

CORNEA & EXTERNAL DISEASE

Revised 2002

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DEFINITIONS

Degeneration: changes secondary to previous disease

Dystrophy: primary changes of genetic origin - bilateral, central, relatively symmetric, avascular, progressive

CONJUNCTIVAL DEGENERATIONS

Pinguecula

environmental exposure to ultraviolet light (actinic)
yellow-white, amorphous, sub-epithelial deposits of abnormal collagen
at the interpalpebral limbus, may be calcified
collagen is fragmented, curly, more basophilic with H&E, stains for
elastin, insensitive to elastase: elastoid or elastotic degeneration
differential: inflammatory, neoplastic, atopic
excision for chronic inflammation, contact lens intolerance, cosmetic

Pterygium

preceded by pinguecula, involves the cornea
actinic exposure, location, elastoid degeneration same as pinguecula
destruction of Bowman's membrane with fibrovascular ingrowth,
epithelium
may be dysplastic, iron line at leading edge (Stocker's line)
excision for chronic inflammation, involvement of visual axis, cosmetic
recurrence rate £ 40%, reduced by Strontium 90 beta irradiation
(necrosis), free conjunctival graft, topical thiotepa (depigmentation)
or mitomycin C

Amyloidosis

avascular, uninfamed, yellow-white or salmon color
primary vs secondary, localized or systemic
primary localized amyloidosis of the conjunctiva most common
(palpebral), lattice and gelatinous droplike dystrophy affect cornea

secondary localized associated with chronic inflammation, e.g.,
trachoma, I.K.

stains with Congo Red, dichroism and birefringence in polarized light,
metachromasia with crystal violet, fluorescence with Thioflavine T
and UV, typical filaments on EM, often subepithelial

Conjunctival Concretions

yellow-white cysts in the fornix or palpebral conjunctiva, associated
with chronic conjunctivitis (trachoma), aging
epithelial inclusion cysts filled with epithelial and keratin debris
can erode overlying conjunctiva to cause FB sensation, easily excised

CORNEAL DEGENERATIONS

Aging Changes

Arcus Senilis - white lipid ring at periphery with lucid interval, starts
inferiorly/superiorly, deposits at Bowman's/Descemet's membrane,
under age 40

work-up for hyperlipoproteinemia, except arcus juvenalis (congenital)

Hassall-Henle bodies - peripheral guttata, normal aging change over 20
years

White Limbal Girdle of Vogt - interpalpebral, (+) lucid interval calcific,
or

(-) lucid interval elastotic degeneration

Cornea Farinata - deep stromal opacities seen best by retroillumination

Crocodile Shagreen - anterior and posterior stromal mosaic pattern

Depositions

Band Keratopathy - interpalpebral, peripheral then central, calcific
degeneration of Bowman's layer, lucid interval, holes

1. chronic inflammation - uveitis in children, I.K., phthisis
2. hypercalcemia - hyperparathyroid, Vit. D toxicity, sarcoid, milk-alkali
3. primary hereditary
4. elevated serum phosphorus, normal calcium (renal failure)
5. chronic exposure to mercury vapors or preservatives in drops
urate deposits are brown, seen with gout or hyperuricemia

Spheroid Degeneration (a.k.a. chronic actinic, labrador, or climatic
droplet

keratopathy, Bietti's nodular dystrophy, etc.) - translucent golden brown
interpalpebral droplets in conjunctiva and superficial stroma of cornea.

- actinic damage and genetic predisposition
- males > females, may be bilateral, associated with band keratopathy

Salzmann's Nodular Degeneration - elevated subepithelial gray- or blue-white nodules on cornea

- late sequella to keratitis, e.g. phlyctenulosis, I.K., trachoma
- focal replacement of Bowman's with hyaline tissue
- remove with superficial keratectomy

Coat's Ring - small white ring in superficial corneal stroma after metallic foreign body, contains iron

Lipid Keratopathy - yellow-white infiltrate with feathery edges in corneal stroma, usually associated with vascularization or scar, e.g., trauma, herpes simplex/zoster

Marginal Corneal Thinning

Mooren's Ulcer - chronic painful peripheral ulceration, progressive, inflammatory, starts circumferentially, then centrally with an undermined

central edge, may lead to diffusely thinned and scarred cornea

- 25% bilateral, variable course, may perforate
- autoimmune disease directed at corneal stromal antigen, not associated with systemic disease
- diagnosis of exclusion, e.g. Wegener's, collagen vascular diseases
- treatment: collagenase inhibitors, steroids, cyanoacrylate adhesive, conjunctival resection, antimetabolites.

Marginal Keratolysis - acute peripheral corneal melt associated with collagen vascular disease, e.g. rheumatoid arthritis, polyarteritis nodosum, lupus

Terrien's Marginal Degeneration - non-inflammatory, slowly progressive thinning of peripheral cornea, 75% males, usually second or third decade, begins superiorly with fine vascularization and lipid infiltration of central edge, causes astigmatism, perforation rare/

Furrow degeneration - benign thinning in lucid interval of arcus senilis

CORNEAL DYSTROPHIES

Anterior

Map-Dot-Fingerprint (Anterior Basement Membrane, Cogan's Microcystic)

bilateral abnormality in epithelial adhesion to the basement membrane resulting in recurrent erosion syndromes

- i. variably dominant inheritance, symptoms usually after 30 years of age
- ii. clinical findings attributed to disruption of normal epithelial maturation by intra- and subepithelial reduplication of basement membrane, best seen on retroillumination, or with broad beam
 - Microcyst: white putty-like intraepithelial lesion
 - Fingerprint: parallel lines of redundant basement membrane
 - Map: geographic area of haze due thickened pannus-like material
 Also seen in chronic corneal edema, diabetics, contact lens wearers

Meesmann's i. (hereditary juvenile epithelial dystrophy, Stocker-Holt)

- i. rare, bilateral, autosomal dominant
- ii. appears early, tiny epithelial vesicles seen by retroillumination
- iii vesicles contain PAS (+) "peculiar substance", b.m. thickened
- iv mild erosive symptoms and slight decrease in acuity, usually no RX

Reis-Bucklers'

- progressive, autosomal dominant
- early onset of recurrent erosions leading to scarring
- subepithelial rings and fine reticular opacification of Bowman's
- pathology: Bowman's membrane replaced by connective tissue
- Rx: PK or lamellar keratoplasty, recurrence common after PK within 5 years

Stromal Dystrophies (see Table)

· Granular dystrophy

- autosomal dominant
- appears early, decreased VA late, erosions rare
- discrete, focal, white anterior stromal deposits, clear zones between
- "bread crumbs" (may be obliterated with progression) spares periphery
- pathology: hyaline, Masson's trichrome (red)
- Rx: PK late, good prognosis, delayed recurrence (superficial)

Lattice Dystrophy

- autosomal dominant
- appears early, frequent painful erosions with scarring
- branching lines, dots, stromal haze between lines, spares periphery
- pathology: amyloid, Congo red (+), metachromatic with Crystal violet, dichroic and birefringent

- PK for decreased vision, recurrence: Reis-Bucklers' > lattice > granular, macular

Macular Dystrophy

- rare, autosomal recessive
- most severe, early visual loss, erosions infrequent
- opacities irregular with indistinct borders, diffuse haze from limbus to limbus, and Descemet's membrane, may develop central thinning
- pathology: glycosaminoglycans (acid mucopolysaccharide), colloidal iron and Alcian blue (+), absence of normal keratan sulphate in blood
- PK for decreased vision earlier than granular, lattice

Schnyder's Central Crystalline Dystrophy

- autosomal dominant
- central deposits of needle-like polychromatic crystals in anterior stroma, prominent arcus
- may be associated with xanthelasma, hyperlipidemia, genu valgum
- pathology: cholesterol, Oil red O (+) in frozen sections

Other Stromal Dystrophies - not vision threatening

- Fleck (Francois-Neetan's): keratocytes contain MPS and lipid
- Pre-Descemet's Dystrophy
- Posterior amorphous stromal dystrophy - rare, autosomal dominant, deposits in posterior stroma, focal endothelial abnormalities, hypermetropia, flat corneas, iris processes to Schwalbe's

Posterior Dystrophies

Endothelial dystrophy (guttata)

- thickened Descemet's with PAS positive excrescences
- decreased endothelial cell density
- specular microscopy: guttata, pleomorphism, and polymegathism
- no stromal edema

Fuchs' dystrophy - guttata with edema

- familial pattern, non-Mendelian inheritance, females > males
- specular microscopy and path same as endothelial dystrophy
- guttata with endothelial dysfunction early - stromal edematous - epithelial edema, bullae, sub-epithelial fibrosis

- pain due to ruptured bullae, resolves with fibrosis
- decreased vision due to epithelial edema - esp. in A.M.
- Rx: Medical - hypertonic/lubricating ointments, contact lens surgery; PK for decreased vision with corneal edema

Posterior polymorphous dystrophy

- SLE endothelium - grouped vesicles, bands with scalloped edges, geographic gray areas, rarely stromal edema, pupil and iris changes similar to ICE syndrome, glaucoma
- Specular microscopy - geographic pleomorphism
- Path: endothelial? Cells look like epithelium, proliferative endotheliopathy
- usually asymptomatic

ECTATIC DYSTROPHIES

Keratoconus

- sporadic, 10% positive family history, bilateral often asymmetric, adolescent onset
- associated with atopy (role of eye rubbing), Downs, contact lens wear
- signs, progressive paracentral corneal thinning, causing irregular astigmatism (early), Fleischer's ring, Vogt's striae, Munson's sign (late)
- Hydrops: acute stromal edema with break in Descemet's, spontaneous resolution weeks to months
- Path: breaks in Bowman's, superficial scarring
- Rx: hard (gas permeable) contact lens in majority. PK in 10%, high success rate

Keratoglobus

- max thinning in mid periphery at base of protrusion
- rare, PK has poor prognosis

Pellucid Marginal Degeneration

- inferior peripheral thinning with protrusion above thinnest area
- irregular astigmatism

MISCELLANEOUS CONDITIONS

Keratoconjunctivitis sicca (K. sicca)

- clinical setting: adult women
- Sjogren's syndrome (dry eyes, dry mouth, arthritis) associated with rheumatoid arthritis, collagen disease
- Symptoms: burning, dryness, foreign body sensation, tearing. Signs: thin tear meniscus, increased mucous,

inferior/interpalpebral corneal and conjunctival staining with Rose Bengal (dead cells) and fluorescein, Schirmer test with anesthetic less than 5mm, lactoferrin

- Deficiency in the middle aqueous layer of tear film (inner layer of mucin is produced by conjunctival goblet cells, outer oily layer is produced by meibomian glands)
- Treatment: artificial tears, in severe cases - punctal occlusion, Lacriserts, tarsorrhaphy

Tear Function Test

- Schirmer I measures total reflex and basic tear secretion, without anesthetic
- Basic secretion test - with anesthetic

Stevens-Johnson Syndrome (erythema multiforme major)

- Precipitating factors - drugs (sulfa, antibiotics, barbituates, dilantin) and infections (herpes simplex, mycoplasma)
- Cutaneous bullous eruption and mucosal ulceration associated with toxemia, 10% mortality
- External disease manifestations - acute pseudomembranous conjunctivitis, loss of goblet cells and dry eye can result in symblepharon, trichiasis, persistent epithelial defects, and corneal scarring

Ocular Rosacea

- Associated with acne-like skin condition of acne in adults, telangiectatic skin vessels, rhinophyma
- External disease findings Blepharitis - teleangiectic vessels
Conjunctivitis - hyperemic Superficial corneal vascularization and infiltrates, ulceration, and rarely perforation
- Treatment Systemic tetracycline or erythromycin
Lid hygiene, antibiotic ointment, occasional cautious use of topical corticosteroids

Ocular Cicatricial Pemphigoid

- Bullous disease of mucous membranes resulting in scarring-
bullae are at level of basement membrane

Etiology

Unknown, probably autoimmune - immune complexes in basement membrane zone

Associated with drug toxicity-miotics, IDU

- Clinical setting and course - women over 60 most frequently, potentially blinding progressive disease with remissions and exacerbations.
- Ocular manifestations
 - Dry eye symptoms
 - Conjunctival symblepharon - hallmark
 - Trichiasis and entropion
 - Severe dry eye due to mucin deficiency
 - Corneal ulcers, vascularization, scarring
- Treatment - difficult
 - Artificial tears and topical steroids in mild cases
 - Immunosuppressive therapy in selected cases
 - Keratoprosthesis - limited success

Vitamin A Deficiency

- Important cause of blindness in certain areas of the world (e.g. Indonesia)
- External disease manifestations
 - Conjunctival xerosis - lack of mucin production. Bitot's spot near limbus
 - Corneal ulceration, keratomalacia, secondary infections
- Treatment - systemic vitamin and protein replacement

Metabolic diseases associated with corneal changes - genetic enzyme deficiencies resulting in tissue accumulation of substance

- Mucopolysaccharidoses, corneal clouding present in some: Hurlers, Scheie, Morquio, Maroteaux-Lamy (I, IV, VI); not in Hunters, Sanfilippo (II, III)

Differential dx of congenital cloudy cornea (Waring)

S - Sclerocornea
 T - Tears Descemet's
 U - Ulcers
 M - Metabolic
 P - Peters
 E - Edema (CHED)
 D - Dermoid

- Mucopolysaccharidoses - corneal clouding in GM gangliosidosis type 1, and mucopolysaccharidoses types I and III
- Sphingolipidoses - most affect retina not cornea except

- Fabry's (renal failure, peripheral neuropathy, skin lesions, X-linked recessive): whorl-like opacities in corneal epithelium, similar to chloroquine, amiodarone
 - Cystinosis - cystine crystals in cornea do not affect vision
- Pigmentations

Iron

- Blood staining of stroma (after hyphema)
- Siderosis - intraocular metallic foreign body-stroma
- Ferry-epithelium anterior to bleb
- Fleisher - epithelium at base of cone in keratoconus
- Hudson-Stahli - epithelium, aging change
- Stocker - epithelium anterior to pterygium

Melanin

- Krukenberg spindle - endothelium
- Adrenochrome deposition - epinephrine drugs
- Ochronosis - peripheral superficial stroma

Copper: Descemet's

- Wilson's hepatolenticular degeneration
- Chalcosis - intraocular copper foreign body

Gold: chryslasis - peripheral stroma - dose related

Silver: agyrosis - deep stroma, conjunctiva

SURGERY

Conjunctival flap

- Indications: non healing sterile ulcers without corneal perforation, bullous keratopathy
- Procedure - Gunderson flap: remove corneal epithelium, thin flap, avoid tension on flap
- Complications - button hole, retraction

Superficial keratectomy

- Histopathology, microbiology specimens

Keratoplasty

- Penetrating - full thickness, lamellar-partial thickness
- Donor material Contraindications - death by unknown cause, Jacob-Creutzfeldt, rabies, sepsis, hepatitis, AIDS, encephalitis, SSPE, congenital rubella Storage - moist chamber 4° C - McCarey-Kaufman (48 hrs) or K-Sol, CSM (5 days)

Penetrating Keratoplasty

- Indications

Edema - aphakic and pseudophakic bullous keratopathy (most common), Fuchs'

dystrophy

Keratoconus

Herpes simplex keratitis

Corneal scars - ulcer, interstitial keratitis, trauma

Dystrophies

Degenerations

Failed grafts

Acute ulcers

Congenital opacities

Chemical burns - consider conjunctival transplantation

- Prognosis depends on pre-operative diagnosis, patient compliance

Favorable prognosis - absence vascularization, inflammation, other eye disease, normal lids, tear film, and sensation

Less favorable prognosis

Ocular diseases - lid abnormalities, dry eyes chemical burns

neurotrophic keratitis, pemphigoid, Stevens-Johnson, uveitis,

glaucoma, macular problems

Cornea - vascularization, thinning, inflammation

Infancy

Procedure

Risk of choroidal hemorrhage: preoperative hyperosmotic agents, digital massage

Graft size, 8mm most common for host, donor oversized .2 - .5mm

Postoperative complications

Flat anterior chamber, wound leak, pupillary block

Iris prolapse, wound dehiscence

Persistent epithelial defects - consider bandage lens

Glaucoma

Bacterial corneal ulcers and suture abscesses

Endophthalmitis

Recurrent disease

Herpes: 15-50%

Dystrophies: especially Reis-Buckler's, lattice

Retrocorneal fibrosis membrane

Cystoid macular edema - in aphakes/pseudophakes, may resolve late

Astigmatism: RPG contact lens, wedge resection, relaxing incisions,
T-cuts
Trauma

Graft Failure

Early - primary donor failure, poor donor endothelium

Late-allograft rejection

Delayed onset - 2 weeks at least

Endothelial rejection:

Early: anterior chamber reaction, keratic precipitates,
vascularization

Late: graft edema, rejection line

Rx: corticosteroids - topical, subconjunctival, +/- systemic,
cyclosporin A

Epithelial rejection:

Subepithelial infiltrates, epithelial rejection line

Rx: topical steroids

Lamellar Keratoplasty - infrequent

- Indications: recurrent pterygium, Reis-Bucklers', scar, dermoid

- Disadvantages

Does not replace deep tissue, endothelium

Interface opacification may limit vision

Difficult technically

- Advantages

Extraocular

Minimizes allograft rejection

Management Corneal Perforation

Diagnosis: Seidel test, shallow-flat anterior chamber

Treatment goal to reform chamber within 48 hours

Pressure patch

Soft contact lens - similar to patch - temporary Rx

Tissue adhesive and bandage lens - cyanoacrylate very useful
for small sterile perforations

Conjunctival flap - inadequate

Patch graft - larger perforations, when large PK
contraindicated

PK - prognosis depends on etiology

Special Procedures

Rotating autograft: PK to rotate central scar to periphery

Keratoprosthesis: pemphigoid, Steven's-Johnson, poor prognosis

Refractive keratoplasty

Myopic keratomileusis - lamellar cap of patient's cornea is frozen, lathed, replaced

Epikeratophakia - donor lenticule placed over host

Bowman's membrane, may be reversible, FDA approval pending for aphakia, keratoconus

Contraindications: ocular surface disease, lagophthalmos, central scars, marginal endothelial function

Radial keratotomy - radial cuts (4-8), > 90% deep to flatten central cornea

Can correct up to 5D myopia. PERK 5 year data:

Undercorrected $\geq 1D$: 20% $\pm 1D$ 60%

Overcorrected $\geq 1D$ 20%

Patients can have fluctuating vision, glare

Problem of increasing hyperopia with time

PERK: +0.25 D per year in 25% of patients

Incisions may rupture with trauma

Difficult to fit contact lens post-op

Astigmatism - T cuts, trapezoidal keratotomy of Ruiz and others

BOARD REVIEW MNEMONICS

CORNEAL DYSTROPHIES

Marilyn Monroe Got Hers in L.A.

Macular Mucopolysaccharide, Granular Hyaline, Lattice Amyloid

CENTRAL RETINAL ARTERY OCCLUSION

CHEAT'M

Collagen Vascular, Hypertension, Embolic, Atherosclerotic, Temporal Arteritis, Migraine

TOXIC OPTIC NEUROPATHY

CLAIMED

Chloroquine, Lead, Alcohol, Isoniazid, Methanol, Ethambutol, Digitalis

SUBRETINAL NEOVASCULARIZATION

HARMS

Histoplasmosis, Angiod Streaks, Rupture of choroid, Myopia, Senile macular degen

ANGIOID STREAKS

PEPSI

Pseudoxanthoma elasticum, Ehler's-Danlos, Paget's, Sickle cell, Idiopathic

CLOUDY CORNEA AT BIRTH**STUMPED**

Sclerocornea, Tears in Descemet's, Ulcers, Metabolic, Peter's, Edema (CHED),
Dermoid
(birth trauma)