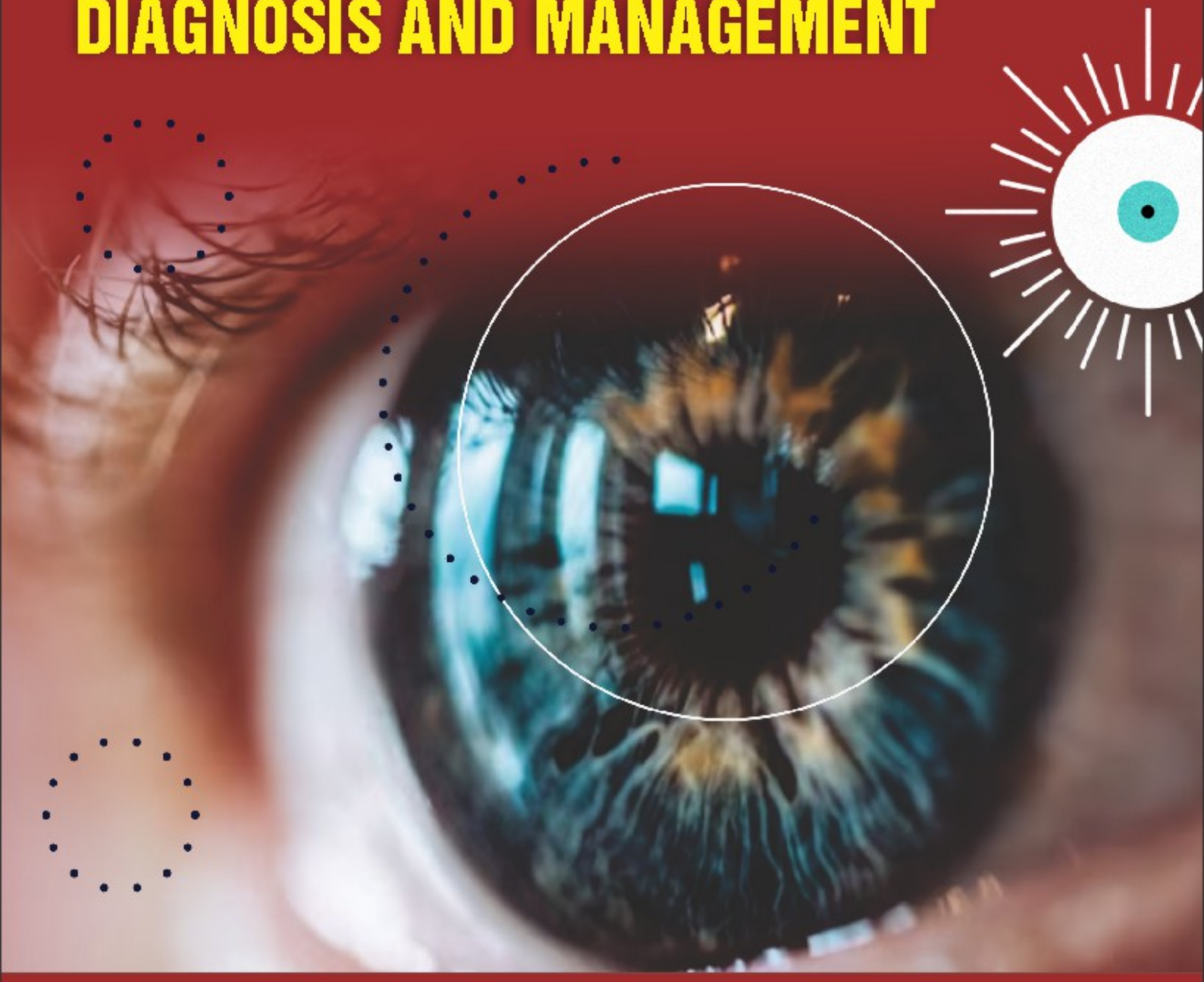
COMMON EYE DISEASE, DISORDERS, DIAGNOSIS AND MANAGEMENT



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Government of Uttar Pradesh

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Processed and Realization

COMMON EYE DISEASE, DISORDERS, DIAGNOSIS AND MANAGEMENT


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MESSAGE

SHRI BRIJESH PATHAK

Shri Brijesh Pathak,
Hon'ble Deputy Chief Minister
Minister of Medical Health and
Family Welfare Department
Government of Uttar Pradesh

The State Health & Family Welfare Institute is playing an important role in enhancing the knowledge of doctors and paramedical staff to provide health services to the poor and common man in the community through continuing medical education. CMEs promote collaboration among healthcare professionals, creating valuable networking prospects.

Primary Health Centers (PHCs) and Community Health Centers (CHCs) serve as the first point of contact with qualified doctors in the public health sector. By implementing structured CME programs, these initiatives aim to upgrade the skills and knowledge of medical officers, thereby significantly improving patient care, fostering patient confidence, and increasing patient satisfaction.

Eyes are an important part of our body without which we cannot even imagine life. In this sequence, by increasing knowledge through continuous medical education for the prevention and treatment of eye infections and various types of disorders, we can cure the eyes of most of the patients.

The Uttar Pradesh government also has the same intention and commitment that all the people of Uttar Pradesh should get the best health treatment. CME will develop and strengthen strategies for "Eye Health" and prevention of visual impairment, provide high quality comprehensive eye care in all districts of Uttar Pradesh and strengthen the basic knowledge of human resources practitioners!

I congratulate the module prepared by the State Institute of Health and Family Welfare and the SIHFW team. I have no doubt that this module will prove to be an important toolkit for the medical officers in the provincial health medical services in Uttar Pradesh to support the well-being and treatment of eye patients. The well-being of patients will increase!

(Brijesh Pathak)


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MESSAGE

Shri Mayankeshwar Sharan Singh

Hon'ble State Minister
Medical Health and Family
Welfare Department
Government of Uttar Pradesh

I take great pride in the fact that the State Institute of Health & Family Welfare, Uttar Pradesh (SIHFW), is addressing the critical need for knowledge enhancement among Medical Officers in the Provincial Health & Medical Services in Uttar Pradesh through its Continuing Medical Education (CME) module focused on Common Eye Disorders, Diagnosis and Management.

Most people have eye problems at one time or another. Some are minor and will go away on their own or are easy to treat at home. Others need a specialist's care. A condition that affects any of the eye components such as cornea, iris, pupil, optic nerve, lens, retina, macula, choroid, conjunctiva or the vitreous. CME on eye disorders are essential to systematically impart recent knowledge and skills, thereby enhancing the existing proficiency of medical professionals.

This module aims to consolidate pertinent information in the domains of eye disorder and its treatment, encompassing screening, detection, referrals, and patient treatment. It is designed to serve as a practical resource that can be periodically reviewed and updated based on the experiences gained from implementing public health services.

In light of these efforts, SIHFW has developed a CME module specifically focused on common eye disorders diagnosis and management for Medical Officers in Provincial Health & Medical Services in Uttar Pradesh. I hope that this CME module is just the beginning of a series of initiatives that will assist our Medical Officers in staying current with intervention practices.

I extend my best wishes to the director and the dedicated team at the State Institute of Health & Family Welfare (SIHFW) in Lucknow, Uttar Pradesh, in their mission to contribute to an improved healthcare delivery system through Continuing Medical Education, especially in the areas of Ophthalmology.

(Mayankeshwar Sharan Singh)


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MESSAGE

Shri Partha Sarthi Sen Sharma

Principal Secretary
Department of Medical, Health
and Family Welfare
Government of Uttar Pradesh

The Continuing Medical Education (CME) module consists of educational activities which serve to maintain, develop, or increase the knowledge, skills, and professional performance and relationships that a physician uses to provide services for patients, the public, or the profession.

Medical officers at the primary level face numerous challenges in managing eye disorder treatments. Continuous improvement in knowledge and skills is essential to effectively address these challenges. However, due to their responsibilities in overseeing healthcare centers and implementing government policies, medical officers have limited time available for learning.

To tackle and rectify this situation, the State Institute of Health & Family Welfare (SIHFW) in Uttar Pradesh has designed a specialized CME module focusing on eye disorder and its treatment for Medical Officers in the Provincial Health & Medical Services. This module has been developed in collaboration with experts in the field.

The module offers a comprehensive overview of common eye disorders and their management. Its primary objective is to enhance the expertise and knowledge of Medical Officers, ultimately leading to an enhancement in healthcare services for the general population.

I want to extend my congratulations to SIHFW team and the other subject matter experts who played a role in crafting this comprehensive module. I am optimistic that this CME module will shed light on the treatment of eye disorder, contributing to improved Ophthalmology outcomes.

(Partha Sarthi Sen Sharma)


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MESSAGE

Dr. Brijesh Rathor
Director General
Medical and Health Services
Uttar Pradesh

Continuing Medical Education (CME) modules provide a means for healthcare professionals to stay abreast of the swiftly evolving practices in the field of Ophthalmology. Particularly in the realm of the common eye disease, disorders, diagnosis and management module, it has become increasingly essential for medical officers to stay updated on treatment methods and management approaches.

Medical officers operating at the primary healthcare level encounter numerous challenges in effectively handling cases involving eye disease and disorders. Ongoing acquisition of knowledge and skills is imperative to tackle these challenges. However, due to their responsibilities in managing healthcare facilities and implementing government policies, medical officers have limited time for further education and skill development.

To address and rectify this situation, the State Institute of Health & Family Welfare (SIHFW) in Uttar Pradesh has formulated a specialized CME module centered on the treatment of common eye disease, disorders for Medical Officers in the Provincial Health & Medical Services in Uttar Pradesh. This module incorporates the common eye disorders, timely diagnosis and management of which can decrease the load of preventable blindness in our country. Its primary objective is to enhance the expertise and knowledge of Medical Officers, leading to an improvement in healthcare services for the population.

I want to extend my congratulations to SIHFW team and the subject matter experts who played a role in creating this comprehensive module. I am hopeful that this CME module will shed light on the effective diagnosis and management of Common eye disease, disorders.

(Dr. Brijesh Rathor)


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MESSAGE

Dr. Shailesh Kumar Shrivastava

Director General Family Welfare,
Directorate of Family Welfare
Uttar Pradesh

Common eye disease, disorders, diagnosis and management is very important in saving lives and serious eye disease and disorder. The reaching of an effected patient to a center which has facilities for treatment of eye disease helps in saving lives and physical impairment.

To meet the specific needs of Medical Officers in the Provincial Health & Medical Services of Uttar Pradesh, the State Institute of Health & Family Welfare (SIHFW) has designed an extensive Continuing Medical Education (CME) program centered on common eye disorders and their management. This program encompasses the latest advancements in the field and offers detailed guidance on essential management approaches for these conditions at the primary level. The objective is to facilitate early screening, detection, referrals, and treatment of patients.

Upon completion of this CME program, it is anticipated that Medical Officers in Uttar Pradesh will be able to elevate their service delivery through proficient screening, effective case management, appropriate referrals, and provision of treatment within their healthcare facilities. Consequently, communities will enjoy enhanced access to healthcare services, heightened patient satisfaction, and improved overall population health. This CME program not only enriches clinical and technical proficiency but also reinforces the delivery of healthcare services, bridging the gap between theoretical knowledge and practical application in healthcare management.

We extend our warmest wishes to the SIHFW team and look forward to the release of many more customized CME modules in the times ahead.

(Dr. Shailesh Kumar Shrivastava)


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MESSAGE

Dr. Narendra Agarwal

Director General (Training)
Medical Health and Family Welfare
Uttar Pradesh

The effective management of Common eye disease, disorders, diagnosis and management is pivotal in preserving lives and preventing serious eye health complications.

This module on Continuing Medical Education (CME) on common eye disorders and their treatment for Medical Officers in Provincial Health & Medical Services in Uttar Pradesh provides a coherent and research-based insight to ophthalmological management. It has been designed and written for Medical Officers and healthcare professionals and takes government perspective in consideration, drawing upon and comparing ideas and developments from national and international health care practices.

Medical Officers in Uttar Pradesh will be able to scale up the services delivery in provide screening, management, referral and treatment in ophthalmological care after this CME, thus benefitting communities. In addition to improving clinical and technical area of expertise, this CME will lead to providing improved access to eye disease and disorder services and enhancing patient satisfaction and population health.

The director and the team at State Institute of Health & Family Welfare, Uttar Pradesh and the team of experts of the field has done a commendable job by publishing this CME module on common eye disease, disorders, diagnosis and management for Medical Officers in Provincial Health & Medical Services in Uttar Pradesh. I hope the participants coming to attend their upcoming CME will take advantage of this initiative and make the most in their field with this handy module.

(Dr. Narendra Agarwal)


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MESSAGE

Dr. Rajaganapathy. R
Director
State Institute of Health and Family Welfare
Uttar Pradesh

The primary goal of Continuing Medical Education (CME) is to ensure that Medical Officers engage in continuous learning and progression, ultimately leading to the delivery of optimal medical care for their patients. CME aims to assist Medical Officers in improving their performance in terms of patient care and satisfaction.

In the realm of healthcare, there has been a notable effort to underscore the importance of effectively managing common eye disorders among Medical Officers in Provincial Health & Medical Services. It has been observed that a lack of systematic management has led to numerous unfortunate outcomes. Therefore, there is a need for a customized CME program tailored to equip Medical Officers in Uttar Pradesh with exposure to the common eye disorders and their management.

I hope that after this CME, Medical Officers in Uttar Pradesh will be able to scale up the services delivery in provide screening, management, referral and treatment in ophthalmic care, thus benefitting communities. In addition to improving clinical and technical area of expertise, this CME will lead to providing improved access to eye disease and disorder treatment services and enhancing patient satisfaction and population health.

To achieve this objective and enhance knowledge, the research and training faculty at the State Institute of Health and Family Welfare (SIHFW), Uttar Pradesh, in collaboration with the assistance of Professor Apjit Kaur, Professor Sandeep Saxena, Dr Nibha Mishra and their team, King George's Medical University (KGMU) in LUCKNOW, has contributed to the development of this CME module. It is expected that this module will be widely distributed, and feedback on its effectiveness will be gathered in the coming months.

(Dr. Rajaganapathy. R)


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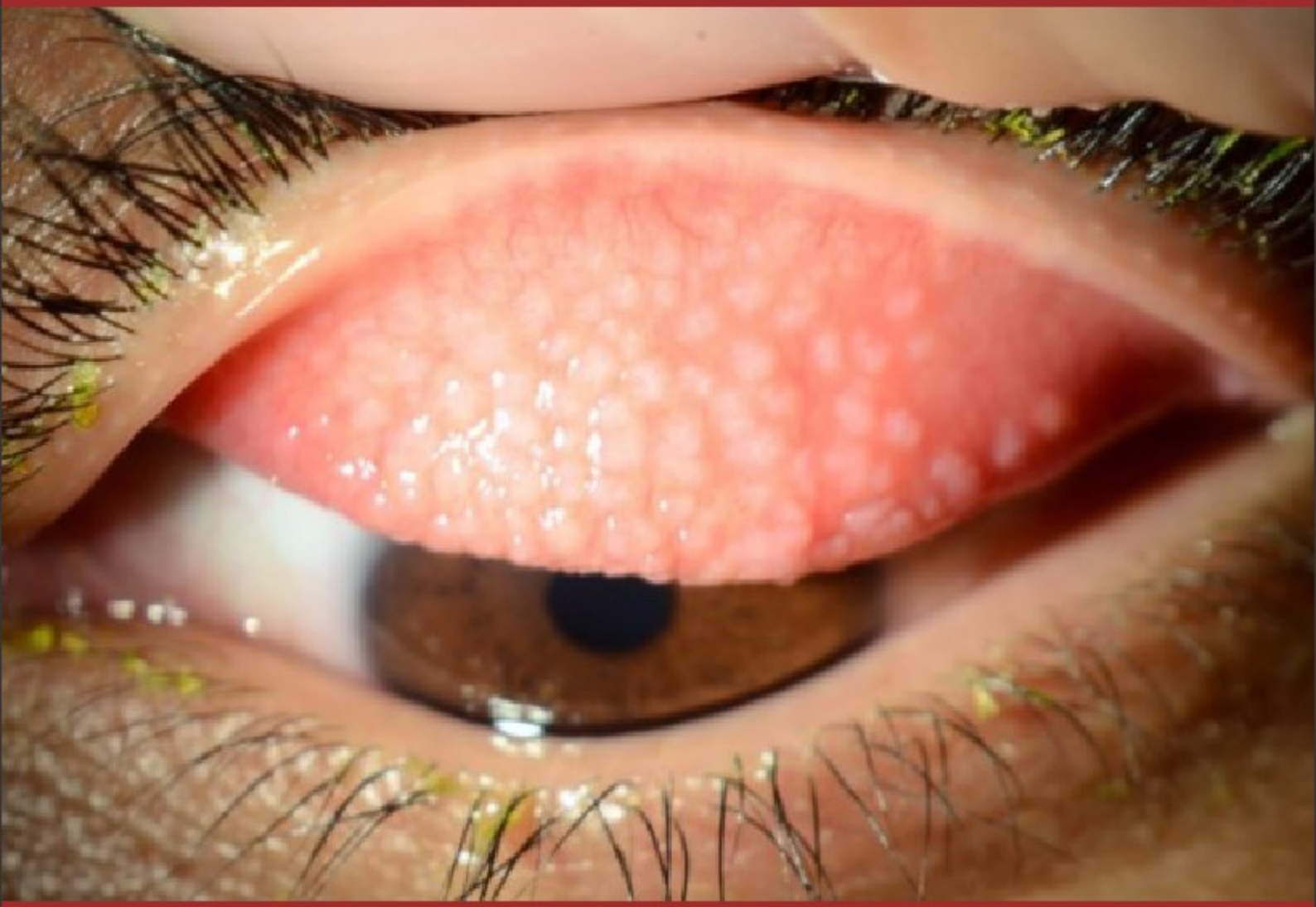
CHAPTER 1



COMMON DISORDER OF CONJUNCTIVA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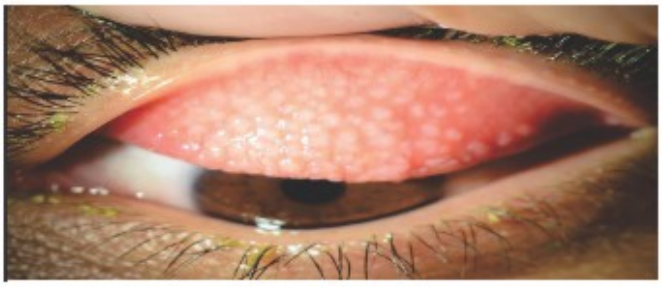


Common Disorders of the Conjunctiva

Introduction

A pterygium is a fibrovascular, wing-shaped encroachment of the conjunctiva onto the cornea. Histopathology shows hyaline degeneration with elastotic proliferation.

Risk factors

Exposure to ultraviolet light[i]

Environmental microtrauma to the ocular surface

A localized limbal stem cell dysfunction

Genetic predisposition

Pathogenesis

Pterygium pathogenesis can be considered as occurring in two stages: the initial disruption of the limbal corneal-conjunctival epithelial barrier, and the progressive □conjunctivalization□ of the cornea

Coronea MT proposed that pterygium occurs due to albedo concentration in the anterior eye (albedo's hypothesis). Light entering the temporal limbus at 90 degrees is concentrated at the medial limbus and this is responsible for the predominance of medial pterygia[ii]

Presentation

Incidental finding

Patients may present with repeated episodes of redness, pain, and watering due to inflammation of the pterygium,

Diminution of vision caused by encroachment of the pterygia onto the pupillary axis or high astigmatism

High resolution anterior segment optical coherence tomography can be used to differentiate pterygia from ocular surface squamous neoplasia (OSSN). In pterygia, the epithelium is of normal thickness with underlying sub epithelial fibrosis.

In comparison in OSSN, the epithelium will appear thickened and hyper-reflective with an abrupt transition from normal epithelium[iii]

Treatment

The following are considered indications for the surgical treatment of a pterygium

1. Encroachment upon the pupillary area causing visual disturbance.
2. Recurrent inflammation.
3. Restriction of ocular movement, with diplopia
4. Cosmetic reasons

Surgical

1. Excision with simple closure of the wound.
2. Mc Gavics bare sclera method: wherein the pterygia is excised and the conjunctival defect is left as it is.

In order to reduce recurrence rates, the use of beta irradiation and thiotepa were considered to reduce the occurrence of the fibroblastic recurrence response.

Excision together with adjunctive therapies such as mitomycin C or 5-fluorouracil can reduce the risk of recurrence to approximately 10%.[iv] However, the use of mitomycin C and 5-fluorouracil can increase the risk of corneal or scleral melt postoperatively[v]

Current Surgical options:

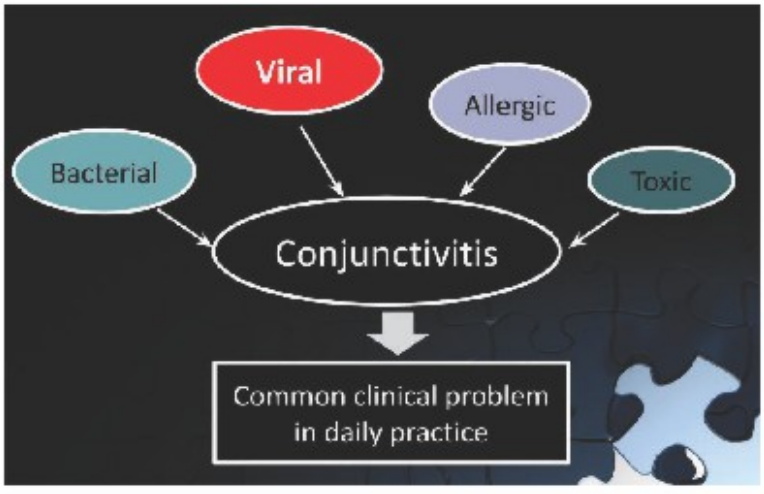
1. Conjunctival-limbal autograft
2. Conjunctival autograft
3. Conjunctival rotational autograft
4. Mitomycin C
5. Mitomycin C + Conjunctival or Conjunctival-limbal autograft
6. Amniotic membrane transplantation
7. Use of fibrin glue with Conjunctival or Amniotic membrane transplants
8. Lamellar keratoplasty in conjunction with pterygium surgery

Surgical options for the Future:

1. Use of intralesional bevacizumab injections □ as an adjunct to surgery Bevacizumab eye drops or subconjunctival injections for treatment of recurrences
2. Conjunctival cultures on Amniotic membrane

Conjunctivitis

Inflammation of conjunctiva characterized by cellular infiltration, vascular dilation and exudation



Allergic Conjunctitvis

They include milder forms like seasonal and perennial allergic conjunctivitis as well as severe forms like vernal and atopic which can be sight-threatening.

Vernal Keratoconjunctivitis - Important Points We Should REMEMBER

- ✓ Vernal keratoconjunctivitis (VKC) is a bilateral, chronic, usually seasonal, recurrent allergic inflammation of the conjunctiva.
- ✓ It mainly affects young boys living in tropical countries
- ✓ Vernal keratoconjunctivitis is type 1 along with a type 4 hypersensitivity reaction

- ✓ Itching is the foremost symptom with which the patient presents along with watering, photophobia, mucoid ropy discharge, blepharospasm, and foreign body sensation.
- ✓ 3 distinct forms of the disease: tarsal (giant cobblestone papillae in the tarsal conjunctiva), limbal (gelatinous limbal infiltrates) and mixed (has features of both tarsal and limbal forms).
- ✓ A personal or family history of atopy is seen in a large proportion of VKC patients[vi]
- ✓ One can find papillary reaction on the tarsal plate with papillae, more frequently in upper than lower or gelatinous limbal hypertrophy.
- ✓ In 1910, Trantas characterized the spectrum of corneal changes seen in VKC[vii]. Aggregates of epithelial cells and eosinophils at the limbus called the Horner Tranta□s dots and conjunctival hyperemia also indicate an active stage of the disease.
- ✓ Corneal involvement includes superficial punctate keratopathy, shield ulcers, and neovascularization.

In the chronic stage of the disease pseudogerontoxon, subconjunctival fibrosis, corneal scarring, keratoconus, and limbal stem cell deficiency have been reported.

Treatment: Management of patients with vernal keratoconjunctivitis has 2 arms: disease and treatment-related.

- Aims of managing the disease-related arm includereducing the frequency of active episodes and
- preventing or curtail the occurrence of complications.

Grade of VKC	Treatment Plan
Grade 0 (Quiescent)	No Treatment
Grade 1 (Mild Intermitted)	Occasional Anti- allergic drops
Grade 2 (Moderate) A) (Intermittent) B) (Persistent)	Daily administration of dual-action anti allergic drops + pulsed topical steroids + Cyclosporine A eye drops
Grade 3 (Severe)	Daily administration of dual-action anti allergic drops + pulsed topical steroids + Cyclosporine A eye drops
Grade 4 (Very Severe)	Daily administration of dual-action anti allergic drops + pulsed high dose topical steroids + Cyclosporine A eye drops

Difference between atopic and vernal conjunctivitis

Features	VKS	AKC
Age of Onset	Childhood/ teens	20-50 years
Duration	Resolved in mid-late teens	Resolved by 50 years
Seasonal Variation	Markedly worse in spring	Variable, worse in winter
Conjunctival papillae	GPC, mainly upper lid	Small/ medium, mainly lower lid
Conjunctival scarring	Uncommon	Symblepharon common
Skin	Uncommon	Often*
Eosinophils	Numerous	Less and less often degranulated
Corneal involvement	Less extensive	More extensive*

Bacterial Conjunctivitis

Etiology

Acute bacterial conjunctivitis -Staphylococcus aureus, Streptococcus pneumoniae, and Haemophilus influenzae. These organisms may be spread from hand to eye contact or through adjacent structure as nasal mucosa.

Hyperacute conjunctivitis -Neisseria gonorrhoeae, transmitted through sex

Chronic conjuctivitis -Chlamydia trachomatis

Risk Factors

- Poor hygenic habits
- Poor contact lens hygiene
- Crowded living or social conditions such elementary schools, military barracks etc
- Ocular diseases including dry eye, blepharitis etc
- Chronic use of topical medications
- Immunocompromised individuals

Diagnosis Symptoms

- Red eye
- Discharge: Classically purulent, but may be thin or thick, muco-purulent or watery
- Irritation, burning, stinging, discomfort
- Tearing
- Fluctuating or decreased vision

Signs

- Bulbar conjunctival injection
- Palpebral conjunctival papillary reaction
- Muco-purulent or watery discharge
- Chemosis
- Lid erythema

Viral V/S acute bacterial are as follows:

- Follicular reaction
- Pre-auricular lymphadenopathy
- Watery discharge
- Itchy eyes
- Concurrent pharyngitis, fever, and upper respiratory infection
- A history of prior conjunctivitis

On the other hand, a history of mucopurulent discharge with "gluing" of the eyelids in the morning is predictive of bacterial conjunctivitis.

Management

Almost all cases of acute bacterial conjunctivitis are self-limited

Antibiotic treatment has been known to decrease the duration of symptoms and speed the eradication of microorganisms from the conjunctival surface.

General treatment

Bacterial conjunctivitis is a contagious condition, so patients are instructed for proper hygiene and hand washing.

Supportive therapy for conjunctivitis consists of cool compresses and preservative free artificial tears two to six times daily.

Topical steroids should be avoided because of the risk of potentially prolonging the course of the disease and potentiating the infection.

However, Holland et al. showed that these perceived risks are associated with long-term steroid uses that are dissimilar to applications for infective conjunctivitis[vii]

Medical therapy

The most common antibiotics used for acute bacterial conjunctivitis are as follows:

- **Fluoroquinolones:**
  - ✓ 2nd generation: Ciprofloxacin 0.3% drops or ointment, or Ofloxacin 0.3% drops
  - ✓ 3rd generation: Levofloxacin 0.5% drops
  - ✓ 4th generation: Moxifloxacin 0.5% drops, Gatifloxacin 0.5% drops, or Besifloxacin 0.6% drops
- **Aminoglycosides:**
  - ✓ Tobramycin 0.3% drops
  - ✓ Gentamicin 0.3% drops

For Neisseria gonorrhoeae and Chlamydia trachomatis, systemic antibiotics are necessary as follows:

- **Chlamydia:**
  - ✓ Macrolides: Azithromycin (1gm single dose) or Erythromycin
  - ✓ Tetracyclines: Doxycycline or Tetracycline (Avoid in pregnant, nursing mothers)
  - ✓ Children less than or equal to 45 kg : Erythromycin 50 mg/kg/day PO divided into four doses daily for 14 days

- **Neisseria gonorrhoeae:**
  - ✓ Ceftriaxone 250mg Intramuscular injection once + Azithromycin 1 gram PO once.
  - ✓ Doxycyline 100mg PO BID for 7 days
  - ✓ For cephalosporin allergy, Azithromycin 2g PO once
  - ✓ For Children < 18 years old: Ceftriaxone 125mg IM once OR Spectinomycin 40mg/kg IM once (max dose 2grams)

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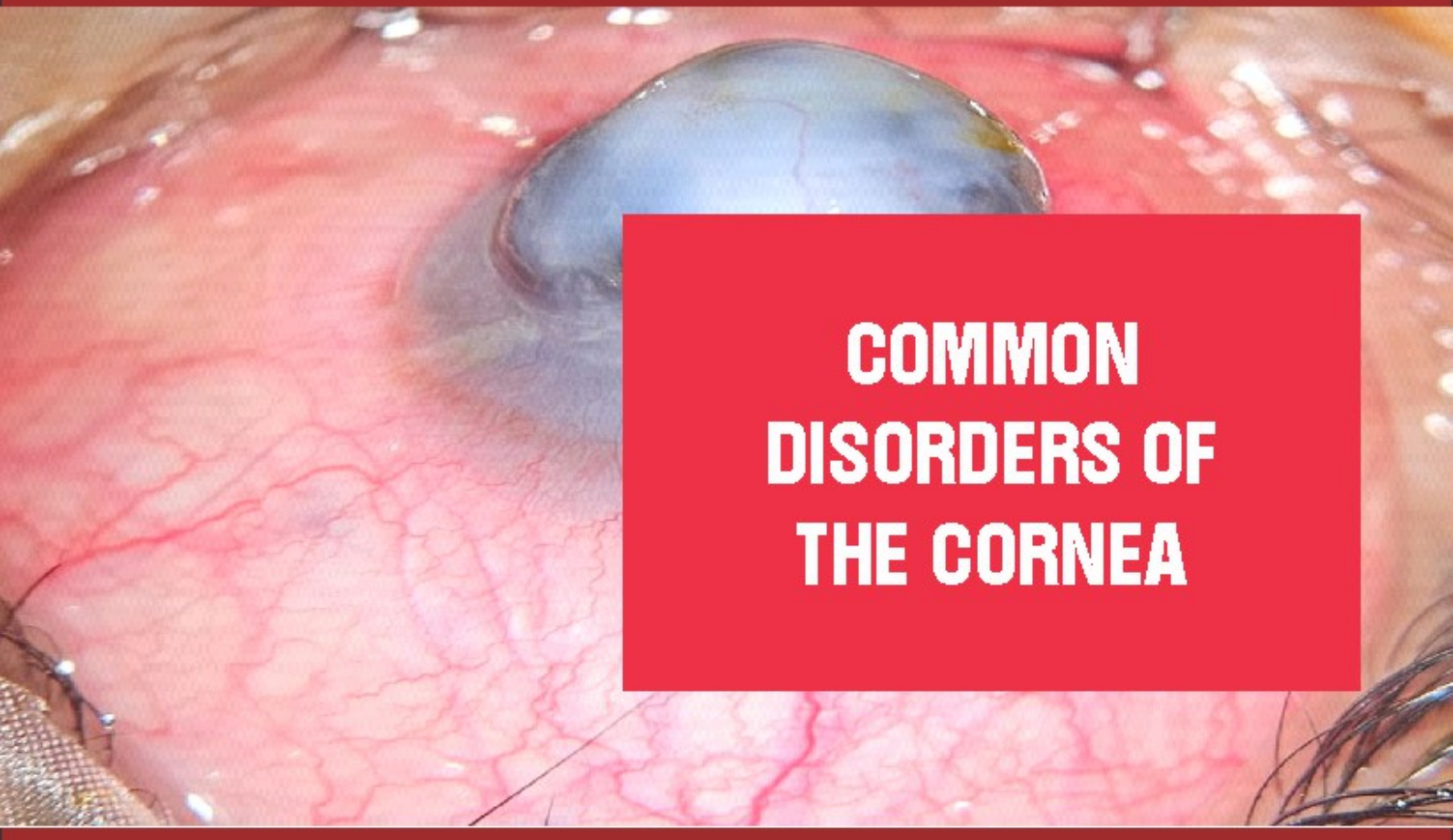
CHAPTER 2



COMMON DISORDERS OF THE CORNEA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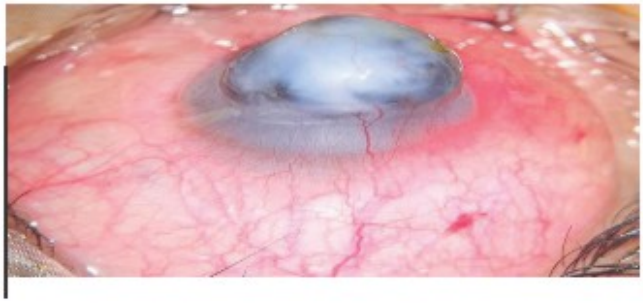


Common Disorders of the Cornea

Introduction

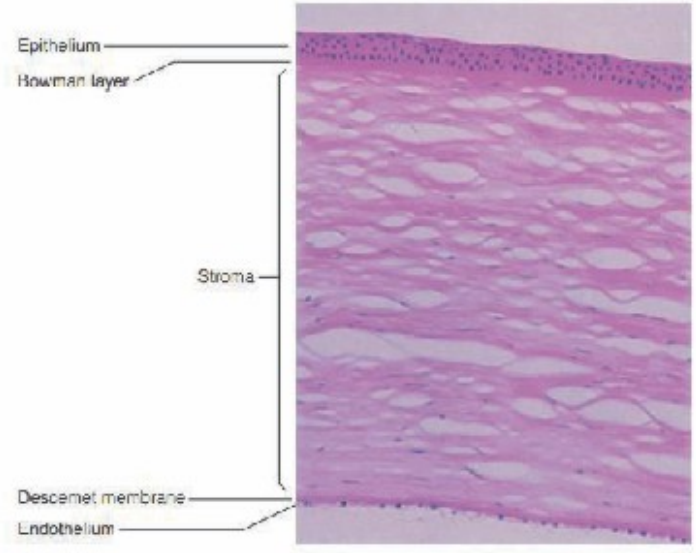
Anatomy and Physiology

The cornea is a complex structure that not only protects the eye but also contributes to about 75% of its optical power. The first division of the trigeminal nerve provides nerves to the subepithelial and deeper stromal layers of the cornea.

The cornea is a transparent, avascular tissue consisting of 5 layers (Figure 1):

- The epithelium is stratified, squamous and non □keratinized.
- The stroma constitutes 90% of corneal thickness, featuring well-organized collagen fibril layers separated by a proteoglycan matrix and modified fibroblasts called keratocytes. Maintaining collagen's orderly arrangement is vital for clear vision.
- Descemet membrane is a distinct sheet of fine collagen fibrils, separate from stromal collagen. It has regenerative potential.
- The endothelium is a single layer of polygonal cells responsible for maintaining corneal hydration. These cells do not regenerate, and when their density falls to around 500 cells per square millimetre, corneal edema occurs, reducing transparency.

- The existence of a proposed sixth corneal layer, the Dua layer, between the stroma and Descemet membrane, is debated, with some experts considering it a continuation of the posterior stroma.



Signs of Corneal Disease

SUPERFICIAL	DEEP
Punctate epithelial erosions (PEE) (Figure 2A)	Infiltrates
Punctate epithelial keratitis (PEK)	Suppurative keratitis
Subepithelial infiltrates	Ulceration
Superficial punctate keratitis	Melting
Filaments	Deep neovascularisation
Epithelial edema	Striate keratopathy (Figure 2C)
Superficial neovascularization (Figure 2B)	Descemetocele (Figure 2D)
Pannus	Corneal perforation

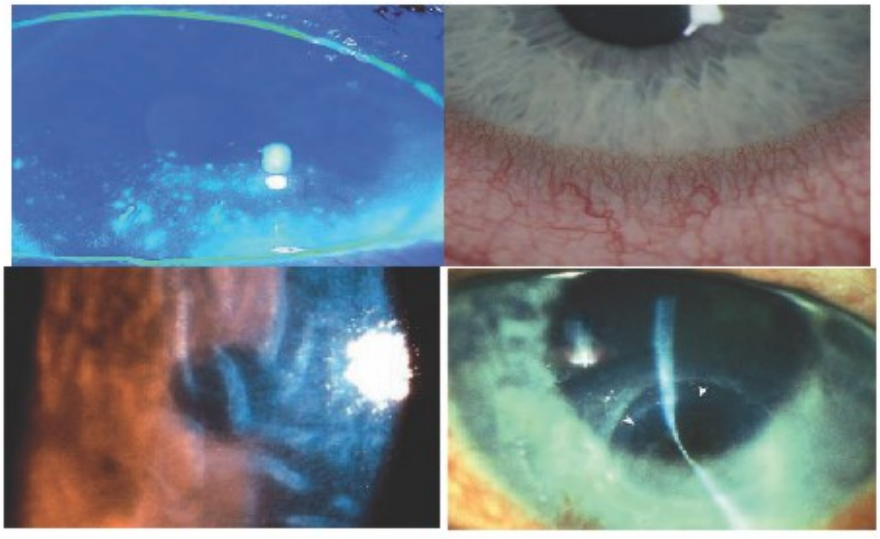


Figure 2 Signs of corneal disease (A) Punctate epithelial erosions stained with fluorescein in dry eye; (B) superficial vascularization; (C) Descemet□s membrane folds; (D) Descemetocele (arrowhead) (Courtesy of C Barry □ figs C)

BACTERIAL KERATITIS

Pathogenesis

Bacterial keratitis typically occurs when ocular defences are compromised. However, certain bacteria like Neisseria gonorrhoeae, Neisseria meningitidis, Corynebacterium diphtheriae, and Haemophilus influenzae can penetrate a healthy corneal epithelium.

Common bacteria	Uncommon bacteria
Staphylococcus aureus	Neisseria spp
Staphylococcus epidermidis	Moraxella spp
Streptococcus pneumoniae and other Streptococcus spp	Mycobacterium spp
Pseudomonas aeruginosa (most common organism in soft contact lens wearers)	Nocardia spp
Enterobacteriaceae (Proteus spp, Enterobacter spp, Serratia spp)	Non□spore-forming anaerobes

	Corynebacterium spp

Risk Factors

Ocular:

- Lid abnormalities: Ectropion, Entropion, Trichiasis, Lagophthalmos
- Ocular surface abnormality: Chronic dacryocystitis, Aqueous/ mucous deficiency
- Compromised corneal epithelium: Contact lens, Trauma, post refractive surgery, Post viral infection
- Contaminated or inappropriate use of antibiotics/steroids

Systemic:

- Local or systemic immunosuppression: Vitamin A deficiency, diabetes mellitus, HIV, Prolonged ventilation, Cancer treatment
- Substance abuse

Signs

In bacterial keratitis, you typically see:

- an epithelial defect with a larger infiltrate (Figure 3A)
- significant conjunctival hyperaemia
- stromal edema
- Descemet membrane folds, and anterior uveitis
- might be accompanied by a hypopyon (pus in the anterior eye chamber) and posterior synechiae
- plaque-like keratic precipitates can appear on the endothelium near the affected area
- chemosis and eyelid swelling may be evident.

Severe ulceration could lead to descemetocele formation and, in cases of Pseudomonas infection, even perforation (Figure 3B) Scleritis may develop, particularly with severe perilimbal infection. Endophthalmitis is rare without perforation.

Improvement is usually characterized by reduced eyelid swelling, chemosis, a smaller epithelial defect, reduced infiltrate density, and fewer anterior chamber signs. Severe scarring and vascularization can occur, affecting vision due to opacification and irregular astigmatism.

Diminished corneal sensation may indicate neurotrophic keratopathy, especially without other major risk factors. Reduced sensation can also be seen in chronic surface diseases, herpetic keratitis, and prolonged contact lens wear.

It is essential to monitor intraocular pressure (IOP) regularly.

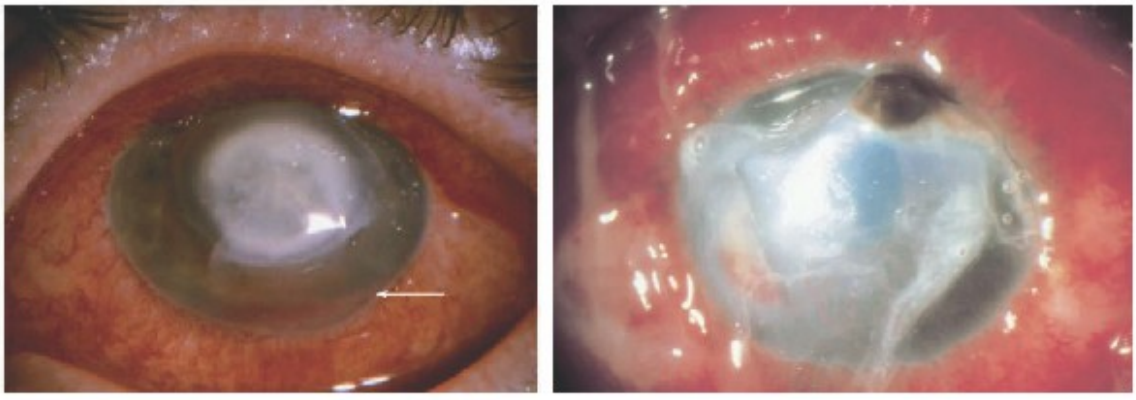


Figure 3 (A) Large Bacterial corneal ulcer (B) Peripheral corneal ulceration and perforation (Courtesy C Barry □ fig. A)

Investigations

- Corneal scraping
- Conjunctival swabs

- Evaluation of contact lens cases, solution bottles, and lenses
- Smears and Culture & Sensitivity report
- Corneal biopsy
- PCR

Commonly used stains and culture media for microbial keratitis

S. No.	Organism	Stain	Media
1	Aerobic bacteria	Gram Acridine orange	Blood agar Chocolate agar Thioglycolate broth
2	Anaerobic bacteria	Gram Acridine orange	Anaerobic blood agar Phenylethyl alcohol agar in anaerobic chamber Thioglycolate or chopped meat broth
3	Mycobacteria	Gram Acid-fast Lectin	Blood agar Lowenstein-Jensen agar
4	Fungi	Gram Acridine orange Calcofluor white	Blood agar (25°C) Sabouraud agar (25°C) Brain□heart infusion agar (25°C)
5	Acanthamoeba	Acridine orange Calcofluor white Gram Giemsa Indirect immunofluorescence antibody	Nonnutrient agar with bacterial overlay (Enterobacter aerogenes, Escherichia coli) Blood agar Buffered charcoal□yeast extract agar

Treatment

General:

- Consider hospitalization for patients who may not adhere to or cannot self-administer treatment

- Discontinuing contact lens wear and wearing a clear plastic eye shield between eye drop applications if there is significant thinning or a risk of perforation.

1. **Specific antibiotics**

Antibiotic monotherapy:

- A commercially available fluoroquinolone is typically chosen for empirical monotherapy, such as Ciprofloxacin or Ofloxacin.
- In areas with widespread resistance to earlier-generation fluoroquinolones, newer options like Moxifloxacin, Gatifloxacin, and Besifloxacin are preferred.
- Ciprofloxacin instillation can lead to white corneal precipitates, potentially delaying epithelial healing.

Empirical duo therapy:

- typically combines two fortified antibiotics □usually a cephalosporin and an aminoglycoside □ to cover common Gram-positive and Gram-negative pathogens. These fortified antibiotics are not commercially available and must be specially prepared.
- Drawbacks of fortified antibiotics include their high cost, limited availability, and the risk of contamination.

2. Anti-inflammatory and analgesics
3. Mydriatics (cyclopentolate 1%, homatropine 2% or atropine 1%) are used to prevent the formation of posterior synechiae and to reduce pain
4. Steroids reduce inflammation but can promote the growth of certain microorganisms. Steroids in corneal ulcer trial (SCUT) found no eventual benefit

in most cases, but severe cases (counting fingers vision or large ulcers involving the central 4 mm of the cornea) tended to do better.

5. Systemic Antibiotics are rarely needed except in severe infections with N. meningitidis, N. gonorrhoeae or H. influenzae and in cases with severe corneal thinning.
6. Cyanoacrylate glue
7. Bandage contact lens
8. Penetrating or deep lamellar keratoplasty should be considered for cases resistant to medical therapy and incipient perforation

FUNGAL KERATITIS

Introduction

Fungi are a group of microorganisms characterized by their rigid cell walls and a distinct nucleus containing both DNA and RNA.

Fungal keratitis is primarily caused by two types of fungi: yeasts, such as Candida, which are responsible for most cases in temperate climates, and filamentous fungi like Fusarium and Aspergillus, which are more common in tropical areas and can exhibit an aggressive course.

Yeasts	Molds (Filamentous)	
	Septate	Non-Septate
Candida spp	Fusarium spp	Mucor
Cryptococcus neoformans	Aspergillus	Rhizopus
Rhinosporadiumspp	Curvularia	Absidia

Predisposing Factors

- Chronic ocular surface diseases
- Prolonged use of topical steroids (often following corneal transplantation)
- Contact lens usage
- Systemic immunosuppression, and diabetes.
- Filamentous keratitis may be associated with minor ocular trauma, often involving plant matter or gardening tools and in immunocompetent hosts.

Clinical Features

The diagnosis of fungal keratitis is often delayed, as it can be initially mistaken for bacterial infection.

Symptoms include gradual onset of pain, a gritty sensation, sensitivity to light, blurred vision, and watery or mucopurulent discharge.

Signs:

- Candida keratitis is characterized by a yellow-white, dense, and purulent infiltrate, while filamentous keratitis typically presents with a gray or yellow-white stromal infiltrate with indistinct, fluffy edges. (Figure 4 A)
- Satellite lesions, feathery branch-like extensions, or a ring-shaped infiltrate (Figure 4 B)
- An intact Descemet membrane can be penetrated, leading to endophthalmitis without apparent perforation.
- Other associated features may include anterior uveitis, hypopyon, endothelial plaque, elevated intraocular pressure, scleritis, and sterile or infective endophthalmitis.
- Differential diagnosis: Bacterial, Herpetic, or Acanthamoeba keratitis

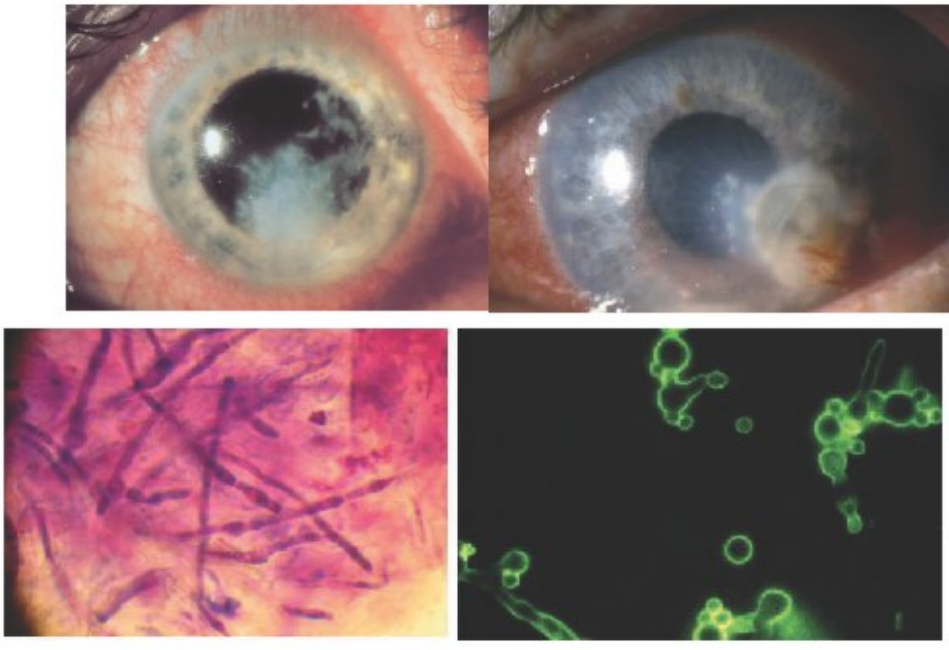


Figure 4 (A) Filamentous keratitis with characteristic dry-appearing, white stromal infiltrate with feathery edges. (B) Ring infiltrate (C) Septate hyphae of filamentous fungus (Fusarium solani). (Diff-Quik stain, original magnification ×100.) (D) Candida mycology stained with calcofluor white (Courtesy of Elmer Y. Tu, MD. Fig C)

Investigations

- Corneal scraping
- Staining techniques:
  - Light microscopy:
    - Potassium hydroxide (KOH) preparation
    - Gram staining
    - Giemsa staining
    - Grocott- Gomori Methenamine Silver (GMS) staining
  - Fluorescent microscopy: Calcofluor white (Figure 4 D)
- Culture on Sabouraud dextrose agar is necessary, but most fungi can also grow on blood agar or in enrichment media.
- Polymerase chain reaction (PCR) analysis of specimens is a highly sensitive (up to 90%) and rapid diagnostic method

- Corneal biopsy may be indicated if clinical improvement is not observed after a certain period.
- For unresponsive cases with endothelial exudate, an anterior chamber tap may be recommended.
- Confocal microscopy is very useful in detecting branching filaments and fungal septae

Treatment

- Improvement in fungal keratitis is typically slower compared to bacterial infections.
- Candida infection can be treated with amphotericin B or econazole, while filamentous infection is typically managed with natamycin or econazole.
- Broad-spectrum antibiotics may also be considered to address or prevent bacterial co-infections.
- Cycloplegia, as used in bacterial keratitis, is necessary.
- In severe cases, subconjunctival fluconazole may be administered.
- Systemic antifungals, such as voriconazole, itraconazole, or fluconazole, may be considered in severe cases, particularly when lesions are near the limbus or when endophthalmitis is suspected.
- Tetracycline, such as doxycycline, may be prescribed for its anti-collagenase effect when corneal thinning is significant.
- Cyanoacrylate glue, bandage contact lens and therapeutic keratoplasty are options considered if perforation occurs.

HERPES SIMPLEX KERATITIS

Introduction

Herpes simplex virus is the leading infectious cause of corneal blindness in developed nations. In developing countries, it may account for up to 60% of corneal ulcers, and approximately 10 million people globally are affected by herpetic eye disease.

Herpes Simplex Virus

Herpes simplex virus (HSV) is an enveloped virus with a cuboidal capsule and a linear double-stranded DNA genome. It has two subtypes: HSV-1 and HSV-2. HSV-1 typically causes infections above the waist, primarily on the face, lips, and eyes. In contrast, HSV-2 is responsible for sexually transmitted infections, such as genital herpes

Primary HSV infection: typically occurs in childhood when individuals have not been previously exposed to the virus. Most primary HSV infections are either mild or subclinical occasionally with mild blepharitis and follicular conjunctivitis.

Recurrent infection: Latent infection in the sensory ganglion with periodic subclinical reactivation various factors like stress, fever, hormonal changes, UV radiation, trauma, or trigeminal injury

Clinical features

- HSV Blepharitis: Focal clusters of vesicles around the lid margin
- HSV Conjunctivitis: Acute follicular with pseudo membranes

- Infectious Epithelial Keratitis: Punctate keratitis, dendrite, geographic (Figure 5 A, B)
- HSV Stromal Keratitis: Hypersensitivity reaction to fixed antigens within stromal keratocytes
- Disciform Keratitis: Endothelitis, Immune ring of Wessley (Figure 5C), reduced corneal sensations
- Neurotrophic Keratopathy: non-healing epithelial defect, recurrent epithelial erosions, persistent stromal ulceration, and perforation (Figure 5D)
- Iridocyclitis: raised IOP due to trabeculitis

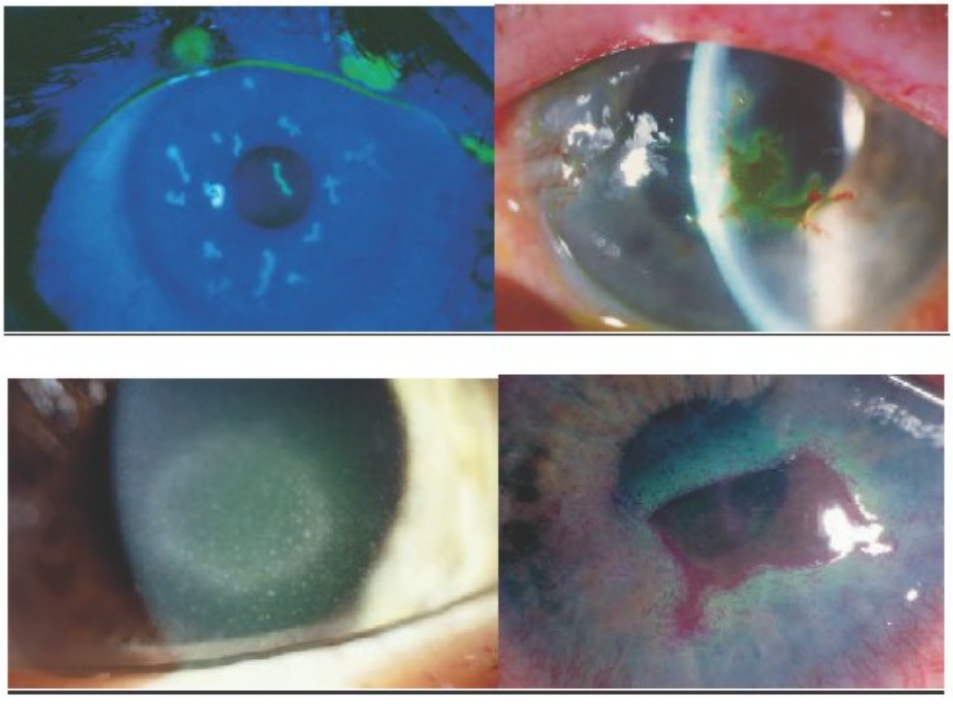


Figure 5 (A) Fluorescent staining in coarse dendritic epithelial HSV keratitis (B Combined fluorescein and rose Bengal staining of geographic HSV keratitis. (Courtesy of Cornea Service, Paulista School of Medicine, Federal University of São Paul (C) Wessely ring (D) Neurotrophic epithelial defect stained with rose Bengal (Courtesy of S Tuft)

Investigations

- Confocal microscopy
- Wright or Giemsa stain
- Viral Culture (Gold Standard)
- PCR
- ELISA
- Electron Microscopy

Treatment

Important Antiviral Agents in Corneal Infections with Herpes Simplex Virus

S. No.	Drug	Mechanism of action	Administration	Dosage
1	Acyclovir	Activated by HSV thymidine kinase to inhibit viral DNA polymerase	3% ophthalmic ointment	5×/day for 10 days
2	Ganciclovir	Cytomegalovirus nucleoside analogue Inhibits DNA polymerase	0.15% topical ophthalmic gel	5×/day until epithelium heals; then 3×/day for 7 days
3	Vidarabine	Purine analogue Inhibits DNA polymerase	3% ophthalmic ointment	5×/day for 10 days
4	Trifluridine	Pyrimidine analogue Blocks DNA synthesis	1% ophthalmic solution	8×/day for 10 days
5	Famciclovir	Prodrug of penciclovir	125, 250, 500 mg	250 mg 3×/day for 10 days
6	Valacyclovir	L-valyl ester of acyclovir	500, 1000 mg	1000 mg 2×/day for 10 days

HERPES ZOSTER KERATITIS

Differentiating Features of Eye Disease Caused by Herpes Simplex Virus and Reactivation of Varicella-Zoster Virus

	Herpes Simples Virus	Varicella-Zoster Virus
Dermatomal distribution	Incomplete	Complete
Pain	Moderate	Severe
Dendrite morphology	Central epithelial ulceration with terminal bulbs; geographic in presence of corticosteroids	Smaller without central ulceration or terminal bulbs; dendritiform mucous plaques occur later
Skin scarring	No	Common
Iris atrophy	Patchy	Sectoral
Bilateral involvement	Uncommon	No
Recurrent epithelial keratitis	Common	Rare
Post herpetic neuralgia	No	Common
Corneal hypoesthesia	Focal or diffuse	May be severe

Post Herpetic Neuralgia

Post-herpetic neuralgia is characterized by persistent pain lasting more than a month after the healing of the rash. It is a condition that affects up to 75% of individuals aged over 70. The pain can be continuous or sporadic, often worse during nighttime and exacerbated by minor triggers like touch and heat, a phenomenon known as allodynia.

Treatment options may include the following:

- Local
- Application of cold compresses.
- Topical use of capsaicin at 0.075% or lidocaine 5% patches.
- Systemic treatment may be employed in a stepwise approach:
- Analgesics: paracetamol, codeine
- Tricyclic antidepressants: nortriptyline or amitriptyline, usually starting at 25 mg nightly and adjusted up to 75 mg over several weeks if needed.
- Carbamazepine at a daily dose of 400 mg for severe pain
- Other: gabapentin (300-600 mg up to three times daily) or sustained-release oxycodone (10-30 mg twice daily), or a combination of these.

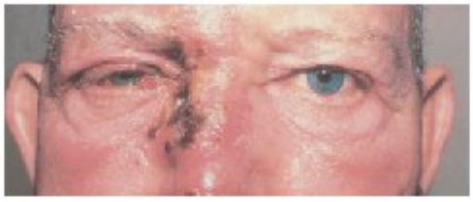


Figure 6 Herpes Zoster Ophthalmicus

ACANTHAMOEBA KERATITIS

Introduction

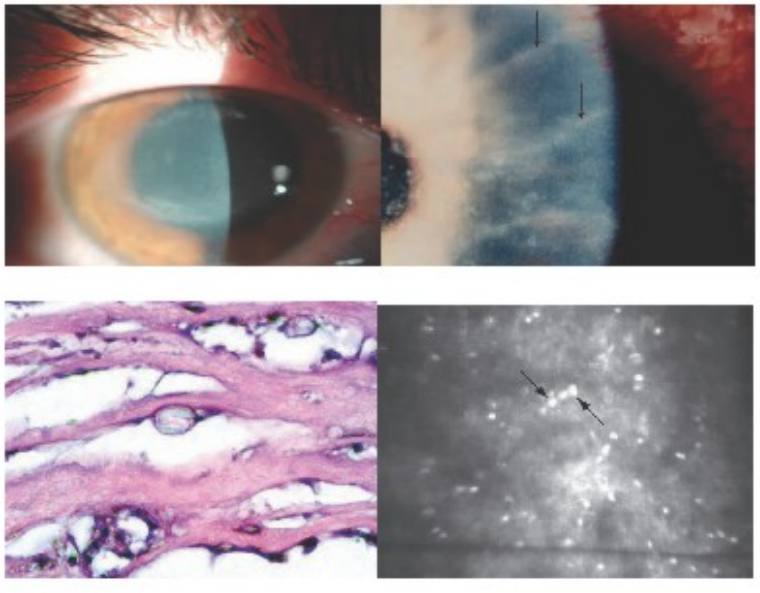
Acanthamoeba spp. are commonly encountered free-living protozoa that exist widely in soil, freshwater, brackish water, and the upper respiratory tract. In developed nations, acanthamoeba keratitis is most frequently linked to the use of contact lenses, particularly when tap water is used for rinsing.

Diagnosis

The condition is often initially misdiagnosed as herpes simplex keratitis, and as it progresses, it should be differentiated from fungal keratitis. Symptoms include blurred vision and discomfort, with pain that is notably severe compared to the clinical signs.

Signs

- **Corneal:**
  - Dirty epithelium with micro erosions
  - Epithelial pseudo dendrites and microcysts
  - Perineural infiltrates (radial keratoneuritis) is nearly pathognomonic (Figure 7B)
  - Ring abscess
  - Neurotrophic keratitis
- **Other:** Scleritis, Limbitis, Glaucoma (inflammatory angle closure)



Investigations:

- Corneal scraping for KOH/Gram/Calcofluor white/Giemsa stains
- Culture on non-nutrient agar with E. coli overlay
- PCR
- In vivo confocal microscopy (Figure 7D)
- Corneal biopsy for Haematoxylin-eosin, PAS and Methamine stain (Figure 7C)

Treatment

- Usually prolonged
- Debridement of affected epithelium to aid in the penetration of eye drops.
- Polyhexamethylene biguanide (PHMB) and chlorhexidine (Biguanides): 1st line of therapy, effective against both trophozoites and cysts.
- Hexamidine or propamidine (Diamidines) may also be used.
- Other: Azole antifungals, simultaneous antibacterial treatment for co-infection
- Topical steroids use controversial
- Therapeutic keratoplasty after complete healing and scarring

PERIPHERAL ULCERATIVE KERATITIS

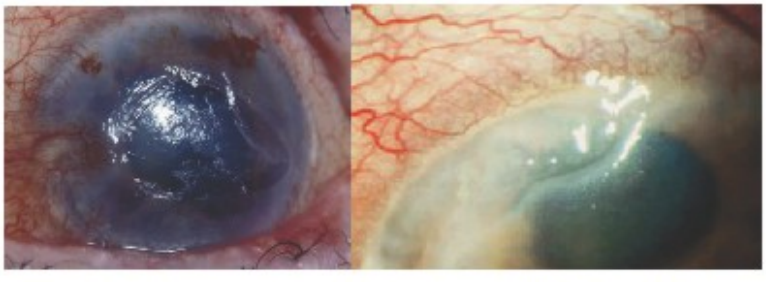


Figure 8 (A) Neurotrophic keratopathy with large epithelial defect (Courtesy of S Tuft) (B) Mooren□s ulcer

Differential Diagnosis

Ocular Conditions and Diseases	Systemic Conditions and Diseases
Microbial Bacterial (Staphylococcus, Streptococcus, Gonococcus, Moraxella, Haemophilus) Viral (herpes simplex, herpes zoster) Acanthamoeba Fungal	Microbial Bacterial (tuberculosis, syphilis, gonorrhoea, borreliosis, bacillary dysentery) Viral (herpes zoster, AIDS, hepatitis C) Helminthiasis
Mooren ulcer (Figure 8B)	Rheumatoid arthritis
Traumatic or postsurgical	Systemic lupus erythematosus
Terrien marginal degeneration	Granulomatosis with polyangiitis (Wegener granulomatosis)
Exposure keratopathy (Figure 8A)	Polyarteritis nodosa
Rosacea	Relapsing polychondritis
	Sjögren syndrome
	Behçet disease
	Sarcoidosis
	Inflammatory bowel disease
	α1-Antitrypsin deficiency
	Malignancy

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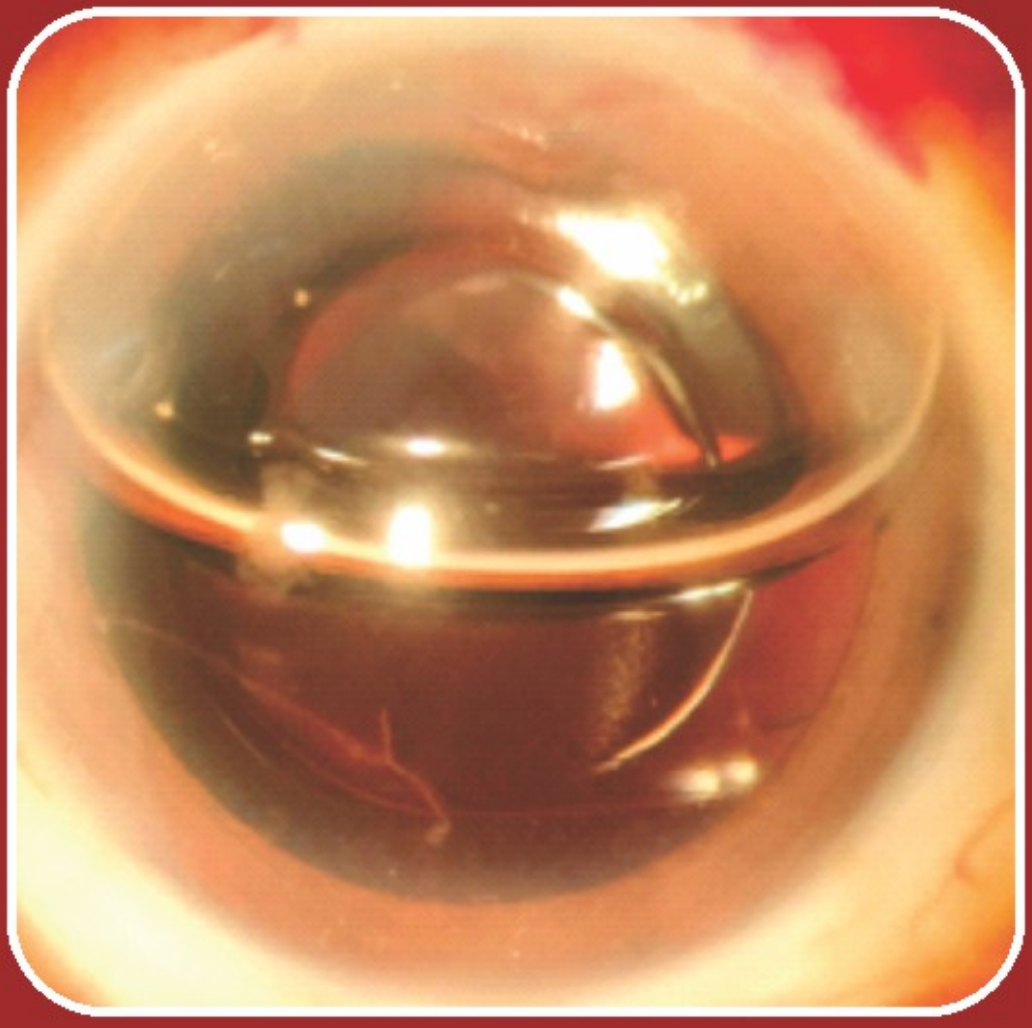
CHAPTER 3



CATARACT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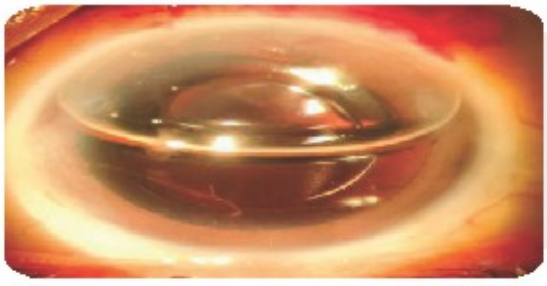

CATARACT

Introduction

Any opacity in the lens capsule or its fibres is called Cataract. Commonly seen in elderly, it is the leading cause of avoidable blindness worldwide. In India, cataract is reported to be responsible for 50-80% of bilateral blindness. It is projected that the number of cataract patients in India shall rise to above 8 million by the year 2020. It is due to this sheer magnitude of the disease, preventing cataract related blindness is the top priority of our National Programme for Control of Blindness (NPCB).

Anatomy and Physiology of Lens

Lens is a biconvex, transparent, globular crystalline structure present in the eye between the vitreous posteriorly and iris anteriorly. The light rays entering the eye through pupil are focused on to the retina by lens. The lens is held in its place by zonules, which attaches it to the ciliary processes of the ciliary body. The part of the lens where zonules are attached is known as the equator of the lens. The lens diameter at equator varies between 8 to 10 mm.

The lens consists of a capsule which is formed by a basement membrane lined by epithelial cells (germinal epithelium) on the inner side. These epithelial cells are concentrated in the equatorial region of the lens and are highly active.

These undergo metaplasia to form lens fibres which are then compacted together and arranged regularly within the capsule giving lens a solid form. In the process, the epithelial cells loose all the intracellular organelles including the nucleus to form transparent lens fibres. The earliest produced fibres are pushed to centre and form the nucleus- the denser central zone of the lens. The newly formed fibres are present in the periphery and form the cortex of the lens. Being avascular structure, the lens is dependent upon aqueous and vitreous for its nutrition.

The lens helps in focusing light rays onto the retina. The lens undergoes changes in its shape for focussing light rays coming from various distances. The change in shape makes the lens more spherical and thereby enhances its refractive power. This flexibility of lens is lost with ageing and it progressively becomes difficult to focus on near objects. This loss of accommodative effort with ageing is known as Presbyopia.

Cataract Pathogenesis

Cataract is caused by degeneration and opacification of the lens fibres already formed, the formation of aberrant lens fibres or deposition of other material in their place. Any factor, physical or chemical, which disturbs the critical intra- and extracellular equilibrium of water and electrolytes or deranges the colloidal system within the fibres tends to bring about opacification. Aberrant lens fibres are produced when the germinal epithelium of the lens loses its ability to form normal fibres. Fibrous metaplasia of the fibres may occur incomplicated cataract. Epithelial cell necrosis leads to focal opacification of the lens epithelium as □glaucomflaken□ in acute angleclosure glaucoma. Radiations can cause cataract by either heat coagulation of lens proteins, free radical induced cellular damage or by altering the cell cycle by causing mutation. Accumulation of metabolic byproducts in lens due to enzymatic defects can cause metabolic cataract.

Furthermore, long term steroid use results in formation of lens-steroid protein complexes which affects the solubility of lens proteins and results in steroid induced cataract. With ageing, there is increase in the non-soluble lens proteins which disturbs the colloidal balance leading to opacification of the lens fibres.

Classification

A. Aetiological Classification

1. Congenital and developmental cataract
2. Acquired Cataract- further sub-classified as:
   - I. Senile cataract
   - II. Traumatic cataract
   - III. Complicated cataract
   - IV. Metabolic cataract
   - V. Electric cataract
   - VI. Radiational cataract
   - VII. Toxic cataract
   - VIII. Cataract associated with systemic disease e.g Myotonic Dystrophy

B. Morphological Classification

Based upon the site of lens opacification, this is a commonly used classification clinically.

1. Capsular cataract- anterior/posterior
2. Subcapsular cataract- anterior/posterior
3. Cortical cataract
4. Nuclear cataract
5. Polar cataract- anterior/posterior capsule/cortex in the polar region

C. Lens Opacities Classification System (LOCS)-III

This is the most recent method of classifying cataract and is widely used in clinical practice. It consists of six slit lamp images for grading nuclear colour (NC) and nuclear opalescence (NO), and five retro-illumination images for grading cortical © and posterior subcapsular (P) cataract.

Senile Cataract

This is the most common type of cataract seen in clinical practice. As the name implies, this type of cataract is age related and is commonly seen in people above 50 years of age. However, sometimes there may be an early onset seen in patient with family history or in those involved in excessive outdoor works e.g farmers. Systemic diseases like Diabetes Mellitus may also cause an early senile cataract.

Two common morphological verities of senile cataracts are observed:

1. ***Cortical senile cataract***

   This type is characterised by hydration and opacification of the cortical lens fibres. Progressive changes in seen in the cortical fibres lead to the following classical stages in its maturation:

   a. Stage of lamellar separation
   b. Incipient cataract
   c. Immature Senile Cataract (IMSC)- A diffuse opacification of most of the cortical lens fibres is seen in this stage. Torch light examination may elicit greyish white reflex in the papillary area. Somtimes, excessive hydration may lead to swelling of the lens and this is referred to as Intumescent cataract. Intumescence often causes papillary block and acute angle closure.

d. Mature Senile Cataract (MSC)- Opacification of whole of the lens fibres is complete. Torch light examination elicits milky white papillary reflex.

e. Hypermature Senile Cataract (HMSC)- Two verities are observed:

   I. MorganianHypermature Cataract: The entire cortex is liquefied and the nucleus is found floating down in the capsular bag.

   II. Sclerotic Hypermature Cataract: Proteins leak out of the capsular bag and the lens capsule becomes wrinkled and sclerotic.

2. ***Nuclear senile cataract***

The cortical lens fibres remain transparent whereas the nucleus undergoes sclerotic changes. This often happens earlier that cortical opacification. The nucleus becomes diffusely cloudy and sometimes may appear yellow, brown or even black. This is due to deposition of pigments derives from amino acids in the lens fibres.

➢ **Clinical Presentation**

Most of the patients present with painless progressive diminution of vision. Cortical cataracts involve the periphery of lens whereas nuclear cataract affects the central part. As a result, night vision is greatly compromised in patients with cortical cataract whereas day vision in nuclear and posterior/anterior subcapsular verities. Secondly, due to more central involvement, glare is often complained of in presence of posterior

subcapsular cataract. Often patients complain of uniocular diplopia and coloured halos. This happens due to irregular refraction taking place due to alters refractive states of different regions of immature lens. Some of the patients experience improvement in near vision. This is because of increase in refractive power of the lens due to nuclear sclerosis. This phenomenon is known as *second sight.*

- **Diagnosis**

A torch light examination will give greyish white papillary reflex in IMSC, pearly white in MSC and milky white in HMSC (Figure 1 & 2). A detailed slit lamp examination can highlight the nuclear colour and its opalescence and also help in grading the amount of cortical and posterior subcapsular cataract.

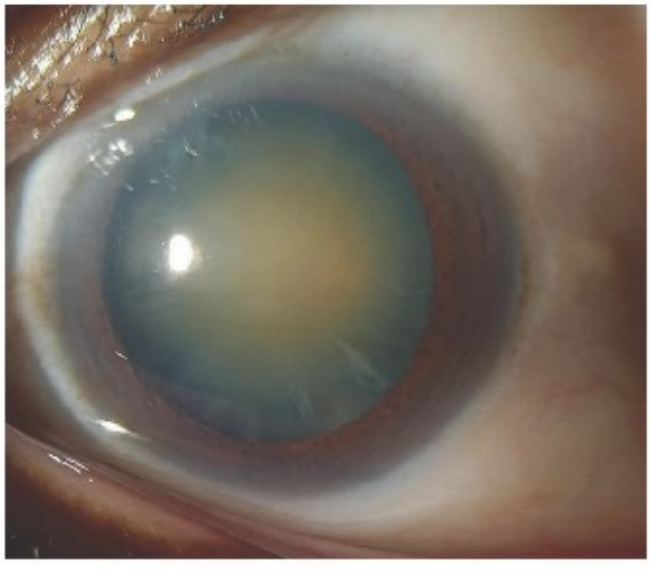

Figure 1. Immature Senile Cataract (IMSC) (photo credit: Dr Shubham Agarwal)

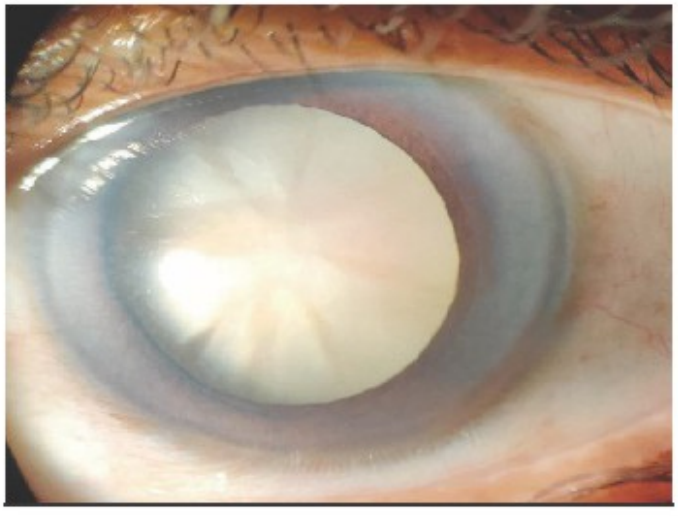

Figure 2. Mature Senile Cataract (MSC) (photo credit: Dr Devanand Bharti)

➢ **Treatment**

Definitive treatment of cataract is replacing the cataractous crystalline lens with transparent artificial intra-ocular lens (IOL). Older surgical techniques involved removal of the entire cataractous lens along with its capsule {Intra-capsular Cataract Extraction (ICCE)} and replacing it with an anterior chamber IOL or by providing aphakic glasses correction. Presently, cataract surgery involves Extra-capsular Cataract Extraction (ECCE) {the lens capsule is left behind and the cataractous lens substance is removed} and posterior chamber (in the bag) IOL implantation (Figure 3). The most widely practiced method of ECCE is by ***Phacoemulsification*** in which ultrasound energy is delivered via probe to break and emulsify the nucleus which is then aspirated along with the cortical fibres. This procedure involves nuclear delivery through a very small incision and implantation of a foldable IOL through the same incision. Manual Small Incision Cataract Surgery (SICS) involves removal of lens nucleus without fragmentation.

Foldable or non foldable IOL can then be implanted in to the eye. This method is relatively cheap as it doesn□t require a phacoemulsification machine. This makes SICS a popular option for camp or low budget cataract surgeries.

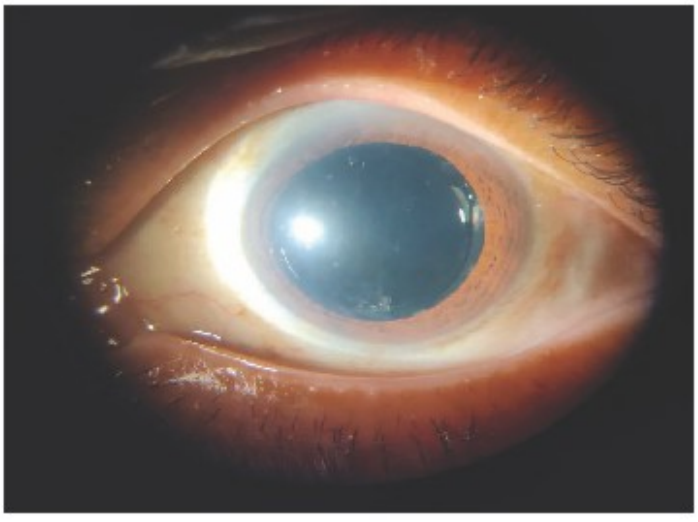

Figure 3. Psuedophakia (artificial intra-ocular lens {IOL} placed in capsular bag. photo credit: Dr Shubham Agarwal)

Congenital and Developmental Cataract

Unlike senile cataract, this occurs in children and young adults. These may be present right from birth (congenital) or may gradually develop over period of time (developmental). Some of these cataracts remain stationary whereas others gradually progress over time. As this occurs very early during the period of visual maturation, congenital/ developmental cataract can have far reaching consequences. As these cataracts affect young population, they affect the socially and economically active population of the country. Inadequate management of congenital cataract will result in many human years of avoidable blindness and social and economic set back to the nation.

➢ **Aetiology**

A variety of causes are thought to result in congenital cataracts. Some of these include the following:

I. Hereditary- Chromosomal anomalies (Trisomy 21) are often associated with congenital cataracts. These types of cataracts may even have an autosomal dominant transmission. Genetic alterations impair lens fibre growth and maturation causing cataract.
II. Maternal factors include malnutrition, infections (TORCH group), radiation exposure and drug ingestion during pregnancy.
III. Foetal factors may include birth hypoxia, metabolic disorders (galactosemia, hypoglycaemia etc.), congenital anomalies like Lowe□s syndrome, Alport syndrome etc.
IV. Birth trauma and malnutrition are common causes.
V. Ocular injury is a common cause of unilateral developmental cataract and signs and history of trauma must be enquired for in unilateral cases.
VI. Idiopathic

➢ **Clinical types**

As congenital/developmental cataract occurs due to an insult during a specific period of lens formation, various clinical morphological types are observed.

I. Punctate Cataract/ Blue dot Cataract- Most common type. This is usually visually insignificant.

II. Zonular Cataract- This variety is most commonly associated with visual compromise. The opacity is limited to a particular zone (usually central) with surrounding clear areas. Occasionally, spoke like opacities may be seen emerging radially from the central cataract (Figure 4).

III. Fusiform Cataract

IV. Nuclear Cataract- These are characterised by opacification of the embryonal nucleus.

V. Sutural Cataract- Punctate opacities are seen distributed along the lens fibre sutures.

VI. Anterior/Posterior Polar (subcapsular) Cataract

VII. Total Cataract

Figure 4. Zonular Cataract (photo credit: Dr Siddharth Agrawal)

- **Clinical Presentation and Diagnosis**

Most commonly children with congenital/developmental cataract present with a white papillary reflex- *Leucocoria*. This may also be seen with Retinoblastoma and should be differentiated. Other common presentation of cataract in children include amblyopia, nystagmus and strabismus due to interference with maturation of visual system from an early age. Incidental detection is also common as these lenticular opacities are often non visually significant.

Examination under anaesthesia (EUA) is often needed for thorough examination of young children with cataract. Ultrasound (B Scan) should be performed to evaluate posterior segment of the eye as a more sinister disease like Retinoblastoma may be hiding behind. Assessment of papillary reactions are important as brisk reactions are indirect indicators of a healthy Optic nerve and Retina and eventual good prognosis post-surgery.

- **Treatment**

Not all congenital developmental cataract warrant surgical extraction as a majority of opacities are not visually significant. A thorough examination followed by prescription of appropriate refractive correction is sufficient. In children with visually significant cataracts, lens aspiration with posterior chamber IOL implantation is procedure of choice in children above 6 months of age. Unilateral cases should be operated as early as possible as the chances of developingamblyopia is higher in such cases. Additionally, primary posterior capsulorrhexis can be done in children less than 8 years toprevent posterior capsular

opacification. Children lesser than 6 months can be given aphakic glasses or contact lens and secondary IOL implantation can be done at a later stage. Post-surgery, care must be taken to treat any underlying amblyopia by advising occlusion therapy and refractive correction. A proper visual rehabilitation following cataract surgery is essential in management of congenital cataract.

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CHAPTER 4

GLAUCOMA


राज्य स्वास्थ्य एवं परिवार कल्याण संस्थान, उ0प्र0
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GLAUCOMA

GLAUCOMA

Introduction

Glaucoma is a group of disorders characterised by progressive optic neuropathy and characteristic visual field defects with raised intra-ocular pressure (IOP) as a common risk factor. It is the leading cause of irreversible blindness worldwide. India is native to around 11 million blind people with Cataract and Glaucoma as the leading cause. Glaucoma accounts for about 6% of blindness in India.

Pathogenesis

Chronic, progressive optic neuropathy is the hallmark of Glaucoma. Mechanical damage due to raised IOP and impaired vascular perfusion of the Optic Nerve Head (ONH) are believed to result in Glaucomatous Neuropathy. Raised IOP is commonly attributed to obstruction of the aqueous outflow. This may be either due to mechanical obstruction of the Trabecular Meshwork (TM) or raised episcleral venous pressure affecting the drainage of aqueous into systemic circulation. Raised IOP is results in compressing the Optic nerve fibres in lamina cribrosa leading to mechanical damage to nerve fibre bundles. Furthermore, raised IOP also alters capillary blood and axoplasmic flow in the ONH.

Thus, mechanical and vascular insults to the ONH impair the axonal flow of the Optic nerve and lead to ganglion cell death. This triggers apoptosis (regularised, non inflammatory cell death) of the adjacent cells. Progressive ganglion cell eventually causes Glaucomatous Optic Neuropathy.

Systemic disorders like Diabetes Mellitus, Hypertension/Hypotension, Thyroid disease are risk factors associated with glaucoma. Advanced age, myopia (short sightedness), low central corneal thickness, smoking, sleep apnea and steroid use are other commonly associated risk factors with glaucoma.

Optic Nerve Head Changes

Progressive structural damage of ONH is characteristic of glaucoma. Neuro-retinal Rim (NRR) and Retinal Nerve Fibre Layer (RNFL) loss suggests glaucomatous neuropathy. These can be seen directly using direct ophthalmoscope, slitlampbiomicroscopy using 90D/78D lenses, fundus photographs. Indirect imaging modalities like Optical Coherence Tomography (OCT), Scanning Laser Ophthalmoscopy (SLO)-HRT, Scanning Laser Polarimerty-GDx can also be used to objectively asses NRR and RNFL loss. Typical ONH signs for glaucoma include the following:

a) Asymmetry in Optic Cup (C) to Disc (D) Ratio (CDR) between eyes (>0.2)

b) CDR >0.5 (Vertical)

c) NRR thinning/pallor

d) Baring of ONH vessels

e) Notching of vessels (Bayonetting)

f) Lamellar Dots

g) Peripapillary atrophy

h) Superficial disc hemmorhages

i) Nasalisation of vessels

Identification of any of these changes and corresponding visual field defect confirms the diagnosis of glaucoma.

Visual Field (VF) Changes

Characteristic VF changes depict functional damage to the Optic nerve. The VF defects correspond with structural damage seen in the ONH. Typically, these visual field defects are limited by the horizontal midline and occur asymmetrically in the upper and lower visual hemi- fields. This is in contrast to VF defects arising out of neurological diseases which tend to be limited by the vertical midline of the visual field. Peripheral visual fields are first affected and central visual field defects are seen in advanced glaucoma. It is due to this pattern in progression of VF defects that glaucoma patients generally do not present with ocular symptoms until advanced stage when central visual defects start appearing. Visual field assessment also known as Perimetry, is essential to the diagnosis of glaucoma. Automated Static Perimetry is currently the most accepted and widely performed procedure for assessing VF. Common VF defects (scotoma) seen in glaucoma include the following:

a) Paracentral Scotoma

b) Bjerrum Scotoma (Arcuate Scotoma)

c) Seidel Scotoma

d) Nasal Step

e) Double Arcuate/ Ring Scotoma

f) Temporal Wedge

g) Generalised Depression

h) Concentric Contraction

These VF defects occur following Optic nerve damage. Structural defect of the ONH may be seen even in absence of VF defects. This is known as pre-perimetric glaucoma. Early detection of VF defects can now be done using Short Wave Automated Perimetry (SWAP) and Frequency Doubling Perimetry (FDP).

Intra-Ocular Pressure

Raised IOP is the commonest risk factor for glaucoma. It is also presently the only modifiable risk factor. Presently, glaucoma therapy is centred upon modifying IOP to within an acceptable range which may preclude further damage (Target IOP). Normal IOP range varies between 10 to 21 mm Hg. Accurate assessment of IOP (tonometry) is essential in the management of glaucoma. IOP assessment can done using various techniques like Schiottz Indentation Tonometry, Goldman Applanation Tonometry, Non Contact Tonometry (NCT)[1], Rebound Tonometry etc. Occasionally, glaucomatous neuropathy also occurs in absence of raised IOP. Such a type of glaucoma is known as Normal Tension Glaucoma (NTG).

Classification

On the basis of gonioscopic appearance of the angle of the eye, glaucoma can be broadly classified into Open Angle and Closed Angle Glaucoma[2]. In absence and presence of any associated ocular or systemic abnormalities, these are further termed as Primary or Secondary Glaucoma respectively.

Common examples of secondary glaucoma include Phacomorphic (lens induced) Glaucoma, Neovascular Glaucoma, Uveitic Glaucoma, Pseudoexfoliative and Pigementary Glaucoma. While managing secondary glaucoma, it is essential to address the underlying cause, failing which the treatment may not be effective.

Glaucoma can occur at any age. Accordingly, glaucoma may also be classified as Congenital/Developmental Glaucoma- (present at birth or shortly thereafter) or Adult Glaucoma-(usually presenting in 5th to 6th decade). Juvenile glaucoma have onset between 5 yrs to 40 yrs of age.

Clinical Presentation

Glaucoma is a group of disorders. It may present with a variety of clinical presentation. Following are some of the common presentations.

I. Chronic Open Angle Glaucoma (COAG)

Age: 6th to 7th decade.

Ocular Complaints: None to painless progressive diminution of vision, constriction of visual fields, frequent change in glasses.

Ocular findings: Normal anterior chamber (AC) depth, open angles, raised IOP, glaucomatous optic nerve head changes, characteristic visual field defects.

II. Primary Angle Closure Glaucoma (PACG)

Age: 5th to 6th decade.

Ocular Complaints: Intermittent redness, pain in eyes, progressive diminution of vision, coloured halos. Symptoms worsen in dark or night.

Associated symptoms: Intermittent headache, nausea.

Ocular findings: shallow AC, iris atrophic patches, peripheral anterior synechia (PAS), closed angles, raised IOP, glaucomatous optic nerve head changes, characteristic visual field defects.

III.Acute Angle Closure (ACG)

Age: 5th to 6th decade

Ocular Complaints: Sudden painful diminution of vision, redness and lacrimation, coloured halos.

Associated symptoms: Intense headache, nausea and vomiting.

Ocular findings: Red congested eye, hazy cornea (oedema), shallow AC, mid dilated non reacting pupil, stony hard eye (raised IOP).

IV. Primary Congenital Glaucoma (PCG)

Age: Birth to 3-5 years

Ocular signs: Buphthalmos (enlarged eyes), photophobia, lacrimation, bleparospasm, bluish cornea, Haab striae (endothelial tears).

Management

The entire management of glaucoma presently revolves around reducing IOP[3]. This may be achieved either by medicines or surgery. Medical management of glaucoma involve the following classes of drugs:

Drug Class Mechanism of Action

1. Prostaglandin Analogues (PGA)- Eye drops.

Latanoprost, Travoprost, Bimatoprost Increase aqueous outflow (uveo-scleral)

2. Beta blockers- Eye drops. Timolol, Betaxolol Reduces aqueous production

3. Alpha Agonists- Eye drop. Brimonidine Reduces aqueous production and increases uveo-scleral outflow

4. Carbonic Anhydrase Inhibitors- Dorzolamide, Brinzolamide-Eye drop Acetazolamide- Tablet. Reduce aqueous production

5. Parasympathomimetics- Eye drop. Pilocarpine Increases aqueous outflow (TM), relieves papillary block

6. Hyperosmotic Agents- Mannitol (I/V), Glycerin Syrup Reduces vitreous volume

PGA are the drug of choice for managing glaucoma. These drugs should be started as monotherapy. In case target pressure is not achieved, combination therapy can be used. Beta blockers should be used with caution in patients with COPD, Heart blocks, hypertension in view of their systemic adverse effects.

Laser procedures like YAG-laser peripheral Iridotomy should be done in management of PACG as this aids in relieving papillary block and improves aqueous outflow. Selective Laser Trabeculoplasty (SLT) using Argon Laser is advised in management of Pigmentary Glaucoma.

When target pressure is not achieved using maximal medical therapy, glaucoma surgery is indicated. Trabeculectomy is the standard surgical procedure for adult glaucoma. In case of failed trabeculectomy procedure, glaucoma drainage devices (GDD) like Ahmad Glaucoma Valve can be used. In some secondary glaucoma like Neovascular Glaucoma, GDD are even considered as the primary choice.

Trabeculotomy with Trabeculectomy is the procedure of choice for managing congenital glaucoma (Buphthalmos). Many a times, repeat surgeries may be required in children due to higher failure rates of glaucoma surgery among them.

Acute angle closure is an ophthalmic emergency and requires prompt management. Immediate IOP control should be achieved using systemic hyperosmotic agents and topical anti glaucoma drops. Pilocarpine eye drop is a must in treating acute angle closure. Oral carbonic anhydrase inhibitors like Acetazolamide tablets also help in reducing IOP[4]. Once the IOP is controlled, definitive therapy in the form of glaucoma surgery or laser procedure should be done. Care must also be taken to perform laser iridotomy in contrlateral eye as these are highly prone to experience such an episode in future. Timely intervention can surely prevent blindness in these patients.

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CHAPTER 5

COMMON DISORDERS PF THE EYELID


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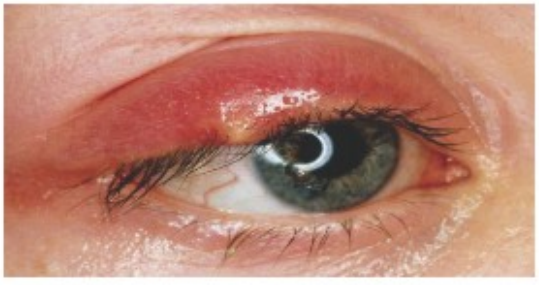

Common Disorders of the eyelid

Common Diseases of the Eyelids

Ectropion

This commonly seen outward turning of the lower eye lidinthe elderly is eminently treatable and responds well to minor surgery. Senile ectropion can begin with slight separation of the lower eyelid from the globe, and the mal-position of the punctum leads to overflow of tears and conjunctival infection. Irritation of the skin by the tears and rubbing of the eyes lead to skin contracture and further downward pulling oftheeyelids. Likeentropion, ectropioncanbe cicatricial and result from scarring of the skin of the eye lids. It can also follow as eventhcranial nerve palsy caused by complete inaction of the orbicularis muscle; this is called paralytic ectropion.

Entropion

This is an inversion of the eye lid. The common form is the inversion of the lower eye lid seen in elderly patients. Often, the patient does not notice that the eye lid is turned in but complains of soreness and irritation. Closer inspection reveals the inverted eyelid, which can be restored to its normal position by slight down- ward pressure on the lower eyelid, only toturn in again when the patient forcibly closes the eyes.

The inwardly turned eyelashes tendtorub on the cornea and, if neglected, the condition can lead to corneal scarring and consequent loss of vision. The condition is often associated with muscular eyelids and sometimes seems to be precipitated by repeatedly screwing up the eyes. Slackening of the fascialsling of the lower eyelid with ageing combined with the action of the orbicularis muscle allows this to happen. This common type of entropion is called spastic entropion and it can be promptly cured without leaving a visible scar by minor eyelid surgery. Entropion can also be seen following scarring of the conjunctival surface of the eyelids and one mustmention the entropion of the upper eyelid caused by trachoma.

Lagophthalmos

This is the term used to denote failure of proper closure of the eyelids caused by inadequate blinking or lid deformity. In all these cases, the cornea is inadequately lubricated and exposure keratitis can develop. If untreated, this can lead to a serious situation; initially, the cornea shows punctate staining when a drop of fluorescein is placed in the conjunctival sac and subsequently, a corneal ulcer might appear. This, in turn, can lead to the spread of infection into the eye and without prompt treatment with antibiotics, the eye might eventually be lost.

As a general principle, it is important to realise that the sight could be lost simply because the eyes cannot blink. The principle applies especially to the unconscious or anaesthetized patient, where a disaster can be avoided by taping or padding the eyelids and applying an antibiotic ointment.

Blepharospasm

Slight involuntary twitching of the eyelids is common and not usually considered to be of any pathological significance other than being a symptom of fatigue or sometimes of an anxiety state. The condition is termed □myokymia□. True blepharospasm is rare. It canbe unilateral or bilateral and cause great in- convenience and worry to the patient. It tends slowly to become more marked over many years. A small proportion of patients eventually develops Parkinsonism. Cases of recent onset need to be investigated because they might result from an intracranial space-taking lesion. In most cases, though, no underlying cause can be found. Patients with this type of blepharospasm (essential blepharospasm) can often be treated quite effectively by injecting small doses of botulinum toxin into the eyelids, but these need to be repeated every few months.

Ptosis

Drooping of one upper lid is an important clinical sign. In ophthalmic practice, ptosis in children is usually congenital and in adults is either congenital or caused by a third cranial nerve palsy. These more common causes must always be kept in mind but there are a large number of other possible ones. When confronted with a patient whose upper lid appears to droop, the first thing to decide is whether the eyelid really is drooping or whether the lid on the other side is retracted. The upper lid might droop because the eye is small and hypermetropic or shrunken from disease. Having eliminated the possibility of such □pseudoptosis□, the various other causes can be considered, beginning on the skin of the eyelid styes, meibomian cysts and advancing centrally through muscle □myasthenia gravis □along nerves □oculomotor palsy, Horner□s syndrome □to the brainstem. Marked ptosis with the eye turned down and out and a dilated pupil is an oculomotor palsy, whereas slight ptosis, often not noticed by the patient or sometimes by the doctor, is more likely

to mean Horner□s syndrome. This syndrome is caused by damage to the sympathetic nervous supply to either upper or lower lids or both and is characterized by slight ptosis, small pupil, loss of sweating on the affected side of the face and slight enophthalmos (posterior displacement of the globe).

The management of ptosis depends on the cause and thus on accurate diagnosis. Surgical shortening of the levator tendon is effective in some cases of congenital ptosis and sometimes in long-standing third cranial nerve palsies. Before embarking on surgery, it is important to exclude myasthenia gravis and corneal anaesthesia. Children with congenital ptosis need to be assessed carefully before considering surgery. In young children, ptosis surgery is indicated where the drooping lid threatens to cover the line of sight and where the ptosis causes an unacceptable backwards tilt of the head. In one rather strange type of congenital ptosis, the problem disappears when the mouth is opened and the patient might literally wink unavoidably when chewing. Careful consideration is needed before making the decision for surgery in these cases.

Causes of Ptosis

- Pseudoptosis: small eye, atrophic eye, lid retraction on other side.
- Mechanical ptosis: inflammation, tumour, and excess skin.
- Myogenic ptosis: myasthenia gravis.
- Neurogenic ptosis: sympathetic □Horner□s syndrome, third cranial nerve palsy, any lesion in the pathway of these, carcinoma of the lung can cause Horner□s syndrome.
- Drugs: guanethidine eye drops cause ptosis.
- Congenital: ask for childhood photograph, ask for family history.

Ingrowing Eyelashes (Trichiasis)

The lashes could grow in an aberrant manner even though the eyelids themselves are in good position. This might be the result of chronic infection of the lid margins or follow trauma. Sometimes one or two aberrant lashes appear for no apparent reason. The lashes tend to rub on the cornea producing irritation and secondary infection. The condition is referred to as □trichiasis. When one or twolashes arefound to be the cause of the patient□s discomfort, it is common practice simply to epilate them with epilating forceps. This produce instant relief, but often the relief is short- lived because the lashes regrow. At this stage, the best treatment is to destroy the lash roots by electrolysis before epilation. Needless to say, before removing lashes it is essential to be familiar with the normal position of the lash line and to realise, for example, that hairs are normally present on the caruncle. When the lash line is grossly distorted by injury or disease, the rubbing of the lashes on the cornea can be prevented by fitting a protective contact lens or, if this measure proves impractical, it might be necessary to transpose or excise the lashes and their roots.

Infections of the Eyelids

Meibomian Gland Infection[20,21,22]

The opening of the meibomian glands could become infected at any age, resulting in meibomitis, seen initially as redness along the line of a gland when the eyelid is everted. A small abscess might then form, with swelling and redness of the whole eyelid, and this can point and burst either through the conjunctiva or less often through the skin. The orifice of a gland could become occluded and the gland thenbecomes distended and cystic. The retained secretions of the gland set up a granulating reaction and the cyst itself might become infected. The patient might complain of sore- ness and swelling of the eyelid, which subsides, leaving a pea-sized swelling that remains for many months and sometimes swells up again.

During the stage of acute infection, the best treatment is local heat, preferably in the form of steam. This produces considerable relief and is preferable to the use of systemic or local anti- biotics. Antibiotics might be required if the patient has several recurrences or if there are signs and symptoms of septicemia. Once a pea-sized cyst remains in the tarsal plate, this can be promptly removed under a local anaesthetic unless the patient is a child, in which case a general anaesthetic might be required. The method of removal involves everting the eyelid and incising the cyst through the conjunctiva and then curetting the contents. Postoperatively, local antibiotic drops or ointment are pre- scribed.

Styes [20]

These are distinct from meibomian infections, being the result of infection of the lash root. The eyelid might swell up and become painful and at this stage, the site of the infection can be uncertain. However, a small yellow pointing area is eventually seen around the base of an eyelash. Hot steaming, again, is effective treatment and once the pus is seen, the eyelash can be gently epilated, with resulting discharge and sub- sequent resolution of the infection. Children aged from about six to ten years sometimes seem to go through periods of their lives when they can be dogged by recurrent styes and meibomian infections, much to the distress of the parents. Under these conditions, frequent baths and hair washing are advised and some- times a long-term systemic antibiotic might be considered. Recurrent lid infections can raise the suspicion of diabetes mellitus but in practice, this is rarely found to be an underlying cause. Eyelid infections such as these rarely cause any serious problems other than a day or two off work and it is extremely unusual for the infection to spread and cause orbital cellulitis. Recur- rent swelling of the eyelid in spite of treatment can indicate the need for a lid biopsy because some malignant tumours can, on rare occasions, present in a deceptive manner.

Blepharitis [21]

This refers to a chronic inflammation of the lid margins caused by staphylococcal infection. The eyes become red rimmed and there is usually an accumulation of scales giving the appearance of fine dandruff on the lid margins. The condition is often associated with seborrhea of the scalp. Sometimes it becomes complicated by recurrent styes or chronic infection of the meibomian glands. The eye itself is not usually involved, although there could be a mild superficial punctate keratitis, as evidenced by fine staining of the lower part of the cornea with fluorescein. In more sensitive patients, the unsightly appearance can cause difficulties, but in more severe cases, the discomfort and irritation can interfere with work. Severe recurrent infection can lead to irregular growth of the lashes and trichiasis. In the management of these patients, it is important to explain the chronic nature of the condition and the fact that certain individuals seem to be prone to it. Attention should be given to keeping the hair, face, and hands as clean as possible and to avoid rubbing the eyes. When the scales are copious, they can be gently removed with cotton wool moistened in sodium bicarbonate lotion twice daily. Dandruff of the scalp should also be treated with a suit- able shampoo. A local antibiotic can be applied to the lid margins twice daily with good effect in many, but not all, cases. In severe cases with ulceration of the lid margin, it might be necessary to consider prescribing a systemic anti- biotic, preferably after identifying the causative organism by taking a swab from the eyelids. Local steroids when combined with a local antibiotic are very effective treatment, but the prescriber must be aware of the dangers of using steroids on the eye and long-term treatment with steroids should be avoided. Steroids should not be used without monitoring the intraocular pressure.

Epidermal lesions

- Epidermal inclusion cysts arise from the infundibulum of the hair follicle and are primarily due to occlusion. These lesions are slow-growing, firm, elevated, round and often have a central pore. Epidermal inclusion cysts are filled with keratin (despite being sometimes called sebaceous cysts), and rupture can incite an inflammatory foreign body reaction. Secondary infection is also possible. Referral for surgical excision is generally recommended.
- Molluscum contagiosum is caused by the molluscum contagiosum virus, a member of the Poxviridae family. Immunocompetent young children and patients who are immunosuppressed are more commonly affected.[1] Lesions are characteristically 1□3 mm white, pink or flesh-coloured nodules with a central umbilication. Molluscum contagiosum may also cause a follicular conjunctivitis because of shedding of the molluscum virus into the tear film. Treatment is usually not required as the lesions will spontaneously resolve over time. For rare cases that are very symptomatic (eg those that cause local irritation), cryotherapy or curettage can be used, but referral to an ophthalmologist may be warranted given the locally destructive treatment modalities.
- Xanthelasma are lesions in the superficial dermis and subdermal tissue containing lipid-laden macrophages. These are sometimes associated with raised cholesterol or congenital disorders of lipid metabolism requiring further investigation and management. Surgical excision can be considered for cosmetic reasons.

Lid Tumours

Benign Tumours[2]

Papilloma

Commonly seen on lids near or on the margin, these can be sessile or pedunculated, and are some times keratinized. These lesions are caused by the papilloma virus and are easily excised, but care must be taken if excision involves the lid margin

Benign melanocytic lesions

Pigmentation can be seen in both benign and malignant lesions and does not necessarily imply melanocytic origin. Conversely, lesions of melanocytic origin may not be visibly pigmented (eg amelanotic naevus). Naevi are flat or raised lesions that arise from melanocytes and are common on the eyelid. Naevi progress through three stages, starting in childhood as a junctional naevus that is a flat, pigmented macule located in the dermoepidermal junction. It then becomes an elevated compound naevus in the second decade, involving both the dermoepidermal junction and dermis, before involuting later in life and losing pigmentation by the seventh decade. Third-stage naevi are known as dermal naevi and involve the dermis only. Transformation to melanoma is rare, but can occur in junctional or compound naevi.

Haemangioma

Infantile haemangiomas, previously known as strawberry or capillary haemangiomas, are lesions with a classic red/pink appearance that are common in children. The vast majority of these lesions□ involute and selfresolve by the age of 10 years. Rarely, they can cause ptosis, refractive error, and amblyopia. All children with eyelid infantile haemangiomas should be referred to a paediatric ophthalmologist to assess for potential refractive error and monitor for amblyopia.[3] Seen as a red □strawberry mark□ at or shortly after birth, this lesion can regress completely during the first few years of life. Figure 5.13 shows a gross example of the rare cavernous haemangioma, which might be disfiguring. This also can regress in a remarkable way. □Port wine stain□ is the name applied to the capillary haemangioma. This is usually unilateral and when the eyelids are involved, there is a risk of association with congenital glaucoma, haemangioma of the choroid and haemangioma of the meninges on the ipsilateral side (Sturge□Weber syndrome). Children with port wine stains involving the eyelids need full ophthalmological and neurological examinations.

Port wine stains

Port wine stains are permanent capillary malformations that are present from birth. They are variably sized macular lesions that can be dark red to blue in colour. The lesion grows in proportion with the child and may also gradually become raised and thicker. Port wine stains involving the eyelid may be associated with glaucoma; approximately 18% of children are affected,[4] particularly patients with bilateral port wine stain or involvement of both upper and lower eyelids. The prevalence is further increased when associated with Sturge-Weber syndrome,[5] with glaucoma affecting 40□60% of these patients.[6,7]

It is therefore important for the patient to be referred to a paediatric ophthalmologist for monitoring and regular follow-up.

Dermoid Cyst

These quite common lumps are seen in or adjacent to the eyebrow. They feel cystic and are sometimes attached to bone. Typically, they present in children as a minor cosmetic problem. The cysts are lined by keratinized epithelium and can contain dermal appendages and cholesterol. A scan might be needed before removal because some extend deeply into the skull.

Xanthelasma

These are seen as yellowish plaques in the skin; they usually begin at the medial end of the lids. They are rarely associated with diabetes, hyper- cholesterolaemia and histiocytosis. Usually, there is no associated systemic disease.

Malignant Tumours[2]

Actinic keratosis

Actinic keratosis is a common precancerous skin lesion that has potential to develop into an SCC and is found on sun-damaged skin. The risk of malignant transformation is only 0.24% per year, but over an extended follow-up period, the incidence of SCC in an individual with multiple actinic keratoses is as high as 12□16%.[2] Actinic keratoses present as scaly, hyperkeratotic plaques with a sandpaper-like texture. Although they are usually treated with cryotherapy, when located on the eyelid margin, surgical excision is generally recommended. Topical imiquimod is an alternative option that requires dermatology referral.

Sebaceous carcinoma [9,12]

Sebaceous carcinoma is a rare but frequently misdiagnosed tumour (Figure 3). It accounts for 1.0□5.5% of all eyelid malignancies and was previously thought to be more common in people of Asian ethnicity, although recent evidence suggests more equal incidence across all ethnicities.[18] Sebaceous carcinoma arises from the Meibomian glands within the tarsus and presents either as a solitary nodule or diffuse eyelid thickening, often with associated inflammatory changes. Anatomically, given the similarities with chalazion, these lesions are often misdiagnosed initially. Although sebaceous carcinomas are rare, any chronic chalazion associated with a gradual increase in size or persistent, diffuse eyelid inflammation and associated thickening (sometimes only evident with eyelid eversion) should raise suspicion. These tumours are aggressive, with metastatic and mortality rates up to 30%, as well as an associated high risk of recurrence.[12] Management generally involves excision with intraoperative margin control and conjunctival mapping biopsies, or Mohs micrographic surgery.

Basal Cell Carcinoma [9-11,13,14]

This is the most common malignant tumour of the lids, usually occurring on the lower lid. It appears as a small lump, which tends to bleed, forming a central crust with a slightly raised hard surround. The tumour is locally invasive only but should be excised to avoid spread into bone. Even large lesions can be approached surgically and □Mohs□ micrographic surgery is recognized as a tissue-sparing gold- standard approach in many centres. Radio- therapy is only occasionally used with a greater risk of recurrence than formal surgical excision.

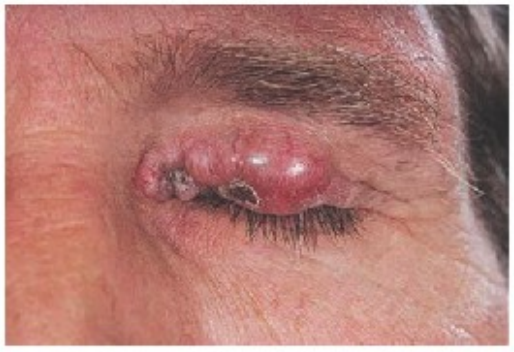

Figure. Cystic basal cell carcinoma that has extended to involve most of the upper eyelid.

Squamous Cell Carcinoma

Squamous cell carcinoma account for approximately 5% of epithelial tumours of the eyelid but are much more aggressive than the more commonly encountered BCC.[15] SCCs develop either spontaneously or from actinic keratosis, Bowen□s disease (SCC in situ), keratoacanthomas or radiation dermatosis. They are more common in immunocompromised patients, particularly following solid organ transplant. SCCs can be difficult to distinguish from BCCs; however, they usually have more scaling and may have an adherent crust or associated ulceration. Prompt referral is required given the higher rates of regional nodal (24%), perineural (8%) and distant metastatic (6%) spread.[16] For this reason, margin-controlled excision is the gold-standard treatment, although newer targeted therapy involving the hedgehog pathway and epidermal growth factor receptor have been promising in patients with advanced metastatic disease.[17]

Malignant Melanoma

This raised black-pigmented lesion is highly malignant, but rare.Melanomas account for <1% of all eyelid malignancies.[19] The lower eyelid is more commonly involved.


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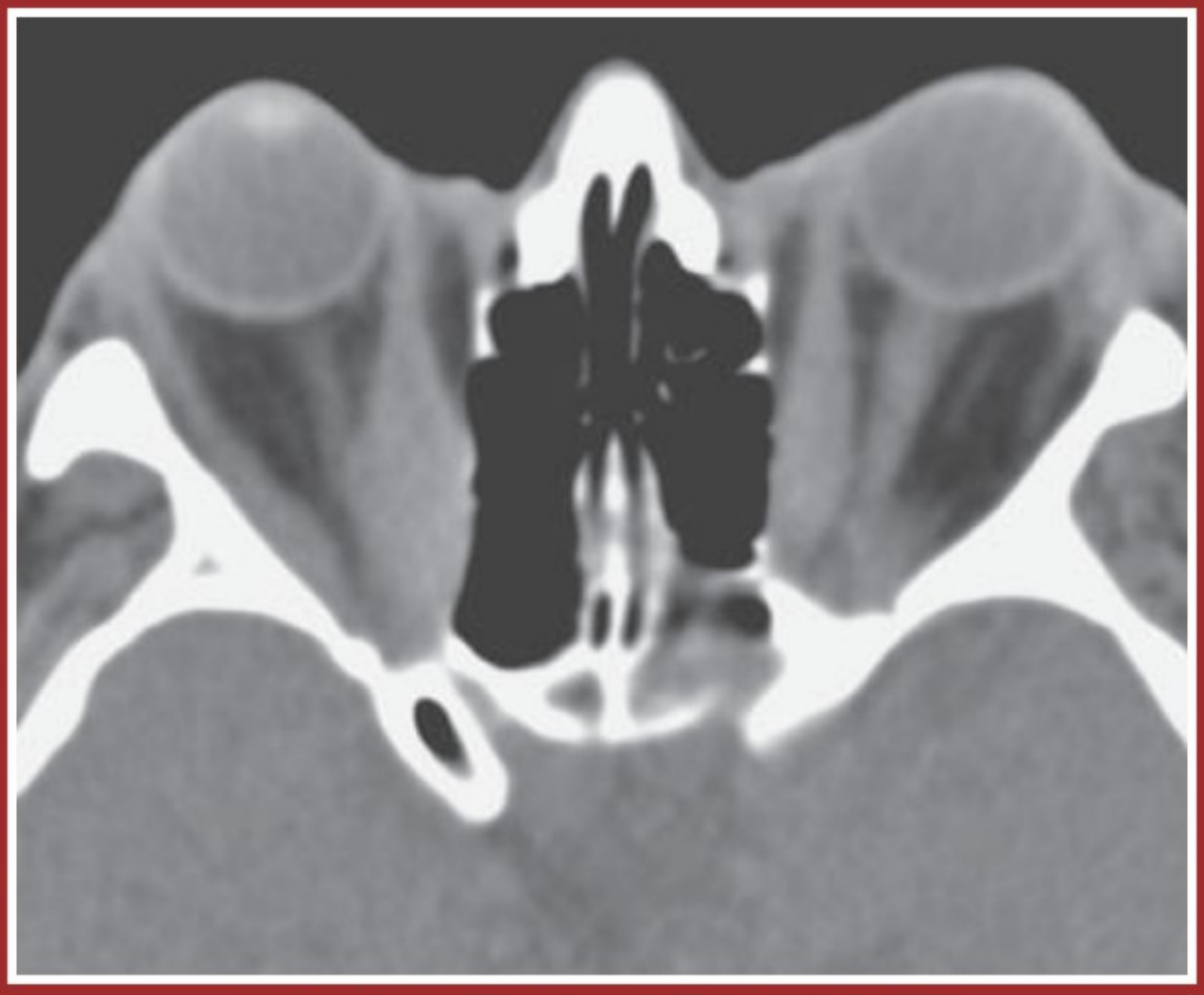
CHAPTER 6



THYROID EYE DISEASE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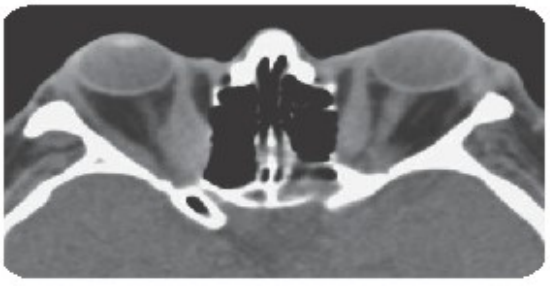


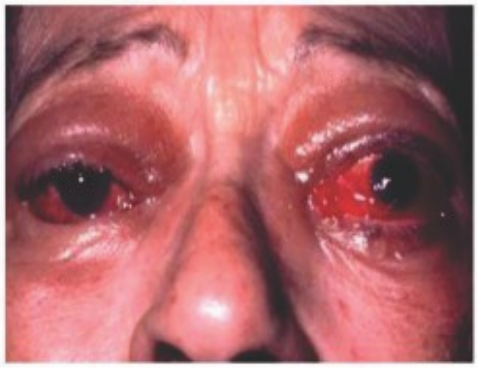
THYROID EYE DISEASE

Introduction

Thyroid eye disease (TED) also known as Graves□ Orbitopathy or Ophthalmopathy is a chronic immune-mediated inflammation of the orbit. It is the most common cause of unilateral and bilateral proptosis in adults.[1] About 25 to 50% of Grave disease (GD) cases present with thyroid eye disease.[2]

Avicenna and Al-Jurjani first described goiter-associated ophthalmopathy in AD 1000. Robert Graves, an Irish physician, described four young women with thyrotoxicosis, palpitations, thyroid gland enlargement, and exophthalmos. Graves ophthalmopathy (or TED) is an orbital inflammation or infiltration involving the soft tissues, proptosis, and ophthalmoplegia.[3] The definition and understanding of TED have evolved over the years.

Thyroid eye disease is a condition in which the eye muscles, eyelids, tear glands and fatty tissues behind the eye become inflamed. This can cause the eyes and eyelids to become red, swollen, and uncomfortable and the eyes can be pushed forward (□staring□ or □bulging□ eyes).



In some cases, there is swelling and stiffness of the muscles that move the eyes so that they no longer move in line with each other; this can cause double vision. Rarely TED can cause reduced vision from pressure on the nerve at the back of the eye or ulcers forming on the front of the eyes if the eyelids cannot close completely. TED can occur in people when their thyroid is overactive, underactive, or functioning normally. It can also occur after treatment for Graves□ disease. People with TED need to be looked after by an eye specialist (ophthalmologist) and a thyroid specialist (endocrinologist).

Epidemiology

Overall, about a quarter of people with Graves□ disease develop TED either before, during, or after their thyroid disorder is diagnosed. In most cases the eye disease is mild. If you have no features of TED by the time the Graves□ disease is diagnosed and you are a non-smoker or ex-smoker then your chance of developing TED is less than one in ten. But if you smoke your chance of developing TED is doubled. If you are a heavy smoker, the chances of developing TED is increased **eight times** compared to non-smokers.

Etiology

The etiology of thyroid eye disease is not well understood. TED involves a complex immune-mediated cycle involving the orbital fibroblasts, adipocytes, and lymphocytes.

IL-1 and prostaglandins.[4] Orbital adipose tissue is a unique fat depot. Robust orbital inflammation produces high levels of pro-inflammatory cytokines interleukin

Orbital fibroblasts are the target cells in the pathogenesis of TED. They have increased expression of TSH receptors and can differentiate into mature adipocytes.[5] A subpopulation of fibroblasts over-expresses the Thy-1 (CD 90) marker.[6] Transforming growth factor-beta (TGF-B) stimulates the Thy-1 + fibroblasts to differentiate into myofibroblasts. The Thy-1 □fibroblasts differentiate into adipocytes on exposure to TGF- B.[7]

TSH receptor (TSH-R) is the primary target of the autoimmune cascade within the orbit.[8] The serum levels of anti-thyrotropin receptor antibodies (TRAb) correlate positively with the severity of TED.[9]

Another possible target molecule is the peroxisome-proliferator-activated receptor-gamma present on Thy-1 - fibroblasts.[10] It is the transcriptional regulator for adipogenesis.[11]

The type 1 insulin-like growth factor receptor (IGF-1R) is another important autoantigen present on Thy-1 + fibroblasts.[12] Its stimulation enhances the synthesis of IL-16 and RANTES complex. These lead to the recruitment of inflammatory CD4+T-cells in the orbital inflammatory cascade.[12]

In summary, the inflammatory cascade is a positive feedback cycle. Thy-1 □ fibroblasts activated by TRAb differentiate into adipocytes, secrete IL-6, and recruit

B-cells and plasma cells. Thy-1 + fibroblasts, on activation by IGF-1R, secrete IL-16 and RANTES to recruit T-cells. T-cells exhibit CD40-CD154 bridges and are responsible for stimulating IL-1 secretion from fibroblasts.[11]

T-cells also produce interferon-gamma and tumor necrosis factor-alpha (TNF-a) to stimulate myofibroblast activity and hyaluronate production. Under the stimulation of IL-6, B-cells produce more auto-antibodies TRAb within the orbit. With prolonged inflammation, the Thy-1 + cell cluster causes fibrosis of EOM - muscle-predominant orbitopathy. TED cases with Thy-1 + cell clusters show enlargement of the orbital adipose tissues - fat-predominant orbitopathy. Individuals younger than 40 years have a higher Thy-1 □response and show orbital fat expansion. TED cases over 70 years of age are more prone to Thy-1 + response and show fusiform muscle enlargement.[13]

Pathophysiology

TED has a self-limiting course owing to the absence of orbital lymphoid tissue.

Rundle explained the natural history of TED.

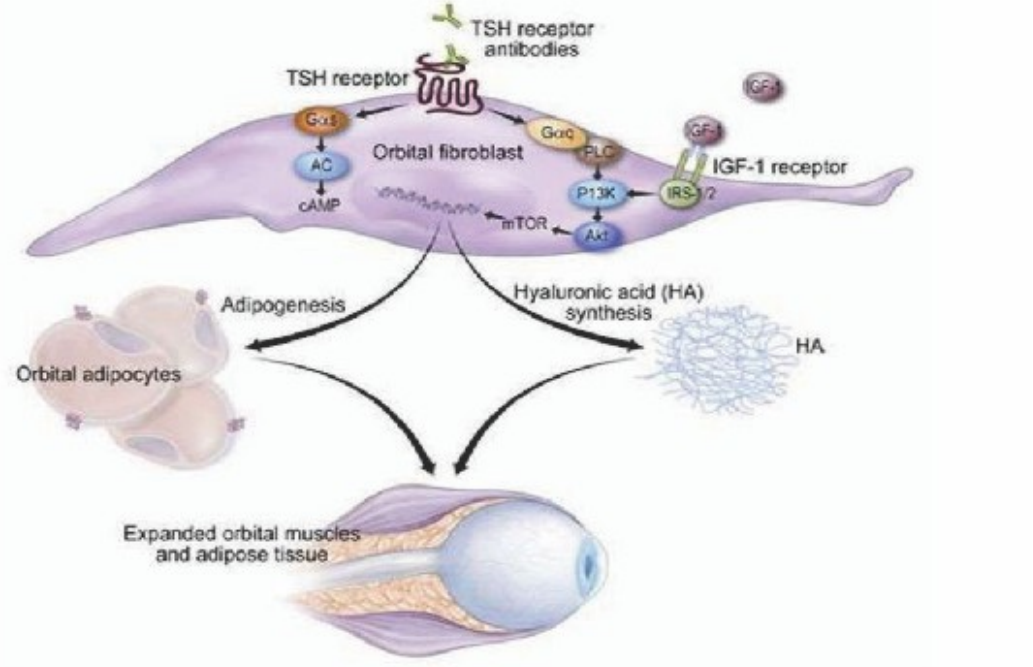
1. Initial phase: A steep rise in disease severity, lasting six months □to 5 years (avg. two years)
2. Inflammatory phase: Active TED duration
3. Stable, inactive phase: TED stabilizes and regresses subsequently beyond 18 months of activity[22]

The disease never returns to baseline. Residual fibrotic changes persist in the orbit. Aggressive immunosuppressive management during the initial active phase can limit the destructive and fibrotic consequences of the immune cascade.

The inactive phase has little response to medical management and warrants surgical intervention.

The □Cone model□ explains the disease progression by an expansion of the muscle cone against a rigid bony orbit into 3 phases:

1. Circumferential cone expansion □displaces the extraconal fat outwards
2. Axial elongation of cone □causes proptosis and muscle strain
3. Cone hypertension and muscle stiffness □ impede the orbital venous drainage[23]



Risk Factors

1. **Ethnicity:** The African-American population exhibits the maximal risk, followed by the White race and Asian populations.[14]
2. **Age:** TED shows a bimodal peak incidence. It occurs in age groups of 40 to 44 years and 60 to 64 years in females, and ages of 45 to 49 years and 65 to 69 years in males.[2] It is more severe in older patients with higher chances of restrictive myopathy and dysthyroid optic neuropathy (DON).
3. **Gender:** There is a female preponderance due to a higher risk of autoimmune diseases. Males cases have more severe ocular involvement and worse outcomes.[15]
4. **Genetics:** CTLA-4, HLA-DRB-1, and TNF-a genes - are most often associated with TED.[16]
5. **Systemic associations:** Autoimmune disorders like pernicious anemia, systemic lupus erythematosus, Addison□s disease, vitiligo coeliac disease, and rheumatoid arthritis - a higher risk of TED.[17]
6. **Environmental factors:** Smoking is strongly associated with the TED incidence.[18]
7. **Dysthyroid status:** At the time of diagnosis, 90% of TED cases are hyperthyroid, 6% euthyroid, 3% have Hashimoto thyroiditis, and 1% are hypothyroid.[2]
8. **Radioactive iodine therapy (RAIT):** causes exacerbation in 24% of TED cases.[19]

9. **Stress:** Psychological stress can aggravate TED by rebound immune hyperactivity following prolonged corticosteroid-induced immune suppression.[20]

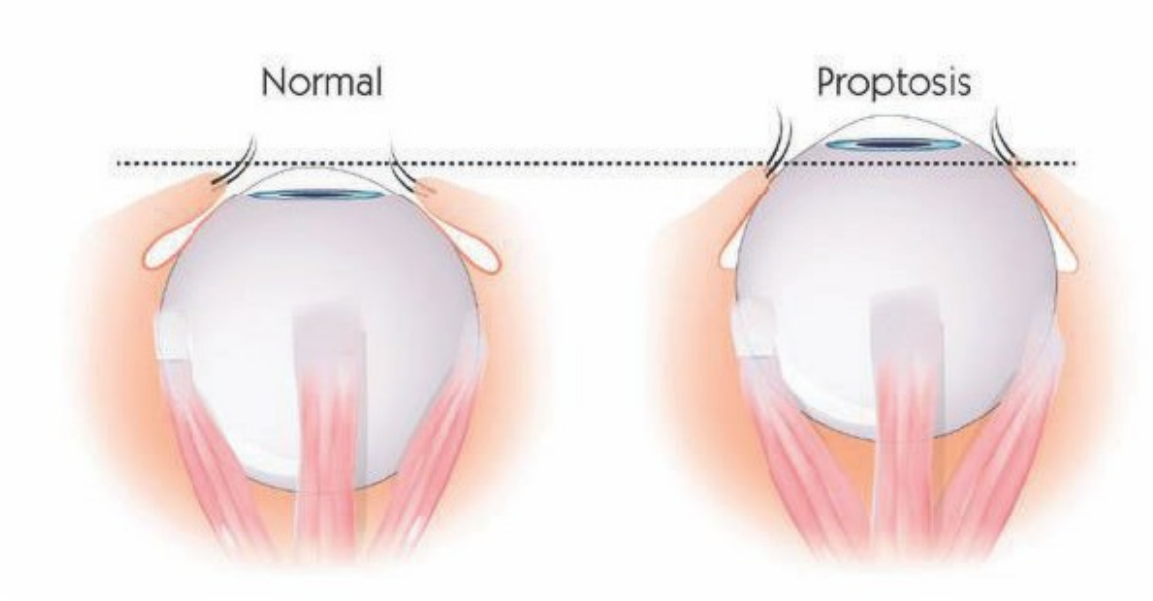
10. **Pregnancy:** New onset or worsening of TED occurs in 30% of GD cases in the post-partum period.[21]

11. **Others:** Trauma can be a stimulus for activating an autoimmune cascade in the orbit. High serum cholesterol may also be a risk factor for TED.[10]

Clinical features of TED

These are the most common symptoms. See your doctor if you have any of the following and ask if it could be TED:

- Change in the appearance of the eyes (usually staring or bulging eyes)
- A feeling of grittiness in the eyes or excessive dryness in the eyes
- Intolerance of bright lights
- Swelling or feeling of fullness in upper or lower eyelids
- New bags under the eyes
- Blurred or double vision
- Pain in or behind the eye, especially when looking up, down or side ways
- Difficulty moving the eyes
- Redness of the eyes due to swelling/irritation of the thin coating (conjunctiva) that covers the white part of the eyes
- Extra tearing of the eyes
- Puffy or red eyelids
- Forward bulging of your eyes (proptosis)



TED can sometimes be difficult to diagnose and patients may be treated for other conditions such as conjunctivitis, allergy or hay fever months before the diagnosis is made. The signs that the diagnosis may be TED rather than any of these conditions are:

- Symptoms may occur in the wrong season for hay fever
- Allergies usually cause itchy eyes, whereas TED does not
- Conjunctivitis usually causes sticky eyes, whereas TED usually does not
- TED often is associated with an ache or pain in or behind the eye, especially when trying to look up or sideways, whereas the other conditions mentioned are not
- TED is sometimes associated with double vision, whereas the other causes of eye symptoms are not

History and Physical

Ocular discomfort - is the most common presentation in thyroid eye disease patients.[24] Other common complaints are dryness, excessive watering, redness,

photophobia, and pain behind the eyes. Visual disturbances like blurring and double vision need prompt intervention. The onset of TED can precede the diagnosis of GD in 19.9% of cases.[25] Asymmetrical bilateral TED is a common presentation. Eyelid retraction is the most common clinical sign of TED, presenting up to 74% of TED cases.

Eyelid Changes

1. Lateral flare □the altered contour of the upper eyelid is a pathognomonic sign.[26] It occurs due to scarring between the lacrimal gland fascia and the levator aponeurosis.
2. Lid lag □on a vertical downward pursuit, the excursion of the upper eyelid lags behind the globe.
3. Lagophthalmos □incomplete eyelid closure is a classical sign of TED
4. Lower lid retraction is seen in up to 49% of TED cases[27]
5. Upper lid retraction is seen in around 90 to 98% of TED patients. The mechanisms proposed are as follows:

    - Enlargement and fibrosis of levator muscle - the most common muscle targeted by the immune cascade
    - Scarring between levator aponeurosis and surrounding soft tissues
    - Overaction of levator muscle to counteract the ipsilateral tight inferior rectus muscle
    - Increased sympathetic stimulation of Muller□s muscle

Ocular Surface Changes (Active TED Phase)

1. Eyelid-tear film-cornea - the interface is destabilized following inflammatory damage to the conjunctival mucous glands.[26]

2. Lacrimal gland inflammation - alters the protein profile of the tear film and reduces the tear secretion rate.
3. Persistent lagophthalmos disturbs the ocular surface, elevates the tear production rate, and elevates the tear osmolarity.[28]
4. Dry eye symptoms and watering occurs in 13 to 20% of patients.
5. Superior limbic keratoconjunctivitis is seen in 0.9% of patients.
6. Persistent dry eye with exposure-keratopathy - 1 to 8% of cases[2]
7. Corneal ulceration, perforation, endophthalmitis - in very severe cases[29]

Orbital Changes

1. Hypertrophy of the orbital fat and EOM within the bony orbit - raises the intraorbital pressure[30]
2. Forward protrusion of the eyeball - proptosis
3. Constriction of the superior ophthalmic vein (SOV) by enlarged EOM - venous stasis in TED[30]
4. Venous congestion - redness and swelling of the eyelids, chemosis, caruncular edema[23]
5. Elevation of the episcleral venous pressure - raised intraocular pressure (IOP), open-angle glaucoma[13]
6. Venous and lymphatic stasis in the orbit - prolongs the half-life of inflammatory cytokines, causing a vicious cycle of inflammation[13]
7. Spontaneous fracture of the medial or inferior wall of the orbit - a true, bony □autedecompression□[31]

EOM Changes

1. Inflammation of EOM - during active TED
2. Infiltration of EOM - accumulation of hyaluronate and late-onset fibrosis[32]
3. Most commonly involved muscle - inferior rectus (IR), followed by the medial rectus (MR), superior rectus (SR), lateral rectus (LR), and oblique muscles[13]
4. Restrictive strabismus and loss of binocular single vision
5. Diplopia at presentation - in 6 to 18% of cases[2]. Diplopia in the primary and inferior gaze is the most debilitating complication.
6. Fluctuation of diplopia with worsening in the morning - during active disease[32]

Optic Nerve Changes

Dysthyroid Optic Neuropathy (DON) is a potentially reversible optic nerve dysfunction in 4-10% of TED patients[2]. Early symptoms include diminished vision, altered color vision, diminished contrast sensitivity, and constriction of visual fields (VF). The possible mechanisms are:

1. Compressive optic neuropathy - most common cause, compression by the enlarged EOM at the orbital apex[23]
2. Optic nerve stretching - in cases of severe fat hypertrophy with proptosis[33]
3. Ischemic optic neuropathy - due to increased resistance to the orbital arterial blood flow, leading to diminished perfusion[34]
4. Enlargement of the superior ophthalmic vein - raises the retro-bulbar pressure and impairs tissue oxygenation.[34]

Evaluation

Thyroid eye disease cases are clinically evaluated as the activity and severity of the disease. The activity represents the grade of active inflammation and defines the progression of the disease. The severity reflects the spectrum of functional and cosmetic deficits. Numerous classification systems have come up over the last century to assess and grade the clinical manifestations of TED.

The most well-known system is the NO SPECS classification.[35] The American Thyroid Association introduced this classification in 1969. It was updated in 1977 to the modified NO SPECS classification.[36]

In 1981, Von Dyek proposed the RELIEF variation of the NO SPECS classification.[37]

The NO SPECS system only grades the clinical severity of TED. It doesn't include the activity of the disease. This classification system dictates the treatment strategies without considering the status of active inflammation. This system is now obsolete.

A new system **Clinical Activity Score (CAS),** was proposed in 1989, considering the classic signs of inflammation pain, swelling, redness, and impaired function. The European Group on Graves Orbitopathy (EUGOGO) later amended the CAS system. As per the amended CAS, active TED has a score of > 3/7 at the first visit or > 4/10 at subsequent visits.[38]

Spontaneous orbital pain Gaze-evoked orbital pain

The **EUGOGO** proposed a severity assessment protocol to grade the severity of TED into mild, moderate-to-severe, and sight-threatening categories as summarised below:

Soft Tissue Assessment (Pain not included)

Eyelid Swelling

1. Absent
2. Mild: none of the features defining moderate or severe categories
3. Moderate: definite swelling, no lower eyelid festoons OR angulation of the upper eyelid skin fold in downgaze
4. Severe: lower eyelid festoons OR upper lid fold becomes rounded at 45 degrees downgaze

Eyelid Erythema

1. Absent
2. Present

Conjunctival Redness

1. Absent
2. Mild: equivocal or minimal
3. Moderate: <50% of definite conjunctival involvement
4. Severe: >50% of definite conjunctival involvement

Conjunctival Edema

1. Absent
2. Present: separation of conjunctiva from sclera present in >1/3 of the total height of the palpebral aperture OR the conjunctiva prolapses anterior to the grey line of the eyelid

Inflammation of Caruncle or Plica Semilunaris

1. Absent
2. Present: plica prolapses through the closed eyelids OR inflammation of caruncle or plica

Lid Margin Assessment (at the mid-pupillary line)

- Palpebral aperture (mm)
- Upper/lower lid retraction (mm)
- Levator function (mm)
- Lagophthalmos - Absent or present
- Bell's phenomenon - Absent or present

Proptosis Assessment - using Hertel exophthalmometery to record the intercanthal distance

Ocular Motility Assessment

- The prism cover test
- Monocular ductions
- Head posture
- Torsion

- Binocular single vision

Corneal Integrity Assessment

- Normal
- Punctate keratopathy
- Ulcer
- Perforation

Optic Nerve Assessment

- Visual acuity (LogMAR or Snellen)
- Afferent pupil defect (present/absent)
- Colour vision
- VF analysis
- Optic disc assessment - normal/atrophy/edema

One or more of the following: Minor lid retraction < 2mm

A novel classification □the **VISA** system, was proposed in 2006 with four parameters □ Vision, Inflammation/congestion, Strabismus/motility restriction, and Appearance/exposure. The International Thyroid Eye Disease Society (ITEDS) 2018 defined separate parameters for the assessment at the first and subsequent visits.

Inflammation (I) score < 4/10, is an inactive disease - manage conservatively. Score > 5/10 with evidence of progression of inflammation - manage aggressively

The clinical assessment and scoring are similar to CAS-EUGOGO recommendations except for the following changes.

Chemosis: +1 point if the conjunctiva lies behind the grey line of the lid, +2 if the conjunctiva extends anterior to the grey line

Lid edema: +1 if no overhanging of tissues, +2 if upper eyelid skin folds or lower lid festoons are present

Strabismus/motility restriction: Ductions - measured to the nearest five degrees in all four gazes, using the corneal reflex method. Any change in the ductions of > 12 degrees in any direction suggests progression.

Clinical assessment protocols given by the VISA and EUGOGO teams are not interchangeable. Hence only a single system is used for a specific patient.

All the scoring systems focus on a qualitative assessment. They give an equal weightage to all the symptoms, regardless of their diagnostic significance. This undermines the accurate monitoring of the disease progression. The arbitrarily chosen cut-off points (3/7 or 4/10 in CAS scoring) may not accurately reflect the extent of the disease.

Orbital Imaging

Orbital imaging provides valuable insights into the diagnosis and management of TED.

Computed Tomography (CT) Scan

1. Characteristic fusiform enlargement of EOM - enlarged muscle belly with relative sparing of tendons. Long-standing cases show significant EOM changes - the "coca-cola sign." Orbital imaging in unilateral TED cases confirms the presence of asymmetric bilateral EOM changes.[39]
2. Barrett's index for quantitative measurement of EOM thickness and apical crowding.[40] The vertical index is the division of the sum of vertical muscle diameters by the height of the orbit. The horizontal index is calculated similarly. The greater of the two ratios is Barret's index. A Barrett's muscle index of >67% is predictive of optic neuropathy.[41]
3. Imaging in DON - soft tissue signs like apical crowding, enlarged superior ophthalmic vein, enlarged EOM (especially MR), Barrett's muscle index >67%, orbital fat prolapse across the superior orbital fissure, perineural fat effacement, and enlarged lacrimal gland. The bony orbit signs - the increased angle of the orbital apex and an increased angle of the medial wall. Coronal CT scan of orbital apex shows a narrow clear ring of low density around the optic nerve due to bulging adipose tissue. Stretch neuropathy is diagnosed by "taut nerve" in severe proptosis cases.
4. Classification of orbitopathy type 1: lipogenic variant, type 2: myogenic variant, and type 3: mixed variant. Accurate coronal images aid the detection of soft tissue remodeling EOM and fat enlargement.
5. CT exophthalmometry - is the gold standard. It is accurate, reproducible, and unaffected by periorbital tissue edema. The interzygomatic line (IZL) connects the ventral zygomatic borders bilaterally in axial view. The various techniques using IZL are:

- The perpendicular distance between the anterior surface of the cornea and IZL corresponds to the Hertel exophthalmometry value.[42]
- The distance between IZL and the posterior sclera (normal value = 9.9 + 1.9 mm).[43]
- The observation of less than 1/3rd of the globe lying behind IZL.[42]

This technique is not feasible in patients who underwent lateral wall decompression surgery. A novel method uses the posterior clinoid (PC) process as a landmark and measures the distance between the PC and the anterior corneal surface[44]

Magnetic Resonance Imaging (MRI) Scan

Better for disease activity assessment. The MR parameters - T2 signal intensity ratio, T1 signal intensity ratio following gadolinium administration, and apparent diffusion coefficient correlate positively with CAS. In T1 weighted images, EOM appears isointense to facial muscles in inactive TED, with enhancement on Gadolinium contrast.[45] In T2 weighted images, EOM appears hyperintense during active TED and hypointense during inactive TED.[39]

Orbital Color Doppler Imaging (CDI)

Evaluates the hemodynamic changes in orbit, secondary to increase in orbital volume. The primary vessels imaged are the ophthalmic artery, central retinal artery, and superior ophthalmic vein. The peak systolic velocity, end-diastolic velocity, and resistivity index are important indicators of ocular perfusion.[46]

Diagnosis of TED

The diagnosis of thyroid eye disease (TED) can be made by your primary care physician, your thyroid doctor/ endocrinologist, or an ophthalmologist. This usually occurs when you tell them about your symptoms, and they examine your eyes. You may also need additional testing such as

- Measurement of the amount of bulging of your eye
- Tests to check your visual field, and colour vision
- A computed tomography (CT) scan or magnetic resonance imaging (MRI) scan of your eye sockets and eye muscles

Treatment / Management

Prevention

Clinical assessment and accurate grading of thyroid eye disease are essential for appropriate management.

Primary Prevention □Smoking cessation[47]

Secondary Prevention □Early detection of any dysthyroid state and prompt management to prevent disease progression.

Tertiary Prevention □ Artificial tears prevent the risk of exposure-keratopathy.[48] Cosmetic and visual rehabilitation is essential.

Medical Management

Prompt restoration of euthyroid status is essential.[49]

Mild TED

Patients with corneal exposure and ocular surface symptoms require extensive lubrication with artificial tears, gels, and ointments. Over-night lid tapping, occlusive eye-pads, cold compresses, or sleeping with head-end elevation are of questionable benefit.

Selenium supplements improve the quality of life, reduce inflammation, and retards TED progression.[50]

Lid retraction < 2 mm is managed by:

- Transconjunctival injection - 5 unit botulinum toxin type A in LPS
- Transconjunctival injection - 10 mg of triamcinolone in LPS

Both techniques show excellent results with the resolution of lid retraction.

Moderate-to-Severe TED

Active Cases

Early immunosuppression is essential.

Corticosteroids: the first-line agent

EUGOGO management protocol is low-dose pulse therapy with intravenous methylprednisolone (IVMP). 500 mg IVMP is administered weekly for the initial six weeks. Over the next six weeks, the dose is tapered to 250 mg weekly.[51] Severe active cases require prolonged oral corticosteroids for six months. Withdrawal of steroids can show disease flare-ups. Adjuvant orbital radiotherapy helps prevent flare-ups.[52]

Immunomodulators: the second-line agents

Indications - steroid intolerance, steroid dependence, disease refractory to steroids, contraindications to steroid use

Methotrexate - weekly dosing of 7.5 to 10 mg shows a significant improvement in CAS and ocular motility within 12 months of treatment[53]

Azathioprine - combined with low dose orbital radiation or IVMP for moderate-to-severe TED[54]

Mycophenolate mofetil-standalone therapy shows better CAS response with minimal disease reactivation[55]

Immunobiologicals

Rituximab - a humanized chimeric monoclonal antibody targeting CD 20 on B-cells, shows 100% response and minimal reactivation in moderate-to-severe TED.[56]

Tocilizumab (anti-IL-6 receptor antibody), adalimumab (anti-TNF-a antibody), and infliximab (anti-TNF-a antibody) also show promising results.

Teprotumumab, a specific IGF-1R blocker, is a novel molecule. It is administered as eight infusions over 24 weeks. The improvement in CAS, proptosis, diplopia, and quality of life, with a reduction in proptosis, is comparable to surgical orbital decompression.[57]

Inactive Cases

For cases with lagophthalmos, dry-eye disease symptoms, and exposure keratopathy, adequate lubrication is advised.

Appropriate surgical management yields good cosmetic results for residual proptosis, strabismus, lid retraction, and significant lagophthalmos.

Sight-Threatening Disease

High-dose systemic corticosteroid, 1 g IVMP for three days, is the most effective therapy for DON cases.[58] Orbital radiotherapy is the second-line management for DON cases, with a reduced need for surgical orbital decompression.

Surgical Management

Elective surgical options are reserved for inactive thyroid eye disease cases not responding to conservative or maximal medical management. During cosmetic rehabilitation, orbital decompression surgery is the primary procedure to correct proptosis. After six months, strabismus surgery achieves adequate ocular alignment. After an additional six months, a definitive lid retraction surgery helps restore the cosmetic and functional status.

Indications for orbital decompression in stable inactive TED are corneal exposure, DON, disfiguring proptosis, chronic pain/ discomfort, and congestion.[59] Urgent orbital decompression is reserved for active TED with DON, not responding to high dose IVMP.[60]

The surgical approaches are customized:

1. Lateral wall decompression - by Kronlein, modified Kronlein, Stallard-Wright, Berke, and lateral eyelid crease incisions. The preferred technique is ab interno bone removal with sparing of the lateral orbital rim.[61] Complications include intraoperative CSF leak, infra-orbital anaesthesia, and new-onset diplopia.[62]
2. Medial wall decompression - using trans-cutaneous, trans-conjunctival, or trans-nasal approaches. The trans nasal endoscopic approach is ideal for medial wall surgeries.[63]
3. Floor decompression - trans-orbital approach by trans-cutaneous or trans-conjunctival incisions
4. Two wall decompressions - combined medial wall and floor removal[64]
5. Combined lateral wall and floor decompression - trans-conjunctival or trans canthal swinging lid crease approach[65]
6. Three walls □floor, lateral wall, and medial wall, and sparing of the orbital roof
7. Four wall decompression □floor, medial wall, lateral wall, posterolateral roof[66]
8. Fat decompression - in fat-predominant orbitopathy [67]
9. Balanced decompression □medial + lateral wall.[68] The rate of new-onset strabismus is lower with a balanced decompression.[69]

Surgical orbital decompression corrects the proptosis of 2 to 2.5 mm per wall.[70] Fat is the fifth wall of the orbit for surgical decompression.[68]

Differential Diagnosis

Non-specific orbital inflammatory disease (NSOID): Bilateral proptosis with lacrimal gland enlargement. EOM enlargement involves the muscle belly and the tendinous origin. The lacrimal gland enlarges and prolapses out of the lacrimal fossa. It can be associated with systemic autoimmune diseases like polymyositis, dermatomyositis, and IGG4-related diseases. Serology and soft tissue biopsy are diagnostic.[71]

Lymphoma: Bilateral proptosis with lymphadenopathy. Hemogram and blood counts are usually normal. Orbital CT scan shows bilateral diffuse soft tissue enlargement with the erosion of the bony orbit. Histopathology and immunohistochemistry features on the soft tissue biopsy are diagnostic.[72]

Blow-out fracture of the orbit: Altered globe position and limitation of EOM movements. History of trauma is followed by enophthalmos and restriction of elevation. An orbital CT scan shows the bony defect with entrapped soft tissues.[73]

Amyloidosis: Bilateral proptosis with neuropathy. Soft tissue biopsy shows eosinophilic material on histopathology with birefringence on polarised light microscopy.[74]

CURRENT MEDICATION OPTIONS FOR THYROID EYE DISEASE

MEDICATION	HOW IS MEDICATION GIVEN?	WHAT DOES THIS MEDICINE IMPROVE?	SIDE EFFECTS
Selenium	By mouth	Mild eye symptoms	High levels can cause diarrhea, nausea, brittle nails, irritability, and skin rashes
Steroids	Intravenous (injection)	Swelling of the eyes	Some people using this medication experience changes in mood, difficulty sleeping, and changes in blood pressure or blood sugar
Teprotumumab	Intravenous (infusion)	Irritation and bulging of the eye May reduce the need for surgery	Some people using this medication experience: high blood sugars, decreased hearing, gastro-intestinal symptoms, and muscle cramps. Cannot be used during pregnancy or breastfeeding.

Prognosis

Approximately 80% of thyroid eye disease cases require conservative management with topical lubricant eye drops. 5% of TED cases need systemic corticosteroids or immunomodulation. About 20% of the patients undergo some form of surgical intervention. Long-term follow-up and strict monitoring for disease complications are essential.

Complications

Thyroid eye disease cases can present with the following complications:

1. Dysthyroid optic neuropathy - compressive or ischemic
2. Optic atrophy

3. Exposure-keratopathy and keratomalacia
4. Open-angle glaucoma
5. Restrictive strabismus and diplopia
6. Persistent proptosis, lid retraction, cosmetic disfigurement
7. Orbital venous stasis and venous occlusions[2]

Postoperative and Rehabilitation Care

Cosmetic rehabilitation is essential in TED management. Asymmetrical proptosis is common during inactive disease. A graded surgical orbital decompression helps achieve a cosmetically symmetrical look.

The surgical plan is customized depending on the amount of proptosis correction, the pattern of strabismus, and the orbital anatomy. The restricted EOM is recessed to achieve orthophoria in the primary gaze. The final correction for the lid retraction is planned at least six months after the strabismus surgery. Blepharotomy, blepahromyotomy, levator recession, and spacer grafts are the common strategies for lid retraction correction.[75]

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राज्य स्वास्थ्य एवं परिवार कल्याण संस्थान, उ0प्र0
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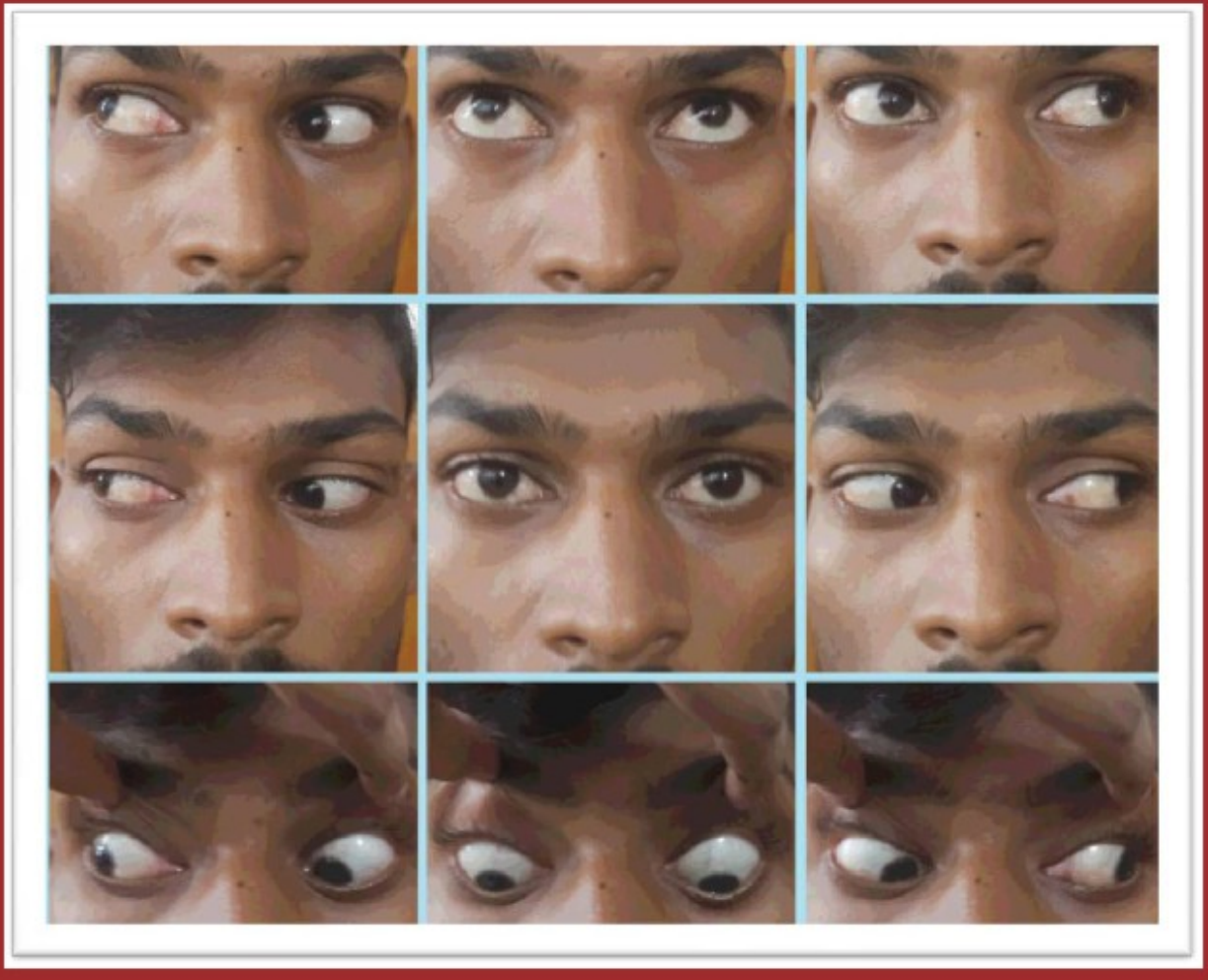
CHAPTER 7



SQUINT


राज्य स्वास्थ्य एवं परिवार कल्याण संस्थान, उ0प्र0
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SQUINT

Introduction

Squint or strabismus has a varied etiology and has a worldwide prevalence of 3-5%.[viii] It is often detected later in life by when irreversible visual damage has occured. Timely diagnosis and treatment of strabismus can lead to better outcomes. This chapter summarizes the basics of squint examination and treatment that can be used as guide for community healthcare.

What is strabismus?

Strabismus or □squint□ as is known in common terms is*the inability of the two eyes to simultaneously direct their foveae at a common object of regard, occasionally or always.*

In slightly technical terms, it is the inability of both the eyes to align their visual axes to common object of regard. Visual axis being the line joining the fovea of the eye to the fixation point.[viii]

What keeps the eyes aligned?

Both the eyes, the extra ocular muscles and the nervous system function together as a sensori-motor unit to keep the eyes aligned. An intact sensory system enables us to binocularly perceive our surroundings in depth (i.e. in third dimension). The

motor system moves the eyes to bring the object of attention onto the fovea and aligns both the eyes to enable binocular single vision. Both the systems work in unison and are mutually reinforcing for each other. A defect in either of them may result in strabismus.

Four recti (superior, inferior, medial, lateral) muscles and two oblique (superior, inferior) muscles comprise the extra-ocular muscles. They form the motor component required for keeping the eyes aligned. Uniocular eye movements are called ductions and binocular movements are called versions.

The sensory mechanisms are the driving force of the motor mechanisms. These reinforce the motor mechanisms to maintain ocular alignment and precisely coordinate ocular movements. Binocular single vision (BSV) involves simultaneous contribution of both eyes to perceive a single image of the object of regard. It is the single most important sensory mechanism driving motor ocular alignment. Fusion and stereopsis are higher grades of binocular vision.

Orthophoria is perfect ocular alignment without any stimulus for fusion. This usually does not occur and a certain amount of heterophoria is commoner in normal population.[viii]

Having understood the mechanisms involved in maintaining ocular alignment and precise ocular movements, we can now understand that aberrations in motor and sensory mechanisms responsible for ocular alignment would result in strabismus.

Classification of strabismus

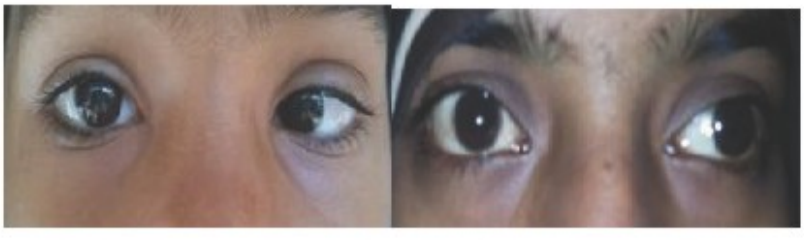
Strabismus is classified broadly into two major forms, comitant and incomitant. Comitant strabismus has the same angle of deviation in all directions of gazewhen for a particular fixation distance.[viii]Strabismusisincomitant when the deviation varies in different gazes or with the eye used for fixation.[viii]Incomitant strabismus is usually

paralytic (due to palsy of the third, fourth, or sixth cranial nerve) or restrictive (due to the involvement of extraocular ocular muscles or their surrounding soft tissue).[viii]

Strabismus can also be classified depending on the axis of deviation.Deviation along the vertical axis causes esotropia (inward deviation of eye) and exotropia (outward deviation of eye). Deviation along the horizontal axis causes hypotropia (downward deviation of eye) and hypertropia (upward deviation of eye).Deviation along the anteroposterior axis causes intorsion (inward rotation of the eye) and extorsion (outward rotation of the eye).[viii]

Differences between comitant and incomitant strabismus are listed in the table below

Symptoms	Comitant	Incomitant
Onset	Insidious	Sudden usually following trauma, viral illness,neuro surgery, poor glycaemic control or hypertension
Duration	Usually since childhood	Usually recent
Diplopia	No	Yes
Signs		
Head Posture (Motor adaptation)	No	Yes
Motility limitation	No	Yes
Secondary deviation>Primary deviation	No	Yes
Sensory adaptations	Yes	No



Photographs showing esotropia and exotropia of left eye in different patients

According to laterality strabismus can be unilateral where one eye deviates while the other eye maintains fixation all the time or alternating when either eye can take the fixation while focusing on an object while the other eye deviates.[viii]

Clinical evaluation

A detailed history should be elicited including the onset, duration, intermittency, aggravating or relieving factors, and associated ocular and systemic complaints. Perinatal period and developmental milestones history should be elicited in infants and children presenting with a history of strabismus since infancy.[viii]A detailed history of antecedent events, including trauma, viral infection, meningitis, and microvascular risk factors such as diabetes mellitus, hypertension, and hyperlipidemia are important clues to potential causes in acquired cases of strabismus.[viii]

Patients with strabismus from early childhood (<3 years) usually adapt to their visual disorder, perhaps with the development of suppression.[viii] Old photographs help figure out the time of onset of strabismus. Those who develop strabismus in adulthood present either with confusion where the patient sees two different overlapping images at the same locus or diplopia where the patient appreciates two different images of the same object at different locus depending on the amount and direction of deviation.[viii] Blurred vision and an awareness of change in head posture are also seen.

Accurate assessment of vision is essential for the management of strabismus. In 6 weeks and older infants, assessing fixation using torch light or brightly colored objects can provide a rough idea about a child□s vision. In children below 5 years, a picture identification test is used, and for those above 5 years, visual acuity assessment is done by Snellen chart.

Cycloplegic refraction forms an essential part of strabismus examination. It assumes greater significance in children who are uncooperative for subjective visual assessment. To ensure full cycloplegia children are often advised to come after instillations at home and this part of examination is then completed on the second visit. Reliable assessment of motor and sensory status is only possible with the patient wearing appropriate glasses.

Table showing different cycloplegic agents used for refraction in different age groups

	Atropine sulphate 1% ointment	Cyclopentolate 1% eye drops	Tropicamide 0.5–0.8% + 2.5–5% phenylephrine eye drops
Indications	• First time refraction in all children <7 years or esotropic children up to 15 years • Subsequent refractions in hypermetropes up to 15 years	• First time refraction in children between 7 and 15 years or esotropic patients above 15 years • Subsequent refractions in hypermetropes over 15 years	• First time refraction above 15 years of age • Subsequent refractions in non-hypermetropes of all ages
Instillation regime	Rice grain size twice daily for 3 days	3 instillations half hour apart, 3–4 h prior	3 instillations 10 min apart, 1 h prior
Recovery	14 days	1–3 days	6–12 h

Strabismus examination

The examination of strabismus can be divided into motor examination and sensory examination.

The motor examination comprises of identifying the actual presence of deviation and quantifying it (both objectively and subjectively). Recognition of limitation in ocular motility, compensatory mechanisms and conditions that may mimic strabismus are also important

Uniocular movements or ductions, synchronous simultaneous movements of both eyes in the same direction or versions, and fusional movements or vergences are assessed.

Hirschberg's corneal reflex test is done to have a rough idea of the amount of deviation.[viii] Each 1 mm decentration of corneal reflection corresponds to 7° of deviation in the visual axis. So, a 2 mm decentration (pupillary margin in a 4 mm pupil) would correspond to a deviation of 14°, and a 5.5 mm decentration (Limbus) would correspond to a deviation of about 40°

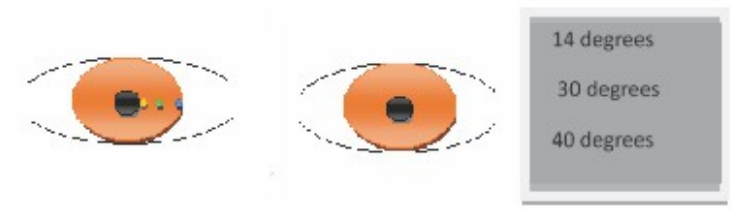


Figure: The Hirschberg corneal reflex test

Prism cover test may be performed with loose prisms or with a prism bar. An alternate cover test is performed for distant and near fixation. The apex of the prisms points in the direction of deviation. The prism that neutralizes deviation and eliminates movement upon alternate cover test is the measurement of deviation (in prism dioptres). The maximum angle of deviation should be measured by increasing the power of prisms till the direction of movement is reversed on the cover test.

Sensory examination of a patient with strabismus comprises of determining the binocular state with various possibilities like 1) diplopia 2) suppression 3) abnormal retinal correspondence or 4) stereopsis. It also involves examination for amblyopia, a condition which persists even after occlusion of the fixating eye.

Differential diagnoses (pseudo-strabismus)

Conditions that have no obvious squint but there is a clinical impression of ocular deviation. It includes:

- Epicanthic folds: prominentepicanthal folds simulate esotropia
- Abnormal interpupillary distance: small simulates an esotropia and large an exotropia
- Angle kappa: A large positive angle kappa may give a pseudoexotropia seen in the temporally displaced macula. A negative angle kappa simulates an esotropia. This occurs when the fovea is situated nasally from its usual position as in high myopia.

Neuroimaging is indicated in all children presenting with acute-onset strabismus and in adults with pupil-involving complete and pupil-sparing partial third cranial nerve palsy. Neuroimaging should also be recommended in acquired strabismus in patients below 50 years, non-resolving till 3 months, or aberrant regeneration in non-traumatic palsy.[viii]

Amblyopia

Amblyopia is a unilateral or bilateral reduction in best-corrected visual acuity, in the absence of any identifiable pathology of the eye or visual pathway.[viii]

Strabismus, refractive errors, and visual deprivation due to conditions like ptosis, corneal opacities, cataracts, etc can lead to amblyopia.[viii] In a child with diminished vision, the diagnosis of amblyopia should be one of exclusion.

Common signs of amblyopia are

(1) Visual acuity of the amblyopic eye is reduced
(2) Visual acuity improves under mesopic conditions

(3) Color, contrast, and accommodation are reduced

(4) A crowding phenomenon occurs, where acuity when measured with single letters is better compared to conventional charts

(5) Abnormalities of pupillary reaction and pursuits may occur

(6) In the presence of strabismus, the non-amblyopic eye strongly prefers to take up fixation.

Complete ophthalmic evaluation excluding organic causes of reduced vision is essential. Principles of treatment include correction of refractive error and occlusion of the sound eye to encourage the use of amblyopic eye.[viii]The younger the patient, the more rapid the improvement but there is a risk of inducing amblyopia in the normal eye. It is therefore necessary to monitor VA regularly in both eyes during treatment.

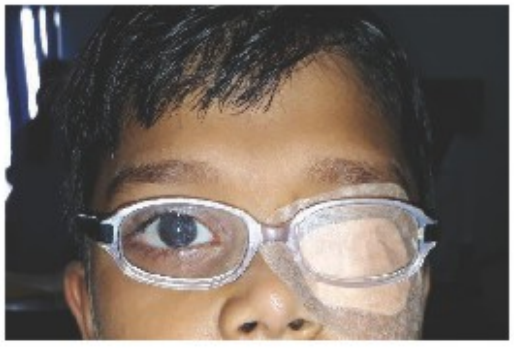
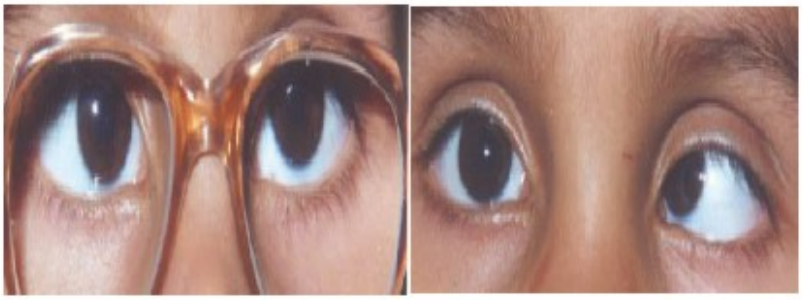


Figure: Child doing patching (occlusion) for amblyopia management

Treatment

The goal of strabismus management is not only to restore motor alignment of the eyes but also to correct any underlying sensory abnormality. While most of the sensory abnormalities are managed conservatively, surgery is often indicated for correcting the static component of the motor misalignment.



The non-surgical approach in strabismus management includes appropriate correction of the refractive error, treatment of associated sensory abnormalities including amblyopia and treatment of the dynamic component of the deviation. Appropriate prescription of glasses and occlusion of the better seeing eye in amblyopia are the mainstay.

Certain types of strabismus require surgical correction. Surgery if indicated should be performed early for better prognosis. Weakening of overacting muscle (recession) and strengthening of the under acting muscle (resection) are commonly performed procedures. Intramuscular injection of botulinum toxin is also used as a muscle-weakening procedure.

Summary

- Strabismus is a common cause of visual disability.
- It is relative misalignment of visual axes of eyes occurring as a consequence of altered sensory and motor mechanisms.
- Clinical evaluation of strabismus involves a systematic and step-by-step approach. Any refractive error should be corrected before proceeding with strabismus evaluation.
- Strabismus can be comitant or incomitant. Incomitant strabismus can be paralytic or restrictive.

- Common cause of comitant strabismus is uncorrected refractive error and that for incomitant is trauma and microvasculopathies (like diabetes mellitus).
- Correction of refractive error, occlusion, orthoptics and surgery are mainstay of strabismus management.
- Delay in management of strabismus can cause amblyopia (reduction in visual acuity due to central suppression) which may be irreversible.

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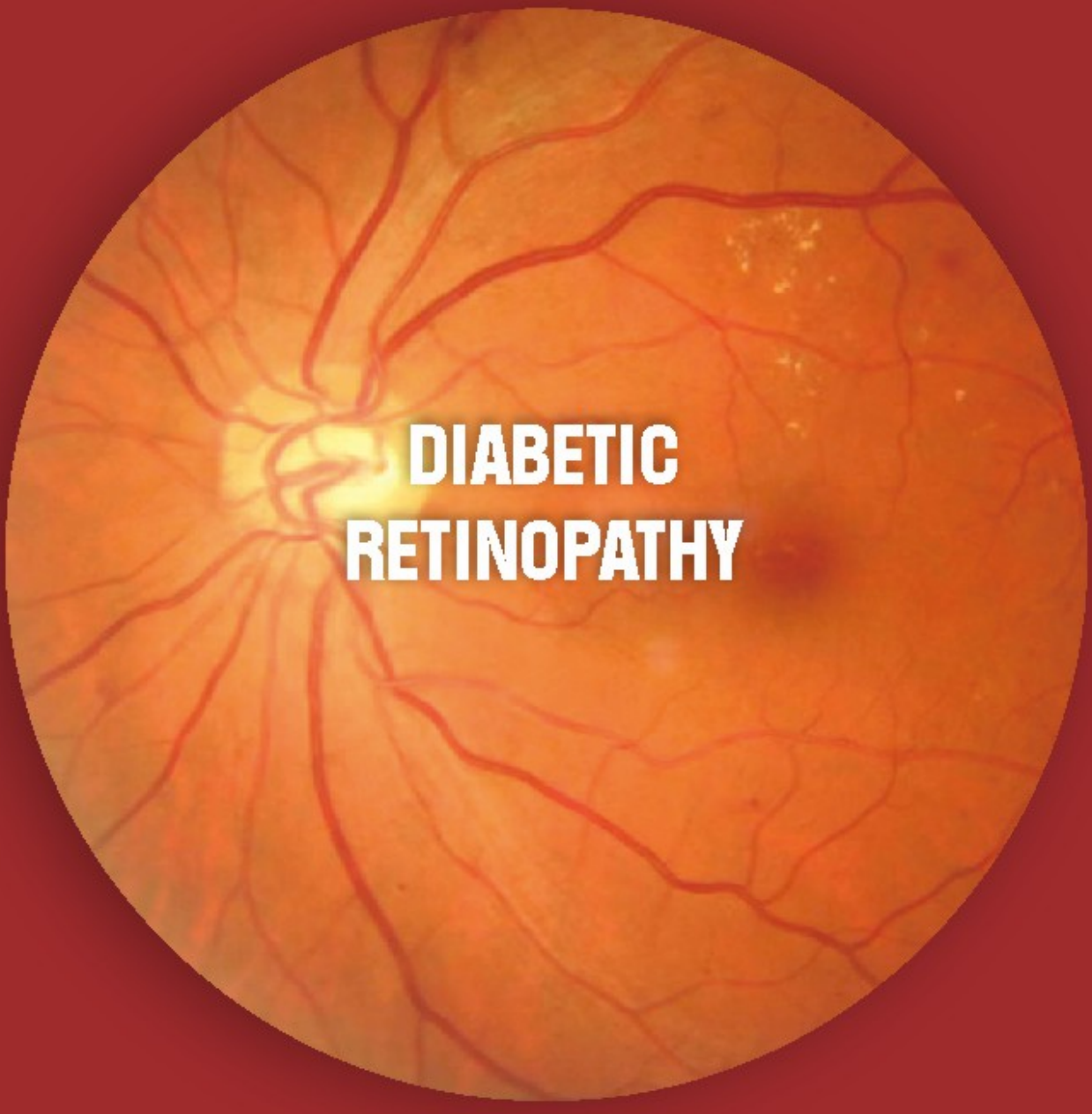
CHAPTER 8



DIABETIC RETINOPATHY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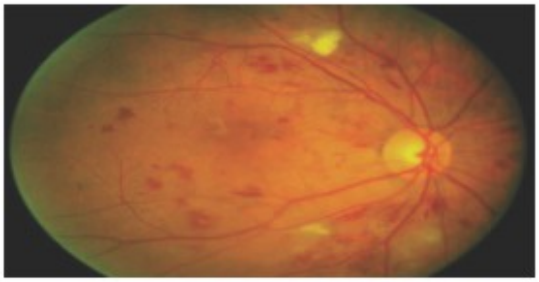


DIABETIC RETINOPATHY

Definition -

Diabetic retinopathy (DR) is a microvascular disorder occurring due to the long-term effects of diabetes mellitus. Diabetic retinopathy may lead to vision-threatening damage to the retina, eventually leading to blindness. Globally, DR impacts approximately 93 million individuals, with around 21 million among them experiencing treatable variations of Diabetic Macular Edema (DME). [1] Within the domain of DR, DME exhibits a prevalence ranging from 11% to 15% [1□3] as the primary contributor to vision impairment. [4] Among those affected, roughly 20% of patients with type 1 Diabetes Mellitus (DM) and 14% to 25% of those with type 2 DM are influenced by DME. [5] Persistent high blood sugar levels trigger a cascade of molecular alterations that culminate in the compromise of the blood-retinal barrier, leading to the onset of DME. The pivotal role played by vascular endothelial growth factor (VEGF) is central to the pathogenesis of DME.

Risk factors - include:

- Pregnancy
- Hypertension
- Obesity
- Dyslipidemia

- Poor glycemic control
- Nephropathy
- Hormonal influence - leptin and adiponectin
- Oxidative stress
- Genetic factors

Pathophysiology -

- Predominantly a microangiopathy
- Chronic hyperglycemia is considered to be the primary pathogenic agent in DR
- Small blood vessels are more vulnerable
- Direct effect on retinal vessels also seen
- VEGF plays a particularly important role by increasing vascular permeability and promoting neovascularization.
- The morphological changes seen in small retinal vessels in DR include early loss of pericytes, basement membrane thickening, loss of endothelial cells, increased vascular permeability, platelet aggregation, leukostasis, and capillary dropout.

Patients might be asymptomatic in the early stages and might be discovered incidentally on fundus examination. As the disease progresses, the symptoms include blurred vision, distorted vision, floaters, and partial or total vision loss.

Signs on fundus examination:

1. Microaneurysms
2. Dot and blot hemorrhages
3. Exudates

4. Venous changes

Early Treatment Diabetic Retinopathy Study (ETDRS)classification:

1.Non-proliferative diabetic retinopathy (NPDR) [Figure 1]

- Very mild NPDR - microaneurysms only
- Mild NPDR - microaneurysms, retinal hemorrhages, exudates, cotton wool spots
- Moderate NPDR - severe retinal hemorrhages (in 1-3 quadrants) or mild IRMA; significant venous beading, cotton wool spots
- Severe NPDR - severe hemorrhages in all 4 quadrants, significant venous beading in 2 or more quadrants, moderate IRMA in 1 or more quadrants
- Very severe NPDR - Two or more criteria for severe NPDR

2.Proliferative Diabetic Retinopathy (PDR)[Figure 2]

- Mild moderate: NVD or NVE
- High risk: NVD greater than 1/3rd disc area, any NVD with vitreous hemorrhage, NVE more than ½ disc area with vitreous hemorrhage.

Diagnosis:

- **Fundus Photo-** both colored and red-free

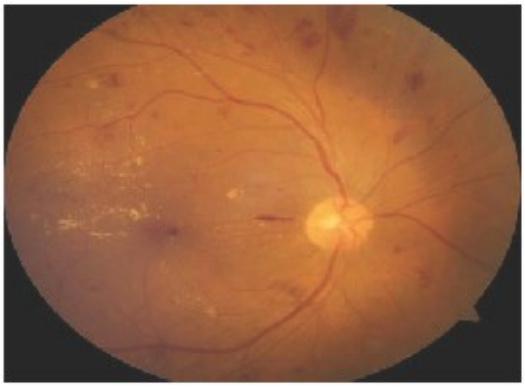


Figure 1: ***Fundus Photo- of the right eye showing moderate nonproliferative diabetic retinopathy with diabetic macular edema. Multiple hemorrhages (flame-shaped and dot blot type) can be seen along with microaneurysms. Hard exudates can be seen on and around the macula with blunting of the foveal reflex.***

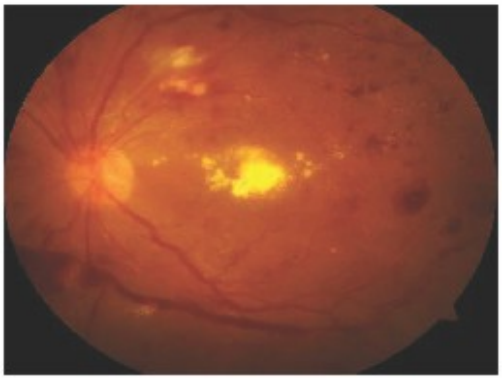


Figure 2: Fundus Photo- of the left eye showing proliferative diabetic retinopathy with diabetic macular edema. Multiple intra-retinal and pre-retinal hemorrhages can be seen along with soft and hard exudates.

- **Fundus Fluorescein Angiography (FFA)** [Figure 4,5]

FFA is indicated in the following situations.

- For the diagnosis of ischemic maculopathy
- To locate capillary dropout areas
- To differentiate IRMA from neovascularization
- To differentiate disc collaterals from disc neovascularization
- To reveal occult new vessels that could not be detected on clinical examination

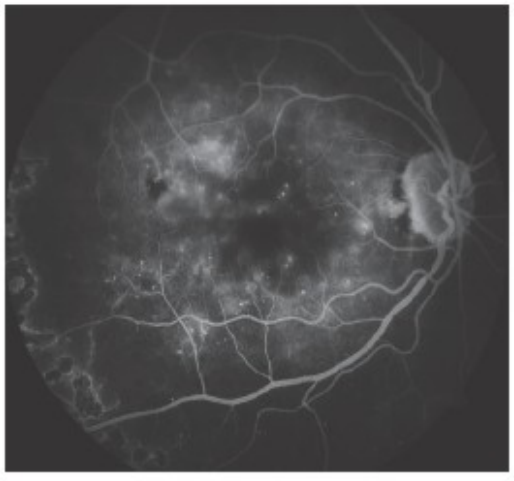


Figure 4: Fundus Photo of Right Eye showing late-phase fundus fluorescein angiography of a patient with proliferative diabetic retinopathy. The hyperfluorescent spots are suggestive of leakage due to macular edema.

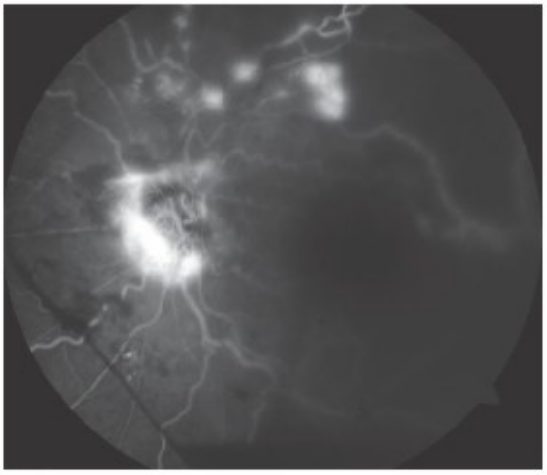


Figure 5: Fundus fluorescein angiography image showing proliferative diabetic retinopathy. Hyperfluorescence at the disc and in the superior quadrant is suggestive of neovascularization at the disc and neovascularization elsewhere. The hypofluorescence is due to blocked fluorescence as a result of hemorrhage.

- **Role of Optical Coherence Tomography (OCT)**[Figure5,6,7]:

➢ To evaluate retinal thickening. Here central subfield thickness (CST) and cube average thickness (CAT) are of utmost importance in diagnosing and managing DME.

➢ To diagnose vitreomacular traction (VMT) and the epiretinal membrane (ERM), which might require surgery (pars plans vitrectomy)

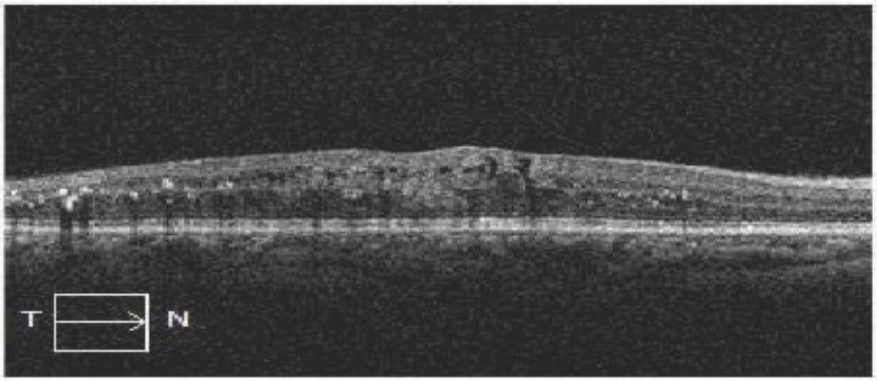
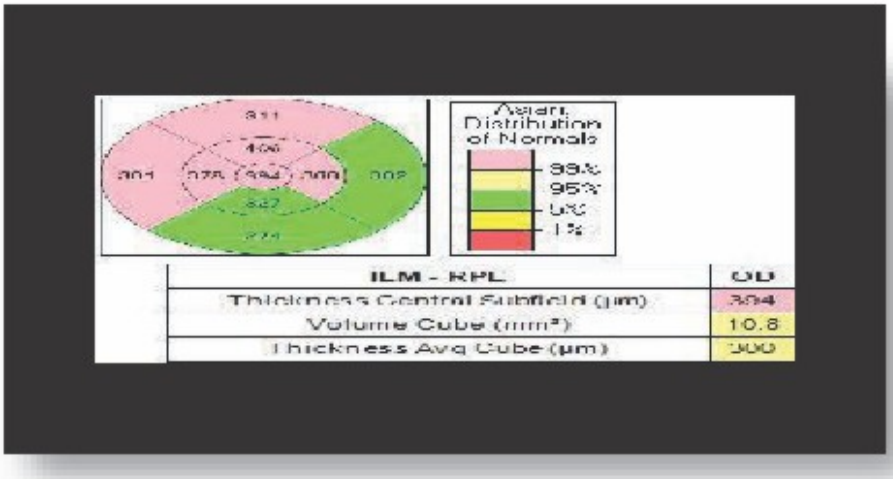


Figure 6: SD-OCT images show Diabetic Macular Edema (DME). The central subfoveal thickness is 394 µm in the centre 1mm area suggestive of Centre Involving DME.



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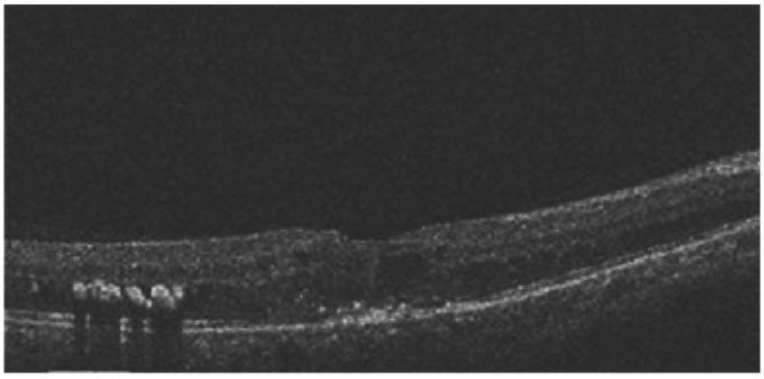

Figure 7SD-OCT image shows diabetic macular edema. Cystic changes can be seen along with hyperreflective spots suggestive of hard exudates.

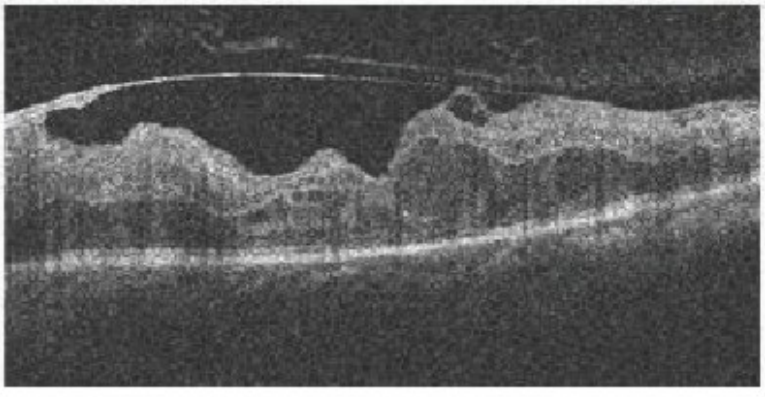

Figure 8: SD-OCT image of a diabetic patient complicated with vitreomacular traction. A posterior hyaloid membrane can be seen exerting traction on the macula.

- **OCT ANGIOGRAPHY (OCT-A)**employs motion contrast imaging to retinal blood flow, generating images similar to fluorescein angiography without the need to inject the dye invasively. [Figure 8]
  - ➢ It provides detailed information on the retinal vasculature
  - ➢ It is helpful for the demarcation of the foveal avascular zone, helping to find out foveal ischemia
  - ➢ It enables accurate detection of even mild IRMA
  - ➢ It helps to delineate capillary dropout areas

- Vascular signs like looping, beading, and dilatation can very well be appreciated on OCTA. OCTA may help the earliest detection of microvascular changes (before the visibility of microaneurysm

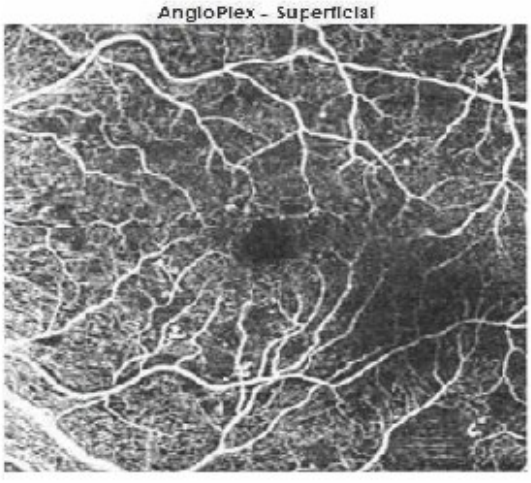

Figure 9: OCT Angiography showing the increased size of the foveal avascular zone along with multiple areas of capillary nonperfusion and leakage in a patient with severe nonproliferative diabetic retinopathy.

Treatment:

1. **Medical management-**
   - Strict glycemic control
   - Normalization of lipid profile
   - Stabilization of serum urea and creatinine levels

2. **Intravitreal anti-VEGF injections**:now considered the main therapeutic option for the treatment of DME and PDR. [Figure 9]

These include:Bevacizumab, Ranibizumab, Aflibercept, and Brolucizumab.

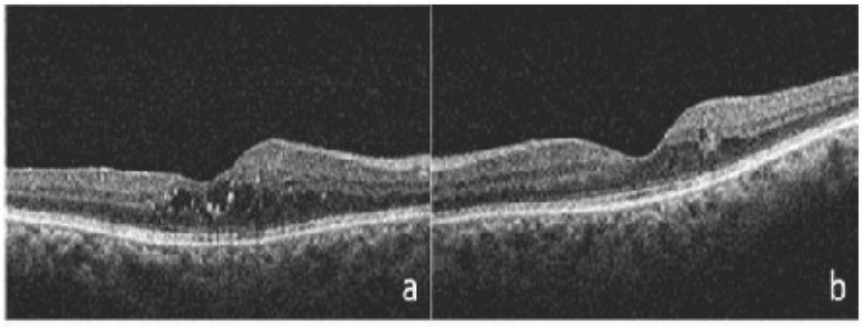

Figure 10: SD-OCT image. (a)Pre- intravitreal injection: shows diabetic macular edema (DME) with cystic changes; (b) Post-intravitreal injection: the macular thickness has decreased. Cystic changes have also decreased.

3. In conditions with refractory DME, **intravitreal triamcinolone and dexamethasone implants** have been tried with some success.
4. **Role of laser:**
   a. **Focal laser-** for leaking microaneurysms
      Spot size- 50-100 µm
   b. **Pan Retinal Photocoagulation-**A retinal burn diameter of 400 micrometers is desirable with the treatment restricted to temporal to macula to reduce the risk of accidental macular damage.
5. **Pars plana vitrectomy** can be considered in patients with:
   a. non-resolving vitreous hemorrhage (blood in the vitreous cavity)
   b. tractional retinal detachment.

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CHAPTER 9

RETINOPATHY OF PREMATURITY


राज्य स्वास्थ्य एवं परिवार कल्याण संस्थान, उ0प्र0
SIHFWUP
ज्ञानादृते न मुक्तिः

RETINOPATHY OF PREMATURITY

Retinopathy of prematurity (ROP) is a disease of retinal vascular and capillary proliferation affecting premature infants undergoing oxygen therapy.[viii] ROP was First described in 1942 by Terry et al and this disease was labelled as retrolental fibroplasia (RLF).[viii] In the 1950s, the association between supplemental oxygen and ROP pathogenesis was first established by controlled studies done in the neonatal intensive care units.[viii] The spectrum of ROP ranges from mild cases that may resolve spontaneously with no visual impairment to advanced cases with bilateral irreversible blindness within the first few months of life.

Epidemiology

India is having largest number of preterm babies.[viii] The incidence of ROP in different regions across India has been reported to range from 38% to 47%[viii] and contributes to nearly 10% of the worldwide estimate of blindness and visual impairment due to ROP.[viii] Significant differences in neonatal care quality between peripheral and tertiary care centers, as well as the improved survival rates of preterm babies, are key factors. The problem is exacerbated by the limited availability of screening and management services, which is due to a lack of ROP awareness among healthcare workers, parents, and counselors. Additionally, the shortage of trained ophthalmologists and neonatologists in the community further compounds the issue.[viii]

Pathogenesis

To understand the pathogenesis of ROP it is important to first understand the normal retinal vascular development. The Vascular supply network for the Retina consists of two main components.

1. The choroidal vessels that supply the outer retinal layers

2. The retinal vessels that supply the inner retinal layers

The Vascular development of choroid is complete by the third month of gestation, but retinal vascular growth is still incomplete in a premature child.[viii] The vascular development of retina begins by the 16th week of gestation. These developing retinal blood vessels reach the nasal ora serrata by 32-36 weeks and the temporal ora by 39-41 weeks. Thus, a premature child is born with incomplete.

peripheral vascularization; the area of avascular retina depending approximately upon the gestational age of the child.

Retinal vascular development occurs in two phases -

Phase 1: Vasculogenesis - During vasculogenesis, vascular precursor cells (VPCs) exit from the optic nerve to form the four major arcades of the posterior retina.

Phase 2: Angiogenesis - It is characterized by the proliferation of endothelial cells, arising from the existing vasculature formed during vasculogenesis.[viii]

Abnormal Vasculogenesis in ROP □

The disease process for the development of ROP occurs in two phases; an initial phase of vessel obliteration followed by the second phase of vessel proliferation.

Phase 1: Hyperoxia-Vaso cessation (Vaso-obliterative) phase - From birth to postmenstrual age of 30 -32 weeks.

In humans, the retina develops in utero where there is low tissue oxygen. The metabolic demands of the developing retina are more than the oxygen supplied by the fetal choroidal circulation resulting in "physiologic hypoxia".[viii] In addition to maternally derived factors, that stimulate angiogenesis, this hypoxia triggers the release of vasoactive factors, like insulin-like growth factor (IGF)-I, vascular endothelial growth factor (VEGF)[viii] and erythropoietin.

With birth, the environment for the retinal development now changes from a low oxygen tension intrauterine environment to a relatively high oxygen tension environment postnatally. A rise in PaO_2 causes a decrease in the hypoxia triggered VEGF and loss of placental and maternal growth factors due to premature birth.[viii] Exposure to supplemental oxygen, which is required to treat associated respiratory distress syndrome (RDS) in premature low birth weight babies, further suppresses retinal growth factors that are already compromised due to preterm birth and poor nutrition. This coupled with a lack of autoregulation of the choroidal circulation in premature babies results in movement of the oxygen from the choroidal to retinal circulation. This retinal hyperoxia and downregulation of growth factors result in phase 1 of vaso-obliteration of existing vessels, retraction of the normal developing retinal vessels, and cessation of the retinal vessel migration (Figure 1). An increase in the oxygen levels also increases the reactive oxygen free radicals, further increasing the damage.[12]

Phase 2 of ROP: Relative hypoxia - revascularization (Vaso proliferative) phase - Begins around 32-34 weeks. Phase 2 is hypoxia driven. In this phase, the infant is weaned from supplemental oxygen. Also because of cessation of the retinal vessels growth, the peripheral retina now becomes a hypoxic and increased release of

growth factors like VEGF, an Insulin-like growth factor is seen. This up-regulation stimulates neovascularization at the border between vascular and avascular retina, whichleads to retinal hemorrhages, vitreous hemorrhage, fibrosis, and tractional retinal detachment leading to visual impairment.[8]

Risk factors for ROP

Definite risk factors include prematurity, low birth weight, and supplemental oxygen administration.

Other risk factors include blood transfusions, failure to gain weight, respiratory distress syndrome (RDS), intermittent hypoxia, intra-ventricular hemorrhage (IVH), anaemia, multiple apnoeic spells, sepsis, hypercarbia and acidosis.[viii]

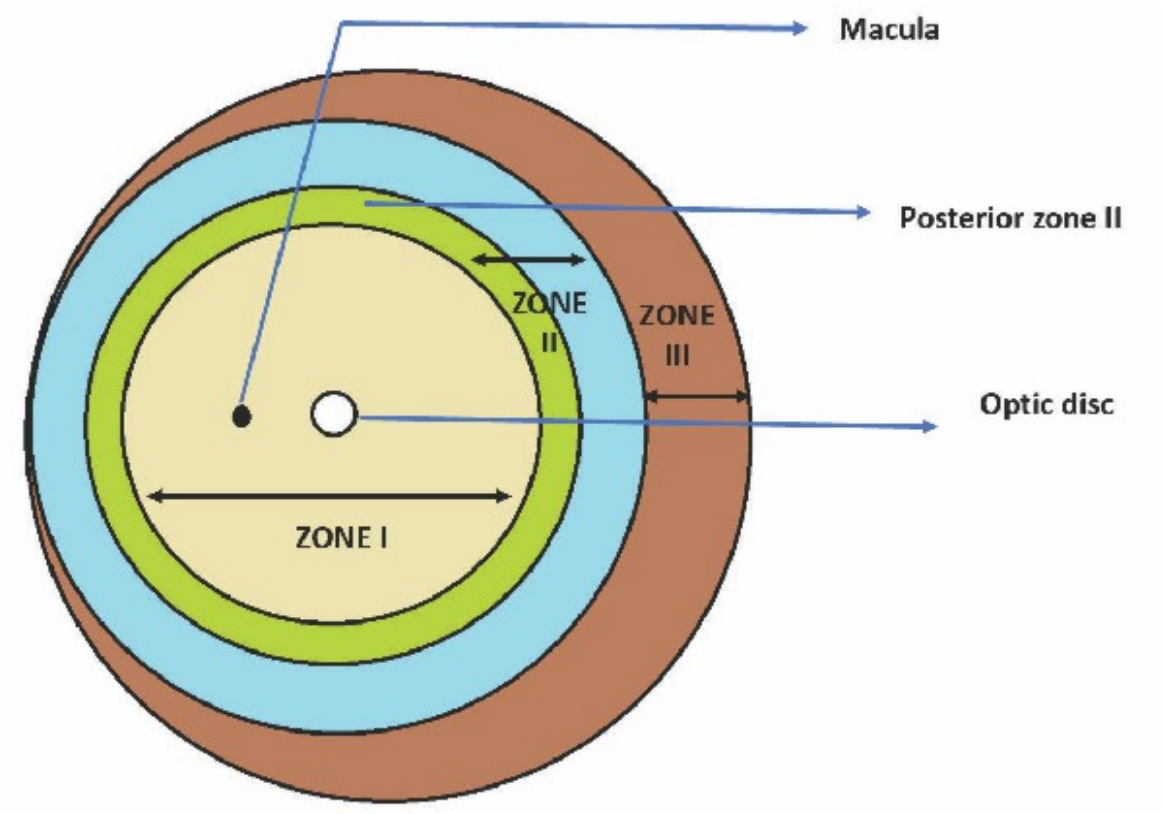
Zones of retinal involvement in ROP[viii]

Zone I is the small circle of retina around the optic disc. The radius of the circle is twice the distance from the macula to the center of the optic disc.

Zone II is a ring-shaped region extending nasally from the outer limit of zone I to the nasal ora serrata and with a similar distance temporally, superiorly, and inferiorly. Posterior zone II is a region of 2-disc diameters peripheral to the zone I border to indicate potentially more worrisome disease than ROP in the more peripheral zone II.

Zone III is a crescent-shaped area of temporal retina.

Zones of ROP



Stages of ROP[14]

The clinical appearance of the stages of ROP is related to the appearance of the retinal vessels at the avascular-vascular junction. More than one stage may be present in the same eye; staging then is determined by the most severe manifestation present.

Immature or incompletely vascularized retina: This is seen prior to the development of ROP and is characterized by dichotomously branching retinal vessels of normal caliber.

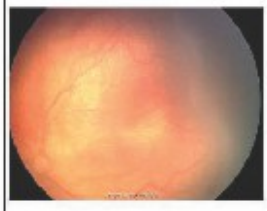
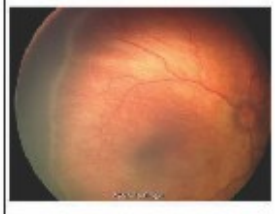
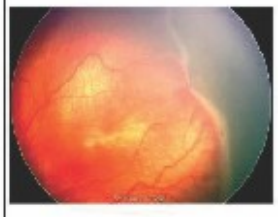
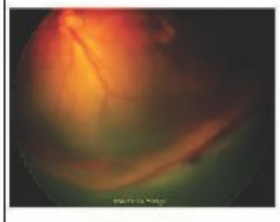
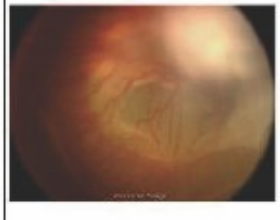
Stage 1: A flat demarcating line is seen delimiting vascularized retina from the anterior avascular retina. Abnormal branching or arcading of vessels is seen leading up to the demarcation line.

Stage 2: The demarcation line develops into a 'ridge'. This ridge is raised and has 'volume'.

Stage 3: Extra-retinal neovascularization into the vitreous is seen with the development of abnormal shunt vessels at the ridge.

Stage 4: ROP associated with retinal detachments are classified into stage 4A (partial retinal detachment, not involving the macula) and stage 4B (involving the macula).

Stage 5: Total retinal detachment is usually tractional and funnel shaped and presents as a leukocoria or white pupillary reflex.

Stage 1 – demarcation line	A thin but definite structure (white line) separating the avascular retina anteriorly from the posteriorly vascularised retina. 
Stage 2 – ridge	A ridge arising from the demarcation line, which has three dimensions (height and width) and extends above the retina. It may be white or pink. 
Stage 3 – extraretinal fibrovascular proliferation	Extraretinal fibrovascular proliferation or neovascularisation extends into the vitreous from the ridge. 
Stage 4 – partial retinal detachment	Retinal detachments are generally concave and most are circumferential. They are further divided into 4A (extrafoveal) and 4B (foveal). 
Stage 5 – total retinal detachment	Retinal detachments are generally tractional but may occasionally be exudative, and are usually funnel-shaped. 

Plus disease: Refers to venous dilatation and arteriolar tortuosity of the posterior retinal vessels in at least two quadrants of the eye. Engorgement of iris vessels, pupillary rigidity and vitreous haze may also be seen.

Pre-plus: It is the term used to denote vascular abnormalities of the posterior retina that are insufficient for the diagnosis of plus disease, but that cannot be considered normal.

Aggressive-posterior ROP (AP-ROP): It is a rapidly progressing, severe form of ROP which if untreated progresses to stage 5 ROP. The features include posterior location (zone I and sometimes posterior zone II), prominence of plus disease, ill-defined nature of the retinopathy, flat network of neovascularization and hemorrhages. The earliest phase of this disease shows abnormal closed-loop vessels (and not the normal dichotomous branching pattern) with mild tortuosity that can develop into the full-blown picture in less than a week. The disease does not proceed from the classical stages of 1 through 3.

Screening guidelines

Whom to screen (Indian Guidelines)[viii]

1 Birth weight < 1750 g

2 Gestational age at birth < 34 weeks

3 Exposed to oxygen >30 days

4 Infants born at < 28 weeks and weighing < 1200 g are particularly at high risk of developing a severe form of ROP

5 Presence of other factors such as respiratory distress syndrome, sepsis, multiple blood transfusions, multiple births (twins/ triplets), apneic episodes, intraventricular haemorrhage increase the risk of ROP. In these cases, screening should be

considered even for babies between 34-36 weeks gestational age or a birth weight between 1750-2000g.

When to screen[15]

The first screen should be performed not later than 4 weeks of age or 30 days of life in infants ≥ 28 weeks of gestational age. Infants <28 weeks or < 1200 grams birth weight should be screened early at 2-3 weeks of age, to enable early identification of AP-ROP.

How to screen[15]

The ideal setting for screening is under a radiant warmer in the NICU, under the guidance of the neonatologist. Discharged and stable babies may be screened in the trained ophthalmologist's clinic or in the NICU itself. The baby should preferably fed one hour prior to examination. Incubator dependant babies can be screened (and even treated) within the incubator itself through the slanting wall without disturbing the equilibrium of the infant.

Pupillary dilatation should be performed about an hour prior to screening. A combination of cyclopentolate 0.5% and phenylephrine (2.5%) drops is used two to three times about 10-15 minutes apart. Tropicamide 0.5-1% is an alternative to cyclopentolate. Excess eye drops should be wiped off to prevent systemic absorption though the cheek skin. Over dosage carries the risk of tachycardia and hyperthermia and must be avoided. A non-dilating pupil could indicate the presence of tunica vasculosalentis and must be confirmed by the ophthalmologist before undue excess medication for dilatation is administered.

The examination is carried out under topical anesthesia without any sedation, using the indirect ophthalmoscope and a 20 D or 28 D condensing lens. Recordings of the findings should be done in the chart or card using standard notations. The date of

subsequent follow-up should be clearly stated. Apnea and bradycardia may rarely develop during the examination in very premature babies. Resuscitation measures should be readily available.

Follow up guidelines[15]

Zone of retinal findings	Stage of retinal findings	Follow up interval
Zone 1	Immature vascularization	1-2 weeks
	Stage 1 or 2	1 week or less
	Regressing ROP	1-2 weeks
Zone 2	Immature vascularization	2-3 weeks
	Stage 1	2 weeks
	Stage 2	1-2 weeks
	Stage 3	1 week or less
	Regressing ROP	1-2 weeks
Zone 3	Stage 1 or 2	Stage 1 or 2
	Regressing ROP	Regressing ROP

Treatment guidelines[v][iii]

ZONE 1	NO PLUS	Stage 1	Follow
		Stage 2	Follow
		Stage 3	Treat
	PLUS	Stage 1	Treat
		Stage 2	Treat

		Stage 3	Treat
ZONE 2	NO PLUS	Stage 1	Follow
		Stage 2	Follow
		Stage 3	Follow
	PLUS	Stage 1	Follow
		Stage 2	Treat
		Stage 3	Treat

When should the screening be terminated?[15]

Retinal examinations may be terminated based on postmenstrual age or retinal findings. The following are the recommendations to guide when to stop further examinations:

a) Full retinal vascularization; this usually occurs at about the 40th week of postmenstrual age and mostly completes by the week 45th week

b) Regression of ROP noted

Treatment :[viii]

While early detection of ROP is crucial, not every case will require treatment. Based upon findings in the Early Treatment for Retinopathy of Prematurity study (ET-ROP), the decision to treat is dependent on the type of ROP.

The first treatment considered both safe and effective for ROP was cryotherapy to the avascular retina. (CRYO-ROP study) In cryotherapy, the sclera, choroid, and full-thickness of the avascular retina are frozen from the surface of the eye. While this treatment resulted in a 50% reduction in retinal detachments in threshold eyes,

it was considered time-consuming and required general anesthesia as well as surgical displacement of the conjunctiva.

Argon and diode laser photocoagulation treatment to the avascular retina has further reduced unfavorable outcomes and has become the standard of treatment for ROP.

Due to the role of VEGF in the development of ROP, the use of anti-VEGF agents is a possible treatment strategy.

Modalities for surgical intervention in stage 4 ROP include scleral buckling or lens sparing vitrectomy. In stage 5 disease, scleral buckling plays a limited role, and the most common approaches include lensectomy with vitrectomy or open sky vitrectomy.

Complications[17]:

Retinal detachment is the most severe complication of ROP and is strongly associated with a poor visual outcome. Macular folds are another common complication. Threats to visual acuity persist through childhood, the most common sequelae is myopia. Other late complications include glaucoma, amblyopia, cataract, and strabismus.

Scan the QR Code for more information

ROP की बीमारी की विस्तृत जानकारी के लिए ऊपर दिए गए QR Code को स्कैन करें!

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CHAPTER 10

RETINAL DETACHMENT


राज्य स्वास्थ्य एवं परिवार कल्याण संस्थान, उ0प्र0
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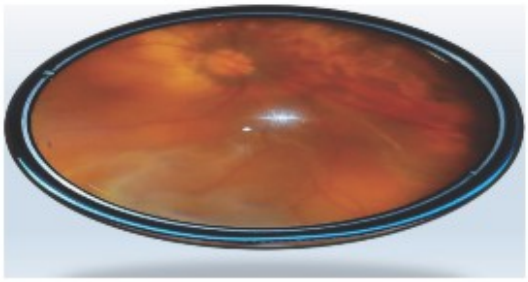


RETINAL DETACHMENT

Introduction

Retinal detachment is an important cause of decreased visual acuity and blindness. It is a sight-threatening disorder, which occurs when the photoreceptors are separated from their vascular supply.[viii] It is one of the most common ocular emergencies today, most frequently affecting the middle aged and elderly. It often requires urgent and sometimes emergent treatment.

The chance of developing a retinal detachment is related to a combination of risk factors. Lifetime risk of retinal detachment is about 0.1% and is higher in patients who are older, have high myopia (nearsightedness greater than 6.0 diopters), have a history of ocular trauma or prior eye surgery, or a family history of retinal detachment.[viii]

There is no specific way to decrease the incidence of retinal detachment, but understanding the symptoms of retinal detachment is important for all patients. The sooner patients can be seen when they have a retinal detachment, the better their visual prognosis will be.

Anatomy

The retina can be compared to the camera's film. It is a thin layer that coats the internal border of the posterior eye. It is a layer of photoreceptors cells and glial cells within the eye that captures incoming photons and transmits them along neuronal pathways as both electrical and chemical signals for the brain to perceive a visual picture[viii]. The retina is comprised of photoreceptors, neurons, and support cells. It is bordered anteriorly by the vitreous and posteriorly by the choroid.The central portion of the retina is the macula. The macula has a high concentration of photoreceptors and is responsible for capturing central vision. More specifically, the highest proportion of photoreceptors is in a central 1.5mm zone called the fovea. This area of high photoreceptor density is important in retinal detachment as its condition dictates the prognosis of the disease.

Internal and anterior to the retina is the vitreous. Consider vitreous as clear jelly inside the eye comprised of type II collagen and hyaluronic acid. It comprises 80% of the volume of the eye and is responsible for providing mechanical support for our eyes during development. However, there is little evidence of a functional purpose of the vitreous after our eyes have fully developed. Also, the vitreous breaks down and liquefies as we age.

External and posterior to the retina are the retinal pigment epithelium (RPE) and the choroid. The retinal pigment epithelium is between the retina and the choroid. It is responsible for nourishing the retina. The choroid is a vascular layer immediately posterior to the RPE which provides blood to the outer layers of the retina (the inner layers of retina supplied by branches of the central retinal artery).

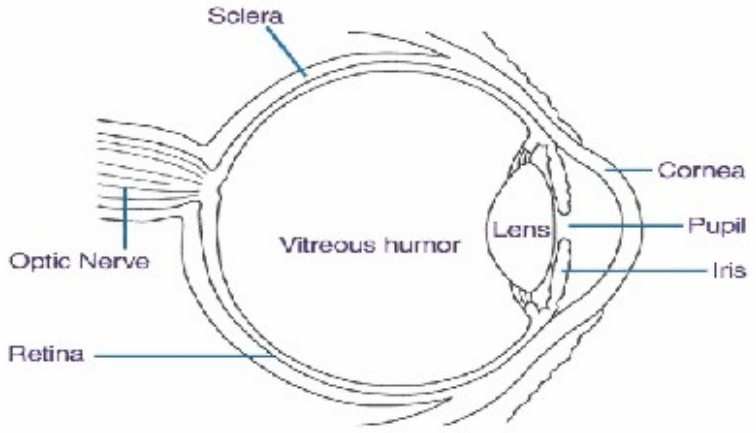


Fig. Diagram of the internal eye. The vitreous is internal and anterior to the retina. Courtesy: National Eye Institute, National Institutes of Health (NEI/NIH).

Sites of vitreous adhesion

Physiological - The peripheral cortical vitreous is loosely attached to the internal limiting membrane (ILM) of the sensory retina.[16]

Sites of stronger adhesion in the normal eye include:

- Vitreous base (very strong).
- Optic disc margins (fairly strong).
- Perifoveal (fairly weak).
- Peripheral blood vessels (usually weak).

Pathological - Abnormal adhesions may lead to retinal tear formation following [16]

- PVD
- Vitreomacular interface disease.
- Lattice degeneration.
- Retinal pigment clumps.
- Cystic retinal tufts.
- Vitreous base anomalies, such as extensions and posterior islands.

- □ □White with pressure□ and □white without pressure□.
- □ Zonular traction tufts.
- □ Vitreomacular traction
- □ Preretinal new vessels, e.g. proliferative diabetic retinopathy.

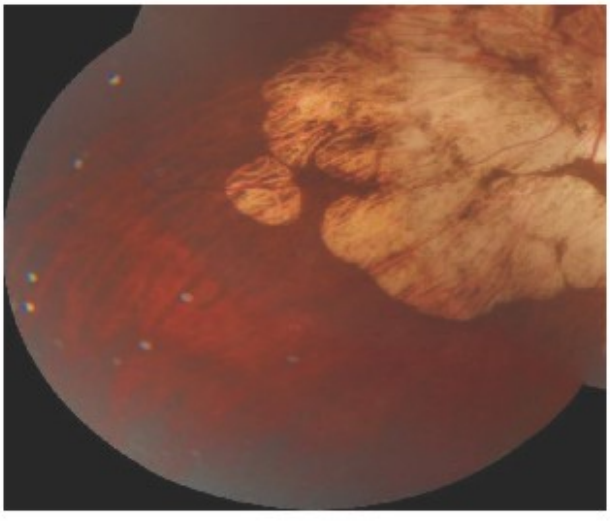


Fig. Peripheral retinal degeneration

RETINAL BREAKS □

Retinal breaks can occur in up to 1 in 5 eyes with symptomatic PVD and are typically the result of traction at sites of vitreoretinal adhesion..In the presence of a break, retrohyaloid fluid has access to the subretinal space. About 8% of the general population has a retinal break that is asymptomatic.

Clinical features □

Timing - Breaks are usually present at or soon after the onset of symptoms of PVD, although in a minority (up to 5%) tear formation may be delayed by several weeks.

Location -Tears associated with PVD are usually located in the upper retina and are more commonly temporal than nasal. Macular breaks related to PVD are rare, but

when they occur are usually round and in a myopic eye. They are aetiologically distinct from age-related macular holes.

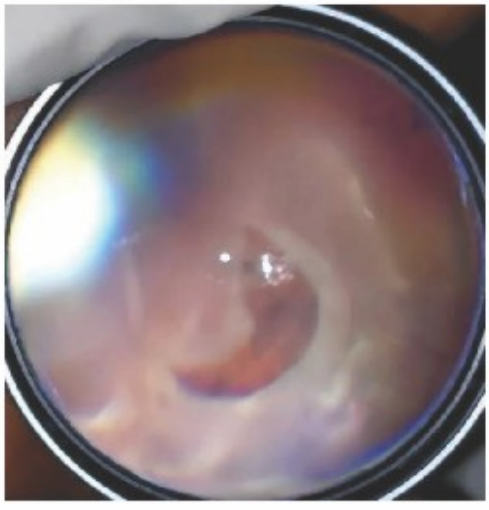


Fig. Horse shoe shaped tear

Morphology

- Retinal breaks may be flat or associated with a surrounding cuff of SRF. If fluid extends more than one-disc diameter from the edge of a break, a RD is said to be present.
- U-tears (horseshoe) consist of a flap, its apex pulled anteriorly by the vitreous, the base remaining attached to the retina.
- Operculated tears in which the flap is completely torn away from the retina by detached vitreous gel to leave a round or oval break. The separated retinal patch is known as an operculum and can usually be seen suspended in the vitreous cavity in the region of the break, which can be difficult to delineate this may be aided by the presence of preretinal blood at the site.
- Retinal holes are often round or oval, smaller than tears, and represent a lower risk of RD. If RD does arise, it most frequently manifests as a shallow, slowly

progressing RD in a young female myope. A PVD is not necessarily present, but if vitreous separation has occurred an operculum may be visible in the nearby vitreous cavity. Round holes may occur in lattice degeneration. Round holes leading to RD may be distinct in most cases from the round atrophic retinal holes that are a variant of paving stone degeneration and probably carry a lower risk, though clinically distinction is not easy.

- A dialysis is a circumferential tear along the ora serrata and is usually a consequence of blunt ocular trauma. Importantly, the vitreous gel remains attached to the posterior margin. It typically appears as a large very peripheral break with a regular rolled edge. The RD is often slowly progressive in the absence of a PVD.
- A giant retinal tear is a variant of U-tear, by definition involving 90° or more of the retinal circumference. In contrast to dialysis, vitreous gel remains attached to the anterior margin of the break. It is most frequently located in the immediate post-oral retina or, less commonly, at the equator.

IDENTIFICATION OF BREAKS

Distribution of breaks in eyes with RD is approximately as follows:

- 60% superotemporal quadrant
- 15% superonasal
- 15% inferotemporal
- 10% inferonasal

The supero-temporal region should therefore be examined in detail if a break cannot be detected initially. It should also be remembered that about 50% of eyes with RD have more than one break, often within 90 degree of each other.

Configuration of SRF - SRF spread is governed by:

- Gravity
- By anatomical limits (ora serrata and optic nerve)
- Location of the primary retinal break.

If the primary break is located superiorly, the SRF first spreads inferiorly on the same side of the fundus as the break and then superiorly on the opposite side, so that the likely location of the primary retinal break can be predicted.

Modified Lincoff□s rules:

- A shallow inferior RD in which the SRF is slightly higher on the temporal side points to a primary break located inferiorly on that side.
- A primary break located at 6 o□clock will cause an inferior RD with equal fluid levels.
- In a bullous inferior RD, the primary break usually lies above the horizontal meridian
- If the primary break is located in the upper nasal quadrant the SRF will revolve around the optic disc 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 primary break located in the periphery nearest its highest border.
- 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.

Treatment techniques - Retinal breaks without RD can be treated with laser (via a slit lamp or BIO) or cryotherapy. Most of the time, laser surgery is the best option since it is more accurate, results in less collateral retinal damage, and has a decreased

risk of developing an epiretinal membraneDue to the need for indentation to visualise the area, adequate treatment of the base of a very peripheral lesion might only be possible with BIO or cryotherapy. For numerous consecutive tears, large lesions, and eyes with hazy media and tiny pupils, cryotherapy may be preferable.

Laser retinopexy - Using slit lamp delivery under topical anaesthesia (occasionally regional or even general anaesthesia is required), typical settings are a duration of 0.1 second, a spot size of 200□300 µm with a three-mirror contact lens or 100□200 µm with a wide-field lens and a starting power of 200 mW. The power should be adjusted as appropriate to obtain moderate blanching. With head-mounted BIO delivery, the spot size is estimated and adjusted by adjusting the condensing lens (usually 20 D) position. The lesion is surrounded with two to three rows of confluent burns. With both forms of laser, care should be taken to identify appropriate landmarks frequently to avoid inadvertent macular damage.

Cryoretinopexy□

- Subconjunctival or regional anaesthesia is commonly required. For lesions behind the equator, a small conjunctival incision may be necessary for access.
- A lid speculum is used. The cryotherapy probe tip must be exposed beyond its rubber sleeve.
- The instrument should initially be purged (e.g. 10 seconds at −25 °C, repeating after 1 minute). The treatment temperature is set (typically −85 °C).
- It is useful to check the effectiveness of the instrument by activating it in sterile water for 10 seconds, when a 5-mm ice ball should form.
- Under binocular indirect ophthalmoscopy visualization, the lesion is indented and the foot pedal depressed until visible whitening of the retina is seen.

- It is critical not to remove the tip from the treated area until thawing occurs (2 3 seconds).
- Care should be taken to maintain orientation of the probe whilst the tip is not visible and not to mistake indentation by the shaft of the probe for that of the tip.
- The lesion is surrounded by a single row of applications, in most cases achieved by one or two applications to a tear.
- The eye is usually padded afterwards and oral analgesia is commonly prescribed.
- After treatment the patient should avoid strenuous physical exertion for about a week until an adequate adhesion has formed.
- Review should usually take place after 1 2 weeks.

CLASSIFICATION

There are many classification schemes for retinal detachment. However, in the simplest terminology, there are three primary forms of retinal detachment. These include rhegmatogenous retinal detachments, tractional retinal detachments, and exudative retinal detachments.

Rhegmatogenous retinal detachment

Rhegmatogenous retinal detachment (RRD) is the most common form of retinal detachment. It affects approximately 0.007-0.018% of the population yearly. Rhegma means break in Greek, and thesretinal detachments are due to full-thickness breaks in the retina. These full-thickness breaks, most commonly due to and held open by vitreoretinal traction, allow fluid from the liquified vitreous to move under the neurosensory retina and further separate it from the retinal pigment epithelium. Risk factors for breaks or tear in the neurosensory retina that can lead to

a rhegmatogenous retinal detachment includes Lattice degeneration, Peripheral retinal excavations , Meridional folds[viii]

Tractional retinal detachment

Tractional retinal detachment occurs when vitreous membranes pull on the retina separating it from the RPE. No tears or holes are present in this type of retinal detachment. Vitreous membranes are usually gliotic, fibrous, vascular, or a combination. They commonly grow in response to proliferative vitreoretinopathies, most notably diabetic retinopathy. Risk factors for the formation of proliferative membranes that cause tractional retinal detachments includes Proliferative diabetic retinopathy, Proliferative vitreoretinopathy, Sickling hemoglobinopathies[viii]

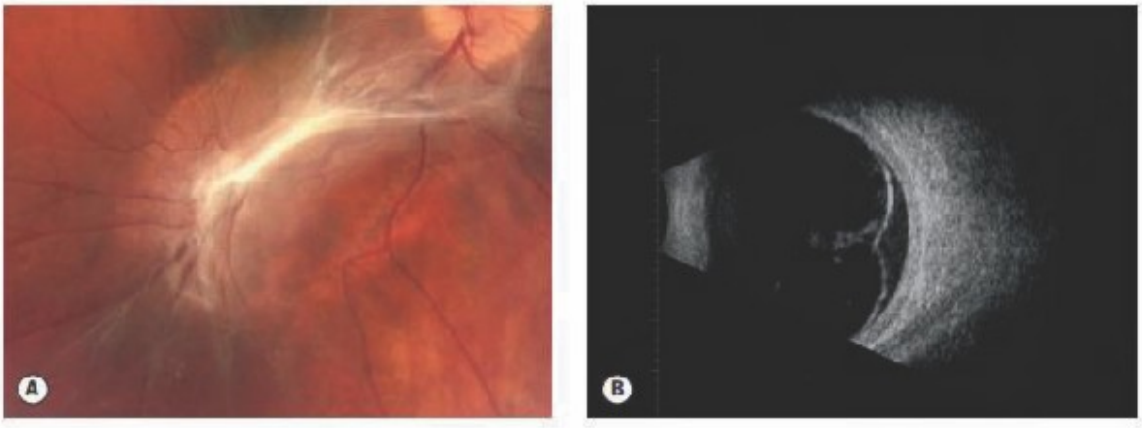


Fig. Tractional Retinal detachment. (A) Localised tractional detachment secondary to preretinal fibrosis; (B) B-Scan (Courtesy- Kanski□s Clinical ophthalmology)

Exudative retinal detachment

Exudative retinal detachment occurs due to an underlying condition causing buildup of fluid (exudate) between the neurosensory retina (photoreceptor layer) and the retinal pigment epithelium (RPE). Inflammatory conditions such as uveitis are the most common conditions responsible for this type of retinal detachment. Other rare

but more serious conditions such as choroidal tumors can be responsible for exudative retinal detachments too[viii].Risk factors or causes for fluid entering the subretinal space and thus causing an exudative or serous retinal detachment includes Primary ocular tumors, Ocular metastases, Sarcoidosis[viii]

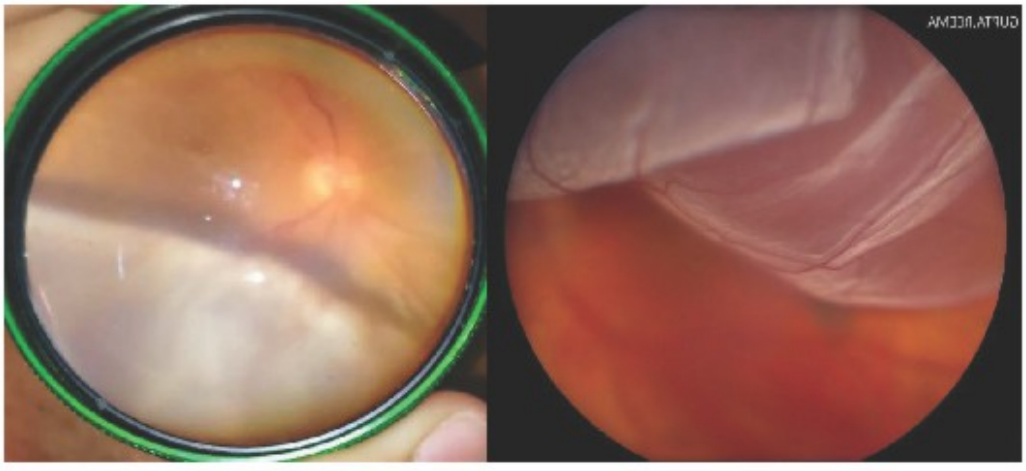


Fig. Bullous Retinal Detachment

SYMPTOMS

- The classic premonitory symptoms reported in about 60% of patients with spontaneous rhegmatogenous RD are flashing lights[viii] and floaters associated with acute PVD.
- A curtain-like relative peripheral visual field defect.
- A lower field defect is usually appreciated more quickly by the patient than an upper defect.
- The quadrant of the visual field in which the field defect first appears is useful in predicting the location of the primary retinal break, which will be in the opposite quadrant.

- Loss of central vision may be due to involvement of the fovea by SRF or, infrequently, obstruction of the visual axis by a large bullous RD.
- Retinal detachments are almost always painless.

SIGNS

General

- Relative afferent pupillary defect (Marcus Gunn pupil) is present in an eye with an extensive RD.
- Intraocular pressure (IOP) is often lower by about 5 mmHg compared with the normal eye. If the intraocular pressure is extremely low, an associated choroidal detachment may be present. It may be raised, characteristically in Schwartz–Matsuo syndrome, in which RRD is associated with an apparent mild anterior uveitis, often due to a dialysis secondary to previous blunt trauma in a young man.
- The aqueous cells are believed in most cases to be displaced photoreceptor outer segments that compromise trabecular outflow.
- Both the aqueous 'cells' and the elevated IOP typically resolve following repair of the RD.
- Iritis is common but usually mild and should be differentiated from Schwartz–Matsuo syndrome (above). Occasionally it may be severe enough to cause posterior synechiae and the underlying RD may be overlooked.
- 'Tobacco dust' consisting of pigment cells is commonly seen in the anterior vitreous.
- Substantial vitreous blood or inflammatory cells are also highly specific.
- Retinal breaks appear as discontinuities in the retinal surface. They are usually red because of the colour contrast between the sensory retina and underlying

choroid. However, in eyes with hypopigmented choroid (e.g., high myopia), the colour contrast is decreased and small breaks may be overlooked.

 Retinal signs depend on the duration of RD ad the presence or absence of proliferative vitreoretinopathy (PVR) as described below.

Fresh retinal detachment

- The RD has a convex configuration and a slightly opaque and corrugated appearance as a result of retinal oedema.
- Loss of the underlying choroidal pattern and retinal blood vessels appear darker than in flat retina.
- SRF extends up to the ora serrata, except in the rare cases caused by a macular hole in which fluid is initially confined to the posterior pole.
- Macular pseudohole -Because of the thinness of the foveal retina, the impression of a macular hole may be given if the posterior pole is detached. This should not be mistaken for a true macular hole, which may give rise to RD in highly myopic eyes or following blunt trauma.
- B-scan ultrasonography shows good mobility of the retina and vitreous. Longstanding retinal detachment
- Retinal thinning secondary to atrophy is a characteristic finding and should not lead to a misdiagnosis of retinoschisis.
- Intraretinal cysts may develop if the RD has been present for about 1 year. These tend to disappear after retinal reattachment.
- Subretinal demarcation lines (high water or tide marks) caused by proliferation of RPE cells at the junction of flat and detached retina are common, taking about 3 months to develop.

Pigmentation tends to decrease over time. Although representing sites of increased adhesion, they do not invariably limit the spread of SRF

HISTORY & EXAMINATION

Every patient encounter should begin with a history of present illness from the patient. When a possible detachment is suspected, the presence or absence of the above symptoms should be documented. Ask about history of prior retinal detachment, retinal tears, and any prior ocularprocedures. Identification of diagnosed ocular diseases and family history of retinal detachment are also very important in the proper workup of these patients.

Examination should start similar to other patients that present to the ophthalmology clinic.

- Visual acuity
- Intraocular pressure
- Visual fields
- Presence or absence of a relative afferent pupillary defect (RAPD)[9]
- Extraocular motility should all be obtained.

After these have been performed, the patient should have their pupils dilated for a thorough fundus exam. Examining both eyes is important as asymptomatic retinal pathology be identified in the fellow eye, too.

Fundus Exam

The primary way to diagnose a rhegmatogenous retinal detachment is by performing a proper fundus exam. When sitting the patient down at the slit lamp biomicroscope,

prior to visualizing the fundus, you should look for *Schaffer□s sign*a finding often present in patients with retinal tears and rhegmatogenous retinal detachments. Schaffer□s sign is positive when you use a thin beam of brightlight without a lens and see fine pigment floating in the anterior vitreous. This pigment is circulating RPE cells released from a retinal break. When visualizing the fundus on the slit lamp or using indirect ophthalmoscopy, you will be checking for retina that appears separated from the normal structure of the eye. In the case of rhegmatogenous retinal detachment, you may see a large bullous separation of the retina. There will always be an associated tear or hole. These are often more peripheral and may be visualized better using an indirect ophthalmoscope. An ophthalmologist or optometrist should repeat the fundoscopic examination with indirect ophthalmoscopy with scleral depression so that the entire retina is visualizable up to the ora Serrata and the examiner can identify any breaks or tears[viii]

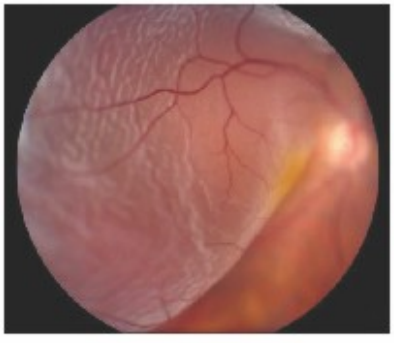


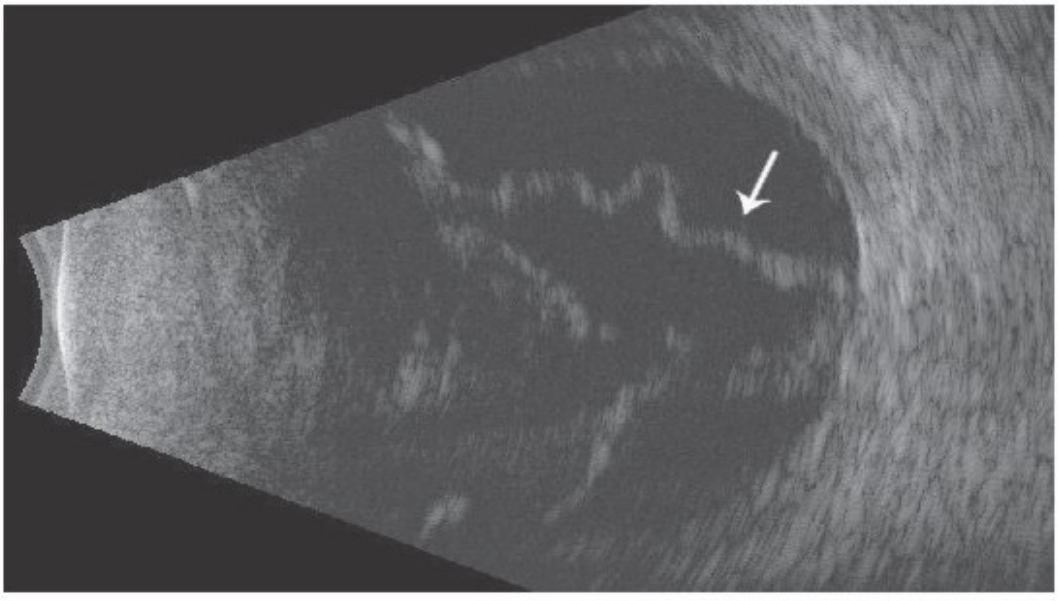
Fig. Bullous superotemporal rhegmatogenous retinal detachment of the right eye. The detachment is in focus on the upper left portion of the picture. Notice how the vessels change course over the detachment, its lighter color, and how it has crinkled upon itself like tissue paper. The tear is in the periphery and is not visible on this image.

Optical Coherence Tomography

OCT allows for visualization of microscopic changes in the retina including small amounts of exudate underneath the retina. OCT is not the gold standard for identifying retinal detachments, but it can be extremely useful for identifying foveal status and tractional or exudative retinal detachments[viii]. If the status of the fovea is still in question despite a good history and exam, obtaining an OCT may support your diagnosis and determine time course for treatment as well as prognosis.

B-Scan

A B-scan is an ultrasound of the eye. If the media of the eye is not clear (e.g. from vitreous haemorrhage or severe cataract), ordering a B-scan is an excellent way to identify retinal detachments.[viii] Point-of-care ultrasound in the hands of an experienced provider can be an effective way of diagnosing a retinal detachment, with one meta-analysis showing a sensitivity of 94.2% and specificity of 96.3%.[viii]



B-scan of an eye with retinal detachment. The bright reflective layer in the posterior pole (indicated by the arrow) corresponds to the retina, detached from the eye wall.

TREATMENT

The treatment for retinal detachment depends upon the type and size of retinal detachment.

- For a small, peripheral RRD, the treatment of choice is cryotherapy of the break or laser photocoagulation around the detachment to prevent it from spreading. Once laser is applied, it takes between 3 and 14 days for maximal retinal adhesion to be achieved.
- For a larger RRD, the primary treatment options are surgical. A scleral buckle, pars plana vitrectomy, or pneumatic retinopexy (all explained below) are the primary interventions used.
- Tractional retinal detachment is addressed most appropriately by treating the underlying disease, such as proliferative diabetic retinopathy. If traction threatens the macula, vitrectomy is usually indicated. Traction can also become severe enough to cause a tear or hole, becoming a RRD.
- Management of exudative retinal detachment involves treating the underlying disease (e.g., uveitis, choroidal tumor, etc.) to decrease the fluid between the neurosensory retina and RPE.

Factors that play into the decision of which technique to use include the patient's presentation, surgeon's training, and cost[viii]

Time Frame for Rhegmatogenous Retinal Detachment

The status of the macula is the primary determinant of the emergency of the situation.

If the macula, or more specifically the fovea, is still attached, the procedure is an emergency and should be performed within 24 hours. This is often referred to as a

□*macon*□retinal detachment and is an emergency because central visual acuity is still preserved. Preventing the detachment from spreading to the fovea is extremely important.

If the macula has detached it is referred to as a □*macoff*□retinal detachment and prognosis for recovery of central acuity is worse, and thus urgent treatment is less critical. Nonetheless, studies show visual recovery is best if the procedure is performed within 7-10 days.

Scleral buckle

The scleral buckle (SB) procedure was introduced in the 1950s and involves the dissection of conjunctival tissue, exposure of the extraocular muscles, and wrapping a buckle underneath the extraocular muscles to support the sclera beneath the retinal detachment.[16]

Indirect ophthalmoscopy is used in coordination with this procedure to provide cryotherapy to the tears and to mark the sclera in the area of detachment.

The marks are used so the buckle can be placed to provide support in the area of the detachment.

The three main mechanisms by which this technique is hypothesised to function include bringing the RPE closer to the retina, altering the fluid dynamics underneath the detachment to allow the RPE to remove fluid, and decreasing traction.

The scleral buckle is often considered for RRD in phakic eyes. This is due to the fact that there is no significant difference in the proportion of primary reattachment between phakic eyes treated with SB and those treated with pars plana vitrectomy (PPV).

In addition, scleral buckle treated eyes have greater 6-month postoperative best corrected visual acuity (BCVA) compared to eyes treated with vitrectomy. This is likely related to the increased incidence of posterior subcapsular cataracts in PPV treated phakic eyes.

However, regardless of lens status, the first-time success rate for retinal reattachment with SB is above 80%.

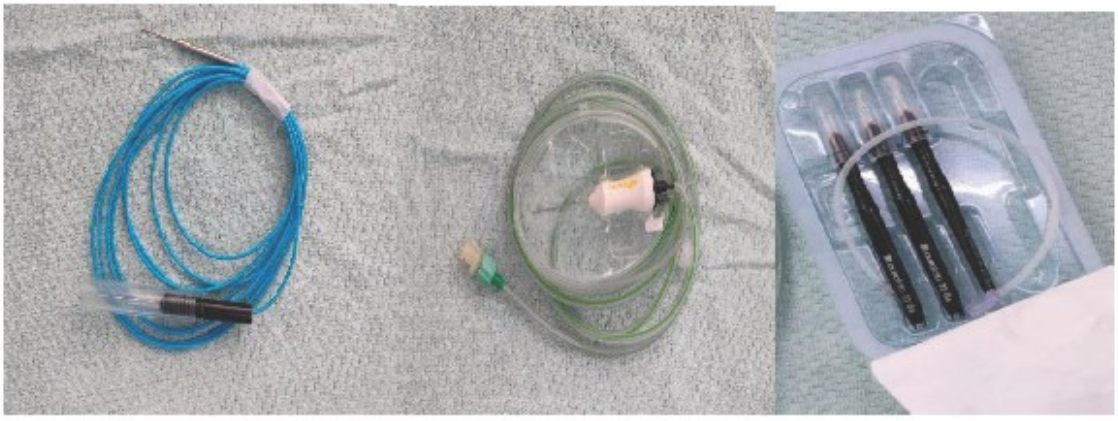
Pars Plana Vitrectomy

The pars plana vitrectomy was introduced in the 1970□s andi considered by some to be superior to SB for the pseudophakic RRD.

The surgeon then can remove vitreous tractioning on the retina and uses cryotherapy or laser around retinal breaks or tears to prevent the worsening of the detachment[viii] In its most simple description, the vitreous is removed by introducing a needle through the pars plana that cuts and aspirates thousands of vitreous slices per second. As vitreous is removed, the eye is continually filled with balanced salt solution to maintain pressure.

The final step involves introducing a medium into the eye (C3F8 gas, SF6 gas, or silicone oil) to hold the retina to the eye wall. Patient positioning based upon the location of the break and the medium used to fill the eye is required after the procedure. The first-time success rate forretinal reattachment, regardless of lens status, is above 90%.

Vitrectomy machine



Light pipe *Vitreous cutter* *Trocar*

Pneumatic retinopexy

Pneumatic retinopexy was introduced in 1986. It is a minimally invasive procedure that can be accomplished in the clinic quickly. Therefore, this procedure can be a cost-effective approach to retinal detachment.

This procedure entails injecting a gas bubble (C3F8 or SF6) into the eye between the retina and the vitreous in an attempt to reapproximate the retina to the retinal pigment epithelium.

However, the success rate for primary retinal detachment at two months for this procedure is approximately 66%.

Furthermore, depending upon the size and location of the break, there is a risk of separating the retina further if bubbles get underneath the detachment. Because a bubble is used, patient positioning is also required after the procedure. If failure does occur, it is usually early within the postoperative course, and re-operation (SB, vitrectomy) results in success rates also above 90%.

COMPLICATIONS

The most common cause of post-operative failure in the affected eye is proliferative vitreoretinopathy.

Other complications include:

- Induced myopia (SB),
- Anterior ocular ischemia (SB),
- Gas migration subretinally or to the anterior chamber (pneumatic retinopexy), cataract (vitrectomy and pneumatic retinopexy),
- Re-detachment (all types of treatment).

The fellow eye is also at an increased risk of retinal detachment.

About 10% of phakic patients will have a retinal detachment in the fellow eye while 20-36% of aphakic patients will have a retinal detachment in the fellow eye.

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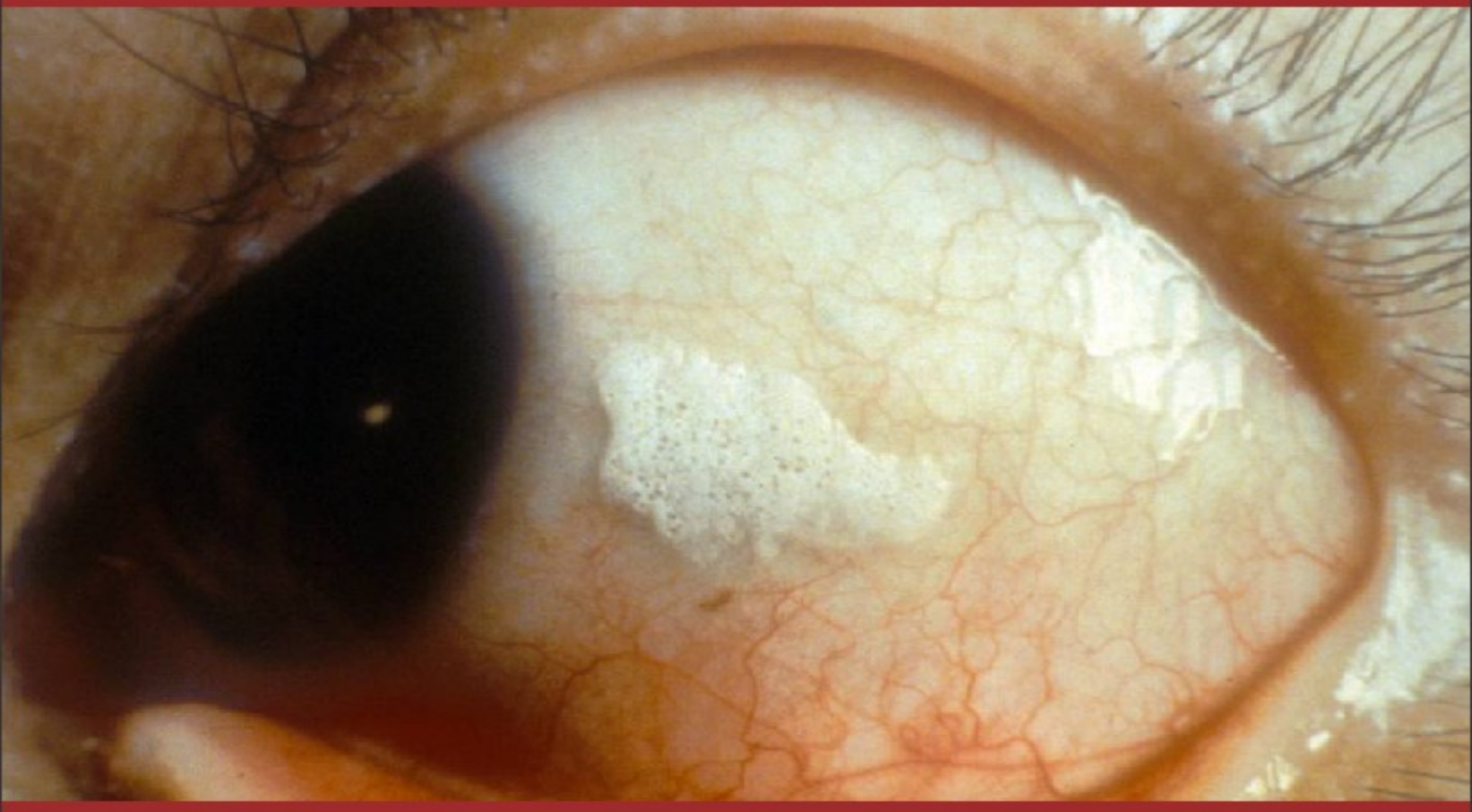
CHAPTER 11



OCULAR MANIFESTATIONS OF SYSTEMIC DISORDERS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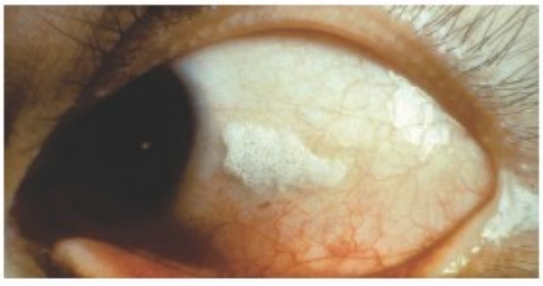


OCULAR MANIFESTATIONS OF SYSTEMIC DISORDERS

INTRODUCTION

An ocular manifestation of a systemic disease is an eye condition that directly or indirectly results from a disease process originating from another part of the body. There are many diseases known to cause ocular or visual changes as a result of systemic disease. Physicians need to consider that systemic disease can involve the eyes and it is important for ophthalmologists to understand that they may be the first to suggest a diagnosis due to underlying systemic disease. In such cases, information obtained from an ocular examination may aid in the diagnosis and management of the underlying systemic disease. For these reasons, the primary care physician should be familiar with the common ocular complications of frequently encountered systemic diseases.

To provide a framework for approaching ocular manifestations of systemic disease, we have categorized it under the following headings: vascular, neoplastic, autoimmune, idiopathic, infectious and metabolic/endocrine.

VASCULAR DISORDERS

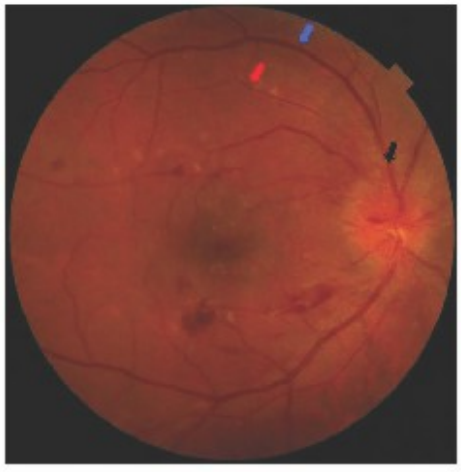
Systemic Hypertension

Systemic hypertension affects the heart, kidney, brain, large arteries, and also the eyes. It is a major risk factor for the development of retinal vascular diseases including hypertensive retinopathy, retinal vein or artery occlusion, embolic events and also increases the risk for the development and progression of diabetic retinopathy. A variety of retinal vascular changes depend in part on the severity and duration of the hypertension. Retinal, choroidal, and optic nerve circulations undergo pathophysiological changes resulting in clinical signs referred to as hypertensive retinopathy, hypertensive choroidopathy, and hypertensive optic neuropathy. Signs of hypertensive retinopathy are predictive of target-organ damage including cardiovascular and cerebrovascular diseases.

Common hypertensive retinal changes are □

- Flame-shaped hemorrhages in the superficial layers of the retina and cotton-wool spots caused by occlusion of the precapillary arterioles with ischemic infarction of the inner retina.
- Long-standing hypertension can produce arteriolar sclerotic vascular changes, such as copper or silver wiring of the arterioles, as shown by the two arrows on the right, or arteriorvenous nicking.
- Another sign of chronic hypertension is lipid exudates resulting from abnormal vascular permeability.

More ominous in this photograph is swelling of the optic disc, seen here by the blurring of the temporal disc margins. This is the hallmark of malignant hypertension, which carries a poor prognosis for the patient□shealth if left untreated



BP must be emergently controlled to decrease the risk of developing heart and renal failure and hypertensive encephalopathy as well as stroke and permanent vision loss.

Embolic Disease

Emboli to the ophthalmic circulation can lodge in the ophthalmic artery or the central retinal artery, producing severe loss of vision that can be transient or permanent. In the elderly, the most common source of emboli is fibrin and cholesterol from ulcerated plaques in the wall of the carotid artery. The so-called Hollenhorst plaque is a refractile cholesterol embolus that lodges at an arterial bifurcation. Emboli of cardiac origin may come from calcified heart valves in patients with a history of rheumatic fever, from an atrial myxoma, or from fibrin-platelet emboli in patients with mitral valve prolapse.

Emboli that temporarily obstruct the ophthalmic or central retinal artery may produce sudden, severe, painless, transient loss of vision, called *amaurosis fugax*. This is a transient ischemic attack involving the ocular circulation.

- The visual loss in amaurosis fugax typically consists of monocular dimming of vision or a sense of a curtain coming down over the eye, depending on what part of the retinal arterial tree is involved.
- Homonymous field defects involving both eyes may also occur due to embolization of the cerebral circulation. Attacks usually lasts for 2–3 minutes, and then vision returns to normal as the embolus travels through the affected artery or the focal vasospasm resolves.

Patients with this symptom require careful assessment of both the cardiovascular and the cerebrovascular systems. The examination should include auscultation and imaging (Doppler and echocardiogram) of the carotid arteries and the heart as well as measurement of blood pressure in both arms. Evaluation by an ophthalmologist may be indicated to look for emboli and evidence of retinal and optic nerve ischemia. Patients with retinal embolization have a greater risk than the general population of developing a cerebral infarction over the next few months, particularly if the amaurosis fugax is accompanied by symptoms of transient cerebral ischemia.

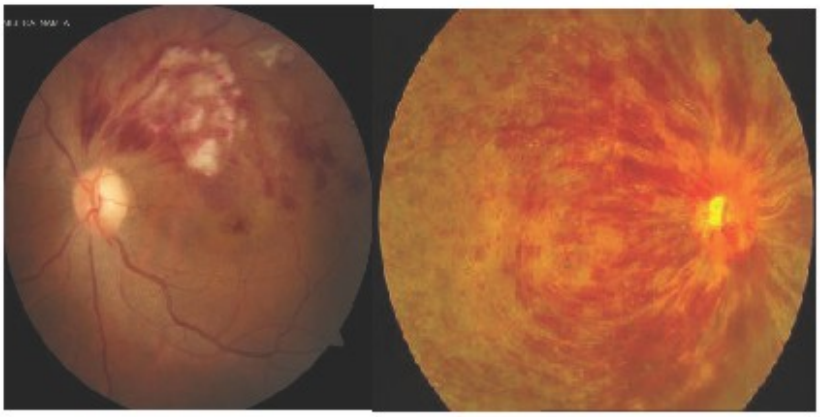
Central Retinal Artery Occlusion - Sudden, persistent visual loss may be due to occlusion of the central retinal artery, and emergency ophthalmologic evaluation is indicated. Ophthalmoscopic examination will reveal –

- Narrowed retinal arterioles and a pale retina.
- Edema with loss of retinal transparency in all areas except the fovea gives rise to the appearance known as the cherryred spot.

Emergency treatment is directed to decreasing intraocular pressure and to vasodilation in an attempt to allow the obstructing embolus to pass into less critical, smaller-caliber vessels.

Central Retinal Vein Occlusion - Another cause of painless vision loss is a central retinal vein occlusion (CRVO). This vision loss may be mild to profound and is often due to macular edema. The onset of a CRVO is usually rapid. Ophthalmic examination will reveal □

- retinal hemorrhages
- cotton-wool spots



The findings of severe vision loss or an afferent pupillary defect indicate a greater risk for the ischemic type of CRVO, which carries a poor prognosis and is more highly associated with rubeotic glaucoma. Fifty percent of patients who have a CRVO have open-angle glaucoma and/or systemic hypertension. A systemic workup in patients with a CRVO should include measurement of blood pressure and exclusion of other vasculopathic risk factors. Blood workup to rule out coagulopathies (including Factor V deficiency), hyperlipidemia, collagen vascular diseases, and paraneoplastic syndromes may be considered.

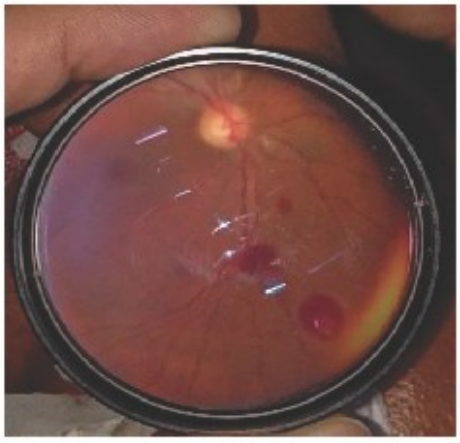
Blood Dyscrasias

A blood dyscrasia is any abnormal or pathologic condition of the blood. Blood dyscrasias with ocular manifestations include hyperviscosity syndromes, thrombocytopenia, and all forms of anemia, including sickle cell anemia.

Anaemia □

Anaemia is a commonest haematological disorder presenting with variety of ocular manifestations. It can affect every part of the eye and adnexa, but predominant features are conjunctival pallor and retinal haemorrhages. Other retinal manifestation includes venous and arteriolar tortuosity, cotton wool spots, macular star and disc oedema. Their high incidence is correlated with severity of anaemia (substrate for retinal metabolism is reduced in anaemia and makes it prone for hypoxic damage because anaemia results in diminished capillary oxygenation, increased permeability and ultimately extravasation of blood and its products). The high-risk group for anaemia are pregnant and lactating females and children while the prevalence of anaemia in 16 to 70 years is lesser. The prevalence of anaemia is higher among females than males and much more in rural than urban areas.

The occurrence of ocular abnormalities is always directly proportional with the severity of anaemia. We should always keep in mind that ocular changes in anaemia are nonspecific and may closely resemble other conditions, so it is important to rule out other ocular and systemic diseases. Normally, the ocular complications are usually reversible with the correction of anaemia. These patients should be monitored frequently with 3 to 6 months follow up evaluation. Small preretinal haemorrhage respond to blood transfusions, while large haemorrhage require posterior hyaloidectomy or vitrectomy to prevent permanent macular damage. In the fundus of eye, the columns of both arterial and venous blood lie exposed, so that they can be observed through the ophthalmoscope, examined in detail with convenient magnification. Of the various blood disorders, the ophthalmologist is thus often the first witness; but the blood is common to every tissue and its diseases may present in diverse sites before the patient reaches the haematologist, whose analysis gives the final diagnosis. Ocular abnormalities increases with the increasing severity of anaemia, so all the patients with moderate-tosevereanaemia should always undergo complete eye checkup, so that early diagnosis and timely treatment can be done. Eye being the direct window to observe the vascular changes in haematological disorders, fundus examination is done to diagnose as well as to observe the progression of a systemic disorder[viii].



METABOLIC/ENDOCRINE DISORDERS

Diabetes

Diabetes commonly produces significant ocular complications that may lead to blindness if not recognized and treated. Diabetic retinopathy is now the leading cause of new blindness in adults aged 20□74 in the United States. Because of its ophthalmologic significance, diabetic retinopathy is covered in detail in Diabetic Retinopathy chapter and is not discussed further here.

INFECTIOUS DISORDERS

Tuberculosis

Tuberculosis (TB) is the world□s leading infectious disease kiⅼⅼr, with one-fourth of the world□s population infected. Approximately 15% of TB ischaracterized as extra-pulmonary, with common locations involving the lymph nodes, pleura, and CNS. Another such specific location is the eyes, with TB being found in the eye, around the eye, and on the ocular surface.

Ocular TB

Ocular TB is uncommon and can present as a primary or secondary disease. In primary disease, the eye is the entry point of the mycobacterium and often has a predilection for the eyelids, conjunctiva, cornea, and sclera. The secondary disease results from the hematogenous spread of infection and preferentially targets the uvea, retina, and optic nerve; TB is a great masquerader and can manifest with any symptoms and signs, and some of the common manifestations are discussed in this brief[viii]. Ocular TB can be categorized into extraocular, which includes structures around and on the eye, and intraocular, related to structures within the eye[viii].

Extraocular TB

Orbit: With orbital TB involvement, proptosis, chemosis, headache, and decreased vision can result[viii].

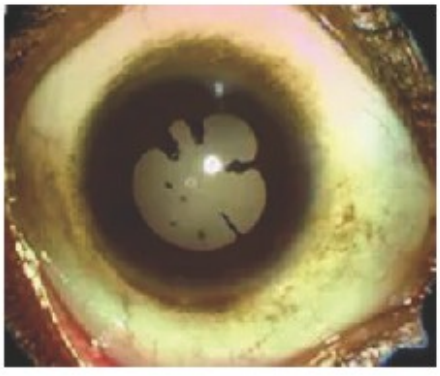
Eyelids/Lacrimal Glands: TB with a predilection for the eyelids can present as □applejelly□ nodules (lupus vulgaris). Lid abscesses and chalazions can also be seen. Lacrimal glands, although technically differentiated from the lids, can also harbor TB and present as infection as well[viii].

Conjunctiva/Cornea: Phlyctenular keratoconjunctivitis, which presents as an inflammatory nodule located at the limbus, causes redness, tearing, photophobia, and epithelial erosions. Specifically for the cornea, TB can present with interstitial keratitis with associated stromal infiltrates[viii].

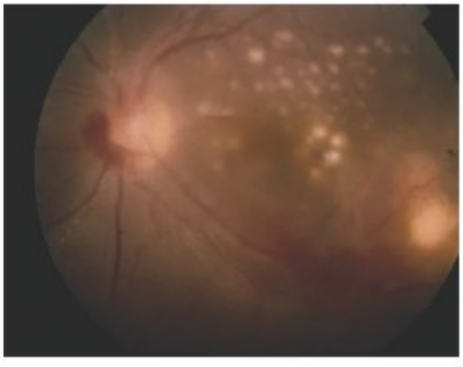
Sclera: Isolated TB scleritis may result from either direct inoculation by the bacterium or through an immune-mediated inflammatory reaction. There is often predilection for the posterior sclera[viii].

Intraocular TB

Anterior Uveitis: TB-related anterior uveitis usually presents as granulomatous uveitis, commonly exhibiting iris granulomas. These granulomas are often in conjunction with Koeppe (located at the pupillary border) and Busacca (directly on the iris surface) nodules. The composition of the nodule includes typical granulomatous features such as epitheloid and giant cells with surrounding lymphocytes[viii].



Posterior Uveitis: The most common presentation of ocular TB is posterior uveitis. Choroidal tubercles can be seen, with a predilection for the posterior pole of the eye. Posterior uveitis due to TB classically produces a serpiginous-like lesion that spares the fovea and causes vitreal inflammation[viii].



Endophthalmitis: Any active TB lesion within the eye can seed the vitreous fluid and lead to TB endophthalmitis. TB endophthalmitis can be sight-threatening and delay in diagnosis and anti-TB therapy can result in significant and permanent loss of vision[viii].

Retina: Retinal involvement in TB is typically secondary to choroidal infection with the bacterium. As with uveitis, tubercles may be present. TB vasculitis of the retina can lead to neovascularization and eventual retinal hemorrhages[viii].

Cranial Nerves: Optic nerve involvement in TB can result from both primary disease and secondary disease. Similar to other infectious or inflammatory causes of optic neuropathy, TB optic neuropathy may present with optic nerve edema, disc granuloma, or may be retrobulbar. TB papillitis can be associated with optic nerve tubercles and anterior or posterior TB uveitis. Other cranial nerve involvement, particularly the abducens nerve, is common and found in over one-third of patients with TB meningitis. TB can also involve the brain parenchyma, the brainstem, cerebellum, or cavernous sinus. TB has also been reported to cause third, fourth, or sixth cranial nerve palsy.

Diagnosis-Pulmonary TB can be divided into active or latent TB. Latent TB may have a positive TB skin test (TST) or a positive Interferon-Gamma Release Assay (IGRA) but the chest x-ray is negative for active TB (i.e., no hilar lymphadenopathy or cavitary lung lesions). Active TB, on the other hand, shows active lesions on chest x-ray and a sputum sample stained for acid-fast bacteria may be diagnostic.In contrast, ocular TB is more difficult to diagnose. Fluid collected from the eye is often negative for TB on both culture and PCR, especially when posterior structures of the eye are affected[viii]. To date, promising diagnostic technologies include IGRAs sampled directly from ocular fluid, as well as further advancement of PCR techniques. Especially in resource-limited

countries where ocular TB is most prominent, access to such diagnostics is scarce and many clinicians are forced to presume a diagnosis of ocular TB when other systemic signs of TB are present in conjunction with expected TST and chest x-ray findings as described above. Additionally, clinical ophthalmic improvement with anti-TB medications has often been used as a retro-diagnostic tool for ocular TB.

Treatment -As with pulmonary TB, ocular TB often requires multi-drug TB therapy (e.g., rifampin, isoniazid, pyrazinamide, and ethambutol). Treatment for ocular TB is similar to pulmonary TB and may require four-drug therapy for up to two months followed by two-drug therapy (rifampin and isoniazid) for up to four months. The role of steroids for ocular TB (systemic or topical) remains controversial.In addition, TB treatment with ethambutol can cause visual loss as a side effect. Ethambutol-induced optic neuropathy can mimic ocular TB (e.g., decreased visual acuity, visual field defects, and dyschromatopsia). Additionally, isoniazid has reportedly been associated with optic neuropathy, retrobulbar optic neuritis, and optic atrophy, although with less of a frequency than with ethambutol.

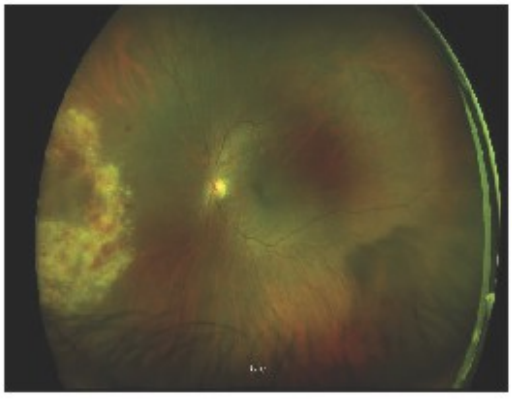
Acquired Immunodeficiency Syndrome (AIDS)

Dry eyes are very common in patients with AIDS, but they are a nonspecific finding.

The three most common classic lesions are retinal cotton-wool spots, cytomegalovirus (CMV) retinitis, and Kaposi□s sarcoma of the eyelid or conjunctiva. Cotton-wool patches, which are due to obstruction of the precapillary arterioles with infarction of the superficial retina, are the most common ocular finding in patients with HIV infection. Associated intraretinal

hemorrhages may also be present and these findings are collectively referred to as HIV noninfectious retinopathy.

Patients with AIDS can develop infectious retinitis secondary to a variety of opportunistic organisms. The most common form is *cytomegalovirus (CMV) retinitis*, which is characterized by discrete, fluffy, white retinal necrotic patches with hemorrhages. Because cytomegalovirus retinitis can begin in the retinal periphery, patients with AIDS should be referred for ophthalmologic evaluation evaluation especially if symptomatic or with reduced T-cell counts. CMV retinitis therapy has evolved significantly. The incidence of CMV retinitis has decreased tremendously with the advent of HAART (Highly Active Anti-Retroviral Therapy). If CMV retinitis is detected in a patient who is not on HAART, the patient must be immune reconstituted with anti-retroviral medications. Induction IV ganciclovir or foscarnet is also necessary, and intravitreal injections of ganciclovir may be considered. As cytomegalovirus infection is usually a systemic infection, intravenous therapy is usually the treatment of choice. The primary care physician and the ophthalmologist must work closely together to monitor efficacy of therapy and side effects of the treatment. As CD4 counts increase and viral load decreases to an acceptable level, IV and intravitreal ganciclovir administration may be withheld as long as the CD4 counts remain above 100. If patients develop CMV retinitis on HAART or have no response to IV therapy, then ganciclovir implants and intravitreal injections are necessary. In patients with AIDS, opportunistic infections such as CMV retinitis occur predominantly when CD4 counts fall below 50 cells/ml.



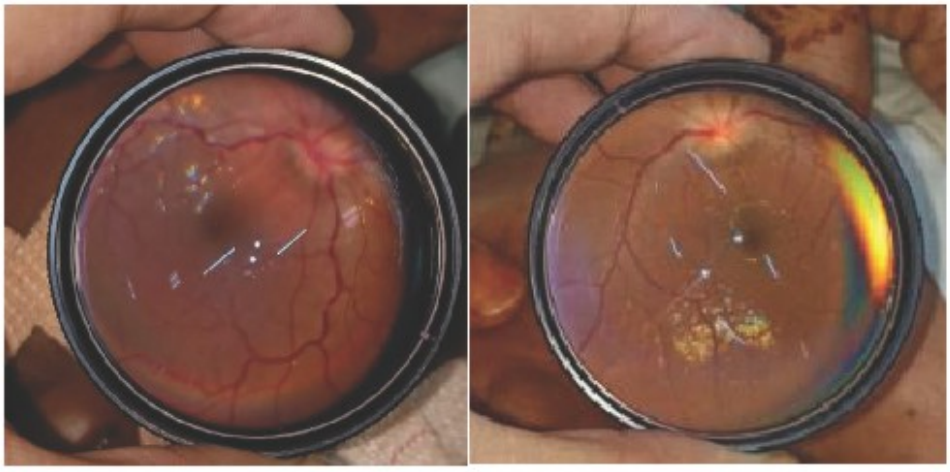
However, other retinal infections such as syphilis, toxoplasmosis, herpes simplex virus, or varicella-related retinitis (acute retinal necrosis syndrome) may occur in immunocompromised or immunocompetent eyes.

IDIOPATHIC DISORDERS

Intracranial Hypertension

The most common ocular manifestation of intracranial hypertension is optic disc swelling, which in this condition is referred to as papilledema. The visual symptoms of papilledema are often mild or absent; the most common are transient visual obscurations, which can range from mild blurring to complete visual loss, usually lasting only a few seconds.

Ophthalmoscopy typically reveals marked disc swelling and vascular engorgement, as seen here. Common causes of intracranial hypertension include brain tumor, meningitis, venous sinus thrombosis, hydrocephalus and the entity pseudotumor cerebri, or idiopathic intracranial hypertension.



Pseudotumor cerebri may be associated with vitamin A or vitamin D intoxication, tetracycline therapy, and steroid withdrawal. Pseudotumor cerebri has a propensity to occur in young, obese women, and in most cases a precipitating factor is not found. Disc edema can also be caused by conditions that are not associated with increased intracranial hypertension, such as sarcoidosis, syphilis, tumor, and pseudo-disc edema from causes such as optic nerve head drusen.

AUTOIMMUNE DISORDERS

Certain autoimmune disorders, such as connective tissue diseases, thyroid eye disease, and myasthenia gravis, can initially present with ocular manifestations only. Thus, it is extremely important for the primary care specialist to screen for those disorders in patients with the most common ocular symptom (dry eyes) so that these patients can receive the appropriate treatment as early as possible in the course of these diseases. Thyroid Eye Disease has been covered in detail in a separate chapter so has not been discussed here.

Ankylosing Spondylitis

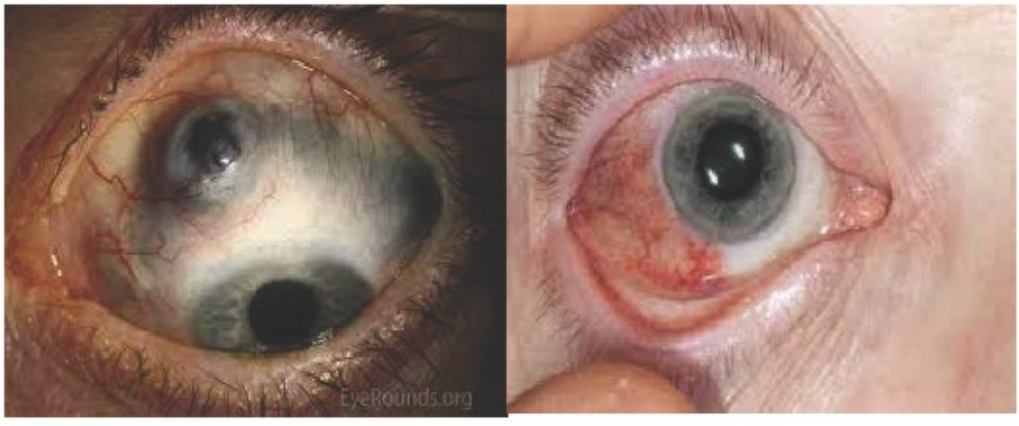
Up to 25% of patients with ankylosing spondylitis have one or more attacks of iritis, a form of intraocular inflammation, which may precede the clinical arthritis.

Patients typically present with photophobia, redness, and decreased vision. Patients with symptoms or signs suggestive of iritis should be referred for evaluation by an ophthalmologist. Iritis usually responds to treatment with topical corticosteroids and dilating agents. However, topical corticosteroids should be prescribed only with the advice of an ophthalmologist, because long-term corticosteroid therapy can lead to glaucoma, cataract formation, or exacerbation of ocular infections, and, in some connective tissue disorders, to ocular perforation.

Rheumatoid Arthritis

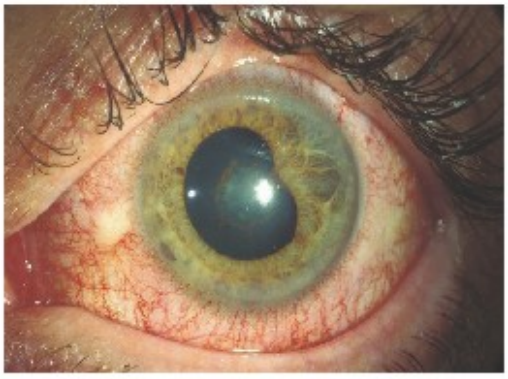
The ocular manifestation of rheumatoid arthritis are most often seen in patients with more active and severe forms of the disease and in those with extra-articular complications. Aside from dry eyes, other common ocular manifestations are inflammation of the episclera and sclera, peripheral corneal ulcers, and uveitis. Episcleritis is inflammation of the superficial tissue overlying the sclera. Typically patients complain of mild to moderate pain and tenderness, and there is localized or diffuse redness of the eye. Scleritis (inflammation of the sclera) may sometimes appear clinically similar to episcleritis. However, severe, deep pain is a distinguishing feature of scleritis. Scleritis may be characterized by active inflammation with redness, as seen on the left, and severe pain. It can progress to necrosis, as seen on the right, and subsequent perforation of the sclera (necrotizing scleritis). Scleromalaciaperforans consists of scleral melting in a white, quiet eye. This condition also can lead to ocular perforation. Peripheral corneal ulceration is another manifestation of rheumatoid arthritis that may result in ocular perforation. Patients with rheumatoid arthritis who develop peripheral corneal ulceration or scleritis have an associated risk for developing potentially lethal systemic vasculitis. Primary care physicians should monitor patients with

active rheumatoid arthritis for symptoms and signs of episcleritis, scleritis, and corneal ulcers; patients who develop these ocular conditions should be referred to an ophthalmologist for treatment.



Juvenile Rheumatoid Arthritis

Ocular involvement in juvenile rheumatoid arthritis typically occurs in patients with a mild form of the disease, the so-called pauci-articular form, and in patients who are rheumatoid-factor negative and ANA positive. Ocular complications may occasionally be the presenting feature of this disease and do not correlate with the severity or course of the systemic signs. The characteristic triad of late ocular complications in juvenile rheumatoid arthritis consists of iritis, cataract, and, as seen here, band keratopathy, which consists of whitish deposits of calcium in the cornea. Band keratopathy is a late sequela of many forms of chronic intraocular inflammation. Iritis or iridocyclitis can occur in up to 15% of patients with JRA and causes few symptoms or signs. The iritis is usually chronic, causing secondary cataract formation and glaucoma. All patients with JRA should be screened and followed by an ophthalmologist.



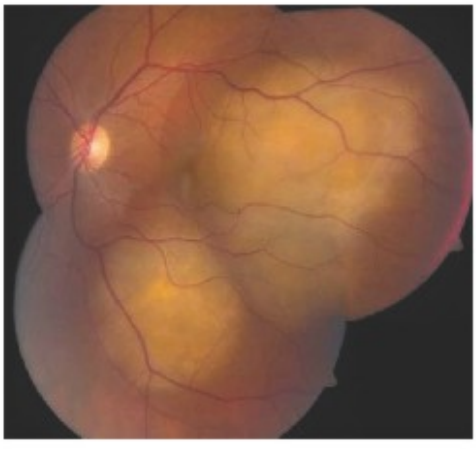
NEOPLASTIC DISORDERS

Ocular malignancies are most commonly metastatic lesions. Neoplasms arising from the uveal tissue give rise to primary ocular melanoma. These melanomas are easily treated when diagnosed early, but they may have fatal metastases if not diagnosed and treated in a timely fashion. Large-cell CNS lymphomas may have their initial presentation in the vitreous cavity of elderly individuals. Diagnosis may be achieved with a diagnostic vitrectomy.

Metastatic Carcinoma

The most common type of intraocular malignancy in adults is metastatic carcinoma, arising from primaries in the breast or lung in women and in the lung in men. Patients are often asymptomatic but may present with decreased or distorted vision. An easily detected iris mass is visible in this patient with metastatic lung carcinoma. An irregularly shaped pupil, iritis, or blood in the anterior chamber may signal a metastatic nodule, as seen here. Because of its rich vascular supply, the choroid is the most common site for ocular metastasis. Choroidal metastases may be solitary or multiple and may affect one or both eyes. Typically they appear as creamy-white lesions, as seen in this patient with metastatic breast cancer. Associated leopard spotting may also be detected.

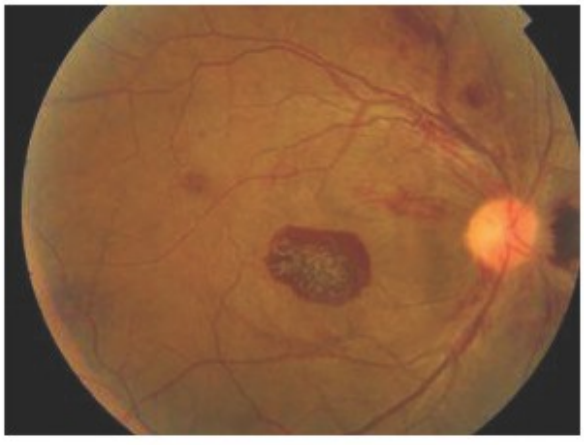
Choroidal metastases are often subtle and difficult to detect with direct ophthalmoscopy and may require referral to an ophthalmologist if suspected or if visual loss or visual distortion develops. Treatment options include local radiation and chemotherapy. Because ocular metastases may represent the smallest clinically detectable lesions of disseminated carcinoma, an ophthalmologist monitoring these lesions at regular intervals may help to assess the efficacy of systemic treatment. However, prognosis for survival after detection of an intraocular metastasis is generally poor, with a mean length of survival of 6 to 9 months.



Leukemia

Ocular involvement of Leukemia is relatively common and vital to assess for as ocular symptoms may be the first indication of manifestation, relapse, or early worsening of the condition. In particular, Leukemic Retinopathy is the most common ocular manifestation of Leukemia[viii]. Leukemia is a myeloproliferative disorder caused by an abnormal proliferation of immature leucocytes. Intraocular involvement in leukemia can be up to 90%.Both acute and chronic leukemia can

cause ocular manifestation. Retinal manifestations are usually due to indirect complications of leukemia especially due to hematological abnormalities.



Fundus of the right eye of a patient with acute myeloid leukemia showing retinal hemorrhages suggestive of leukemic retinopathy

Ocular complications of leukemia can either be[viii] : Primary/direct due to infiltration of the orbit, iris, choroid, optic nerve, and other tissues by leukemic tumour cells or indirect/ secondary as

- Hematological abnormalities such as anemia and thrombocytopenia, leading to intraretinal hemorrhages, white-centered retinal hemorrhages, cotton-wool spots, macular hemorrhages, subhyaloid hemorrhages, and vitreous hemorrhages.

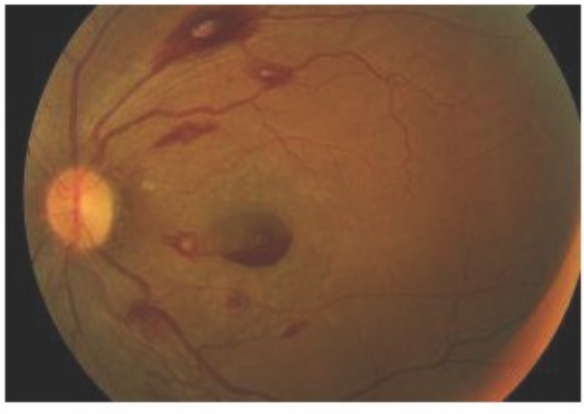
- CNS involvement through infiltration of the optic nerve, causing papilledema due to high intracranial pressure, and cranial nerve palsies.

- Opportunistic infections

- Chemotherapy related; high doses of glucocorticoids can cause ocular hypertension, cataracts, diplopia, and various other disorders[viii].

Signs:

2. Dilated and tortuous veins □ early manifestations due to hematological disturbances
3. Retinal hemorrhages at all levels □especially in the posterior pole, and extension to the vitreous. Preretinal hemorrhages, Superficial hemorrhages, Dot and blot hemorrhages, White centered hemorrhages/ Roth Spots, Sub-ILM hemorrhages, Subhyaloid hemorrhage and Vitreous hemorrhage



Fundus photo of the left eye showing white centered hemorrhages or Roth Spots

ROTH SPOTS[viii]

White centered hemorrhages known as □Roth spots□ result from retinalapillary rupture and extrusion of whole blood. This is followed by platelet adhesion to the damaged endothelium initiating a coagulation cascade and formation of a white lesion in the centre of the hemorrhage which is a platelet-fibrin thrombus. In leukemia, the white centre could correspond to an accumulation of leukemic cells.

3.Cotton wool spots

4.Leukemic Infiltrates: It is generally associated with high blood counts, fulminant disease and early mortality. Usually, but not always seen with surrounding hemorrhage[viii]. Grey-white streaks along vessels caused by local perivascular infiltrates. Subretinal infiltrates- referred to as subretinal hypopyon. Optic nerve infiltration. Choroidal infiltrates □ Serous retinal detachments, RPE detachments, discrete choroidal masses. Vitreous infiltrates: Internal limiting membrane acts as an effective barrier for leukemic cells infiltration. But they can rarely invade the vitreous from the optic disc. Can be associated with vitreous hemorrhage.

5. Vascular occlusions- Bilateral CRVO due to hyperviscosity.

6. Peripheral Microaneurysms- due to viscosity of elevated WBC count, does not correlate with hemoglobin or platelet level

7. Peripheral neovascularization similar to sickle cell anemia seen in CML- capillary closure associated with chronic elevated WBC count causing focal ischemia

8. Retinal detachments

9. Vitreous infiltrates

10. Choroidal infiltrates

11. Opportunistic infections □CMV retinitis, Ocular toxoplasmosis, Viral retinitis

12. Optic nerve involvement

13. Ocular Hypertension

Diagnosis:

- History of leukemia
- Detailed fundus evaluation
- Laboratory tests
- Complete blood count □ to look for anemia, thrombocytopenia, pancytopenia
- Peripheral blood smear- for blast cells
- Bone marrow biopsy □infiltration by blast cells
- Flow cytometry and immunophenotyping

Management:

Patients should be treated for the underlying leukemia by chemotherapy, immunotherapy or radiotherapy. Chemotherapy is the primary treatment modality and depends on the type of leukemia, as well as the phase of progression. ALL treatment consists of various combinations of vincristine, prednisone, and L-asparagine, while AML is treated with Daunorubicin, cytarabine, and thioguanine. CML on the other hand, is initially treated with busulfan or hydroxyurea. If chemotherapy fails to diminish intraocular leukemic infiltrates, direct radiation therapy is recommended. Leukopheresis and allogeneic bone marrow transplant are also sometimes necessary depending on severity and disease progression[viii]. One retrospective cohort study on 11 eyes treated with methotrexate injections showed improvement in inflammatory reactions and tumor cell infiltration in all treated eyes. Although retinal hemorrhages were not resolved, there was considerable improvement of other symptoms suggesting such approaches may be beneficial[viii].

Patients with clinical leukemic retinopathy may have more aggressive systemic disease that might lead to a worse prognosis. [viii]

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