Conjunctiva

**Applied anatomy:**
The conjunctiva is a transparent mucous membrane lining the inner surface of the eyelids and the anterior surface of the globe as far as the limbus. It is richly vascular, supplied by the anterior ciliary and palpebral arteries. There is a dense lymphatic network, with drainage to the preauricular and submandibular nodes corresponding to that of the eyelids. It has a key protective role, mediating both passive and active immunity. Anatomically, it is subdivided into the following:

1. **The palpebral conjunctiva** starts at the mucocutaneous junction of the lid margins and is firmly attached to the posterior tarsal plates. The underlying tarsal blood vessels can be seen passing vertically from the lid margin and fornix.

2. **The fornical conjunctiva** is loose and redundant.

3. **The bulbar conjunctiva** covers the anterior sclera and is continuous with the corneal epithelium at the limbus.

**Histology:**

1. **The epithelium** is non-keratinizing and around five cell layers deep. Basal cuboidal cells evolve into flattened polyhedral cells before they are shed from the surface. Goblet cells are located within the epithelium and are densest inferonasally and in the fornices.

2. **The stroma** (substantia propria) consists of richly vascularized loose connective tissue. The adenoid superficial layer does not develop until about 3 months after birth, hence the inability of the newborn to produce a follicular conjunctival reaction. The deep fibrous layer merges with the tarsal plates. The accessory lacrimal glands of Krause and Wolfring are located deep within the stroma. Mucus from the goblet cells and secretions from the accessory lacrimal glands are essential components of the tear film.

**Clinical features of conjunctival inflammation:**

**Symptoms:** Non-specific symptoms include lacrimation, grittiness, stinging and burning. Itching is the hallmark of allergic disease,
although it may also occur to a lesser extent in blepharitis and dry eye.

Significant pain, photophobia or a marked foreign body sensation suggest corneal involvement.

**Discharge:**

1) **Watery** discharge is composed of a serous exudate and tears and occurs in acute viral or acute allergic conjunctivitis.

2) **Mucoid** discharge is typical of chronic allergic conjunctivitis and dry eye.

3) **Mucopurulent** discharge typically occurs in chlamydial or acute bacterial infection.

4) **Severe purulent** discharge is typical of gonococcal infection.

**Conjunctival reaction:**

1) **Hyperaemia:** that is diffuse, beefy-red and more intense away from the limbus is usual in bacterial infection and should be distinguished from the ciliary injection of iridocyclitis.

2) **Haemorrhages:** may occur in viral conjunctivitis, when they are often multiple, small and discrete; and severe bacterial conjunctivitis, when they are larger and diffuse.

3) **Chemosis (conjunctival oedema):** is seen as a translucent swelling, which when severe may protrude through the eyelids. Acute chemosis indicates a hypersensitivity response e.g. pollen whereas chronic chemosis has numerous causes e.g. chronic allergic conjunctivitis.

4) **Membranes:**

   a) **Pseudomembranes** consist of coagulated exudate adherent to the inflamed conjunctival epithelium. They can be peeled easily leaving the underlying epithelium intact.
b) **True membranes** involve the superficial layers of the conjunctival epithelium so that attempted removal leads to tearing.

c) **Causes**
- Severe adenoviral conjunctivitis.
- Gonococcal conjunctivitis.
- Ligneous conjunctivitis.
- Acute Stevens–Johnson syndrome.
- Bacterial infection (*Streptococcus* spp., *Corynebacterium diphtheriae*).

5) **Subconjunctival scarring**: may occur in trachoma and other types of cicatriz ing conjunctivitis.

6) **Follicles**:
   a) **Signs.** Multiple, discrete, slightly elevated lesions resembling translucent grains of rice, most prominent in the fornices. Blood vessels run around or across rather than within the lesions.
   b) **Causes** include
      - Viral conjunctivitis.
      - Chlamydial conjunctivitis
      - Parinaud oculoglandular syndrome
      - Hypersensitivity to topical medications.

7) **Papillae**: can develop only in the palpebral conjunctiva and in the limbal bulbar conjunctiva where it is attached to the deeper fibrous layer.
   a) **Signs** In contrast to follicles, a vascular core is present.
      - Micropapillae form a mosaic-like pattern of elevated red dots as a result of the central vascular channel.
      - Macropapillae (<1 mm) and giant papillae (>1 mm) develop with prolonged inflammation.
   b) **Causes** include
• bacterial conjunctivitis
• allergic conjunctivitis
• chronic blepharitis
• contact lens wear
• superior limbic keratoconjunctivitis
• Floppy eyelid syndrome.

*Lymphadenopathy:*
The most common cause of lymphadenopathy associated with conjunctivitis is viral infection. It may also occur in chlamydial and severe bacterial conjunctivitis (especially gonococcal), and Parinaud oculoglandular syndrome. The preauricular site is typically affected.

*Laboratory Investigations:*
There is no need to do routine investigations for every patient presented with conjunctivitis unless has one of the following indications.

**Indications:**
- Severe purulent conjunctivitis.
- Follicular conjunctivitis (viral, chlamydial).
- Atypical conjunctivitis.
- Neonatal conjunctivitis.

*Bacterial Conjunctivitis*
1- **Simple bacterial conjunctivitis:**
It is a common disease, and usually it is *self-limiting condition.*
Common causative organisms are:
- Staphylococcus epidermidis.
- Staphylococcus aureus.
- Others like Streptococcus pneumoniae, H. influenzae.

**Symptoms:**
- Acute onset of redness.
- Grittines.
- Burning.
- Discharge.
- On morning, eyelids are stuck together due to accumulation of exudates during the night.
- Both eyes are usually involved.

**Signs:**
- The eyelids are oedematous (mild oedema).
- Mucopurulent discharge.
- Beefy-red injection, maximally in the fornices.
- Pseudoembranes in severe cases.
- Corneal involvement is uncommon.
  * Blurred vision may occur due to mucus not due to corneal involvement.

**Treatment:**
- Usually resolves within 10-14 days and laboratory tests are not routinely performed.
- Irrigation to remove excessive discharge.
- Topical drops (Antibiotics): Chloramphenicol, ciprofloxacin, ofloxacin, gentamicin, neomycin, tobramycin.
  - Antibiotic ointments: it gives higher concentration for long period and usually given at night because it causes blurred vision. e.g. chloramphenicol, gentamicin.

**2- Neonatal bacterial Keratoconjunctivitis:**
  * bacterial conjunctivitis in neonate is one cause for Ophthalmia neonatorum (any infection of the conjunctiva within the first month after delivery).
  - Usually appears at 1-3 days of life.
  - it is rare condition.

**Signs:**
- Hyperacute presentation.
- Chemosis.
- Pseudo-membranes.
- Corneal involvement.

**Treatment:** Systemic and topical antibiotics.
Viral Conjunctivitis

1- Adenoviral keratoconjunctivitis:
- It is a highly contagious virus.
- Transmission is via respiratory or ocular secretion.
- Dissemination is by contaminated towels or equipments (e.g. tonometer: an instrument used to measure the intraocular pressure).
- Incubation period is 4-10 days; it is an occupational hazard of ophthalmologists (due to contamination of their hands with their patients).

 Conjunctivitis:
Presentation: acute onset of watery discharge, redness, discomfort and irritation, both eyes are affected in 60% of cases.

Signs:
- Eyelids are oedematous.
- Watery discharge.
- Follicular reaction.
- Subconjunctival haemorrhages.
- Pseudomembranes. and - Lymphadenopathy is tender.

Keratitis:
Multiple, corneal sub epithelial infiltration and opacification.

Treatment:
a- Avoid transmission following examination of patients:
- Washing of hands.
- Meticulous disinfection of ophthalmologic instruments.
- Infected hospital personnel should not be in contact with patients.

b- Medications:
i- For conjunctivitis:
- Spontaneous resolution occurs within 2 weeks.
- Antiviral agents are ineffective (has no role).

- Topical steroids are indicated only in very severe inflammations and when Herpes simplex infection has been excluded. The
treatment with steroids is symptomatic and supportive (not used routinely).

- Artificial tears q.i.d. may be useful for symptomatic relief. Preservative-free preparations may give superior comfort, and if supplied in single-dose units may reduce transmission risk.
- Cold (or warm) compresses for symptomatic relief.
- Removal of symptomatic pseudomembranes or membranes.
- Topical antibiotics if secondary bacterial infection is suspected.

ii- For keratitis:
- Topical steroids, which are indicated only if the eye is uncomfortable or there is diminishing of the visual acuity by corneal subepithelial infiltrates and opacifications, Steroids should not be used till exclusion of Herpes simplex infection.

Note: Steroids do not shorten the natural course of the disease but suppress the inflammation and relief symptoms.

2- Herpes simplex conjunctivitis:
Conjunctivitis may occur in patients with primary Herpes simplex infection.
- when the person catches the infection for the first time it is primary, after treatment, the virus get dormant in the trigeminal nerve ganglia. If for any reason, the person gets decrease immunity, then secondary herpes infection is developed.

Signs:
- The eyelids and periorbital skin show unilateral herpetic vesicles, which may be associated with edema.
- Watery discharge.
- Ipsilateral follicular reaction.
- Lymphadenopathy is tender.
- Keratitis is uncommon.
- Herpes simplex infection is very severe and it can lead to dendritic ulcer of the cornea.
- No subconjunctival hemorrhage.

**Treatment:** Antiviral agent (as Acyclovir "Zovirax™") for 21 days to prevent keratitis.

**Chlamydial Conjunctivitis**

1- Adult chlamydial Keratoconjunctivitis:
It is a sexually transmitted disease caused by the obligate intracellular bacterium *Chlamydia trachomatis*(serotypes D-K).
- Patients are usually young and at least 50% have a concomitant genital infection (cervicitis in ♀ or urethritis in ♂).

**Mode of transmission:**
- Autoinoculated from genital secretions.
- Eye to eye spread is rare.

**Incubation period:** 1 week.

**Presentation:**
Subacute onset of unilateral or bilateral mucopurulent discharge.
* Without treatment conjunctivitis persists for 3-12 months. So, in chronic conjunctivitis we should think about Chlamydial Keratoconjunctivitis.

**Signs:**
- Eyelids are lightly oedematous.
- Mucopurulent discharge.
- Large follicles are formed at the inferior fornix.
- Lymphadenopathy (tender).
- Keratitis is uncommon, if it occurs:
  * Epithelial Keratitis.
  * Sub-epithelial keratitis (opacities).
  * Marginal infiltrates (circumferential, i.e. involvement of the limbus and the periphery of cornea).
- Conjunctival scarring.
- Pannus (sub-epithelial corneal neovascular or fibrovascular membrane, i.e. affects the cornea not the conjunctiva).

**Treatment:**

a- Topical therapy: Tetracycline ointment 4 times\ day for 6 weeks.
b- Systemic therapy: One of the following:
   i- Doxycycline: 100mg X 1 for 1-2 weeks.
   ii- Tetracycline: 250mg X 4 for 6 weeks.
   iii- Erythromycin: 250mg X 4 for 6 weeks.

2- Neonatal chlamydial conjunctivitis:
- The *most* common cause of neonatal conjunctivitis (ophthalmia Neonatorum).
- It may be associated with systemic infection, e.g. otitis, rhinitis or pneumonitis.
- It is transmitted from the mother genital tract during delivery.

**Presentation:**
The child is usually presented between 5 & 19 days after birth.

**Signs:**
- Papillary conjunctivitis (there is no follicular reaction as the lymphoid tissue develops 3 months after delivery).
- Mucopurulent discharge.

**Complications (if not treated):**
There is Conjunctival scarring and superior corneal pannus.

**Treatment:**

a- Topical Erythromycin.
b- Oral Erythromycin, 250mg/kg body weight daily for 14 days.

3- Trachoma:
(Compare it with Adult Chlamydial Keratoconjunctivitis)
- It is an infection caused *Chlamydia trachomatis*(*serotypes A,B,Ba and C*).
- It is a disease of underprivileged populations with poor conditions of hygiene (low socioeconomic status).
Transmission: Common fly is the major vector, currently trachoma is the leading cause of preventable blindness in the world.

Presentation: is usually during childhood.

Signs:
1- Follicular reaction.
2- Chronic conjunctival inflammation causes conjunctival scarring that involves the entire conjunctiva but most prominent on the upper tarsus.
3- Keratitis: either * Superficial epithelial keratitis.
* Anterior stromal inflammation and pannus formation.
4- Progressive conjunctival scarring: if it is severe lead to:
* Destruction of lids.
* Trichiasis: Misdirection of eyelashes towards the cornea causing rubbing of cornea, it is either true Trichiasis (due to affection of hair follicles) or pseudo (due to entropion of lid margin).
* Entropion: the inward turning of the eyelid.
* Dry eyes, due to destruction of conjunctival goblet cells, accessory lacrimal cells and lacrimal ducts of main lacrimal duct.
5- End-stage trachoma:
* Corneal ulceration (due to dry eye and Trichiasis). Superficial corneal ulcers usually heal by regeneration so the cornea remains transparent, while deep ulcers do not regenerate but heal by fibroblasts to fibrous tissue leading to opacification, which lead to diminished visual acuity or even blindness in severe cases.

World Health Organization (WHO) grading:
TF: Trachoma follicles (5 or more follicles in the superior tarsal conjunctiva).
TI: Trachomatous intense inflammation diffusely involving the tarsal conjunctiva.
TS: Trachomatous conjunctival scarring.
TT: Trachomatous trichiasis touching the cornea.
CO: Corneal opacity.
**Treatment of trachoma:** indicated for stages I & II (TF & TI) only, as there is no benefit from treating stages III, IV & V (there is no active inflammation).
- Preventive measures: strict personal hygiene, especially washing the face of young children (single face wash at the morning is enough to prevent the infection).
- Topical Tetracycline or Erythromycin eye ointment plus Single dose of systemic erythromycin.

**Neonatal conjunctivitis**

is defined as conjunctival inflammation developing within the first month of life. It is the most common infection of any kind in neonates, occurring in up to 10%.

**Causes:**
- *C. trachomatis, N. gonorrhoeae* (now rare in developed countries) and occasionally herpes simplex virus (typically HSV-2), which may be associated with severe ocular or systemic complications.
- Staphylococci are usually responsible for mild conjunctivitis
- Topical preparations used as prophylaxis against infection may themselves cause conjunctival irritation.

**Diagnosis:**

1) **Timing of onset**
- Chemical irritation: first few days.
- Gonococcal: first week.
- Staphylococci and other bacteria: end of the first week.
- Herpes simplex: 1–2 weeks.
- Chlamydia: 1–3 weeks

2) **History**
• Instillation of a prophylactic chemical preparation.
• Parental symptoms of sexually transmitted infections.
• Recent conjunctivitis in close contacts.
• Systemic illness such as pneumonitis, rhinitis and otitis in chlamydial infection, skin vesicles and features of encephalitis in herpes simplex.
• Prior persistent watering without inflammation may indicate an uncanalized nasolacrimal duct.

3) Signs
• The type of discharge varies according to the underlying cause.
• Reflux of mucopurulent material on pressure over the lacrimal sac is suggestive of delayed canalization of the lacrimal duct.
• Severe eyelid oedema occurs in gonococcal infection.
• Eyelid and periocular vesicles may occur in HSV infection.
• Keratitis in gonococcal or HSV infection.

Allergic conjunctivitis

1- Acute allergic conjunctivitis:

is a common condition caused by an acute conjunctival reaction to an environmental allergen, usually pollen. It is typically seen in younger children after playing outside in spring or summer.

Presentation is with acute itching and watering, associated with severe chemosis.

Treatment is not usually required and the conjunctival swelling settles within hours as the acute increase in vascular permeability resolves. Cool compresses can be used and a single drop of adrenaline 0.1% may reduce extreme chemosis.

2- Vernal keratoconjunctivitis (spring catarrh):
is a recurrent bilateral disorder in which both IgE- and cell-mediated immune mechanisms play important roles. It primarily affects boys and onset is generally from about the age of 5 years onwards (mean age 7 years). Ninety-five per cent of cases remit by the late teens although many of the remainder develop atopic keratoconjunctivitis. VKC often occurs on a seasonal basis, with a peak incidence over late spring and summer.

Classification

1) Palpebral VKC primary involves the upper tarsal conjunctiva. It may be associated with significant corneal disease as a result of the close apposition between the inflamed conjunctiva and the corneal epithelium.

2) Limbal disease typically affects black and Asian patients.

3) Mixed VKC has features of both palpebral and limbal disease.

Clinical features:

1) Symptoms consist of intense itching, which may be associated with lacrimation, photophobia, a foreign body sensation, burning and thick mucoid discharge. Increased blinking is common.

2) Palpebral disease
   • Early-mild disease is characterized by conjunctival hyperaemia and diffuse papillary hypertrophy on the superior tarsus.
   • Macropapillae (<1 mm).
   • Progression to giant papillae (>1 mm) can occur, as adjacent smaller lesions amalgamate when dividing septa rupture.
   • Mucus deposition between giant papillae.

3) Limbal disease
   • Gelatinous limbal conjunctiva papillae that may be associated with transient apically-located white cellular collections (Horner-Trantas dots).
4) **Keratopathy** is more frequent in palpebral disease and may take the following forms:

a **Superior punctate epithelial erosions.**

b **Epithelial macroerosions** caused by a combination of epithelial toxicity from inflammatory mediators and a direct mechanical effect from papillae.

c **Plaques** and ‘**shield’ ulcers** may develop in palpebral or mixed disease when the exposed Bowman membrane becomes coated with mucus and calcium phosphate, leading to inadequate wetting and delayed reepithelialization.

d **Subepithelial scars** that may affect vision.

e **Pseudogerontoxon** can develop in recurrent limbal disease. It is characterized by a paralimbal band of superficial scarring.

**Treatment:**

1- Topical steroids: (its use is mandatory)
- As the patients will not cure until around puberty by any drug, so we should use weak steroids as fluorometholone or Clobetasone. Potent topical steroids likes dexamethasone, betamethasone or prednisolone should be avoided as their corneal penetration and their risk to increase IOP and causing cataract is more than weak steroids.
- It should be of short course.

2- Mast cell stabilizers:
- nedocromil 0.1% drops *2 daily
- or lodoxomide 0.1% drops *4 daily.
- or sodium cromoglycate 2% *4 daily

They are not effective as steroids in controlling **acute** exacerbation.

3- Acetylcysteine 5% drops *4 daily, as treatment of early plaque formation (mucolytic).

4- Topical cyclosporin A: used in steroids resistant cases.
5- Debridement: of early mucus plaques to get speed repair of persistent epithelial defect, done under topical anesthesia with cotton-tipped applicator.

6- Lamellar keratectomy: For densely adherent plaques or subepithelial scarring, and sometimes we may need corneal replacement (corneal graft).

7- Supratarsal injection of steroids: it is very effective in patients with severe disease and Giant tarsal papillae. It is used to avoid ocular side effect of topical medications.

**Conjunctival Degenerations**

1- Pinguecula:
It is an extremely common lesion which consists of a yellow-white deposit on the bulbar conjunctiva adjacent to the nasal or temporal aspect of the limbus and it is usually asymptomatic.

**Histology:** There is degeneration of the collagen fibers of the conjunctival stroma, thinning of the overlying epithelium and occasionally calcification.

Some pingueculae may enlarge very slowly but surgical excision is seldom required. (usually, it need no treatment)

2- Concretions (ocular lithiasis) :
- They are small yellow-white deposits.
- Commonly present in the palpebral conjunctiva of the elderly.
- Also in patients with chronic meibomian gland disease.
- Usually asymptomatic, but occasionally causes foreign body sensation when erode through the epithelium.

**Treatment:** They can be easily removed with a needle.

3- Pterygium:
- It is a triangular sheet of conjunctival fibrovascular tissue invades the cornea.
- Occurs in patients who have been living in outdoor, hot climates.
- May represent a response to chronic dryness and exposure to the sun
**Signs:**

a- Small, grey, corneal opacities near the nasal limbus.

b- Then, the conjunctiva overgrows these opacities and progressively invades onto the cornea in a triangular fashion.

c- A deposit of iron (Stocker line) may be present in the corneal epithelium anterior to the advancing head of the pterygium.

* Usually asymptomatic.

**Treatment:**

a- Surgical excision: **indicated only** in the following cases:

i- If it is threatening the visual axis.

ii- Severe irritation.

iii- For cosmetic reason.

b- Lamellar keratoplasty: required if the visual axis is affected by opacification.

Surgical excision, it is an easy procedure but should be avoided unless there is indication because the recurrent rate is high (about 80%) and the recurrent pterygium is uglier, rapidly progress and causing more severe symptoms.

**Subconjunctival Haemorrhage:**

is a very common phenomenon that may result from surgery, conjunctivitis and trauma (from minor unnoticed to severe skull base), but is often idiopathic and apparently spontaneous, particularly in older patients. The bleed is usually asymptomatic until noticed by the patient or others. Coughing, sneezing and vomiting are common precipitants. In younger people contact lens wear is a common association, and in older individuals systemic vascular disease is prevalent, especially hypertension. Bleeding diatheses are a very rare association.

The vision is usually unaffected. Spontaneous resolution over a week or two is typical.