERENTIAL DIAGNOSIS

Central serous chorioretinopathy (CSCR) must be differentiated from a neural retinal detachment secondary to:

- **Subretinal choroidal neovascularization (CNV):** CNV present with thickening at the level of the RPE, notched PEDs and subretinal or subpigment epithelial blood that are absent in CSCR. In addition, there will be coexistent ocular findings related to the generation of new blood vessel growth in eyes with CNV. Indocyanine green angiography of subretinal choroidal neovascularization usually reveals only one area of hyperfluorescence that progressively enlarges during the later frames of the study.
- **Tumors and infiltrative conditions** (leukemia, amelanotic melanoma, or metastatic disease) these lesions generally have a different color than the surrounding normal choroid; USG would show thickening of the choroid serous PEDs are absent.
- **Inflammatory (posterior scleritis or Harada's disease):** There will be signs of intraocular inflammation such as iritis or vitritis, and other sign's such as patches of yellowish discoloration in the posterior pole, papillitis,

thickening of the choroid on USG. These should always be considered for chronic and multifocal cases.

- **Polypoidal choroidal vasculopathy:** Indocyanine green angiography of polypoidal choroidal vasculopathy demonstrates small-caliber, polypoidal choroidal vascular lesions and no areas of choroidal hyperpermeability.
- **Optic disc pit:** The optic nerve pathology is visible on ophthalmoscopy. There are no leaks on fluorescein angiography. OCT can show the tract connecting to optic nerve head along with splitting of retinal layers, at times with an impending macular hole.

INVESTIGATION

Fundus Fluorescein Angiography

- Fundus fluorescein angiography is not required in routinely, but is a good practice for documenting the baseline disease, in chronic forms and when suspecting other disorders.
- Fundus fluorescein angiography classically shows, dye from the choroid leaks through a focal RPE defect and pools in the subretinal space (**Figs 2 and 3**). In more than 75% of patients, this pooling occurs within 1 disc diameter of the fovea, very common in the superior nasal area.
- Fundus fluorescein angiography findings can be described as '*smokestack leak*' or the more common '*inkblot leak*' patterns. Multiple leaks may be seen in multifocal disease.



Fig. 2: Fundus photograph of a patient of CSR. Note the fluid accumulation beneath the fovea and the superior-temporal pigment mottling



Fig. 3: Fluorescein angiography (FA) picture of the patient in Figure 1. Large ink blot leak can be seen. Staining is also visible in the area of pigment mottling

Indocyanine Green Angiography

- Earlier considered gold standard, choroidal ischemia and dilatation of larger choroidal vessels and hot spots corresponding to leaking areas can be seen.
- Staining appears in the mid phase of the indocyanine green angiography (ICGA) and fades in the late phase.
- It helps to differentiate CSC from polypoidal choroidal vasculopathy, choroidal neovascularization.
- Pick-up CNVMs when doubtful.

Optical Coherence Tomography

- Demonstrate the presence of subretinal fluid (**Fig. 4**).
- Helps to quantify and follow the amount and extent of subretinal fluid and to demonstrate thickening of the neurosensory retina.
- Helps in diagnosis of doubtful cases.
- Choroidal OCT imaging can reveal pachychoroidal epitheliopathy in both eyes, now considered a precursor of CSR.
- Posteriorly loculated fluid in choroid can also be seen on choroidal imaging.

Optical Coherence Tomography Angiography

Role is under investigation. It can pick up CNVMs and has shown increased choroidal vascularity in both the eyes.

TREATMENT

Observation

Majority of cases of central serous chorioretinopathy (CSC) resolve spontaneously over period of 3–4 months. Most often, as per conventional teaching, the initial treatment of choice is observation. If the patient is using corticosteroids, these should be discontinued if medically possible. The patient must be advised to avoid tobacco and smoking.

Acetazolamide

Systemic acetazolamide treatment promotes the resorption of subretinal fluid and case reports suggest that it may reduce subretinal fluid in CSC. However, there is no evidence that treatment promotes healing of the retinal pigment epithelium (RPE) lesion, long-term preservation of visual function, or a reduced rate of recurrence.

Laser Photocoagulation

- *Indication*
 - Extrafoveal leaks who fail to improve after 4–6 months
 - Demonstrate permanent changes from CSC in the other eye
 - Demonstrate multiple recurrences
 - *Occupational:* Require improved vision for work.
- Laser photocoagulation is applied to the site of fluorescein leakage. The technique of laser

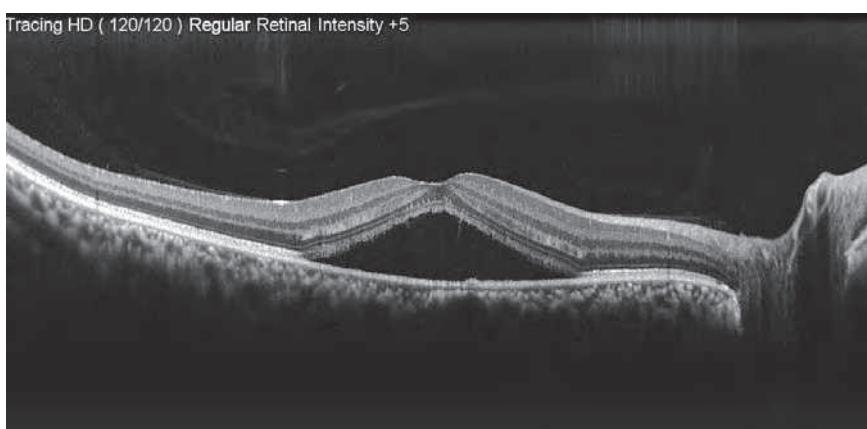


Fig. 4: OCT image showing subretinal fluid

- photocoagulation involves using a green-wavelength laser to produce a light scar over the focal RPE leak.
- Typically, 6–12 laser burns of 50–200 µm spot size at 0.1-second duration and 75–200 mW are used. Permanent RPE change is induced at the site of the laser scar.
 - Treatment should be avoided if the leak occurs within 300 µm of the center of the foveal avascular zone.

Photodynamic Therapy

- Photodynamic therapy has been used to treat chronic CSC (defined as >6 months' duration of disease) with diffuse compensation of the RPE and lacking focal FA leak. However, recent evidence from East Asia supports its role in acute uncomplicated CSR as well, especially when done at low fluence.
- Photodynamic therapy is treatment that is more effective with a lower complication rate for patients with subfoveal or juxtapapillary leaks.

Transpupillary Thermotherapy

Few studies suggest that this treatment may accelerate the resolution of CSC, but long-term safety and efficacy are not known.

Others: Several other modalities have been described.³

- The beta-adrenergic receptor blocker propranolol and the mixed alpha and beta adrenergic receptor blocker labetalol.
- Mifepristone as an antagonist of progesterone and glucocorticoid receptors.
- Ketoconazole as an adrenocorticoid antagonist that has been shown to lower endogenous cortisol.
- Intravitreal bevacizumab has been investigated for treatment of CSR; theoretically, the antipermeability characteristics of this antibody to vascular endothelial growth factor (VEGF) may allow for reduced leakage, favoring resorption of the exudative retinal detachment in CSR.
- Aspirin:** Plasminogen activator inhibitor-1 (PAI-1) is increased in CSCR and aspirin is

effective in lowering PAI-1 levels and platelet aggregation.

- Rifampicin is another drug that has been tried for CSR, though evidence level is low.

VIVA QUESTIONS

- Q.1. What are the risk factors associated with CSCR?**

Ans. See Table 1.

- Q.2. What is the clinical course and outcome of CSCR?**

Ans. The visual prognosis is good in majority of cases of CSCR. The majority of patients suffer no significant permanent visual loss. Although visual acuity usually improves, patients may continue to have persistent metamorphopsia probably due to a photoreceptor misalignment causing a *Stiles-Crawford effect*.

- Q.3. Mechanism of action of acetazolamide in CSCR.**

Ans. Helps in absorption of the subretinal fluid by inhibiting carbonic anhydrase pump located in the RPE and creating a localized acidic milieu.

Table 1 Risk factors and associations with central serous chorioretinopathy

Systemic conditions	Type A personality, emotional stress pregnancy Organ transplantation Systemic lupus erythematosus Tobacco and alcohol use Membranoproliferative glomerulonephritis type II <i>Helicobacter pylori</i> infection Gastroesophageal reflux disease Systemic hypertension
Medications	Corticosteroids Antihistamines Sildenafil citrate Psychopharmacologic medications Amphetamine Antacids and anti-reflux medications Sympathomimetics Antibiotics

Q.4. Hypothesis for pathogenesis of CSCR.

Ans. Choroidal circulation anomaly of the middle choroidal layers leading on to focal choroidal ischemia, choroidal edema which sets up a vicious cycle. This leads to accumulation of fluid in the choroid, formation of PEDs which eventually give way to cause leakage and manifest as SRF. Choroidal imaging confirms this by demonstrating pachychoroid epitheliopathy, localized choroidal fluid and increased compensatory vascularity.

Q.5. Histopathological classification.

Ans. Type 1: Only neurosensory detachment
Type 2: Neurosensory with pigment epithelium detachment.

Q.6. What are the indications for treatment of CSR?

Ans. See chapter for answer.

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DIABETIC MACULAR EDEMA

Brijesh Takkar, Dhaval Patel

INTRODUCTION

Macular edema is important cause of decrease in vision in cases with diabetes mellitus (DM). Determination of diabetic macular edema (DME) is important for ophthalmologists for the early treatment and visual rehabilitation. DME is very frequently kept as short case or a spotter.

HISTORY

Chief Complaints

A known case of DM will give history of diminution of vision and other macular symptoms such as scotoma or distorted vision. The patient may also give history of inadequate control of the blood sugar levels, or recent fluctuation in blood sugar levels or even recent change in diabetic medication. Sometimes, DME may be picked up on routine diabetic screening without symptoms, especially when noncenter involving. Also such patients often present after referral by an endocrinologist with minimal visual symptoms.

Past History

In this condition, there should always be a parallel focus on the systemic features apart from a meticulous ocular workup. Past history of diabetes mellitus, hypertension, coronary artery disease, asthma, diabetic nephropathy should be recorded. Conditions such as pregnancy and dyslipidemias are other risk factors, and should always be carefully recorded. History of use of insulin and the type of antidiabetic drugs should be recorded as they influence macular findings and treatment outcomes.

Importantly, the record of past fundus examinations with grade of diabetic retinopathy recorded in last visits are essential.¹⁻³ If any treatment, e.g. Laser or intravitreal injections was given in past, then detailed record, including the number of setting of PRP, time since last panretinal laser photocoagulation (PRP), number of intravitreal injections given, should be noted.

Family History

Family history of DM should be recorded. It is essential to ask for family history because DM has familial inheritance. Each relative having

DM should undergo the fundus examination according to the type and duration since diagnosis.

EXAMINATION

Systemic Examination

Since DM is a disease affecting various systems of the body, detailed examination of cardiovascular, central nervous system, respiratory system, renal system, should be done to rule out any comorbidity associated with diabetic retinopathy DR.

Ophthalmic Examination

Uncorrected visual acuity and Best corrected visual acuity should be noted.

Eyeball may not show any specific finding. But it's not uncommon for a patient of DM to have cranial mononeuropathy. If such mononeuropathy is present, the patient will have corresponding squint.

Eye lids—blepharitis can be seen in patients of DM, lid edema may indicate nephropathy.

Conjunctiva does not show any specific finding, signs of dryness may be seen as a complication of neuropathy and chronic conjunctivitis may be present.

Cornea—diabetic neuropathy can lead to neurotrophic keratopathy. So assessment of corneal sensation is important. Dryness and epitheliopathy may be noticed on slit-lamp examination.

Anterior chamber and angle—neovascularization of iris (NVI) must always be ruled out.

Lens—status should be noted, since macular edema can be precipitated or aggravated by cataract surgery and may cause decrease in visual acuity. Snowflake cataract is typically seen in uncontrolled young diabetics.

Vitreous body should be examined for any hemorrhage, pigments. Asteroid hyalosis is a known association of DM and can preclude fundus examination.

IOP measurement is important to rule out glaucoma, open-angle glaucoma (OAG) is a known association.

Fundus Examination

Documentation of details of disc finding should be done, including the cup disc ratio, neuroretinal

rim, arteriovenous ratio, foveal reflex along with evidence of vitreomacular adhesion (VMA), retinal thickening, hard exudates, microaneurysms and soft exudates. One should perform a careful peripheral retinal examination for features of proliferative diabetic retinopathy (PDR) and slitlamp biomicroscopy examination is a must for classifying the macular edema (**Fig. 1**).

DIFFERENTIAL DIAGNOSIS

- Retina vein occlusion
- Ruptured macroaneurysm
- Irvine-Gass syndrome
- Radiation retinopathy
- Hypertensive retinopathy
- Subfoveal choroidal neovascularization.

CLASSIFICATION

- The diabetic retinopathy study (DRS) first gave the term DME. Later, the early treatment diabetic retinopathy study (ETDRS) defined clinically significant macular edema as presence of:
 - Retinal edema located at or within 500 µm of the center of the macula.
 - Hard exudates at or within 500 µm of the center if associated with thickening of adjacent retina.
 - A zone of thickening larger than 1 disc area if located within 1 disc diameter of the center of the macula.



Fig. 1: Fundus photograph depicting diabetic macular edema (DME). Hard exudates can be seen along with retinal thickening within the central area. Other signs of non-proliferative diabetic retinopathy (NPDR) can also be seen

To characterize the severity of macular edema and for treatment guidelines, the term clinically significant macular edema (CSME) is used.

- The international classification system classifies DME as mild, moderate or severe, depending on proximity of retinal thickening to the foveal center.
- Based on fundus fluorescein angiography (FFA), DME may be classified as focal, diffuse or ischemic.
- Recently, Diabetic Retinopathy Clinical Research (DRCR) network has classified it as a center involving (within 300 µm) and peripheral.

INVESTIGATIONS

Fluorescein Angiogram

The fluorescein angiogram (FA) is used to identify areas of increased vascular permeability, for example, leaking microaneurysms or capillary beds, and to evaluate retinal ischemia. Leakage on the angiogram does not necessarily indicate retinal edema since extracellular edema requires that the rate of fluid ingress into the retina (i.e., as indicated by leakage on the FA) exceeds the rate of fluid clearance from the retina (e.g. via the RPE pump).

CSME is further classified into *focal* or *diffuse*, depending on the leakage pattern seen on the fluorescein angiogram (FA). In *focal* CSME, scattered points of retinal hyperfluorescence are present on the FA due to focal leakage. The source of this focal leakage are microaneurysms. It is hypothesized that leaking microaneurysms are cause of retinal thickening. Commonly, these leaking microaneurysms are surrounded by circinate rings of hard exudates. The exudates are lipoprotein deposits in the outer retinal layers.

In *diffuse* DME, areas of diffuse leakage are noted on the FA due to intraretinal leakage from a dilated retinal capillary bed and/or intraretinal microvascular abnormalities (IRMA), and/or (in severe cases) from arterioles and venules without discrete foci of leaking microaneurysms (**Fig. 2**). There may be associated cystoid macular edema. Cystoid macular edema results due to fluid accumulation, primarily in the outer plexiform layer.

Ischemic maculopathy (**Fig. 3**) in presence of large capillary nonperfusion (CNP) areas, macular

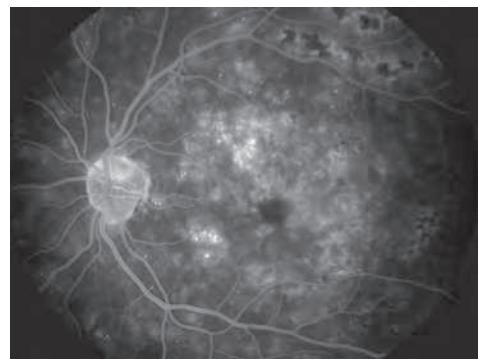


Fig. 2: Fluorescein angiography (FA) picture of diffuse diabetic macular edema (DME). Diffuse leaks with few scattered microaneurysms can be seen. Peripheral laser marks are also visible

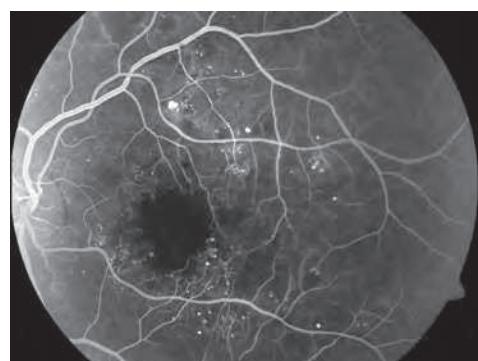


Fig. 3: Fluorescein angiography (FA) picture of macular ischemia. Distortion of FAZ with increased size is seen, irregular borders are accompanied by pruned vasculature

collaterals and foveal avascular zone (FAZ) changes like irregular shape, increased size with pruned arterioles.

Optical Coherence Tomography

The optical coherence tomography (OCT) has been used for high-resolution imaging of the retina and detection of increased retinal thickness (**Fig. 4**). There are several studies done for use of OCT in case of CSME. OCT can be used for measuring macular volume, determining central retinal thickness and determining the type of edema. Recently, distortion of inner retinal layers has been described for ischemic DME.

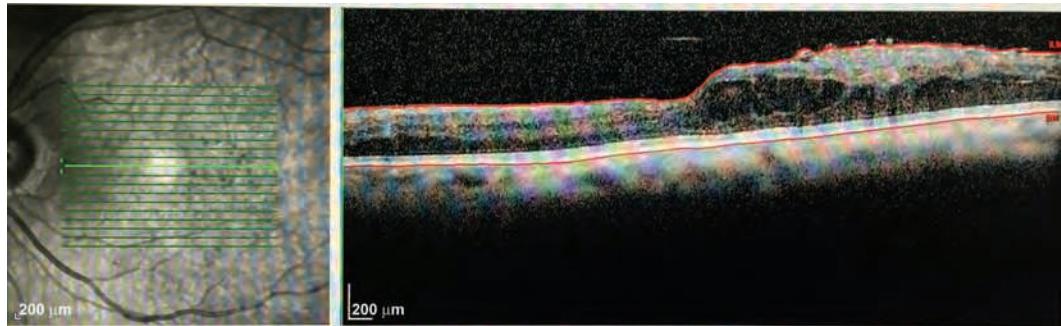


Fig. 4: Optical coherence tomography (OCT) picture of hemi-field DME.
Large cystoids spaces are visible in middle retinal layers

Hyper-reflective foci are also seen in DME. Choroidal thickness is under evaluation for DME with special focus on treatment-induced changes.

Patterns of OCT findings associated with CSME:

- Spongiform
- Cystoid
- Sensory detachment
- VMT
- TRD and mixed.

Macular thickness map is a specific protocol used for analysis of macular thickness on OCT that measures in 9 thickness sectors centered on fovea in 3 rings of diameter of 1, 3 and 6 mm.

Compared to clinical examination, OCT is a more sensitive and specific method for macular evaluation. It is an excellent tool for follow up and deciding treatment endpoints, prognosis and measuring response to therapy.

OCT has several advantages as a retinal imaging technique:

- It is noninvasive (no injection of dye involved) and well tolerated.
- It is highly sensitive and specific for retinal thickness measurement.
- It clearly reveals the presence and extent of vitreomacular traction.
- Other investigations like OCTA are useful for visualizing FAZ, microaneurysms, capillary density and choroidal changes.

Ultrawide imaging and VR interface enhancement with OCT is under investigation for use in DME. These are currently under investigation but are expected to play important roles in deciding treatment protocols soon.

Multifocal electroretinography (MFERG) and micropertimetry: These are more of research tools.

MANAGEMENT

Medical Therapy

This includes:

- Strict control of diabetes, hypertension, and hypercholesterolemia
- Diet modification
- Weight loss
- Exercise.

Controlling systemic parameters are extremely important. High-grade evidence in support has been given by DCCT, UKPDS, ACCORD and FIELD trials. The standard of treatment for CSME has been focal laser photoocoagulation in the days of ETDRS with 50% prevention of moderate visual loss at the end of 2 years (**Table 1**). Conventionally, In "focal" CSME, a focal laser pattern is used to treat leaking microaneurysms identified on the FA that contribute to the retinal edema. In 'diffuse' CSME, intraretinal leakage is noted on the FA from dilated retinal capillary beds or intraretinal microvascular abnormalities (IRMA) without isolated, discrete foci of leakage. Modified ETDRS macular grid laser was advocated for managing DDME (see **Table 1** for details).

Pharmacotherapy

Up till anti-VEGF intravitreal treatment came to the fore, laser was standard of care for managing CSME. While this still holds true for non-center involving DME, current evidence states that

Table 1 Different laser procedures for diabetic macular edema

Parameters	Focal laser	Classic grid laser	Modified grid laser
Wavelength	Argon Green, Double Frequency Nd:YAG		
Duration	100 ms		
Spot size	50 μ	50 μ	
Power	80 mw (Titrated according to requirement)	50 mw (Titrated according to requirement)	
Interburn distance	–	2 burns	
Intensity of burn	Grade 2–3 (dirty white)/ Blanching or darkening of microaneurysms	Grade 1–2 (Faint white)	
Area of laser	Based on FA findings and location of microaneurysms. Central ring is spared	Laser burns are given at 500 μ from the center of macula to all microaneurysm within 3000 μ	Laser burns are given at 500 μ from the center of macula in a C-pattern sparing papillomacular bundle. Can be done up to 2 DD from the center of macula
Follow-up	1-week, 1 month, 4-month (FFA)	1 week, 1 month, 4-month (FFA)	1 week, 1 month, 4-month (FFA)

intravitreal anti-VEGF provides more effective treatment for CSME than monotherapy with laser or steroid in center involving edema. This conclusion has been drawn from long-term results of a study from diabetic retinopathy clinical research (DRCR) network, which found monthly loading therapy with ranibizumab followed by as needed (also called *pro re nata* or PRN schedule) maintenance to have best results in center involving DME via a vis early laser, only laser and steroid injection. 5-year data has confirmed these results. Though repeated intravitreal injections have the financial constraints and obviously can lead to untoward ocular complications, the final visual acuity and macular anatomy is better than managing with laser monotherapy. As discussed above for ETDRS, laser chiefly halted moderate visual loss, but did not improve acuity. Triamcinolone injections have poorer results as well as more complications than anti-VEGF.

Other notable studies on anti-VEGF are READ, RISE, RIDE, BOLT, RESTORE and RESOLVE studies. Further, DRCR has analyzed afibercept for DME and found it to be useful in patients with worse initial visual acuity; da Vinci study is

another notable study. A newer analyzed drug is steroid implant-dexamethasone (BEVORDEX study) and flucinolone (FAME study). Basic advantage of implants is frequency of injections with noninferior results. Typically, they are useful in presence of hard exudates and may be for macular ischemia.

Combined Therapy

These therapies may be combined, the most fruitful example is combination of ranibizumab with deferred laser.

Surgical Management

Pars plana vitrectomy (PPV) for removal of VMT may be considered. The posterior hyaloid is removed along with any posterior cortical vitreous strands to the foveal edge and any visually significant epiretinal membrane. 50% of eyes will have reduction in central subfield thickness to <250 μm. As per the DRCR net study, only 28%–49% of such eyes will have improvement of visual acuity, and between 13% and 31% may have worsening of visual acuity. The

effectiveness of PPV for DME in the absence of VMT is unclear. ILM peeling has been evaluated as a treatment for chronic DME as well as primary treatment with differing outcomes.

Treating Refractory DME

Though no fixed definition is quotable, commonly used dictum is failure of response to therapy with multiple anti-VEGF and, at least, one sitting of laser. The available options for management include checking diagnoses, checking systemic control and ruling out anatomical causes. Steroids, higher frequency or dosing of anti-VEGF, change in anti-VEGF drug peripheral laser, surgery and newer molecules like tyrosine kinase based therapies (TIME study), angiopoietin and AGE inhibitors may be tried.

Managing Macular Ischemia

Outcomes remain bad. Often these patients have poor systemic control. Lasers and anti-VEGF are relative contraindications in presence of ischemia. These patients may benefit from peripheral laser and steroids/implants.

Pseudophakic ME and DME

Differentiation may be difficult, presence of microaneurysms typically indicate DME while late disc stippling indicates Irvine Gass syndrome.

In patients with DME, simultaneous treatment with intravitreal injections is indicated for prevention of exacerbation following cataract surgery.

VIVA QUESTIONS

Q.1. What is the basic pathogenesis of DME?

Ans. Breakdown of inner and outer blood retinal barrier, anatomical disturbance of the VR interface, blood flow changes like hyperviscosity and other changes like retinal neuropathy.

Q.2. Differentiate between different anti-VEGF agents.

Ans. See table of chapter on proliferative diabetic retinopathy (PDR).

Q.3. What are steroid implants used for DME management?

Ans. See Table 2.

Q.4. What was conclusion of ETDRS regarding DME?

Ans. ETDRS had defined CSME. It also defined moderate visual loss as loss of 15 letters or more, or doubling of visual angle, over 2 visits spread 4 months apart. ETDRS concluded that lasering CSME prevented moderate visual loss in 50% of patients till 2 years of follow up. Visual gain was however seen in roughly around 15% of the patients.

Table 2 Comparison of dexamethasone implant and fluocinolone acetonide

Parameters	Dexamethasone implant (Ozurdex)	Fluocinolone acetonide (Iluvien)
Formulation	Biodegradable implant	Non-biodegradable implant
Dose	0.7 mg	0.19 mg
Duration of action (months)	≤6	24–36
Efficacy (15-ETDRS-letter BCVA gain at 3 years)	18.4–22.2 (% patients)	28.7–27.8% (% patients)
IOP rise	34–36%	37–45%
Cataract	64–67%	81–88%
Incisional glaucoma surgery	0.3–0.6%	4.8–8.1%

Note: The values are from two studies FAME (Fluocinolone acetonide for macular edema) and MEAD (dexamethasone intravitreal implant in patients with diabetic macular edema)

Lower complication (in the range given in table) were associated with lower dose [i.e. Dexamethasone intravitreal implant 0.35 mg vs 0.7 mg; fluocinolone acetonide low-dose intravitreal implant (0.2 µg/day vs 0.5 µg/day)]⁴

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EPIRETINAL MEMBRANE

Dhaval Patel, Brijesh Takkar

INTRODUCTION

An epiretinal membrane (ERM) is a sheet-like fibrocellular structure that develops on or above the surface of the retina. Epiretinal membrane (ERM) can be given as a short case or spot case for ophthalmoscopy examination.

HISTORY

Chief Complaints¹

- *Loss of vision:* Ranges from no symptoms at all to severe visual dysfunction, usually progressive and painless.
- Metamorphopsia is common; due to distortion of the sensory retina.
- Early stages hamper monocular function, while late stages cause binocular disturbance also.
- Patients with idiopathic ERM may also give history suggestive of acute posterior vitreous detachment (PVD) in recent past preceding the ERM related symptoms.

Past History

A careful past history can often point towards the probable underlying cause. Following things must be recorded carefully:

- Trauma
- Previous retinal tears
- Retinal detachment
- Retinal vascular occlusive diseases
- Ocular inflammatory diseases

- Vitreous hemorrhage
- Diabetic retinopathy.

Past Surgical History

- Previous history of intraocular surgery may or may not be present
- Photocoagulation or cryotherapy can also be the cause for ERM.

EXAMINATION

Ocular Examination²

- Uncorrected and best corrected visual acuity (UCVA and BCVA) should be recorded, Amsler grid or M charts may be used to document metamorphopsia.
- Anterior segment examination can often be normal. Signs of previous intraocular surgery or trauma or inflammation must be examined carefully.
- *Vitreous:*
 - Posterior vitreous detachment (PVD) is present in the most eyes (75 to 90%) with idiopathic ERMs, although it is not a prerequisite.
 - Signs of degenerative vitreous may be seen.
- *Fundus:*
 - An irregular or glistening light reflex from the retinal surface may be the only sign in asymptomatic patients, similar to cellophane maculopathy (**Fig. 1**).



Fig. 1: Fundus photograph of early stage ERM with minimal distortion of retinal vessels. Absence of signs of chronicity and retinal distortion indicate good prognoses



Fig. 2: Thick mature epiretinal membrane (ERM). Gross distortion of retina and pigmentary changes are visible. Such membranes ensue poor prognosis

- In more advanced cases, in symptomatic patients with actual contraction or shrinkage of the membrane, distinct retinal findings can be appreciated, such as retinal striae radiating from the center of the ERM, retinal vessels straightened toward the membrane center, or tortuosity of retinal vessels and dilated retinal veins (**Fig. 2**). Wrinkling of the retina may be noted.
- Pigmentary changes indicate chronicity of the disease with poorer prognoses
- A pseudohole can also be there.
- Peripheral examination should always be done for retinal breaks.
- Gass Grading System is useful in describing the clinical findings
 - ♦ *Grade 0:* Cellophane maculopathy—an irregular translucent sheen is present in early ERM, best detected using green (red-free) light.
 - ♦ *Grade 1:* Crinkled cellophane maculopathy—membrane thickens and contracts, becomes more obvious and causes mild distortion of blood vessels
 - ♦ *Grade 2:* Macular pucker—distortion of blood vessels, marked retinal wrinkling and striae and obscuration of underlying structures.

DIFFERENTIAL DIAGNOSIS

- *Vitreomacular traction (VMT):* OCT and careful 90D examination can rule out VMT, though both may be present simultaneously.
- *Cystoid macular edema (CME):* Presence of cystic spaces and absence of characteristic distortion of blood vessels helps in differentiating this entity.
- *Macular hole or pseudohole:* Watzke-Allen test and red beam test and in doubtful cases OCT can differentiate this entity.

INVESTIGATION

Following investigative modalities are useful in ERM.

Ocular Coherence Tomography

- By far, the modality of choice.
- Ocular coherence tomography (OCT) provides good visualization of the vitreoretinal juncture and shows the membrane on the retinal surface as a hyper-reflective structure (**Fig. 3**).
- Ocular coherence tomography (OCT) also may play a role in preoperative and postoperative evaluation of surgery for ERMs by indicating prognostic markers.
- It also helps in differentiating detaching vitreous cortex from ERM, differentiating pseudoholes and true lamellar holes.

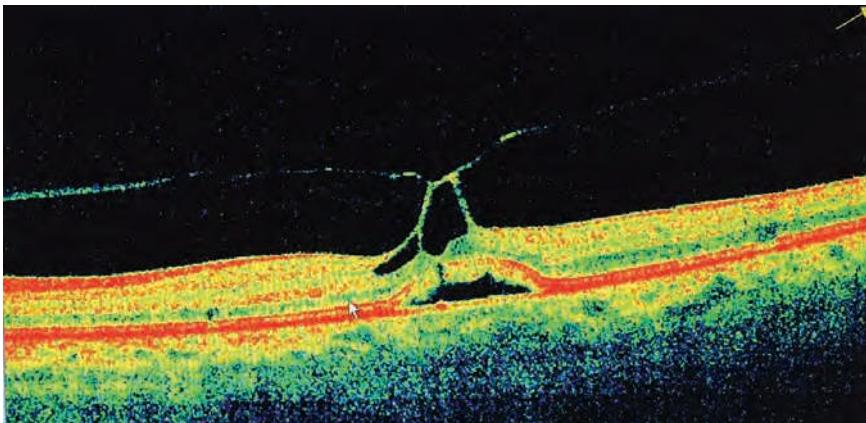


Fig. 3: Ocular coherence tomography (OCT) picture of vitreomacular traction (VMT) with fine epiretinal membranes (ERM). An impending full thickness macular hole is visible

- Disruption of the outer most hyper-reflective bands, previously termed IS-OS junction, may be associated with a worse visual outcome following surgery. However, recent focus for prognostication is now shifting towards the inner retinal layers.
- Enhancement of the VR interface by vitreous windowing helps in studying it on detail using OCT.
- *Secondary associations:*
 - Vascular disease (diabetic retinopathy, CRVO)
 - Inflammatory disease (posterior uveitis)
 - Trauma
 - Retinal surgery (RD surgery, laser photocoagulation, cryotherapy)
- *Iatrogenic*
 - *Postoperative:* Cataract/Retinal detachment/Silicone oil/Retinopexy/Laser or cryotherapy.

Fluorescein Angiography

- Not required routinely.
- Anatomic features of retinal distortion may be better seen on FA, such as straightened retinal vessels, retinal vascular tortuosity, foveal ectopia, and macular dragging.
- Fluorescein leakage and macular edema secondary to ERM traction-induced vascular leakage also may be assessed.
- One of the important role of FA is to detect the presence of other retinal pathology, such as a choroidal neovascular membrane (CNVM).

CLASSIFICATION

The different classification systems used for ERM are as follows.

Standard Classification

- *Idiopathic:*
 - Age-related/PVD related
 - Up to 20% are bilateral

Gass clinical grading system: It has been described in the examination section.

Foos Classification

- *Simple ERM:* Incidental without contraction features or associated ocular disease.
- *Intermediate ERM:* Thicker than simple ERMs and contain contraction features and pigment.
- *Complex ERM:* Present after retinal detachment surgery or after trauma and may be secondary to other ocular conditions. Traction retinal detachments may develop as a result of contraction of such membranes.

International vitreomacular traction study (IVTS) Group optical coherence tomography (OCT)-based anatomic classification system for diseases of the vitreomacular interface (VMI) has been described in **Table 2** of chapter on macular hole.

Other classification systems based on OCT and confocal scanning laser ophthalmoscopy (CSLO) are also notable, but not in common clinical use.

MANAGEMENT

The management options for ERM has been described below:

Observation: It is always advisable to have a short period of observation before embarking upon surgery. In early stages with good visual acuity (e.g. better than 6/12), absence of visually disturbing symptoms and if membrane is nonprogressive observation is the rule. Spontaneous resolution of symptoms can occurs, due to separation of the ERM from the retina as a previously incomplete PVD completes and also some times in secondary cases.

Medical management with enzymatic vitreolysis: Use of ocriplasmin (microplasmin) has been described by MIVI-TRUST trials. In this trial 27% vitreomacular adhesion (VMA) resolved as compared to 10% in placebo. But given the expenses and nonavailability is currently not preferred.

Surgical intervention with pars plana vitrectomy and epiretinal membrane peeling: Indications for surgery:³

- High visual requirements (occupation, young age)
- VA < 20/60
- Associated CME or tractional detachment.

Whether internal limiting membrane (ILM) peeling should be combined with ERM removal or not is controversial, one of school of thought indicates lesser recurrences while the other is based on neuronal damage caused by the ILM peel itself. Intraoperative OCT is now commercially available and may be seen to have a greater role in future (PIONEER study). Long-term results, up to 5 years, have revealed low recurrence rates with ILM peeling but with associated progressive thinning of regional macular thickness. See the chapter on macular hole for discussion on surgical technique and vital dyes.

VIVA QUESTIONS

Q.1. How do epiretinal membranes (ERM) develop?

Ans. A dehiscence of the internal limiting membrane allows retinal glial cells [predominant cellular constituent, probably derived from the indigenous posterior hyaloid membrane (PHM) cell population (laminocytes), myofibroblasts and fibroblasts] to proliferate along the retinal surface. Contraction of these membranes causes cellophane maculopathy or macular pucker. Detachment of the posterior vitreous is present in almost all eyes. PVD may be responsible by inducing micro-retinal breaks.

Q.2. What is the chance of recurrence after surgery?

Ans. Recurrence of the membrane after PPV is uncommon. Reported recurrence rates are low, with visually significant recurrences up to 5%.

Q.3. What is VMA?

Ans. As per definition, it refers to largely attached cortical vitreous with some areas of detachment not causing retinal structural changes. In contrast, VMT causes tractional disturbance in the retinal architecture and in presence of symptoms it termed VMT syndrome. VMA is more likely to have a smooth contour rather than ERM. The terminology and classification system for different diseases of the vitreomacular interface (VMI) has been described in **Table 2** of chapter on macular hole.

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FUNDAL COLOBOMA

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INTRODUCTION

Coloboma (plural-colobomata) is derived from Greek word “koloboma” meaning mutilated or curtailed. Walther introduced term “coloboma”. Coloboma of the fundus is a congenital ocular malformation, which generally results from failure of the fetal or choroidal fissure to close during 5th to 7th week of fetal life, at 7–14 mm stage. This is the period between the invagination of the optic vesicle and the closure of fetal fissure. Closure starts at the equator of eye/ciliary body region and continues anteriorly and posteriorly. A coloboma may extend from the iris margin to the optic disc and involve one or more defects along line of fusion. Any ocular structure can be involved including cornea, iris, ciliary body, zonules, choroid, retina and optic disc or optic nerve.¹⁻³

Coloboma can be unilateral or bilateral, the latter being seen in 60–70% of cases. Bilateral colobomas are usually inherited in an autosomal dominant fashion with variable penetrance. Recessive inheritance has also been reported. If fetal fissure fails to close posteriorly, then a coloboma affecting the retinal pigment epithelium, neurosensory retina or choroid may occur. Typical coloboma occurs in the inferonasal quadrant. There can be associated with apparent lens coloboma due to persistence of mesodermal vascular remnants that prevent development of zonules in that area leading to flattening of the lens edge. Mutation in *PAX6* gene has been reported in association with syndromic forms of colobomata.

HISTORY

Chief Complaints

Usual history is of a child or young adult presenting with diminution of vision for distance. In some cases, parents may present complaining about small size or different shape of eye. Sometimes presence may be noted only at time of complications like cataract or retinal detachment (RD).

Presenting Complaints

The visual loss is typically painless detected on routine examination in a child or suddenly due to its complications. This would vary from cases to case. In severe cases, the child may present with nystagmus, microphthalmos or even inability to follow objects. With concomitant iris defects, the presentation may be for cosmetic reasons. In peripheral colobomas, the visual acuity is spared but other complications may be the cause of presentation.

Past History

This is rather necessary as syndromic association is well-defined and actually may even be the reason for presentation. Typical syndromes have been discussed later.

Family History

Analysis of pedigree charts is mandatory to identify inheritance patterns. Genetics has been discussed later in the chapter.

EXAMINATION

Visual Acuity

Varies depending on the type and laterality of coloboma. Peripheral colobomas sparing macula usually have good visual acuity than those involving macula. Similarly, unilateral colobomas may have accompanying refractive error that may lead to anisometropic amblyopia with consequent poor visual acuity, even when macula is spared.

Motility and Eyeball

Usually, not associated with ocular motility defects. Unilateral cases may have history of long standing squint. Nystagmus/nystagmoid movements may be noted. Microphthalmos may also be seen.

Lids and Conjunctiva

Usually, unaffected unless in syndromic association.

Cornea

Usually pear shaped in cases with iris involvement.

Iris and Pupils

“Key hole” pupil due to associated Iris coloboma (**Fig. 1**). Iris coloboma may be typical/atypical, complete/incomplete/partial/total.

Lens

There can be nuclear sclerosis of varying degree with associated cortical component, with associated zonular coloboma inferiorly (**Fig. 2**). True lens colobomas are rare, albeit to surface ectoderm origin of the lens vis-a-vis the coloboma.

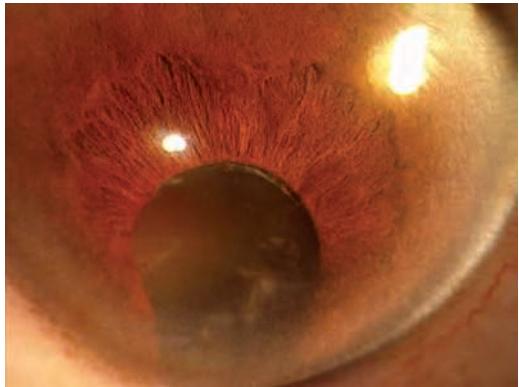


Fig. 1: “Key hole” pupil due to associated Iris coloboma

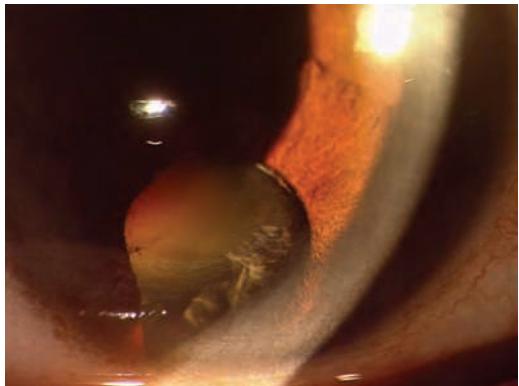


Fig. 2: Nuclear sclerosis with associated zonular coloboma inferiorly

Intraocular Pressures

Usually normal, can be low in cases of RD or thigh in those associated with glaucoma.

Fundus Examination⁴⁻⁶

Following findings must be noted:

- On ophthalmoscopic examination, the white background of the sclera usually showing a glistening white sheen replaces normal color of the fundus (**Fig. 3**).
- Typically, coloboma is oval.
- Usual location is downwards and inwards.
- Posterior end frequently stops short of the disc (see classification later).
- Anterior end sometimes reaches forwards beyond the limits of ophthalmic examination, due to involvement of the ciliary body region as well.
- Sometimes the defect can be relatively small, round, or transversely oval, or several isolated defects can be scattered along the line of fissure.
- Edges are usually cleanly cut and frequently pigmented.
- Floor of the coloboma is usually depressed below the level of the rest of the fundus.
- Two types of vessels can be seen, retinal vessels that dip down into the coloboma as they pass from the normal fundus and choroidal vessels, more tortuous and broader lying at a deeper level (**Fig. 4**).



Fig. 3: Fundal coloboma with sparing of disc and macula (Type 3 coloboma)

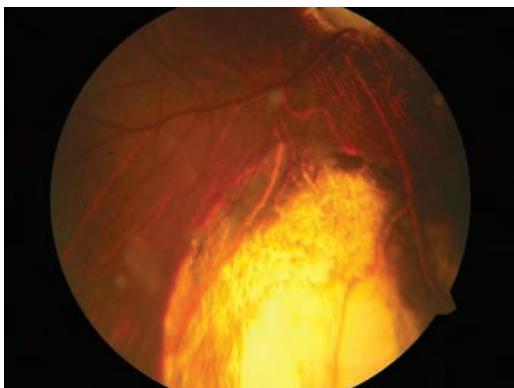


Fig. 4: Choroidal excavation in the area of the coloboma with overlying retinal vessels

Macular colobomas are atypical coloboma; with causation different from that of the choroidal coloboma. Peripheral examination must be conducted for presence of peripheral retinal breaks and retinal degenerations. Scleral depression may be necessary for areas not visible to the eye as such. One must look for retinal breaks at the edge of the coloboma also. While total RD may be seen, sometimes it is present only in the colobomatous area.

DIFFERENTIAL DIAGNOSIS

Choroidal colobomas may be confused with infective conditions like toxoplasmosis in macular cases and Zika virus infections in predisposed patients. Pathological myopia may also have staphylomas with scleral ectasia giving false appearance of a coloboma. Causes of large chorioretinal atrophy areas should also be kept in mind (also see viva questions).

INVESTIGATIONS

Systemic investigations should be done for syndromes as applicable. Genetic tests may also be needed. In hazy media, ultrasonography (USG) is necessary for charting the coloboma and identifying RD. Although not compulsory, OCT, with its enhanced penetration, is a handy adjunctive investigation, which is currently more of a research tool. It helps in identifying retinal breaks, examining changes at the edge of

coloboma, though still not advocated for routine clinical use. VER may have a prognostic value and be useful in surgical decision making in long standing cases of RD.

MANAGEMENT

Amblyopia

Uniocular coloboma not involving the macula can be associated with refractive errors that need prompt correction to avoid development of amblyopia. In cases with bilateral coloboma, severe refractive errors may lead to ametropic amblyopia. Such cases, again, are good candidates for correction of refractive errors.

Family and Genetic Screening

Some cases of coloboma may be associated with genetic variations. Family history, including close relatives may be helpful in identifying such cases. Genetic screening and genetic counseling in such cases may help. Other associated anomalies arising due to the defective genes may be picked up in unsuspecting family members that may be amenable to treatment.

Retinal Detachment

Retinal detachment is a known and frequent complication of choroidal colobomas. Colobomas may present with different forms of retinal detachments (see Viva questions). Prophylactic role of laser photocoagulation to coloboma edges is proven effective in decreasing chances of retinal detachment. Laser photocoagulation may be performed at the earliest possible time. Surgery for retinal detachment usually involves pars plana vitrectomy, endolaser photocoagulation and silicone oil tamponade. Most of the cases have a retinal break in and around the edge of the coloboma. Use of an encircling element is controversial, though, may be advocated in cases with significant proliferative vitreoretinopathy. These cases usually have poor surgical outcomes after silicone oil removal with high re-detachment rates that may necessitate long-term oil tamponade and oil exchanges instead of removal to maintain retinal attachment. Buckling surgery has poor outcome in cases where the primary break is in

the colobomatous region. It may be used in cases where a peripheral primary break is causative.

Cataract

Earlier onset of cataract is a known finding in colobomas. Most common type of cataract detected is nuclear sclerosis, being seen in almost half of cases. A distinct type of linear cataract may also be seen in the area of coloboma. As these eyes may be associated with microphthalmos and microcornea, different surgical techniques such as scleral tunnel phacoemulsification have been advocated in such cases. Use of capsular tension rings to stabilize the area of coloboma has also been described. Implantation of intraocular lens in cases with apparent small eye is aided with ultrasound biomicroscopy to measure the sulcus size.

Choroidal Neovascularization

Though rare, development of choroidal neovascularization developing at the edge of the coloboma has been described in literature. Use of both photodynamic therapy and anti-VEGF agents have been described in such cases.

VIVA QUESTIONS

Q.1. What is the embryological defect in a case of coloboma?

Ans. Following points must be remembered:

- Cranial end of differentiating CNS forms neural folds
- Optic pits appear at 21 days of life, on each side of neural groove
- Optic grooves (recognizable by 4 weeks) in neural folds
- Neural ectoderm evaginates from each groove towards surface (recognized by 25th day) as optic vesicles.
- Optic vesicle is connected to forebrain by optic stalk.
- Surface ectoderm overlying optic vesicle thickens forming lens placode - lens pit - lens vesicle.
- Optic vesicle invaginates forming double layered optic cup; lens vesicle gets pinched off by 4th week, lies in the optic cup.

- Margins of the optic cup do not grow over inferior part of the lens, showing a deficiency in this part known as choroidal/fetal fissure (usually closes by 6th week, failure to close by 6th to 7th week results in typical coloboma).
- Outer layer of the optic cup forms retinal pigment epithelium, inner layer forms neurosensory retina.

Q.2. What are the various types of coloboma?

Ans. The different types are as follows

Iris coloboma

- Typical/atypical iris coloboma
 - *Typical coloboma* is in the inferonasal quadrant as this is the site of closure of embryonic fissure
 - *Atypical coloboma*: Located anywhere other than inferonasal quadrant
- Complete/incomplete iris coloboma
 - *Complete coloboma*: Full thickness defect involving both pigment epithelium and iris stroma.
 - *Total*: Extending to iris root (keyhole pupil)
 - *Partial*: Involving pupillary margin (oval pupil)

- *Incomplete coloboma*: Partial thickness defect involving either pigment epithelium or iris stroma.

- Wedge shaped
- Demonstrated by transillumination

- Lens coloboma—misnomer as it is actually zonular coloboma that manifests as flat lens surface visible through pupillary defect.

- Posterior segment coloboma—retinochoroidal coloboma
- Optic nerve coloboma

Lid colobomas have been discussed in relevant chapter. They should not be confused with ocular coloboma as involved embryonic layers are different.

Q.3. What is the pathophysiology of choroidal coloboma?

- Ans.**
- In eyes with defective closure of fetal fissure, inner layer destined to form neurosensory retina grows faster than outer layer destined to form retinal pigment epithelium, leads to eversion.

- Gradual displacement of retinal pigment epithelium, leading to development of double layer of photoreceptors facing each other.
- Absence of retinal pigment epithelium.
- Since choroid development is influenced by retinal pigment epithelium, choroid is absent in areas of coloboma.

Q.4. What is the histopathology of coloboma and colobomatous border?

Ans. *Histopathology of coloboma:*

- Sclera is thinned by loss of its inner layers, ability for ectasia increases.
 - Absence of choroid and choriocapillaries
- Hermann Schubert, described the histopathology of the colobomatous border:*
- Retina splits into two layers near the margin of the coloboma. The split in the layers of the retina has been identified at the level of inner nuclear or outer plexiform layer or both.
 - The inner layer continues as the *intercalary membrane* onto the coloboma, while the outer layers turn back, become disorganized, and fuse with the retinal pigment epithelium.
 - The choroid is terminated as a distinct pigmented layer peripheral to the point of reversal. The junction where this reversal occurs has been termed "*locus minoris resistentiae*".
 - The intercalary membrane progressively becomes thinner as it is traced centrally.

Q.5. What are the various systemic associations with coloboma?

Ans. There are many syndromes, decreasing the specificity of coloboma as an association. For example,

- *CHARGE syndrome:* Colobomatous microphthalmos, heart defects, atresia (choanal), retarded growth, genital anomalies, and ear anomalies.
- *AICARDI syndrome:* Retinal cystic dysplasia, occipital encephalocele, polydactyly, pulmonary hypoplasia.
- *WARBURG syndrome:* Hydrocephalus, agyria, retinal dysplasia.
- Goltz syndrome

- Basal cell nevus syndrome
- Meckel-Gruber syndrome
- Trisomy 13 (patau), 18 (Edward)
- 13 q deletion syndrome
- Cat eye syndrome, Rubinstein-Taybi syndrome.
- Posterior fossa malformations hemangiomas-arterial anomalies-cardiac defects-eye (PHACE) syndrome.

Q.6. Differential diagnosis of various colobomata.

Ans. *Iris coloboma*

- Iatrogenic—postsurgery
- Traumatic—open globe injury
- Congenital—sporadic, familial, syndromic.

Choroidal coloboma

- *Retinal scars:* Toxoplasma, toxocara
- *Congenital anomalies:* Torpedo maculopathy, staphyloma

Disc coloboma

- Excavated disc anomalies: Coloboma, morning glory syndrome, peripapillary staphyloma, optic disc pit.

Q.7. What are the various classifications of fundal coloboma?

Ans. See Tables 1 and 2.

Q.8. What is incidence of retinal detachment in patients with coloboma?

Ans. Incidence of rhegmatogenous retinal detachment in patients with retinochoroidal coloboma is 23–40%.

Q.9. What are the various locations of retinal breaks in coloboma?

Ans. Breaks can occur at two locations:⁷

- At the locus minoris resistentiae
- In the intercalary membrane:
 - 63.8% of breaks are located within 2 disc diameter (DD) of the margin of coloboma and rest in the central portion of the coloboma.
 - 54.1%—breaks at margin
 - 24.7%—within coloboma
 - 8.2%—macula

Various clinical situations depending on the combination of the breaks:

- Break at the locus minoris resistentiae only—cannot lead to retinal detachment.

Table 1 Ida Mann classification

I	Above the disc
II	Superior border of the disc
III	Below the disc (separated from the optic disc by normal narrow area of retina)
IV	Isolated disc coloboma (inferior crescent below the disc)
V	Peripheral with normal retina above and below (isolated gap in the line of fissure)
VI	Pigmentary disturbance
VII	Extreme peripheral coloboma

Table 2 Lingam Gopal classification (1996); Types of optic disc involvement in fundus coloboma

I	Disc outside the fundus coloboma and totally normal (27.8%)
II	Disc outside the fundus coloboma and abnormal (10.4%)
III	Disc outside the fundus coloboma and independently colobomatous (8.9%)
IV	Disc within the fundus coloboma and normal (5%)
V	Disc within the fundus coloboma and colobomatous (44.3%)
VI	Disc shape not identified; blood vessels emanating from superior aspect of the large fundus coloboma

Note: High myopia is more common in types I-III with better visual acuity. Microphthalmos is more common in types IV-VI.

- Break in the intercalary membrane only—detachment of intercalary membrane only.
- Break in both intercalary membrane and the locus minoris resistentiae—leads to clinical retinal detachments.
- Breaks in the normal peripheral retina alone—the retinal detachment will be seen to stop short of the colobomatous border.
- Breaks in the peripheral retina and the locus minoris resistentiae but no break in the intercalary membrane—the retinal

detachment will be seen to extend into the colobomatous area.

- Breaks in peripheral retina, locus minoris resistentiae, intercalary membrane—total retinal detachments.

Q.10. Why is it difficult to localize breaks in colobomatous area?

Ans. It is difficult to localize breaks in colobomatous area because of:

- Little contrast in colobomatous area due to absence of choroid and RPE
- Thinned out retina
- Nystagmus
- Ectatic sclera.

Q.11. What is the pattern of retinal breaks and detachments in coloboma?

Ans. • *Type I:* Retinal detachment does not extend into coloboma.

- *Type II:* Retinal detachment extends into coloboma to a variable extent with or without retinal detachment outside coloboma.
 - *II A: Subclinical*—Restricted to coloboma.
 - *II B:* Visible break within coloboma.
 - *II C:* Visible break both within and outside coloboma.
 - *II D:* Break only in peripheral retina.
 - *II E:* Break not visible.

Q.12. What are the causes of low vision in coloboma?

Ans. Following can be the causes:

- Refractive error
- Subluxated lens
- Optic disc anomalies
- Macular involvement
- Retinal detachment
- Cataract
- Choroidal neovascular membrane.

Q.13. What are the various complications associated with retinochoroidal coloboma?

Ans. Complications:⁸

- Retinal detachment
- Cataract/lens subluxation
- Amblyopia
- Anisometropia
- Sensory strabismus
- Subretinal neovascularization
- Secondary glaucoma.

Q.14. What is the management of retinal detachments in retinochoroidal coloboma?

Ans. It includes following:

- Prophylactic laser photocoagulation posteriorly along the edge of the coloboma for prevention of detachment.
- Proper localization of breaks—if breaks are outside the coloboma with an RD not extending into coloboma than buckling surgery may be indicated.
- Vitrectomy—for all retinal detachments where breaks are at the margin or inside colobomatous region.

Q.15. Role of prophylactic laser photocoagulation in fundal coloboma.

Ans. Reduces the incidence of rhegmatogenous retinal detachment. A recent study⁸ highlighted the importance of prophylactic laser in coloboma for prevention of retinal detachment. They reported prevalence of retinal detachment to be 2.9% in laser treated eyes compared with 24.1% in untreated eyes with a total prevalence of 17.9%.

Q.16. Which laser is preferred?

Ans. Diode laser is preferred over argon because of less damage to retinal nerve fiber layer owing to deeper penetration. Currently frequency doubled Nd:YAG (532 nm) green laser is laser of choice for all retinal photocoagulation.

Q.17. How are various types of coloboma lasered?

Ans.

- **Type 1 (Ida Mann):** Laser spots are applied initially along the superior margin of the coloboma and then continued along the whole nasal margin. Temporal margin is lasered inferior to the presumed inferotemporal vascular arcade and superiorly up to the superotemporal arcade sparing the macula.
- **Type 2 (Ida Mann):** Laser spots are applied starting from nasal to the optic disc. The nasal margin is lasered. Temporally, laser is performed inferior to the presumed inferotemporal vascular arcade.

- **Type 3 (Ida Mann):** Margins of the coloboma is lasered sparing the area within the temporal vascular arcade and nasally up to 0.5 mm from the disc.
- **Type 5 (Ida Mann):** Coloboma is surrounded by three rows of laser.

Q.18. Why is buckling difficult in retinochoroidal coloboma?

Ans. External buckling is difficult in retinochoroidal coloboma because of:

- Difficulty in identifying breaks in intercalary membrane.
- Impossibility of creating adhesion around breaks due to absence of choroid and retinal pigment epithelium.
- Posterior location of breaks.

Q.19. Why is PPV preferred?

Ans. Pars plana vitrectomy is preferred because of:

- Ease of identifying breaks in the intercalary membrane with more certainty.
- Removal of traction
- Closure of breaks or sealing off colobomatous regions with laser retinopexy.

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GIANT RETINAL TEAR

Shipra Singh, Brijesh Takkar

INTRODUCTION

A giant retinal tear (GRT) is a full-thickness neurosensory retinal break that extends circumferentially around the retina for three or more clock hours. It accounts for around 1.5% of rhegmatogenous retinal detachments (RRD). Most GRTs are idiopathic (55–66%). The most common predisposing factors for the development of a GRT are trauma (4–31%), hereditary vitreoretinopathies (14.5%), and high myopia (9.7%).¹ It can be given as a short case in postgraduate exams.

HISTORY

Epidemiology/Demography

Giant retinal tear (GRTs) have a significant male preponderance, between 65% and 91%. The mean age of patients ranges from 30 to 53 years of age. Right eyes appeared to be more frequently affected, with most studies reporting a right eye incidence of 48% to 67%. GRTs have been estimated to be the cause of the RD in 0.5–8.3% of cases in adults. In contrast, in the pediatric population (16 years or younger), the prevalence is higher and is between 18% and 31.7%.¹

Chief Complaint

The patient usually presents with sudden loss of vision in eye, flashes, floaters, and photopsia. It may be associated with dull ocular pain due to inflammation.

History of Present Illness

The sudden loss of vision in eye is commonly associated with floaters; presentation can be unilateral or bilateral. It may be rapidly progressive. History of associated trauma or use of high power glasses must be recorded in such cases.

History of Past Illness

Past history of trauma, cryo may be there. There may be history of recent ocular surgery like scleral fixated intraocular lens (SFIOL) or phakic

intraocular lens (IOL) in an already predisposed patient.

Family History

Family history may be there (Marfan's, Stickler, Ehlers Danlos syndrome).

Past Surgical History

Past history of intraocular surgery may be there. Conventionally, GRTs would be found at the edge of heavy cryo burns.

EXAMINATION

Systemic Examination

Giant retinal tear (GRT) may be associated with Wagner, Stickler, and Marfan syndrome.

Ocular Examination

Visual acuity: Visually, acuity is commonly very low with inaccurate PR in large GRTs due to massive receptor dysfunction, especially in displaced flaps.

Eyeball: Eyeball may appear large in high myopic patient.

Lid: Lids are generally normal except signs of previous trauma such as scar.

Conjunctiva: Conjunctiva is generally normal.

Cornea: It may be large and corneal thinning may be there (Myopia).

Sclera: Scleral thinning may be there (blue sclera in collagen vascular disease). Globe tenderness can be elicited in presence of inflammation.

Anterior chamber (AC): AC may be deep in high myopic eyes. AC inflammation is frequent in cases of GRT.

Iris: Iridodialysis or atrophy may be there in cases of previous trauma.

Pupil: An eccentric pupil may be there in Marfan's syndrome.

Intraocular pressure (IOP): There is usually hypotony in cases of GRT. This is a characteristic feature of GRTs and is observed due to rapid egress of fluid via the exposed choroidal circulation.

Gonioscopy: Angle recession or cyclodialysis may be there in case of trauma.

Lens: Lens may be subluxated or dislocated. Zonular dialysis may be there. Phacodonesis may be present there in cases of Marfan's syndrome or Ehlers-Danlos syndrome or trauma. When the tear involves retina with patent vasculature, vitreous hemorrhage may develop.

Anterior vitreous: There may be presence of vitreous pigments (Shaffer's sign) or hemorrhage. Shaffer's sign/tobacco dusting is seen in virtually all patients with GRT.

Fundus: To examine retina in cases of displaced flaps (**Fig. 1**), patient positioning may be adjusted accordingly (*Note:* In virtually all patients with a GRT, the tear is either partially or completely inverted. The posterior flap of the tear may invert over the optic disc or even the whole macula, making it difficult to assess the full extent of the associated RD. For inverted and mobile GRT, positioning of the patient appropriately may unfold the tear, facilitating a more accurate examination). Choroidal detachment and multiple tears are very common. Following points must be noted:

- Vitreous syneresis/liquefaction, posterior vitreous detachment (PWD)



Fig. 1: Intraoperative photograph of a GRT stabilized partially with PFCL. Note the large flap of the retinal tear that has fallen over the retina. Underlying bare choroid is also visible

- Extent of tear (in degrees or clock hours), location of tear (posterior, equatorial or anterior)
- Lattice or other degenerations
- Proliferative vitreoretinopathy (PVR)/macular pucker (*Note:* PVR is a well-recognized feature of GRTs. The large surface area of exposed RPE increases the propensity for the liberation of RPE cells and subsequent PVR)
- Retinal detachment; extent of retinal detachment (total or subtotal), retinal tear flap if displaced or mobile.

Fellow eye must be examined carefully to look for myopic changes, lattice, vitreous condensation, white without pressure (WWOP) changes, retinal breaks, giant retinal tear and retinal detachment. Up to 50% of fellow eyes may be predisposed to RD.

DIFFERENTIAL DIAGNOSIS

Giant retinal dialysis: A retinal dialysis is a circumferential retinal disinsertion at the ora serrata, frequently secondary to blunt trauma. The differentiating points are discussed in **Table 1**.

Table 1 Difference between GRT and GRD

Giant retinal tear	Giant retinal dialysis
Break may extend beyond the posterior limit of the vitreous base insertion	The break is located anterior to the posterior limit of the vitreous base insertion
Vitreous attached to anterior flap	Vitreous attached to posterior flap hence the tear is prevented from rolling over or inverting
PVD is usually present	PVD is usually absent
Massive preretinal vitroproliferation and macular pucker is present	PVR not massive, macular pucker is rare
Radial posterior tear extensions can be there	Absence of the radial posterior tear extensions
Vitreoretinal surgery is needed	Rarely needed; RD surgery is generally successful

Abbreviations: PVR, proliferative vitreoretinopathy; PVD, posterior vitreous detachment

INVESTIGATIONS

Ultrasonography (USG) is useful in presence of media haze precluding fundus evaluation. Ultrawide image documentation may be considered. Systemic diseases should be screened in cases of GRT.

MANAGEMENT

It should be aggressive. One may consider pre-operative local steroids if delay is expected. Traditionally, primary scleral buckling and buckle pneumatics have been considered for early GRT. Vitrectomy is now generally preferred. In the pre perfluorocarbon liquids (PFCL) era, prone position fluid-air exchange and retinal tacks have been used. PFCLs have over all revolutionized typically a GRT-RD surgery by acting as the "Third hand". Management of GRT depends on the extent and associated PVR changes.²

Conventional Protocol

- *GRT without displacement:* Treatment is by either cryopexy or laser (contiguous and at edge of tear reaching up to or at edge)
- *GRT with displacement, mobile post flap:*
 - Extent <180°—Scleral buckling (DACE)
 - Extent ≥ 180°—Vitreoretinal (VR) surgery
- *GRT with everted/rolled up posterior retinal flap with or without star folds/macular pucker:*
 - Treatment—vitreoretinal surgery.

Other Indication of Vitreoretinal Surgery

- Opaque media (lenticular opacity, vitreous hemorrhage)
- Retained intraocular foreign body (RIOFB)
- Retinal and vitreous incarceration (trauma).

It should however be remembered that in today's era, vitrectomy is generally preferred for GRT related RD.

Role of silicone oil: Generally, preferred except in early stages. Silicon oil restores and holds flap in position until the time retinopexy occurs. It also counters the occurrence of postoperative PVR.

Role of perfluorocarbon liquids (PFCL): PFCL is a great help by helping in un-displacing the retinal flap and keeping it in position until retinopexy is done. It acts as the third surgical hand. In highly

complicated cases, surgeons have left PFCL *in situ* to attain attachment, and performed silicone oil exchange as a secondary procedure. There after 3-5 rows of endolaser are placed to hold the flap in position. For SRF drainage, PFCL silicone oil exchange, or PFCL-air, followed by Air-PFCL exchange is done. Particularly, the edge of the GRT has to be kept dried during this maneuver.

Role of lensectomy: Lensectomy has to be done in following cases:

- Increased risk of development of cataract within 2 years
- Subluxation of lens
- Presence of PVR especially in anterior PVR to get access to vitreous base region.

Surgical Objectives

- Vitrectomy, PVD and restoration of folded flap to original position
- Remove PVR, may remove the anterior retinal flap and manage edge of GRT
- Retinopexy under PFCL
- To drain all SRF
- To hold flap in position until retinopexy adhesion occur.

Management of Fellow Eyes

Cryotherapy: It is indicated in all retinal holes, small dialysis and small retinal tears located anterior to equator.

Photocoagulation: All retinal holes, and small retinal tears located posterior to equator should be photocoagulated.

Scleral buckling: Large retinal tears, multiple retinal tears, and tears associated with vitreous hemorrhage.

Prophylactic Scleral Buckle in High-risk Eye

The following characteristic puts the patient at high-risk of having GRT:

- High myopia >10 diopters.
- Increasing white without pressure (WWOP).
- Increasing vitreous base condensation.

Role of Pneumatic Retinopexy

Expansile gases with increased longevity are indicated in cases of small GRT and Co-operative

patient with good compliance. Its advantages are it avoids complication of VR surgery and the procedure is relatively simple and easy. However, the chances of failure are high and chances of slippage of flap are higher than silicon oil.

Role of Vitrectomy with Scleral Buckle

This is a highly debated topic. Scleral buckle would help by supporting vitreous base and decreasing tractional forces. On the other hand, it may result in flap slipping and fish mouthing.

Complications of surgery: Complications of GRT surgery are summarized in **Table 2**.

Prognosis: Primary and final anatomical success is from 70% to over 90%, but less than 50% of patients will achieve 20/40 or better acuity. Poor visual prognosis factors³ are macular detachment, hypotony, pseudophakia/aphakia, high grade PVR, GRT>180 degree, poor visual acuity at presentation, and persistent retinal detachment.¹

VIVA QUESTIONS

Q.1. GRT definition.

Ans. A giant retinal tear (GRT) is a full-thickness neurosensory retinal break that extends circumferentially around the retina for three or more clock hours in the presence of a posteriorly detached vitreous.

Q.2. Difference between GRT and GRD.

Ans. See Table 1.

Table 2 Complications of GRT surgery

Intraoperative	Slippage (around 3–15%) Vitreous hemorrhage Retinal folds Rolled edge
Postoperative	Recurrent retinal detachment (40–50%) Cataract (40–50%) Macular pucker Hypotony (IOP ≤5 mm) Corneal decompensation Vitreous hemorrhage Hyphema Phthisis bulbi

Abbreviation: GRT, giant retinal tear

Q.3. What is risk of developing RD in fellow eye?

Ans. The incidence of bilateral non-traumatic GRT at presentation ranges between 0% and 21%. The fellow eye is also at risk of developing a RD unrelated to a GRT. The rate of fellow eye RD ranges from 6% to 42%.¹

Q.4. Classification of GRT.

Ans. See Tables 3 and 4.

Q.5. Syndromes associated with GRT.

Ans. See Table 5.

Q.6. Most common complications.

Ans. See Table 2.

Q.7. Role of PFCL.

Ans. See text.

Q.8. Indication of lensectomy in GRT.

Ans. See text.

Q.9. Pathogenesis of idiopathic GRT.

Ans. Central vitreous liquefaction followed by vitreous condensation and formation of equatorial membranes, transequatorial forces lead to formation of large break

Table 3 GRT classification (based on extent)

GRT I	<180°
GRT II	180–270°
GRT III	>270–<360°
GRT IV	360°

Abbreviation: GRT, giant retinal tear

Table 4 GRT classification (based on PVR severity)

GRT I	Without displacement
GRT II	With displaced; mobile posterior retinal flap
GRT III	With everted or rolled up posterior retinal flap
GRT IV	With everted or rolled up posterior retinal flap and star fold/macular pucker

Abbreviation: GRT, giant retinal tear

Table 5 Etiology of GRT

Ocular	Systemic
Idiopathic (75–80%)	Stickler's syndrome
Traumatic (10–20%)	Marfan's syndrome
Myopia	Ehlers-Danlos syndrome
Lattice degeneration	
Previous retinal cryotherapy	
Intravitreal surgery	

Abbreviation: GRT, giant retinal tear

at posterior edge of vitreous base, as if a zipper has opened.

Q.10. Most common associations of GRT.

Ans. The most common predisposing factors for the development of a GRT is; trauma

(4–31%), hereditary vitreoretinopathies (14.5%) and high myopia (9.7%).^{1–3}

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POSTERIOR SEGMENT CYSTICERCOSIS

Harika Regani, Karthikeya R, Yamini Attiku, Atul Kumar

INTRODUCTION

Ocular cysticercosis is most commonly caused by *Cysticercus cellulosae*, the larval form of the *Taenia solium* (pork tapeworm), though other species may also be involved. It is endemic in tropical areas such as Sub Saharan Africa, India, Latin America and East Asia. The posterior segment is involved in approximately 68% cases.¹ In the posterior segment, vitreous cavity is the most commonly involved site followed by subretinal space.²

Posterior segment cysticercus is discussed here, which can be a short case/spotter in the examination with specific questions.

HISTORY

Chief Complaint

The patient is typically a young males and presents with diminution of vision. An aware patient can also complain of scotoma due to the presence of a cyst, retinal detachment or scarring. Pain during ocular movements can occur if optic nerve is involved or there is concomitant extraocular infection.

History of Present Illness

Onset may be sudden or insidious depending on the presentation. It could be painful and associated with redness (particularly dying cyst causes severe inflammation and vitritis) or painless (in case of retinal detachment or submacular scarring). The presentation is usually unilateral but can be bilateral in cases of disseminated cysticercosis. Most commonly affected are patients from lower socioeconomic strata due to poor hygienic practices and food habits (contaminated fruits and vegetables with tapeworm ova). Patient may be vegetarian by diet.²

History of seizures, headache, vomiting, subcutaneous nodules need to be elicited in patients suspected of cysticercosis. The central nervous system (CNS) and skin involvement are more common than ocular involvement. It is rather very common to have CNS involvement in cases of ocular cysts, while solitary ocular cysts per se are less common. Over all, CNS manifestations are most frequent, up to 90% in some descriptions.¹

Past and family history are usually not significant in such cases.

EXAMINATION

Systemic Examination

In general, any organ system may be affected.

- Thorough work-up of the CNS (motor, sensory and all cranial nerves) for any signs of focal neurological deficit.
- *Musculoskeletal system:* Palpate major muscle masses (forearm, arm, thighs and legs) for evidence of cysts in the muscle belly.
- Skin examination for subcutaneous nodules.

Ocular Examination

Adnexal and orbital examination and its findings are covered elsewhere in the book: Particularly subconjunctival cysts should be looked for, even in absence of findings like proptosis and ocular movement disorders.

Vision: Best-corrected visual acuity with projection of rays is recorded in both the eyes. Vision can be very poor in cases with severe vitritis or retinal detachment but can also be surprisingly well maintained in a few cases.

IOP: It can be normal or decreased (uveitis) or increased (neovascular glaucoma).

Anterior segment: It can show evidence of active inflammation (AC cells, flare, keratic precipitates) or past inflammation [old keratic precipitates (KPS), flare, pigments on endothelium, frank endothelitis]. Occasionally, a cysticercus can migrate in to the anterior chamber from the posterior chamber through zonules.

Posterior segment: The cyst can be found subretinally (eighty percent of the time being at the posterior pole, or anywhere in the fundus), in the vitreous and rarely on the optic disc. Sometimes multiple or dumbbell shaped cysts (half in vitreous and half subretinal) may also be encountered.

Gross examination of the cyst: Globular, elongated or oval, milky white transilluminant cyst with translucent wall and a white, opaque, dot like area at one end, which indicates the position of the scolex (**Fig. 1**). This is typical for a live cyst. On illumination of the cyst with a bright light, such as that of the indirect ophthalmoscope, the cyst shows undulating movements of the

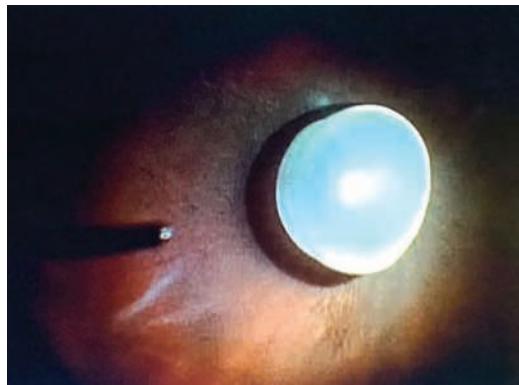


Fig. 1: Intraoperative photo of an intravitreal cyst along with its scolex. Presence of scolex is diagnostic for the parasite

cyst wall, which is movement of the cyst wall due to a mobile scolex. The size of the cyst may vary from 0.5 cm to 3 cm in diameter.

Posterior segment findings

- *Subretinal cysts:* May vary in size from 3 to 6 DD
- *RPE disturbances:* Because of presence or migration of the cyst through the subretinal space, which causes mild inflammation and subsequent RPE changes. Sometimes they may represent the site of access to subretinal space from the choroid.
- *Intraretinal hemorrhage.*
- *Vascular sheathing:* Thought to be immune mediated reaction to the antigens of the cysticercus.
- *Retinal detachment.*
 - *Rhegmatogenous* (Rheuma being the site of exit of the cysticercus from the subretinal space)
 - *Tractional:* Due to proliferation of the cells over the retina caused due to inflammation.
- *Submacular/subretinal scarring.*
- *Severe vitritis and a picture like endogenous endophthalmitis:* Due to a dying cyst which leaks contents into the surrounding vitreous which are strongly antigenic.
- *Calcified cyst/granuloma:* A dead cyst can get calcified and may lead to a granuloma formation.

DIFFERENTIAL DIAGNOSES

In presence of mobile cysts with scolex, the diagnosis is rather straightforward. Dead cysts may cause difficulty. Else other diagnoses of retinal cysts-old RD, hamartomas, retinal mass vs calcified cyst, dropped lens as a USG finding in hazy media, ciliary body cyst, etc.

INVESTIGATIONS

Head imaging should always be done, regardless of symptoms (see above). Following investigations are carried out:

- *Complete blood count*: To look for eosinophilia
- *Stool examination*: To find the eggs or proglottids of the worm.
- *Ultrasonography*: Cyst can be seen as a sonolucent area with well-defined anterior and posterior margins. An echo dense, curvilinear, highly reflective structure is present within the cyst corresponding to the scolex. USG is better than CT for the detection of the scolex. High amplitude spikes correspond to the cyst wall and the scolex. The scolex shows a high amplitude spike due to presence of calcareous corpuscles. Presence of high reflective scolex within a clear cyst is diagnostic of cysticercus.
- *CT scan*: Nonenhanced circular area of low attenuation with tiny areas of increased attenuation within the lesion. This confirms the diagnosis and helps to rule out neurocysticercosis.
- *MRI brain*: If neurocysticercosis is suspected.
- *ELISA*: Rarely helpful. Positive for anti-cysticercal antibodies (cystic lesions without a scolex with positive ELISA for anticysticercal antibodies is diagnostic).

MANAGEMENT

In cases of neurocysticercosis, ophthalmic examination should be first done to rule out cysticercosis before starting the patient on cysticidal drugs. Starting cysticidal drugs in the presence of an intraocular live cysticercus can lead to disastrous consequences by leading to severe intense inflammation and eventual loss of eye. Therefore, in cases with neurocysticercosis and intraocular cysticercosis, ocular management

should precede neurological management, albeit without delay.

Intraocular cysts are best managed by surgical removal.^{2,4} They are the treatment of choice in the modern era. Historically, the cysts used to be removed in-toto using large sclerotomies but the current best practice is to rapidly lyse the cyst *in vivo* and aspirate the cyst contents with the vitrector using high suction and high cut rate. In toto removal has the advantage of allowing a histopathological documentation.

Dead cyst or dying cyst with severe inflammation is best managed by steroids. Anterior segment cysts may be managed by using visco expression.

VIVA QUESTIONS

Q.1. What is the life cycle of cysticercosis?

Ans. In the life cycle of *Taenia solium*, man is the definitive host where sexual reproduction occurs and the eggs are produced. Man acquires *Taenia* infection by eating raw or undercooked pork infested with the cysticerci. These cysticerci exvaginate in the stomach, attach to the intestinal wall through scolex and develop into the adult worms. Adult tapeworms develop, (up to 2 to 7 m in length and produce less than 1000 proglottids, each with approximately 50,000 eggs) and reside in the small intestine for years.

The eggs/proglottids excreted in the excreta are ingested by the intermediate hosts, pigs, in whom the eggs hatch in the stomach, pierce the stomach, reach skeletal muscle through blood and lead to cysticercus formation. The life cycle is complete when human consumes raw or undercooked pork. This cycle usually does not lead on to ocular involvement, unless autoinfection occurs with the human ingesting eggs or retrograde peristalsis.

Typically, cysticercosis of humans occurs when man acts as an accidental intermediate host and consumes vegetables (salad) contaminated with eggs of the *Taenia solium*.³

Q.2. How do the cysticerci reach the posterior segment?

Ans. Cysticercosis is caused by the ingestion of the eggs of *Taenia solium* or by reflux of gravid proglottids in a patient with taeniasis from lower intestines into stomach and their subsequent excystment. The embryos hatched out of the eggs penetrate the walls of the stomach, reach bloodstream, and lodge at sites with high blood circulation like the eye, skeletal muscle, skin, heart and brain. It reaches the orbit through the ophthalmic artery and the posterior segment through the posterior ciliary arteries. It penetrates the choriocapillaris and reaches the subretinal space. Macula has been noted to be the preferred site for the lodgment of the cysticercus possibly due to the rich blood supply. From the macular subretinal space, it can enter the vitreous cavity through a break in the overlying neurosensory retina. When this migration occurs, the defect in the retina thus formed can give rise to rhegmatogenous retinal detachment or more commonly, this site heals with a scar due to the inflammation associated with the cysticercus migration and leads to an area of scarring in the retina. An alternate route of entry for cysticercus into the vitreous cavity has been hypothesized to be directly from the retinal blood vessel or the ciliary body.²

Q.3. When does cysticercus lead to inflammation?

Ans. A live cysticercus has mechanisms to evade the host immune system and only cause mild inflammation. A dying cyst, however,

has faltered immune evading mechanisms, develops micro leaks in the cyst wall and leads to severe inflammation. This is the reason why a patient with live intraocular cysticercosis requires treatment for removal of cyst even if he is 6/6 at the time of presentation, and not cysticidal therapy. A dead cyst does not incite significant inflammation and may not be removed.

Q.4. What is the prognosis of a case of intraocular cysticercosis?

Ans. Prognosis depends on the presentation of the condition. An uncomplicated intravitreal live cysticercosis can be managed with pars plana vitrectomy with cyst lysis and aspiration with good outcomes (if no pre-existing macular scar). In cases with retinal detachment, prognosis is guarded. In cases with subretinal cysticercosis, macular scarring, tractional retinal detachment prognosis is guarded.⁴

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CATARACT IN SILICONE OIL-FILLED EYES

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INTRODUCTION

Silicone oil with its biomechanical properties of buoyancy, surface tension and viscosity is a very good agent for endotamponade and has been used along with pars plana vitrectomy

especially in complicated rhegmatogenous retinal detachments, old detachments with proliferative vitreoretinopathy changes, giant retinal tears, endophthalmitis, etc. But, at the same time silicone oil implantation has been associated with its own set of changes in the eye when kept for a

long time, namely, oil in the anterior chamber, emulsification, cataract in phakic eyes, glaucoma and keratopathy. Management of cataract in silicone oil filled eyes is different from senile cataract not only due to difficulty in getting the true biometry in these patients but also due to the anatomical challenges.

HISTORY

Chief Complaint

Usually, recurrent loss of vision following vitrectomy or in some cases no gain in vision following vitrectomy.

History of Presenting Illness

The history is generally straightforward; there is usually the history of gain in vision following vitreoretinal surgery followed by gradual diminution of vision. In most of the cases cataract develops within a year of vitrectomy, before or following its extraction. However, some patients can present within days or weeks with total cataract—in such cases iatrogenic damage to the lens capsule should be suspected. It is important to take a detailed history of the nature of the vitreoretinal pathology and the extent of previous surgery as they have a direct bearing on the success or complexity of the phacoemulsification procedure and its overall visual benefit to the patient.

Past History

History of trauma, detailed history of the vitreoretinal procedure and pathology for determining the visual prognosis.

Family History

This is usually not significant to work-up.

EXAMINATION

Eyeball, lids and adnexa should be examined as in any other case.

Cornea: One should look for band-shaped keratopathy (BSK), corneal pigments and corneal opacity, which may have been incurred during the vitrectomy.

Scleral and episcleral scarring should be noted and recorded.

Anterior chamber: Oil bubbles inside the anterior chamber (Hyperoleon sign; **Fig. 1**) and signs of emulsification are common.

Pupil: Pupil dilation, regularity, and neovascularization of the iris (NVI) should be noted. Direct light reflex in the index eye or consensual reflex of the other eye may be used as good prognostic indicators.

Lens: Presence of iridophacodonesis indicating compromised zonules, lens subluxation, anterior capsular plaque, posterior capsular plaque/defect (**Fig. 2**). Cataract should be graded as in any other case. Sometimes emulsified oil bubbles may be found stuck to the anterior or posterior capsule.

Fundus should be carefully examined especially to know the optic nerve status and the integrity of macula. One should refer to pre-operative retinal findings and intraoperative findings for determining prognosis if retina cannot be examined due to media haze.

DIFFERENTIAL DIAGNOSIS

Includes other causes of vision loss following vitreoretinal surgery: Secondary glaucoma, band shaped keratopathy, refractive error, retinal complication like RD, epiretinal membrane, cystoid macular edema, retinal toxicity, optic neuropathy.

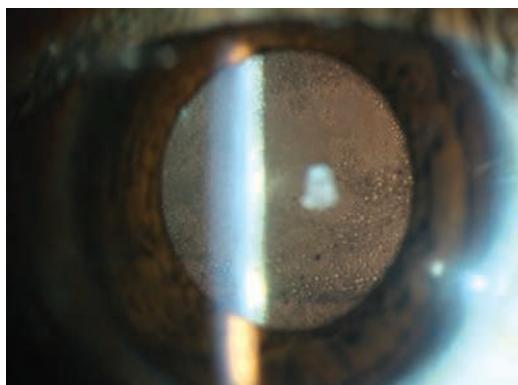


Fig. 1: Oil bubbles stuck behind the lens

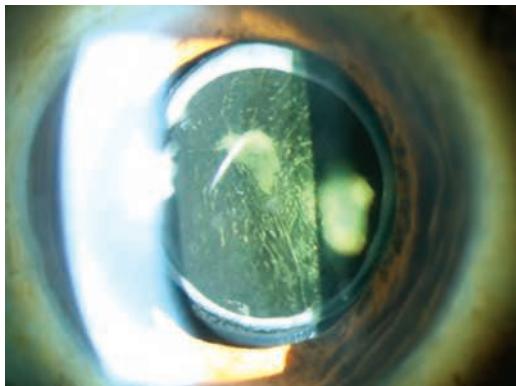


Fig. 2: Slit-lamp photograph depicting posterior capsule plaque behind the IOL after phacoemulsification. Such plaques may be later tackled with laser capsulotomy

INVESTIGATIONS

B-scan Ultrasonography

One should remember that due to the differing sound speed in oil, the eyeball appears to be large and enhanced depth mode should be utilized. In eyes with advanced cataract, fundus evaluation with an indirect ophthalmoscopy may not be feasible and an assessment using a B-scan should be made. Here the imaging is best carried out in sitting position to determine inferior RDs as well. In addition to that, careful evaluation of the posterior capsule by ultrasound B-scan can be done if direct visualization is not possible. If the ultrasound shows an abnormally large lens thickness or an out-pouching of the posterior lens surface, a defect in the posterior lens capsule should be suspected.

Biometry

Biometry should be performed for IOL power calculation. However, axial length measurement in an oil filled eye is a big challenge. In ultrasonography, due to change of velocity of sound in different viscosity, axial length measurements also vary as compared to normal vitreous in silicone oil filled eyes. Velocity of sound in physiological vitreous filled phakic eye is 1532 m/s. Velocity of sound in oil is slower, being 987 m/s in oil of viscosity 1000 cst, causing measured axial length to be longer in oil filled eyes.

Determining the length of the anterior chamber, lens and vitreous cavity separately and adding these values together can calculate the true AL.

$AL = ACD + LT + VCD$ (AL = axial length; ACD = anterior chamber depth; LT = lens thickness; VCD = vitreous cavity depth).

Theoretically, the velocity of sound in silicone oil of viscosity 1000 centistokes compared with the velocity of sound in vitreous humor decreases by a factor of 0.64 ($987 \text{ m/s} \div 1532 \text{ m/s}$). It is therefore possible to calculate the true depth of the vitreous cavity ($VCD_{\text{oil}} \times 0.64$) and hence the true AL.

The conversion factor of 0.71 multiplied by the measured axial length has been reported by Murray¹ to correct for the apparent increase in axial length induced by silicone oil of viscosity 1300 cSt.

Other alternative methods include partial coherence interferometry (IOL Master, Zeiss), which is preferred over ultrasonography to calculate the axial length of the silicone oil filled eye. It should be remembered that light speed is not affected to a level significant enough to cause falsifications in AL calculation as in USG. Axial length of the fellow eye can be used in certain cases in which axial length measurement of the oil filled eye is not possible. Previous records if available can also be used especially if scleral explants have not been used. Intraoperative retinoscopy has also been used for IOL power calculation.

Specular Microscopy

In the post-vitrectomized eyes, the corneal endothelium is often compromised especially in those cases where silicone oil is present in the anterior chamber, so it is important to perform specular microscopy in these patients.

Anterior segment OCT (ASOCT) may also be used to analyze PC when appropriate to document integrity of the PC.

TREATMENT

Cataract surgery, typically using phacoemulsification and intraocular lens implantation, is recommended for individuals with visually significant lens opacities. Phacoemulsification with IOL implantation can be performed safely in post-vitrectomized eyes.² Patients who need both

cataract surgery and silicone oil removal can undergo either a combined or two step surgical approach. Most of the studies show similar visual outcome and complication rates with both the approaches; however, combined surgery offers the advantages of a single surgical event and a faster visual rehabilitation.³ Silicone IOLs should be avoided. In presence of PC defect oil bubbles are suddenly seen in AC. Frequent AC wash may be needed during surgery for removing the emulsified oil, and AC tends to collapse often, as oil tends to rise in supine position. Capsulorhexis may be difficult to plaques and retroillumination assisted maneuvers are typically difficult due to poor glow. The capsular opening tends to run out. Use of viscohesive should always be considered.

VIVA QUESTIONS

Q.1. What is the incidence of cataract following vitreoretinal surgery with silicone oil injection in phakic patients?

Ans. All eyes with silicone oil injection inadvertently undergo cataract formation in almost 100% cases. The incidence of development of visually significant cataract ranges from 8 to 80% for nuclear sclerotic cataract and 4–34% for posterior subcapsular cataract (PSC) in various studies.^{4,5} Although, early removal of oil has been associated with a decreased risk of cataract formation, however, cataracts have been reported even months after oil removal.

Q.2. What are the common morphologies of cataract seen in oil-filled eyes?

Ans.

- Posterior subcapsular feather opacity, seen in early postoperative periods.
- Development of posterior fibrous pseudodemetaplasia and finally posterior subcapsular cataract and posterior capsular plaque.
- Formation of lens vacuoles in posterior part of lens
- Early lens opacities leading to nuclear sclerosis, with or without brunescence.
- Rapid progression of nuclear sclerosis to white cataract with hypermaturity, often leading to leaking of proteins and uveitic changes.

Q.3. Which is the most common type of cataract seen in oil-filled eyes?

Ans. Progressive nuclear sclerosis is the most common type followed by posterior subcapsular cataract in the young patients.

Q.4. What are the various risk factors for development of cataract in post vitrectomized eyes?

Ans.

- Older age
- Degree of preoperative nuclear sclerosis
- Intraoperative lens touch
- Diabetic retinopathy
- Silicone oil injection.

Q.5. What is the pathomechanism of cataract formation in oil-filled vitrectomized eyes?

Ans. However, the exact cause of cataract formation in oil filled eye is not known entirely. However, it has been postulated that altered metabolism at the lens-oil interface and direct oil induced toxicity may be responsible, both leading to oxygen stress to the lens proteins leading to their oxidation. Also, increased oxygen exposure to the lens following vitrectomy, lens toxicity from intraocular irrigating solution, intraoperative lens touch by surgical instruments, use of intravitreal steroids during vitrectomy, removal of barrier function provided by the vitreous, permeability changes in lens capsule, uveitis were the various other reported causes of cataract formation following vitrectomy.^{6,7}

Q.6. What are the various refractive changes seen in aphakic and phakic patients following silicone oil injection?

Ans. Refractive state in silicone oil filled eyes depends on the extent of oil fill inside the vitreous cavity and the shape of the anterior oil surface. In aphakics, the anterior surface is convex; hence acting similar to the crystalline lens and due to the induced myopia may bring these eyes towards emmetropia. However, in phakic eyes, this anterior surface being concave and refractive index of oil being higher than that of the crystalline lens, the oil acts as a minus

lens rendering the eye hypermetropic. These myopic and hypermetropic shifts have been on an average close to 6D. Further changes may occur depending on whether or not an encirclage was used during vitreoretinal surgery.

Q.7. What are the fallacies in measuring axial length using A-scan ultrasound and other methods to measure axial length in silicone oil-filled eyes?

Ans. Refer to the chapter above.

Q.8. Which type of IOL should be preferred in silicone oil filled eye?

Ans. As silicone oil can interact with various intraocular lens biomaterials with a potential of reducing the optical quality of the lens, the type of IOL used becomes an issue. It has been postulated that it is the hydrophobia of silicone oil, which influences its interaction with intraocular lenses. The more hydrophobic a lens biomaterial is the more the adherence of silicone oil; the more hydrophilic, the less the adherence. Interaction of silicone oil was seen maximal with silicone lenses, so they should be best avoided. Acrylic lenses or polymethylmethacrylate (PMMA) lenses can be successfully used. As convexo-plano lens with the plane surface facing posteriorly induces minimal refractive change, they are preferred in silicone oil filled eyes.

Q.9. How to choose an appropriate IOL power in silicone oil-filled eyes?

Ans. Silicone oil due to its higher index of refraction (1.40) as compared to vitreous behaves like an intraocular minus lens in pseudophakia. Therefore, without appropriate power adjustment, significant hyperopic overcorrection would be expected. The more curvature or power incorporated in the posterior surface of the lens, the greater is the postoperative error. The convexo-plano lens with the plane surface facing posteriorly induces minimal refractive change.

The following formula have been suggested by Patel (1995) and Meldrum⁸ to find the

Table 1 Surgical difficulties and intraoperative complications

Cornea	Peripheral corneal injury Stripped Descemet's membrane
Anterior chamber	Fluctuations in AC depth Infusion deviation syndrome
Iris	Prolapse Miotic pupil
Lens	Tears in rhelix margin Marked zonular laxity/dehiscence Posterior capsular plaque Unplanned posterior capsulorhexis Posterior capsule rupture Unplanned AC intraocular lens (IOL)
Posterior segment	Nuclear drop/dropped lens fragment Suprachoroidal hemorrhage
Others	Conversion from topical to intracameral anesthesia

Table 2 Early and late postoperative complications

Cornea	Moderate to severe corneal edema Pseudophakic bullous keratopathy
Anterior chamber	IOP spike Wound leak
Iris	Chronic postoperative iritis Irregular pupil Rubeosis iridis
Lens	Incorrect intraocular lens power Intraocular lens decentration or dislocation Capsulorhexis contraction Posterior capsular opacification
Posterior segment	New or persistent macular edema Retinal detachment

additional IOL power to be added to the calculated IOL power to arrive at the power of IOL to be implanted in a silicone oil filled eye:

$$\text{Additional IOL power} = \{(Ns-Nv)/(AL-ACD)\} \times 1000$$

Ns: Refractive index of silicone oil (1.4034)

Nv: Refractive index of vitreous (1.336)

AL: Axial length in millimeters
ACD: Anterior chamber depth in millimeters.

Q.10. What are the various surgical difficulties and intraoperative and postoperative complications in silicone oil-filled eyes?

Ans. Surgical difficulties and intraoperative complications are summarized in **Table 1**.² Early and late postoperative complications are summarized in **Table 2**.²

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SILICONE OIL-INDUCED SECONDARY GLAUCOMA

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INTRODUCTION

Silicone oil (polydimethylsiloxane) is a linear synthetic polymer made of repetitive Si-O units and is used as an internal tamponade agent in vitreoretinal surgeries. First introduced by Paul Cibis in 1960s, it has become an important adjunct in vitreoretinal surgery. Secondary glaucoma can occur at any time in the postoperative period, and may range from mild and transient to severe and sustained resulting in vision loss.

HISTORY

Chief Complaint

Patients are generally asymptomatic. However, few cases may present with acute pain, redness, blurred vision and colored halos following vitrectomy.

History of Presenting Illness

As most of these patients are asymptomatic most of the cases will be detected with glaucoma/high intraocular pressure (IOP) on follow-up.

Some patients may develop very high IOPs in immediate/late postoperative period and may present with complaint of nausea, vomiting, pain, redness and blurred vision. The patient can present with these symptoms within hours or years after surgery. Some cases present with history of gradual painless loss of vision following vitreoretinal surgery.

Past History

Detailed history of vitreoretinal pathology for which surgery was done, history of pre-existing glaucoma, trauma, any history of steroid intake in past or present and its mode and duration should be taken. Other eye history should also be recorded, as that of other risk factors of glaucoma. OT notes may be reviewed for amount of oil fill if available.

Family History

Family history of glaucoma is important, as patients with positive family history can be steroid responders.

EXAMINATION

Eyeball, lids and adnexa should be examined as in any other case.

Cornea: Corneal edema and bullous keratopathy are suggestive of raised IOP. Any band shaped keratopathy, corneal pigments and corneal opacity should be documented.

Scleral and episcleral scarring with special concern to its site and extent should be noted, it is especially important if one is planning trabeculectomy.

Anterior chamber: AC depth should be carefully examined as patients with pupillary block glaucoma or malignant glaucoma will present with shallow AC. Presence of any AC cells, flare, hyphema, emulsified oil (**Fig. 1**) or oil globules in anterior chamber should be noted as it helps in knowing the etiology.

Angle: Gonioscopy should be performed to look for emulsified oil in angle (superior angle), NVI, PAS, increase pigmentation, and angle recession. These patients are prone to surgical failure.

Intraocular pressure measurement: IOP should be measured using Goldmann applanation tonometer.

Iris: Pupillary ruff atrophy, sphincter tear, NVI, and any iridotomies and its patency if present should be noted.

Pupil: Direct and consensual light reflex should be checked as it gives the gross idea of optic nerve status.



Fig. 1: Hyperoleon: along with bubbles of silicone oil. These bubbles induce fibroses in the angle leading onto glaucoma

Lens: Aphakic, phakic or pseudophakic status as well as presence of any subluxation should be documented.

Fundus should be carefully examined especially to know the optic nerve status (vertical cup disc ratio, neuroretinal rim, bayonetting, baring of circumlinear vessels, pallor) and the integrity of macula. A retinal examination should be performed keeping in mind the original indication of surgery ant OT notes, and findings carefully documented.

INVESTIGATIONS

Pachymetry

As variation of central corneal thickness (CCT) in normal corneas can lead to falsely higher pressure readings with thicker corneas and falsely lower with thinner corneas, it is important to measure CCT to know the corrected IOP.

Visual Fields

Static perimetry (HVF/Octopus) should be performed wherever possible as it helps in diagnosing as well as in detecting progression of glaucoma. If HVF/Octopus is not possible due to poor vision, Goldmann visual field should be performed.

B-scan Ultrasonography

It should be performed if media is hazy and fundus evaluation is not possible by indirect ophthalmoscopy. It can also be used to detect glaucomatous cupping of 0.7 or greater in eyes in which optic nerve cannot be examined due to media haze.

RNFL-OCT may be done, scanning laser based or otherwise. Comparisons with unaffected fellow eye are helpful to loss of NRR.

MANAGEMENT

Treatment is directed towards treating the etiology (see viva questions). If planning for surgery, oil removal should be considered in cases with emulsification.

Medical Therapy

- Corticosteroids and cycloplegics are indicated to reduce the inflammation. Aqueous

- suppressants are generally preferred to reduce the IOP. Hyperosmotic agents can be used for short-term control of IOP.
- Success rate of medical therapy in controlling high IOP in silicone oil-filled eyes varies from 30% to 78% in various studies.^{1,2}

Prophylactic Peripheral Iridectomy

Inferior peripheral iridectomy (PI) described by Ando³ helps to prevent pupillary block glaucoma in aphakic. As silicone oil floats superiorly (specific gravity 0.97), an iridectomy (ideal size 150–200 µ) done at 6 o'clock position prevents pupillary block by allowing aqueous passage from the posterior to the anterior chamber. Superior PI is done in cases where heavy silicone oil is used.

However, postoperative closure of the PI has been reported in about one-third of eyes undergoing silicone oil surgery. If the PI is not patent, treatment involves reopening the peripheral iridectomy, either with a YAG laser or surgically. If the cause is a blockage by fibrin or clot, injection of tissue plasminogen activator (tPA) into anterior chamber has been reported with success.

Selective Laser Trabeculoplasty

Selective laser trabeculoplasty (SLT) may be considered as a treatment option for the patients with open-angle glaucoma (OAG) secondary to emulsified SO which are not at high risk for progressive glaucomatous damage to save time before more invasive surgical interventions are performed.⁴ It acts by activating the macrophages loaded with SO and remodeling the extracellular matrix in the trabecular meshwork by releasing cytokines, hence increasing trabecular outflow. Typically, recurrences are seen needing alternative therapy in due course.

Silicone Oil Removal

The benefit of early SO removal before the emulsification was demonstrated to be effective for IOP regulation in higher proportion of the eyes. However, the late removal of emulsified SO does not necessarily prevent the development of glaucoma as prolonged contact of emulsified silicone oil with trabecular meshwork causes organic changes in the endothelium and collagen component

of trabecular meshwork leading to its collapse and sclerosis. Furthermore, SO removal itself can cause IOP elevation by several mechanism; Firstly, due to edema of the trabecular meshwork because of postoperative inflammation. Secondly, the mechanical impact of balanced salt solution during silicone oil removal may split the silicone oil droplets into much smaller drops, which are more likely to obstruct the trabecular meshwork.⁵ Therefore, whether oil removal helps or not is still a matter of debate.

Filtration Surgery

Conventional filtration surgery has a limited role and success rate in the management of glaucoma after pars plana vitrectomy and silicone oil injection.⁶ Trabeculectomy in these eyes is also technically difficult because of conjunctival scarring from previous retinal surgeries. Increased postoperative inflammation and emulsified silicone oil may lead to blockage of internal ostium and trabeculectomy failure. Inferior trabeculectomy is not advisable as it carries high risk of endophthalmitis.

Glaucoma Drainage Device

Glaucoma drainage implants offer a good surgical option and have better surgical outcomes as compared to trabeculectomy in oil filled eyes. However, oil migration can occur through the tube into subconjunctival space inciting an inflammatory reaction and its failure.

Cyclodestructive Procedures

Transscleral photocoagulation can be used to control IOP in oil filled eyes, but as it carries a risk of visual loss, it is generally reserved for cases with poor visual outcome.

VIVA QUESTIONS

Q.1. What is the incidence of secondary glaucoma following vitreoretinal surgery with silicone oil injection?

Ans. The true incidence of glaucoma after silicone oil injection is difficult to ascertain from the literature. First reported by Cibis, the incidence of high IOP intraocular

pressure ranges from 2.2% to 56% in various studies,^{7,8} depending on the definition of elevated IOP and the time considered.

In the silicone study, 8% of the cases that underwent SO tamponade experienced glaucoma at 36-month follow-up.

Q.2. What are the various risk factors for development of glaucoma in post-vitrectomized eyes?

Ans. Following are the risk factors for developing silicone oil-induced glaucoma

- Pre-existing glaucoma
- Diabetes
- Trauma
- Aphakia
- Oil in the anterior chamber
- Emulsification of the oil
- Use of low viscosity silicone oils as compared to high viscosity oils
- Heavy silicone oils
- Duration of oil tamponade.

Q.3. What is the pathomechanism of glaucoma in oil-filled vitrectomized eyes?

Ans. Several mechanisms have been proposed for secondary glaucoma following the use of silicone oil in vitreoretinal surgeries:

Early postoperative rise in IOP

- Pupillary block
- Migration of silicone oil into the anterior chamber with consequent mechanical impediment to filtration
- Inflammation
- Overfill
 - Absolute
 - Relative—due to increase choroidal thickness
- Pre-existing glaucoma.

Late postoperative rise in IOP

- Infiltration of the trabecular meshwork by silicone bubbles
- Chronic inflammation
- Synechial angle closure
- Rubeosis iridis
- Migration of emulsified and non-emulsified silicone oil into the anterior chamber
- Idiopathic open-angle glaucoma.

Q.4. What is the ideal site of peripheral iridectomy in silicone oil-filled eyes?

Ans. It should be inferior at 6 o'clock, peripheral and not more than 2 mm because larger more centrally located inferior iridectomy may allow silicone oil to enter the anterior chamber, creating a form of reverse pupillary block with a deep anterior chamber.

Q.5. State whether silicone oil removal helps in controlling IOP in oil-filled eyes.

Ans. See discussion in chapter above.

Q.6. What are the causes of failure of trabeculectomy in silicone oil-filled eyes and ways to prevent it?

Ans. Scleral and episcleral scarring from previous surgery and increased postoperative inflammation are the main causes of trabeculectomy failure in oil-filled eyes. Emulsified oil droplets may block the ostium/bleb. Use of antimetabolites (MMC or 5-FU) during trabeculectomy, making large ostium, performing cyclodialysis combined with trabeculectomy may decrease the chance of failure.

Q.7. What are the other causes of glaucoma after VR surgery?

Ans. Tight explants, steroid induced, gas overfill, improper concentration of gas, NVG, malignant glaucoma, lens intumescence, inflammatory, choroidal hemorrhage, etc.

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POSTERIOR DISLOCATED LENS

Shipra Singhi, Brijesh Takkar

INTRODUCTION

Posterior dislocation of lens is one of the worst complications of cataract surgery. Rarely cases of spontaneously dislocated lens can also be seen in clinical practice. Such cases are commonly given as short cases. These may include lens drop/IOL drop/lenticular fragment drop/subluxation of lens/decentered intraocular lens (IOLs).

HISTORY

Chief Complaint

The usual presenting symptoms are loss of vision, pain and redness of the affected eye.

History of Present Illness

The patient may present with sudden loss of vision in eye after trauma or no visual gain after intraocular surgery or gradual visual loss in disorders associated with slow zonular dehiscence. There may be complaints related to recent inflammation. In the cases where subluxation preceded dislocation, there may be history of diplopia/edge effect related astigmatism.

History of Past Illness

History of trauma, intraocular surgery, coloboma, pseudoexfoliation syndrome or systemic diseases associated with ectopia lentis must be ruled out.

Family History

Family history may be there in cases of ectopia lentis (Marfans, homocysteineuria, sulfite oxidase

deficiency syndrome, hyperlysineemia, focal dermal hypoplasia) and coloboma.

Past Surgical History

Recent history of cataract surgery may be there in case of IOL dislocation or lenticular fragment dislocation.

EXAMINATION

General Examination/Specific Systemic Examination

A thorough systemic examination is carried out when ectopia lentis is supposed to be the underlying cause.

Ocular Examination

Visual acuity: Uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA) both undilated and dilated (esp. in cases of decentered IOLs/ partially subluxated lens) should be checked as final management depends on the same.

Eyeball: Large eyeball is seen in high myopic patient while small eyeball may be seen in cases of coloboma. Nystagmus or squint may be present in cases of coloboma.

Lid: Lid findings are usually normal.

Conjunctiva: Scar may be present in case of previous surgery. Ciliary as well as diffuse conjunctival congestion can be there due to associated inflammation.

Cornea: Cornea may be pear shaped in coloboma. Krukenberg spindle may be present in pseudoexfoliation. Corneal edema or Descemet folds

may be present in cases with history of recent complicated cataract surgery. This finding is extremely important in deciding the timing of surgery. In cases of lens drop during phacoemulsification, the wound might have been extended in an attempt to deliver the nucleus, in such cases careful examination (with fluorescein staining) has to be done to ensure proper wound closure. In addition, any vitreous twig extending to corneal wounds must be ruled out.

Sclera: Scleral thinning may be there in cases of connective tissue disorders (e.g. blue sclera in collagen diseases) and pathological myopia. In cases of nucleus drop following small incision cataract surgery (SICS) careful examination of the wound integrity must be done.

Anterior chamber (AC): AC may be deep in high myopic eyes or shallow in pseudoexfoliation. Anterior chamber cell and flare may be present (more in case of dislocated crystalline lens). ACD should be checked as an ACIOL may be implanted during rehabilitation. Presence of vitreous in AC must be ruled out by careful slit-lamp examination. If vitreous is touching corneal, endothelium there is a chance of corneal decompensation, in such cases the decision to go ahead with surgery has to be expedited.

Iris: Iridodialysis (in trauma) or atrophy may be there. Transillumination test is positive in pseudoexfoliation syndrome. Iridodonesis is common in such cases.

Pupil: Pupillary abnormalities that can be seen in such cases include eccentric pupil in Marfan's syndrome, and a poorly dilating pupil in pseudoexfoliation syndrome. Size of the pupil must be evaluated, vis-a-vis. secondary IOL implantation.

Intraocular pressure (IOP): IOP may be raised in case of inflammation or pseudoexfoliation.

Gonioscopy: Angle recession or cyclodialysis may be there in case of trauma. Dense pigmentation of the angles is seen in pseudoexfoliation.

Lens: IOL may or may not be present, depending on initial management by the phaco surgeon. It is necessary to look for presence and status of the capsular rim, as the best option is a sulcus IOL implant for rehabilitation. One should carefully

look for presence of the anterior vitreous in pupil plane/AC or otherwise.

Fellow eye: Lens may be subluxated or dislocated in bilateral diseases. Broken zonules or zonular dialysis may be there. Pseudoexfoliation material may be present over anterior lens capsule. A posterior polar cataract may be present, partially explaining the complicated surgery in the other eye. Traumatic cases would generally have a normal fellow eye. In cases of pseudophakia in the other eye, look for evidence of posterior capsular rent (PCR) in the other eye; that may suggest a posterior polar cataract as the predisposing factor for lens drop.^{1,2}

Anterior vitreous: Presence of vitreous pigments also known as tobacco dusting or Shaffer's sign may be there (*Note: Shaffer's sign is one of the characteristic sign of rhegmatogenous retinal detachment, however, both trauma and surgery can produce this sign.*)

Distant direct examination: On distant direct examination in fellow eye may reveal subluxation or dislocation. There will be a poor glow in the aphakic eyes and characteristic crescent reflex is seen in cases of subluxation in the other eye.

Fundus: Indirect ophthalmoscopy is the most important examination. Dislocated lens (**Fig. 1**) or IOL (**Fig. 2**) may be entangled into vitreous/vitreous base or may be situated inferiorly. The location depends on status of vitreous degeneration. One should look for vitreous hemorrhage,



Fig. 1: Intraoperative photograph depicting dropped sclerotic lens over the posterior pole. Note nuclear sclerosis

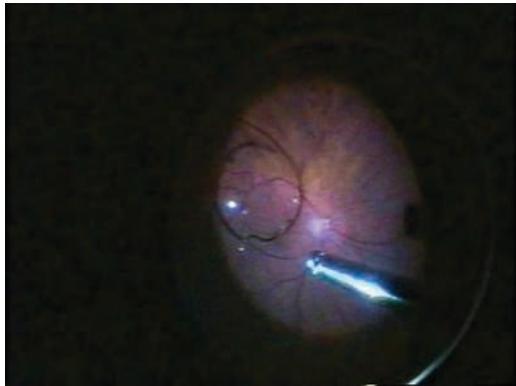


Fig. 2: Intraoperative photograph of dropped rigid IOL. The haptics are being freed of vitreous

status of PVD, retinal tear, its extent (in degrees or clock hours), location of tear, retinal detachment, extent of retinal detachment (total or subtotal), macular edema. In myopia or Marfans disease, there may be accompanying signs of vitreoretinal degeneration.

In case of lens drop, size of fragment must be noted as up to 20% sized fragments may be traditionally left alone. Only cortical drop can be managed easily with steroid therapy and inflammation control. Grade of nuclear sclerosis must be noted, harder lens would need fragmentation while softer lens are amenable to cutter dissection. In cases of IOL drop, it should be noted if the IOL is rigid or foldable, broken or intact. If IOL power is suitable, the IOL may even be repositioned in the sulcus.

Fellow eye: One should look for posteriorly dislocated lens, myopic changes, lattice, retinal tear and retinal detachment in the fellow eye.

DIFFERENTIAL DIAGNOSIS

Usually, the cases are straightforward. In patients with media haze, however, Ultrasonography (USG) finding can have differentials like endophthalmitis, cysticercosis, IOFB, etc.

INVESTIGATIONS

Axial length and keratometry or optical biometry (if possible) is done, if secondary IOL implantation is planned.

Ultrasonography

Ultrasonography is done in presence of media haze.

- *Ultrasonography appearance of dropped nucleus:* Seen as a biconvex body, which may be mobile or fixed. Lens fragment usually produces vitritis that can be seen as multiple mild-moderate amplitude spikes.
- *USG appearance of dropped IOL:* Appears similar to a foreign body showing high reflectivity and shadowing effect behind it.

UBM

UBM is useful in cases of angle recession, and for sulcus assessment.

Specular Count

It is done for evaluation of corneal endothelium, and it is necessary for complicated surgeries.

OCT

Optical coherence tomography (OCT) is done to rule out CME, only if suspected.

MANAGEMENT

The management of dropped nucleus begins at the time of first surgery itself.

Recommendation for Anterior Segment Surgeon

- Attempt lens fragment removal if only accessible.
- Perform anterior vitrectomy to avoid vitreous prolapse in limbal wound.
- Insert PCIOL or ACIOL whenever possible (unless fragment is very hard and later limbal extraction is planned).
- Close wound in standard fashion and ensure watertight closure.
- All vitreous and viscoelastic must be removed completely.
- Postoperative medication must include intensive steroid for inflammation control (both systemic and topical), cycloplegics and antiglaucoma medication. Include topical hypertonic saline drops if corneal edema is present.

- Refer to posterior segment surgeon as soon as possible.

Conservative Therapy

For smaller nuclear fragments and cortical drop, conservative management may be planned. Though in the era of safe vitrectomy, usually surgery is recommended. Until the time surgery is awaited, delayed, or planned, careful control of IOP, inflammation and corneal edema should be planned, along with regular posterior examinations.

Lens Removal (Phacofragmentation)

Surgical removal is preferred within 2 weeks after original cataract surgery.

Indications of surgery includes following:

- Nuclear size >2 mm or >25%
- Inflammation not responding to treatment by 1–2 weeks despite optimum therapy. Nucleus is full of antigens that can incite inflammation.
- Persistently raised IOP despite medical therapy.
- Retinal detachment, retinal tear, endophthalmitis and other complications.

Factors affecting the technique of removal of lens includes:

- Size of lens
- Matter-nuclear or cortical
- Time since surgery
- Presence of inflammation.

Surgery

Two routes can be used—either limbal or pars plana. The various techniques that can be used include vitrectomy cutter (for cortical matter); Ultrasonic fragmentation (for grade 2/3 hardness of nucleus); mechanical crushing between two instruments; limbal extraction of hard nuclear fragment (advanced grades/brunescent cataract). However, with modern day vitrectomy machines, vitrectomy with fragmentation is the preferred technique.

Role of Perfluorocarbon Liquid (PFCL)

It floats nucleus anteriorly and decreases complication. Chattering in the vitreous cavity

is rather frequent. PFCL helps in management of such small pieces as well, while preventing macular damage.

Prognosis

Careful case selection and timing of surgery along with postoperative care results in better prognosis. Around 60–80% patients achieve a visual acuity of >20/40 with proper care.³

Other types of posterior surgeries: Torsional fragmentation, Four-port vitrectomy with chandelier, limbal vitrectomy with electrical cutter, PFCL levitation and removal through limbus for hard cataracts, using micro vitreo-retinal knife (MVR) for lens elevation.

INTRAOCULAR LENS (IOL) DISLOCATION

Inadequate posterior capsular support from capsular/zonular rupture due to trauma is usually the basis of IOL dislocation. It can be early or late.

Early Dislocation

Completely dislocated PCIOL usually occurs in first week. Placing the IOL on anterior hyaloid through posterior capsule rupture or spontaneous IOL haptic rotation can cause early dislocation.

Late Dislocation

Late dislocation is less common. Trauma or spontaneous loss of zonular support as in pseudoexfoliation syndrome or Laser capsulotomy (After YAG capsulotomy dislocation of IOL, characteristically foldable IOL dislocate due to release tension from fibrosis.) can cause late dislocation.

IOL Removal

Three different approaches are followed IOL removal, IOL removal with IOL exchange or IOL removal with IOL repositioning. For IOL repositioning capsular rim should be at least, six clock hours/180 degree in which three clock hours should be intact inferiorly. Best way to judge is retroillumination.

Indication for Removal

Mobile IOLs with attached vitreous cortex can typically cause complications and should

be removed. In addition, IOLs stuck over the posterior poles causing visual dysfunction need removal. Conventionally immobile IOLs away from posterior pole with detached cortical vitreous have been left *in situ*. However, again, in today's era of safer vitrectomy, most IOLs are removed.

Other Indications

Substantial intraocular inflammation, CME, retinal detachment, vitreous in wound/attached to iris.

Surgery involves vitrectomy, PVD induction, PFCL injection, freeing the IOL from all vitreous tags, grasping the IOL at optic-haptic junction, careful removal through the limbus while maintaining IOP and protecting endothelium. Secondary IOL may be placed, wound closed and vitrectomy completed with PFCL removal. Complications are similar to lens drop.

VIVA QUESTIONS

Q.1. What are predispositions to complicated cataract surgery, and what are the signs for posterior polar cataract.

Ans. See chapter on posterior polar cataract.

Q.2. Management of PCR during phacoemulsification with prevention of nucleus drop.

Ans. It is important to recognize risk factors for complicated surgery before beginning the cataract surgery. See risk factors above. Next the surgeon should recognize presence of PCR early (see chapter on polar cataract). Further management should depend on the size of PCR, size of lenticular fragments pending for emulsification and surgeon's ability. If drop is imminent it would be wiser to enlarge the wound using appropriate viscoelastics and deliver out the lenticular fragments manually.

See recommendations for anterior segment above in chapter.

Q.3. What are causes of ectopia lentis?

Ans. See the chapter on ectopia lentis.

Q.4. Discuss management of dropped lens.

Ans. This has been discussed above.

Q.5. What is optimum timing for management of dropped lens during phacoemulsification?

Ans. There are two opinions on this. Immediate surgery at the time of the drop has the advantage of a single surgery with less patient anxiety and quicker rehabilitation. Later surgery after corneal edema and inflammation control has the advantage of better and easier surgery planned IOL rehabilitation and already loosened vitreo-retinal attachments. However, most surgeons believe if cornea is clear enough to allow for surgery and vitreoretinal expert is available, it is better to go for immediate surgery.

Q.6. How to rehabilitate an aphakic patient?

Ans. Spectacle, contact lens, and secondary IOLs (SFIOL/ACIOL/Sulcus IOL) are the options. Surgery may be deferred if poor visual function is anticipated. See relevant chapters for discussion.

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STARGARDT DISEASE

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INTRODUCTION

Stargardt disease, or fundus flavimaculatus (Fundus flavimaculatus is the term designated for the phenotypic presentation of Stargardt disease in which “flecks” are distributed throughout the fundus) is an inherited form of juvenile macular degeneration.¹ It causes progressive vision loss usually to the point of legal blindness. It is the most common childhood inherited macular dystrophy. It is commonly kept as a short case in postgraduate examination.

HISTORY

Symptoms

The disease is bilateral and symmetric, though asymmetric presentations may be seen. Main symptom is loss of visual acuity. Complaints of diminution of vision may first be recognized as early as 5 years but may even be seen as late as 50 years or more. Very early onset patients usually have a fairly severe *ABCA4* genotype and more sensitive foveal cones.

History of Presenting Illness

Apart from painless, gradual in onset vision loss, other symptoms includes:

- Wavy vision/metamorphopsia
- Central scotoma
- Blurring
- Impaired color vision
- Difficulty in adapting to dim lighting
- Photophobia
- Slow dark adaptation.

Vision is most noticeably impaired when the macula (center of retina and focus of vision) is damaged, leaving peripheral vision more intact. Peripheral visual fields also tend to stay stable.

Family History

This is extremely important. Typically autosomal recessive pattern may be traced on pedigree analysis.

Genetics

Stgd 1: Most common form of mutation in Stargardt disease. It is the recessive form caused by mutations in the *ABCA4* gene.

Stgd 3: Seen in dominant form of Stargardt disease caused by mutations in the *ELOVL4* gene.

Stgd 4: Autosomal dominant transmission. *PROM1* gene-heterozygous mutation.

Disease spectrum is determined largely by the total amount of residual *ABCA4* function.²

EXAMINATION

Systemic Examination

Systemic examination may not reveal findings in isolated ocular disease and are typically absent.

Ocular Examination

Visual acuity: Best corrected visual acuity should be recorded. Refractive errors may be seen. Loss of visual acuity, can be as mild as 20/30 or as severe as 20/200.

Examination of anterior segment, eyeball, lid adnexa and orbit usually does not show any findings.

Posterior segment: While 90 D examination is a must for macular examination, peripheral examination with 20 D/28 D lens should also be done. Peripheral lesions like retinal degenerations and pigmentary changes may be associated with macular dystrophy. Typical findings includes:

- Abnormal fundus appearance that is incidentally discovered.
- Light-colored flecks at the level of the retinal pigment epithelium—*more elongated than round*.
- *Pisciform (fish-tail)*: Two adjacent flecks form an obtuse angle.
- Many different fleck configurations.
- Fairly reliable diagnostic sign: *Relative sparing of the peripapillary retinal pigment epithelium (RPE)*.

- Uniform vermillion or light-brown color to the fundus with complete obscuration of the underlying choroidal details.
- Frank RPE atrophy is commonly seen in the center of the macula and the bases of these atrophic lesions have a metallic sheen (**Fig. 1**). “Beaten-bronze” appearance.
- Choroidal neovascular membranes (CNVMs) and subretinal bleed may be seen as complications.

There is interplay of three factors:

1. Severity of *ABCA4* genotype (determines rate at which toxic bisretinoids are formed in the photoreceptors).
2. Relative sensitivity of the foveal cones to the genotype.
3. Relative sensitivity of the retinal pigment epithelium to the genotype.

DIFFERENTIAL DIAGNOSIS

Differentials of Bull's eye maculopathy:

- Stargardt diseases
- Cone and cone-rod dystrophy
- Chloroquine retinal toxicity
- Age-related macular degeneration (ARMD)
- Chronic macular hole
- Central areolar choroidal dystrophy
- Olivopontocerebellar atrophy
- Ceroid lipofuscinosi

Other macular dystrophies should be kept as differential diagnosis.



Fig. 1: Macular atrophy and flecks in a case of macular dystrophy. Note the pigment mottling and temporal disc pallor

INVESTIGATIONS

Autofluorescence

Due to lipofuscin deposits, hyper-auto-fluorescence may be elicited. However, diagnostic reliability is low as some patients can have hypo-autofluorescence also. Amount/density of autofluorescence may be utilized in follow-up also.³

Fundus Fluorescein Angiography Finding

- Complete masking of the choroidal circulation.
- With angiography, the dye-filled retinal vessels lie upon a completely hypofluorescent background that results in a finding variously known as a dark, silent, or masked choroid.⁴

Optical Coherence Tomography

Optical coherence tomography (OCT) can reveal the extent of outer retinal loss and RPE atrophy and it can also distinguish the anatomic level of flecks with accuracy. Choroidal layer changes have also been studied, though concrete evidence is lacking. Choriocapillaris may be lost. Late stages reveal thinned out macula and may catch CNVMs or SRF.

Electrophysiology

As full-field ERG represents a mass response of all photoreceptors, it is typically normal in patients with Stargardt disease. Cone and rod functions may be affected in severe *ABCA4* genotypes.⁵ Multifocal electroretinogram (mfERG) is a sensitive tool in detecting very early involvement in even clinically normal cases. Significant decrease in ERG waveform amplitudes is noted in all rings, even the most peripheral eccentricity group 10°–31°, although the change from normal goes on decreasing as we move from central to peripheral eccentricity rings.

Visual Field Testing

Visual field testing in Stargardt patients is often normal in early disease stages.

Over time, relative central scotomas develop which progress to absolute central scotomas. Color vision and contrast sensitivity may be done for progressions or as ancillary tests, but do not add to diagnosis.

MANAGEMENT

There is currently no proven treatment for this disease. Since a primary defect in *ABCA4* associated retinal disease is an accumulation of toxic bisretinoids in the RPE and photoreceptors, drugs that modulate the visual cycle (e.g. Isotretinoin and fenretinide), have been investigated for their potential to slow the formation of these toxic products.

Gene therapy and cell replacement may be upcoming treatment modality.

Visual Rehabilitation

Low vision aids (LVA)—such as magnifying glasses may be help in cases with macular atrophy.

Patient Counseling

- Stargardt patients should be encouraged to maintain good sun protection, as exposure to bright light can lead to the formation of all-transretinal in photoreceptors and contribute to lipofuscin accumulation.
- Avoidance of cigarette smoking or avoidance of high-dose vitamin A supplements, including AREDS vitamins, because of their potential to increase the formation of bisretinoids in the retina.
- Sibling screening and genetic counseling is important.
- These patients should be kept on follow-up for documenting progression and treating complications.

VIVA QUESTIONS

Q.1. Name few macular dystrophy.

Ans. See Table 1.

Table 1 Common examples of macular dystrophy

	<i>Macular dystrophy</i>	<i>Gene</i>	<i>Chromosome</i>	<i>Pattern</i>
1	Best macular dystrophy	<i>BEST1</i>	11	AD/AR
2	Stargardt disease	<i>ABCA4</i>	1	AR
3	Stargardt-like dominant macular dystrophy	<i>ELOVL4</i>	6	AD
4	Pattern dystrophy	<i>PRPH2</i>	6	AD
5	Sorsby fundus dystrophy	<i>TIMP3</i>	22	AD
6	Autosomal dominant radial drusen	<i>EFEMP1</i>	2	AD

Q.2. What are differential diagnoses of Bull's eye maculopathy?

Ans. See the section on differential diagnosis.

Q.3. What is Stargardt-like dominant macular dystrophy (SLMDM)?

Ans. *Stargardt-like dominant macular dystrophy (SLMDM)*.

- Autosomal dominant
- Chromosome 6
- Elovl4* gene: Elongation of very long chain fatty acids-4
- Most-characteristic features of this disease are circular zone of RPE atrophy, a pigmented spot beneath the fovea, and a ring of flecks just beyond the margin of the atrophy
- ERG is usually normal.

Q.4. What are the fundus findings in Stargardt disease?

Ans. See above.

Q.5. What is the pathophysiology of Stargardt disease?

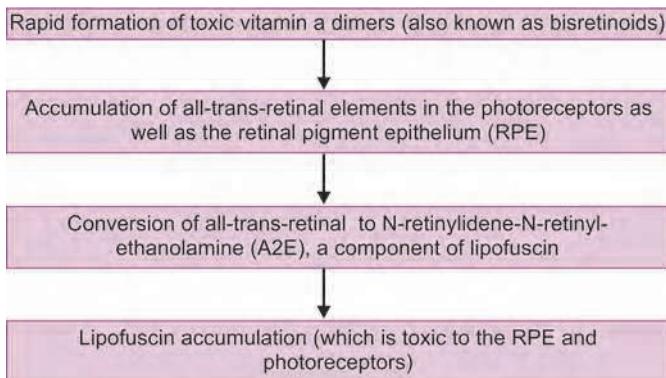
Ans. See Flow chart 1.

Q.6. What is Fishman classification of Stargardt disease?

Ans. See Table 2.

Q.7. What is fundus flavimaculatus?

Ans. Fundus flavimaculatus and Stargardt disease are varied clinical presentation of the same disease process and belong at different ends of the clinical spectrum. Pure Stargardt disease presents with macular involvement and pure fundus flavimaculatus presents with multiple mid peripheral 'fleck' lesions with preservation of macular region. In most cases, a mixed presentation is usually seen. In general,

Flow chart 1: Pathophysiology of Stargardt disease**Table 2** Fishman classification of Stargardt disease

Stage 1	<i>Fundus:</i> Pigmentary change in macula, "beaten-bronze" appearance. <i>ERG:</i> Normal.
Stage 2	<i>Fundus:</i> Flecks beyond 1 DD from margin of fovea, extending beyond arcade. <i>ERG:</i> Normal. Prolonged period of dark adaptation
Stage 3	<i>Fundus:</i> Diffuse flecks and choriocapillary atrophy at macula <i>ERG:</i> Subnormal cone and rod amplitude Central field defect as well as peripheral/midperipheral field impairment
Stage 4	<i>Fundus:</i> Diffuse flecks and extensive RPE atrophy throughout the fundus <i>ERG:</i> Reduced cone and rod amplitude Peripheral field—Moderate to extensive restriction

patients with extensive extramacular flecks have poorer long-term visual prognosis than patients with only macular involvement.

Q.8. What are fleck lesions?

Ans. These are accumulations of lipofuscin seen at the RPE level. They are usually more elongated than drusens and may connect with each other forming a net like branching pattern. Different shapes, size, color and location can be seen. They may remain stable in number and location with preservation of visual acuity or may grow in size leading to widespread atrophy and decline in vision.

Q.9. What is Best dystrophy? What are its stages? How is it different from Stargardt?

Ans. Best disease is a juvenile onset vitelliform macular dystrophy that is characterized

by classic single bilateral macular egg yolk like vitelliform lesions, though, multiple lesions involving the posterior pole may be seen. It has an autosomal dominant mode of inheritance in typical cases, although autosomal recessive inheritance as well as adult onset has been described. The classic lesions typically appear in early childhood, though are not usually picked up as visual acuity remains very good till very late in the disease process. Different stages for the lesions are described but the disease may not follow specific staging pattern.

Stages:

- Previtelliform
- Vitelliform
- Pseudohypopyon
- Vitelliruptive
- Atrophic

On SD-OCT, the vitelliform lesions represent accumulation of hyper-reflective material in the subretinal space. Full field ERG is typically normal. EOG is a specific investigation for Best disease. An Arden ratio of <1.5 is said to be characteristic of Best disease.

Cases with Best disease differ from Stargardt disease in many ways:

- Presence of a well-defined yellow lesion at the macula
- Maintained visual acuity till late stages
- Absence of flecks
- Electrooculogram (EOG) <1.5 with normal ERG
- Characteristic SD-OCT with presence of subretinal hyper-reflective material.

It may become difficult to clinically distinguish the two in cases with atrophic Best disease as only well-defined central atrophy might be present in such cases. EOG may be diagnostic in such cases. Also, autosomal dominant inheritance with presence of lesions in otherwise asymptomatic relatives may help in diagnosis.

Q.10. What is Ardens ratio?

Ans. Electrooculogram is a measure of the difference in standing potential of the eye between the cornea that is electrically positive and the RPE that is electro-negative. As there is much variation in EOG

amplitudes, a ratio known as the Arden ratio, which represents ratio between the maximal height of potential in the light (light rise) and minimal potential in the dark (dark trough) is used to quantify the EOG values. Most of the response is manifested due to photoreceptor activity and RPE.

Electrooculogram is a specific investigation for Best disease. A highly abnormal EOG with normal ERG is diagnostic of Best disease.

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TRAUMATIC RETINAL DETACHMENT

Priyanka Ramesh, Shreyas Temkar, Dheepak Sundar, Atul Kumar

INTRODUCTION

Traumatic retinal detachment accounts for 12% of all rhegmatogenous retinal detachment (RD) and is the most common cause of rhegmatogenous RD (RRD) in children. RD can occur both following open globe and closed globe injury. In closed globe injury, the detachment is following a retinal tear or dialysis, whereas in an open globe injury, the retinal detachment is due to vitreous traction following vitreous prolapse or direct injury related break.¹

HISTORY

Sometimes it is easy to link trauma to RD, whereas sometimes the patient may try to hide the history or may even have forgotten it. The onus is on the ophthalmologist to identify the precipitating event in the latter case.

Chief Complaints

The patient can present in following ways:

- Sudden onset of field loss and diminution of vision.

- Incidental RD may also be detected while managing for other manifestations of trauma. It is usually seen in young male patients with definitive history of trauma either blunt or penetrating. Patients can present either immediately following trauma or can present until usually about 2 years following trauma.

History of Presenting Illness

Detailed history about when the trauma occurred, the mode of injury has to be taken. In addition, following points must be enquired:

- History of any surgical intervention like corneal/scleral perforation repair has to be noted.
- If a patient is presenting late after trauma, then the previous ocular findings, visual acuity has to be reviewed. This may help in case wise prognostication. Children typically present late after trauma. All these points become very crucial in a medicolegal case.
- History of trauma should always be ruled out on leading questions in unexplained ophthalmic cases.

Past History

History of any surgical procedures done before the trauma or for its management has to be taken. History of recurrent trauma may indicate patient abuse or even self-mutilation (mentally challenged) or poor functional status of vision.

Family History

In doubtful cases, family history of retinal disorders must be inquired for.

EXAMINATION

Systemic Examination

History of loss of consciousness, ENT bleeds and seizures have to be evaluated in case of multiple injuries. In cases of polytrauma, other system involvement has to be assessed. These patients would require multidiscipline management.

Ocular Examination

Visual acuity: Best-corrected visual acuity of both eyes with projection of rays has to be checked.

While pure retinal detachment may cause inaccurate PR rarely, it can be present in post-traumatic cases, which suggests concomitant optic nerve damage and hence poor visual prognosis.

Eyeball: Presence of squint, ocular movement restrictions, enophthalmos, discontinuity in the orbital rim has to be checked to rule out any orbital trauma. It is not uncommon to see signs of blow out fractures.

Lids, conjunctiva: May show signs of trauma. There may be lid laceration or subconjunctival hemorrhage. Complex lacerations may need a plastic surgical review.

Sclera: In fresh cases, one should always look at the integrity of the globe and rule out the presence of any scleral rupture. In doubtful delayed cases, a thorough examination should be done as posterior as possible for signs of old repaired scleral wounds.

Cornea: In fresh cases, there may be a corneal laceration and in old cases, there might be scars of previously operated corneal laceration or of a self-sealed corneal wound. Limbal scars are common in blunt trauma related open globe injury.

Anterior chamber: In acute injury there might be hyphema in the anterior chamber. Detailed examination must be done to check for any signs of inflammation like cells and flare.

Iris: There might be associated iridodialysis, which appears as a D shaped pupil and best confirmed on a distant direct examination. The iris may also show presence of sphincter tears and traumatic mydriasis, which causes anisocoria. Sphincter tears may also be seen.

Gonioscopy: It is necessary to do gonioscopy in all patients with trauma to rule out angle recession. Findings must always be compared with the other eye. There will be increased width of the ciliary body band and increased pigmentation. Cyclodialysis can also be picked up on gonioscopy.

Lens: It can be cataractous ranging from total cataract to posterior subcapsular variety, typically the rosette cataract. There can also be associated subluxation/dislocation of the lens. These patients will have phacodonesis and iridodonesis. One should keenly examine for presence of the Vossius ring.

Pupillary reactions: Direct and consensual reflexes must be checked in both eyes and swinging torch light test must be done for relative afferent pupillary defect (RAPD). In case the affected eye has traumatic mydriasis or there is obscuration of the pupil due to hyphema then the consensual in the other eye becomes a very important predictor of an intact optic nerve.

Intraocular pressure (IOP): In the presence of retinal detachment, the IOP is usually low, but in the presence of angle recession or increased inflammation, there might be raised IOP.

Posterior segment: The idea is two pronged: Identify signs of trauma and work-up for RD. The vitreous cavity may show the presence of vitreous hemorrhage in acute cases. If the posterior segment details are obscured due to vitreous hemorrhage, an ultrasonography (USG) of the posterior segment is required to rule out retinal detachment.

If the fundus is visible then the fundus has to be examined thoroughly to look for:

- All retinal breaks has to be localized
- Indentation indirect ophthalmoscopy has to be done to check for dialysis and vitreous base avulsion.
- Retinal dialysis is typical for blunt trauma; SN is pathognomonic while IT is most common.^{2,3}
- Other indicative breaks include giant retinal tear (GRT), ragged margin multiple tears, etc. As such, any kind of break may be seen. Work-up should be done as for retinal detachment. Young patients with delayed

presentation will have chronic RD often with signs of proliferative vitreoretinopathy (PVR) (Fig. 1).

- Other signs of trauma like commotio retinae, subretinal bleed, choroidal rupture, macular hole should be looked for.⁴
- Optic disc must be evaluated for presence of traumatic optic neuropathy or for glaucomatous changes.
- Other eye examination is necessary for satisfying Cox's postulates in doubtful cases.

See Table 1 for posterior segment signs of trauma.

DIFFERENTIAL DIAGNOSIS

See chapter on RD. Specifically in a patient with GRT differentials like myopia, iatrogenic

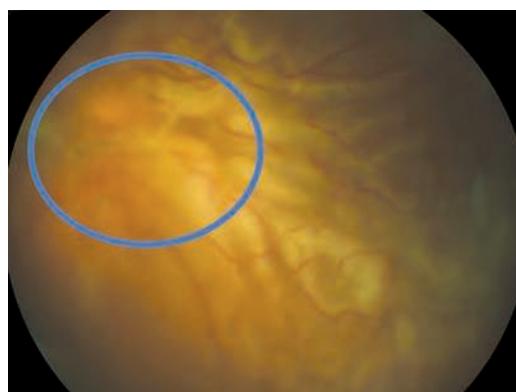


Fig. 1: PVR in a case of traumatic RD. Note the encircled peripheral retinal fold

Table 1 Posterior segment signs of trauma

Closed globe injury	Open globe injury
Vitreous base avulsion Retinal tears (dialysis, horseshoe tears, operculated holes, tears with ragged margins) Retinal detachment Commotio retinae Macular hole Choroidal rupture Subretinal bleed Vitreous hemorrhage Choroidal hemorrhage Posteriorly dislocated lens/IOL Retinitis scropetaria	Scleral rupture/penetration Retinal tears Retinal detachment Proliferative vitreoretinopathy Retained intraocular foreign body Endophthalmitis

and idiopathic, and in patients with retinal dialysis, inferior temporal retinal dialysis of young should be kept in mind (see discussion). Ragged margin breaks may also be due to viral retinitis related necrosis.

INVESTIGATIONS

USG B scan: Can be used to rule out RD in patients where the visualization of the retina is hampered. It can show vitreous incarceration in few cases. USG is also useful to rule out presence of retained intraocular foreign body.

X-ray orbit: Used to rule out orbital fractures or any retained intraocular foreign body.

Optical coherence tomography: May be done for concomitant macular changes due to trauma.

Visual evoked response (VER): It is useful in cases of old RD and those in which traumatic neuropathy is suspected.

MANAGEMENT

Medicolegal cases need proper documentation while multidepartment approach may be needed. Other concomitant manifestations of trauma may need management. See chapter of RD for detailed management and figures. In patients with blunt trauma, it is necessary to rule out retinal dialysis. PVD is typically absent in these patients. Prognostication is of essence as these patients typically need recurrent surgeries and have poor outcomes. Complications like postoperative glaucoma and cataract are frequent.

In patients with open globe injury, it is necessary to secure the wound in the coats.

VIVA QUESTIONS

Q.1. What are the mechanical changes in the globe following blunt trauma?

Ans. Changes occur in four phases

1. Compression
2. Decompression
3. Overshooting
4. Oscillations

Blunt trauma typically causes antero-posterior compression with equatorial expansion of the globe.

Q.2. What are the types of retinal breaks seen following blunt trauma and what is the mechanism of breaks?

Ans. Blunt trauma (ocular contusion) results in numerous types of breaks like retinal dialysis, horseshoe tears, giant retinal tears (GRT), operculated holes and macular hole. These breaks can be due coup injury causing breaks at the site of trauma or counter coup, opposite the site of trauma and are usually located predominantly in the vitreous base region. Breaks caused by retinal necrosis occur slowly and show ragged uneven edges.

Q.3. What is the definition of retinal dialysis and what is the most common location of dialysis following trauma?

Ans. Retinal dialysis is defined as disinsertion of the retina from the nonpigmented epithelium of the ciliary body at the ora serrata. It accounts for 8 to 14% of the retinal detachments. GRT and dialysis account for 69% of all traumatic detachments.

Most common location is inferotemporal accounting for 66% of cases. This is because the inferotemporal quadrant is least protected based on orbital anatomy. Superonasal location is the most pathognomonic of trauma. Weidenthal and Schepens reported that nasal retina has greater susceptibility to traumatic retinal dialysis secondary to its narrow vitreous base. Mean size of post-traumatic dialysis is around 2.4 clock hours.

Q.4. When does retinal detachment occur following trauma?

Ans. Retinal detachment immediately following trauma is rare and in general the detachment progresses slowly occurring weeks to months following trauma. This is because of the presence of formed vitreous in young patients. Following points must be remembered:

- 12% detachments are identified immediately.
- 30% detachments are identified within 1 month.
- 50% detachments are identified within 8 months.

- 80% detachments are identified by 24 months.

GRT following trauma usually shows a rapid progression.

Q.5. What is the mechanism of retinal detachment following open globe injury?

Ans. In the presence of open globe injury, the vitreous is incarcerated in the wound and there is fibrous ingrowth along the vitreous scaffold. There is also break down of blood retinal barrier, which initiates an inflammatory response causing proliferation of pigment epithelial cells, fibroblasts and glial cells. These produce collagenous extracellular matrix, which causes contraction. This causes traction on the peripheral retina, rolling forward at the vitreous base and junction of the ora. Over weeks, the proliferation progresses and causes cyclitic membrane, epiretinal membrane and retroretinal membrane. There can also be abrupt PVD causing retinal breaks.

Q.6. What are the seven rings of trauma?

Ans. Blunt trauma can result in injury to various tissues of the eye. Seven rings of tissues affected by blunt trauma to the eye are:

1. Tears in Sphincter pupillae—seen as disruption of pupillary margin on slit lamp.
2. Iridodialysis—seen as dehiscence of iris from the sclera with a D shaped pupil.
3. Angle recession—characterized by separation of circular muscle fibers from longitudinal fibers of ciliary body. There is posterior displacement of the iris and widening of ciliary body band on gonioscopy. It is always important to confirm this finding by comparing with the fellow eye.
4. *Cyclodialysis*: Separation of ciliary body attachment from scleral spur. This can result in hypotony.
5. Trabecular meshwork tears.
6. Zonular dialysis resulting in subluxation of the crystalline lens.
7. Retinal dialysis—disinsertion of the retina from nonpigmented epithelium of ciliary body at the ora serrata.

Inferotemporal quadrant is most commonly involved but superonasal dialysis is pathognomonic of trauma.

Q.7. What are the posterior segment signs of trauma?

Ans. See Table 1.

Q.8. What are the Cox's postulates for traumatic retinal detachment?

Ans. In some cases it is difficult to differentiate between spontaneous retinal detachments from those occurring due to trauma. Cox, Schepens and Freeman gave certain postulates, which could point towards occurrence of retinal detachment from trauma. They include:

- Unilateral retinal detachment preceded by ocular contusion.
- Objective signs of contusion in the affected eye.
- Absence of visible vitreoretinal degeneration of the types known to cause retinal breaks in both the affected and fellow eyes.

Q.9. What is inferior temporal dialysis of young?

Ans. The patient is typically young male and has unilateral or bilateral retinal dialysis in the inferior temporal area. Sometimes other changes like WWOP, retinal cystic degeneration and pigmentation/holes may be there. The causation is related to abnormal development of the inferior temporal pars plana, which normally develops the last. This is an important differential of a case of traumatic RD with retinal dialysis.

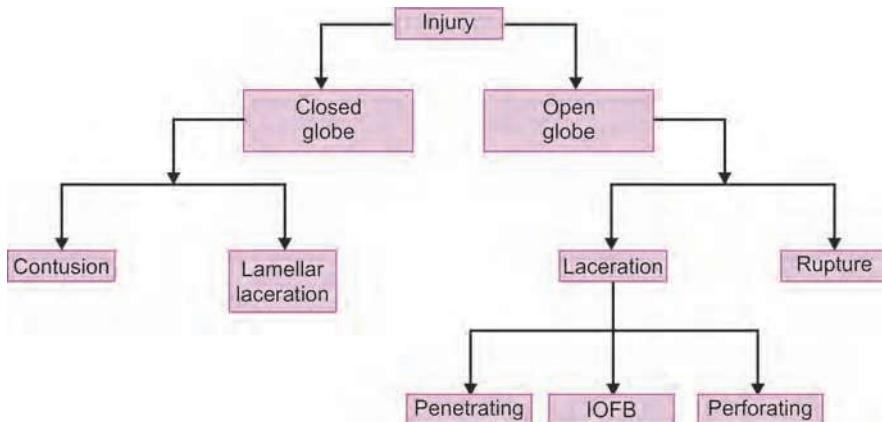
Q.10. Tell in brief about BETT classification.

Ans. This system utilizes definitions that refer to the entire globe, not to a specific tissue. This solves the problem of using confusing terms with respect to individual tissues.

Flow chart 1 showing clinical classification of injuries based on BETT system.

BETT system also defines these injuries as follows:

- *Eye wall*: Sclera and cornea
- *Closed globe injury*: No full-thickness wound of eye wall

Flow chart 1: Classification of ocular injury

Abbreviation: IOFB, intraocular foreign body

- **Open globe injury:** Full-thickness wound of the eye wall
- Contusion no wound of the eye wall. The damage may be due to direct shock wave by the object (e.g. choroidal rupture), or to changes in the shape of the globe (e.g. angle recession)
- **Lamellar laceration:** Partial-thickness wound of the eye wall
- **Rupture:** Full-thickness wound of the eye wall, caused by a large blunt object
- **Laceration:** Full-thickness wound of the eye wall, caused by a sharp object
- **Penetrating injury:** An entrance wound is present
- **IOFB:** One or more foreign objects are present
- **Perforating injury:** Both an entrance and an exit wound are present.

Based on the Birmingham Eye Trauma Terminology, injured eyes are categorized by four parameters:

1. **Type** (based on the mechanism of trauma):

Closed globe injury

- Concussion
- Lamellar laceration
- Superficial foreign body
- Mixed

Open globe injury

- Rupture

- Penetration
- Perforation
- Retained intraocular foreign body
- Mixed

2. **Grade** (based on visual acuity at presentation):

- VA > 20/40
- VA 20/50–20/100
- VA 19/100–5/200
- VA 4/200–light perception
- No light perception.

3. **Pupil:**

- Positive afferent pupillary defect
- Negative afferent pupillary defect

4. **Zone** (based on the extent of the injury):

- Cornea and limbus
- Up to 5 mm from limbus
- > 5 mm from limbus.

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CHAPTER

5

Neuro-ophthalmology and Strabismus

LONG CASES

THIRD CRANIAL NERVE PALSY

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INTRODUCTION

Cranial nerve palsies can be given as long case in exam. The third cranial nerve supplies majority of extraocular muscles (MR, SR, IR, IO), levator palpebrae superioris (LPS) and contains pupillomotor fibers. A complete lesion of the III nerve involving both branches will result in a deficit of elevation, adduction and depression in abduction leading to the characteristic down and out position of the eyeball. Most of the cases are acquired. Following discussion is primarily on acquired palsy.

HISTORY

Chief Complaint

A case of third nerve palsy may present with following:

- Diplopia
- Deviation of eyes
- Limitation of movements
- Drooping of eyelid
- Diminution of vision for near, head posture, face turn, facial asymmetry, protrusion of eye, chemosis.

History of Present Illness

Age at onset: It is important to note the age of onset to differentiate between congenital and

acquired form. At times a close observation of old photographs may be helpful. Age less than 50 years warrants urgent imaging to rule out ICSOL.

Mode of Onset

Acute onset of diplopia or deviation warrants immediate neuroimaging to rule out life-threatening conditions, hence, the type of onset is extremely important to note.

Diplopia

It is the presenting symptom in majority of cases. Primarily seen as horizontal and vertical binocular diplopia. It must be remembered that patients due to ptosis may not volunteer diplopia. It may also be absent in patients with long standing disease with early age of onset resulting in suppression.

Pain

Headache, localized pain in the orbit, and periorbital region can be there suggestive of orbital inflammatory disease like Tolosa-Hunt syndrome. Aneurysm of posterior communicating artery can be associated with severe pain or headache. Ischemic mononeuropathy (e.g. DM) can be associated with variable degree of pain.

Poor Visual Acuity, Abnormal Head Posture, Facial Asymmetry

Presence of these suggests congenital nature of the disease.

Glare

Rarely a dilated pupil (due to involvement of pupillomotor fibers).

Associated Symptoms

Although rare patient may complain of difficulty in reading, protrusion of eye, chemosis, headache, pain, vomiting. Patient may present with other neurological symptoms like contralateral hemiparesis in Weber's syndrome, contralateral tremors in Benedict syndrome and ipsilateral ataxia in Nothnagel syndrome.

History of Past Illness

A careful past history is helpful in identifying the probable cause of third nerve palsy. Important causes include etiologies for oculomotor palsy: vasculopathic process (diabetes, hypertension, CAD), trauma, compression (e.g. aneurysm, ICSOL) and/or infiltrative (e.g. leukemia), inflammatory, infection, demyelinating disease, toxic (e.g. chemotherapy).

Similar episodes in past must be enquired. Recurrent third nerve palsy can occur in DM, aneurysm, and ophthalmoplegic migraine.

Past Surgical History

History of any previous neurosurgical procedure must be recorded.

Family History and Birth History

In cases of congenital third nerve palsy both these history are important.

EXAMINATION

General Examination/Specific Systemic Examination

A thorough review of systems should be conducted, including enquiry about other neurological symptoms, giant cell arteritis, trauma and symptoms of ear disease. Neurological

examination must include other cranial nerves and the peripheral nervous system. In a child, an otorhinolaryngological review may be sought.

Ocular Examination

Visual Acuity

It is necessary to lift the ptotic lid to evaluate visual acuity. Vision may be reduced due to mydriasis, particularly for near visual acuity due to loss of accommodation. It may be reduced due to amblyopia in congenital or early age onset 3rd CN palsy. Visual acuity must be checked with and without glasses.

Face

Head posture: Head posture is taken to position the eye away from direction of action of paralytic muscles so as to minimize the deviation which can be fused to avoid diplopia. So, for left 3rd CN palsy—face turn to right with head tilt to left with chin elevation.

Facial asymmetry—should be noted in congenital cases. This can be assessed by measuring the lateral canthus to angle of mouth distance and comparing with that of other side.

Palpebral fissure asymmetry—measurement of palpebral fissure should be done using transparent ruler in primary gaze, in adduction and abduction and depression to rule out aberrant regeneration.

Eyeball

- The characteristic position of the eyeball is “down and out” (**Fig. 1**) due to unopposed



Fig. 1: Characteristic “down and out” position of the eyeball in 3rd nerve palsy

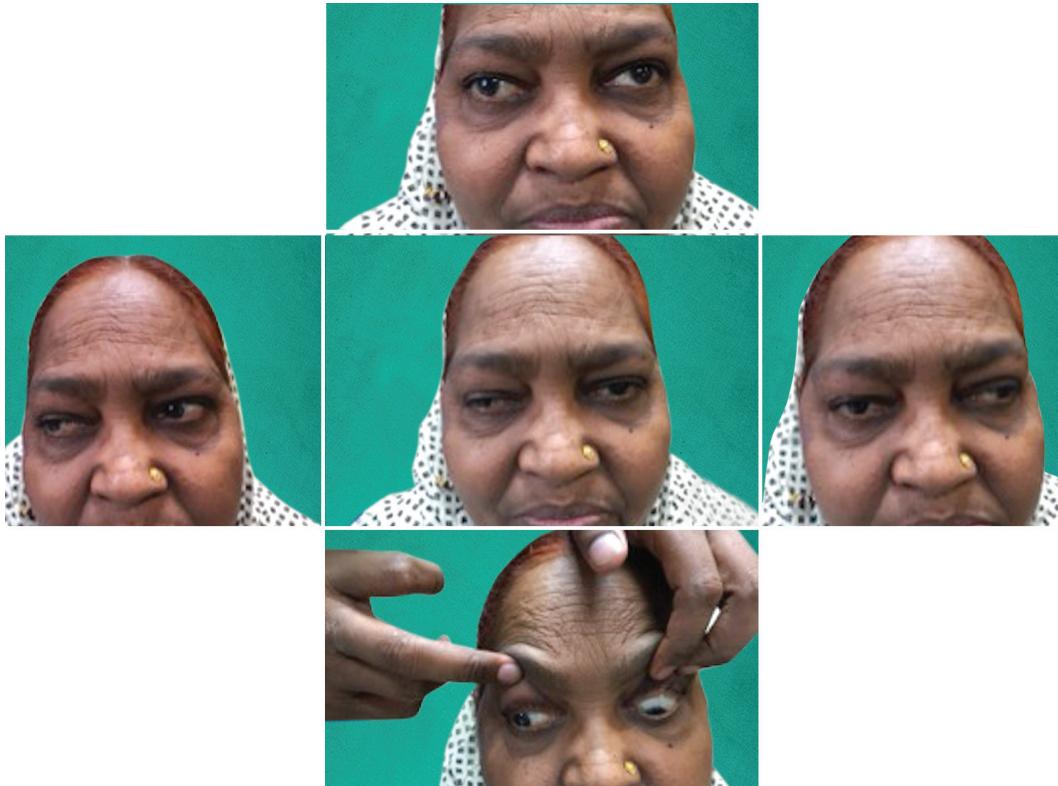


Fig. 2: Limited elevation (SR), depression (IR) and adduction (MR) in 3rd nerve palsy

action of the lateral rectus and superior oblique muscles.

- There will be limited elevation (SR), depression (IR) and adduction (MR), which may be complete or partial limitations, depending on the extent of paresis/palsy (**Fig. 2**).
- The intact superior oblique muscle also causes intorsion of the eye at rest, which increases on attempted down gaze.
- Check for the presence of IV nerve function by asking the patient to attempt to look down and outwards and observe for the presence of incyclotorsion during this movement. This can be checked by observing the movements of the nasal limbal vessels.
- In case of partial third cranial nerve palsy the deficit of adduction, supraduction, and infraduction should be apparent even if partially paralyzed. One can also check for saccades which will be floating in direction of action of paretic muscles.

- In very mild cases, latent deviation or phoria can be elicited by Maddox rod or alternate cover testing (exo and hypo deviation) to dissociate the 2 eyes and interrupt fusion.

Lid

Ptosis is usually severe and the upper lid will have to be raised by the examiner (or an assistant) in order to perform the ocular motility assessment. If there is ptosis, one must look for lid fatigue or lid twitch (kindly see myasthenia gravis case), because these might indicate myasthenia gravis. Lagophthalmos should be checked in all such cases. Aberrant regeneration to LPS from extraocular motor nerve fibers should be checked which might improve ptosis on attempted duction movements of the respected involved recti muscles (e.g. Pseudo von Graefe sign—lid retraction seen on attempted downgaze). Aberrant regeneration is important to document as it helps in guiding the surgical management.

Conjunctiva

Conjunctival injection or chemosis can be present in cases of lymphoma and thyroid dysfunction.

Cornea/Sclera/Iris

Usually normal, corneal sensation should be checked in all cases of CN palsy, which may be lost in orbital inflammatory disease.

Pupil

3rd CN palsy generally presents with anisocoria more prominent in daylight. This sluggish or absent reaction to light is there due to involvement of parasympathetic fibers that originate in the Edinger-Westphal subnucleus of the third cranial nerve complex. Aberrant regeneration to pupil should also be checked. This can be from ciliary body resulting in light near dissociation (tonic pupil) or from extraocular motor nerve fibers which can be assessed by checking pupillary constriction on attempted duction (e.g. if from MR than on attempted adduction).

IOP/Lens/Vitreous

Usually normal.

Fundus

Usually normal. However always rule out papill-edema (raised ICT), any vasculitis, vascular disease and choroidal fold (orbital mass lesions).

Special Tests for Squint/3rd Nerve Palsy

Measurement of deviation (kindly see the chapter of 6th nerve palsy and esotropia).

Convergence

This will be absent if the medial rectus muscle is paralyzed.

Accommodation

If the underlying cause of the lesion has resulted in pupillary dilatation, then fibers to the ciliary body are also likely to be involved so that accommodation will be defective.

Binocular Function

Binocular function should be assessed after neutralization of deviation. This is usually absent especially in congenital and early age onset 3rd CN palsy with large angle of deviation. Those with late onset and in partial 3rd CN palsy binocular function are usually intact.

Worth Four-dot Test

This is a dissociation test using red-green glasses, which can be used with both distance and near fixation and differentiates between BSV, ARC and suppression. Results can only be interpreted if the presence or absence of a manifest squint is known at time of testing. If two red and three green lights are seen, diplopia is present.

Bagolini Striated Glasses

This is a test for detecting BSV, ARC or suppression. Each lens has fine striations that scatter and convert point source of light into line perpendicular to the striations, as with the Maddox rod.

Double Maddox rod test

- Red and green Maddox rods, with the cylinders vertical, are placed one in front of either eye.
- Each eye will therefore perceive a more or less horizontal line of light.
- In the presence of cyclodeviation, the line perceived by the paretic eye will be tilted and therefore distinct from that of the other eye.
- One Maddox rod is then rotated until fusion (super-imposition) of the lines is achieved.
- The amount of rotation can be measured in degrees and indicates the extent of cyclodeviation.

Diplopia Charting

- *Diplopia charting using red-green glasses:* It is done by using red-green glasses and projecting a streak of light on a screen testing the patient at 1 meter [see 6th nerve palsy]
- *Synoptophore:* The synoptophore compensates for the angle of squint and allows stimuli to be presented to both eyes simultaneously.

It is useful in:

- To investigate the potential for binocular function in the presence of a manifest squint

and is of particular value in assessing young children (from age 3 years), who generally find the test process enjoyable.

- It can also detect suppression and ARC.
- It can measure horizontal, vertical and torsional misalignments simultaneously and is valuable in determining surgical approach by assessing the different contributions in the cardinal positions of gaze.
- *Hess chart:* The affected eye will show a markedly constricted field whereas the other eye demonstrates overaction of its muscles.

Left third nerve palsy—The area enclosed on the left chart is much smaller than that on the right.

- Left exotropia—note that the fixation spots in the inner charts of both eyes are deviated laterally. The deviation is greater on the right chart (when the left eye is fixating), indicating that secondary deviation exceeds the primary, typical of a paretic squint.
- Left chart shows underaction of all muscles except the lateral rectus.
- Right chart shows overaction of all muscles except the medial rectus and inferior rectus, the ‘yokes’ of the spared muscles.
- In inferior rectus palsy, observing intorsion on attempted depression can only assess the function of the superior oblique muscle. Observing a conjunctival landmark using the slit lamp best performs this. Hess charting in case of left third nerve palsy

Forced Duction Test

The forced duction test is an attempt by the examiner to move a patient’s eye farther in a given direction than the patient can move it. Topical anesthetic is placed on the appropriate limbal location (generally 180° away from the duction limitation) with a small cotton swab and the limbal conjunctiva is grasped firmly with a toothed forceps. The patient is asked to rotate the eye fully in the direction of the limited duction. An attempt is then made by the examiner to rotate the eye beyond the position attained by the patient while avoiding globe retraction. Care must be taken not to abrade the cornea. Patients who have pure nerve palsy exhibit no restriction to full movement by the examiner; patients who have pure restriction

(dysthyroid orbitopathy, entrapment of ocular contents after blowout fracture) exhibit restricted movements (sometimes termed a positive forced duction test). Some patients initially have pure nerve palsy, but contracture of the antagonist muscle results in secondary mechanical restriction of movement. Suction cup devices have been developed for examiners who are wary of using toothed instruments at the limbus; a cotton swab may be a sufficient tool in some patients.

Active Force Generation Test

Active force generation testing may be used to evaluate the ability of a muscle to move the eye against a resisting force. The forceps is placed at the limbus of the anesthetized (topical) globe in the meridian of the muscle whose duction is limited and the patient requested to rotate the eye in the direction of the limited duction; the examiner judges through the forceps the relative amount of force generated. Strain gauges have been devised that enable quantitation of this force. In case of positive AFGT, strengthening surgical procedures can be done on involved paretic muscle (e.g. resection or plication). If negative the involved muscle should be left untouched.

Aberrant Regeneration (Oculomotor Synkinesis)

Change in the actions of muscles supplied by the third nerve due to regrowth of damaged nerve fibers following complete or severe third nerve palsy. It is liable to occur when trauma, tumor or an aneurysm has caused the breach of endoneurial sheath. It may occur from weeks to months after the onset of the III nerve paresis. Aberrant regeneration is known to involve pupil, LPS and to other extraocular muscles.

INVESTIGATION

- Acute onset paralytic squint always warrants an immediate neuroimaging unless the physician is certain about the diagnosis.
- Neuroimaging is indicated in following cases of acquired 3rd CN palsy—all cases with age less than 50 years; age more than 50 years, if patient has headache, nausea, vomiting,

- other neurological signs and symptoms, involvement of pupil, ocular pain, proptosis, papilledema, loss of corneal sensation, history of trauma, nonresolving or worsening cases and lastly a willing patient.
- Remember, majority (around 60%) of cases are idiopathic and of presumed microvascular lesions in older patients. However, a wide-range of life-threatening causes (e.g. aneurysm) can be there hence a low threshold should be adopted for neuroimaging.
 - CT angiography is usually the preferred modality by most physicians. Newer modalities such as MRI brain and orbits with venography can provide additional information.
 - Vascular risk factor assessment (ESR, CRP, CBC, blood sugar, lipid profile, blood pressure, homocysteine levels, etc.) similar to that for retinal arterial disease should be done to rule out microvascular causes.
 - Supplementary investigation (e.g. lumbar puncture) may be required if a rare etiology such as infection (e.g. syphilis, Lyme disease) or vasculitis (including giant cell arteritis) is suspected.
 - For surgical purpose it can be divided into three groups
 - Complete 3rd CN palsy—supra-maximal LR recession, periosteal fixation of LR, transposition of LR to MR, Scott procedure, Peter's procedure (SO to MR).
 - Partial third CN palsy—MR resection and LR recession (adjustable procedure for co-operative patient), vertical transposition of SR and IR to MR, surgeries on SR and IR for correction of vertical deviation.
 - Aberrant regeneration to LPS—to do surgery on the normal eye which takes the advantage of fixation duress for correction of ptosis, and same side surgery may worsen the same
 - Scott procedure:* Transposition of the insertion of the SO tendon to a point anterior and medial to the insertion of the SR muscle without trochleotomy combined with large recessions of the LR muscle and, occasionally, recession-resection procedures of horizontal rectus muscles of noninvolved eyes can result in a satisfactory cosmetic outcome and alignment in primary position in some cases.

MANAGEMENT

Observation

- Appropriate in presumed microvascular cases; Majority of cases show signs of recovery at 2 weeks and recover by 3–6 months.
- Temporary (e.g. Fresnel stick-on) prisms may be useful if the angle of deviation is small, but uniocular occlusion may be necessary to avoid diplopia if the ptosis component is partial or recovering.
- Young children should be treated with alternate patching to prevent amblyopia.

Surgical Treatment

- Surgical treatment of the ocular motility element and ptosis should be contemplated only after spontaneous improvement has ceased, usually not earlier than 6–12 months from onset.
- The aim is to provide binocular fusion in at least primary position and if possible in downgaze and to correct vision limiting or cosmetically annoying upper lid ptosis.

- For surgical purpose it can be divided into three groups
 - Complete 3rd CN palsy—supra-maximal LR recession, periosteal fixation of LR, transposition of LR to MR, Scott procedure, Peter's procedure (SO to MR).
 - Partial third CN palsy—MR resection and LR recession (adjustable procedure for co-operative patient), vertical transposition of SR and IR to MR, surgeries on SR and IR for correction of vertical deviation.
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Botulinum Toxin

Its role in the management of acute or chronic third-nerve paresis has not been adequately investigated. Botulinum toxin injection into the uninvolved lateral rectus muscle is sometimes used to prevent its contracture when recovery time is prolonged.

Permanent Prism

It is used, as an alternative to surgery, to get rid of troublesome but mild residual deviation.

VIVA QUESTIONS

Q.1. What are the causes of isolated third nerve palsy?

- Ans.**
- *Microvascular disease (ischemic mononeuropathy)* associated with hypertension and diabetes is the *most common* cause of third nerve palsy. Marked periorbital pain is often associated with this.

- *Aneurysm of the posterior communicating artery* at its junction with the internal carotid [remember ischemic mononeuropathy is usually associated with pain in the periorbital region, and pupil is often spared (75% of cases) inspite of significant restriction of motility. In contrast, pain is variably present in aneurysm and pupillary involvement is almost always present inspite of less severe restriction of motility].
- *Trauma*, both direct and secondary to subdural hematoma with uncal herniation can produce isolated third nerve palsy.
- *Miscellaneous uncommon causes* include tumor, inflammatory disease

such as syphilis, Lyme disease and sarcoidosis, giant cell arteritis and vasculitis associated with collagen vascular disorders.

Q.2. What are the causes of recurrent isolated 3rd nerve palsy?

Ans. Episodes of third nerve dysfunction with spontaneous recovery over 3–6 months can occur in:

- Ophthalmoplegic migraine
- Diabetes mellitus
- Aneurysm
- Raised ICT.

Q.3. What are the causes and localization of 3rd cranial nerve palsy?

Ans. Summarized in Table 1

Table 1 Causes and localization of third cranial nerve palsy

<i>Level of lesion</i>	<i>Etiology</i>	<i>Manifestations</i>
Nuclear portion	Infarction Hemorrhage Neoplasm Abscess	<ul style="list-style-type: none"> • Paralysis of the contralateral SR • Bilateral ptosis • Ipsilateral IR, MR, IO palsy • Patients with damage to the oculomotor nuclear complex need not have ipsilateral pupillary dilation, but when involved, it indicates dorsal rostral damage.
Fascicular midbrain portion	Infarction Hemorrhage Neoplasm Abscess	<ul style="list-style-type: none"> • Lesions at this level can produce complete or incomplete palsies • Lesion at the superior cerebellar peduncle (Nathan's syndrome) presents ipsilateral 3rd nerve palsy and cerebellar ataxia. • Lesions at the red nucleus (Benedikt's syndrome) are characterized by ipsilateral third nerve palsy and contralateral involuntary movement. • Lesion at the cerebral peduncle (Weber's syndrome) produces ipsilateral third nerve palsy and contralateral hemiplegia. • Isolated dysfunction of either the superior and inferior division
Fascicular subarachnoid portion	Aneurysm Infectious meningitis—bacterial, fungal/parasitic, viral Meningeal infiltrative Carcinomatous/lymphomatous/leukemic infiltration, granulomatous inflammation (sarcoidosis, lymphomatoid granulomatosis, Wegener granulomatosis) Ophthalmoplegic migraine	<ul style="list-style-type: none"> • CN III palsy with fixed dilated pupil in case of surgical lesion • CN III palsy without pupil involvement in case of medical disease

Contd...

Contd...

Level of lesion	Etiology	Manifestations
Fascicular cavernous sinus portion	Tumor—Pituitary adenoma, meningioma, craniopharyngioma, metastatic carcinoma Pituitary apoplexy (infarction within existing pituitary adenoma) Vascular Giant intracavernous aneurysm Carotid artery—cavernous sinus fistula Carotid dural branch—cavernous sinus fistula Cavernous sinus thrombosis Ischemia from microvascular disease in vasa nervosa Inflammatory—Tolosa—Hunt syndrome (idiopathic or granulomatous inflammation)	<ul style="list-style-type: none"> Most commonly associated with other cranial nerves dysfunctions. It presents as paresis of oculomotor, trochlear and abducens nerves with associated maxillary division of trigeminal nerve, producing pain.
Fascicular orbital portion	Inflammatory—Orbital inflammatory pseudotumor, orbital myositis Endocrine (thyroid orbitopathy) Tumor (e.g., hemangioma, lymphangioma, meningioma)	<ul style="list-style-type: none"> Lesions within the orbit are associated with visual loss, ophthalmoplegia and proptosis. Third nerve ophthalmoplegia can be associated with trochlear and abducens nerves palsies. It is important to remember that at the orbit the oculomotor nerve divides into superior (SR, LPS) and inferior division (IR, MR, pupillomotor fiber). This can cause partial oculomotor nerve palsies.

Q.4. What is the importance of pupil sparing nerve palsy?

- Ans.**
- Pupillary involvement usually suggests an underlying '*Surgical*' lesion such as aneurysms, trauma and uncal herniation. These lesions characteristically involve the pupil by compressing the pial blood vessels supplying the superficially located pupillary fibers (parasympathetic fibers).
 - Pupillary sparing usually suggests an underlying '*Medical*' lesion such as hypertension and diabetes. The microangiopathy involves the vasa nervorum, causing ischemia of the main trunk of the nerve, leaving the superficial pupillary fibers intact.
 - However, it must be remembered exceptions can be there. Pupillary involvement may develop a few days after the onset of diplopia in case of aneurysm as it gradually expands. In few cases such as basal meningitis and uncal herniation pupillary involvement may be the only

sign of third nerve palsy, so mild pupillary signs may be clinically significant in such cases. Lastly, however, pupil sparing in children (unlike in adults) may not be helpful in differentiating the causes of the palsy and third nerve.

Q.5. What is the course of third cranial nerve?

- Ans.** Nucleus at the level of the superior colliculi ventral to the Sylvian aqueduct.

↓

Fasciculus (efferent fibers) that pass from the third nerve nucleus through the red nucleus and the medial aspect of the cerebral peduncle.

↓

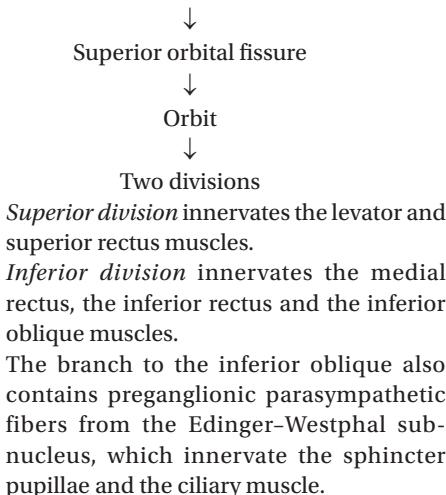
Basilar part starts as a series of 'rootlets' that leave the midbrain on the medial aspect of the cerebral peduncle, before coalescing to form the main trunk.

↓

Enters the cavernous sinus by piercing the dura just lateral to the posterior clinoid process.

Contd...

Contd...



Q.6. Enumerate the subnuclei of third nerve nucleus complex.

- Ans.** • *Levator subnucleus is unpaired* and innervates *both levator muscles*. Lesions confined to this area will therefore give rise to bilateral ptosis.

- *Superior rectus subnuclei are paired—* each innervates the respective *contralateral superior rectus*. Nuclear third nerve palsy will therefore spare the ipsilateral, and affect the contralateral, superior rectus.
- *Medial rectus, inferior rectus and inferior oblique subnuclei are paired* and innervate their corresponding *ipsilateral muscles*.

Q.7. What are the childhood causes of third nerve (oculomotor) palsy?

- Ans.**
- Trauma; subdural hematoma
 - Neoplasm
 - Ophthalmoplegic migraine
 - Postoperative cause
 - Meningitis/encephalitis/viral or post-
upper respiratory tract infection/
Varicella-zoster virus
 - Aneurysm
 - Orbital cellulitis
 - Sinus disease
 - Mesencephalic cyst
 - Poison.

SIXTH CRANIAL NERVE PALSY

Shipra Singhi, Swati Phuljhale

INTRODUCTION

The sixth nerve nucleus is located in the pons. The sixth nerve contains only somatic efferent fibers. Runs a long course from the brainstem to the lateral rectus muscle, through the superior orbital fissure and into the orbit through the middle part of superior orbital fissure and then to lateral rectus. The VI cranial nerve supplies the lateral rectus muscle only. A lesion affecting the nerve will result in defective abduction of the eye. Sixth nerve has the longest subarachnoid course of all the cranial nerve, which makes it vulnerable to injury at many levels. Due to close association between sixth nerve and seventh nerve (facial) in the brainstem, there may be involvement of seventh nerve also in some cases.^{1,2}

HISTORY

Chief Complaint

A case of sixth nerve palsy can present in following ways:

- Inward deviation of eyes
- Diplopia in acquired cases
- Face turn on the same side amblyopia may be present in congenital cases
- Patient may complain of headache, hearing problem, depending on the location of involvement of sixth nerve.

History of Present Illness

Following points must be noted in history:

Age at Onset

Patient has history of deviation of eye inwards and limitation of movement towards outwards. The congenital sixth nerve palsy is present since birth. In acquired type the onset can be at any age, depending upon the underlying cause. Inspection of previous photographs may be useful for the documentation of strabismus. Deviation may be large or small.

Mode of Onset

Acute onset of diplopia or deviation warrants immediate neuroimaging to rule out life-threatening conditions, hence, the type of onset is extremely important to note.

Diplopia

Patient usually complains of horizontal diplopia, which is characteristically worse in the distance and/or on lateral gaze and less or absent for near fixation (Direction of the action of paralyzed muscle).

Head Posture

Face turn on the ipsilateral side is present. Face turn is seen in acquired cases. Face turn in congenital cases may prevent amblyopia and maintain binocular single vision.

Past History

Any history of febrile disease such as viral or bacterial, diabetes mellitus, raised intracranial tension (ICT), trauma or cerebral palsy must be asked for. Adult: History of DM, hypertension, thyroid disease, other diseases (duration, treatment), trauma, medication taken must be enquired for.

Past Surgical History

History of any previous neurosurgical procedure must be recorded as it gives a clue about diagnosis.

EXAMINATION

Systemic Examination

The other cranial nerves and the peripheral nervous system should be examined, if necessary by an appropriate specialist. It is important to

examine specifically for V, VII and VIII nerve to locate the site of lesion, particularly, at the level of cerebellopontine angle. Moreover the fasciculus of VII nerve form a bend around the VI nerve nucleus before emerging from the pons, and thus in a case of nuclear VI nerve palsy the VII nerve involvement is frequently seen.

Ocular Examination

Visual Acuity

This may be reduced if the affected eye fails to fixate properly due to the presence of a marked deviation. Amblyopia will develop due to presence of convergent strabismus.

Abnormal Head Posture

The face is turned towards the affected side.

Ocular Motility

- Esotropia in the primary position (As shown in **Figure 1**, right eye sixth nerve palsy with right esotropia in primary gaze) due to relatively unopposed action of the medial rectus and the deviation (and symptomatic description) is characteristically worse for distance than near fixation.
- Limitation of abduction is characteristically on the side of the lesion (**Fig. 2**, showing limitation of adduction in right eye in right sixth nerve palsy).

Normal adduction of the affected eye is seen (as shown in **Figure 3** in case of right sixth nerve palsy).

Lid: It is usually normal.



Fig. 1: Esotropia of right eye in primary position in a case of right sixth nerve palsy



Fig. 2: Limitation of adduction in right eye in right sixth nerve palsy



Fig. 3: Normal adduction of the right eye in a case of right sixth nerve palsy

Conjunctiva: Conjunctival injection or chemosis can be present in cases of lymphoma and thyroid dysfunction.

Cornea/Sclera/Iris: Usually normal. Corneal sensation may be reduced in acoustic neuroma. It is first sign in acoustic neuroma while first symptom is hearing loss hearing loss.

Pupil: It is usually normal.

IOP/Lens/Vitreous: Usually normal.

Fundus: Papilledema may be present due to raised ICT.

Special Tests

Cover test: An esodeviation is present that is often greater on distance testing. The test should be carried out with and without an abnormal head posture, if one is present. It should be done in all nine gazes, at least in dextroversion and levoversion to look presence of incomitance. The amount of deviation will always be more in the direction of the involved muscle. Similarly, the

cover test should be done with either eye fixing to differentiate the primary (fixing with the normal eye) and secondary deviation (fixing with affected eye). In all paralytic strabismus, the secondary deviation is always more than the primary deviation.

Past pointing: Presence of past pointing indicates recent onset. It can be tested by asking the patient to point with his finger the object viewed by the paretic eye (hand-eye coordination) with a septum not allowing him to have a visual feedback to correct the coordination due to paresis. In the presence of paresis extrainnervation is required for a movement in the direction of field of action of the paretic muscle which is perceived by the brain as if the object is located farther than it is, giving extrainnervation to the hand for pointing. This causes past pointing. For example, paretic right lateral rectus palsy requires more innervation to fixate an object in dextroversion causing past pointing.

Diplopia charting: The subjective deviation is recorded by asking the subject to quantify the separation between the double images, which are dissociated by red-green glasses. This is repeated in all the nine diagnostic positions. In paralytic strabismus, the separation is maximal in the field of action of the paretic muscle. Using a slit, horizontal for vertical strabismus and vertical for horizontal strabismus, one can also know the subjective cyclotropia. Three points to be remembered are:

1. Maximum separation is in the direction in which the muscle acts most (field of action)
2. The image that appears farthest belongs to the deviating eye.
3. The image is displaced in the direction of action of the paralyzed muscle.

In case of lateral rectus, palsy image shifts to outwards.

Binocular function: This is often retained in the presence of an abnormal head posture. As the angle of deviation is often smaller for near fixation, binocular function is usually present on near fixation. In cases of head trauma, fusion may have been lost. Binocular function can be assessed with any of the following tests; Worth four dot test, Bagolini's striated glasses, Maddox rod and synoptophore.

Hess charting: The affected eye will show a markedly constricted field whereas the other eye

demonstrates overaction of its muscles. Following points must be remembered while interpreting:

- The smaller chart indicates the eye with the paretic muscle.
- The larger chart indicates the eye with the overacting yoke muscle.
- The smaller chart will show its greatest restriction in the direction of action of the paretic muscle.
- The larger chart will show its greatest expansion in the main direction of action of the yoke muscle.
- The degree of disparity between the plotted point and the template in any position of gaze gives an estimate of the angle of deviation (each square = 5°).

Force duction test (FDT): The FDT is done to look in mechanical restriction due to medial rectus. Under the topical anesthesia, the examiner passively moves the patient's eye in the direction opposite to that in which mechanical restriction is suspected. For example, in a case right lateral rectus limitation, there may be contracture of right medial rectus. After the topical anesthesia, the medial limbal conjunctiva is grasped firmly with a toothed forceps and the globe is lifted up from the orbit. The patient is asked to look in abduction so that the medial rectus is relaxed. The examiner then tries to passively move the eye in abduction. Care must be taken not to abrade the cornea. If examiner can successfully manage to move the eye until the lateral limbus touches the lateral canthus that means that there is no mechanical restriction and, the motility defect is clearly caused

by paralysis of the lateral rectus muscle. And if resistance is encountered it means that the FDT is positive, mechanical restrictions do exist medially which may be due to contracture of the medial rectus muscle, conjunctiva, or Tenon's capsule. Important causes for medial rectus contracture include thyroid eye disease, entrapment of medial contents after fracture, myositis, and cysticercosis. Some patients initially have pure nerve palsy, but contracture of the antagonist muscle results in secondary mechanical restriction of movement. FDT can be falsely negative if the globe is not lifted out of the orbit while performing the test for recti muscle and if not depressed inside the orbit while performing the test for oblique muscles.

Active force generation test (AFGT): AFGT may be used to evaluate the ability of a muscle to move the eye against a resisting force. After topical anesthesia, the paralytic muscle is held with the fixation forceps and the patient is asked to look in the direction of the limited duction; the amount of force generated by the muscle is felt as a tug by the examiner. The test should be repeated in the other eye for the comparison of the forces.

DIFFERENTIAL DIAGNOSIS

See Table 1.

MANAGEMENT

Investigations are tailored depending on the suspected etiology. In an elderly patient

Table 1 Differential diagnosis of sixth nerve palsy

Diseases	Features
Duane's retraction syndrome	Difficulty on abduction and adduction with eyelid retraction
Grave's orbitopathy (TED)	Proptosis + decreased ability of eye movement + diplopia
Orbital trauma	Orbital fracture + Muscle swelling + eye restriction + diplopia
Infantile esotropia	Esotropia + limit in abduction (improve after doll's head maneuver) + IO overaction + nystagmus + vertical deviation
Spasm of the near reflex	Triad of intermittent : esotropia + accommodative spasm +Miosis
Myasthenia Gravis	Muscle restriction, diplopia and ptosis
High myopia	Can lead to progressive loss of abduction

investigations to rule out diabetes, hypertension, dyslipidemia, coronary artery disease, should be done.

The indications for neuroimaging are:

- VI nerve palsy along with involvement of other cranial nerves like V, VII, VIII is suggestive of lesion at brainstem and cerebello-pontine angle
- VI nerve and presence of disc edema (Pseudo localizing sign)
- Isolated VI nerves palsy in patient with <60 yrs of age
- No improvement or if worsening seen within 6 weeks of onset in cases of ischemic nerve palsy
- Development of other neurological signs in patients with systemic risk factors.

Observation

Since most of the idiopathic and microvascular lesions recover on their own it is advisable not to jump to surgery immediately. In meantime the aim is to avoid diplopia.

Occlusion: Use of frosted gasses in spectacles, occluder patches for spectacles, pirate patches, occluder contact lenses, etc. are the various methods employed for patching depending upon the patient's demands and comfort

Prismatic (e.g. temporary Fresnel stick-on) for correction of diplopia can be done if deviation is small angle. Young children should be treated with alternate patching to prevent amblyopia.^{1,2}

Botulinum toxin injection into the ipsilateral medial rectus may be used to prevent contracture, assess residual function and sometimes to facilitate

prismatic correction with a large deviation. It may have to be repeated and it is rarely curative.

Surgery should be considered only when adequate time has been allowed for maximal spontaneous improvement, typically at least 6–12 months from onset.^{1,2} The aim of the surgery is to correct diplopia and head posture.

Partial palsy (paresis), if some force is felt on AFGT, then adjustable medial rectus recession and lateral rectus resection in the affected eye can be done.

Complete palsy is treated by transposition of the superior and inferior recti to positions above and below the affected lateral rectus muscle. This may or may not be coupled with weakening of the ipsilateral medial rectus depending on FDT. If FDT is positive then one should recesses the medial rectus to release the globe. In such cases where medial rectus recession is required, a partial tendon transposition is done instead of full tendon. Three rectus muscles should not be detached from the globe at the same procedure because of the risk of anterior segment ischemia. Various types of transposition surgeries are described for the sixth nerve palsy; Hummelsheim (full tendon transposition of superior and inferior recti to lateral rectus), Jensen (tying of the inferior half the lateral rectus belly with the temporal half of the inferior rectus belly and tying of the superior half of the lateral rectus to the temporal half of superior rectus).

INVESTIGATION

See **Table 2** for investigations.

Table 2 Investigations in sixth nerve palsy

Forced duction test (FDT)	For diagnosing the presence of mechanical restriction of ocular motility
Force generation test (FGT)	To assess muscle strength of an extraocular muscle To differentiate paretic from restrictive strabismus
Magnetic resonance imaging (MRI)	Provides greater resolution of the orbits, cavernous sinus, posterior fossa, and cranial nerves
Cerebrospinal fluid (CSF)	Help diagnose disease affecting the brain and spinal cord If vasculitis is suspected clinically
Erythrocyte sedimentation rate and/ or C-reactive protein	Help detect inflammation associated with conditions such as infections, cancers, and autoimmune diseases

VIVA QUESTIONS**Q.1. What is the course of sixth nerve?**

Ans. Nucleus at the mid-level of the pons, ventral to the floor of the fourth ventricle



The fibers (fasciculus) leave the brainstem ventrally at the pontomedullary junction.



The basilar part of the nerve enters the prepontine basilar cistern, passes upwards close to the base of the skull and is crossed by the anterior inferior cerebellar artery.



Dorello canal (underneath the petroclinoid ligament)



Intracavernous part intercavernous sinus



Superior orbital fissure

Contd...



Intraorbital part enters orbit



Lateral rectus muscle

Q.2. What are the causes of sixth nerve palsy?

Ans. Causes of sixth nerve palsy are summarized in **Table 3**. The four most common causes were idiopathic (26%), hypertension alone (19%), coexistent diabetes and hypertension (12%), and trauma (12%).

Q.3. What is false localizing sign?

Ans. Raised intracranial pressure may cause stretching one or both sixth nerves due to their long intracranial course or the compression against the petrous tip, in this situation sixth nerve palsy that may be bilateral, is a false localizing sign.

Q.4. What is management of diplopia?

Ans. Monocular occlusion or prismatic (e.g. temporary Fresnel stick-on) correction of

Table 3 Causes of sixth nerve palsy

Causes	Examples	
Congenital		<ul style="list-style-type: none"> • Following birth trauma • Hereditary • Infection (maternal) • Failure of lateral rectus development
Acquired	Children	<ul style="list-style-type: none"> • Space-occupying lesions • Infections, bacterial or viral • Trauma • Raised intracranial pressure • Decompensated esophoria • Infantile esotropia with cross-fixation • Mobius syndrome • Duane's retraction syndrome
	Young adults	<ul style="list-style-type: none"> • Trauma • Space-occupying lesions • Post-viral inflammation • Multiple sclerosis • Diabetes • High myopia • Ophthalmoplegic migraine
	Older adults	<ul style="list-style-type: none"> • Vascular • Hypertension • Diabetes • Space-occupying lesions • Senile lateral rectus weakness

Table 4 Total vs partial 6th nerve palsy

Tests	Finding
Forced generation test	Residual lateral rectus function—feel a tug on forceps
Botulinum toxin injection into a contracted medial rectus	If abduction past midline—partial LR palsy
Saccadic velocity analysis	<ul style="list-style-type: none"> • Mild paresis—varies from 40 degrees per second • Complete paralysis—slow lateral saccades (160 degrees per second)
Electromyography	<ul style="list-style-type: none"> • Record action potential in LR muscle • Increased signal in attempt to abduction→ residual LR function

diplopia is appropriate in idiopathic and presumed microvascular lesions; up to 90% will recover spontaneously, usually over weeks to several months. Young children should be treated with alternate patching to prevent amblyopia.

Q.5. How will you do diplopia charting?

Ans. See 3rd nerve palsy.

Q.6. How will you do Hess/Lees charting?

Ans. See 3rd nerve palsy.

Q.7. What is relationship of sixth nerve with other structures in cavernous sinus?

Ans. The intracavernous section runs below the third and fourth, and the first division of the fifth nerves. The sixth nerve is the most medially situated and runs through the substance of the sinus in close relation to the internal carotid artery. Occasionally, intracavernous sixth nerve palsy is accompanied by a postganglionic Horner syndrome (Parkinson syndrome) due to damage to the paracarotid sympathetic plexus.

Q.8. Can a patient present with isolated nuclear sixth nerve palsy?

Ans. Nuclear sixth nerve presents as horizontal gaze palsy, where there's limitation of abduction due to sixth nerve nucleus involvement as well as adduction limitation on contralateral side due to lack of impulse to contralateral MLF. Convergence may be preserved in such cases, e.g. Facial (seventh) nerve fibers wrap around the sixth nerve nucleus, so ipsilateral lower

motor neuron (LMN) facial nerve palsy is also common. Isolated sixth nerve palsy is never nuclear in origin.

Q.9. What is Foville syndrome?

Ans. Foville (inferior medial pontine) syndrome is most frequently caused by vascular disease or tumors involving the dorsal pons. It is characterized by sixth nerve paresis, horizontal conjugate gaze palsy, ipsilateral V, VII, VIII cranial nerve palsy and ipsilateral Horner's syndrome.

Q.10. What is Millard-Gubler (ventral pontine) syndrome?

Ans. Millard-Gubler (ventral pontine) syndrome involves the fasciculus as it passes through the pyramidal tract and is most frequently caused by vascular disease, tumors or demyelination. In addition to ipsilateral sixth nerve palsy, there is contralateral hemiplegia and often an ipsilateral LMN facial nerve palsy.

Q.11. What is the muscle function test/How to differentiate total or partial sixth nerve palsy?

Ans. See Table 4.

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FOURTH CRANIAL NERVE PALSY

Swati Phuljhale, Shipra Singh, Patil Mukesh Prakash

INTRODUCTION

Fourth cranial nerve (CN) is the thinnest and longest CN (75 mm) and the only CN that comes out from the dorsal aspect of the brainstem. It is the only CN, which crosses completely to the opposite side. This originates from the contralateral nucleus. The IV cranial nerve supplies the contralateral superior oblique muscle. Its nucleus lies at the level of the inferior colliculus. Any lesion affecting the nerve may result in difficulties of depression in adduction, incyclotorsion and abduction of the eye. The acute onset of vertical diplopia in the absence of ptosis, combined with a characteristic head posture, strongly suggests fourth nerve involvement. Peripheral lesions cause ipsilateral and nuclear lesions contralateral superior oblique weakness. In postgraduate exams, it may come as a long case.

HISTORY

Chief Complaint

A case of fourth nerve palsy may present with following:

- Sudden hypertropia
- Diplopia
- Head posture
- Although amblyopia may be associated in congenital cases, it is rarely seen in presence of a head posture.

History of Present Illness

Following points must be recorded.

Age at Onset

It is important to note the age of onset (to differentiate between congenital and acquired form). Inspection of previous photographs may be useful for the documentation of head posture.

Diplopia

Vertical diplopia which worse in down gaze is a characteristic symptom in acquired cases. Since

diplopia is worse in down gaze, it usually associated with difficulty in climbing stairs or reading.

Post-traumatic superior oblique palsy often bilateral and these patients may complain of torsional diplopia in downgaze

Past History

Past history should include following:

- Any history of febrile disease (viral or bacterial), diabetes mellitus, space-occupying lesions.
- Since trauma is the most important cause of fourth nerve palsy it should always be ruled out, particularly blow to the dorsal aspect of mid brain.
- In adults history of diabetes mellitus, hypertension, thyroid disease, and myasthenia gravis, other diseases (duration, treatment), trauma, and medication should be taken.

Past Surgical History

History of any previous neurosurgical procedure must be recorded.

Birth History

Birth history, including period of gestation, birth weight and any problems in utero, with delivery or in the neonatal period should be taken thoroughly.

Family History

History of strabismus in the parents or siblings may be positive. It shows autosomal dominant inheritance.

EXAMINATION

General Examination/Specific Systemic Examination

A thorough review of systems should be conducted, including enquiry about trauma, diabetes, hypertension, etc. and symptoms viral illness. Neurological examination must include other cranial nerves and the peripheral nervous system.

Ocular Examination

Visual Acuity

Vision may be reduced in congenital cases due to amblyopia. Visual acuity must be checked with and without glasses.

Facial Asymmetry and Abnormal Head Posture

- A compensatory head posture avoids diplopia. The functions of SO muscle include in torsion, depression and abduction. To compensate for each of these there is a characteristic head posture. For example, in a case of right SOP the held tilt would be towards left shoulder to compensate for in torsion, chin depression is present to compensate for depression action and there will be face turn to same side to compensate for abduction. In bilateral cases since in torsion and abduction of both the eyes is affected there's no head tilt or face turn, unless the involvement is asymmetrical. Facial asymmetry in form of (plagiocephaly) causes congenital weakening of superior oblique muscle. The premature fusion of coronal axis on one side causes posterior placement of trochlea, thus making superior oblique muscle more parallel to the coronal than the sagittal axis (de-sagittalization). The posterior placement of trochlea causes laxity of the SO tendon thus reducing all of its action.
- Bilateral cases demonstrate chin depression but there will be no face turn or head tilt unless one side is affected more than the other.
- Persistent abnormal head posture following surgery for IV nerve palsy should be investigated to exclude sternocleidomastoid muscle tightness that may have developed in congenital cases.

Lid

If there is ptosis, one must look for third nerve involvement.

Conjunctiva

Conjunctival injection or chemosis can be present in cases of lymphoma and thyroid dysfunction.

Cornea/Sclera/Iris

Usually normal, corneal sensation should be checked in all cases of CN palsy.

Pupil

It is usually normal. It may be mydriatic in third nerve palsy.

IOP/Lens/Vitreous

Usually normal.

Special Examination of Squint

Cover Test

All the strabismus examination should be performed after correcting the compensatory head posture. A latent deviation exists if a compensatory abnormal head posture is adopted. When the test is repeated with the head straight, the deviation will increase and may become manifest. The affected eye shows a hyperdeviation and an associated esodeviation.

There will be hypertropia of the affected eye which increases on opposite gaze and same side head tilt, also known as Park's three step test.

Park's Three-step Test

The test is illustrated with the example of left superior oblique paresis (SOP). It should be noted that the test is only for identifying the paralyzed cyclovertical muscle.

Step 1: To assess which eye is hypertropic in the primary gaze (**Fig. 1A**).

In case of left hypertropia, the following muscles could be involved:

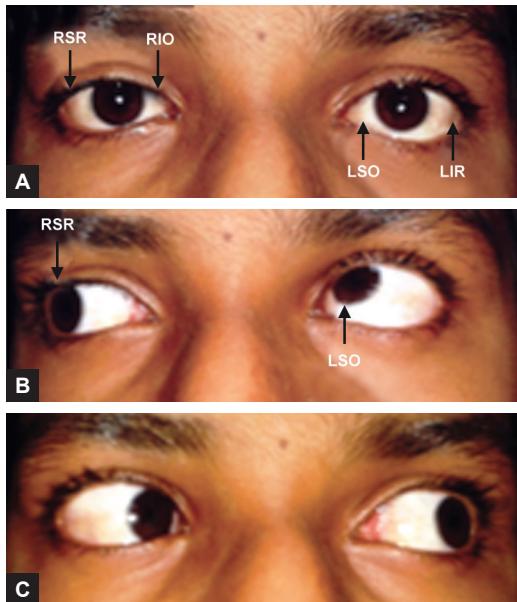
1. Depressors of the left eye, i.e. superior oblique and inferior rectus causing hypertropia of left eye.
2. Elevators of the right eye, i.e. the superior rectus or inferior oblique causing hypotropia of right eye.

Step 2: To assess which lateral direction has worse hypertropia (**Fig. 1B**).

If the left hypertropia increases on right gaze implicates a left superior oblique or right superior rectus involvement.

Increase in the left gaze implicates that either the right inferior oblique or left inferior rectus are involved.

In this case, the deviation will be worse in opposite gaze, so now from four muscles we have zeroed down to two muscles left SO or right SR deviation is *Worse On Opposite Gaze (WOOG)*.



Figs 1A to C: Left superior oblique palsy: (A) Left hypertropia. Four muscles could be involved; Left superior oblique (LSO), left inferior rectus (LIR) or right superior rectus (RSR), right inferior oblique (RIO); (B) Since the hypertropia worsens on right gaze; we have zeroed down to 2 muscles; RSR or LSO; (C) On head-tilt test, the hypertropia worsens on left tilt due to overaction of LSR muscle

Step 3: Also known as *Bielschowsky's head tilt test* is done to assess, in which head tilt direction is the hypertropia worse (**Fig. 1C**)

- The head tilt test is performed with the patient fixating at a straight-ahead target at 3 meters.
- Increase in left hypertropia on left head tilt implies the left superior oblique is involved, and increase in right hypertropia on left head tilt indicates the right superior rectus is involved. Since tilt on left side will cause extorsion in right eye, which needs to be compensated by an intorsion of the eye to balance head movement. In addition, since the SO is paralyzed the SR needs to overact to bring about the desired intorsion, which is accompanied by elevation. This increased elevation is seen as worsening of hypertropia on same side head tilt.

In fourth nerve palsy the deviation is better on opposite tilt (boot).

Bilateral involvement should always be excluded, particularly following head trauma.

- There is alternate hypertropia in adduction. Right hypertropia in left gaze and left hypertropia in right gaze, though orthophoria may be present in primary position.
- Greater than 10° of cyclodeviation (measured using double Maddox rods or by synoptophore) and a tendency towards reversal of any hyperdeviation or diplopic images on lateral gaze.
- 'V' pattern esotropia is often present.
- Bilaterally positive Bielschowsky head tilt test
The primary underaction of the affected superior oblique muscle results in a number of sequelae.
- There is overaction of the contralateral inferior rectus and of the ipsilateral inferior oblique muscles.
- The contralateral superior rectus shows secondary underaction.

The combination of these muscle effects is variable and often depends on whether or not the deviation is long standing.

Hess Charting

The affected eye will show a markedly constricted field whereas the other eye demonstrates overaction of its muscles.

For example, recently acquired left fourth nerve palsy would have following abnormalities:

- Left chart (chart of left eye with right eye fixing) is smaller than the right (chart of right eye with left eye fixing).
- Left chart shows underaction of the superior oblique and overaction of the inferior oblique.
- Left chart shows overaction of the inferior rectus and underaction (inhibition palsy) of the superior rectus.

Evaluation of Torsion

Unilateral fourth nerve palsy is characterized by less than 8 degree of cyclodeviation whilst bilateral cases may have greater than 10 degree of cyclodeviation.

Double Maddox rod test: It includes following steps

- Red and green Maddox rods, with the cylinders horizontal, are placed one in front of either eye.

- Each eye will therefore perceive vertical line of light.
- In the presence of cyclodeviation, the line perceived by the paretic eye will be tilted and therefore distinct from that of the other eye.
- One Maddox rod is then rotated until till both lines become parallel to each other
- The amount of rotation can be measured in degrees and indicates the amount of cyclodeviation.

Fundus—Indirect ophthalmoscopy and fundus photography: Useful methods for evaluation of cyclodeviation. Normally the fovea is located between the two horizontal lines, one passing through the center of disc and the other cutting the lower pole of the disc tangentially. The usual location is in the middle of these two horizontal lines, in cases of SOP because of extorsion it is displaced downwards.

Field charting: Vertical displacement of blind spot suggests torsion.

Forced duction test (FDT): Exaggerated forced duction test was described by Guyton is done to look for laxity on the SO tendon. The globe is grasped with Pierce Hoskins forceps in superotemporal and inferonasal quadrant. The globe is retracted inside the orbit and the eye is elevated and adducted. The globe is rocked in intorsion and extorsion movement. A normal taut SO tendon will cause globe to pop up during this maneuver and a click is felt by the examiner. It is always imperative to compare it with other eye to differentiate between the normal and lax tendon. To test tension in the inferior oblique muscle—the globe is grasped inferotemporal and superonasal quadrant and is then retracted, depressed and adducted.

Checking fourth cranial nerve function in third palsy: Vertical actions cannot be tested, as there is third CN involvement (adduction). To solve this, note a limbal or conjunctival landmark. Ask the patient to look down. The patient will not be able to look down as the eye is abducted and not adducted. However, the eye should intort as the SO works. Check for the conjunctival landmark to see if the eye is intorting.

If the conjunctival landmark is moving the eye is intorting, thus the fourth CN is intact.

DIFFERENTIAL DIAGNOSIS

A case of fourth CN palsy has to be differentiated from following:

- Thyroid eye disease
- Ocular surgery
- Orbital fracture
- Neurosurgery
- Childhood strabismus
- Skew deviation
- Third nerve palsy
- Myasthenia gravis
- Decompensated hyperphoria.

INVESTIGATION

Blood investigations to rule out risk factors like diabetes, hypertension, and other cause of microangiopathy should be done. Neuroimaging is required only when it is associated with other neurological signs.

MANAGEMENT

Observation

Congenital decompensated and presumed microvascular palsies commonly resolve spontaneously. All patients are seen every 1–2 months whilst being monitored for stability/recovery. Unilateral cases of vascular origin usually recover within 6 months. Small-unrecovered deviations with vertical/horizontal diplopia can be managed long-term by incorporating prisms in to spectacles. [Also, see chapter on sixth nerve palsy].

Surgical Management

The choice of surgical options is influenced by various factors:

- Laxity of SO tendon
- Presence of IO overaction
- Amount of deviation in primary position
- Gaze of maximum deviation

Table 1 shows the algorithm for the management of superior oblique palsy according to Knapp's classification. To correct for torsion Harada-Ito procedure is done. For bilateral acquired cases, perform bilateral Harado-Ito procedure is done to correct torsion.

Table 1 Management of IV nerve palsy (Von Noorden modification of Knapp's classification): for a case of left superior oblique palsy

Class	Maximum deviation in gaze	Management
1	Dextroelevation (L/R maximum in this gaze)	Left inferior oblique recession
2	Dextrodepression	Left superior oblique tuck or Harada-Ito's procedure ± Right inferior rectus recession
3	All right gazes	If hypertropia < 25 PD then left inferior oblique recession If hypertropia > 25 then add left superior oblique tuck
4	All down and right gazes	Treatment plan as in 3 with right inferior rectus recession or left superior rectus recession
5	All down gazes	Left superior oblique tuck with right inferior rectus recession
6	Bilateral with a "V" pattern	Bilateral surgery as in class 5
7	All downgazes, primary gaze and dextroversion	Explore trochlea

VIVA QUESTIONS

Q.1. What is the course of fourth nerve?

Ans. The nucleus is located at the level of the inferior colliculi ventral to the Sylvian aqueduct.



The fasciculus consists of axons that curve posteriorly around the aqueduct and decussate completely in the anterior medullary velum.



The trunk leaves the brainstem on the dorsal surface enters the cavernous sinus.



Superior orbital fissure



Intraorbital part enters orbit



The intraorbital part innervates the superior oblique muscle.

Q.2. What are the causes of isolated fourth nerve palsy?

Ans. *Idiopathic lesions* are common, and many of these are thought to be congenital although symptoms may not develop until decompensation occurs in adult life due to reduced fusional ability.

Trauma frequently causes bilateral fourth nerve palsy.

Microvascular lesions are relatively common.

Aneurysms and tumors are extremely rare.

Q.3. What is relationship of fourth nerve with other structures in cavernous sinus?

Ans. The intracavernous part runs in the lateral wall of the sinus, inferior to the third nerve and above the first division of the fifth. In the anterior part of the cavernous sinus, it rises and passes through the superior orbital fissure above and lateral to the annulus of Zinn.

Q.4. Why fourth nerve is so vulnerable to trauma?

Ans. It is the thinnest and longest cranial nerve (75 mm). It is the only CN that comes out from the dorsal aspect of the brainstem.

Q.5. How would you differentiate between unilateral and bilateral SOP?

Ans. See Table 2.

Q.6. How would you differentiate between congenital and acquired SOP?

Ans. See Table 3.

Q.7. How would you differentiate between congenital vs ocular torticollis SOP?

Ans. See Table 4.

Table 2 Differences between unilateral and bilateral superior oblique palsy

<i>Investigations</i>	<i>Unilateral</i>	<i>Bilateral</i>
Cover test	Hyperdeviation in 1° position Reflects extent of palsy	Often only slight hyperdeviation in 1° position
Ocular motility	No reversal of hypertropia and diplopia on lateral versions Slight V pattern may be noted	Reversal of hypertropia and diplopia on lateral versions Large V pattern
Abnormal head posture	Chin depression, head tilt and head turn	Chin depression
Torsion	Slightly extorsion	Extorsion >100

Table 3 Differences between congenital vs acquired SOP

<i>Parameters</i>	<i>Congenital</i>	<i>Acquired</i>
History	Long standing head tilt No history of trauma	No long standing head tilt history of acute trauma
Facial asymmetry	Present	Absent
Ocular motility	No diplopia	Diplopia +
Force duction test	Lax superior oblique tendon	No lax superior oblique tendon
Vertical fusional reserve	>40 prism diopters	<20 prism diopters
Torsion (Double Maddox rod test)	No extorsion	Extorsion<150

Table 4 Congenital vs ocular torticollis

<i>Congenital</i>	<i>Acquired</i>
Onset at birth	Rarely before 18 months
Passive straightening of head difficult	Easy passive straightening
Neck muscles firm	Palpation negative
No visual disturbances	Diplopia is frequent
Tilt not affected by occlusion	Generally straightens on occluding the paralytic eye

Q.8. How would you do Parks–Bielschowsky three-step tests?

Ans. Given in examination.

Q.9. How do you localize the lesion in case of fourth nerve palsy?

Ans. Fourth nerve palsy may be due to lesions in the nucleus or fascicular lesions of the midbrain. It can be difficult to differentially diagnose nuclear and fascicular lesions as the IV nerves decussate immediately after exiting the nuclei and exit the dorsal midbrain after a very short intra-midbrain course. The IV nerve is not only susceptible to damage as it exits the midbrain but also is vulnerable in the cavernous sinus and orbital apex.

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OPTIC NEURITIS

Ritu Nagpal, Adarsh Shashni

INTRODUCTION

Optic neuritis (ON) is the term used for the inflammation of optic nerve. It is also called papillitis (when the head of the optic nerve is involved) and retrobulbar neuritis (when the posterior of the nerve is involved). It is caused by many different conditions, and it may lead to complete or partial loss of vision. The most common cause is acute demyelinating optic neuritis often associated with multiple sclerosis (MS).¹⁻³

In exams, ON can be given as both long and short case.

HISTORY

Chief Complaint

Usual history is a young adult patient, typically less than 45 years of age, (but may be of any age) presents with unilateral vision loss developing over a period of several hours to few days.

This may be associated with:

- Periorbital pain (seen in almost 53–92% of cases), especially with eye movement that may precede or coincide with visual loss.
- Reduced contrast and color vision—loss of color and contrast at times out of proportion to loss of visual acuity strongly suggests optic nerve pathology. Abnormal color vision by Ishihara plates was found in 88% of involved eyes in the optic neuritis treatment trial (ONTT). Many a times patient may complain of color desaturation refers to a qualitative inter-eye difference in color perception that can be tested by comparing vision of a red object with each eye. A patient with monocular “red desaturation” may report that the red color appears “washed out,” pink, or orange when viewed with the affected eye. It is important to remember that problems of color vision can persist even after complete clinical resolution. Few symptoms when present strongly points toward an association with multiple sclerosis such as:
- Bright flashes of light with movement of affected eye (phosphenes)

- Flashes of light induced by noise, smell, taste, touch (photism)
- Diplopia, nystagmus, dysarthria, dysphagia
- Electric shock like sensation on neck movement (*Uhthoff phenomenon*)
- Sudden worsening of vision on exercise or increase in body temperature (*Lhermitte sign*)
- *Pulfrich phenomenon*, in which anomalous perception of the direction of movement of an object occurs due to asymmetry of conduction velocity in the optic nerves
- Weakness and stiffness of lower limbs
- Numbness and paresthesias
- Sphincter disturbances.

History of Present Illness

The onset and progression shows a characteristic pattern in a typical case of optic neuritis. Visual loss is acute or subacute, varies from mild reduction to no perception of light and progresses over 7–10 days before reaching a nadir. By 2–3 weeks the visual acuity starts improving and almost complete recovery occurs by 4–5 weeks of onset.

The pain is typically dull aching type exacerbated by touching or moving the eye. It reaches maximal severity within 24–36 h and spontaneously abates within 48–72 h in few cases it may persist for a long time and atypical causes of ON must be ruled out in such cases.

Past History

Similar episodes in past may be there. In the ONTT, the recurrence rate was 35% within 10 years. Subgroup analysis showed a higher recurrence rate (48%) in patients with MS compared to those without MS (24%).^{1,2}

Past Surgical History

History of prior surgery; such as shunt surgery, optic nerve fenestration, cardiac or any spinal surgery must be recorded carefully.

Past Medical History

A careful systemic history is required to rule out other causes of optic nerve dysfunction such as NAION.

Hypertension, diabetes mellitus, hyperlipidemia, collagen vascular disease, antiphospholipid antibody syndrome, erectile dysfunction, hypertension, hyperhomocysteinemia, sleep apnea syndrome, previously diagnosed multiple sclerosis and any previous cerebrovascular accident must be noted carefully. Prior history of peptic ulceration and tuberculosis is important especially when IV steroid therapy is planned.

EXAMINATION

Systemic Examination

A complete neurological work-up is a must in all cases of optic neuritis.

Ocular Examination

Visual Acuity

Uncorrected as well corrected visual acuity (VA) must be recorded in all cases. VA on presentation and VA of the other eye often guides the initial treatment. Serial VA monitoring helps in differentiating typical from atypical form of optic neuritis. It must be remembered VA in optic neuropathies but does not correlate perfectly with the extent of optic nerve dysfunction, so it is a somewhat insensitive measure.

Eyeball

Usually normal. However, nystagmus and ocular motor nerve palsies may be seen in some cases.

Lids, Conjunctiva, Cornea

Usually normal.

Pupils

Presence of relative afferent pupillary defect (RAPD) is an important sign of optic nerve dysfunction. It must be remembered that RAPD is a nonspecific sign of optic neuropathy. In bilateral cases, or in cases with a pre-existing optic neuropathy in the fellow eye, an RAPD may not be apparent.

Anterior Segment/IOP

Usually normal.

Posterior Segment

(Slit lamp biomicroscopic examination using a 90D/78D lens and indirect ophthalmoscopy)

- Vitreous—in a typical case of ON vitreous is usually normal.
- Optic disc
 - Papillitis with hyperemia and swelling of the disk (**Fig. 1**), blurring of disk margins, and distended veins (**Fig. 2**) is seen in one-third of patients with optic neuritis.
 - Two-thirds of these patients have retrobulbar neuritis with a normal funduscopic examination.
 - It must be remembered that the disc swelling of demyelinating ON is diffuse and presence of any segmental changes,

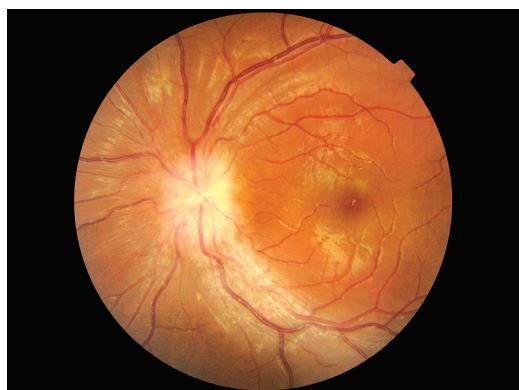


Fig. 1: Papillitis with hyperemia and swelling of the disk

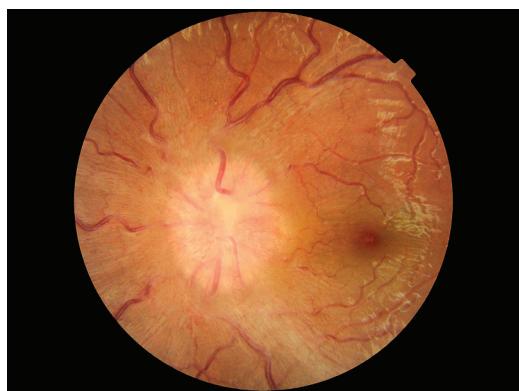


Fig. 2: Papillitis with blurring of disk margins, and distended veins

altitudinal swelling, pallor, arterial attenuation, and splinter hemorrhages suggests some alternate diagnosis.

- Papillitis is more common in children less than 14 years old and in certain ethnic populations, including black South Africans and Southeast Asians.
- Peripapillary hemorrhages are rare in optic neuritis, but are a common accompaniment to papillitis due to anterior ischemic optic neuropathy Normal or edematous.
- **Macula:** A typical case of ON may not show any abnormality. Presence of edema, exudates or star formation suggests atypical nature of the disease.
- Perivenous sheathing or periphlebitis retinae can be seen in about 12% of patients with ON and implies a *high risk for MS*.
- Examination of fellow eye is important. Disc pallor (commonly temporal disc pallor which may extend beyond the disc margin into adjacent RNFL) in the fellow eye suggests previous optic neuritis.

INVESTIGATIONS

The diagnosis of ON is usually made on clinical grounds.

- Color vision and contrast sensitivity
 - Decreased color vision and contrast sensitivity are highly characteristic of optic neuritis.
 - Poor color vision, particularly out of proportion to loss of acuity, is a very sensitive indicator of optic neuropathy
- Visual field
 - The most common field defect seen in demyelinating optic neuritis is diffuse depression of sensitivity in the entire central 30° followed by altitudinal/arcuate defects and focal central/centro-cecal scotomas.
- Visual evoked potential (VEP)
 - Decrease in amplitude and prolongation of latency can be seen. A delay in the P100 of the visual evoked response (VER) is the electrophysiologic manifestation of slowed conduction in the optic nerve as a result of axonal demyelination.
- This test is not specific for diagnosis of acute optic neuritis.
- In ONTT 67% cases had fellow eye abnormalities.
- Magnetic resonance imaging (MRI)
 - MRI of the brain and orbits with gadolinium contrast provides confirmation of the diagnosis of acute demyelinating optic neuritis. *MRI with FLAIR (fluid attenuated inversion recovery) sequencing and gadolinium infusion and fat suppression* when available is the preferred modality.
 - Usual finding shows white matter abnormalities characteristic of MS such as ovoid periventricular (>3 mm) and corpus callosum plaques with long axis perpendicular to the ventricular margins dark on T2 and hyperintense on T1. The longitudinal extent of nerve involvement as seen on MRI correlates with visual impairment at presentation and with visual prognosis.
 - The reported prevalence of white matter abnormalities varies from 23% to 75%. In the ONTT, almost 40% of patients had MRI lesions.
 - It also provides important prognostic information regarding the risk of developing MS. Individuals with white matter abnormalities are at a higher risk of developing MS.
- Lumbar puncture
 - Lumbar puncture is not an essential diagnostic test in optic neuritis, but should be considered in atypical cases.
 - Abnormality is seen in >90% cases. It shows leucocytosis, raised IgG levels, raised IgG/albumin index and oligoclonal IgG bands.
- *Optical coherence tomography (OCT):* OCT shows RNFL thinning in most (85%) of patients with optic neuritis. However, it does not have any diagnostic value since these abnormalities are also common in patients with MS who do not have a clinical history of optic neuritis.
- *Additional investigations:* To be done in the presence of atypical features
 - Complete hemogram with ESR and CRP
 - Antinuclear antibody, anti-ds-DNA antibody

- Mantoux test
- IFN- γ release assay (Quantiferon TB Gold)
- Chest X-ray
- Gallium scan
- S. ACE levels
- Serum and CSF VDRL and FTABs
- S. NMO IgG levels
- Spinal MRI
- Anti-Lymes antibody titer
- Mitochondrial gene mutation (11778 and 14484).

DIFFERENTIAL DIAGNOSIS

The differential diagnoses for unilateral sudden decrease in vision include following:¹⁻³

- Optic neuritis
 - Sudden onset vision loss with subsequent improvement (visual acuity usually between 6/18-6/60)
 - Cellular reaction in the vitreous overlying the optic disc and presence of retinal exudates suggestive of papillitis
 - Normal appearing optic disc in retrobulbar neuritis
 - Central visual loss (central scotoma).
- Ischemic optic neuropathy
 - Sudden onset vision loss with no or incomplete improvement
 - Chalky white edematous disc with overlying hemorrhages
 - Sectoral disc edema
 - Nerve fiber bundle-type field defects (originating from and involving the physiologic blind spot) typically respecting the horizontal meridian.
- Compressive optic neuropathy
 - Slowly progressive vision loss
 - Chronic disc edema with optociliary shunt vessels
 - Presence of pseudodrusen
 - Central visual loss (central scotoma)
- Papillophlebitis
 - Mild vision loss (6/12 or better)
 - Slow progression compared to optic neuritis or NAION
 - Mild disc swelling
 - Disc surface telangiectasia
 - Spontaneously resolves.
- Central retinal vein occlusion (CRVO)
 - Sudden onset of visual blurring with severity depending on the type of CRVO; ischemic or nonischemic
 - Dilated and tortuous vessels with dot/blot and flame hemorrhages in all 4 quadrants, most numerous in the periphery
 - Cotton wool spots, optic disc and macular edema
 - FFA—delayed A-V transit time, blockage by hemorrhages
 - Disc collaterals, epiretinal gliosis and pigmentary changes at macula in chronic stage.
- Leber's hereditary optic neuropathy
 - Acute or subacute painless loss of central vision
 - Sequential involvement of the fellow eye within weeks or months
 - Disc hyperemia with obscured margins
 - Dilated and tortuous posterior pole vasculature (telangiectatic microangiopathy)
 - Swelling of the peripapillary nerve fiber layer (pseudoedema)
 - FFA—absence of dye leak
 - Central or centrocecal scotoma
 - Usually poor prognosis.

CLASSIFICATION OF OPTIC NEURITIS

Optic neuritis may be classified either on the basis of ophthalmoscopic findings or on the basis of underlying etiology.

Ophthalmoscopic Classification

- Retrobulbar neuritis—characterized by normally appearing optic nerve head. This is the most common type seen in adults and is frequently associated with multiple sclerosis.
- Papillitis—characterized by hyperemia and edema of the optic disc with or without peripapillary flame-shaped hemorrhages and cells in the posterior vitreous. This is the most frequently encountered in children.
- Neuroretinitis—characterized by papillitis associated with inflammation of the nerve fiber layer and a macular star development. This is the least common type of optic neuritis.

Table 1 Difference between typical and atypical optic neuritis

Feature	<i>Typical optic neuritis</i>	<i>Atypical optic neuritis</i>
Onset	Acute	Chronic
Age	Young patient (mean age in ONTT was 32 years)	Older patient
Sex	Caucasian female	Male
Laterality	Typically unilateral	Bilateral simultaneous or rapidly sequential
Pain	> 90% have pain with eye movements. This helps to differentiate optic neuritis from NAION	Lack of pain or protracted pain
Optic disc	Appears normal in 2/3rd cases	Significant papillitis
Hemorrhage	Usually not seen	Marked hemorrhages
Exudates	Uncommon	Macular star may be seen
Uveitis	Rare	Pars planitis, choroiditis, phlebitis
Course	Vision worsens over several days to 2 weeks and then begins to improve. About 75% patients recover visual acuity of 6/9 or better	Lack of improvement or progression

Etiological Classification

- Demyelinating—the most common type
- Parainfectious—usually occurs following a viral infection or immunization
- Infectious—occurs due to sinus infections or in association with cat scratch fever, syphilis, lyme disease, cryptococcal meningitis in patients with AIDS and herpes zoster
- Noninfectious—occurs in association with systemic causes such as sarcoidosis, systemic lupus erythematosus, polyarteritis nodosa and other forms of vasculitis.

Depending upon Course of the Disease

Typical and atypical (see Table 1).

TREATMENT

Acute Therapeutic Options for Optic Neuritis

Routine treatment of typical demyelinating ON with corticosteroids is not advised due to lack of long-term benefit and the potential for side-effects.¹⁻³ There are specific situations where corticosteroids may be offered to shorten the period of functional impairment. Corticosteroids, therefore, are considered for following patients:

- Who require faster recovery, such as occupational requirements

- Patients with severe bilateral visual loss
- Poor vision in the fellow eye.

Regimen: Intravenous methyl prednisolone 1g daily for 3 days followed by oral prednisolone (1 mg/kg/day) for 11 days and then tapered over 3 days. Oral corticosteroids were associated with an increased risk of recurrence of optic neuritis in ONTT hence this form of therapy should be avoided.

VIVA QUESTIONS

Q.1. What are the signs of optic nerve dysfunction?

- Ans.** Signs of optic nerve dysfunction include:
- Reduced visual acuity for distance and near
 - Afferent pupillary defect
 - Dyschromatopsia mainly affecting red and green
 - Diminished light brightness sensitivity
 - Diminished contrast sensitivity
 - Visual field defects depending on the underlying pathology.

Q.2. How do you differentiate typical optic neuritis from atypical optic neuritis?

- Ans.** See Table 1.

Q.3. What were the results of optic neuritis treatment trial (ONTT)?

- Ans.** • The objectives of the study were to evaluate the efficacy of corticosteroid for

the treatment of acute optic neuritis and to investigate the relationship between optic neuritis and multiple sclerosis.

- Patients were randomized into three arms: placebo, oral (low-dose) prednisone (1 mg/kg/day for 14 days) and high-dose intravenous methyl prednisolone (250 mg 4 times daily for 3 days), followed by oral prednisone (1 mg/kg/day for 11 days).
- At 6 months, color vision and contrast sensitivity and visual fields were found to be significantly better in the methyl prednisolone arm; however, after 1 year, there was no significant difference between treated and untreated patients in any of the functional outcome.
- Intravenous methyl prednisolone was found to accelerate the rate of visual recovery over the first 15 days. By day 30 nearly complete recovery occurred in all patients.
- No significant difference was found between oral prednisolone and placebo in any of the parameter. At 12 months, all three groups were similar in terms of visual functions.
- In a subsequent analysis, patients randomized to receive treatment with high-dose intravenous methylprednisolone in conjunction with 11-day low-dose oral prednisone taper exhibited a significantly reduced risk of developing clinically definite MS (defined by the development of new neurologic symptoms attributable to demyelination other than optic neuritis in either eye occurring at least 4 weeks after the study entry and lasting more than 24 hours with abnormality documented on neurological examination) over the subsequent 2 years. Beyond 2 years no significant disease-modifying effects of steroids was seen.

Q.4. What is the overall risk of developing multiple sclerosis in a patient presenting with optic neuritis?

Ans. Approximately 15–20% of MS patients present with optic neuritis. In patients with

established MS optic neuritis occurs in 50% cases at some point of time. The overall 10 years risk of developing MS following an acute episode of optic neuritis with one or more characteristic brain lesions, normal brain MRI is 56% whereas it is 22% if the MRI is normal. At 15 years the risk increases to 25% in patients with normal baseline MRI and 70% in patients with abnormal baseline MRI.¹⁻³

Q.5. What is the role of brain MRI?

Ans. The likelihood of progression of optic neuritis to MS is best predicted by brain MRI done at the time of diagnosis. In the ONTT baseline, brain MRI was found to be the most powerful predictor of likelihood of clinically definite multiple sclerosis (CDMS).

Q.6. What are the low risk factors for MS?

Ans. Lack of pain, severe disc edema, peripapillary hemorrhage, retinal exudates and mild visual acuity loss.

Q.7. What are the diagnostic criteria for diagnosis of MS?

Ans. *Mc Donald criteria:* Clinical history and presentation in the presence of neuro-imaging abnormalities with or without CSF abnormalities or abnormal VEP response. Recurrent optic neuritis in the absence of other clinical or laboratory manifestations is not sufficient for diagnosis.

Q.8. What is neuromyelitis optica?

Ans. Neuromyelitis optica or Devic's disease, is characterized by necrotizing demyelinating lesions of bilateral optic nerves and spinal cord. The spinal lesions extend contiguously over three or more vertebral segments. Serum antibody, NMO-IgG, which targets the autoantigen aquaporin-4, is a useful marker for diagnosis. Treatment with rituximab has been tried to be beneficial.

Q.9. What are the treatment modalities available for acute optic neuritis apart from corticosteroids?

Ans. Treatment modalities available for acute optic neuritis are described below:^{4,5}

- *Short-acting agents (for acute exacerbations):* High dose intravenous steroids.

- Longer-acting agents (delay the development of CDMS):
 - Disease modifying drugs: Interferon β -1a and 1b, glatiramer acetate
 - Immunosuppressives: Mitoxantrone, Natalizumab, Fingolimod
- Newer treatment options
 - *Intravenous immunoglobulins (IVIg)*: have been tried for acute optic neuritis but with no long-term effects on visual function or on the latency of VEP responses after AON.
 - *Plasma exchange (PLEX)*: PLEX has demonstrated efficacy in the treatment of refractory AON and in AON associated with neuromyelitis optica (NMO). The addition of PLEX to intravenous methylprednisolone in the acute treatment of NMO-associated AON has showed significant improvement in high-contrast acuity, visual fields and temporal retinal nerve fiber layer (RNFL) thickness, but not low-contrast letter scores or color vision. The early, first-line use of PLEX in the treatment of AON is yet to be evaluated. PLEX is presumed to mediate a therapeutic effect, at least in part, through the removal of pathogenic humoral and plasma factors.
 - *Erythropoietin*: Systemic infusion of erythropoietin with and without methylprednisolone has demonstrated beneficial effects on retinal ganglion cell (RGC) function and survival in a rat model of experimental autoimmune encephalomyelitis. Erythropoietin administration increases protein levels of various antiapoptotic factors such as phospho-Akt, phospho-MAPK 1 and 2 and Bcl-2 which helps to limit the apoptosis of retinal ganglion cells after AON. Erythropoietin administration has shown partial recovery of pattern-reversal VEPs and improvement in flash electroretinograms and significant improvement in the

thickness of peripapillary retinal nerve fiber layer.

- Teriflunomide
- Adrenocorticotropic hormone
- Dimethyl fumarate
- Antibody against LINGO1 (anti-LINGO), a CNS protein that acts as a negative regulator of oligodendrocyte precursor differentiation to promote CNS remyelination
- Phenytoin.

Q.10. What are the newer investigative modalities available for the management of acute optic neuritis?

Ans. Various investigative modalities are as follows:

- *OCT and SLP*: To demonstrate RNFL edema which is evident in approximately 80% of the affected optic nerves. On an average, patients with AON lose 22 μ m more RNFL in their affected eye than in their unaffected eye at 3–6 months after the inception of visual symptoms.
- *Diffusion tensor imaging (DTI)*: Provides a sensitive modality to complement RNFL structural injury in the evaluation of acute ON injury.
- *Electrophysiology*: Prolongation of the VEP P100 latency is used as a measure of conduction delay through the optic nerve and is a sensitive marker of demyelination. Reduction in the amplitude of VEP serves as a measure of axonal injury. The sensitivity of mfVEP is further enhanced by using low-contrast pattern-reversal stimuli allowing detection of mild residual injury or occult damage in the so-called ‘unaffected’ eye. The traditional ERG with optical nerve head component (ONHC) waveform—The ONHC waveform represents the transformation of slow membrane conduction to fast salutatory conduction, as axons traverse the lamina cribrosa and become myelinated. After AON, the ONHC waveforms are abolished and later recover, representing the transient effects of conduction block due to reversible demyelination. Eyes with

previous optic neuritis in patients with MS exhibit changes or loss in the ONHC waveform that correlate with reduction in low-contrast letter acuity, retinal nerve fiber layer (RNFL) thickness, visual field depression and amplitude loss and latency delay on mfVEP.

- **Biomarkers:** Serum and plasma neurofilament levels, heavy (NfH) and light (NfL), are elevated in patients with ON, independent of the inflammatory mechanism. The levels of NfH and NfL have been observed to correlate with the extent of vision loss and the loss of retinal nerve fiber thickness following ON.

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ESODEVIATION

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INTRODUCTION

Esodeviations are the most common type of ocular misalignment. It represents 50% of ocular deviations in pediatric age group. In exams, it is given as long case.

HISTORY

Chief Complaint

- Deviation of eyes
- Diminution of vision
- Head posture.

History of Present Illness

- Following points must be recorded in history:
 - Age at onset
 - Constant or intermittent
 - Unilateral or bilateral
 - Progression
 - Abnormal movement of the eyes
 - Preceding history of febrile illness, meningitis, or any neurological events
 - Exacerbating and ameliorating factors
- Patient has history of deviation of eyes that can be present since birth or after some time and can be associated with diminution of vision.

- The earlier the onset, the more likely the need for surgical correction. The later the onset, the greater is the likelihood of an accommodative component (mostly arising between 18 and 36 months).
- The longer the duration of squint in early childhood the greater the risk of amblyopia, unless fixation is freely alternating.
- Inspection of previous photographs may be useful for the documentation of strabismus.
- History of head posture, chin position or face turn may be there.

Past History

Previous ocular history including refractive prescription and compliance with spectacles or occlusion, previous surgery or prisms is important to decide upon the treatment options and prognosis.

Birth History

Including period of gestation, birth weight and any problems *in utero*, type of delivery (normal or forceps) is important. Following factors increases the risk of ET in a child:

- Maternal smoking during pregnancy

- Maternal age (>30 years)
- LBW (low birth weight) baby
- Retinopathy of prematurity and Down's syndrome.

Family History

Note down any history of strabismus in the parents or siblings. There is 73% concordance rate of esotropia in monozygotic twins, as compared to 35% in dizygotic twins.

EXAMINATION

General Examination

A careful examination especially focusing on development of the child and the neurological system must be carried out.

Local Examination

Visual Acuity

- Visual acuity chart (for elderly children)
- VER (< 6 months).

Fixation preference tests (for young kids)

- Central, steady and maintained (CSM)
- *Fixation preference:* Alternation
- *Maintenance of fixation:* 15 secs
- 10 pd BD/BU prism test
- 25 pd BI alternation test
- *Cross fixation:* Tracking past midline.

Measurement of Alignment

Light reflex tests

- Generally used to assess deviations in small children and in patients who cannot fixate with either or both eyes.
- Require minimal cooperation from the patient
- *Drawback:* Assess only tropias and less accurate than cover testing.
- In cases where the goal of surgery is improved appearance and an angle kappa is present, light reflex tests (especially the Krimsky test) are essential as they are likely to be the best choice for determining surgical dosages.

Hirschberg test

- A pen torch is shone into the eyes from arm's length and the patient asked to fixate the light.

- Placement of the corneal light reflexes is observed (more or less centered in the pupil of the fixating eye, but will be decentered in a squinting eye, in the direction opposite to that of the deviation).
- The distance of the corneal light reflection from the center of the pupil is noted. Each millimeter of light displacement across the cornea is equivalent to 7° of decentration or 14Δ.
- A light reflection at the pupillary border signifies a 15° or 30Δ deviation, at the mid-iris a deviation of 30° or 60Δ, and at the limbus a deviation of 45° or 90Δ.
- The Hirschberg method relies on a pupil size of 4 mm and performing in a case with dilated pupil is not reliable.
- It provides rough estimate of the angle of strabismus in cases where the patient may not allow prisms to be placed in front of the eyes.

Krimsky test

- Preferred over the Hirschberg test as it allows a more exact estimate of the alignment.
- However, it requires a cooperative patient.
- Corneal reflex assessment is combined with prisms to measure the angle in a manifest deviation.
- A neutralizing prism is placed (A prism bar starting with a relatively low prism power) over either eye to position the corneal light reflex in its normal position.
- Generally, the prism is placed over the fixing eye to improve visualization of the light reflex in the deviating eye. Few authors call it *prism reflection test* when the prism is placed in front of the deviating eye until the corneal light reflections are symmetrical.

Bruckner test

- Done with the help of a direct ophthalmoscope and watching the red reflex.
- If the red reflex coming from one eye is different from the other, strabismus is suspected. The deviating eye gives a brighter reflex.
- Easy to perform, but it does require some expertise.
- Generally used for screening purposes only. It is an excellent test to screen a preverbal child for strabismus, anisometropia or amblyopia.

Cover-uncover test: The gold standard for evaluating strabismus is the cover-uncover test. It can diagnose both the tropia and phoria components. When performed with prisms, it can be quantitative also. It has to be done for both near and distance and with and without refractive correction. The fixation distance should be 33 cm for near and 6 meters for distance. For distance fixation target is given of a figure or letter size of 6/9 of Snellen's chart.

Prerequisites

- Both eyes must be able to fixate the target.
- Both eyes must have central fixation.
- No severe motility defect.

Cover test

- To start with, cover the apparently fixating eye.
- Observe if the apparently deviating eye moves to take up fixation.
- If the uncovered eye moves, tropia exists.

Uncover test

- It is done to unmask the phoria.
- After covering the eye fusion breaks and if there is any heterophoria the eye behind the cover deviates. This can be observed with the use of translucent occluder (Spielmann's occluder).
- After removing the cover if it remains deviated, it confirms a latent squint with poor fusion (poor recovery). If it recovers, the examiner observes the speed of recovery, which shows strength of fusion and it, is important prognostic sign.

Alternate cover test

- The alternate cover test induces dissociation to reveal the total deviation when fusion is disrupted. It should be performed only after the cover-uncover test.
- One eye is covered for several seconds. The occluder is quickly shifted to the opposite eye for 2 seconds, then back and forth several times.
- After the cover is removed, the examiner notes the speed and smoothness of recovery as the eyes return to their predissociated state.
- A patient with a well-compensated heterophoria will have straight eyes before and after the test has been performed whereas a patient with poor control may decompensate to a manifest deviation.

Prism Bar cover test

- The prism cover test measures the angle of deviation on near or distance fixation and in any gaze position.
- The procedure is similar to the alternate cover test, but prisms of increasing power are placed in front of one of the eyes until the eyes stop shifting.
- The apex of the prism is towards the direction of the deviation. Thus, the position of prism is base-out for esotropia, base-in for exotropia, and base-down for a hypertropia.
- The amplitude of the refixation movement should gradually decrease as the strength of prism approaches the extent of deviation.
- The end-point is approached when no movement is seen. To ensure the maximum angle is found, the prism strength can be increased further until a movement is observed in the opposite direction (the point of reversal) and then reduced again to find the neutral value; the angle of deviation is then taken from the strength of the prism.
- In cases of incomitant strabismus, both primary and secondary deviations should be determined [primary deviation—deviation of the paretic eye when normal eye is fixating; secondary deviation—deviation of the normal eye when paretic eye is fixating]. The secondary deviation is always larger than the primary deviation.

Accommodative Convergence to Accommodation Ratio

It characterizes the difference in alignment observed between distance and near fixation. A normal accommodative convergence to accommodation ratio (AC/A Ratio) allows the eyes to remain aligned and in focus as a target moves closer. Preoperative determination of AC/A ratio may be helpful in predicting the extent to which a patient may respond to plus lenses when a surgical overcorrection is obtained.

AC/A ratio can be determined by following methods:

- **Gradient method:** IPD is not needed as vergence is measured at the same distance. At 33 cm with patient wearing his proper refractive correction, deviation is measured with and without +3.0DS lens (if assessed using

distance target -3.0SD Lens is used) placed in front of both the eyes.

Prolonged mono-ocular occlusion used to break vergence after effect before test.

AC/A = Deviation without lens – deviation with lens

Power of the lens in diopters.

- **Heterophoria method:** Deviation measured at distant vision with full optical correction (no accommodation exerted), and at a near distance (e.g. 33 cm).

$AC/A = IPD + ND - DD / AN$ [IPD = inter pupillary distance (cm); ND = near deviation (Diopters); DD = Distance deviation (Diopters); AN = Accommodation for near ($1/3 = 3$ Diopters)]
[Note: Esotropia + sign is used and for Exotropia - sign is used for deviation while calculating AC/A ratio].

- Graphic method, fixation disparity method and haploscopic method are other methods for AC/A ratio:

Routine AC/A ratio is normally not done clinically; instead, the difference in measurements at distance and near is assessed. Any difference of >10 PD suggests an abnormal AC/A relationship and should be considered into the treatment plan for the patient.

Maddox Wing

- The Maddox wing dissociates the eyes for near fixation (1/3 m) and measures heterophoria.
- The instrument is constructed in such a way that the right eye sees only a white vertical arrow and a red horizontal arrow, whereas the left eye sees only horizontal and vertical rows of numbers.
- Horizontal deviation is measured by asking the patient to which number the white arrow points.
- Vertical deviation is measured by asking the patient which number intersects with the red arrow.
- The amount of cyclophoria is determined by asking the patient to move the red arrow so that it is parallel with the horizontal row of numbers.

Maddox Rod

- The Maddox rod consists of a series of fused cylindrical red glass rods that convert the appearance of a white spot of light into a red streak. The optical properties of the rods cause the streak of light to be at an angle of 90° with the long axis of the rods; when the glass rods are held horizontally, the streak will be vertical and vice versa.
- The rod is placed in front of the right eye. This dissociates the two eyes: the red streak seen by the right eye cannot be fused with the unaltered white spot of light seen by the left eye.
- The amount of dissociation is measured by the superimposition of the two images using prisms. The base of the prism is placed in the position opposite to the direction of the deviation.
- Both vertical and horizontal deviations can be measured.

Fusional Amplitudes

Fusional amplitudes measure the efficacy of vergence movements. It can be tested with prisms bars or synoptophore. A progressively increasingly strong prism is placed in front of one eye, which will then abduct (base-in prism) or adduct (base-out prism) to maintain binocular fixation. Thus for fusional amplitude of convergence base-out prism is used and for divergence base in prism is used. When the power of prism exceeds the fusional amplitude, diplopia is reported or one eye drifts in the opposite direction, indicating the limit of vergence ability. This is known as break point and gradually then decreases the strength of the prism till patient realign his eyes this is the recovery point. This should be checked for both distance and near fixation.

Near Point of Convergence

It is the nearest point on which the eyes can maintain binocular fixation. It can be measured with the RAF ruler that rests on the patient's cheeks. A target is slowly moved along the rule towards the patient's eyes until one eye loses fixation and

drifts laterally (objective NPC). The subjective near point of convergence (NPC) is the point at which the patient reports diplopia. Normally, the NPC should be nearer than 10 cm without undue effort.

Near Point of Accommodation

It is the nearest point at which the eyes can maintain clear focus. It is also measured with the RAF ruler. The patient fixates a line of print, which is then slowly moved towards the patient until it becomes blurred. The distance at which this is first reported is the near point of accommodation (NPA). The NPA continuously recedes with age. At the age of 20 years, the NPA is 8 cm and by the age of 50 years approximately 46 cm.

Inter-pupillary Distance (IPD)

It is measured with the help of two scales or synoptophore.

Diplopia Charting

Test requires red green glasses. Diplopia charting is done in all 9 gazes with the help of a linear light source.

Tests for Binocular Vision and Sensory Anomalies

Worth Four-dot Test

- A dissociation test used with both distance and near fixation.
- Differentiates between BSV (binocular single vision), ARC (anomalous retinal correspondence) and suppression.
- Presence or absence of a manifest squint must be known at time of testing.
- *Procedure:* The patient wears a red lens in front of the right eye (which filters out all colors except red) and a green lens in front of the left eye (filter out all colors except green). The patient then views a box with four lights—one red, two green and one white.
- *Results*
 - BSV is present when all four lights are seen

- When all four lights are seen in the presence of a manifest deviation, harmonious ARC is present
- Two red lights are seen if left eye suppression is present
- Three green lights are seen if right suppression is present
- If two red and three green lights are seen, diplopia is present.
- If the green and red lights alternate, alternating suppression is present.

Bagolini Striated Glasses

- Test for detecting BSV, ARC or suppression.
- Each lens has fine striations that convert a point source of light into a line similar to the Maddox rod.
- *Procedure:* The two lenses are placed at 45° and 135° in front of each eye and the patient fixates on a focal light source. Each eye perceives an oblique line of light, which is perpendicular to that perceived by the fellow eye.
- When the two streaks intersect at their centers in the form of a cross (X), the patient has BSV with NRC if the eyes are straight, or harmonious ARC in the presence of manifest strabismus.
- When the two lines are seen but they do not form a cross, diplopia is present.
- When only one streak is seen, there is no simultaneous perception and suppression is present.
- If a small gap is seen in one of the streaks, a central suppression scotoma is present (e.g. microtropia). However, it is often difficult to appreciate by the patient and the patient describes a cross. This scotoma can be confirmed clinically with the 4 Δ prism test.

Four Δ Prism Test

- It distinguishes bifoveal fixation (normal BSV) from foveal suppression (also known as a central suppression scotoma (CSS) in microtropia).
- *With bifoveal fixation:* The prism is placed base-out (microtropia is commonly esotropic not exotropic) in front of the right eye with

deviation of the image away from the fovea temporally, followed by corrective movement of both eyes to the left [kindly read it once, the message is not clear].

- The left eye then converges to fuse the images
- *In left microtropia:* The patient fixates a distance target with both eyes open and a 4Δ prism is placed base-out in front of the eye with suspected CSS. The image is moved temporally in the left eye but falls within the CSS and no movement of either eye is observed.
- The prism is then moved to the right eye which, adducts to maintain fixation; the left eye similarly moves to the left consistent with the Hering law of equal innervation, but the second image falls within the CSS of the left eye and so no subsequent re-fixation movement is seen.

Base-out Prism

This is a simple method used for detecting fusion in children. The test is performed by placing a 20Δ base-out prism in front of one eye of the patient. The prism displaces the retinal image temporally resulting in diplopia. Most children with good BSV can overcome a 20Δ prism from the age of 6 months; if not, weaker prisms (16Δ or 12Δ) may be tried, but the response is then more difficult to identify.

After Image Testing (with Synoptophore)

It is a dissociative test to know suppression, ARC or central scotoma.

Stereopsis

Various tests, using differing principles, are employed to assess the stereoacuity. Random dot tests (e.g. TNO, Frisby) provide the most definitive evidence of high grade BSV. Where this is weak and/or based on ARC, contour-based tests (e.g. Titmus) may provide more reliable information.

- *Titmus test:* The Titmus test consists of a three-dimensional polarized vectograph comprising two plates in the form of a booklet viewed through polarized spectacles. On the right is a large fly, and on the left is a series of circles and animals. The test should be performed at a distance of 40 cm.

- *Randot test:* It uses Julesz's random dot background to mask the monocular clues. It requires Polaroid glasses. Near randot is done at 40 cm and distance randot is done at 3 m.
- *TNO test:* The TNO random dot test consists of seven plates of randomly distributed paired red and green dots viewed with red-green spectacles, and measures from 480 down to 15 seconds of arc at 40 cm.
- *Frisby Davis distance test:* this is a real depth test. Measured at 6 m, 3 m or 1 m measure stereoacuity from 4 sec to 200 sec of arc.
- *Lang's pencil gross stereopsis test:* Pencils held horizontally to avoid patient seeing end on view. We ask the patient to touch the pencil tip held by him to that of the examiner. Simple bedside test works well to demonstrate gross stereopsis (3000–5000 sec of arc).
- *Synoptophore test:* The synoptophore compensates for the angle of squint and allows stimuli to be presented to both eyes simultaneously.
- It can thus be used to investigate the potential for binocular function in the presence of a manifest squint and is of particular value in assessing young children (from age 3 years), who generally find the test process enjoyable. It can also detect suppression and ARC.
- The instrument consists of two cylindrical tubes with a mirrored right-angled bend and a + 6.50 D lens in each eyepiece. This optically sets the testing distance as equivalent to about 6 m.
- The synoptophore can measure horizontal, vertical and torsional misalignments simultaneously and is valuable in determining surgical approach by assessing the different contributions in the cardinal positions of gaze.
- *Hess/Lees testing:* A Hess chart is plotted to aid in the diagnosis and monitoring of a patient with incomitant strabismus, such as an extraocular muscle palsy (e.g. third, fourth or sixth nerve paresis) or a mechanical or myopathic limitation (e.g. thyroid ophthalmopathy, blow-out fracture or myasthenia gravis). The chart is commonly prepared using either the Lees or Hess screen, which facilitate plotting of the dissociated ocular position as a measure of extraocular muscle action. Information provided by the Hess chart should be regarded

in the context of other investigations such as the field of binocular single vision.

Hess Screen

The Hess screen contains a tangent pattern displayed on a dark gray background. Red lights that can be individually illuminated by a control panel indicate the cardinal positions of gaze within a central field (15° from primary position) and a peripheral field (30°); each square represents 5° of ocular rotation. The eyes are dissociated by the use of reversible goggles incorporating a red and a green lens, the red lens in front of the fixating eye and the green lens the nonfixating eye. Red points of lights are illuminated at selected positions on the screen. The patient holds a green pointer, and is asked to superimpose a green light over each red light in turn. In orthophoria the two lights should be more or less superimposed in all positions of gaze. The goggles are then reversed and the procedure repeated. Software is available that facilitates the plotting of a Hess chart using a standard desktop computer screen.

Lees Screen

This apparatus consists of two opalescent glass screens at right-angles to each other, bisected by a two-sided plane mirror that dissociates the eyes; each of the eyes can see only one of the two screens. Each screen has a tangent pattern (two-dimensional projection of a spherical surface) that is revealed only when the screen is illuminated. The patient is positioned facing the nonilluminated screen with his or her chin stabilized on a rest. Using a pointer, the examiner indicates a target point on the illuminated tangent pattern and the patient positions a pointer on the nonilluminated screen, at a position perceived to be superimposed on the dot indicated by the examiner. The non-illuminated screen is briefly illuminated by the examiner using a footswitch to facilitate recording of the dot indicated by the patient. When the procedure has been completed for one eye, the patient is rotated through 90° to face the previously illuminated screen and the procedure repeated.

Interpretation

- The smaller chart indicates the eye with the paretic muscle (right eye).

- The larger chart indicates the eye with the overacting yoke muscle (left eye).
- The smaller chart will show its greatest restriction in the main direction of action of the paretic muscle (right lateral rectus).
- The larger chart will show its greatest expansion in the main direction of action of the yoke muscle (left medial rectus).
- The degree of disparity between the plotted point and the template in any position of gaze gives an estimate of the angle of deviation (each square = 5°).

Forced Duction Test

The forced duction test (FDT) is an attempt by the examiner to move a patient's eye farther in a given direction than the patient can move it. Topical anesthetic is placed on the appropriate limbal location (generally 180° away from the duction limitation) with a small cotton swab and the limbal conjunctiva is grasped firmly with a toothed forceps. The patient is asked to rotate the eye fully in the direction of the limited duction. An attempt is then made by the examiner to rotate the eye beyond the position attained by the patient while avoiding globe retraction. Care must be taken not to abrade the cornea.

Patients who have pure nerve palsy exhibit no restriction to full movement by the examiner; patients who have pure restriction (dysthyroid orbitopathy, entrapment of ocular contents after blowout fracture) exhibit restricted movements (sometimes termed a positive forced duction test). Some patients initially have pure nerve palsy, but contracture of the antagonist muscle results in secondary mechanical restriction of movement. Suction cup devices have been developed for examiners who are wary of using toothed instruments at the limbus; a cotton swab may be a sufficient tool in some patients. Forced duction testing of oblique muscles may be performed, but two forceps are used and the globe is depressed forcibly into the orbit.

Active Forced Generation Test

Active force generation testing may be used to evaluate the ability of a muscle to move the eye against a resisting force. The forceps is placed

at the limbus of the anesthetized globe in the meridian of the muscle whose duction is limited and the patient requested to rotate the eye in the direction of the limited duction; the examiner judges through the forceps the relative amount of force generated. Strain gauges have been devised that enable quantitation of this force. This is done in patients with paralytic squint (example- in esotropia due to 6th CN palsy).

CLASSIFICATION

- *Esophoria*: Latent deviation that is controlled by fusion under binocular conditions
- *Intermittent esotropia*: Deviation that is controlled by fusion sometimes, but manifests in exertion/illness
- *Esotropia*: Deviation is constantly manifested Right, left or alternating
Comitant (**Table 1**) vs incomitant (**Table 2**)
Primary/secondary/consecutive
- *Primary*: No other cause. Most of the esotropias are primary
- *Secondary*: Consequence of loss or impairment of vision
- *Consecutive*: Overcorrection of an initial exotropia.

MANAGEMENT

In all patients of esotropia should undergo full cycloplegic refraction before measurement of deviation.

Occlusion therapy should be given to those with amblyopia.

Table 1 Types of comitant esotropia

Accommodative	Nonaccommodative
• Refractive accommodative	• Infantile esotropia
• Nonrefractive accommodative	• Acute onset
• Partially accommodative	• Acquired or late onset
• Hypoaccommodative	• Microtropia
	• Cyclic esotropia
	• Nystagmus blockage syndrome

Table 2 Incomitant esotropia types

Paralytic	6th CN palsy, divergence palsy, myasthenia
Restrictive	Eso DRS, tumor, postoperative, strabismus fixus, endocrine myopathy
Spastic	

It depends upon the type of esotropia:

- For accommodative esotropia—all patient requires is full cycloplegic refraction with or without near add depending upon AC/A ratio for correction of their deviation fully (**Table 3**).
- For partially accommodative esotropia—the accommodative element requires correction with glasses and for the nonaccommodative element surgery is needed.
- For nonaccommodative esotropia surgery is needed. For convergence excess (near

Table 3 Classification of accommodative esotropia

	Refractive normo-accommodative	Refractive hyper-accommodative	Nonrefractive hyper-accommodative	Nonrefractive hypo-accommodative
Refractive error	Hyperopia	Hyperopia	Not significant	Not significant
AC/A ratio	Normal no convergence excess	Increased	Increased	Normal
NPA	–	–	–	Remote
NPC	–	–	–	Remote
N-D deviation (prism Diopter)	<15	>15	>15 No significant esotropia for distance	>15

>distance by 10PD) bimedial recession or medial recti recession with posterior fixation is done. For divergence insufficiency (distance > nearby 10 PD) bilateral LR resection is preferred. For basic type (near distance disparity less than 10 PD) either monocular MR recession and LR resection or bimedial recession is done.

VIVA QUESTIONS

Q.1. What is accommodative esotropia?

Ans. See Table 1 for types

- *Refractive accommodative:* (*Normal AC/A ratio*) esotropia restored to orthotropia at all fixation distances and in all positions of gaze by optical correction of underlying refractive error.
 - Onset between 6 months—5 years of age
 - Associated hyperopia
 - Insufficient fusional divergence
 - Often hereditary
 - Intermittent at onset—becoming constant
 - *Deviation:* 20–40 Δ
 - Precipitation—trauma, illness
- *Treatment of refractive accommodative esotropia:*
 - Cycloplegic refraction
 - Full cycloplegic correction of hypermetropic refractive error
 - Initial atropinization to relax accommodation
 - 60–70% of these patients respond well to treatment with glasses; the remaining require surgical treatment (Dyer et al.)
 - It is important to treat the entire accommodation (latent + manifest)
 - Orthoptic treatment to overcome suppression and build fusional divergence.
- *Nonrefractive accommodative:* (*High AC/A ratio*)
 - Esotropia N > D
 - Abnormally high AC/A ratio
 - *Normal NPA*
 - Age: 2–3 years
 - Usually has hypermetropia (2.25 D) but may have myopia

- Accommodative component is present—greater deviation at near
- Accommodation is not linked to refractive error; there is synkinesis with accommodative convergence
- Costenbader: Small refractive error, remote near point of accommodation, small distance but large near deviation
- Excessive accommodative effort and a large persistent deviation with the refractive error fully corrected

Management: Treat with bifocals and miotics

- Miotics—echothiophate iodide 0.06% or 0.125%/BE OD for 6 weeks—dose may be reduced subsequently
- Complications—RD, iris cysts, etc.
- Most patients improve with therapy
- *Surgery:* Advocated if nonaccommodative component develops
- Partially accommodative esotropia
 - Esotropia having both accommodative and non-accommodative elements are considered as partially accommodative esotropias.
 - *May be:* Decompensated accommodative esotropia
 - Esotropia with subsequent development of accommodative component.
- *Treatment:*
 - Eventually amblyopia therapy with or without surgery is needed.
 - Cycloplegic refraction with *bifocals*.
 - Surgical correction of residual deviation (nonaccommodative part)
 - Explaining to parents that children would still require glasses after surgery.
 - Alignment of the eyes with glasses or surgery alone usually does not make the eyes work together. Vision therapy does.
 - Occasionally the deviation may increase after patient gains stereopsis for near; one should repeat refraction at this point.
 - Supportive orthoptic treatment to promote fusional divergence.
- Hypoaccommodative:
 - Esotropia N > D

- Unrelated to refractive error
- Weakness in accommodation (primary or secondary) → excess accommodative effort → excess convergence
- *The NPA is receded*

Q.2. Describe clinical features and management of essential infantile esotropia.

Ans. Essential infantile esotropia:

- Manifest esodeviation
- Onset between birth and 6 months of age
- Neurologically normal infant prevalence: - 0.1% of newborns
- Even with this reduced prevalence it is the most common form of strabismus

Clinical characteristics

- Onset from birth to 6 months
- Large angle ($\geq 30\Delta$)
- Stable angle
- Initial alternation with cross fixation
- No clinically apparent CNS involvement
- Asymmetrical optokinetic nystagmus—OKN asymmetry is present in all infants but becomes symmetrical by 6 months in the normal. Patients with congenital ET retain OKN asymmetry
- Temporal to nasal (T/N) OKN—smooth, following and rapid refixation.
- Nasal to temporal (N/T) OKN—jerky inaccurate movements with halting refixation.
- *Incidence: 1-2%*

Variable findings^{1,2}

- Amblyopia
- Apparently defective abduction
- Apparently excessive adduction
- Up or down shoot on adduction
- A or V pattern
- Inferior oblique over action (68%)
- DVD/DHD (50%)
- Manifest latent nystagmus (33%)
- Manifest nystagmus (rare)
- Anomalous head posture
- *Heredity:* Transmission may be irregular autosomal dominant, or recessive. Waardenburg reported concordance in monozygous twins to be 81%, compared with 9% in dizygotic
- History of strabismus in the parents or siblings—positive

- *Refractive errors*—Most commonly associated with mild hyperopia, followed by moderate and high hyperopia, and lastly myopia associated with hypermetropia (> 85 %) rare in myopia (6-8 %).

Ciancia syndrome

- Essential infantile esotropia
- Latent nystagmus
- Head turn toward adducting eye
- Apparently limited abduction in both eyes

Lang syndrome

- Esotropia
- DVD
- Excycloduction of the nonfixating eye
- Abnormal head posture

Differential diagnosis

- **Congenital**
 - Bilateral abducens paralysis
 - Duane syndrome type 1
 - Mobius syndrome
- **Acquired**
 - Sensory esotropia
 - Refractive accommodative esotropia
 - Nystagmus blockage syndrome
 - Esotropia in association with CNS problems

Management

Goals of treatment

- Restoration of single binocular vision
- Normal visual acuity
- Normal stereoacluity
- Normal retinal correspondence
- Stable sensory and motor fusion

Nonsurgical treatment

- Correct all hypermetropias (full cycloplegic refraction)

Amblyopia treatment

- Conventional, full time occlusion.
- End-point being free alternation of the two eyes which is equally maintained.
- It should be treated before surgery because...
 - The earlier the treatment betters the results.
 - The diagnosis of amblyopia and monitoring of fixation preference difficult, once eyes aligned.
 - Patient neglect their follow-up appointment for amblyopia.

- The outcome of surgery is less favorable.
- The only situation when surgery is indicated in the face of residual amblyopia is a *tight medial rectus muscle* that causes one eye to be buried in the medial canthus even when the good eye is patched.

Surgical management

- *Timing of surgery*
 - Early surgery provides better chances of functional improvement.
 - A secondary change that occurs in extraocular muscles, the conjunctiva, and Tenon's capsules makes a surgical correction at later stages more difficult and less predictable.
 - In some cases of infantile esotropia, persisting deviation warrants early surgery (3–4 months)
 - Treatment of infantile esotropia must be started at an early age frequently at 6 months.
 - *Esotropia:* Surgery done within a year of misalignment yields better stereopsis.
- *Surgical approaches:*
 - Bilateral medial rectus (MR) recession
 - MR recession with lateral rectus (LR) resection
 - *Safe limits lesser in infants* MR: 5.5 mm, LR: 6.5 mm for recession.
 - 3 or 4 muscle surgery has also been advocated
 - Inferior oblique overaction: Muscle weakening procedures
 - *Alignment within 7–8 Δ of orthophoria:* Acceptable. However, orthotropia/small—esotropia— *better in comparison*
 - One must carefully look at the fixation pattern to make sure that there is no amblyopia.
 - Treatment after 2 years reduces prognosis for re-establishment of binocular vision.
 - Older children with infantile isotropic need both surgical intervention if the turn is large and vision therapy.

- Smaller turns may only require vision therapy.

Botulinum toxin: It is an effective treatment modality for the management of infantile esotropia in infants.

Q.3. What are microtropias? Describe its clinical features and management.

- Ans.**
- These are ultra-small angle esodeviations which may be missed by ordinary methods of examination.
 - Can be primary or secondary, latter are residual deviation postsurgery.
 - Park monofixation syndrome has macular scotoma with good peripheral fusion and fusional amplitude with gross stereopsis.
 - Lang's microtropia—small angle heterotropia (<5°) these have harmonious ARC with mild amblyopia and partial stereopsis. These are of 3 types—type 1 has central fixation; type 2 has eccentric fixation without identity; type 3 has eccentric fixation with identity (this means that angle of anomaly is same as the eccentricity of fixation)
 - *Clinical features*
 - Amblyopia
 - ARC
 - Relative scotoma at fixation spot
 - Near normal fusional amplitude
 - Defective stereopsis
 - Size of deviation (5°–8°)
 - Foveal or eccentric fixation
 - Presence or absence of anisometropia
 - *Test used for diagnosis*
 - Bagolini's glasses—detects central scotoma
 - 4 prism diopter test—already explained
 - *Management:* Primarily involves treatment of amblyopia.

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EXODEVIATION

Shipra Singh, Adarsh Shashni

INTRODUCTION

Exotropia (XT) is outward deviation of the eyes. It is less more frequently seen than esotropia (ET). The approximate ratio of XT to ET is 1:3. According to some studies XT is more prevalent in the Middle East, the Orient, and Africa. Most studies report a normal distribution of refractive errors with XT.

In exams, it can be given as a long case.

HISTORY

Chief Complaint

- Deviation of eyes
- Headaches, eyestrain, blurring of vision (older children and adults)
- Difficulty with prolonged period of reading
- Diplopia, photophobia, image is perceived as becoming smaller and coming closer

History of Present Illness

Patient (parents in case of small children) may complain of headaches, eyestrain, blurring of vision (older children and adults), and difficulty with prolonged period of reading.

- *Deviation of eyes:* Deviation of eyes towards outside which can be intermittent or constant. Deviation may be present since birth or shortly after birth.
- *Diplopia:* Seen in adults with a mature visual system, which can be intermittent. Children with intermittent or constant exotropia are less symptomatic as suppression eliminates diplopia.
- *Photophobia:* Bright light dazzles the retina so that fusional vergence is disrupted, causing manifest deviation. Child closes one eye to avoid confusion and diplopia [this phenomenon is called Diplopia- Phobia]
- *Micropsia:* Rare, patient uses accommodative convergence to maintain BSV. Image is perceived as becoming smaller and coming closer.

- *Refractive error:* Patient may have uncorrected myopia, high degree of uncorrected hypermetropia, anisomyopia, anisoastigmatism can also be there.

History of past illness: Any history of febrile disease or cerebral palsy must be noted. Previous ocular history including refractive prescription and compliance with spectacles or occlusion, previous surgery or prisms is important to future treatment options and prognosis.

Birth History

- Children with craniofacial anomalies more likely to exhibit XT.
- Maternal smoking during pregnancy increases the risk of XT [maternal smoking is more commonly associated with ET and for XT it is controversial].
- Low birth weight (LBW) baby increase the risk.
- Retinopathy of prematurity and Down's syndrome increases the risk of XT.

Family history: Note down any history of strabismus in the parents or siblings. There is 17-fold increased risk in monozygotic twin.

EXAMINATION AND SPECIAL TESTS

For examination please refer to chapter of esotropia.

Classification: Based on difference in measurement of deviation for distance and near, intermittent exotropia can be divided into following types:

- Divergence excess pattern—distance deviation exceeds near deviation by 10 prism diopters
- Convergence insufficiency pattern—near deviation exceed distance deviation by 10 prism diopter
- Basic exodeviation—when distance and near deviation is same or does not exceed 10 prism diopter.
- Simulated or pseudodivergence excess—these are basic deviation but appear as divergence excess exotropia due to either tenacious proximal fusional convergence (TPFC) or due

to accommodation as in patients with high AC/A ratio. Following test differentiates the true and pseudodivergence excess.

Occlusion test of Scobee-Burian: Differentiate true and simulated divergence excess due to TPFC.

- Distance and near deviation is measured
- U/L occlusion of one eye for 24 hour (Scobee)/ 30–45 min (Burian)
- Ensure that patient does not use both eye simultaneously even momentarily
- Measurement of deviation for near fixation is repeated.

In simulated divergence excess after patching there is increase in near deviation, so that it equals or exceeds that at distant fixation.

True divergence excess is not influenced by occlusion.

+ 3.0DS lens test: Differentiate true and simulated divergence excess due to accommodative convergence.

- A +3.0DS lens is used and deviation for near fixation is repeated.
- A large increase of near deviation indicates a high AC/A ratio.
- These patients are good candidate for over minus therapy, i.e. using more minus for myopic and using less plus for hypermetropic to stimulate accommodation that aids in decreasing or controlling the amount of exodeviation.
- Preoperative determination of AC/A ratio may also be helpful in predicting the extent to which a patient may respond to plus lenses when a surgical overcorrection is obtained.

TREATMENT

Optical

- Full cycloplegic refraction to be done.
- Over minus therapy as described above can be prescribed specially in patients with high AC/A ratio.

Prisms

- Indicated in overcorrected/under corrected exotropia.
- Base out prisms to stimulate fusional convergence.

- 1/2 to 1/3rd of deviation is corrected in intermittent exotropia.

Orthoptics

- Anti-suppression exercises—appreciation of diplopia.
- Convergence exercise is done with the help of a convergence trainer. These do not affect the basic deviation but decrease the manifestation of tropia to phoria.
- Should be done only after antisuppression exercises in cases of suppression.
- Should not be done in intermittent exotropia for distance only in whom surgery is planned as can cause postoperative over convergence.
- Exercises on synoptophore should always be supplemented by home exercises.
- Aim is to obtain normal near point of convergence.

Occlusion Therapy

- Useful in small angle exotropia.
- Occlusion of the preferred eye for 3–5 hours per day decreases the angle of deviation—evaluate 4 monthly.

Surgery

Indications: The indications for surgery in—

- Intermittent exotropia include following:
 - Exotropia > 50% of waking hrs
 - Newcastle scoring >3 (**Table 1**)
 - Deviation ≥ 20 D
 - Asthenopic symptoms
 - Increasing basic deviation
 - Secondary convergence insufficiency with asthenopic symptoms
 - Development of suppression
 - Decreasing stereopsis
- *In constant exotropia:* Surgery is almost always indicated with preoperative and postoperative orthoptic treatment.

Timing of surgery: Knapp advocated early surgery to prevent sensory changes especially in patients with infantile exotropia.

The best approach is to assess the timing in each case individually.

Factors to consider before surgery:

- Age

Table 1 Newcastle scoring for intermittent exotropia

<i>Home control</i>	<i>Score</i>
X(T) or mono-ocular eye closure- never seen	0
<50% times for distance fixation	1
<50% times for near fixation	2
>50% times for both distance and near fixation	3
<i>Clinic control</i>	
<i>Distance</i>	
Immediate realignment after cover test	0
Realignment after blink or refixation	1
No realignment/manifest spontaneously	2
<i>Near</i>	
Immediate realignment after cover test	0
Realignment after blink or refixation	1
No realignment/ manifest spontaneously	2

- Type and size
- Comparative deviation at 33 cm, 6 m, and in the far distance (20 m).
- The size of the AC/A ratio and determining whether the patient has a true or simulated divergence excess.
- If there is a change of deviation on lateral versions.
- Lateral gaze inhibition (i.e. decrease in deviation on lateral gaze) If there is a V or A phenomenon with or without associated inferior oblique or superior oblique overaction. These should not be missed especially A pattern as this is a risk factor for postoperative residual exotropia.

Aims

- Phoria for distance and near in primary position.
- In children aim of surgery is to either give optimal correction or slightly under correct (up to 8 PD is desirable) as consecutive esotropia can result in amblyopia.
- In adult surgery can be aimed at slight overcorrection (up to 8PD) as there is risk

of exotropic drift in postoperative period especially in patients with poor vision.

- No suppression.
- Stereopsis should be salvaged by performing early surgery especially in very young children with constant deviation.

Types of Surgery

- True divergence excess type:* Bilateral recession of lateral recti.
- Basic exotropia and stimulated divergence excess:* Unilateral rectus recession and medial rectus resection.
- Convergence insufficiency:* Bilateral resection of medial recti.
- Lateral gaze inhibition:* Bilateral lateral recti recession should be avoided.

VIVA QUESTIONS

Q.1. How will you perform occlusion test of Scobee-Burian?

Ans. Given in examination section.

Q.2. Differentiate between true and simulated divergence and name the tests used for that.

Ans. Given in examination section.

Q.3. What is epidemiology of exotropia?

Ans. Incidence

Exotropia appears less frequently than esotropia (ET). The approximate ratio of XT to ET is 1:3

In Costenbader's series of 472 patients with IDS, deviation was present

- At birth - 204
- 6 months - 16
- 6–12 months - 72
- After 5 years - 24
- Sex - women (approximately 60–70%)

Other associations

- Facial symmetry associated with exodeviations
- Children with craniofacial anomalies more likely to exhibit exotropia
- Maternal smoking during pregnancy
- LBW
- 17-fold increased risk in monozygotic twin.

Table 2 Difference between alternating and unilateral constant exotropia

<i>Alternating</i>	<i>Unilateral</i>
Visual acuity is almost equal in both eyes	Fixation preference
Angle of deviation is large, nearly equal for distance and near	Deviation is large
Associated commonly with secondary vertical deviation, deviating abducted eye is elevated	Vertical deviations are more common
If there is NRC and bifoveal fusion-suppression of deviating eye	Marked suppression in the deviating eye
	Amblyopia is less severe than esotropia
	Treatment is almost always surgical

Q.4. What is constant (early onset) exotropia?

Ans. Constant (early-onset) exotropia has following features:

Presentation is often at birth. Primary constant infantile exotropia is rare

Signs

- Normal refraction
- Large and constant angle
- DVD may be present
- Neurological anomalies are frequently present, in contrast with infantile esotropia.
- Treatment is mainly surgical and consists of lateral rectus recession and medial rectus resection.

Differential diagnosis is secondary exotropia, which may conceal serious ocular pathology.

Difference between alternating and unilateral constant exotropia is summarized in

Table 2.**Q.5. Classify exodeviation.**

Ans. A. Classification

*Concomitant/incomitant**Comitant*

- Primary
 - Infantile exotropia
 - Intermittent exotropia

Table 3 Classification intermittent exotropia

<i>Burian classification</i>	<i>Kushner classification</i>
Divergence excess	High AC/A ratio Strong proximal convergence
Simulated divergence excess	Tenacious proximal fusion
Basic pattern	Basic pattern
Convergence insufficiency	Low AC/A ratio Fusional convergence insufficiency Pseudoconvergence insufficiency

- Secondary
 - Sensory exotropia
 - Consecutive exotropia

Incomitant

- Paralytic
- Restrictive
- Musculofascial anomalies
- Dissociated horizontal deviation
- B. On the basis of underlying fusional reserve
 - Exophoria XP
 - Intermittent exotropia X(T)
 - Manifest exotropia XT
- C. Burian's classification of intermittent exotropia
 - *Basic pattern*: Distance and near deviation is almost equal
 - *Convergence insufficiency*: Near deviation is larger than distance deviation by >15 pd
 - *Divergence excess*: Distance deviation exceeds near deviation by >15 pd
 - *Simulated divergence excess*: Initial distance deviation exceeded the near deviation by > 15 pd, but after 1 hr of monocular occlusion 2 measurements showed difference of < 15 pd.

Burian classification did not specify the type of convergence that was insufficient (accommodative or fusional) which was included in Kushner classification

(Table 3).*D. Duane's classification:*

- Divergence excess pattern
- Convergence insufficiency pattern



Fig. 1: Left exotropia

- Basic exodeviation
- Simulated or pseudodivergence excess

True divergence excess

- Exophoria—exotropia at distance, normal near point of convergence, adequate prism convergence, intermittency, equal vision, good stereopsis, and ARC when exodeviated
- *Costenbader*—definition of divergence excess
- *Near*: Distance > 15 pd
- Associated with a high AC/A ratio in 60% Kushner

Simulated divergence excess:

- Exodeviation distance—near > 15pd
- After breaking fusion, distance—near < 10 pd
- Due to vergence after effect (tonic and accommodative). Dissipated by prolonged mono-ocular occlusion
- Over 80% of divergence excess type patients

Convergence insufficiency

- Near deviation—distance >15pd
- Patients have either a low AC/A ratio or a fusional convergence insufficiency
- Patient usually in teens
- Asthenopic symptoms with intermittent diplopia at near
- No X or X(T) initially at distance or near. Seen as disease progresses.

Q.6. What are Calhounz's phases of exodeviation.

- Ans.**
- Intermittent exotropia at distance, orthophoria at near, asymptomatic
 - Exotropia (**Fig. 1**) at distance, orthophoria/exophoria at near, symptomatic for distance, no suppression scotoma
 - Exotropia at distance, exotropia or intermittent exo at near, binocular vision for near, suppression scotoma develops for distance
 - Exotropia for distance and near. Lack of binocularity.

Q.7. What are the causes of pseudoexotropia?

- Ans.** Pseudoexotropia:

- Hypertelorism
- Positive angle kappa
- Large interpupillary distance
- Broad nasal bridge
- Narrowing of lateral canthi

Q.8. What are the causes of pseudoesotropia?

- Ans.**
- Negative angle kappa
 - Small interpupillary distance
 - Epicanthus.

Q.9. What are rules of thumb for prescribing spectacles for young children refractive error without strabismus?

- Ans.**
- Hyperopia greater than 5 D
 - Myopia greater than 3 D
 - Astigmatism greater than 2 D if not oblique, greater than 1 D if oblique
 - Anisometropia greater than 2 D for myopic, greater than 1 D if hyperopic, greater than 2 D if astigmatic Refractive error with strabismus; treat:
 - Hyperopia or hyperopic astigmatism greater than astigmatism greater than 1.25 D (esotropia)
 - Myopia greater than 1 D (exotropia) child's age and symptoms as well as other factors must be taken into account.

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SHORT CASES

DUANE RETRACTION SYNDROME

Shipra Singh, Saranya Devi K

INTRODUCTION

Duane retraction syndrome (DRS) forms a part of a group of conditions called congenital cranial dysinnervation disorders (CCDD), which occur due to the developmental errors in the innervation of ocular and facial muscles. In Duane retraction syndrome (DRS) there is failure of innervation of the lateral rectus by a hypoplastic sixth nerve nucleus, with anomalous innervation of the lateral rectus by the third nerve. The condition is often bilateral. Up to half of the patients have associated systemic defects such as deafness, external ear abnormalities, speech disorder and skeletal abnormalities. Associated mutations in several genes have been found. Approximately 10% of cases are familial muscles.¹

HISTORY

Chief Complaints

Patients present with deviation of either eye, limitation of extraocular movements, abnormal movement of eye (upshoot and downshoot), shortening of eye (leash phenomenon), bigger size of eye (retraction of globe), diminution of vision, abnormal head and face posture.

History of Present Illness

Patients may complain of inward or outward deviation of either eye. Complete or less often partial, absence of outward movement (abduction) of the affected eye or deficiency of inward movement (adduction) of the affected eye. Abnormal movement of eye (upshoot and downshoot) can be there while doing inward movement. Abnormal head posture is adopted in order to obtain better vision (binocularity). A face turn is typical, conferring binocular single vision (BSV) in the primary position and avoiding amblyopia. Narrowing of the palpebral

aperture (co-contraction of muscles) can be there. Diminution of vision may be there (Anisometropia/amblyopia).

History of past illness—history of fever/illness

Family history—may be hereditary.

EXAMINATION

General Examination/Specific Systemic Examination

Preauricular tag, hemivertebra, low hair line, torticollis, malformation of the jaw, cheek and ear, usually on one side of the face, radial ray defect, Klippel-Feil anomaly, deafness, congenital paresis of facial and abducens cranial nerves, abnormalities of the upper limbs and heart may be present.

Ocular Examination

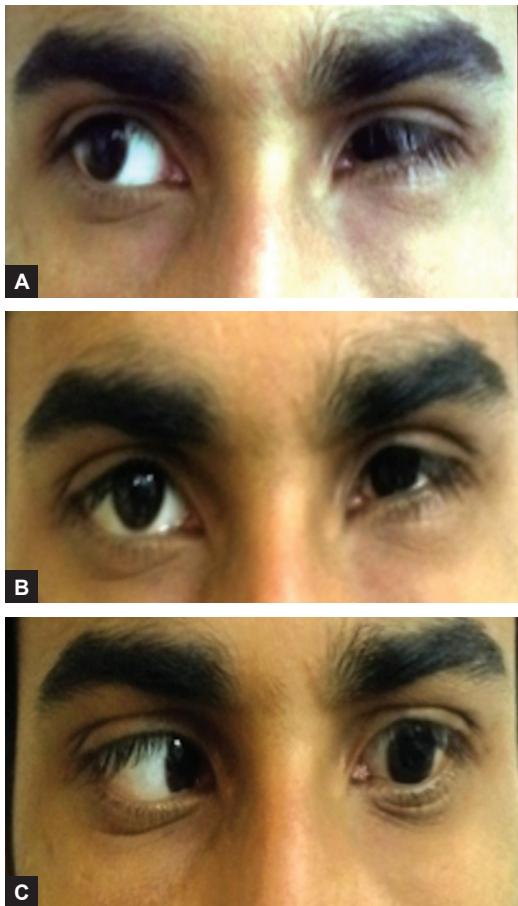
Head posture: Abnormal head posture is adopted to achieve alignment of the two eyes in order to obtain binocularity. Longstanding torticollis (since birth) leads to craniofacial asymmetry.

Face turn: A face turn is typical, conferring BSV in the primary position and avoiding amblyopia; usually a face-turn to the affected side in types 1 and 3 and to the opposite side in type 2.

Eyeball: Retraction of the globe on adduction because of co-contraction of the medial and lateral recti with resultant narrowing of the palpebral fissure (**Figs 1A to C**).

Extraocular Movement (EOM)

- Complete or less often partial, absence of outward movement (abduction) of the affected eye
- Partial, or rarely complete, deficiency of inward movement (adduction) of the affected eye
- Partial closure of the eyelids (pseudoptosis) of the affected eye when it is adducted.



Figs 1A to C: Left Eso-DRS with left eye limitation of abduction with globe retraction

- An upshoot or downshoot in adduction may be present; in some cases, this is produced by a tight lateral rectus muscle slipping over or under the globe to produce an anomalous vertical movement.
- **Strabismus:** 76% of individuals have frank strabismus in primary gaze.
- Poor binocular vision.
- Deficiency of convergence in which the affected eye remains fixed in the primary position while the unaffected eye is converging.

Reviews of DRS patients have shown hypermetropia of greater than +1.50 in 71% of the patients.

Amblyopia (anisometropia) occurs in about 10% of individuals and will respond to standard therapy if detected early.

Special examination for squint: See section on esotropia long case.

Lid: Partial closure of the eyelids (pseudoptosis) of the affected eye when it is adducted.

Conjunctiva—previous scar of surgery may be there.

Fundus—Disc anomaly may be there. (Morning glory syndrome).

DIFFERENTIAL DIAGNOSIS

It includes:

- Congenital sixth nerve palsy
- Infantile esotropia
- Mobius syndrome.

MANAGEMENT

Nonsurgical

- Spectacles or contact lenses for refractive error
- Prism glasses to improve the compensatory head position
- Treat amblyopia with standard therapy
- *Botulinum toxin:* Botulinum toxin decreases the amount of deviation and leash phenomenon (upshoot or downshoot of globe with adduction).

Surgical

The aims of surgery are:

- To correct a manifest strabismus
- To centralize the field of binocular single vision,
- To overcome or reduce the need for a large compensatory head posture.

Surgery is indicated for the following reasons:

- Decomposition, giving rise to manifest strabismus
- Abnormal head posture
- Severe globe retraction with or without upshoot and downshoot
- Avoid lateral rectus resection.

Different scenarios

- *For types 1 and 3 with head turn:* Recession of medial rectus muscle or horizontal transposition of vertical rectus muscles

- For types 1 and 3 with leash phenomenon and/or severe globe retraction: Recession of both medial and lateral rectus muscles with possible Y-splitting of the lateral rectus muscle
- For type 2 with head turn and fixation with uninvolved eye: Recession of ipsilateral lateral rectus muscle
- For type 2 with head turn and fixation with involved eye: Recession of contralateral lateral rectus muscle
- For type 2 with leash phenomenon: Recession of lateral rectus muscle with possible Y-splitting
- Associated V phenomenon with inferior oblique overaction with upshoot: Horizontal recti plus inferior oblique recession.
- Associated a phenomenon with superior oblique overaction with downshoot: Ipsilateral horizontal recti recession plus superior oblique weakening.
- Resection of the horizontal recti of the same eye should not be attempted even to correct the ocular deviation.
- Recession and retroequatorial myopexy (Faden) of the contralateral synergist can also be done to correct face turn and may improve the limitation of abduction of the involved eye.
- Y splitting of lateral recti can be done in upshoot and downshoot.

Complications of surgery:

- Undercorrection of primary position esotropia and the compensatory head turn
- Overcorrection leading to secondary exotropia
- New vertical deviations can occur after vertical rectus transposition procedures.

VIVA QUESTIONS

Q.1. What is epidemiology of DRS?

Ans. Epidemiology:

- Prevalence of about 1/1000 in general population
- Females (60%) > Males (40%)
- Accounts for up to 4% of all strabismus cases
- Most common type of congenital aberrant ocular innervation
- 80% of cases occur unilaterally, with LE predominance

- 70% of cases are isolated
- 30% of cases are associated with other congenital anomalies.

Isolated cases: 90% occur sporadically and are commonly unilateral. Remaining 10% are inherited and these are commonly bilateral.

Syndromic forms:

- *Oklahomo syndrome:* Duane syndrome and radial ray defects
- *Goldenhar syndrome:* Malformation of the jaw, cheek and ear, usually on one side of the face
- *Wildervanck syndrome:* Duane syndrome, Klippel-Feil anomaly, and deafness
- *Moebius syndrome:* Congenital paresis of facial and abducens cranial nerves
- *Holt-Oram syndrome:* Abnormalities of the upper limbs and heart
- *Morning glory syndrome:* Abnormalities of the optic disc.

Q.2. Name the systemic syndromes associated with DRS.

Ans. See the discussion part.

Q.3. What is pathogenesis of DRS?

Ans. Various theories are as follows:

- *Myogenic theory:* This theory, suggested by earlier studies, indicates there is fibrosis or inelasticity of the lateral rectus muscles and that the medial rectus muscle inserts abnormally far posteriorly.
- *Neurogenic theory:* There is a disturbance in embryologic development between weeks 4–8 which results in an absent abducens nerve with anomalous innervations of the lateral rectus muscle by a branch of the oculomotor nerve. Simultaneous activation of the medial and lateral rectus muscles, as demonstrated by EMG studies, may be the cause of global retraction.

Q.4. Describe surgical management in DRS—indications and procedures.

Ans. See management.

Q.5. Classify DRS.

Ans. See Tables 1 and 2.

Table 1 Classification of DRS

Type 1	Type 2	Type 3	Type 4
Poor abduction, good adduction	Poor adduction, good abduction	Poor adduction, poor abduction	Paradoxical abduction on attempt adduction
Agenesis of 6th nerve, 3rd nerve split innervate LR, MR, Adduction intact as most of the nerve goes to MR	6th nerve intact, 3rd nerve split innervate LR, MR, Poor adduction as LR contract against MR	6th nerve agenesis, 3rd nerve split innervate LR, MR, The split is equal	6th nerve agenesis, 3rd nerve split innervate LR, MR, Most of the nerve innervates LR

Abbreviations: LR, lateral rectus; MR, medial rectus; ADD, adduction; ABD, abduction

Table 2 Classification (Huber) of DRS

Type I	Type II	Type III
Most common, characterized by— <ul style="list-style-type: none">• Limited or absent abduction.• Normal or mildly limited adduction• In the primary position, straight or slight esotropia	Least common, characterized by: <ul style="list-style-type: none">• Limited adduction• Normal or mildly limited abduction• In primary position, straight or slight exotropia	Characterized by <ul style="list-style-type: none">• Limited adduction and abduction.• In the primary position, straight or slight esotropia• In some cases phenotypic variants have been allied to differing genotypes

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OCULAR MYASTHENIA GRAVIS

Shipra Singh, Adarsh Shashni

INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disease in which antibodies mediate damage and destruction of postsynaptic acetylcholine receptors in striated muscle. The resultant impairment of neuromuscular conduction causes weakness and fatigability of skeletal musculature, but not of cardiac and involuntary muscles. This resulting in progressive muscle weakness with use of the muscle and recovery of strength after a period of rest. Weakness is experienced once number of receptors is 30% or less.¹

HISTORY

Chief complaint: Drooping of eyelid, double vision, limitation of eye movements, abnormal eye movement, difficulty in eye closure, light sensitivity, fatigue of eye muscles, difficulty in swallowing, speech, breathing, muscular weakness, lack of facial expression.

Past history: Previous history of similar complaints or any history of thymoma, thyroid dysfunction, intracranial mass, lung carcinoma.

Pastsurgical history: Any history of surgery of extraocular muscles or ptosis or thymoma, thyroid dysfunction, intracranial mass, lung carcinoma.

Systemic Myasthenia

- Symptoms are typically of onset in the third decade and may include painless fatigue, often brought on by exercise, commonly in conjunction with ptosis and diplopia.
- Fatigability affects the musculature of the limbs, facial expression, ocular movements, chewing and speech. Bulbar symptoms include dysphagia and dysarthria; difficulty with breathing is rare.
- Signs:** The most important feature is peripheral weakness, particularly of the arms and proximal leg muscles, with wasting in long-standing cases. There is characteristically a lack of facial expression (myopathic facies).

There may be several reasons why eye muscles are more frequently involved. However, this is not completely understood.

One hypothesis is that patients may simply notice eye weakness more often than mild weakness in other muscle groups in the body. Another hypothesis is that the eye and eyelid muscles are structurally different from muscles in the trunk and limbs. For example, they have fewer acetylcholine receptors, which is where the defect occurs in autoimmune MG. Eye muscles contract much more rapidly than other muscles and may be more likely to fatigue.

Perhaps the most important difference between eye and eyelid muscles compared with other muscles of the body is that eye muscles respond differently to immune attack. The differences in the response of eye muscles to immune attack may explain why eye muscles are also targeted in other autoimmune conditions, such as autoimmune thyroid disease.

Ocular Myasthenia

Ocular involvement (**Table 1**) occurs in 90% of cases and is the presenting feature in 60%. Two-thirds of patients have both ptosis and diplopia. Less than 10% of patients have ptosis alone and less than 30% have diplopia alone.¹

Ptosis: Ptosis is insidious, bilateral and frequently asymmetrical.

- Typically worse at the end of the day.
- Worse on prolonged (60 second) upgaze due to fatigue.

Table 1 Ocular signs of myasthenia gravis

Muscle involved	Clinical sign
Levator palpebrae superioris	Ptosis Cogan's lid twitch Lid hopping Enhanced ptosis
Extraocular movements (EOMs)	Cranial nerve III, IV, or VI weakness Gaze palsies Pseudo-internuclear ophthalmoplegia (unilateral or bilateral) Complete ophthalmoplegia Intrasaccadic fatigue End gaze nystagmus
Orbicularis oculi	Weakness of forced closure Peek sign

- Cogan twitch sign is a brief upshoot of the eyelid as the eyes saccade from depression to the primary position.
- If one eyelid is elevated manually as the patient looks up, the fellow eyelid may show fine oscillatory movements.

Diplopia: Diplopia is frequently vertical, although any or all of the extraocular muscles may be affected. This most often occurs when looking up or to the side. To compensate for the weakness, the patient may tilt his/her head or turn their face to allow the stronger eye to work. For example, if the muscle which allows the eye to look upward is weak, the patient could tilt their head back to look up.

Nystagmoid movements: Nystagmoid movements resemble nystagmus, but the initial pathological defoeveating movement is a saccadic intrusion.

Ocular flutter and opsoclonus: These entities consist of saccadic oscillations with no inter saccadic interval; in ocular flutter oscillations are purely horizontal, and in opsoclonus they are multiplanar. Causes include viral encephalitis, myoclonic encephalopathy in infants ('dancing eyes and dancing feet'), as a transient idiopathic occurrence in healthy neonates, or may be drug-induced.

Ocular bobbing: Ocular bobbing manifests with rapid downward conjugate eye movements

with a subsequent slow drift up to the primary position. Causes include pontine lesions (usually hemorrhage), cerebellar lesions compressing the pons, and metabolic encephalopathy.

Peek sign: A test to check for fatigue and weakness of the eye muscle which may be done by the examining doctor includes attempting to open the eyes while the patient tries to hold them shut, sometimes called a “peek sign”. This may result in one or both eyes opening, and the patient appears to “peek” at the examiner.

Forced duction test: It differentiates from paralytic strabismus.

DIAGNOSIS

The edrophonium (Tensilon) test is a first line test for diagnosis of MG. The Tensilon test consists of injecting a small amount of medication edrophonium intravenously. If the patient has MG the ocular muscle weakness, the ptosis, and general muscle weakness and/or nystagmus will improve dramatically for a short period of time.

In recent years an *ice test* is being more widely used. This is when ice is applied to the eyes, after a short period of time; the eyes will have an improvement of ocular symptoms. Usually, a blood test called acetylcholine receptor antibody titer (AChR Ab) is ordered as well. Additional blood work may include other antibody studies, thyroid profile, and a sedimentation rate.

Investigations

Blood

- AchR-Ab—Positive in 80% with generalized MG. Positive in only 50% with ocular involvement only also present in 90% of patients with penicillamine-induced MG
- Antistriated muscle Ab
- Anti-muscle specific kinase Ab (Anti-MuSK Ab – positive in patients with AChR Ab -ve).

Imaging

- CXR (*chest x-ray*)—thymus (anterior mediastinal mass), aspiration pneumonia
- Thoracic imaging (MR, CT, CT/PET) to detect thymoma, present in 10%. Imaging may also be used to rule out a lung tumor if Lambert-

Eaton syndrome is suspected, or an intracranial mass for ocular myasthenia.

Ice pack test: This test for an improvement after an ice pack is placed on the ptotic eyelid (or other affected muscle) for 2 minutes, as cold inhibits the breakdown of acetylcholine by acetylcholinesterase. It is around 75% sensitive but highly specific.

Sleep test: The “sleep test”, which is based on the tendency for MG symptoms to improve following rest, may be used in small children and patients who have allergies or sensitivity to anticholinesterase drugs such as Tensilon. The patient is placed in a quiet, darkened room and instructed to close their eyes for 30 minutes. The patient is photographed and eye movement is measured before and after the test. The test is considered positive if there is improvement in the ptosis and/or eye movement (motility) following the 30 minutes rest period.

The morning/evening comparison test is similar in concept to the sleep test. The patient is photographed, and the ptosis and ocular motility are compared at different times during the day. Old photos are very helpful to determine how long the patient has had drooping of the upper eyelid.

Fatigue test: Another simple test for ptosis is the “fatigue” test. This consists of having the patient look at an object held up by the examiner in front of the patient. After a short period of time the eyelid (s) will droop in the person with ocular MG.

Acetylcholine receptor (AChR) antibodies: Antibody testing supports a diagnosis of MG and predicts the likelihood of thymoma. Testing is confounded by recent (within 48 hours) general anesthesia with muscle relaxants. Present in around 90% of systemic cases but only 50–70% of ocular myasthenics. Rarely present in Lambert-Eaton.

MuSK protein antibodies are positive in 50% of those negative for AChR antibodies; positive patients are less likely to have ocular features and thymoma.

Striational antibodies: Antibodies against several contractile elements of skeletal muscle (e.g. titin) may be present; they are found in 80–90% of those with thymoma and one-third of those without and can be a marker of more severe MG.

Voltage-gated calcium channel antibodies are characteristic of Lambert-Eaton syndrome.

Edrophonium (Tensilon) test: Edrophonium is a short-acting anticholinesterase that confers a transient improvement of weakness in MG. The estimated sensitivity is 85% in ocular and 95% in systemic MG. Diagnostic and distinguishes from cholinergic crisis.

- An intravenous test dose of 0.2 mL (2 mg) edrophonium hydrochloride is given. If definite symptomatic improvement (or adverse reaction) is noted, the test is terminated.
- The remaining 0.8 mL (8 mg) is given after 60 seconds if necessary. Pre- and post-procedure measurements of ptosis and/or motility (Hess chart) are compared; the effect lasts only 5 minutes.
- Cardiac monitoring for bradycardia and asystole (Rx with atropine).
- 1 mg test dose and up to 10 mg.
- In cholinergic crisis, will get increased salivation, etc.
- Potential but uncommon complications include bradycardia and death; resuscitation facilities and appropriate expertise must be readily available on site in case of emergency, and its use may be limited to cases in which less invasive tests have given equivocal results.
- Atropine 0.3 mg is given intravenously to minimize muscarinic side effects.

Electromyography shows characteristic features.

Muscle biopsy reveals neuromuscular junction antibodies and characteristic electron microscopy features, but is not commonly performed.

Thyroid function testing should be performed as autoimmune thyroid disease can be associated with MG.

Electrodiagnostic Studies

Repetitive nerve stimulation test—shows a decrease in the compound muscle action potential by 10% in the 4th or 5th response to a train of nerve stimuli.

Single fiber nerve electromyography—evidence of neuromuscular blockade with increased jitter.

GRADING

Myasthenia Gravis Foundation of America

- Grade 1—affects the ocular muscles only
- Grade 2—mild weakness affecting muscles other than ocular muscles
- 2A—affects the limb and axial muscles
- 2B—affects the respiratory and bulbar muscles
- Grade 3—moderate weakness (3A and 3B)
- Grade 4—severe weakness (4A and 4B)
- Grade 5—intubation required.

Osserman's Grading

- I: Ocular
- II A: Mild generalized with slow progression
- II B: Moderate generalized
- III: Acute fulminant MG
- IV: late severe MG (takes 2 years to progress from I to II).

DIFFERENTIAL DIAGNOSIS

- Fourth nerve palsy
- Third nerve palsy
- Progressive external ophthalmoplegia.

TREATMENT

Emergencies in crisis (ABC)—treat exacerbating factors, stop medications that can exacerbate, treat fever with antipyretics, treat infections.

- Oral pyridostigmine, neostigmine, steroids, azathioprine, cyclosporine
- Plasmapheresis
- Intravenous immunoglobulin (IVIG).

Ocular Myasthenia Gravis

People with ocular MG and their caregivers should balance the severity of the symptoms with the risks and benefits of treatment. People who have primarily cosmetic problems due to ptosis or diplopia may consider no pharmacological treatment, such as:

- Wearing dark glasses in bright light, which some patients find helpful.
- Using eyelid tape (a special type of tape used to hold the eyelids open without injuring the eyelids). This can be used for ptosis and may be preferable to drug therapy that alters

- the immune system using agents such as glucocorticoids (prednisone or similar agents),
- Azathioprine (Imuran), cyclosporine or mycophenolate mofetil (CellCept).
- Applying a patch to one eye. This permits patients with double vision to see one image. If the same eye is consistently patched, vision in that eye will decrease. Therefore, it is important to alternate the patch from one eye to the other to avoid permanent vision loss. Another method is wearing one contact lens which is opaque (cannot be seen through). This may also be changed periodically from one eye to the other. Special prism glasses may also help to correct double vision in some cases. The use of non-allergenic tape such as paper tape is suggested.
- Using *eyelid crutches* (clever devices attached to glasses to hold the eyelids open) for ptosis and eyeglass prisms for diplopia. These are rarely used, older methods of treatment for ocular MG. Once again, *alternating taping of eyelids* is recommended to prevent eye strain. Another way to hold one or both eyelids open is to have *ptosis bars* or eyelid crutches attached to the eyeglasses. These are thin, flexible wires which attach at the bridge of the nose and are free-floating at the other end or attached to the frame near the hinges. The wires rest against the eye socket and hold the eyelid open like a brace or crutch. It is important to remove the glasses frequently to allow the eyes to close so that they can be moistened. Artificial tear drops and forced blinking may also help.
- Weakness of the muscles that control eye closure (*orbicularis oculi*) may result in the patient getting soap in their eyes when bathing, and in excessive tearing due to incomplete blinking. The use of non-irritating shampoo, such as baby shampoo, may be of help. *Swimming goggles* may also be worn when bathing or swimming to prevent eye irritation.
- Medication such as *baclofen* and *gabapentin* may be helpful.
- *Botulinum toxin* injection into the extraocular muscles has had some success but can be unpredictable and long-term treatment is required.
- *Surgery for nystagmus* with a null point is aimed at moving muscles in order to mimic

muscle tension while the eyes and face are straight and may be performed to address a compensatory head posture. Recession of all horizontal recti has been successful in reducing the amplitude of nystagmus in some patients without a significant null point.

- When ptosis does not respond to medication, or conservative treatment, surgery may be suggested to lift the eyelid or lids. Surgery is only done in very rare cases.
- When ocular symptoms are severe or disabling, treatment with immune system
- Modulating therapy may be considered.
- Agents that improve neuromuscular transmission, such as *Mestinon* may be helpful for ptosis, but are generally not very useful for diplopia.

Thymectomy

Thymectomy is usually not considered for people with ocular MG unless these treatments offer only a temporary improvement and repeated treatments are necessary to sustain the effect. While thymectomy (removal of the thymus gland) is often recommended for patients with generalized MG, it is rarely used in purely ocular MG unless a thymoma is suspected. The clinical observations which distinguish ocular myasthenia from generalized MG include: highly restrictive ocular symptoms such as diplopia, ptosis, and weak eye closure. The good news for patients with ocular MG is that if they continue to have only ocular symptoms for three years, there is a very good chance their symptoms will not increase. The use of the above strategies can make it easier to live with ocular MG.

VIVA QUESTIONS

Q.1. How common is the thymus involved?

- Ans.**
- 75% of cases of which 15% are thymomas and 85% are thymic hyperplasia
 - Myasthenia gravis may be ocular, bulbar (affecting the cranial nerves arising from the lower brainstem) or generalized. Congenital and juvenile forms are rare. A similar clinical picture is found in the

Lambert-Eaton myasthenic syndrome mediated by antibodies against pre-synaptic voltage gated calcium channels; in 60% this is a paraneoplastic phenomenon associated with a lung tumor. Patients positive for anti-MuSK (muscle-specific kinase) antibody may have a distinct form of MG. A range of drugs can exacerbate MG, and should be avoided if possible; those with ophthalmic relevance include many antibiotics, and beta-blockers.

Q.2. How common is the thyroid involved?

Ans. Up to 30% of patients with MG have antithyroid antibodies.

Q.3. What are the common presentations?

Ans.

- Age- 2 peaks.
- 20 to 30 years old with female predominance overall, the ratio of affected females to males in generalized MG is 3:2 or higher.
- >50 years old with male predominance.
- Ptosis, diplopia
- Dysarthria, difficulty swallowing (isolated bulbar muscles involvement occurs in 20%).
- Generalized weakness or reduced exercise tolerance.
- Respiratory failure in 1%.
- Tends to occur extraocular muscles first, then to facial to bulbar and to limbs and truncal.

Over two-thirds of all patients with myasthenia gravis (MG) begin with symptoms relating to their vision. Overall, the ratio of affected females to males in generalized MG is 3:2 or higher. In ocular myasthenia, men are more frequently affected, especially after the age of 40. In addition, the average age of onset for generalized myasthenia is 33 years, while that of ocular MG is 38 years. The ocular motor system may be especially vulnerable to MG since it cannot adapt rapidly to variable weakness. The most common symptoms seen in patients with ocular MG are diplopia (double vision), ptosis (droopy eyelids), and incomplete eye closure. Compared to other involved skeletal muscles, only slight weakness of

the extra ocular muscle may cause diplopia and visual disturbances to occur. These symptoms occur due to weakness of the muscle that control eyeball and eyelid movement. Light sensitivity due to sluggish pupils may occur in some patients.

Q.4. What are the complications?

Ans.

- Myasthenic crisis
- Severe exacerbation of MG
- 10% require intubation
- Treatment complications
- Cholinergic crisis.

Q.5. What can exacerbate MG or precipitate crisis?

Ans.

- Noncompliance to medications
- Infection
- Emotions
- Drugs
- *Antibiotics:* aminoglycosides, tetracyclines, macrolides and fluoroquinolones
- *CVS:* Beta blockers, calcium channel blockers (verapamil)
- *Others:* Chloroquine, quinidine, procainamide, Li, Mg, prednisolone, quinine, penicillamine. Symptoms are frequently influenced by environmental, emotional, and physical factors. Some of these factors include bright sunlight, extreme temperature, emotional stress, illness, surgery, menstruation, and pregnancy, among others. Symptoms tend to be worse at the end of the day.

Q.6. Ocular involvement is seen in how many patients of myasthenia gravis? What is the most common presenting ocular feature in it?

Ans. Ocular involvement occurs in 90% of cases and is the presenting feature in 60%. Two-thirds of patients have both ptosis and diplopia. Less than 10% of patients have ptosis alone and less than 30% have diplopia alone.

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CHAPTER

6

Lens

LONG CASES

ZONULAR CATARACT

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INTRODUCTION

Zonular cataract is the most common visually significant variant of pediatric cataract. It may be congenital or occur at a later stage of development, and is characterized by an opacity which occupies a discrete zone in the lens. It is usually bilateral, and has an autosomal dominant inheritance pattern.

It may be given as a long or short case in postgraduate/DNB/Diploma examination.

HISTORY

Chief Complaints

The informants are usually the parents who notice few or all of the following symptoms:

- Child does not recognize objects, toys or parents (diminution of vision)
- White pupillary reflex (*leukocoria*)
- Involuntary continuous rhythmic movements of the eye (*nystagmus*)
- Deviation of eye (*Strabismus*).

History of Present Illness

Etiology and genetics: It is usually hereditary with an autosomal dominant genetic pattern. This type of congenital cataract may be caused by mutations

in the heat-shock transcription factor-4 gene (HSF4) located at 16q21-q22.1.

An environmental form of zonular cataract may occur and is associated with vitamin D deficiency. Occasionally, maternal rubella infection contracted between 7th and 8th week of gestation may also cause zonular (lamellar) cataract.

Age at presentation: Patients with zonular cataract usually present in early childhood, though occasionally, they may present soon after birth.

Presenting features: Bilateral involvement is characteristic of zonular cataracts. Since the patients are often in the pre-school age group, a definitive history of diminution of vision may be difficult to elicit. The parents usually notice that the child is unable to see toys placed nearby, stumbles often and does not recognize faces of familiar persons. The parents may notice a white reflex or leukocoria. In cases where there is an asymmetric involvement of both eyes, strabismus may be the presenting complaint. Congenital cases may have associated involuntary ocular movements due to impaired development of fixation.

Antenatal and perinatal history: A history of fever associated with rash may be present in the mother in the antenatal period, which may point towards

rubella as the causative etiology. It is essential to rule out maternal malnutrition and history of drug or toxin intake in the antenatal period. Recurrent neonatal infections and malnutrition should be ruled out.

Family history: A positive family history of congenital or developmental cataract is present.

EXAMINATION

General Examination/Specific Systemic Examination

Zonular cataract is familial and usually not associated with any underlying systemic disorder.

However, a detailed examination is essential to rule out systemic disorders that are commonly associated with bilateral congenital cataracts, such as Toxoplasmosis, Other Agents, Rubella, Cytomegalovirus, and Herpes simplex (TORCH) syndrome, galactosemia and various mutational syndromes. The presence of microcephaly, deafness, cardiac abnormalities and developmental delay point towards an underlying systemic etiology and warrants a need for further investigations.

Ocular Examination

Visual acuity: Visual acuity may be difficult to establish in very young children. Indirect evidence of diminution of vision include:

- Child does not follow objects or light
- Inability to maintain central steady fixation
- Child resists occlusion of the good eye
- Strabismus (usually convergent squint)
- Nystagmus

Objective assessment of visual acuity may be made by the following tests:

- *Infants:* Preferential looking tests, Teller acuity cards, Catford drum test, Optokinetic nystagmus and visual-evoked responses
- *1–2 years:* Worth's ivory ball test, Sheridan's ball test, Boek's Candy test
- *2–5 years:* Dot acuity test, Miniature toy test, Sheridan-Gardiner test (HOTV) test, Tumbling E test, Allen picture cards, Beale-Collins picture chart tests, Kay picture test, Landolt C test, Snellen's chart

Eyeball: Strabismus may be present, usually convergent squint. Nystagmus is present in cases with congenital onset of cataract

Eyelids, conjunctiva, cornea, sclera, iris, and pupil: Examination is usually unremarkable. Microcornea may be present in cases with underlying systemic syndrome.

Intraocular pressure is usually normal.

Lens: Typically, zonular cataract occurs in the zone of fetal nucleus surrounding the embryonic nucleus. The main mass of the lens internal and external to the zone of cataract is clear, except for small linear opacities like spokes of a wheel (riders), which may be seen towards the equator (**Figs 1 and 2**).

Vitreous and fundus: Examination is usually normal in bilateral zonular cataract. Salt and

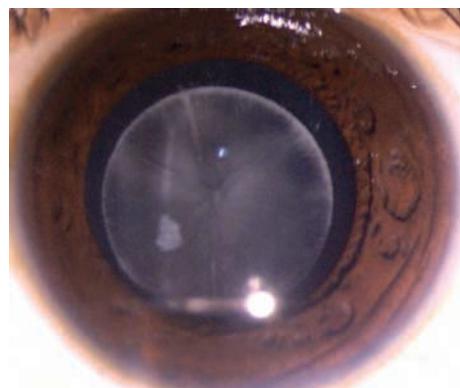


Fig. 1: Zonular cataract with clear periphery and riders

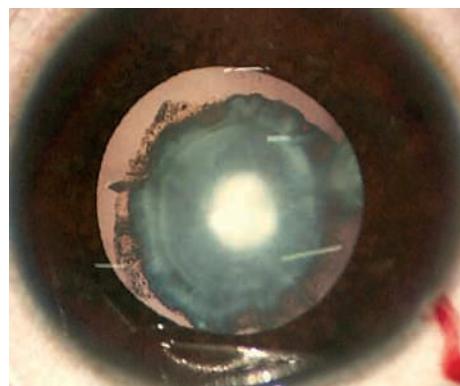


Fig. 2: Zonular cataract retroillumination

pepper retinopathy may be present in congenital rubella syndrome. Persistent hyperplastic primary vitreous may be associated, especially in unilateral cases.

DIFFERENTIAL DIAGNOSIS

- Persistent hyperplastic primary vitreous
- Retinoblastoma
- Endophthalmitis
- Retinal detachment
- Toxocariasis
- Coat's disease
- Retinopathy of prematurity
- Astrocytic hamartoma
- Vitreous hemorrhage.

INVESTIGATIONS

Systemic Investigations

Zonular cataract with positive family history and established hereditary basis for the cataract does not warrant any further investigation.

In other cases with bilateral cataract, the investigations should include the following:

- *Serology for intrauterine infections:* TORCH titres (TORCH = toxoplasmosis, rubella, cytomegalovirus, herpes simplex virus, other viruses such as varicella), VDRL titres for syphilis.
- *Urine examination:* Urinalysis for the presence of reducing sugars (galactosemia); urine chromatography for amino acids (Lowe's syndrome).
- Serum electrolytes (serum calcium and phosphorus)
- Fasting blood glucose
- Serum galactokinase
- Thyroid function tests
- Referral to a pediatrician may be warranted for dysmorphic features or suspicion of other systemic diseases. Genetic testing and chromosome analysis may be useful in this context.

Ocular Investigations

- *Visual evoked responses (VER):* To assess visual acuity and estimate visual potential

- *Biometry:* Axial length and keratometry measurements for IOL power calculation
- A-scan ultrasonography to give an estimate of axial length in infants and children uncooperative for biometry
- *B-scan ultrasonography:* To rule out any posterior segment pathology.

MANAGEMENT

Conservative Management

Partial cataracts, cataracts with less than 3 mm diameter and pericentral cataracts may not immediately require surgery and can be observed. Pupillary dilatation with 2.5% phenylephrine and part time occlusion of good eye may be tried in unilateral partial cataracts.

Surgical Management

Indications for Treatment

- Cataract >3 mm diameter
- Dense nuclear cataract obstructing view of fundus
- Associated strabismus/nystagmus
- VA < 20/80.

Time of Surgical Intervention

- Bilateral dense cataracts require early surgery within 6–8 weeks of age to prevent the development of stimulus deprivation amblyopia. In asymmetrical cataract, the eye with the denser cataract should be addressed first.
- Unilateral dense cataract should be operated as soon as possible, ideally before 4–6 weeks of age. Results are often poor due to dense amblyopia and non-compliance with occlusion therapy.
- Bilateral partial cataracts may not require surgery until later, if at all. In case of doubt, it may be prudent to defer surgery. Monitor lens opacities and visual function and intervene later, if vision deteriorates.
- Partial unilateral cataract can usually be observed or treated non-surgically with mydriasis, and possibly part-time contralateral occlusion to prevent amblyopia.

Biometry and IOL Power Calculation

Accurate measurements of axial length and keratometry may be difficult in the preoperative period because of poor patient cooperation and poor fixation. Usually, examination under anesthesia has to be performed to determine axial length and keratometry. Immersion biometry is more predictable than the contact method for IOL-power calculation.

An under-correction of the IOL power is usually recommended in cases of pediatric cataract to account for the myopic shift following IOL implantation. Dahan et al. suggest an under-correction of 10% in children between 2 to 8 years and under-correction of 20% in children less than 2 years of age. They also suggested IOL power selection based on axial length alone (**Table 1**).

In cases with unilateral cataract, emmetropia may be aimed for to minimize the risk of amblyopia. Piggyback IOL or IOL exchange may be needed at a later date in such cases.

Surgical Procedure

The primary surgical management consists of *lens aspiration or lensectomy*. Coaxial or bimanual lens aspiration via limbal route is preferred. Pars plana lensectomy may be undertaken in cases where IOL implantation is not planned.

Anterior capsulorhexis may pose a challenge due to the elastic pediatric anterior capsule, which has a propensity to extend. Cohesive OVD such as Healon GV facilitates anterior capsulorhexis as it maintains anterior chamber stability and offsets the vitreous upthrust.

Posterior continuous curvilinear capsulorhexis (PCCC) with limited anterior vitrectomy is recommended for children less than 7 years of age

to minimize the risk of visual axis opacification (VAO) and subsequent additional surgical procedures. In children older than 7 years, lens aspiration with IOL implantation is performed.

Primary IOL implantation is preferred in all unilateral cataract cases as well as bilateral cases when possible. In-the-bag implantation of single-piece hydrophobic IOL is preferred. Multipiece IOL in the sulcus may be implanted when in-the-bag IOL implantation is not possible.

Wound closure by stromal hydration alone may be inadequate because of low scleral rigidity, and sutures are often required to effectively seal the corneal incisions.

Postoperative Visual Rehabilitation

Postoperative occlusion therapy and visual rehabilitation is essential to achieve optimal outcomes, as postoperative amblyopia may limit the visual potential in even a well-done cataract surgery. Optical correction in an aphakic child depends upon the patient age and laterality of aphakia.

- Aphakic glasses are effective for visual rehabilitation in older children with bilateral aphakia. However, they result in unacceptable anisometropia and aniseikonia in unilateral aphakia. Aphakic glasses are heavy, cosmetically unattractive and result in spherical as well as prismatic aberrations.
- Contact lenses provide a superior optical solution for both unilateral and bilateral aphakia. Tolerance is usually reasonable until the age of about 2 years; problems with compliance may start after this period as the child becomes more active and independent. Contact lens may become dislodged or lost, leading to periods of visual deprivation with the risk of amblyopia. Maintenance of hygiene may be problematic in young children, leading to a risk of microbial keratitis. The maintenance issues and financial cost limits the widespread usage of contact lenses.
- IOL implantation is increasingly being performed in young children and even infants, and appears to be effective and safe in selected cases. Awareness of the rate of myopic shift, which occurs in the developing eye, combined with accurate biometry, allows the

Table 1 IOL power based on axial length (Dahan's formula)

Axial length (mm)	IOL power (D)
17 mm	28 D
18 mm	27 D
19 mm	26 D
20 mm	24 D
21 mm	22 D

calculation of an IOL power targeted at initial hypermetropia (correctable with spectacles), which will ideally regress towards emmetropia later in life. However, final refraction is variable and emmetropia in adulthood cannot be guaranteed.

- Occlusion therapy to prevent and treat amblyopia is vital in order to achieve optimal outcomes, especially in cases that have undergone unilateral cataract surgery. Atropine penalization may also be considered.

Complications

- *Visual axis opacification (VAO)* is nearly universal, if the posterior capsule is retained in a child under the age of 6 years. An intact anterior hyaloid phase provides a scaffold for proliferation of lens epithelial cells and may result in VAO despite posterior capsulorhexis. The incidence of opacification is reduced when posterior capsulorhexis is combined with vitrectomy. Surgical membranectomy via limbal or pars plana route is required for management. Nd: YAG capsulotomy may be tried in cooperative children.
- *Secondary membranes* may form across the pupil, particularly in microphthalmic eyes or those with associated chronic uveitis. A fibrinous postoperative uveitis in an otherwise normal eye, unless vigorously treated, may also result in membrane formation. Thin membranes can be treated with laser capsulotomy, thick membranes may require surgical excision.
- *Secondary glaucoma* may develop in 3–32% of eyes undergoing pediatric cataract surgery. Pupillary block glaucoma may occur in the immediate postoperative period, especially in microphthalmic eyes. Secondary open-angle glaucoma may also develop years after the initial surgery. It is therefore important to monitor the intraocular pressure regularly for many years.
- *Retinal detachment* is an uncommon and late complication after cataract surgery. The incidence of retinal detachment following cataract surgery has been reported between 1% and 1.5%.

VIVA QUESTIONS

Q.1. What is the etiology of congenital cataracts?

Ans. *Etiology of bilateral cataracts:*

- Idiopathic
- Familial (hereditary); usually autosomal dominant
- Chromosomal abnormality—Trisomy-21 (Down), Trisomy-18 (Edward), Trisomy-13(Patau). Other translocations, deletions, and duplications
- *Craniofacial syndromes:* Hallermann-Streiff, Rubinstein-Taybi, Smith-Lemli-Opitz.
- Musculoskeletal—Conradi, Albright, myotonic dystrophy
- Renal—Lowe, Alport
- Metabolic—Galactosemia, Fabry, Wilson, mannosidosis, diabetes mellitus
- Maternal infection (TORCH diseases)—Rubella, cytomegalovirus, varicella, syphilis, toxoplasmosis
- Ocular anomalies—Aniridia, Anterior segment dysgenesis syndrome
- Iatrogenic—Corticosteroids, Radiation (may also be unilateral)

Etiology of unilateral cataracts:

- Idiopathic
- Ocular anomalies—Persistent fetal vasculature (PFV), anterior segment dysgenesis, retinal detachment
- Traumatic (rule out child abuse)

Q.2. What are the contraindications for IOL implantation in pediatric cataract?

Ans. *Contraindications of IOL implantation are:*

- Microphthalmos
- Rubella cataract
- Aniridia
- Uveitis

Q.3. What are the surgical challenges faced in pediatric cataracts?

Ans. *The intraoperative challenges faced in pediatric cataracts are:*

- Difficulty in capsulorhexis formation
- Positive intravitreal pressure
- Intraoperative miosis
- Wound leak

Table 2 Morphological variants of pediatric cataract associated with systemic diseases

<i>Systemic disease</i>	<i>Cataract morphology</i>	<i>Associated findings</i>
Fabry syndrome	Spoke-like	Corneal whorls
Mannosidosis	Spoke-like	Hepatosplenomegaly
Diabetes	Vacuoles	↑ Blood glucose level
Hypoparathyroidism	Multicolor flecks	↓ serum calcium
Myotonic dystrophy	Multicolor flecks	Characteristic facial features, tonic "grip"
Wilson disease	Green "sunflower"	Kayser-Fleischer corneal ring
Lowe syndrome	Thin disciform	Hypotonia, glaucoma

Q.4. What are characteristic morphological variants of pediatric cataracts associated with systemic diseases?

Ans. Refer Table 2.

Q.5. Explain IOL power calculations in pediatric patients.

Ans. Refer text.

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ECTOPIA LENTIS

Ruchita Falera, Manpreet Kaur, Prafulla Kumar Maharana

INTRODUCTION

Ectopia Lentis (subluxation of lens) is characterized by partial displacement of the lens from the patellar fossa. The first case of lens dislocation was reported by Berryat in 1749 and the term *Ectopia Lentis* was coined by Stellwag in 1856.¹ The terms *ectopia lentis* and *subluxated lens* have been used interchangeably in literature, it is however, preferable to use ectopia lentis in cases of subluxation secondary to inheritable causes. Lens subluxation may be heritable without associated systemic syndrome, heritable with associated systemic syndrome, in association with ocular comorbidities or because of trauma (**Table 1**).

The most common cause of lens subluxation is trauma, which accounts for nearly 50% of all cases.

Marfan's syndrome is the most common heritable cause of ectopia lentis. Disruption or dysfunction of the zonular fibers of the lens is the underlying pathophysiology of ectopia lentis, regardless of cause (trauma or heritable condition). The degree of zonular impairment determines the degree of lens displacement.

It is given as a long or short case in post-graduate/DNB/Diploma examination.

HISTORY

Epidemiology

Ectopia lentis can occur at any age. It may be present at birth, or it may manifest late in life. A male preponderance is reported, as males appear more prone to ocular trauma than

Table 1 Etiology of subluxated lens

- Traumatic subluxation of lens
- Hereditary causes without systemic associations
 - Isolated ectopia lentis
 - Ectopia lentis et pupillae
- Hereditary causes with systemic associations
 - Marfan's syndrome
 - Homocystinuria
 - Weill-Marchesani Syndrome
 - Hyperlysinemia
 - Sulfite oxide deficiency
 - Ehlers-Danlos syndrome
 - Crouzon's syndrome
 - Oxycephaly
- Associated with other ocular diseases
 - Mature or hypermature cataract
 - Buphthalmos
 - High myopia
 - Megalocornea
 - Pseudoexfoliation
 - Retinitis pigmentosa
 - Eales disease
 - Retinal detachment

females. Isolated ectopia lentis and Marfan's syndrome have an autosomal dominant mode of inheritance.

Chief complaints: The patients may present with the following symptoms:

- Decreased or fluctuating vision
- Photophobia
- Glare
- Monocular diplopia
- Suboptimal correction with spectacles

History of present illness: Heritable ectopia lentis is bilateral, symmetric and stable from early childhood. Time of onset of disease, its progression and its effect on visual function should be noted. There is frequent change in glasses with a progressive increase in the power of glasses. Subluxation of lens associated with trauma can present with sudden diminution of vision or other symptoms like photophobia and monocular diplopia.

Past medical history: Ectopia lentis may be associated with underlying systemic disorders and a careful history must be elicited regarding the following:

- Any history of previous cardiac illness must be taken. Cardiovascular manifestations

of Marfan's syndrome include aortic and pulmonary artery dilatation, mitral and tricuspid valve prolapse with or without regurgitation. Dilatation of the sinus of Valsalva is found in 60–80% of adult and mitral valve prolapse (MVP) is present in 80% patients.^{1,2}

- Homocystinuria is a recessively inherited disorder caused by deficiency of cystathione synthase leading to accumulation of homocysteine and methionine. Affected persons have tall, thin habitus similar to Marfan's syndrome patients but infrequent arachnodactyly. Any history of developmental delay or mental retardation should be elicited as homocystinuria is associated with subnormal intelligence.
- History of recurrent fractures, hip dislocation or any musculoskeletal abnormalities should be asked to rule out presence of any connective tissue diseases such as Ehlers-Danlos syndrome.

Family History

A three generation pedigree chart must be prepared. History of similar complaints in siblings and parents should be specifically asked.

EXAMINATION

Systemic Examination

A careful systemic examination must be carried out and the findings suggestive of underlying systemic disorders must be noted.

Marfan's syndrome may present with the following systemic signs:

- Long thin limbs
- Arachnodactyly-long spider like fingers
- *Arm span:* Height ratio > 1.05
- Upper segment of body (Head to pubic bone): Lower segment ratio < 0.86
- Scoliosis
- Chest wall deformities (Pectus excavatum/ Pectus carinatum)
- Thumb sign (The thumb sign is positive when the entire distal phalanx of the adducted thumb extends beyond the ulnar border of the palm)
- Wrist sign (The wrist sign is positive when the tip of the thumb covers the entire fingernail

of the fifth finger when wrapped around the contralateral wrist.)

- High-arched palate

Musculoskeletal anomalies are also present in homocystinuria, Weill-Marchesani syndrome and connective tissue disorders.

Cardiovascular examination should be performed to rule out underlying valvular heart defects in Marfan's syndrome

Homocystinuria may have associated mental retardation and may necessitate IQ testing and evaluation of higher mental functions.

Ocular Examination

Visual acuity: Visual acuity should be carefully assessed considering the following points:

- Uncorrected visual acuity and BCVA must be assessed in all cases
- Near vision should be documented
- Refraction should be carried out through phakic and aphakic zones (**Fig. 1**).

Eyeballs: Strabismus may be associated with Marfan's syndrome, and if uncorrected in children can result into amblyopia. It may be a presenting sign of the disorder. Delayed and inadequate correction of refractive errors as well as deficient fibrillin in extraocular muscle pulleys causing their instability may explain the high incidence of strabismus in Marfan's patients.

Conjunctiva is usually normal.

Cornea: Patients with Marfan's syndrome can present with flat cornea (cornea plana) or steep cornea. Associated keratoconus may be present.

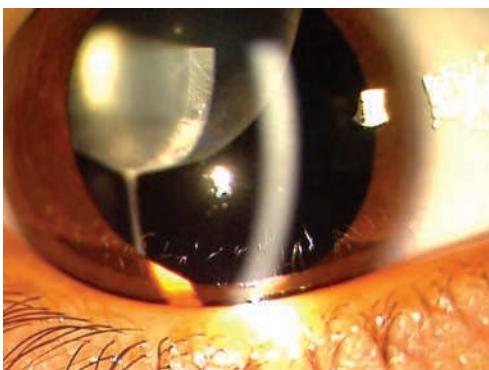


Fig. 1: Phakic and aphakic zones in ectopia lentis

Sclera: Thinning of sclera may be present, giving it a bluish hue in Marfan's Disease as well as in cases of connective tissue disorders such as osteogenesis Imperfecta and Ehler-Danlos syndrome.

Anterior chamber and angle:

- Ectopia lentis is usually associated with a deep anterior chamber, however, it may be irregular
- Gonioscopy must be done in all cases to rule out angle recession (in post-traumatic subluxation of lens)

Pupil:

- The pupil may be eccentrically placed as in cases of ectopia lentis *et pupillae* where the pupil is displaced opposite to the direction of subluxation.
- The pupil may be poorly dilating on account of hypoplastic dilator muscles
- Relation of the lens with respect to the undilated pupil should be noted.

Lens:

- Any evidence of phacodonesis should be documented
- Evidence of cataract, if any should be documented
- Extent of subluxation should be noted in clock hours.
- Direction of subluxation (**Fig. 2**) must be noted.
- **Zonules:** Condition of the zonules should be documented as they may be stretched in cases of Marfan's disease (**Fig. 3**) or broken in case of homocystinuria

The subluxation of the lens is generally superotemporal in cases of Marfan's syndrome.

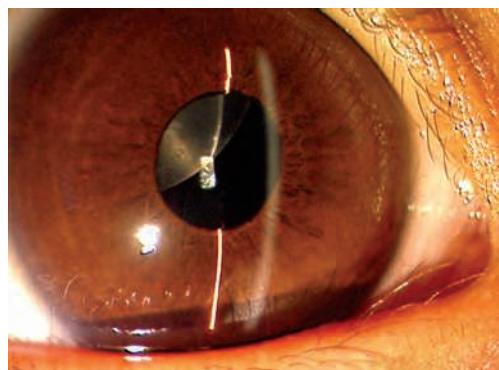


Fig. 2: Superotemporal displacement

Preferential focusing of ultraviolet B light on the inferonasal quadrant of the crystalline lens is hypothesized to explain the predominantly supero-temporal dislocation (**Fig. 2**) of the lens in Marfan syndrome, while it is inferonasal in cases of homocystinuria. However, the direction of subluxation is not pathognomonic, and it may occur in any direction. Premature cataracts and other lens and capsule opacities are commonly found in Marfan's syndrome with presentation at a younger age (30–50s) compared to the general population.

In some cases, the patients may be aphakic with posterior dislocation of the lens into the vitreous cavity.

Intraocular pressure: Intraocular pressure should be documented in all cases. Primary open-angle glaucoma is most common, but glaucoma can be secondary to anterior lens dislocation or anterior chamber angle abnormalities.

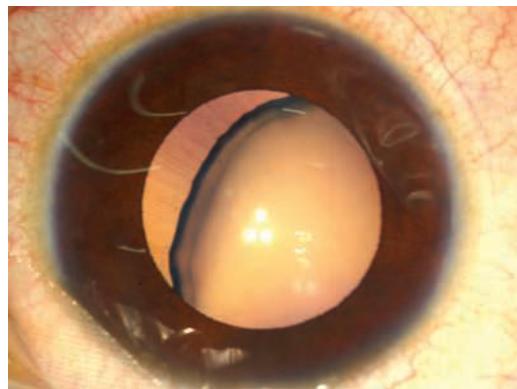


Fig. 3: Stretched zonules in cases of Marfan's disease

Fundus examination:

- **Distant direct ophthalmoscopy examination:** A crescent-shaped reflex seen on distant direct ophthalmoscope is pathognomonic of subluxated lens.
- Detailed fundus examination is mandatory in all cases. Retinal detachment may occur in 5–11% of patients with Marfan's syndrome, and its incidence increases to 8–38% in the presence of ectopia lentis.¹ Unstable subluxated or dislocated lens capsule exerts traction on the vitreous base, leading to small tears or holes in the retinal periphery. Axial myopia presents in Marfan's syndrome predisposes to early vitreous liquefaction and posterior vitreous detachment, retinal thinning, lattice degeneration, and peripheral breaks.

DIFFERENTIAL DIAGNOSIS

Ectopia lentis is diagnosed clinically on the basis of slit-lamp examination. Various etiologies responsible for ectopia lentis are tabulated in **Table 1**. Marfan's syndrome and homocystinuria are common heritable systemic disorders associated with ectopia lentis and their differentiating features are summarized in **Table 2**.

INVESTIGATIONS

Systemic Investigations

A case of ectopia lentis must be managed with a multidisciplinary approach along with a pediatrician, cardiologist and orthopedician.

Table 2 Differentiating features of Marfan's disease and homocystinuria

Clinical features	Marfan's disease	Homocystinuria
<i>Etiology</i>	Fibrillin-1 (FBN1) gene mutation on chromosome 15	Deficiency of cystathione synthase leading to accumulation of homocysteine and methionine
<i>Mode of inheritance</i>	Autosomal dominant	Autosomal recessive
<i>Mental retardation</i>	Absent	Present
<i>Direction of subluxation</i>	Superotemporal subluxation of lens	Inferonasal subluxation of lens
<i>Condition of zonules</i>	Primarily present with stretched zonules	Absent and broken zonules

It should be evaluated for underlying systemic abnormalities.

- X-ray Chest/ECG/2D Echo should be done in all cases to rule out cardiac abnormalities in Marfan's syndrome.
- Sodium nitroprusside test (in urine) must be done to rule out homocystinuria.
- X-ray of spine and extremities are undertaken to evaluate the skeletal deformities

Ocular Investigations

- *Biometry* should be done to calculate IOL power
- *B-scan ultrasonography*: In cases of mature cataract where the fundal view is obscured, a USG must be done to rule out retinal detachment or any posterior segment pathology.

MANAGEMENT

Conservative Management

- A complete refraction considering the undilated central pupillary position, size of the phakic and aphakic zones and preferred visual axis needs to be done.
- Appropriate spectacle correction, aphakic glasses or contact lens can be given.
- Other methods such as miotics to minimize diplopia or mydriatics to enlarge the aphakic zone are rarely used these days.

Surgical Management

Indications for Surgery

- Subluxated lens bisects the pupil leading to a phakic and aphakic zone in an undilated pupillary axis
- Cataractous lens
- Associated complications like glaucoma or pupillary block
- Presence of lenticular astigmatism
- Anteriorly or posteriorly dislocated lens

Surgical management of subluxated lens depends on the degree of subluxation. The following are the modalities of management are mainly for secondary causes of lens subluxation.

- *Subluxation < 3 clock hours*: In cases of lens subluxation of less than 3 clock hours, slow

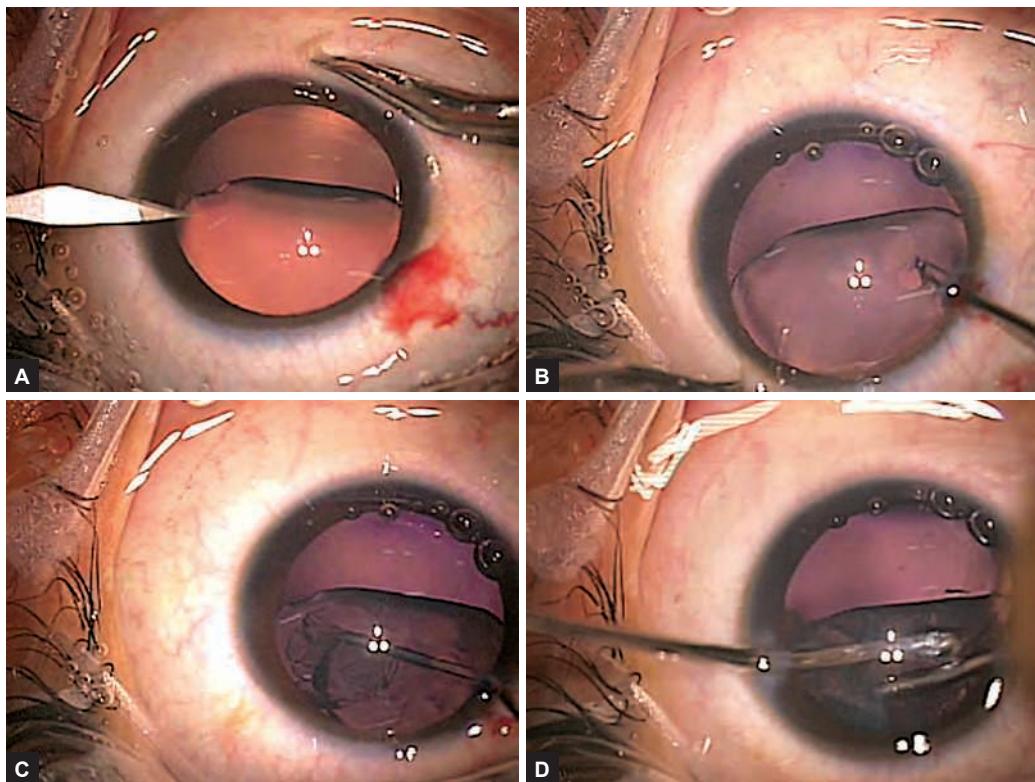
motion phacoemulsification with PCIOL implantation in the bag can be attempted. Slow motion phacoemulsification includes phacoemulsification at low flow rate, low vacuum and low infusion bottle height in order to minimize stress on the zonules

- *Subluxation of 3–5 clock hours*: In case of lens subluxation of 3–5 clock hours, slow motion phacoemulsification can be done. Insertion of capsular tension ring (CTR) or capsule tension segments (CTS) may be needed to support the bag. With the use of CTR, any force that is transmitted to the capsule does not directly impact the adjacent zonules, but is rather distributed to the entire zonular apparatus.
- *Subluxation of 5–7 clock hours*: Slow motion phacoemulsification with the use of Cionni ring with PCIOL implantation can be attempted in cases of severe or progressive zonular weakness. Cionni ring has a hook, which needs to be kept opposite to the direction of decentration. A transcleral suture applied to it allows it to be pulled peripherally thereby counteracting the capsular bag decentration.
- *Subluxation of > 7 clock hours*: Intracapsular cataract extraction (ICCE) with sclera fixated IOL or ACIOL implantation can be done in cases with extensively subluxated cataractous lens.
- In cases with significant posterior subluxation of lens, pars plana lensectomy (PPL) with pars plana vitrectomy (PPV) can be done, followed by IOL implantation in the anterior chamber or sulcus-fixated IOL.

The use of capsular support devices is not preferred in cases of progressive zonular weakness. These are of particular importance in secondary causes of subluxation such as post-traumatic subluxation of lens and pseudoexfoliation where the basic zonular anatomy is not compromised.

In heritable ectopia lentis with or without underlying systemic disorders, *intralenticular lens aspiration (Figs 4A to D)* is the preferred technique, which is described as follows:

- In this technique, two openings are made in the lens capsule with a microvitrectorial (MVR) blade and the lens matter is aspirated using a bimanual irrigation and aspiration system.



Figs 4A to D: Intralenticular lens aspiration

- The capsular bag is then cut and aspirated using a vitrectomy probe.

This technique has several advantages such as:

- The lens can be stabilized with the irrigation cannula, the area to be aspirated can be brought into focus, and a complete lens aspiration can be easily performed.
- Additionally, the irrigation cannula hydrates the cortical matter, enabling complete aspiration.
- Furthermore, creating two small capsular openings in the midperiphery of the lens that are directly visible often eliminates the problem of poor visibility.
- There is less chance of vitreous becoming hydrated and lens matter falling into the vitreous cavity, as aspiration is intralenticular.
- Another added advantage is that the capsular rim is left intact. This may allow IOL implantation in the sulcus once the capsular

rim fibroses, thus avoiding the complications and difficulties associated with anterior chamber and sulcus-fixated IOLs.

VIVA QUESTIONS

Q.1. What is the etiopathogenesis of Marfan's disease?

Ans. Marfan's syndrome is an autosomal dominant disorder with near complete penetrance and variable expression. There is a mutation in the Fibrillin locus (FBN1), which lies on the long arm of chromosome 15 (15q21). This results in abnormal biosynthesis of fibrillin, a 350 kd cysteine rich glycoprotein which is a major constituent of microfibrils present in connective tissue of suspensory ligaments of crystalline lens.

Q.2. What are the differences between Homocystinuria and Marfan's disease?

Ans. Refer Table 2.

Q.3. Type of astigmatism seen in subluxation of lens.

Ans. Irregular/compound myopic astigmatism is seen due to following mechanism:

- Weak zonules lead to relaxation of lens capsule (which is normally in a state of stretch by zonules) making the lens more spherical along the axis with increased lens power and consequent myopia.
- Area where zonules are still intact, the lens remains as such or may slightly bulge.
- Therefore, there is more myopia in one axis while less myopia in other axis.

Q.4. What are the diagnostic criteria for Marfan's syndrome?

Ans. Marfan's Disease is diagnosed according to Modified Ghent's Criteria

In absence of family history:

- Aortic root dilation (Z score >2) and Ectopia lentis
- Aortic root dilation and FBN1 mutation
- Aortic root dilation and systemic score >7 points
- Ectopia lentis and FBN1 with known aortic root dilation

In presence of family history:

- Ectopia lentis and family history: Marfan's syndrome
- Systemic score (>7 points) and family history of Marfan's syndrome
- Aortic dilation and family history of Marfan's syndrome

Systemic score:

- Wrist and thumb sign -3 (Wrist or thumb sign -1)
- Pectus carinatum deformity -2 (pectus excavatum or chest asymmetry -1)

- Hind foot deformity-2 (plain pes planus -1)

- Pneumothorax -2

- Dural ectasia -2

- Protrusio acetabuli -2

- Reduced US/LS and increased arm/height and no severe scoliosis -1

- Scoliosis or thoracolumbar kyphosis -1

- Reduced elbow extension -1

- Facial features (3/5) -1 (dolichocephaly, enophthalmos, down-slanting palpebral fissures, malar hypoplasia, retrognathia)

- Skin striae -1

- Myopia > 3 diopters -1

- Mitral valve prolapse (all types) -1

Maximum total: 20 points; score \geq 7 indicates systemic involvement.

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SHORT CASES

LENTICONUS

Manpreet Kaur, Prafulla Kumar Maharana, Jeewan S Titiyal

INTRODUCTION

Lenticonus is characterized by a localized conical protrusion of the anterior or posterior lens capsule and the underlying cortex. The anomaly is usually restricted to the axial area and can reach a diameter of 2–7 mm. Posterior lenticonus is more common than anterior lenticonus and is usually unilateral and axial in location. Anterior lenticonus is bilateral and usually associated with Alport syndrome.

It is given as short case in postgraduate/DNB/Diploma examination.

HISTORY

Chief Complaints

- Decrease in visual acuity
- Minimal improvement with spectacle or contact lenses.

History of Present Illness

Epidemiology: Anterior lenticonus occurs bilaterally in patients with Alport syndrome, which is a hereditary systemic disease with a prevalence of 1/5000 in a normal population. Alport syndrome is X-linked in 85%, autosomal recessive in 10% and autosomal dominant in only a small fraction of the patients.

Posterior lenticonus is a unilateral congenital defect that usually occurs in a sporadic manner, with a prevalence of 1–4 per 100,000 children. It has no predilection for either sex. It may also occur in association with Lowe syndrome (oculocerebrorenal syndrome).

Age at presentation: Anterior lenticonus manifests before the age of 30 years, most commonly in the second decade. Posterior lenticonus is a congenital anomaly and the age at diagnosis lies between 3 and 7 years.

Presenting features: Patients with anterior lenticonus present with gradual progressive diminution of vision in both eyes. It is not amenable to correction by either spectacles or contact lenses.

Posterior lenticonus is unilateral and amblyopia is the most significant visual problem associated with it. Amblyopia may be a result of the optical distortion induced by the conical protrusion of the lens surface, anisometropia or by visual deprivation due to cataract.

Associated ocular features: Anterior lenticonus may be associated with the following ocular anomalies:

- Dot-and-fleck retinopathy
- Posterior polymorphous corneal dystrophy
- Temporal macular thinning
- Subcapsular and cortical cataract.

Posterior lenticonus may be associated with the following ocular manifestations:

- Amblyopia
- Subcapsular and cortical cataract
- Strabismus
- Glaucoma (in Lowe syndrome).

Family history: A positive family history of hematuria, early onset deafness, and renal insufficiency may be present, especially in male patients with anterior lenticonus.

EXAMINATION

Systemic Examination

Alport syndrome is characterized by progressive renal failure and sensorineural deafness in addition to anterior lenticonus. Gross or microscopic hematuria is the most common and earliest manifestation of Alport syndrome; microscopic hematuria is observed in all males and in 95% of females. Proteinuria develops in males with X-linked Alport syndrome and in

males and females with autosomal recessive Alport syndrome. It progresses with age and can occur in the nephrotic range in as many as 30% of patients. Hypertension is usually present in males with X-linked Alport syndrome and in males and females with autosomal recessive Alport syndrome. Incidence and severity increases with age and degree of renal failure.

Bilateral, high-frequency sensorineural hearing loss begins by late childhood and is present in approximately 50% of male patients with X-linked disease by the age of 25 years, and about 90% are deaf by the age of 40 years.

Posterior lenticonus may be associated with Lowe syndrome (oculocerebrorenal syndrome). It is a rare X-linked recessive disorder characterized by congenital cataracts, hypotonia and areflexia, intellectual disability, proximal tubular acidosis, aminoaciduria, phosphaturia, and low-molecular-weight proteinuria.

Ocular Examination

Eyeball: Strabismus may be present in cases with posterior lenticonus. Eyeball shape and movements are normal.

Lid: Eyelids are normal.

Conjunctiva: Conjunctival examination is normal.

Cornea: Posterior polymorphous corneal dystrophy may be observed in cases with anterior lenticonus. Posterior lenticonus may be associated with microcornea.

Sclera: Scleral examination is normal

Iris: Iris examination is normal

Pupil: Pupils are normal

Intraocular pressure: Glaucoma may be present in 50% of cases with Lowe syndrome.

Lens: Transparent, localized, sharply demarcated conical projection of the lens capsule and cortex is observed, usually axial in localization (**Fig. 1**). There is an increase in lens thickness.

'Oil-droplet' reflex is observed on retro-illumination (**Fig. 2**).

Associated subcapsular and cortical opacities appear in advanced stages of lenticonus.

Vitreous: Posterior lenticonus may be associated with persistent hyperplastic primary vitreous.

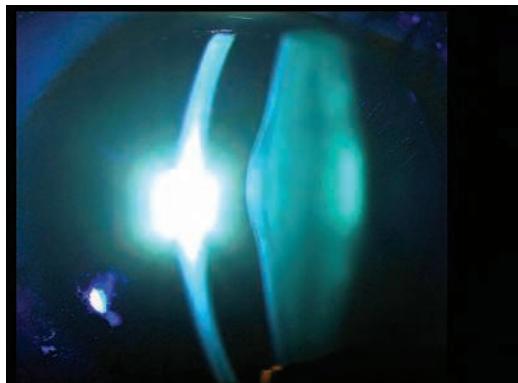


Fig. 1: Transparent, localized, axial, sharply demarcated conical projection of the lens capsule and cortex in anterior lenticonus. There is an increase in lens thickness

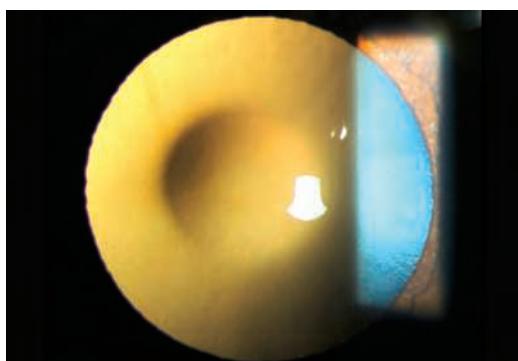


Fig. 2: Oil-droplet reflex observed on retro-illumination in a case of anterior lenticonus

Fundus: A dot-and-fleck retinopathy may be observed in cases with anterior lenticonus. Temporal macular thinning may also be observed in cases with anterior lenticonus.

Retinoscopy: Scissoring reflexes are observed on retinoscopy.

DIFFERENTIAL DIAGNOSIS

The diagnosis of lenticonus is clinical in nature and is easily confirmed on a slit-lamp examination. The differences between anterior and posterior lenticonus are highlighted in **Table 1**.

Anterior lenticonus is rare and bilateral, and may be associated with the following syndromes:

- Alport syndrome (most common association with anterior lenticonus)
- Waardenburg syndrome (rare)

Table 1 Differentiating features of anterior and posterior lenticonus

Clinical features	Anterior lenticonus	Posterior lenticonus
Laterality	Bilateral	Unilateral
Age at presentation	Second decade	3–7 years
Etiology	Associated with Alport syndrome	<ul style="list-style-type: none"> • Usually sporadic • May be associated with Lowe syndrome
Sex	M > F	M = F
Associated ocular features	<ul style="list-style-type: none"> • Posterior polymorphous corneal dystrophy • Cataract • Dot-and-Fleck retinopathy • Temporal macular thinning 	<ul style="list-style-type: none"> • Amblyopia • Strabismus • Cataract • Glaucoma (in Lowe syndrome)
Associated systemic features	<ul style="list-style-type: none"> • Renal dysfunction • Sensorineural hearing loss 	<ul style="list-style-type: none"> • Usually none • Renal and cerebral manifestations in Lowe syndrome
Management	Lens aspiration with IOL implantation	<ul style="list-style-type: none"> • Lens aspiration with IOL implantation • Amblyopia therapy

Posterior lenticonus is more common and unilateral. It may be associated with the following conditions:

- Sporadic (most common)
- Associated with persistent hyperplastic primary vitreous
- Associated with hyaloid artery remnant
- Familial posterior lenticonus and microcornea
- Lowe syndrome (oculocerebrorenal syndrome)
- Trauma

INVESTIGATIONS

Systemic investigations should be undertaken to evaluate for associated syndromes.

- Renal function tests
- *Urine examination*: Hematuria and proteinuria
- *Audiometry*: Evaluate sensorineural hearing loss

Ocular Investigations

- A-scan ultrasonography may reveal an increased lens thickness
- B-scan ultrasonography may show herniated lenticular material, suggestive of a lenticonus
- Aberrometry reveals lenticular astigmatism and aberrations
- Biometry to calculate intraocular lens power.

MANAGEMENT

- Lens aspiration with *in-the-bag* intraocular lens implantation is the treatment of choice.
- Amblyopia management with occlusion therapy is mandatory in cases with unilateral posterior lenticonus to achieve optimal visual outcomes.

VIVA QUESTIONS

- Q.1. Describe the pathogenesis of anterior lenticonus associated with Alport syndrome.**

Ans. Alport syndrome is caused by mutations affecting the gene that encodes for type IV collagen. Type IV collagen is present in the basement membranes of the glomerulus, cochlea, lens capsule and cornea. Histopathologic examination of the anterior lens capsule shows thinning and vertical dehiscences. Initially, an increase of the lens thickness is observed with thin anterior capsule in the central area, followed by progressive central protrusion of the capsule-cortex complex and development of anterior lenticonus.

Q.2. Describe the pathogenesis of posterior lenticonus.

Ans. The pathogenesis of posterior lenticonus is unclear; traction on the posterior lens capsule by remnants of the hyaloid artery system as well as a disturbance in the tunica vasculosa have been suggested as possible mechanisms. Viritis or an overgrowth of posterior lens fibers that produce a phakoma of the lens have also been suggested as possible pathophysiologic mechanisms.

In bilateral cases, a genetically determined congenital weakness of the posterior lens capsule may be the causative factor.

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POSTERIOR POLAR CATARACT

Manpreet Kaur, Devika S Joshi, Jeewan S Titiyal, Sandeep Gupta

INTRODUCTION

Posterior polar cataract is a rare form of congenital cataract with incidence ranging from 3 to 5 in 1000. It is bilateral in 65–80% of the cases. It poses a surgical challenge due to its fragile posterior capsule and an increased risk of posterior capsule rupture with vitreous loss.

It is given as short case in postgraduate/DNB/Diploma examination.

HISTORY

Chief complaints: The patient presents with the following complaints:

- Diminution of vision for distance and near
- Glare, especially during night driving
- Intolerance to bright light.

History of Present Illness

Epidemiology and genetics: Posterior polar cataract has an autosomal dominant inheritance pattern, although it may occasionally be sporadic. Positive family history may be present in 40–55% of the patients. There is no gender predilection and the disease is usually bilateral in nature.

Presenting features: Early cases may present with complaints of glare and reduced vision in bright light. There is a difficulty in near work and intolerance to bright light. The cause of glare, reduced contrast sensitivity and decreased visual

acuity is forward light scattering (light scattering toward the retina). The diminution of vision is progressive in nature.

Patient profession must be noted carefully, since it may influence decision making before cataract surgery.

EXAMINATION

General Examination/Specific Systemic Examination

Posterior polar cataract may be associated with number of systemic disease such as:

- Psychosomatic disorders
- Ectodermal dysplasia
- Rothmund disease
- Scleroderma
- Incontinentia pigmenti
- Congenital dyskeratosis
- Congenital ichthyosis
- Congenital atrophy of the skin.

Ocular Examination

- **Eye balls:** Microphthalmia may be an associated feature
- **Eyelids** are usually normal.
- **Conjunctiva** is usually normal
- **Cornea:** Microcornea may be present
- **Sclera, iris and pupil** are usually normal
- **Intraocular pressure** is normal.

Lens: Dense, circular plaque is present in the central posterior part of the lens giving rise to the classic Bull's-eye appearance. Concentric rings of opacity are present around the central opacity (onion peeling) (**Fig. 1**). It can be surrounded by vacuoles and smaller areas of degenerated lens material.

Co-existent nuclear sclerosis may be present in advanced cases.

In cases where the other eye has already undergone cataract surgery, it is important to examine the posterior capsule status of the fellow eye carefully. This is especially important where the cataract is in an advanced stage and it is difficult to rule out posterior polar cataract. In presence of any sign of posterior capsule rent in the operated eye (such as posterior capsular rupture, decentered IOL, vitreous strands, pupillary peaking, IOL in sulcus, etc.), the cataract in the other eye must be suspected as posterior polar cataract and all precautions during surgery must be taken.

Vitreous: Examination of the anterior vitreous may reveal oil-like droplets or particles. The presence of such finding should raise the possibility of pre-existing capsular opening (**Fig. 2**). This is also known as 'fish-tailing'.

Fundus: Examination is usually normal; signs of incontinentia pigmenti may be present, if associated.

DIFFERENTIAL DIAGNOSIS

- **Posterior subcapsular cataract:** There is generally a clear space between the posterior subcapsular cataract and the posterior capsule

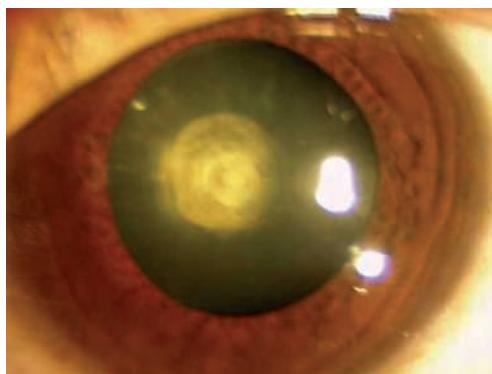


Fig. 1: Posterior polar cataract with concentric rings of opacity (onion-peeling or Bull's eye appearance)

- **Posterior lenticonus:** There is a conical protrusion of the posterior capsule and underlying cortex, which may or may not be associated with cataract.

CLASSIFICATION

Three different classification systems have been described as:

Duke Elder Classification

- **Stationary form (most common—accounts for 65% of cases):** Well-circumscribed circular opacity, localized on the central posterior capsule. The concentric thickened rings around the central plaque opacity give an appearance of a Bull's eye. The opacity may be camouflaged by nuclear sclerosis or smaller satellite rosette lesions may be present adjacent to the central opacity.
- **Progressive form:** Whitish opacification changes take place in the posterior cortex in the form of a radiating rider opacity. It has feathery and scalloped edges but they do not involve the nucleus, and does not extend as far anteriorly as the original opacity.

Singh Classification

- **Type 1:** Posterior polar opacity is associated with posterior subcapsular cataract.
- **Type 2:** Sharply defined round or oval opacity with ringed appearance such as an onion with or without grayish spots at the edge.



Fig. 2: Pre-existing posterior capsular defect in a case of posterior polar cataract with whitish particles in anterior vitreous

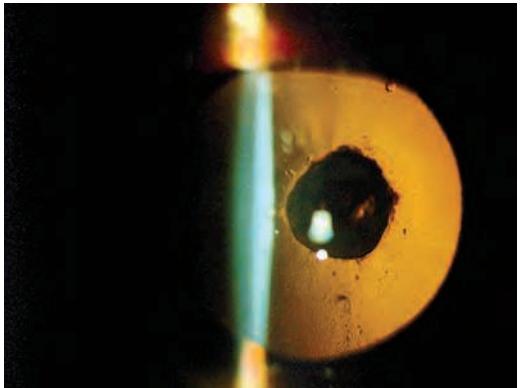


Fig. 3: Disc-like opacity in the posterior capsule on retroillumination

- **Type 3:** Sharply defined round or oval white opacity with dense white spots at the edge often associated with thin or absent posterior capsule. These dense white spots are a diagnostic sign (Daljit Singh sign) of posterior capsule leakage with or without repair and extreme fragility.
- **Type 4:** Combination of the above 3 types with nuclear sclerosis.

Schroeder Classification

Based on the effect of opacity on pupillary obstruction in the red reflex testing

- **Grade 1:** Small opacity without any effect on the optical quality of the clear part of the lens (**Fig. 3**).
- **Grade 2:** Two-thirds obstruction without other effects.
- **Grade 3:** Disc-like opacity in the posterior capsule is surrounded by an area of further optical distortion. Only the dilated pupil shows a clear red reflex surrounding this zone.
- **Grade 4:** Opacity is totally occlusive; no sufficient red reflex is obtained by dilation of the pupil.

MANAGEMENT

Preoperative counseling: It is essential to inform the patient of the possibility of a PC rupture, a relatively long-operative time, secondary posterior segment intervention, and a delayed visual

recovery. In addition, the possibility of leaving the patient aphakic should be explained. Also, the need for Nd:YAG capsulotomy for residual plaque should be discussed.

Surgery in posterior polar cataract: Posterior polar cataract poses a unique surgical challenge, with a high incidence of posterior capsular rupture ranging from 8% to 36%. Various techniques have been described to avoid intraoperative complications in posterior polar cataract, such as inside-out phacoemulsification, slow motion phacoemulsification, bimanual microphacoemulsification, viscodissection, pre-surround division technique and layer-by-layer phacoemulsification, etc. The basic surgical principle governing these techniques is avoidance of hydrodissection, and attempting to create a cushion of cortical matter with careful hydrodelineation. The aim is to avoid stress on the compromised posterior capsule during surgery.

Capsulorhexis: Aim is to keep an adequate sulcus (approximately around 5 mm) so that the IOL can be placed in sulcus in case of PCR.

Hydrodissection should be avoided as posterior polar opacities adhere firmly to the posterior capsule around the opacity. Hydrodissection may result in rupture of the thinned posterior capsule or widen any congenital capsular opening. If at all it is done, it should be performed gently in multiple quadrants with minimal fluid. A fluid wave should not be allowed to pass across the posterior capsule in the center where the posterior capsule is weak.

Hydrodelineation is also performed with minimal fluid. Careful hydrodelineation is done to achieve multiple planes of separation (seen as multiple golden rings in co-axial illumination) so that *layer-by-layer* nuclear aspiration can be done. Not more than 0.2 cc of irrigating fluid should be used for hydrodissection and hydrodelineation.

Phacoemulsification parameters: Slow motion phacoemulsification with low parameters should be used in cases with posterior polar cataract. The power should be 60%, bottle height 55–70 cm, aspiration rate 15–25 mL/min, vacuum 30–100 mm Hg. The low vacuum and aspiration rates help to maintain a very stable chamber and the reduced infusion drives less fluid around the lens.

Nucleus emulsification: A fine chopper should be used to incise the endonucleus in perpendicular

meridians, dividing the nucleus into small quadrants. This should be done without countertraction and the quadrants are then emulsified.

Epinucleus removal: Epinucleus can be effectively removed using viscodissection. Ophthalmic viscoelastic device (OVD) is injected under the anterior capsular margin in one quadrant to elevate the epinucleus, which can then be aspirated using irrigation/aspiration (I/A) handpiece. The peripheral cortex is aspirated first using I/A handpiece. To avoid fluctuations in anterior chamber depth, an attempt should be made to keep the I/A tip always occluded. The central posterior portion of cortex is elevated with viscoelastic and aspirated.

Adequate anterior chamber stability: It is provided by the low-infusion and low-vacuum system. Biaxial microincisional phacoemulsification may be used to enhance safety and reduce risk of complications. Anterior chamber should not be allowed to collapse at any step during surgery.

Residual plaque: Sometimes, the opacity may come off spontaneously due to infusion pressure during removal of the peripheral cortex. However, in some cases, part of the opacity may be firmly adherent to the posterior capsule and may not be separated. In such cases, residual plaque can be left *in situ* and later removed by Nd:YAG capsulotomy.

Management of posterior capsular defect (pre-existing/iatrogenic): If a defect is present in the posterior capsule, a dispersive OVD such as Viscoat should be injected over the area of defect before withdrawing the phaco or I/A probe from the eye. Convert the posterior capsular defect into posterior capsulorhexis followed by anterior vitrectomy, if necessary. IOL can be implanted in the bag in cases with a small PCR. If in-the-bag IOL implantation is not possible, sulcus implantation of a multipiece IOL may be done followed by optic capture in the bag, if needed.

VIVA QUESTIONS

Q.1. Describe the pathogenesis of posterior polar cataract.

Ans. The developing lens requires nutrition that is obtained through the tunica vasculosa lentis (TVL), which is a vascular network, supplied posteriorly by the hyaloid artery, a branch of the primary dorsal ophthalmic artery, and anteriorly from an anastomosis with vessels in the pupillary membrane. It has been suggested that posterior polar cataracts are caused by persistence of the hyaloid artery or invasion of the lens by mesoblastic tissue. The genetic mutation is expressed as an abnormality in lens development, specifically in the lens fibers that fail to develop normally and form an opacity close to and sometimes adherent to the posterior. Posterior polar cataract forms during embryonic life or early in infancy and usually becomes symptomatic 30–50 years later.

Q.2. What is the inheritance pattern of posterior polar cataract?

Ans. Refer text.

Q.3. Classify posterior polar cataract.

Ans. Refer text.

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MICROSOPHEROPHAKIA

Manpreet Kaur, Devika S Joshi, Prafulla Kumar Maharana

INTRODUCTION

Microspherophakia is a developmental abnormality and is characterized by a crystalline lens, which has a small diameter and spherical shape. The entire lens diameter can be characteristically visualized during slit-lamp examination with a fully dilated pupil.

It is given as short case in postgraduate/DNB/Diploma examination.

HISTORY

Chief complaint: The patient with microspherophakia presents with the following features

- Diminution of vision
- Acute painful red eye with diminution of vision (*acute angle-closure episode*)

History of Present Illness

Genetics: Isolated spherophakia is an autosomal recessive disorder resulting from homozygous mutations in LTBP2 (13q24.1-q32.12). Parental consanguinity was present in reported families.

Microspherophakia is a clinically and genetically heterogeneous disorder and usually found in association with Weill-Marchesani syndrome. Other syndromes that may be associated include Marfan's syndrome, Peter's anomaly, Alport syndrome, Lowe syndrome, homocystinuria, mandibulofacial dysostosis, and Klinefelter's syndrome.

Etiopathogenesis: Microspherophakia is a result of the faulty development of the secondary lens fibers during embryogenesis. The underdeveloped zonules of Zinn are unable to exert enough force on the lens to make it form the usual oval shape.

Presenting features: The disease is bilateral in nature. The patient presents in childhood with diminution of vision and the use of high minus lenses as a result of the lenticular myopia. The lens may subluxate into the vitreous cavity in advanced cases. Secondary angle-closure glaucoma may occur because of pupillary block induced by the spherical lens. The pupillary block manifests as an

acute onset diminution of vision associated with pain and circumciliary congestion.

EXAMINATION

General Examination/Specific Systemic Examination

Systemic examination should be undertaken to evaluate the manifestations of the associated syndromes.

Features of *Weill-Marchesani syndrome* include short fingers (i.e. brachydactyly) and muscular hypertrophy. *Marfan's syndrome* is associated with arachnodactyly, tall stature, high-arched palate and cardiac valvular anomalies.

Homocystinuria, mandibulofacial dysostosis, Alport's syndrome and Klinefelter's syndrome may also rarely be associated with microspherophakia.

Ocular Examination

The *eyeballs and eyelids* are usually normal.

Conjunctiva: Circumciliary congestion may be present in cases presenting with acute angle-closure episode

Cornea: is usually normal. Corneal opacity is usually present in Peter's anomaly

Sclera: Scleral thinning and posterior staphyloma is present in Marfan's syndrome

Anterior chamber is shallow

Iris and pupil: Sphincter dysplasia may be present and pupils may be ectopic

Intraocular pressure is raised in cases of pupillary block.

Lens: There is a decrease in the equatorial lens diameter and the whole lens is visible with full mydriasis (**Fig. 1**). The anteroposterior lens diameter is increased and the lens assumes a relatively spherical shape. The lens may move with changes in posture, and may dislocate or subluxate into the anterior chamber or vitreous.

Vitreous: Posteriorly dislocated lens may be visible in the vitreous cavity in advanced cases.

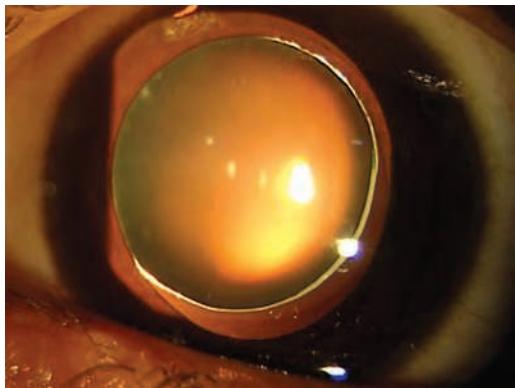


Fig. 1: Whole lens is visible with full mydriasis in a case of microspherophakia

Fundus: Glaucomatous optic nerve head cupping may be visible in cases with co-existent secondary glaucoma. Posterior staphyloma, myopic crescent and retinal detachment may be present.

Refraction: High myopia is present without an increase in axial length.

DIFFERENTIAL DIAGNOSIS

The lens findings on slit-lamp examination are pathognomonic and characteristic of microspherophakia. The differential diagnoses for the etiology of microspherophakia are described in **Table 1**.

INVESTIGATIONS

Systemic Investigations

Systemic investigations are directed towards the underlying syndrome, and may include X-rays of spine and extremities, cardiac ECHO and genetic testing as needed.

Ocular Investigations

Specular microscopy: For endothelial cell count, especially in cases with co-existent glaucoma.

Perimetry: To evaluate visual fields in cases with secondary glaucoma.

Biometry: Axial length and keratometry for IOL power calculations.

B-scan ultrasonography: To evaluate cases with posterior staphyloma or posteriorly dislocated lens.

MANAGEMENT

Management of Lens

Clear lens extraction is the treatment of choice for myopia and glaucoma in microspherophakia.

Indications for Lens Extraction

- Cataract
- Corneolenticular touch
- High myopia
- Intermittent pupillary block
- Secondary glaucoma.

Surgical Approach

- Lens aspiration via limbal route
- Pars-plana lensectomy.

Surgical Challenges

Capsulorhexis: Iris hooks may be needed to stabilize the lens.

Intraocular Lens Implantation

- Successful in-the-bag implantation of acrylic single piece hydrophobic lens has been described; however, phacodonesis persists in the postoperative period.
- Capsular support using a modified capsular tension ring (M-CTR) and capsular tension segment (CTS) sutured to the sclera along with implantation of a foldable intraocular lens inside the bag may be tried.
- Scleral fixated IOL in the same sitting or a second sitting can be done in cases without capsular bag support.
- Aphakic glasses or contact lens may be prescribed in cases where IOL is not implanted.

Management of Glaucoma

The pupillary-block glaucoma associated with microspherophakia is also known as *inverse glaucoma* as miotics aggravate the condition by stimulating ciliary muscle contraction, thereby loosening the zonules and further increasing anterior lens displacement. Mydriatics tighten the zonules and are the preferred treatment.

Nd: YAG laser peripheral iridotomy is useful in relieving angle-closure glaucoma and

Table 1 Differential diagnoses for the etiology of microspherophakia

Features	Familial microspherophakia	Weill-Marchesani syndrome	Marfan's syndrome	Peter's anomaly	Klinefelter's syndrome	Alport's syndrome	Lowe syndrome
Inheritance	Autosomal recessive	Autosomal dominant, rare autosomal dominant	Autosomal dominant	Autosomal dominant, autosomal recessive	X-Linked (Aneuploidy)	X-linked	X-linked recessive
Other ocular features (in addition to microspherophakia)	Ectopia lentis, lenticular myopia, posterior staphyloma, ectopic pupil, retinal detachment, glaucoma	Ectopia lentis (displaces inferiorly), posterior synechiae, glaucoma	Ectopia lentis, glaucoma, axial myopia, retinal detachment, blue sclera, iris hypoplasia	Anterior segment dysgenesis (coneal opacity, glaucoma, sclerocornea, corectopia, iris hypoplasia, cataract)	Microphthalmia, colobomas of the iris, choroid and optic nerve, strabismus	Lenticus, posterior polymorphous corneal dystrophy, dot-and-fleck retinopathy, temporal macular thinning	Congenital cataract, glaucoma
Systemic features	None	Short stubby fingers (brachydactyly), short stature, broad hands, joint stiffness	Cardiac and musculo-skeletal anomalies	Developmental delay, dysmorphic facial features, cardiac, genitourinary, and central nervous system malformation	Tall stature, gynecomastia, small testes, and infertility	Renal dysfunction, sensorineural hearing loss	Central nervous system and renal anomalies, hypotonia

should be done prophylactically in all cases of microspherophakia.

Raised IOP may be managed with topical and oral anti-glaucoma medications; trabeculectomy may be required in chronic cases refractory to conservative medical therapy.

VIVA QUESTIONS

Q.1. Describe the pathogenesis of microspherophakia.

Ans. An arrest of development of the secondary lens fibers or the insertion of abnormally thin secondary fibers are said to be responsible for the development of microspherophakia. Both may be secondary to a nutritional deficiency from defects in the tunica vasculosa lentis and occur at the 5–6 months of embryonic life when the lens is normally spherical.

An alternative theory suggests that microspherophakia is caused by a lack of

tension in the rudimentary zonular fibers of the lens, which arrests development so that the lens remains spherical.

Q.2. What is inverse glaucoma?

Ans. Refer text.

Q.3. What are the syndromes associated with microspherophakia

Ans. Refer Table 1.

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POSTERIOR CAPSULAR OPACIFICATION

Prafulla Kumar Maharana, Manpreet Kaur

INTRODUCTION

Posterior capsular opacification (PCO) or aftercataract is the most common complication of cataract surgery with an incidence of 2–63% three years after phacoemulsification. It is a major cause of diminution of vision in the postoperative period after an uneventful extracapsular cataract surgery.

It may be given as a short case in postgraduate/DNB/Diploma examination.

HISTORY

Chief complaint: The patient presents with the following complaints:

- Diminution of vision
- Glare.

History of Present Illness

The patient presents few months to few years after undergoing an extracapsular cataract extraction.

The interval between surgery and PCO ranges from three months to four years after the surgery. There is an inverse correlation with age and young age is a significant risk factor for PCO. There is a history of good gain in visual acuity following cataract surgery, following which there is a gradual, painless, progressive diminution of vision. In early cases, the best corrected visual acuity may be optimal but the patient may complain of glare.

EXAMINATION

General Examination/Specific Systemic Examination

Systemic examination is usually unremarkable.

Ocular Examination

Visual acuity: There is a decrease in the uncorrected as well as best spectacle corrected visual acuity (BSCVA), both for distance and near. Refraction must be done in all cases to find out the BSCVA.

The *eyeballs and eyelids* are usually normal.

Conjunctiva is usually normal. Conjunctival scars may be present in cases that have undergone ECCE or SICS.

Cornea: Scars of previous cataract surgery may be present. Sutures or suture marks may be present.

Sclera: Scleral incision may be visible in cases that have undergone SICS.

Iris: Usually normal; however, in complicated cases iris atrophy, chafing, peripheral anterior synechiae or capsuloiridic adhesion must be noted carefully

Pupil: Usually normal; however, in complicated cases abnormality in shape and size may be there. In cases with dense PCO, pupillary reflexes must be noted carefully to rule out relative afferent pupillary defect (RAPD) to determine the visual prognosis.

Intraocular pressure is usually normal. Following Nd: YAG laser capsulotomy, a transient rise in IOP often occurs. So any raised IOP or glaucoma must be controlled with medication before proceeding for capsulotomy.

Lens: Intraocular lens is present in the bag, or rarely in the sulcus. Any IOL decentration, adhesion between anterior capsular margin and posterior capsule or between iris and posterior capsule must be noted carefully as these clinical conditions increases the risk of early PCO formation.

Posterior capsular opacification is visible behind the lens. Different morphological variants of PCO may be observed, such as fibrotic type (**Fig. 1**), Elschnig pearls and Soemmering's ring (**Fig. 2**).

Vitreous: Usually normal; may not be clearly visible as a result of media haze induced by PCO.

Fundus: A thorough fundus examination is essential to rule out any retinal tear/hole/traction, since Nd: YAG laser capsulotomy increases the risk of retinal detachment. Cystoid macular edema must be ruled out as the inflammation induced by laser capsulotomy predisposes towards the development of macular edema. Indirect ophthalmoscopy must be done in all cases.



Fig. 1: Posterior capsular opacification fibrotic type

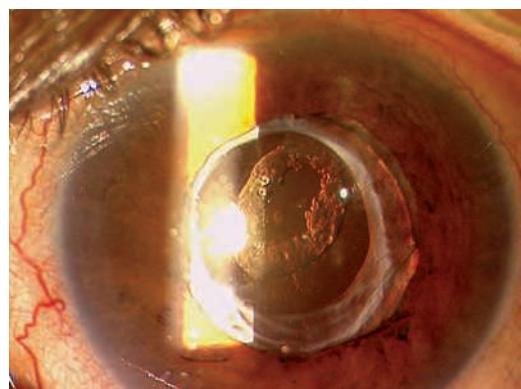


Fig. 2: Soemmering's ring

DIFFERENTIAL DIAGNOSIS

Localized Endophthalmitis

Propionibacterium acnes may induce a chronic endophthalmitis with low-grade inflammation that may mimic a PCO. The bacteria are sequestered within the capsular bag and form whitish precipitates and plaques. Laser capsulotomy is contraindicated in such cases to avoid dispersion of the infective material into the vitreous cavity.

Cell Precipitates and Membranes

Breakdown of the blood-aqueous barrier as a result of cataract surgery may lead to inflammation and the aqueous dispersion of erythrocytes, chronic inflammatory cells such as macrophages and giant cells as well as protein, pigments and

fibrin. They may form thin, translucent diffuse or punctate opacities that may mimic PCO. Increased frequency of topical steroid instillation may help resolve such inflammatory membranes.

Capsular Bag Distention Syndrome

Capsular bag distention syndrome (CBDS) is a complication of continuous curvilinear capsulorhexis done in phacoemulsification and in the bag IOL implantation. It usually presents in the immediate postoperative period, with shallowing of the anterior chamber, unexpected myopic refraction and accumulation of liquefied substance between the implanted lens and posterior capsule. It may rarely present many years after surgery with reduced vision but no significant refractive change. The management consists of Nd: YAG capsulotomy or capsular bag lavage.

INVESTIGATIONS

- *B-scan ultrasonography:* To rule out any posterior segment complications. Presence of PVD is a good sign before proceeding for laser capsulotomy since risk of traction and subsequent retinal detachment is less. It also helps to rule out low-grade endophthalmitis, especially *P. acnes* endophthalmitis.
- *Pentacam:* Not done routinely. Scheimpflug imaging may be useful to document a distended capsular bag with fluid accumulation behind the lens in CBDS.

CLASSIFICATION

- Clinically, PCO can be divided into two types:
 1. *Regenerative PCO:* Regenerative PCO is a result of migration of lens epithelial cells along the posterior capsule, behind the IOL. These cells (also known as bladder cells due to their appearance) proliferate to form layers of lens material and *Elschnig pearls*, leading to opacification. When arranged in a form of ring (between anterior capsular rim and posterior capsule), it is called *Soemmerring's ring* (Fig. 2). It is more common and is one of the important cause of a decrease in visual function after cataract surgery.

Table 1 Sellman and Lindstrom posterior capsule opacification (PCO) grades

Grade	Definition
1	No or slight PCO without reduced red reflex, also no pearls at all or pearls not to the IOL edge
2	Mild PCO reducing the red reflex, Elschnig pearls to the IOL edge
3	Moderate fibrosis or Elschnig pearls inside IOL edge but with a clear visual axis
4	Severe fibrosis or Elschnig pearls covering the visual axis and severely reducing the red reflex

2. *Fibrotic PCO:* In fibrotic PCO, lens epithelial cells of the anterior capsule undergo transformation to myofibroblasts, causing fibrosis and contraction of the capsule bag. This can lead to decentration of the IOL and hinder visualization of the peripheral retina.

- Sellman and Lindstrom has described four grades of posterior capsule opacification (Table 1).

MANAGEMENT

Conservative Management

Cases with mild PCO that achieve optimal visual acuity with refraction may be observed and kept on regular follow-up. Refraction with prescription of glasses may be adequate in such cases.

Nd: YAG Laser Capsulotomy

- *Indications*
 - Interference with daily activities
 - Decreased vision
 - Increased glare
 - Difficulty visualizing the fundus
- *Preoperative preparation:* Before beginning the capsulotomy, informed consent should be obtained. One hour before the laser capsulotomy, a drop of a pressure-lowering drug such as apraclonidine may be administered along with a mydriatic to dilate the pupil. Topical anesthesia drops are administered.

- Procedure/laser parameters:** An Abraham YAG capsulotomy lens is used in conjunction with a coupling agent, such as 2% hydroxypropyl methylcellulose. Laser spots are applied in a cruciate, circular, inverted U or 'Christmas-tree' pattern. Cruciate pattern is most commonly used. The capsulotomy should be centred on the visual axis with diameter slightly larger than the mesopic pupil size. Laser energy is set at 1-3 mJ and posterior offset of laser beam is set at 125–150 microns to avoid hitting the lens.
- Post-laser medication:** After the procedure, topical anti-glaucoma medications may be prescribed for a week along with topical steroids to reduce inflammation.

Membranectomy

Surgical membranectomy may be indicated in the following situations:

- Pediatric patients
- Uncooperative or mentally challenged patients
- Dense fibrotic PCO.

Surgical Approach

- Limbal route—with anterior vitrectomy cutter
- Pars-plana route:* Especially, in dense fibrotic PCO with *in-the-bag* IOL, where it may be difficult to access the posterior capsule via limbal route.

VIVA QUESTIONS

Q.1. Describe the prevention of PCO.

Ans. Following factors may help to minimize the incidence of PCO:

Surgical techniques to prevent PCO formation

- Cortical cleaving hydrodissection and cortical clean-up
- In-the-bag IOL fixation
- Optimally sized continuous curvilinear capsulorhexis with 360° IOL coverage

IOL-related factors ("Ideal" IOL)

- Biocompatible IOL material to reduce stimulation of cellular proliferation
- Maximal IOL optic—posterior capsule contact, angulated haptic, 'adhesive' biomaterial to create a 'shrink wrap'
- IOL optic geometry—square, truncated edge

Q.2. Describe the pathogenesis of PCO.

Ans. The development of PCO is a very dynamic process, and involves three basic phenomena: proliferation, migration, and differentiation of residual lens epithelial cells (LECs). LECs left behind in the capsular bag after cataract surgery convert from epithelial to mesenchymal cells, deposit collagen and generate lens fibers, leading to PCO development.

Q.3. What do you mean by 'A' and 'E' cells?

Ans. The anterior-central zone (corresponding to the zone of the anterior lens capsule) consists of a monolayer of flat cuboidal, epithelial cells with minimal mitotic activity. In response to a variety of stimuli, these anterior epithelial cells ('A' cells) proliferate and undergo fibrous metaplasia. Continuation of anterior lens cells around the equator form the equatorial lens bow ('E' cells). Unlike within the A-cell layer, cell mitoses, division and multiplication are quite active in this region, and new lens fibres are continuously produced in this zone throughout life.

Q.4. Describe the Soemmering's ring and Elschnig pearls.

Ans. Elschnig pearls consist of clusters of swollen, opacified epithelial "pearls" or clusters of posteriorly migrated equatorial epithelial (E) cells (Bladder or Wedl cells)

The Soemmering's ring (**Fig. 3**) is a dumb-bell or donut-shaped lesion that often forms following any type of

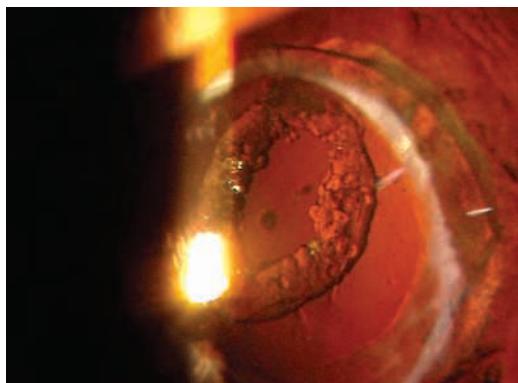


Fig. 3: Soemmering's ring with bladder cells

ECCE (manual or phacoemulsification). Equatorial cells (E-cells) are responsible for formation of a Soemmering's ring. The pathogenetic basis of a Soemmering's ring is rupture of the anterior lens capsule with extrusion of nuclear and some central lens material. Soemmering's ring is a direct precursor to PCO.

Q.5. What are the drugs/agents used intra-operatively to reduce PCO?

Ans. Intraocular application of pharmacologic agents has been investigated to prevent PCO. The basic principle is to selectively destroy the LECs and avoid toxic side effects on other intraocular tissues such as corneal endothelium. Pharmacologic agents being investigated include antimetabolites (such as methotrexate, mitomycin, daunomycin, 5-FU, colchicine, and daunorubicin), anti-inflammatory substances, hypo-osmolar drugs, and immunological agents. Sealed capsular irrigation (SCI) device has

been developed to precisely deliver the pharmacological agents within the capsular bag, while minimizing the potential for collateral ocular damage. Implantation of intracapsular ring may prevent central PCO after cataract surgery by mechanically blocking migration of lens epithelial cells towards the central visual axis.

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TRAUMATIC CATARACT

Deepali Singhal, Ruchita Falera, Manpreet Kaur

INTRODUCTION

Cataract formation is a well-known complication of blunt and penetrating trauma. It results from direct lens trauma or concussion effect on the lens and is often associated with trauma to cornea, iris, angle and posterior segment.

It is given as short case in postgraduate/DNB/Diploma examination.

HISTORY

Chief complaint: Presenting complaints depend on the type of injury.

Blunt trauma

- Progressive diminution of vision
- Whitish opacity
- Monocular diplopia, if associated with subluxation

Penetrating trauma

- Sudden diminution of vision
- Whitish opacity

History of present illness: Onset, duration and mode of trauma should be recorded.

- Onset and duration of diminution of vision and whitish opacity should also be noted.
- Any history of deviation of eye or limitation of motility should be noted
- It is important to note, if there is any medico-legal case associated with trauma.

Past history: Any history of ocular surgery or glaucoma should be enquired.

EXAMINATION

Systemic Examination

A complete systemic examination should be done including cranial nerves examination, especially in cases associated with acute onset diplopia. It is important to remember the ABC (airway, breathing, circulation) in a case of multisystemic trauma presenting with acute trauma.

Ocular Examination

Visual acuity: Uncorrected and best-corrected visual acuity (BCVA) helps in planning the treatment, especially in early cataract. It is important to note projection of rays, since it can suggest presence of posterior segment complications of blunt trauma such as retinal detachment (RD).

Eyeball: Ocular deviation and both unioocular and binocular movements should be tested

Eyelid: Laceration or scarring may be seen.

Conjunctiva: Subconjunctival hemorrhage, chemosis or scar may be present.

Cornea: On slit-lamp biomicroscopy, following signs must be noted.

- Corneal clouding/edema
- Corneal perforation
- Scar may be seen
- Sutures may be seen in repaired perforations
- Intrastromal foreign body may be present.

Sclera: Repaired scleral perforation or scar should be looked for.

Anterior chamber: Anterior Chamber (AC) cells, flare, hyphema, vitreous or lens matter must be looked for.

Iris: Iridodonesis/iridodialysis/posterior synechiae/iris atrophy may be present.

Pupil: Sphincter tear, eccentric pupil/traumatic mydriasis (**Fig. 2**), oval/peaking pupil/irregular/vitreous entangling pupillary area should be ruled out. Direct and consensual light reactions of both eyes should be recorded. Presence of relative afferent pathway defect (RAPD) suggests posterior segment complications such as RD or traumatic optic neuropathy.

IOP: IOP may be raised due to angle recession/subluxation or trabecular damage.

IOP may also be low in case of globe perforation or vitreous loss. In acute cases of trauma, IOP is low due to ciliary shock.

Gonioscopy: Angle recession, pigmentation, PAS, cyclodialysis, zonular dialysis and trabecular meshwork splitting may be seen.

Lens: Lens examination should include:

- Determination of type and extent of cataract

- Intumescent or normal thickness lens
- Associated intact or ruptured anterior capsule
- Status of the zonules.

In majority of young patients, the opacity is localized and stationary, which starts in subcapsular zone and eventually lies deeply due to the formation of new lens fibers.

Whereas, older age group is associated with more diffuse and progressive cataract due to activation of degenerative process of senile cataract.

Morphological classification of traumatic cataract due to blunt trauma is as follows.

Vossius Ring

Vossius ring is the epicapsular deposition of iris pigment. It is a reddish-brown ring corresponding to the pupillary aperture, about 1 mm in breadth formed due to extreme miosis at the time of trauma. It is usually segmented due to constrictions on the posterior surface of iris. At times, a double ring can be seen due to immediate pupillary constriction followed by dilatation.

Localized Subcapsular Opacities

- **Disseminated subepithelial opacity:** Small, discrete/flake like anterior subcapsular opacities, which are commonly stationary. This can also present as a large, round, discrete-layered opacity called as *Cataracta Nodiformis*.¹
 - **Cobweb opacity:** It presents as a subcapsular and a more diffuse filmy structure supporting fine dust-like opacities commonly in young patients. This can be seen in both blunt and penetrating trauma. It is permanent, occurs in the absence of capsular rupture and may be due to mechanical damage to the epithelium.¹
 - **Zonular (Lamellar) opacity:** It is the result of disseminated opacities occurring extensively over the lens or rosette opacity. This is a rare presentation as a unilateral zonular cataract, seen in young patients. The density may vary while the outline is irregular and typical riders may be evident.
 - **Rosette cataract:** Early/late.
- Early rosette cataract**
- It is recognized shortly after trauma, few hours to few weeks.

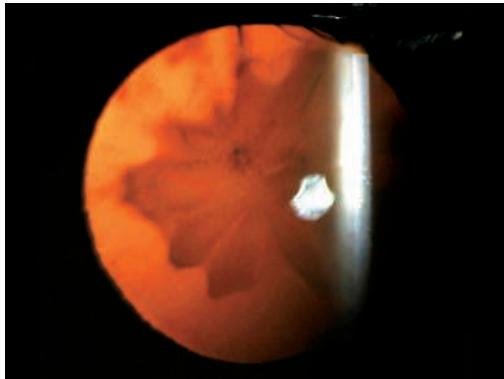


Fig. 1: Vossius ring

- It may be seen in anterior subcapsular area in concussive injuries or in posterior subcapsular area in penetrating injuries.
- Initially seen as fine-fluid droplets formed between the radiating lens fibers, which then form feathery parallel rays radiating from the dark suture lines (**Fig. 1**).
- In mild injuries, these are translucent and may disappear within a few days.
- More commonly, they are permanent, stationary, and cause vision impairment. It is gradually buried deeply in cortex due to formation of new lens fibers.

Late rosette cataract

- Seen few years after trauma
- It is located deep in the cortex or nucleus and is due to minimal degree of damage to subcapsular fibers.
- In early rosette, the sutures run upto the center of petals and the rays run from them as a midriff whereas, in late rosette, the sutures run between the petals which are formed by the outcrop of rays from two neighboring sutures. It can also extend much further in the periphery and may turn backwards to form a second posterior rosette.
- **Post-traumatic atrophy of the lens:** It may be seen few years after a severe blunt trauma where lens capsule is intact. It is characterized with thinning of the lens substance and associated with shrinkage of the nuclear and cortical matter, which can be symmetrical or asymmetrical leading to deformation of whole architecture. Anterior capsule seems to

be flatter without folds, which are present in penetrating trauma.

- **Presenile and senile changes:** These can be observed in the form of coronary cataract, water clefts, punctate cortical opacities and sclerotic nuclear opacities. There is rapid and premature progression of such changes as compared to senile cataract.

Diffuse concussion cataract: It is rare, and is usually associated with capsular tear. It is due to rapid imbibition of aqueous by the lens matter leading to opacification. In case of a large tear, the swollen lens fibers may herniate into anterior chamber and vitreous, and later become granular and necrotic. In young patients, slow and total absorption of cataract may occur; whereas, in the old, iritis and secondary glaucoma may occur.

Vitreous: Vitreous hemorrhage may be present or vitreous base avulsion with a bucket handle appearance may be seen.

Fundus: Retinal dialysis, giant retinal tear with retinal detachment and macular hole can occur due to trauma. Indirect ophthalmoscopy with indentation of periphery is a must in all cases of trauma. Other features include commotio retinae, traumatic optic neuropathy or disc avulsion.

DIFFERENTIAL DIAGNOSIS

- Uveitic cataract
- Developmental cataract (unilateral)
- Glaucomafleckens.

INVESTIGATIONS

- **Biometry:** Axial length and keratometry
- **Visual potential assessment:** Laser Interferometry or VER
- **Ultrasonography:** For posterior segment evaluation
- **NCCT head and orbit/X-ray orbit:** To look for IOFB and orbital injuries
- **UBM:** To identify occult zonular damage and posterior capsular rupture.

MANAGEMENT

Standard recommendation in acute-onset traumatic cataract with penetrating/perforating injuries is primary globe closure followed by a

secondary lens aspiration with IOL placement. This is because the degree and visual significance of cataract may not be apparent in the acute setting and a small opacity may become visually insignificant later. Moreover, IOL power calculation and decision about the type of lens and positioning may be compromised in acute setting and surgery may be difficult due to hazy media.^{1,2}

Indications of Surgery

- Anterior capsular rupture with swollen lens or lens matter in AC require primary lens aspiration
- Lens-induced glaucoma or inflammation
- Visually significant cataract causing diminution of vision
- Poor visualization of posterior segment, which impedes management of posterior segment injuries.

Primary cataract removal helps control inflammation and allows early direct visualization of posterior segment. In children, cataract surgery should be performed within one year of ocular trauma to reduce the risk of amblyopia. In the acute setting, accurate IOL calculations may be difficult to obtain so data from the other eye can also be taken.

Surgical Management

The surgical approach depends upon the capsular and zonular status and degree of lens injury (**Fig. 2**). There can be four different scenarios such as:

1. Nondislocated cataract with intact capsule
2. Anterior capsular rupture with cataract
3. Posterior capsular rupture with cataract
4. Subluxated lens with cataract (**Fig. 3**).

Nondislocated Cataract with Intact Capsule

Standard phacoemulsification technique can be used with associated glaucoma and iris injuries taken into consideration. Adequate size capsulorhexis should be made with capsular staining which will help in better visibility. Anterior capsular staining can be performed with trypan blue 0.06%. Generous hydrodissection should be done with low flow phacoemulsification to avoid stress on the zonules.²



Fig. 2: Early rosette cataract

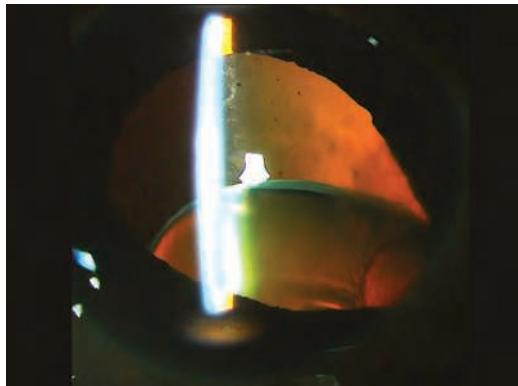


Fig. 3: Late rosette cataract

Anterior Capsular Rupture with Cataract

Primary lens aspiration should be performed in these cases to decrease the chances of inflammation and secondary glaucoma. After the initial incision, viscoelastic should be injected and the extent of anterior capsular rupture along with the presence of vitreous prolapse should be determined. Vitrectomy cutter should be used in cut/IA mode to remove the vitreous and cortical matter from AC. Then, the anterior capsulorhexis can be completed and lens aspiration is done. In cases of thick fibrotic capsule, vannas scissors can be used to complete the capsulorhexis. Femtosecond laser assisted anterior capsulorhexis can also be performed to minimize zonular stress.^{1,2}

Posterior Capsular Rupture with Cataract

The management depends upon the type and the size of tear. In type I tears the margins are *thickened and fibrosed*, so there are less chances of extension with irrigation. Type 2 tears are present in early surgeries and they have *thin, transparent* margins, which may rapidly enlarge during irrigation. Tears larger than 6 mm are unable to support in the bag IOL. When using an anterior approach, further hydration of vitreous and extension of tear should be avoided by using dry aspiration techniques and meticulous control of infusion and anterior vitrectomy. Phacoemulsification with low-flow settings should be used. Posterior pars plana approach is used in cases of posterior dislocation, and if there is associated retinal pathology.²

VIVA QUESTIONS

Q.1. Describe the pathophysiology of cataract in trauma.

Ans. Several mechanisms have been described for cataract formation after ocular trauma, which includes coup injury, countercoup, and equatorial expansion. Coup injury is

the direct trauma to the lens epithelium and capsule leading to imbibition of aqueous and cataract formation. Countercoup refers to damage occurring at a distal site due to shock waves, which can disrupt the capsule and the lens fibers. Blunt trauma causes anteroposterior compression and equatorial expansion of the globe, which results in transmission of shock waves. This may result in damage to capsule causing necrosis and increased permeability, or damage to lens fibers, or zonular dehiscence. Damage to lens fibers can also result from the impact of aqueous and iris or lens rebound mechanism.

Q.2. Discuss the seven rings of trauma.

Ans. See section of traumatic RD.

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CHAPTER

7

Instruments

OPHTHALMIC INSTRUMENTS

Pranita Sahay, Devesh Kumawat

The ophthalmic instruments can be classified into the following.

LID SPECULUM

It is used to keep the lids open during any ocular surgery. The two commonly used lid speculums are described below.

Universal Metallic Eye Speculum

As the name suggests, the same speculum can be used for either eye (right or left) but the disadvantages are that it is heavy in weight and cannot keep the eyelashes away from the operating field (**Fig. 1**).

Self-retaining Barraquer Eye Speculum

This lid speculum has a screw that helps in giving desired exposure of the surgical site which can be changed as per the surgery or surgeon's choice.

The disadvantage is that the screw increases pressure over the eyeball and thereby increases the intraocular pressure. Hence, it is not advisable in perforated cases (**Fig. 2**).

Uses

- All intraocular surgeries like cataract surgery, glaucoma surgery, keratoplasty, buckling and other vitreoretinal surgery

- Removal of conjunctival and corneal foreign body
- Examination of children and patients with severe blepharospasm.



Fig. 1: Universal metallic eye speculum



Fig. 2: Self-retaining Barraquer eye speculum

FORCEPS

Forceps of different design are available for different purposes.

Plain Forceps

It is a blunt forceps without any tooth.

Its tip has serrations (either horizontal/vertical) for holding tissue (**Fig. 3**).

Uses

- For holding conjunctiva, scleral flap or skin
- For holding the sutures while tying.

Globe Fixation Forceps

The tip of this forceps is toothed for better grip while holding the tissue.

It is used to hold the conjunctiva and episcleral tissue near the limbus (**Fig. 4**).

Uses

- For fixing the eyeball during surgery
- For holding the eyeball during forced duction test.

Superior Rectus-holding Forceps

It is a toothed forceps with 'S' shaped curve specially designed to fit into the orbit while trying to grasp the muscle belly (**Fig. 5**).

Colibri Forceps

It is a fine-toothed forceps for holding flaps of cornea or sclera and rarely the iris (**Fig. 6**).



Fig. 3: Plain forceps

Lim Forceps

It is also a toothed forceps for holding the cornea or sclera and rarely the iris (**Fig. 7**).

Iris Forceps

These are toothed forceps especially designed for holding the iris for the purpose of iridectomy.



Fig. 4: Globe fixation forceps



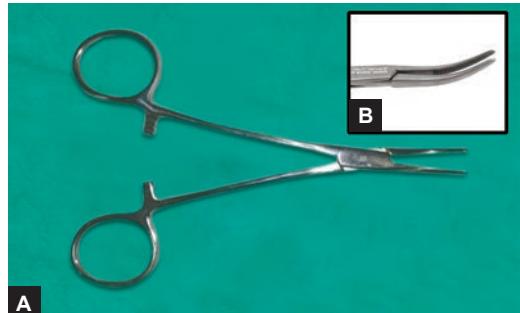
Fig. 5: Superior rectus-holding forceps



Fig. 6: Colibri forceps



Fig. 7: Lim forceps



Figs 9A and B: Artery (hemostatic) forceps:
(A) Plain; (B) Curved (Inset)



Fig. 8: Epilation forceps



Fig. 10: Utrata capsulorhexis forceps

Epilation Forceps

It is a small stout forceps with blunt and flat ends (**Fig. 8**).

Uses

- Epilation of cilia in trichiasis and stye
- Removal of cilia after electrolysis and cryolysis.

Artery (Hemostatic) Forceps

It is a blunt-tipped forceps with multiple serrations near the tip and a locking mechanism near the other end. It is available in various sizes small, medium and large. The small-sized forceps are called mosquito forceps and are the most commonly used variety in ophthalmic surgeries (**Figs 9A and B**).

Uses

- Holding the bleeders during surgery
- To crush the muscle before cutting in squint surgery.

Utrata Capsulorhexis Forceps

This forceps has a fine titanium tip with a sharp point that enables to initiate the capsular tear then securely grasp the capsule to perform the capsulorhexis. It has an “iris stop platform” at 8.5 mm from the tip to stop the shaft of the forceps from completely closing when tips are closed (**Fig. 10**).

McPherson Forceps

It is a fine sharp tipped non-toothed forcep with angulation (**Fig. 11**).

Uses

- Holding the intraocular lens (IOL) while implanting it
- Holding the suture while tying the knot
- Suture removal.

Pierce-Hoskin Forceps

It is a fine toothed tissue holding forceps (**Fig. 12**).



Fig. 11: McPherson's forceps



Fig. 13: Lens hook/Von Graefe retractor



Fig. 12: Pierce-Hoskin forceps



Fig. 14: Green hook

Uses

- Holding the corneal tissue firmly
- For suture tying
- For forced duction test.

HOOKS AND RETRACTORS

Lens Hook/Von Graefe Retractor

It has a flat metal handle which is curved at its end and has a knob (**Fig. 13**).

Uses

- For applying pressure on the limbus at 6 o' clock position during delivery of lens in intracapsular cataract extraction as well as extracapsular cataract extraction
- It can be used as an alternative to muscle hook in squint surgery.

Green Hook

It has a straight shaft with flat-ended hooked tip. It is used for hooking the muscle during squint or enucleation surgery (**Fig. 14**).

Jameson Hook

It has a straight shaft with flat hooked end and paddle shaped tip. It is used for retrieving the rectus muscles at their insertion site during squint or enucleation surgery (**Fig. 15**).

Desmarre Retractor

It is a saddle-shaped instrument available in two sizes—small and large (**Fig. 16**).

Uses

- For double eversion of the eyelid and evaluation of superior fornix



Fig. 15: Jameson hook



Fig. 17: Barraquer needle holder



Fig. 16: Desmarre retractor

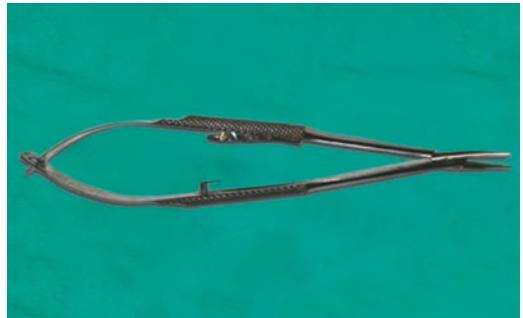


Fig. 18: Castroviejo needle holder

- For retraction of the upper eyelid while removing corneal sutures or foreign body
 - For retraction of the conjunctiva after peritomy in buckling surgery.
- The only disadvantage with this instrument is that it is not self retaining.

Cat's Paw Lacrimal Wound Retractor

It is used to retract the soft tissue from the operative field during lacrimal sac and lid surgery. It has an added advantage of having a hemostatic effect.

Müller's Self-retaining Adjustable Hemostatic Retractor

It has two limbs with three pins in each. As the name suggests, it has the advantage of being hemostatic and self-retaining along with retracting the skin from the surgical site in dacryocystorhinostomy (DCR) surgery.

NEEDLE HOLDERS

Barraquer Needle Holder

It is available in two designs with or without locking system.

It has fine serrations at its jaw for better grip while passing the suture through conjunctiva, cornea, sclera and extraocular muscles (**Fig. 17**).

Castroviejo Needle Holder

It is a needle holder with S-shaped locking system. The uses are same as that of Barraquer needle holder (**Fig. 18**).

Arruga Needle Holder

It is a large needle holder with one end being flat for placement of the surgeon's thumb and the other end having serrations for better grip of the

suture. It is available in two designs—with and without a locking system (**Fig. 19**).

Uses

- In eyelid surgery
- For passing superior rectus bridle suture.

CASTROVIEJO CALIPER

It is a divider-like instrument with a graduated scale at one end (marking in millimeters) and the other arm moves by a screw over the scale (**Fig. 20**).

Uses

- Measuring the diameters of host or donor cornea
- Marking the site for muscle insertion in recession surgery
- Marking the site for pars plana entry for either surgery or intravitreal injection.

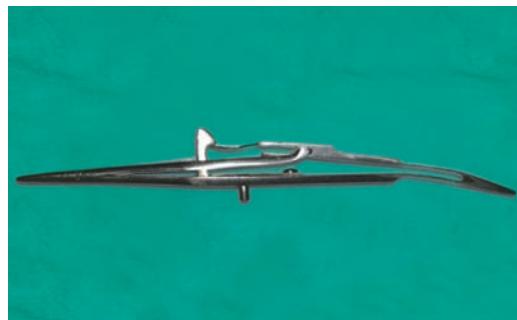


Fig. 19: Arruga needle holder

KNIVES

Von Graefe Knife

It is a long, narrow, thin blade with a sharp tip with cutting edge on one side. It was used for making the corneoscleral entry in cataract surgery.

Keratome

It is a thin blade with a diamond-shaped apex and cutting edge on both sides. It is available in both straight and curved design as well as in various sizes (2.8 mm, 3 mm, 3.5 mm and 5.5 mm). It is used for making self-sealing corneal incisions in cataract surgery, iridectomy and keratoplasty (**Fig. 21**).

MVR or V-Lance Blade

It is a fine straight instrument with triangular knife at its distal end having cutting edge on both the sides. It is used for making the side port entry at the limbus (**Fig. 22**).

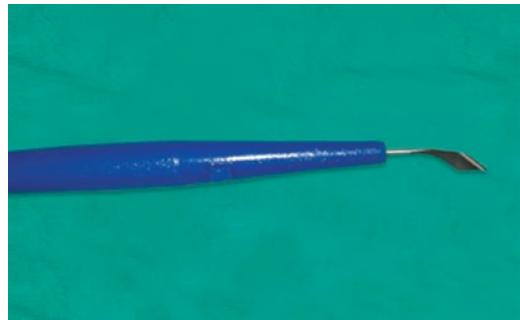


Fig. 21: Keratomes



Fig. 20: Castroviejo caliper

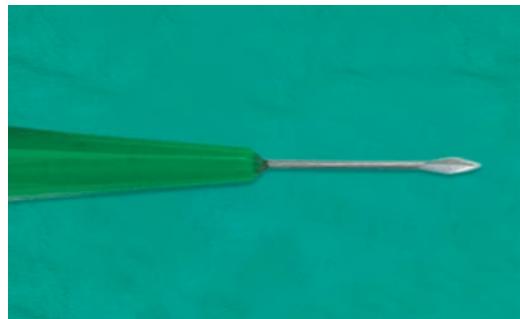


Fig. 22: MVR or V-Lance blade

Crescent Knife

It is blunt-tipped instrument with bevel side of the knife up and having cut-splitting action on both the sides (**Fig. 23**).

Uses

- For dissection in pterygium surgery
- For dissection of the scleral flap in trabeculectomy/small incision cataract surgery (SICS)/ Descemet's stripping automated endothelial keratoplasty (DSAEK)
- For corneal dissection in anterior lamellar keratoplasty.

SCISSORS

Steven Tenotomy Scissors

It is a plain scissors with blunt end. It comes in two design—straight and curved (**Fig. 24**).

Uses

- For cutting the muscle



Fig. 23: Crescent knife

- For blunt dissection of the soft tissue in squint and oculoplasty procedures.

Castroviejo Corneoscleral Scissors

It is a fine-curved scissors that works on spring action (**Fig. 25**).

Uses

- To enlarge the corneal or corneoscleral incision for intracapsular cataract extraction (ICCE)/ extracapsular cataract extraction (ECCE)
- To enlarge corneal incision in keratoplasty
- To cut the scleral tissue flap.

DeWecker Scissors

It is a fine scissor with small blades at right angle to the arm that works on spring action (**Fig. 26**).

Uses

- For performing iridectomy
- For cutting the vitreous strands prolapsing from the wound.



Fig. 25: Castroviejo corneoscleral scissors



Fig. 24: Steven tenotomy scissors



Fig. 26: DeWecker scissors



Fig. 27: Westcott scissors



Fig. 29: Enucleation scissors



Fig. 28: Vannas scissors



Fig. 30: Lens spatula

Westcott's Scissors

It is a stout scissor with straight or curved blades that work on spring action.

It is used for conjunctival dissection (**Fig. 27**).

Vannas Scissors

It is a fine scissor that works on spring action. It has two wings to operate—one sharp and one blunt (**Fig. 28**).

Uses

- For cutting sutures
- For anterior capsulotomy in ECCE
- For cutting the vitreous strand while performing anterior vitrectomy.

Enucleation Scissors

It is a thick-curving scissor with a blunt tip used for cutting the optic nerve in enucleation surgery (**Fig. 29**).

OTHER INSTRUMENTS

Cataract Surgery

Lens Spatula

It has a metallic handle with a spoon-shaped end which is used to apply pressure at the 12 o'clock position for expression of nucleus in Smith's technique in extracapsular cataract extraction (**Fig. 30**).

Wire Vectis

It is a wireloop attached to a metallic handle (**Fig. 31**).

Uses

It is used to remove subluxated lens in ICCE as well as nucleus in ECCE.

Irrigating Wire Vectis

It is a modification of the wire vectis. It has a hollow rim with a 0.3 mm opening at the anterior end



Fig. 31: Wire vectis



Fig. 34: Dastoor iris repositor



Fig. 32: Irrigating wire vectis



Fig. 33: Simcoe irrigation and aspiration cannula

and a hollow handle at the posterior end which is attached to a hub similar to that of a hypodermic needle through which fluid can be injected (**Fig. 32**).

Uses

It is used for hydro/viscoexpression of the nucleus in ECCE and SICS.

Simcoe Irrigation and Aspiration Cannula

It is available in the classical and reverse design with both right-handed and left-handed models available in each design. It has an irrigation system through the main port and aspiration system through the port on the side which is attached to a syringe through a silicon tube (**Fig. 33**).

Uses

- For irrigation and aspiration of cortical matter in ECCE and open sky cataract surgery in keratoplasty
- For aspiration of hyphema.

Dastoor Iris Repositor

It is a flat and straight/bent blade with blunt edges (**Fig. 34**).

Uses

- To reposit the iris in the anterior chamber
- To tuck the donor cornea underneath the host cornea in keratoplasty surgery.

Cystotome Needle

It is prepared with a 26-gauge needle by bending the needle tip down while holding the bevel up. Then, while maintaining this needle orientation, bend the needle up near the hub (**Fig. 35**).

Uses

- It is used to make the anterior capsulotomy in ECCE as well as capsularhexis in phacoemulsification
- Posterior capsularhexis in pediatric cataract surgery.



Fig. 35: Cystotome needle



Fig. 37: IOL-holding forceps



Fig. 36: Arruga intracapsular (capsule holding) forceps



Fig. 38: Sinskey hook or IOL dialer

Arruga Intracapsular (Capsule Holding) Forceps

This forcep has a cup at inner side of the tip of each limb. The edges of the cup are smooth and atraumatic to the lens capsule (**Fig. 36**).

Uses

- For removal of the lens during forceps method of intracapsular cataract extraction
- For removal of the lens capsule remnant after accidental extracapsular cataract extraction.

IOL-holding Forceps

It is a spring action forceps with short, blunt and curved blades smooth edges and tips. It is used to hold the optic of nonfoldable polymethylmethacrylate (PMMA) intraocular (IOL) during implantation (**Fig. 37**).

Sinskey Hook or IOL Dialer

It is a fine instrument with a bent tip. The tip can engage the dialing holes of the IOL (**Fig. 38**).

Uses

- Dialing of the nonfoldable PMMA IOL for proper positioning in the capsular bag or sulcus
- For nucleus manipulation in phacoemulsification.

Chopper

It is similar in appearance to the Sinskey hook but the difference lies in the tip which is sharp with cutting edges in a chopper. It is used to split or chop the nucleus into smaller pieces during phacoemulsification (**Fig. 39**).

**Fig. 39:** Chopper**Fig. 41:** Kelley's punch**Fig. 40:** Phaco needle tip**Fig. 42:** Flieringa ring

Phaco Needle Tip

It is made of titanium with a distal opening 0.9 mm in diameter with a silicon sleeve which has two openings on the side 180° apart, through which the irrigation fluid flows. The phaco needle threads directly onto the phaco handpiece (**Fig. 40**).

The tip can have bevel with 0°, 15°, 30°, 45° or 60°. The greater is the angulation of the bevel tip, better is the sculpting effect and visibility of the tip but leads to poor occlusion. The 30° bevel offers the best compromise and leads to better sculpting, visibility as well as occlusion. The silicon sleeve acts as an insulator and the fluid flowing through the sleeve keeps the tip cool and prevents wound burn.

The Kelman tip has a 22° angulation of the shaft 3.5 mm from the tip. This enhances the emulsification as well as allows the surgeon to use the phaco tip for manipulation of nucleus during surgery.

The flared tip has an outer diameter greater at the distal end of the tip than 1–2 mm behind it.

This helps to enhance the emulsification effect and reduce the postocclusion surge.

The Cobra tip is a bell-shaped tip, which increases the surface producing the ultrasound to reduce the level of energy required.

Glaucoma Surgery

Kelley's Punch

It is used to perform bone punch in dacryocystorhinostomy (DCR) surgery but can also be used to perform punch sclerectomy in trabeculectomy surgery (**Fig. 41**).

Keratoplasty

Globe Fixation Rings

Flieringa Ring

It is made of stainless steel and is useful for maintaining the architecture of the globe once the host corneal button has been removed. They are available in 11 sizes from 12 mm to 22 mm (**Fig. 42**).



Fig. 43: RK marker



Fig. 44: Disposable handheld trephine

Uses: Keratoplasty in aphakic eyes especially where vitrectomy has been performed. Keratoplasty in pseudophakic eyes and pediatric eyes as the eyeball has a tendency to collapse in these cases after trephination.

Disadvantage is that it can distort the shape of the eyeball and cause an oval cut during trephination and subsequent high astigmatism.

McNeill-Goldman Ring

It provides support at four strategically placed sutures. The ring has medial and temporal openings for greater access to the surgical field and two lid retractors to prevent eyelid closure by the patient. It is available in three sizes—small, medium and large.

Corneal Marking Instruments

RK marker, Vajpayee corneal marker (20 radial arms) and Anis corneal marker (8 radial arms) are the various instruments that guide the optimal placement of sutures in keratoplasty (**Fig. 43**).

Corneal Trephines

Types of Trephines

- **Conventional circular cutting trephines**
 - **Handheld**
 - ♦ Ranging from 3 mm to 17 mm in diameter. In some trephines, there is a central obturator, which can be adjusted to select the depth of the corneal cut and hence an inadvertent entry into the anterior chamber (**Figs 44 and 45**).
 - ♦ However, the obturator obscures the view of central cornea which may



Fig. 45: Handheld trephine with obturator

result in inaccurate centration during trephination of the recipient's cornea

- ♦ The examples of hand-held trephines with obturator are the Castroviejo trephine and the Grieshaber-Franceschetti trephine.

– **Mechanized:** The disadvantages associated with motor driven trephines include corkscrew edge effect on the corneal stroma.

Suction-fixation type

- ♦ It is devised to obtain a perpendicular cut in the recipient cornea. These trephine systems essentially consist of an outer corneal suction ring for fixation and an inner circular cutting blade.
- ♦ Hessburg-Barron trephine has a cross hair device for improved centration and an outer ring of corneal marks at equal intervals to assist in suture placement. It is available in diameters.



Fig. 46: Hessburg-Barron trephine



Fig. 47: Paton spatula

- 6.0–9.0 in 0.5 mm increments as well as diameter of 7.75 mm. For each spoke (90 degrees) turned, the blade is lowered or raised approximately 0.06 mm (**Fig. 46**).
- The barron vacuum punch features a solid stainless steel blade which is permanently mounted in a nylon housing. Four steel guide posts align with four corresponding holes in the cutting block base, automatically centering the blade over the donor cornea.

Special-Purpose Type

- The olson calibrated cornea trephine system used to trephinate both the donor and recipient corneas. The system consists of the anterior chamber maintainer, the reusable blade holder (with micrometer setting), and the suction ring. One revolution of the micrometer is equivalent to 500 microns.
- **Skin biopsy punches:** The skin biopsy punches, which have been used in dermatological practice, are especially useful in harvesting of small patch grafts used for tectonic purposes in cases of impending/frank perforation.
- **Single point cutting trephines:** The single point cutter trephines were designed to decrease corneal torsion, e.g. Leiberman single point cutter.
- **Combination trephines:** Hanna trephine system has got a circular razor-cutting blade and incorporates many of the salient features of single point cutting trephines.



Fig. 48: Teflon block

- **Noncontact trephines (Lasers):** Laser non-contact trephination eliminates corneal topography distortion, provides the visualization of the entire cornea and enhances centration.

Graft Holder (Paton Spatula)

Graft is placed over viscoelastic and is kept covered till the recipient dissection is complete (**Fig. 47**).

Cutting Block

The various cutting blocks available for corneal grafting are paraffin block, Teflon block and polycarbonate and nylon blocks (**Fig. 48**).

The Kaufmann corneal cutting block is the simplest design which consists of a Teflon block with a metal cover.

The Brightbill polytef cutting block is the modern, compound curved block which approximates the central, midperipheral and peripheral curvature of the donor tissue.



Fig. 49: Blade breaker

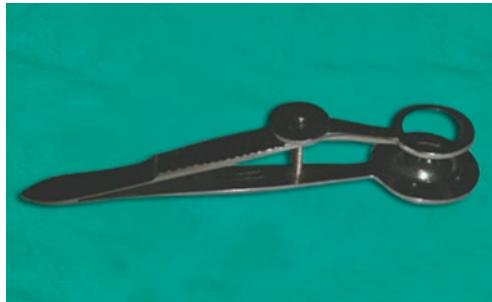


Fig. 50: King's clamp

Corneal Endothelial Punches

To cut a donor button from endothelial side corneal punches are also available which use disposable trephine blades. The advantage of corneal punch is that they yield sharp vertical cuts without beveling, e.g. Cottingham corneal punch, Troutman corneal punch, IOWA PK press corneal punch, Lieberman gravity-action punch, Rothman-Gilbard corneal punch.

Cutting Instruments

Blade Breaker

A disposable razor blade is broken and mounted on the tip of a metallic pencil handle. It is used for a controlled entry into the anterior chamber (Fig. 49).

Diamond Knife

This is the sharpest cutting instrument and is available in various sizes and shapes. It is the most durable and useful instrument for stab incisions as well as to complete the trephine cuts.

Forceps with special functions

- *Double corneal forceps, colibri style:* It has two 2.75 mm long tips separated 1 mm with 0.4 mm pierce tips. It is 72 mm long and has a serrated handle.
- *Colibri-style Polack double Corneal forceps:* It is used for the first corneal suture. The cut edge of the graft is gently grasped at the junction of the epithelium and stroma with fine toothed forceps.

Instruments for donor cornea dissection in lamellar keratoplasty

- *Barron's artificial anterior chamber and clamp:* The chamber is used to mount the

donor tissue and maintain adequate pressure while lamellar dissection or full thickness trephination is being performed. It is designed in a bright blue color to provide a high contrast background for visualizing the cornea and aiding in the lamellar dissection of the cornea.

- King's clamp (Fig. 50).

Lamellar Dissectors

Tooke knife: The pocket for the initiation of the lamellar dissection may be performed with a Tooke's knife. It has a smooth blade at one end, which can be inserted intralamellarly to create a pocket.

Paufique knife: It has a double-edged sharp angled blade that helps in outlining the graft, making the pocket and in dissecting the lamellar plane.

Desmarre lamellar dissector: It is used in the open type of dissection, which has a curve in its vertical meridian and it is used to sweep across the fibers in a cutting and teasing motion. A duckbill shape lamellar dissector is used for closed type of dissection, which is curved in the horizontal dimension.

Gill's lamellar dissector: It has a 3 mm wide blade which can be either straight or curved.

Guarded diamond knife: It is a micrometer adjusted guarded diamond knife, useful for obtaining irregular shaped lamellar grafts.

Crescent knife: This is another useful instrument for the lamellar dissection. It has a 2.0 mm blade.

Automated Lamellar Therapeutic Keratoplasty Machine

The Moria automated lamellar therapeutic keratectomy (ALTK) microkeratome system



Fig. 51: Moria automated lamellar therapeutic keratectomy microkeratome system



Fig. 53: DSAEK spatula (Stripper)



Fig. 52: Moria artificial chamber maintainer



Fig. 54: Busin glide

utilizes the CBm microkeratome and an artificial chamber which is manually driven by the surgeon. Multiple microkeratome heads may be used to achieve dissection of various thicknesses ranging from 130 to 350 (130, 150, 250, 300, 350 micrometer). The Moria ALTK artificial anterior chamber requires a donor scleral rim that is symmetrically greater than 16 mm (max 19 mm) in diameter to provide proper vacuum during the microkeratome pass. The surgical time is greatly reduced as compared to manual dissection technique (**Figs 51 and 52**).

DSAEK Spatula (Stripper)

It is designed to strip the recipient's Descemet's membrane during the DSAEK procedure. The DSAEK strippers, made of surgical steel, are available in 45 and 90 degrees angled models, in both irrigating and nonirrigating versions. The angled tips facilitate the efficient dissection

and removal of Descemet's membrane without inadvertent damage to the stroma (**Fig. 53**).

Busin Glide

It allows insertion of the taco by pull through technique through 3.2 mm incision. It facilitates the unfolding of the graft and simplifies centration of the donor button in the anterior chamber. It helps to minimize intraoperative manipulation of the graft and the possibility of endothelial loss (**Fig. 54**).

DSAEK Busin Forceps

It is a microincision forceps with 20G diameter and distal action. It is designed to position the graft in the glide and to pull it from the glide into the anterior chamber. Its tips have been specifically designed to contact the periphery of the graft such that the endothelial and the stromal surfaces remain untouched in the optical zone.

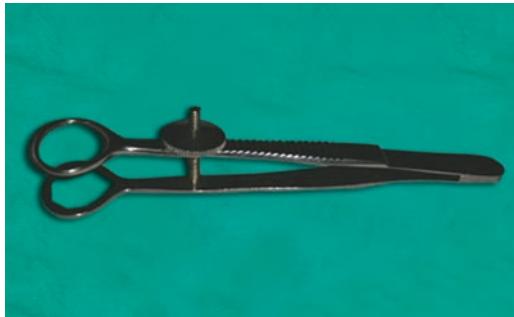


Fig. 55: Chalazion clamp



Fig. 57: Jaeger's lid spatula



Fig. 56: Chalazion scoop



Fig. 58: Lid clamp or Snellen's entropion clamp

Lid Surgery

Chalazion Clamp

It consists of a circular disc attached to a circular rim attached to each other with the help of a handle that can be tightened with a screw. The disc side is placed toward the skin while the rim is placed towards the conjunctiva. It is available in various sizes from 10 mm to 21 mm. It is used to stabilize the lid and chalazion, and also provides hemostasis while performing incision and curettage of the chalazion (**Fig. 55**).

Chalazion Scoop

It has a small cup with sharp margins attached to a narrow handle. It is used to scoop out the contents of chalazion during incision and curettage (**Fig. 56**).

Jaeger Lid Spatula

It is a simple metal plate having a slightly convex surface on both ends. It is used to support the lid,

as well as protect the globe during lid surgeries such as entropion, ectropion, ptosis, etc. (**Fig. 57**).

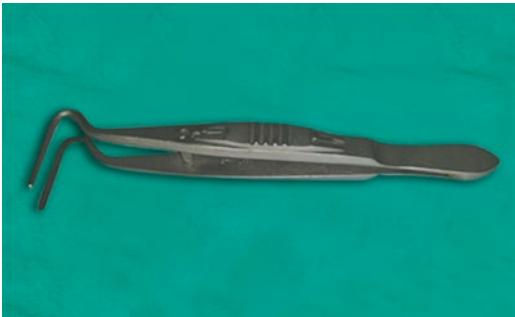
Lid Clamp or Snellen's Entropion Clamp

It has a D-shaped plate attached to a U-shaped rim which when tightened with the help of a screw clamps the tissue and provides hemostasis. There are separate clamps for the right and left eye. The plate is placed on the conjunctival side while the rim is placed on the skin side and the handle is always directed temporally (**Fig. 58**).

It offers the advantage of being self-sustaining and providing hemostasis. The disadvantage is that it reduces the surgical field and can cause pressure necrosis of the tissue, if applied too tightly. It is used in lid surgeries such as ectropion and entropion to stabilize the lid, protect the eyeball and provide hemostasis.

Berke's Ptosis Clamp

It is a clamp with J-shaped end with internal serrations. It has a locking mechanism as well.

**Fig. 59:** Berke's ptosis clamp**Fig. 61:** Bowman lacrimal probe**Fig. 60:** Nettleship's punctum dilator**Fig. 62:** Freer periosteal elevator

It is used to hold the levator palpebral superioris muscle during ptosis surgery (**Fig. 59**).

Crawford's Fascia Lata Stripper

It is used in ptosis surgery for harvesting the fascia lata. It has a proximal slot for holding the fascia lata and has the advantage of harvesting the tissue through a small incision.

Lacrimal Sac Surgery

Nettleship Punctum Dilator

It has a conical pointed tip and is used to dilate the puncta prior to probing or syringing. It is available in multiple sizes corresponding to the probe sizes (**Fig. 60**).

Bowman Lacrimal Probe

It is available in sizes ranging from 0000 to 4 with size 0=1 mm diameter (**Fig. 61**).

Uses

- Probing the lacrimal canaliculi and naso-lacrimal duct to find the location of block
- DCR surgery
- Therapeutic probing in children.

Freer Periosteal Elevator

It has a concavoconvex end which is used to lift the periosteum and lacrimal sac from underlying fossa (**Figs 62 and 63**).

Thudichum Nasal Speculum

It is used for anterior rhinoscopy (**Fig. 64**).

Kerrison Bone Punch

It is available in various sizes ranging from size 0=1 mm to size 4=5 mm. It has a cutting end up or down design. It is predominantly used to create an ostium in DCR surgeries (**Fig. 65**).

Enucleation and Evisceration Surgery

Wells Enucleation Spoon

It is a spoon-shaped instrument with a central cleavage to engage the optic nerve during



Fig. 63: Lacrimal sac dissector and curette



Fig. 66: Wells enucleation spoon



Fig. 64: Thudicum nasal speculum



Fig. 67: Mule evisceration spatula



Fig. 65: Kerrison bone punch

enucleation procedure so that it can be easily cut with an enucleation scissor (**Fig. 66**).

Mule Evisceration Spatula

It consists of a handle with small but stout rectangular blade with convex surface and blunt edges at its distal end. It is used to separate the

uveal tissue from sclera in evisceration surgery (**Fig. 67**).

Evisceration Curette

It consists of a round cup with blunt margins attached to a handle. It is used to curette out the intraocular contents during evisceration surgery.

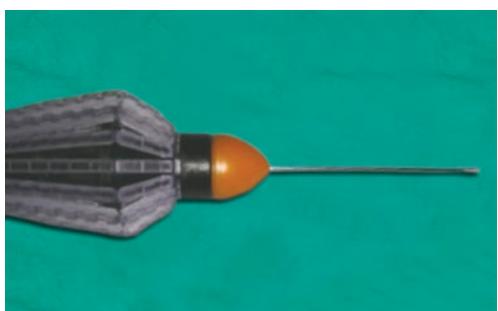
Vitreoretinal Surgery

Trocar and Cannula

Trocars are used to make pars plana sclerotomy entries. Trocar needle can be 20G/23G/25G/27G.

Microcannulas made up of polyimide, are preloaded on the needle trocars. Microcannula can be valved or nonvalved. Valved cannulas eliminate the need for plug placement while exchanging instruments or removing it.

Combined components of the trocar needle, microcannula, and trocar handle are referred to as the trocar-cannula assembly. This system

**Fig. 68:** Trocar**Fig. 70:** Vitrectomy cutter**Fig. 69:** Infusion cannula**Fig. 71:** End-grasping forceps

maintains the alignment between the entry holes in conjunctiva and sclera, as well as provides unobstructed instrument access (**Fig. 68**).

Infusion Cannula

Self-retaining infusion cannula of different sizes according to microcannula (20G/23G/25G/27G) are used to introduce irrigating solution into the vitreous cavity (**Fig. 69**).

Vitrectomy Cutter

Vitreous cutters utilize suction and inclusive shearing force to cut vitreous.

These can be of two broad types:

1. *Electrodynamic cutters:* It is heavy, becomes hot causing fatigue and exacerbates tremors.
2. *Pneumatic cutters:* It is light, so cause fewer tremors and are cheap.

Vitrectomy cutters are of three types based on the cutting mechanism:

1. *Cutters using rotating mechanism:* There is risk of vitreous spooling and traction on retina.

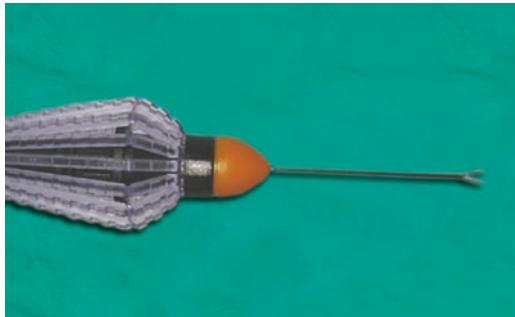
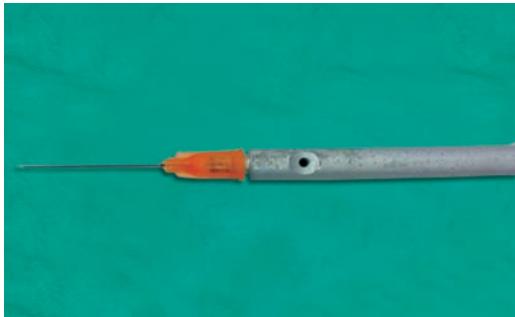
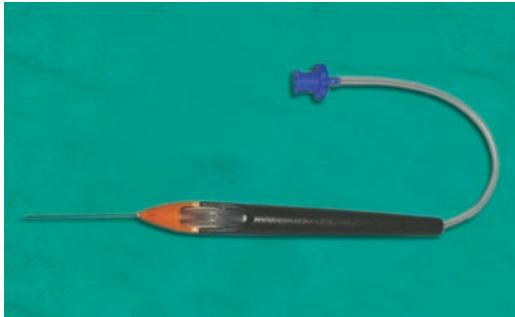
2. *Cutter using oscillating mechanism/Peyman type:* This type of cutter is considered to be superior to the first one as it has less shearing effect.
3. *The Guillotine type cutters:* It has an outer tube which is fixed and has an opening through which vitreous is aspirated. The inner tube slides across the port thus cutting the vitreous (**Fig. 70**).

End-grasping Forceps

These forceps have jaws at the tip to hold tissues at the edge only. The tips are fine and allow visualization of the tissue while grasping. These are used for epiretinal membrane peeling (**Fig. 71**).

ILM Forceps

These have fine tips with smaller jaws which help in picking up of delicate tissues like ILM. These are used for internal limiting membrane peeling in macular hole surgery (**Fig. 72**).

**Fig. 72:** ILM forceps**Fig. 74:** Charles flute needle**Fig. 73:** Foreign body forceps**Fig. 75:** Back flush

Serrated Forceps

These have large flat grasping blades without jaws, which help to attaining strong grip over tissues while managing proliferative vitreoretinopathy. These are used in tough epiretinal membrane peeling and retinal pucker release.

Foreign Body Forceps

These are large gauge forceps with serrated or diamond dusted tips for removal of intraocular foreign bodies. These have stout jaws which help in firm holding of the foreign bodies (Fig. 73).

Extrusion Instruments

Charles flute needle: It consists of a blunt needle attached to a detachable handle. It is used for controlled passive extrusion of fluid during internal drainage of subretinal fluid, removal of preretinal blood, and fluid-air exchange. Internal channel leads to an exit port on the side of handle.

Egress of fluid occurs when cannula tip is in fluid and exit port is open, driven by infusion pressure which is above the atmospheric pressure. The blunt tip can be replaced with a soft silicone tip needle as well which decreases the risk of iatrogenic retinal damage (Fig. 74).

Backflush is a modified flute handle with large silicone reservoir. Pressure on this reservoir leads to retrograde flushing of the fluid or accidentally aspirated/incarcerated tissues. It can also be used to disperse sedimented preretinal bleed. It can be used with either blunt or soft tip needle (Fig. 75).

Cannula

Cannula tips can be of several types:

- **Silicone brush tip cannula:** The soft silicone brush tip allows gentle brushing and manipulation of the retina. These are excellent for manipulation and removal of blood from the retina surface.



Fig. 76: Soft silicone tip cannula



Fig. 77: Diamond-dusted membrane scraper

- *Diamond dusted soft silicone tip cannula:* These are used for triamcinolone removal.
- *Charles flute cannula:* This helps to aspirate blood and debris from the posterior segment. Smooth, finished tip provides atraumatic entry and reduces risk of trauma to surrounding tissue.
- *Soft silicone tip cannula:* The soft flexible tip on the cannula provides atraumatic entry through retinal or macular tears or holes. These are used for fluid-fluid or fluid-air exchange in vitrectomy surgery (**Fig. 76**).
- *Dual bore cannula:* Simultaneous infusion of heavy liquids and aspiration of intraocular fluids with dual bore cannula helps to control constant intraocular pressure during injection. Cannula can be connected to flute handle or backflush handle or active extrusion handle.

Diamond-dusted Membrane Scraper

Tano diamond dusted membrane scraper (DDMS) helps to find the edge of the epiretinal membranes. It is made of tongue shaped soft silicone with inert diamond dust. Perfectly suited for both internal limiting membrane (ILM) and epiretinal membrane (ERM) removal, the diamond dusted, soft silicone tip helps in finding and grasping the edge of the membrane quickly and easily (**Fig. 77**).

Vitreoretinal Scissors

Horizontal scissors are used for delamination during epiretinal membrane removal. Their cutting edge moves conformal to the retinal surface.



Fig. 78: Vitreoretinal scissors

Their blades can have a gentle curve or can be straight, with angle of 30 or 45° to the shaft.

Vertical scissors have vertical blades with pointed tips that move along the axis of shaft.

Proximal blade moves down toward the fixed distal blade to cut the tissue vertically. These are used for epiretinal membrane segmentation (**Fig. 78**).

Gass Retinal Detachment Hook

Used for localization of retinal breaks onto the sclera in retinal detachment surgery (**Fig. 79**).

Magnets

These are used to remove magnetic intraocular foreign bodies. Electromagnets are more powerful than rare earth magnets (REM) and their magnetic force can be varied but they are used only as



Fig. 79: Gass retinal detachment hook



Fig. 81: Schocket scleral depressor



Fig. 80: Magnets

external magnets. Rare earth magnets are available for both intra-ocular and extraocular use (**Fig. 80**).

Schocket Scleral Depressor

It has a rounded end designed for depressing the sclera, and a curved marking end for reaching behind the globe (**Fig. 81**).

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