CONJUNCTIVA:
Inflammatory and degenerative lesions

Anat Stemmer-Rachamimov
Associate Professor
Massachusetts General Hospital
Harvard Medical School
Boston MA
Outline

• Introduction:

• Inflammatory lesions:
  – Follicular
  – Papillary
  – Cicatricial

• Malformative/developmental

• Degenerative
The normal Conjunctiva

- The conjunctiva lines the surface of the eye and posterior aspect of the eyelids
  
- 3 parts:
  - Bulbar: lines the globe
  - Palpebral: lines the post aspect of the eyelids
  - Forniceal: where it reflects to
    - globe, cul de sacs
Two special modifications are present in the medial fornix:

- The plica semilunaris, a crescentic fold of conjunctiva just lateral to caruncle

- The caruncle; medial to the plica semilunaris, A small fleshy nodular prominence in nasal portion of interpalpebral fissure (inner angle of eye) between skin and conjunctiva
A mucous membrane

- **Epithelium**: Non-keratinized stratified epithelium containing goblet cells (more in nasal area; plica semilunare)
- **Other cells**: melanocytes, Langerhans cells, inflammatory cells
- **Connective tissue/stroma**: epithelium rests on loose connective tissue; substantia propria; subepithelium
Regional differences

- Number of goblet cells varies: more prominent in fornices, semilunar fold, and the caruncle

- Layers of epithelium: varies; 6 in the bulbar and palpebral; 3 in the fornices

- Adherence of conjunctiva to connective tissue: most adherent at the limbus, most loose at the fornices (redundancy to allow movement)
Areas of transition

- **Limbus** – gradual to the corneal epithelium; site of corneal epithelial stem cells

- **Lid margin** – marginal mucocutaneous margin; abrupt transition to skin

- **Caruncle** – composed of modified conjunctiva containing hair, sebaceous glands, fat, lacrimal glands
Conjunctiva – binds together eyelid and globe

- Forms a barrier to exogenous agents from outside world
- Lubrication of the eye cornea through tear film
Conjunctival defense mechanisms

• Intact epithelium
• Eyelid blinking: mechanical removal of pathogens
• Tear film:
  – antimicrobial proteins (lysozymes, Ig, lactoferrin)
  – mucins
• Specific mucosal immune system: conjunctival associated lymphoid tissue
• Normal tear film is important for the homeostasis of the conjunctiva

• The tear film is composed of lipid, aqueous, and mucoid layers
  – the mucoid layer is apposed to the corneal epithelium
  – the lipid layer is at the tear film : air interface

• Multiple disorders are associated with abnormal tear film and secondary ocular surface changes.
The conjunctiva produces hydrophilic mucins
Secreted by goblet cells and epithelial cells

Heavily glycosylated proteins with multiple roles:
1) clearance of allergens and pathogens
2) lubrication
3) antimicrobial activity
 Conjunctival lesions in adults

Large study review of over 2000 conjunctival biopsies (1923-1984), Wilmer Ophth. Inst

Inflammatory/degenerative lesions 41%
Aquired epithelial lesions 26%
Pigmented lesions 12%
Aquired subepithelial lesions 6%
Congenital lesions 2%

Grossniklaus et al; 1987
Inflammatory/degenerative lesions:

- Pterygium: 44%
- Chronic inflammation: 17%
- Pyogenic granuloma: 10%
- Pinguecula: 9%
- Sarcoidosis: 4%

Increased incidence of pterygium in men
Increased incidence of Sarcoidosis in women

Grossniklaus et al; 1987
Inflammatory - conjunctivitis

• Clinical course:
  – Acute
  – Chronic

• Cause:
  – Infectious
  – Immune mediated

• Morphology:
  – Papillary, follicular, cicatricial,
  – Hemorrhagic, membranes, pseudomembranes
Patterns of conjunctival reaction

Acute conjunctivitis:

• Edema (chemosis), hyperemia, and cellular exudates

• Inflammatory membranes:
  – *True membrane*: consists of an exudate of fibrin–cellular debris firmly attached to the underlying epithelium by fibrin; removal strips the epithelium and leaves a raw, bleeding surface.

• Seen in Stevens–Johnson syndrome, and infections caused by bacteria
– *Pseudo membrane*: a loose fibrin–cellular debris exudate not adherent to the underlying epithelium. Can be easily stripped, usually without bleeding.
Chronic conjunctivitis

- Epithelium: Hyperplasia and increase in number of goblet cells
- *Pseudoglands (Henle)*: Infoldings of the proliferated epithelium and goblet cells may resemble glandular structures
- Pseudoretention cyst formation: clogging of surface openings of the pseudoglands, (inferior palpebral conjunctiva). Cysts contain mucinous secretions and degenerative epithelial cells.
Papillary conjunctivitis

- Papillary hypertrophy is primarily a vascular response.
- Conjunctiva is thrown into folds.
- Papillae:
  - covered by hyperplastic epithelium
  - Central core of vessels
  - surrounded by edematous subepithelial tissue infiltrated with lymphocytes, plasma cells, eosinophils
Clinically, cobble stone pattern
- Papillae appear as small, regular hyperemic projections
- Marked in the upper palpebral conjunctiva,
- contain a central tuft of vessels.
- The valleys between the projections are pale
- Most commonly

Associated with
Immune mediated conjunctivitis

Clinical Ophthalmology/Kanski
Follicular conjunctivitis

• Represents follicular hyperplasia

• Clinically, large gelatinous masses without a central vascular core
- Histologically: lymphoid aggregates, sometimes with germinal centers
- Associated with infections: viral, chlamydia.
- Also with drug toxicity, allergy
Inflammatory disorders

• Infectious
  – Bacteria
  – Viruses
  – Chlamydia

• Immune mediated
  – Local: allergic, contact lens wear, giant papillary, vernal
  – Systemic: Steven Johnson, Mucous membrane pemphigoid
Case #1

5 year old child complains of burning in the eye (left). Following day, the second eye is burning as well.

In addition patient complains that in the morning, eyes are stuck together. His mom describes yellow crust on they eyelids.
On examination: There is purulent exudate and the conjunctiva is injected.

Additional findings on exam:
- Mucus strands and
- Superficial corneal erosions
Diagnosis: Bacterial Conjunctivitis

- **Bacteria** is most common form in children (50%);
- Uncommon in adults (5%)

- **Gram positive:** Haemophilus Influenza, Strep pneumonia

- Usually self limiting; resolves within a week
Histology (not done):
neutrophilic infiltrates in epithelium

Eye pathology/Eagle
Bacterial conjunctivitis as part of a systemic infection: **Gonococcal**

Transmission:
- By contact of eye with infected genital secretions
- Fetus infected while in transit in the birth canal

Ocular clinical manifestations:
- Severe lid edema and erythema
- Hyperacute, severe purulent conjunctivitis
- Membrane formation

*Clinical Ophthalmology/Kanski*
• Corneal ulceration if not treated
• Perforation and endophthalmitis

Systemic manifestations:
• Urogenital infection may be present
• Marked lymphadenopathy

Diagnosis:
• Diploccoci on Gram stain
• Culture
Case #2

- 23-year-old man
- 6-week duration of red eyes associated with mucous discharge, foreign body sensation, tearing, blurred vision, and swollen eye lids.
- These symptoms started in his right eye a few days later, his left eye also became affected.
Has been treated with polymyxin B drops for a week but symptoms persisted.

Had multiple female sexual partners in the past, does not use protection

On examination:

- Palpable preauricular lymph nodes
- Conjunctival injection
- Follicular reaction involving the inferior fornix
- Peripheral corneal infiltrates
Differential diagnosis

- Chlamydia
- Bacterial
- Viral
- Masquerade syndrome

Laboratory investigation
Corneal scrapings were sent for culture: positive for Chlamydia.

Clinical Ophthalmology/Kanski
Diagnosis:
Adult chlamydial conjunctivitis

- Adult chlamydial conjunctivitis is a sexually transmitted disease (STD)
- All ages but particularly young adults
- More women than men affected
- the most common cause of chronic follicular conjunctivitis
- 20% of acute follicular conjunctivitis
- C. trachomatis serotypes D-K
• Patients can present with a wide range of acuity and severity of symptoms.
  – more common - mild symptoms
  – acute, mucopurulent conjunctivitis
  – often unilateral disease but can involve both eyes.
  – pink/red eye, mucous discharge, lids stuck together, swollen lids, tearing, photophobia, foreign body sensation, and decreased vision.
  – Often also have genitourinary symptoms
• If left untreated, adult chlamydial conjunctivitis resolves spontaneously in 6-18 months.
• Because genito urinary tract is also involved- systemic treatment
• Partner has to be treated as well
• Gonorrhea coinfection has to be ruled out.
Chlamydia

- Gram-negative, basophilic, coccoid or spheroid bacteria
- Obligate intracellular organisms
- Order Chlamydiales; 4 species: *trachomatis psittaci*, *pneumonia* and *pectorum*. Only *trachomatis* and *psittaci* are associated with disease.
- Chlamydias cause:
  - trachoma,
  - Adult inclusion conjunctivitis,
  - Neonatal chlamydia conjunctivitis
  - lymphogranuloma venereum
  - ornithosis (psittacosis)
Neonatal chlamydial conjunctivitis

- Neonate infected through passage in birth canal
- Clinical manifestation - 2 weeks after birth
- Acute bilateral eyelid edema and mucopurulent discharge
- May involve other systems: pneumonia, otitis.
- Differential diagnosis: Gonorrhea and Chlamydia.
Trachoma

• Chlamydia trachomatis is a major cause of ocular infection and blindness (especially in the Middle East).

• Different strains and depending on the age and immune system of the host cause different forms of ocular disease:
  - Serotypes A, B and C are associated with trachoma
  - Serotypes D-K cause neonatal and adult inclusion conjunctivitis.
Tracoma:

• Chronic, cicatrizing conjunctivitis

• Infection is spread by direct contact with infected eye secretions; often through flies or contaminated water

• Common in crowded, poor environment
McCallan’s Four Stages

Stage I: Epithelial hyperplasia and neovascularization.

• Early formation of conjunctival follicles, subepithelial conjunctival infiltrates, diffuse punctate keratitis and early pannus

Hyperplastic conjunctival epithelium containing clearly defined, intracellular minute elementary bodies and large basophilic bodies, or inclusion bodies of Halberstaedtler and Prowazek

Cornea, Conjunctiva
Stage II: Follicular conjunctivitis

- Florid inflammation, mainly of the upper tarsal conjunctiva with the early formation of follicles appearing like sago grains, and then like papillae. Pannus becomes larger
Trachomatous pannus growing over the superior conjunctiva
Stage III: Scarring (cicatrization):

• in the peripheral cornea, involution of follicles leaving a row of shallow depressions (*Herbert's pits*);
• as the palpebral conjunctiva heals, a white linear horizontal line or scar forms near the upper border of the tarsus (*von Arlt's line*).
• Cicatricial entropion and trichiasis may result.
Stage IV

- Corneal opacification and blindness

Laboratory diagnosis procedures:

- Molecular methods (PCR-DNA detection)
- Immunofluorescence
- Culture: McCoy cell culture
- Conjunctival smears (Giemsa, PAS). Inclusions in epithelial cells; neonatal form
Case #3

- eight-year-old boy
- complaining of a four month history of decreased distance visual acuity
- Hx seasonal allergic rhinitis
On examination

– Moderate photophobia
– 20/40
– Conjunctival injection
– Limbal and palpebral papillae

• Corneal scrapings: eosinophils and debris
Diagnosis: vernal keratoconjunctivitis

- Vernal keratoconjunctivitis is an allergy associated inflammatory disease
- Boys, before puberty (11-13)
- characterized by bilateral palpebral and/or bulbar conjunctiva papillae, corneal keratopathy and severe itching, thick muous discharge (chewing gum)
- higher incidence in warm, dry climates (Africa)
• family history positive for atopic disease (asthma, rhinitis, and eczema).
• self-limiting disease, typically lasts 4-10 years with remission at puberty.
• Mucous discharge and corneal scrapings show numerous eosinophils.
• pathogenesis is multifactorial.
• type I IgE mediated.
• hypersensitivity reaction.

Ocular Pathology/Yanoff & Sassani
Viral conjunctivitis

- Most common form in adults
- Adenovirus ("pink eye") occurs in epidemics
- Highly contagious and can be transmitted through medical instruments cleaned with alcohol
- 2 broad clinical diseases:
  - Epidemic keratoconjunctivitis: follicular
  - Pharyngoconjunctival fever: children, lymphadenopathy, sore throat, fever
Case # 4

- 4 year old child presented with bilateral large, yellowish-white soft tumors near the temporal canthus, extending backward and upward.

- Present since birth
• Resected specimen composed primarily of mature adipose tissue
Diagnosis: Dermolipoma

• Dermolipoma is a choriostoma
• **Choristomas**: mature tissue elements not normally present at the site of occurrence.
• Choristomas are the most common epibulbar and orbital tumors in children.
• may arise from the cornea, limbus or subconjunctival space
• range in appearance from a small, flat lesion to a large masses
Other choriostoma:

- limbal dermoid,
- ectopic lacrimal gland,
- episcleral osseous choristoma.
Case #5

• 80 year old man presented with complaints of dryness and foreign body sensation in left eye

• On examination: pinkish triangular wedge of vascular conjunctiva on the surface
Histology:

There is subepithelial elastotic degeneration of collagen fibers

DD: pseudo pterygium (conjunctival fold)
• Incidence and prevalence of pterygium and pingeucula vary with race and location
• Positive association with UV exposure esp. in early childhood
• Positive association with rural environment (dust?)
• More common in non-whites