

PRACTICING OPHTHALMOLOGISTS
CURRICULUM 2014-2016

Cornea/ External Disease

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Practicing Ophthalmologists Curriculum

Authors and Financial Disclosures

The Practicing Ophthalmologists Curriculum was developed by a group of dedicated ophthalmologists reflecting a diversity of background, training, practice type and geographic distribution.

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The Academy gratefully acknowledges the contributions of the Cornea Society.

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Background on Maintenance of Certification (MOC)

Developed according to standards established by the American Board of Medical Specialties (ABMS), the umbrella organization of 24 medical specialty boards, Maintenance of Certification (MOC) is designed as a series of requirements for practicing ophthalmologists to complete over a 10-year period. MOC is currently open to all Board Certified ophthalmologists on a voluntary basis; time-limited certificate holders (ophthalmologists who were Board Certified after July 1, 1992) are required to participate in this process. All medical specialties participate in a similar process.

The roles of the American Board of Ophthalmology (ABO) and the American Academy of Ophthalmology relative to MOC follow their respective missions.

The mission of the American Board of Ophthalmology is to serve the public by improving the quality of ophthalmic practice through a process of certification and maintenance of certification that fosters excellence and encourages continual learning.

The mission of the American Academy of Ophthalmology is to advance the lifelong learning and professional interests of ophthalmologists to ensure that the public can obtain the best possible eye care.

The role of the ABO in the MOC process is to evaluate and to certify. The role of the Academy in this process is to provide resources and to educate.

Background on the Practicing Ophthalmologists Curriculum (POC)

At the request of the ABO, the Academy developed the Practicing Ophthalmologists Curriculum (POC), a knowledge base that identifies and defines areas of knowledge important to the delivery of quality eye care as a basis for the content of examinations for the MOC process. The content in the POC is comprised of the information deemed as the most relevant clinical information for a practicing ophthalmologist.

The ABO has agreed that their Periodic Ophthalmic Review Test (PORT) and closed-book Demonstration of Ophthalmic Cognitive Knowledge (DOCK) examinations will be based on the POC. The ABO is solely responsible for creating the PORT and DOCK exams and for certifying MOC candidates. The Academy has developed study tools based on the POC to assist doctors preparing to meet these MOC requirements.

Organization of the POC

The Practicing Ophthalmologists Curriculum comprises 10 practice emphasis areas (PEA), plus Core Ophthalmic Knowledge. The ABO has designated the following as practice emphasis areas:

- Comprehensive Ophthalmology
- Cataract/Anterior Segment
- Cornea/External Disease
- Glaucoma
- Neuro-Ophthalmology and Orbit
- Oculoplastics and Orbit
- Pediatric Ophthalmology/Strabismus
- Refractive Management/Intervention
- Retina/Vitreous
- Uveitis

In addition to two practice emphasis areas of choice, every diplomate sitting for the DOCK examination will be tested on Core Ophthalmic Knowledge. Core Ophthalmic Knowledge is defined as the fundamental knowledge every practicing ophthalmologist must have whatever their area of practice.

Each PEA is categorized into topics presented in an outline format for easier reading and understanding of the relevant information points by the reader. These outlines are based on a standard clinical diagnosis and treatment approach found in the Academy's Preferred Practice Patterns.

For each topic, there are Additional Resources that may contain journal citations and reference to textbooks. These resources are supplemental to the topic outline, and should not be necessary for MOC exam preparation purposes.

Creation of the POC

The POC was developed by panels of practicing ophthalmologists in each of the ten practice emphasis areas. The panels reflect a diversity of background, training, practice type and geographic distribution, with more than 90 percent of the panel members being time-limited certificate holders.

The panels ranked clinical topics (diseases and procedures) in terms of clinical relevance to the subspecialist or comprehensive ophthalmologist. The panelists created outlines for the topics deemed Most Relevant, based on what an ophthalmologist in a specific practice emphasis area needs to know to provide competent, quality eye care (i.e., directly related to patient care). These outlines were reviewed by subspecialty societies and the American Board of Ophthalmology.

Revision Process

The POC is intended to be revised every three years. The POC panels will consider new evidence in the peer-reviewed literature, as well as input from the subspecialty societies, the American Board of Ophthalmology and the Academy's Self-Assessment Committee, in revising and updating the POC.

Prior to a scheduled review the POC may be changed only under the following circumstances:

- A Level I (highest level of scientific evidence) randomized controlled trial indicates a major new therapeutic strategy
- The FDA issues a drug/device warning
- Industry issues a warning

Cornea/External Disease

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Anatomy and embryology of the cornea

I. Describe relevant aspects of corneal embryology

- A. **Week 5 of gestation: surface ectoderm forms corneal and conjunctival epithelium**
- B. **Mesenchymal cells from the neural crest of the surface ectoderm extend under the epithelium from the limbus to form corneal endothelium**
- C. **At week 6 of gestation: mesenchymal cells of neural crest origin begin forming corneal stroma and sclera**
- D. **At birth, infant's globe is 80% of adult size**
- E. **Distensible postnatal sclera and cornea become more rigid during first 2 years of life**

II. Describe relevant aspects of corneal anatomy

- A. **11-12mm horizontally, 10-11mm vertically**
- B. **nutrition: glucose from aqueous humor; oxygen from tear film and limbal vessels (peripheral cornea)**
- C. **very high density of nerve endings (extend from long ciliary nerves and form subepithelial plexus)**
- D. **Epithelium**
 - 1. Thickness: 50 microns
 - 2. Stratified squamous epithelial cells optically smooth
 - 3. Limbal stem cells (found in palisades of Vogt) are source of continuous proliferating basal epithelial cells
 - 4. Basement membrane is secreted by basal epithelial cells
- E. **Bowman layer: acellular compact layer of anterior stroma (8-12 microns thick)**
- F. **Stroma**
 - 1. Made up of about 200 regularly arranged flattened collagen lamellae (mainly collagen types I, V and VI) and proteoglycans synthesized by keratocytes
 - 2. Keratocytes are sparsely distributed, form an interconnected network, and are generally quiescent unless exposed to injury
 - 3. After injury, some keratocytes undergo apoptosis and others transform into activated keratocytes or myofibroblasts
 - 4. Anterior stromal collagen lamellae are short, narrow sheets with extensive interweaving
 - 5. Posterior stroma has long wide, thick lamellae extending from limbus to limbus
 - 6. Water content 78%
- G. **Descemet membrane**

1. Basement membrane of the corneal endothelium
2. Increases in thickness from 3 microns at birth to 10-12 microns in adults

H. Endothelium

1. Closely interdigitated cells arranged in a mosaic pattern of mostly hexagonal shapes
2. Cell density is typically 2400-3200 cells/mm² in adults
3. Human endothelial cells do not proliferate in vivo
4. Cell loss results in enlargement and spread of neighboring cells to cover the defective area
5. Pump function is critical to keep cornea compact and transparent. Both Na⁺ K⁺ ATPase and carbonic anhydrase are important in this process

Additional Resources

1. AAO, Basic and Clinical Science Course. External Disease and Cornea: Section 8, 2013-2014.

Slit-lamp biomicroscopy: performance and record-keeping

I. Describe the instrumentation and technique

A. Instrumentation

1. Viewing arm (corneal microscope)
 - a. Magnification depends on eyepieces and objective lens changer settings
 - i. Magnification numbers on knob apply to one set of oculars
 - ii. For higher power oculars, magnification increases by proportionate amount
 - b. Eyepieces
 - i. Adjust dioptric power to compensate for observer's refractive error and/or accommodation and for any instrument misalignment
 - ii. Eyepiece settings and calibration can be confirmed using focusing rod
2. Illuminating arm
 - a. Illumination arm swings in an arc on a co-pivotal axis with the corneal microscope to allow coaxial alignment with a parfocal and isocentric light beam
 - b. Beam length generally available with pre-set increments and with continuous-length adjustment; beam width varies from open spot to narrow slit
 - c. Light filters may include grey filter, cobalt-blue filter, and red-free filter; heat absorption screen often part of lighting system
3. Base
 - a. Allows both corneal microscope and slit illuminator to be horizontally and vertically mobile, controlled by joystick
 - b. Arresting lock or lever for stabilization
4. Patient positioning frame

B. Illumination methods

1. Diffuse and direct illumination
 - a. Diffuse illumination
 - i. Gives overview of eyelids, ocular surface, and anterior segment of eye
 - ii. Use full height and broad width
 - iii. Light diffuser may be used for photography
 - b. Direct focal illumination and slit illumination
 - i. Allows detection and localization of structures, including differences in refractive

index

- ii. Use medium to narrow beam width to illuminate a parallelepiped of transparent tissue and use very narrow slit beam to illuminate an optical section
 - iii. Use shortened beam to evaluate Tyndall flare effect in the anterior chamber and to detect cells in the convection currents of the aqueous humor or in the tear film to detect slow tear turnover or presence of inflammatory cells
 - c. Tangential illumination
 - i. Shine light across anatomical surface, such as cornea or iris
 - ii. Observe shadowing effects
- 2. Indirect illumination, retroillumination, and sclerotic scatter
 - a. Indirect, proximal illumination and lateral illumination
 - i. Purposely focus or reflect the illuminator's light beam at a different, though adjacent site as the corneal microscope
 - ii. Useful to highlight abnormalities that have a refractive index similar to their surroundings and that are difficult to discern by direct illumination
 - iii. Abnormalities visualized by light scattered from its irregular surface or glowing by internal reflection
 - iv. Three-dimensionality may be enhanced by oscillatory movements of light beam
 - b. Retroillumination
 - i. Direct retroillumination
 - i) Used to examine darkened abnormalities against an illuminated background (e.g., keratic precipitates against illuminated iris)
 - ii. Indirect retroillumination
 - i) Used to examine illuminated abnormalities against a darkened background (e.g., microcystic epithelial edema against dark pupil)
 - iii. Fundus retroillumination
 - i) Used to examine darkened (e.g., posterior subcapsular cataract), illuminated (e.g., keratoconus), or transilluminated (e.g., focal iris atrophy) against "red reflex" background
 - c. Sclerotic scatter
 - i. Used to detect subtle corneal abnormalities that distort the total internal reflection property of the normal cornea
 - ii. Detect scattering of light while shining light onto limbus
- 3. Specular reflection
 - a. Used mainly to examine corneal endothelium (second Purkinje light reflex), although can also examine corneal epithelium and lens epithelium

- b. Monocular viewing
- c. Estimate endothelial cell density, evaluate endothelial cell pleomorphism and polymegethism, and detect abnormal areas of nonreflectivity (e.g., guttate changes and pseudoguttata)

C. Devices used with the slit-lamp biomicroscope

- 1. Linear measurement tools
 - a. Length and width reticules of the illuminating arm
 - b. Eyepiece micrometer of the viewing arm
- 2. Applanation tonometer
 - a. Falsely high measurement of intraocular pressure with increased corneal thickness
 - b. Falsely low measurement of intraocular pressure with corneal thinning
 - c. Misleading estimation of intraocular pressure with high astigmatism
- 3. Gonioscopy tools for examining the anterior chamber angle
 - a. Goldmann single-mirror gonioscope
 - b. Koeppe goniolens
 - c. Four-mirror gonioprism
 - d. Zeiss four mirror lens
- 4. Lenses for examining the vitreous cavity and posterior segment
 - a. Hruby lens
 - b. Goldmann fundus contact lens
 - c. Three-mirror contact lens
 - d. Condensing lens for indirect ophthalmoscopy
- 5. Optical pachymetry for measuring corneal thickness

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 3: Optics, Refraction and Contact Lenses 2013-2014.
- 2. Leibowitz HM, Waring GO III, eds. Corneal Disorders: Clinical Diagnosis and Management. 2nd ed. Philadelphia: Saunders; 1998:34-81.

Tear film evaluation: static and dynamic assessments; tear break-up time, Schirmer

I. List the indications/contraindications

A. Indications

1. Keratoconjunctivitis sicca
2. Evaluation of ocular discomfort
3. Evaluation of intermittent blurred vision
4. Neurotrophic keratopathy
5. Exposure keratopathy
6. Preoperative evaluation for refractive or cataract surgery

B. Contraindications

1. Inability to cooperate with testing

II. Describe the instrumentation and technique

A. Slit-lamp biomicroscopic examination

1. Measure tear meniscus height
 - a. Below 0.3 mm is abnormal
2. Observe for presence of debris, mucus in the tear film using slit beam
3. Observe rate of disappearance of dye, such as fluorescein

B. Vital stains

1. Fluorescein
 - a. Available as .25% solution with an anesthetic, 2% non-preserved unit-dose eyedrop, and impregnated paper strip
 - b. Moisten a fluorescein strip with a drop of non-preserved saline and touch the inferior palpebral conjunctiva
 - c. Observe using cobalt blue light
 - d. Measure location and intensity of staining
 - e. Stains areas where epithelial is missing
2. Rose bengal or Lissamine Green

- a. Available in impregnated strips
- b. Moisten strip with a drop of non-preserved saline and touch the inferior palpebral conjunctiva
 - i. Be sure to maximize amount of dye in tear film to avoid false negatives
- c. Observe using white light
- d. Measure location and intensity of staining
- e. Stains areas of devitalized epithelium (missing mucin layer)

C. Tear break-up time

- 1. Tear break-up time should be measured prior to the instillation of any eyedrops
- 2. Moisten a fluorescein strip with a drop of non-preserved saline and touch the inferior palpebral conjunctiva
- 3. Observe using cobalt blue light
- 4. The patient is asked to blink, then hold the eye open without blinking
- 5. Time from the last blink until the tear film thins and "breaks up"
- 6. Take at least three readings

D. Schirmer

- 1. Without anesthetic
 - a. Any tear present is removed from the lower fornix by gentle blotting
 - b. Whatman #41 filter paper strip (5 mm wide and 35 mm long) is placed across the lower lid at the outer 1/3 of the lid margin
 - c. The patient is advised not to squeeze the eyelids together
 - d. After 5 minutes the strips are removed and the amount of wetting measured
 - e. If no tear production at 5 minutes, consider nasal stimulation
- 2. With anesthetic
 - a. Same as above except a drop of topical anesthetic is first placed into the eye, and then removed by gentle blotting

III. Describe the considerations in interpretation for this diagnostic procedure

A. Vital stains

- 1. Fluorescein
 - a. Detects disruptions of intercellular junctions
 - b. If abnormal, consider pattern of staining
 - i. Diffuse
 - i) Keratoconjunctivitis sicca (severe)

- ii) Viral conjunctivitis
 - iii) Trauma
 - iv) Toxicity
 - ii. Inferior staining
 - i) Lagophthalmos
 - ii) Blepharitis
 - iii) Trichiasis
 - iv) Exposure keratopathy
 - iii. Interpalpebral
 - i) Exposure keratopathy
 - ii) Neurotrophic keratopathy
 - iii) Dry eye syndrome
 - iv. Superior
 - i) Superior limbic keratoconjunctivitis
 - ii) Foreign body under upper lid
 - iii) Trichiasis
 - v. 3 and 9 o'clock
 - i) Contact lens
2. Rose Bengal or Lissamine Green
- a. Stains epithelium devoid of surface glycoproteins (mucin)
 - b. Interpalpebral staining- dry eye syndrome

B. Tear break-up time

- 1. Normal tear break-up time is over 10 seconds
- 2. If rapid tear break up time- evaporative type dry eye
- 3. Consider lipid deficiency or mucin deficiency

C. Schirmer test

- 1. Normal values
 - a. With anesthetic: over 10 mm
 - b. Without anesthetic: over 15 mm
- 2. Test with anesthesia measures basal level of tear production
- 3. Test without anesthesia measures reflex and basal level of tear production
- 4. Test widely available

5. Test is very operator dependent
6. Poor reproducibility
7. Low value suggests aqueous tear deficiency

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Dry Eye, Module #5, 2006.

Detection of altered structure and differentiation of signs of inflammation affecting the eyelid margin, conjunctiva, cornea, sclera, and iris

- I. Describe the instrumentation and technique (See Scanning-slit topography, 3-D imaging, wavefront analysis, and anterior segment optical coherence tomography, corneal aberrometry)**
 - A. External examination**
 - 1. Observation under room light
 - 2. Focal illumination
 - 3. Palpation of eyelid tumors and adenopathy
 - B. Slit-lamp biomicroscopy, using diffuse, focal, retro, specular, indirect, and sclerotic scatter forms of illumination**
 - C. Ultrasonic or optical measurement of corneal thickness**
 - D. Specular microscopy of corneal endothelium**
 - E. Anterior segment imaging**
 - 1. Ultrasonic biomicroscopy
 - 2. Scheimpflug analysis
 - 3. Scanning slit
 - 4. Optical coherence tomography
 - F. Anterior segment angiography**
 - G. Confocal microscopy**
 - H. Additional instruments may be of value under special circumstances**
 - 1. Indirect ophthalmoscope with a +20 condensing lens focused on the anterior segment and ocular adnexa when unable to perform slit lamp evaluation
 - 2. The operating microscope and/or portable slit lamp biomicroscope during a sedated or general anesthesia evaluation

I. Meibography to visualize meibomian glands

II. Describe the considerations in interpretation of this diagnostic procedure

- A. Detection of altered structure and differentiation of signs of inflammation: Diagnostic considerations**

1. Eyelid
2. Conjunctiva
3. Cornea
4. Sclera
5. Iris

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Diagnostic techniques for infectious diseases of the cornea and conjunctiva, including specimen collection methods for microbiologic testing and diagnostic assessment of the normal ocular flora

I. List the indications/contraindications

A. Indications

1. To determine the microbiologic (viral, bacterial, fungal, or protozoal) etiology of an infectious process of the cornea and conjunctiva, in order to aid in the selection or modification of appropriate anti-infective agents for treatment
2. To determine the normal ocular flora of a patient

B. Relative contraindications

1. Severe thinning of the cornea by the infectious process that might result in perforation of the globe by the specimen collection
2. In conditions where obtaining the specimen might cause further dissemination of the infectious process

II. List the alternatives to this procedure

A. Diagnosis based on clinical appearance

B. Broad-spectrum treatment

III. Describe the instrumentation and technique

A. Specimen collection

1. Eyelid margin specimen
 - a. Microbial cultures are obtained by swabbing the abnormal area with a sterile applicator moistened with thioglycollate broth followed by direct inoculation of appropriate culture media and slides
 - b. Viral eyelid vesicles or pustules can be opened with a sterile small-gauge needle or a sharp pointed surgical blade
 - c. Material for cytology is smeared onto a glass slide and fixed in methanol or acetone for immunofluorescent staining

- d. Collected vesicular fluid can be inoculated into chilled viral transport medium for culture isolation or polymerase chain reaction (PCR) testing now rather widely available in hospitals
2. Conjunctival specimen
 - a. Sterile Dacron swabs moistened with thioglycollate broth are used to collect surface conjunctival cells
 - b. Swabbed material can be plated onto solid media, smeared on slides, and inoculated into the broth tube
 - c. Conjunctival biopsy may also be performed with forceps and scissors
3. Corneal specimen
 - a. Corneal infiltrates can be scraped using a sterile spatula, e.g., Kimura platinum spatula, needle, jeweler's forceps, or surgical blade, or swabbed
 - b. Specimens may be immediately inoculated onto room temperature microbiologic media in rows of C-shaped streaks or placed into transport medium
 - c. Contamination and false positives must be avoided by not allowing the blade or swab to touch the eyelids
 - d. Viral specimen can be obtained with a swab, and then inoculated into chilled viral transport medium
 - e. Corneal biopsy can be performed with a 2-3 mm trephine to create a partial-thickness incision; forceps and scissors are then used to excise a lamellar piece of cornea
 - f. The specimen is divided for histopathology and microbiology
4. Contact Lenses
 - a. Consider also swabbing/scraping contact lenses or contact lens cases if applicable.
5. Tear Specimen
 - a. Immunochromatography to detect Adenoviral infection

B. Isolation techniques

1. Bacteria and fungal culture plates and broth are examined periodically to detect visible growth
2. Microorganisms are identified by chemical staining and reactions, and may be tested for antimicrobial susceptibility
3. Acanthamoeba may be identified by trophozoite trails on blood agar, but optimally on non-nutrient agar with an overlay of killed E. Coli
4. For viral and chlamydial infections, an appropriate tissue-culture cell line is selected for inoculation and examined for the development of cytopathic effects and cellular inclusions

C. Culture media and stains

1. Aerobic bacteria
 - a. Media: blood agar, chocolate agar, thioglycollate or thiol broth
 - b. Stain: Gram, acridine orange

2. Anaerobic bacteria
 - a. Media: anaerobic blood agar, phenyl ether alcohol agar in anaerobic chamber, thioglycollate or thiol broth
 - b. Stain: Gram, acridine orange
3. Mycobacteria
 - a. Media: blood agar, Lowenstein-Jensen agar, Middlebrook agar
 - b. Stain: Gram, acid-fast, lectin
4. Fungi
 - a. Media: blood agar (25°C), Sabouraud's agar with antibacterial agent (25°C), brain-heart infusion (25°C)
 - b. Stain: Gram, acridine orange, calcofluor white, Gomori's methenamine silver, wet mount (potassium hydroxide preparation)
5. Acanthamoeba
 - a. Media: non-nutrient agar with bacterial overlay, blood agar, buffered charcoal-yeast extract agar
 - b. Stain: acridine orange, calcofluor white, Giemsa, PAS
6. Viruses
 - a. Cell culture
 - b. PCR testing of fluids or scrapings
 - c. Electron microscopy
 - d. Enzyme immunoassay
 - e. Serologic testing to detect circulating antibodies

IV. Describe the considerations in interpretation of this diagnostic procedure

A. False-negative cultures

1. Inadequate specimen
2. Recent antimicrobial treatment
3. Poor survival in transport media

B. False-positive cultures

1. Contamination with normal ocular flora
2. Contamination during inoculation or transport of culture media

C. Criteria used in laboratory for nonviral infection may differ to include

1. Sparse growth on a single culture medium
2. Growth on two or more media

3. Growth on at least one culture medium of the same organism identified on the smear
4. Confluent growth at inoculation sites on at least one solid culture medium
5. Anaerobic growth in an anaerobic culture medium
6. Amoebic trails on culture plate, with microscopic confirmation of trophozoites from culture

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Applications of New Laboratory Diagnostic Techniques in Cornea and External Disease, Module #9, 2002.

Diagnostic techniques for neoplasia of the cornea, conjunctiva, and eyelid margin, including specimen collection methods for histopathological testing

I. List the indications

- A. Suspected malignant lesion
- B. Cosmetically undesirable or uncomfortable lesion
- C. Lesion interfering with vision

II. Describe the pre-procedure evaluation

A. History

- 1. Age of onset, including congenital or acquired
- 2. Growth pattern, including speed of growth, color changes, ulceration, and bleeding
- 3. Risk factors, including sun or chemical exposure, pre-existing lesion, previous injury, or systemic disease

B. Clinical examination

- 1. Distinguish epithelial from subepithelial lesions
- 2. Distinguish cystic from solid tumors
- 3. Determine presence of inflammation
- 4. Evaluate pigmentation
- 5. Evaluate with Rose Bengal to define size of conjunctival lesion
- 6. Determine movability versus adherence to underlying structure
- 7. Determine extent and focality versus multifocality of lesion
- 8. Consider likely origin of cells producing neoplasia
 - a. Epithelial or epidermal cells
 - b. Melanocytes
 - c. Cells of the substantia propria, including lymphocytes
- 9. Assess regional lymph nodes
- 10. Presence or absence of abnormal vessels extending to the lesion

III. List the alternatives to this procedure

- A. Periodic observation**
- B. Sequential photographs**

IV. Describe the instrumentation and technique

- A. Exfoliative or impression cytology**
- B. Incisional biopsy to remove a representative portion of the lesion**
- C. Excisional biopsy to remove entire lesion**
 - 1. Superficial debridement to remove superficial lesion of the epithelium
 - 2. Shave biopsy to remove superficial lesion of the epidermis
 - 3. Complete excision of deeper lesion
- D. Preparation of biopsy for histopathological processing**
 - 1. Minimize crush artifact during excision
 - 2. Apply specimen onto moist carrier or paper, keeping specimen flat with epithelial side up
 - 3. Indicate orientation, such as by snipping corner of absorbent mount, making a penciled drawing to map location of biopsy, or tagging a margin of the specimen with a suture
 - 4. Frozen section for intraoperative decision-making
 - 5. Place specimen into fixative solution for histopathological processing
 - 6. Consult with the pathologist regarding appropriate studies

V. List the complications of the procedure, their prevention and management

- A. Structural alteration during healing, including distortion and scarring**
- B. Lesion recurrence**
- C. Inadequate material for adequate histopathological evaluation**

VI. Describe the considerations in interpretation of this diagnostic procedure

- A. Determine cell type involved in neoplasia**
 - 1. Histopathological examination
 - 2. Flow cytometry
- B. Distinguish histopathological features of neoplasia**
 - 1. Benign
 - 2. Dysplastic
 - a. Abnormal or precancerous growth of cells

- b. Cellular atypia is a set of histopathological features involving cellular polarity; number, size, and shape of nuclei; and number of mitoses
- 3. Malignant
 - a. Invasion of dysplastic cells beneath the basement membrane into adjacent tissue
 - b. Metastatic spread with secondary centers of neoplastic growth

C. Correlate clinical appearance with histopathological findings

- 1. Gelatinous lesion may have acanthosis (thickening of epithelial layer with increased mitoses of basal epithelial cells)
- 2. Papilliform lesion may have hypertrophy (increased size of cells) and hyperplasia (increased number of cells)
- 3. Epidermalization and leukoplakia may have hyperkeratosis (excessive formation of keratin) and dyskeratosis (abnormal formation of keratin)

D. Use diagnostic results to determine need for further therapy, including surgery, cryotherapy, radiotherapy, or chemotherapy

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
- 2. AAO, Focal Points: Applications of New Laboratory Diagnostic Techniques in Cornea and External Disease, Module #9, 2002.
- 3. Shields CL, Shields JA. Tumors of the conjunctiva and cornea. *Surv Ophthalmol* 2004;49:3-24.
- 4. AAO, Focal Points: Ocular Surface Neoplasia, Module #1, 2007.

Corneal pachymetry

I. List the indications/contraindications

A. Indications

1. Diagnosis and management of glaucoma, glaucoma suspect, and ocular hypertension
2. Preoperative planning for keratorefractive surgery
3. Corneal thinning disorders - diagnosis, ongoing assessment
4. Endothelial dysfunction - ongoing assessment, preoperative planning for patients with visually significant cataract, following corneal transplants

II. Describe the instrumentation and technique

A. Ultrasonic pachymetry

1. Topical anesthesia

B. Followed by applanation of cornea in area to be measured

C. Scheimpflug imaging (e.g., Pentacam, Galilei)

D. Scanning-slit (e.g., Orbscan)

E. Optical coherence tomography

F. Optical pachymetry, focusing technique

1. Measure distance between focused images of anterior and posterior surfaces (e.g., specular microscopy)

G. Perpendicular alignment of measuring instrument to cornea is essential

H. Employ universal precautions, particularly for contact procedures (See Universal precautions for minimizing transmission of infectious agents)

III. List the complications of this procedure, their prevention and management

A. Corneal abrasion

1. Prevention
 - a. Careful applanation
2. Management (See Traumatic corneal abrasion)

IV. Describe the considerations in interpretation for this diagnostic procedure

A. Falsely elevated readings if instrument is not perpendicular to cornea, or, for central corneal thickness (CCT), not centered properly

- B. Consistent pachymetry values (at least 3 measurement values)**
- C. Compensating for intraocular pressure readings based on CCT**
- D. Evaluation for corneal refractive surgery based on corneal thickness**
- E. Corneal thickness should be compared with the appearance of the corneal endothelium**
 - 1. For example, in the preoperative evaluation of cataract patients with concomitant corneal endothelial dysfunction, increased corneal thickness should be correlated with corneal endothelial changes on slit-lamp biomicroscopic examination because patients with evidence of corneal decompensation from Fuchs endothelial dystrophy may benefit from corneal transplantation

V. Describe appropriate patient instructions

- A. Explain relationship between corneal thickness and disease process**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
- 2. Price FW Jr, Koller DL, Price MO. Central corneal pachymetry in patients undergoing laser in situ keratomileusis. *Ophthalmology* 1999;106:2216-20.
- 3. Seitzman GD; Gottsch JD, Stark WJ. Cataract surgery in patients with Fuchs corneal dystrophy; expanding recommendations for cataract surgery without simultaneous keratoplasty. *Ophthalmology* 2005;112:441-6.
- 4. Arce CG, Martiz J, Alzamora JB, et al. Sectorial and annular quantitative area pachymetry with the Orbscan II. *J Refract Surg* 2007;23:89-92. Review.

Corneal esthesiometry

I. List the indications/contraindications

A. Indications

1. Determine the presence of abnormal corneal sensation in the presence of suspected disease
2. Monitor return of corneal nerve function
 - a. During the recovery from disease
 - b. Postoperatively
3. Estimate prognosis prior to contact lens wear, corneal surgery

II. Describe the instrumentation and technique

A. Cotton tipped swab

1. Qualitative, gross assessment
2. No topical anesthetics for 24 hours prior to testing
3. Wisp of cotton fiber from tip of swab brought in from side to avoid startle reflex
4. After touching central cornea of each eye, patient responds as to which eye is more sensitive, and examiner observes the interocular difference in blink reflex and verbal response

B. Dental floss

C. Cochet-Bonnet aesthesiometer

1. More objective, quantitative
2. No topical anesthetics for 24 hours prior to testing
3. Handheld "mechanical pencil" like device with 6 cm long adjustable nylon monofilament for testing
4. Longest extension of filament (6 cm) exerts 11 mg/mm² pressure, shortest extension (1 cm) exerts 200 mg/mm² pressure when applied perpendicularly to cornea
5. Perception of touch at full extension (6 cm) indicates normal corneal sensation
6. Tip progressively shortened in 0.5 cm increments until patient can feel corneal touch
7. Record length at which filament is first felt to quantify level of corneal sensation

III. List the complications of this procedure, their prevention and management

A. Corneal abrasion

1. Prevention
 - a. Careful applanation of wisp of cotton, dental flex or nylon filament

2. Management (See Traumatic corneal abrasion)

IV. Describe the considerations in interpretation for this diagnostic procedure

- A. Accuracy depends on consistency in testing same area of cornea each time**
- B. Confirm values by increasing and decreasing filament length by 0.5 cm from recorded measurement**
- C. Insure tip of monofilament is perpendicular to corneal surface**
- D. Recognize expected variances in corneal sensation**
 1. Ocular sensitivity greatest in central cornea, except in elderly where peripheral cornea can be more sensitive
 2. Long term contact lens wearers can have significant decrease in corneal sensation
 3. Topical medications (glaucoma medications) can decrease corneal sensation
 4. Penetrating keratoplasty grafts are anesthetic initially and never recover full sensation
 5. Endothelial keratoplasty corneas will have reduced corneal sensation only at the area of the wound, similar to cataract surgery patients
 6. Radial keratotomy reduces corneal sensation
 7. Laser refractive surgery such as photorefractive keratectomy (PRK) and LASIK reduce corneal sensation

V. Describe appropriate patient instructions

- A. Explain relationship between corneal sensation and disease process**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Krachmer J, Mannis M, Holland E, eds. *Cornea: Fundamentals, Diagnosis and Management*. 2nd ed. St. Louis: Elsevier Mosby; 2005.
3. Brennan NA, Bruce AS. Esthesiometry as an indicator of corneal health. *Optom Vis Sci* 1991;68:699-702.
4. Rao GN, et al. Recovery of corneal sensitivity in grafts following penetrating keratoplasty. *Ophthalmology* 1985;92:1408-11.

Ultrasound biomicroscopy for the anterior segment

I. List indications and contraindications

A. Indications

1. To provide an image of the anterior chamber (AC) angle when gonioscopy is not possible (e.g., with a cloudy cornea or hyphema)
2. To qualitatively and quantitatively image and assess up to 4-5 mm in depth the normal anatomy of the
 - a. Anterior chamber angle structures
 - b. Cornea
 - c. Ciliary body
 - d. Anterior choroid and sclera
 - e. Pars plana
 - f. Zonular apparatus
 - g. Posterior chamber
 - h. Anterior crystalline lens
3. To qualitatively and quantitatively image and assess abnormalities of the anterior segment associated with
 - a. Evaluation of pigmented conjunctival lesions, nevi, for presence of cysts
 - b. Evaluation of conjunctival melanoma for sclera invasion and depth
 - c. Scleral invasion of squamous tumors
 - d. Iris and ciliary body tumors and cysts
 - e. Traumatic angle damage and recession
 - f. Cyclodialysis clefts
 - g. Ciliary effusions
 - h. Phacomorphic angle-closure
 - i. An anterior or posterior chamber intraocular lens position
 - j. Retained AC or posterior chamber foreign bodies or lens fragments
 - k. Filtration blebs and glaucoma drainage devices
 - l. Zonular dehiscence due to trauma or exfoliation syndrome
 - m. Acute and chronic angle-closure

B. Contraindications

1. An open globe (relative, can be done gently through the lids)
2. Inability to remain supine for examination

II. Describe the pre-procedure evaluation

- A. Complete anterior segment examination with slit-lamp gonioscopy, if possible, to allow for clinical comparison and correlation with subsequent ultrasound biomicroscopy findings**

III. List alternatives to the procedure

- A. Slit lamp biomicroscopy to assess tumors on the conjunctiva, with mobility of tumor**
- B. Gonioscopy with a standard 4 mirror gonioscopy lens or 3-mirror retinal lens before and after pupil dilation, with attention to the angle anatomy, ciliary processes, peripheral lens, zonules and anterior, peripheral retina**
- C. Anterior segment optical coherence tomography (OCT) for 2 dimensional imaging of the cornea, AC angle, and anterior lens surface**

IV. Describe the instrumentation and technique

- A. Ultrasound biomicroscope**
 1. Optical cross-section of the eye in 2 dimensions
 2. B-mode imaging system at 5-10 frames per second
 3. 25 and 50-MHz transducer
 4. 4-5 mm depth tissue penetration
 5. 0.08-0.2 axial resolution
- B. Place patient supine**
- C. Anesthetize the cornea**
- D. Insert eye cup with methylcellulose for coupling**
- E. Control ambient illumination and patient fixation and accommodation of the fellow eye for standardization of pupil size and angle anatomy**
- F. Examiner comfortable with hand steadied on patients forehead**
- G. Orient probe perpendicular to structures of interest for best image**

V. List the complications of the procedure, their prevention and management

- A. Corneal abrasion**
- B. Corneal infection**
- C. Make sure imaging probe (which can come to within 2 mm of the cornea) does not contact the**

cornea during examination, adequate gel

VI. Describe the considerations in interpretation of this diagnostic procedure

- A. Scleral invasion of conjunctival tumor may be difficult to ascertain**
- B. Resolution of tumor low compared with OCT**
- C. Accommodation, pupil position and patient fixation of the fellow eye may affect the angle anatomy.**

Additional Resources

1. Pavlin CJ, Sherar MD, Foster FS. Subsurface ultrasound microscopic imaging of the intact eye. *Ophthalmology* 1990;97:244-30.
2. Pavlin CJ, Harasiewicz K, Sherar MD, et al. Clinical use of ultrasound biomicroscopy. *Ophthalmology* 1991;98:L287-95.
3. Pavlin CJ, McWhae JA, McGowan HD, et al. Ultrasound biomicroscopy of anterior segment tumors. *Ophthalmology* 1992;99:1220-28.
4. Hiroshi I, Liebmann JM, Ritch R. Quantitative assessment of the anterior segment using ultrasound biomicroscopy. *Curr Opin Ophthalmology* 2000;11:113-39.
5. Bianciotto C, Shields CL, Guzman JM *et al.* Assessment of anterior segment tumors with ultrasound biomicroscopy versus anterior segment optical coherence tomography in 200 cases. *Ophthalmology* 2011; 118:1297-1302.

Anterior segment ocular coherence tomography (AS-OCT)

I. List indications and contraindications

A. Indications for OCT

1. Assessment of corneal pathologies, iris pathologies and angle configuration
2. Assess depth of corneal pathology prior to lamellar surgery
 - a. Depth of scarring, dystrophy, prior LASIK flaps
3. Corneal pachymetric mapping
 - a. Assess corneal configuration and focal thinning/thickening
4. Evaluate ocular surface tumors
 - a. Help differentiate ocular surface squamous neoplasia (OSSN) from other entities
 - b. Evaluate for cysts in pigmented lesions such as conjunctival nevi
5. Assess tear film
6. Measurement of angle and central and peripheral anterior chamber depth
 - a. Population screening: non-contact exam, relatively quick procedure
 - b. Pre iridotomy and post iridotomy and/or iridoplasty
 - c. Possible new dark room provocative test for angle closure suspect eyes to evaluate the need for potential treatment
7. Assessment of conjunctival filtration blebs and glaucoma implants for function/scarring or patency and assessment of non-penetrating glaucoma surgical procedures

B. Contraindications

1. Lack of patient cooperation

C. Advantages

1. Non-contact, comfortable technique
2. Seated position of patient
3. Rapid image acquisition
4. Some devices provide image of scan localization
5. High resolution, cross sectional images are reproducible and accurate
6. Ability to image an eye immediately preoperatively and postoperatively without contact with the eye
7. Easy for technician to acquire skill in examination technique

8. Avoids potential mechanical distortion of the anterior segment of the eye and change in angle/iris anatomy
9. Can provide "optical biopsy" in some cases for differentiating ocular surface squamous neoplasia from pterygia and other entities
10. Can follow tumor resolution when treating OSSN with medical therapies such as mitomycin, 5 fluorouracil, and interferon
11. May help detect early recurrences of OSSN and map disease
12. Can be used intra-operatively or post Descemet stripping endothelial keratoplasty to assess donor/host apposition
13. Can assess potential depth of corneal pathology prior to phototherapeutic keratectomy, automated lamellar keratoplasty etc.
14. Dynamic investigation of anatomical angle variation and occludability with changes in illumination intensity
15. Potential for large scale, population screening at the primary care setting, in areas where angle closure glaucoma is highly prevalent

D. Disadvantages

1. High cost of the device
2. Limited depth of penetrance (especially in spectral domain OCT)
3. Shadowing often occurs due to keratinization, or depth > about 400 μm
4. Cannot determine atypia as seen with histopathology
5. Tumors in locations such as caruncle, inferior or superior fornix difficult to image
6. Cannot image structures behind the iris such as the ciliary body, ciliary processes, lens equator, zonules, and lesions or tumors in these areas
7. Inability to perform dynamic compression to discriminate appositional from synechial angle closure
8. Potential for over diagnosis of angle closure by AS-OCT compared to under diagnosis by conventional gonioscopy

II. Describe the pre-procedure evaluation

- A. Select the appropriate patient for the imaging**
- B. Describe the procedure to the patient**
- C. Adequate fixation is required, ability to move eye to evaluate lesion in not near limbus**
- D. Select the appropriate illumination for the study**
- E. Anesthesia is not necessary**
- F. Lid manipulation may be necessary**

III. Device characteristics

- A. Non-contact, optical technology to image the eye with the patient in the upright and seated position (unlike ultrasound biomicroscopy [UBM])**
- B. Provides real-time, in vivo, cross sectional images (tomography) of the ocular anterior segment (more detailed than UBM)**
- C. Enables detailed visualization of cornea, bulbar conjunctival surface, iris, anterior chamber angle, and anterior lens surface, but not ciliary processes, due to light attenuation by pigment epithelium (not as deep as UBM)**
- D. Employs low coherence interferometry to compare the time delay of tissue reflections against a reference reflection, with image correction for the effect of refraction at the cornea air interface**
- E. Instrument scans a beam of light laterally to create a series of axial scans (A-scans) which are combined into a composite image**
- F. A-scans contain information on the strength of the reflected signal as a function of depth**
- G. Time-domain (TD) OCT**
 - 1. Visante OCT (Carl Zeiss Meditec, Inc., Dublin, CA, USA FDA approved October, 2005)
 - a. Axial resolution of up to 17 μm and transverse resolution of up to 60 μm
 - b. Scan width of 16 mm and depth of up to 6 mm
 - c. Images 4 meridians and 8 angles simultaneously in 0.5 seconds
 - d. Requires lid manipulation to image superior angle
 - e. High intra and interobserver reproducibility
 - f. Better than FD-OCT for anterior chamber (AC) biometry of AC depth, angle-to-angle width, iris profile and angle anatomy
 - 2. Slit-lamp biomicroscopy OCT (Heidelberg Engineering, GmbH, Dossenheim, Germany)
 - a. Axial resolution of less than 25 μm and transverse resolution of 25-100 μm
 - b. Images only 1 meridian and 2 angles simultaneously
 - c. Requires manual beam rotation to image non-vertical meridians
 - d. Software calculates central corneal thickness, central AC depth, volume of the AC, and the inter-spur distance
- H. Fourier-domain (FD) OCT**
 - 1. RTVue (Optovue, Inc., Fremont, CA, USA FDA approved September 2007)
 - a. Axial resolution of up to 5 μm (>3 times higher than TD-OCT)
 - b. Spectrometer with a high speed line camera captures 26,000 A scans per second (13 times faster than TD-OCT)
 - c. Better for corneal and conjunctival pathologies, biometry to map corneal thickness, and assess internal corneal structure than TD-OCT
 - d. Higher speed reduces motion artifact and produces higher resolution, more detailed images than TD OCT
 - e. Can image Schlemm's canal, Schwalbe's line and the trabecular meshwork better than

IV. List the alternatives to this procedure

- A. Slit-lamp biomicroscopy to evaluate tumors, corneal pathologies**
- B. Conventional slit-lamp gonioscopy with a gonioprism and clinical grading of the angle by the Shaffer, Scheie or Spaeth classification systems**
- C. Ultrasound biomicroscopy**
- D. Corneal topographic slit-lamp device**
- E. Confocal biomicroscopy**
- F. Histopathologic biopsy for tumors**

V. Describe the technique

- A. Position the patient comfortably at the device**
- B. Maintain proper fixation to image the appropriate angle/meridians of interest**
- C. Adjust ambient illumination for most appropriate imaging**
- D. Optimize the scan image**
- E. Select the scan acquisition protocol**
- F. Select the scan analysis protocol**
 - 1. Display raw image and averaged image in devices able to do this
 - 2. Measure depth/thickness when appropriate
- G. Archive and/or print the scan image for appropriate interpretation of the scan results for clinical assessment and billing purposes**

VI. List the complications of the procedure, their prevention and management

- A. None known**

VII. Describe the considerations in interpretation of this diagnostic procedure

- A. Acquisition of a good quality scan**
- B. Accurate interpretation of the qualitative and quantitative scan results**
- C. Comparison of scan results with findings from clinical biomicroscopy**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. External Disease and Cornea: Section 8, 2013-2014.
- 2. Ramos JL, Li Y, Huang D. Clinical and research applications of anterior segment optical

coherence tomography - a review. Clin Experiment Ophthalmol 2009;37(1):81-9.

3. Bianciotto C, Shields CL, Guzman JM, et al. Assessment of anterior segment tumors with ultrasound biomicroscopy versus anterior segment optical coherence tomography in 200 cases. Ophthalmology 2011;118(7):1297-302.
4. Shields CL, Belinsky I, Romanelli-Gobbi M, et al. Anterior segment optical coherence tomography of conjunctival nevus. Ophthalmology 2011;118(5):915-9.
5. Kieval JZ, Karp CL, Abou Shousha M, et al. Ultra-high resolution optical coherence tomography for differentiation of ocular surface squamous neoplasia and pterygia. Ophthalmology 2012;119(3):481-6.
6. Shousha MA, Karp CL, Perez VL, et al. Diagnosis and management of conjunctival and corneal intraepithelial neoplasia using ultra high-resolution optical coherence tomography. Ophthalmology 2011;118(8):1531-7.
7. Vajzovic LM, Karp CL, Haft P, et al. Ultra high-resolution anterior segment optical coherence tomography in the evaluation of anterior corneal dystrophies and degenerations. Ophthalmology 2011;118(7):1291-6.
8. Nolan W, See JL, Chew PTK, et al. Detection of primary angle-closure using anterior segment optical coherence tomography in Asian eyes. Ophthalmology 2007; 114:33-39.
9. Radhakrishnan S, See J, Smith SD, et al. Reproducibility of anterior chamber angle measurements obtained with anterior segment optical coherence tomography. Invest Ophthalmol Vis Sci 2007; 48:3683-3688.
10. Wolffsohn JS, Davies LN. Advances in anterior segment imaging. Curr Opin Ophthalmol 2007; 18:32-38.
11. Nolan W. Anterior segment imaging: ultrasound biomicroscopy and anterior segment optical coherence tomography. Curr Opin Ophthalmol 2008; 19:115-121.
12. Ramos JLB, Li Y, Huang D. Clinical and research applications of anterior segment optical coherence tomography—a review. Clin Experiment Ophthalmol 2009; 37:81-89.
13. Jancevski M, Foster CS. Anterior segment optical coherence tomography. Semin Ophthalmol 2010; 25:317-323.

Confocal and specular microscopic imaging

I. List indications and contraindications

A. Indications

1. Corneal endothelial cell imaging
 - a. Determination of endothelial cell density
 - i. Prior to intraocular surgery
 - i) Cataract surgery
 - ii) Secondary intraocular lens implantation
 - b. Identification of endothelial pathology (such as guttae)
2. Diagnosis of infectious keratitis
 - a. Fungal
 - b. Protozoal
3. Diagnosis of non-infectious keratitis
 - a. Corneal dystrophies
 - i. Fuchs endothelial dystrophy (confocal and specular microscopy)
 - ii. Corneal stromal dystrophies (confocal microscopy)
 - b. Interface opacities following lamellar corneal surgery
 - c. Corneal intraepithelial neoplasia

B. Contraindications

1. None, although imaging may not be successful in setting of limited patient cooperation

II. Describe the pre-procedure evaluation

A. Patient history

1. Infectious keratitis
 - a. Decreased vision, pain, conjunctival injection
2. Non-infectious keratitis
 - a. Corneal dystrophies
 - i. Decreased vision
 - ii. Pain (in the presence of epithelial edema)

- b. Interface opacities following lamellar corneal surgery
 - i. Asymptomatic or decreased vision

B. Examination

- 1. Infectious keratitis
 - a. Corneal opacity
- 2. Non-infectious keratitis
 - a. Corneal dystrophies
 - i. Corneal stromal opacities
 - ii. Corneal endothelial abnormalities (guttae, endothelial bands, etc)
 - b. Interface opacities following lamellar corneal surgery
 - i. Debris under LASIK flap or between donor and host corneas (Descemet stripping endothelial keratoplasty) or donor cornea and host Descemet membrane (deep anterior lamellar keratoplasty)

III. List the alternatives to this procedure

A. Corneal endothelial cell imaging

- 1. If stromal opacification prevents endothelial cell imaging with specular microscopy, confocal microscopy can be used
- 2. Specular reflection performed with slit lamp

B. Diagnosis of infectious keratitis

- 1. Fungal
 - a. Corneal scraping for culture and sensitivities
 - b. Corneal biopsy
- 2. Protozoal
 - a. Corneal scraping for culture and sensitivities
 - b. Corneal biopsy

C. Diagnosis of non-infectious keratitis

- 1. Corneal dystrophies
 - a. Clinical examination
 - b. Molecular genetic analysis
- 2. Interface opacities following lamellar corneal surgery
 - a. Optical coherence tomography
 - b. LASIK surgery

- i. Lifting flap and removing opacities for further analysis

IV. Describe the instrumentation and technique

A. Confocal microscopy

1. Technique
 - a. Uses spatial filtering techniques to eliminate or reduce out-of-focus light, thus minimizing image degradation, when performing serial optical sectioning of the cornea
2. Types of confocal microscopes
 - a. Slit scanning
 - b. Laser scanning
3. Procedure
 - a. Topical anesthesia for contact confocal microscopy
 - b. Positioning of the patient's head
 - c. Patient fixation
 - d. Automated scan and analysis

B. Specular microscopy

1. Technique
 - a. Based on imaging of the light reflected from an optical interface, such as the corneal endothelium and the aqueous humor
2. Types of specular microscopes
 - a. Widefield scanning slit
 - b. Scanning spot confocal
 - c. Contact
 - d. Non-contact
3. Procedure
 - a. Topical anesthesia for contact specular microscopy
 - b. Positioning of the patient's head
 - c. Patient fixation
 - d. Automated scan and analysis

V. List the complications of the procedure, their prevention and management

A. Confocal microscopy

1. Corneal epithelial abrasion

- a. Prevention - Use of viscous artificial tear prior to application of applanator
- b. Treatment - Topical antibiotics +/- bandage soft contact lens

B. Specular microscopy

- 1. Non contact - No complications associated with performance of the procedure
- 2. Contact - Corneal epithelial abrasion (see above)

VI. Describe the considerations in interpretation of this diagnostic procedure

A. Confocal microscopy

- 1. Image quality:
 - a. Dependent upon:
 - i. Operator experience
 - ii. Patient cooperation
 - iii. Degree of corneal opacification
- 2. Image interpretation:
 - a. Dependent upon
 - i. Reader experience
 - b. Corneal endothelial cell imaging
 - i. Provides
 - i) Endothelial cell density (see below)
 - ii) Pachymetry
 - ii. Does not provide
 - i) Coefficient of variation (see below)
 - ii) Average cell size
 - iii) % hexagonal cells (see below)

B. Specular microscopy

- 1. Image quality:
 - a. Dependent upon:
 - i. Degree of corneal opacification
 - i) Unable to visualize endothelium in cases of corneal opacification
- 2. Image interpretation
 - a. Dependent upon:
 - i. Reader experience - less than confocal microscopy

- b. Corneal endothelial cell imaging
 - i. Mode
 - i) Automated - appropriate when endothelial mosaic well-visualized
 - ii) Manual - appropriate when endothelial cell borders not well visualized or endothelial mosaic interrupted by guttae
 - ii. Endothelial cell density
 - i) Normal adult endothelial cell density is 2400-3200 cells/mm²
 - iii. Endothelial cell morphology - cell shape and size
 - i) Coefficient of variation - Average cell size divided by the standard deviation of the average cell size
 - (i) Normally < 0.30
 - (ii) Polymegathism - increased variation in cell size, which is an indication of poor cell function
 - ii) Percentage of hexagonal cells
 - (i) Should approach 100%
 - (ii) Polymorphism (Pleomorphism) - increased variability in cell shape. Less than 50% hexagonal cells may be an indication of poor cell function

Additional Resources

1. AAO, Basic and Clinical Science Course. External Disease and Cornea: Section 8, 2013-2014.
2. Kumar RL, Cruzat A, Hamrah P. Current state of in vivo confocal microscopy in management of microbial keratitis. *Semin Ophthalmol.* 2010;25:166-70.
3. Tu EY, Joslin CE, Sugar J. The relative value of confocal microscopy and superficial corneal scrapings in the diagnosis of *Acanthamoeba* keratitis. *Cornea* 2008;27:764-772.
4. Wang Y, Le Q, Zhao F, Hong J, Xu J, Zheng T, Sun X. Application of in vivo laser scanning confocal microscopy for evaluation of ocular surface diseases: lessons learned from pterygium, meibomian gland disease, and chemical burns. *Cornea.* 2011 Oct;30 Suppl 1:S25-8.

Corneal topography/Placido disc imaging

I. List the indications/contraindications

A. Indications

1. Preoperative management
 - a. Refractive surgery
 - b. Corneal surgery
2. Postoperative management
 - a. Refractive surgery
 - b. Penetrating keratoplasty
 - c. Post-cataract surgery astigmatism
3. Evaluation of corneal ectasia, including keratoconus
4. Irregular astigmatism
5. Evaluation of cornea scars (trauma or previous infection)
6. Contact lens fitting
7. Evaluation of unexplained decreased vision

B. Contraindications

1. Inability to cooperate with testing

II. Describe the instrumentation and technique

A. Computerized corneal topography: Placido disc

1. Digitally captures keratoscopic images and analyzes with computer
2. Placido disc-based computerized topography
 - a. Collects reflected data points from the concentric rings and creates a map of the cornea
 - b. Uses color-coded map to present the data with warmer (red and orange) colors representing steeper curvature of the cornea and cooler (blue and green) colors representing flatter curvature.
3. Maps that can be obtained
 - a. Power maps
 - b. Simulated keratometry
 - c. Probability of having keratoconus, etc.
 - d. Elevation maps

- e. Corneal wavefront maps

III. Describe the considerations in interpretation for this diagnostic procedure

A. Computerized corneal topography: Placido disc

1. Useful in detecting irregular astigmatism or multifocal corneas- irregular corneal reflex, scissoring reflex
2. Useful for contact lens fitting and intraocular lens power calculation
3. Critical screening tool for refractive surgery
4. Identifies changes in astigmatism over time or after surgery
5. Identifies corneal ectasias
6. Identifies contact lens induced warpage
7. Useful in postoperative management of corneal transplant patients
8. Helpful in determining etiology for unexplained decreased vision or unexpected post-surgical results including: under corrected aberrations, induced astigmatism, decentered ablations, irregular astigmatism, etc
9. Requires skill to interpret test results
10. Quality and reproducibility of images is operator dependent and dependent on quality of tear film
11. Non-standardized data maps; user can manipulate appearance of data by changing scales; colors may be absolute or varied (normalized)
12. Other limitations: misalignment may lead to error

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Computerized Corneal Analysis, Module #5, 1996.
3. Arce CG, Martiz J, Alzamora JB, et al. Sectorial and annular quantitative area pachymetry with the Orbscan II. J Refract Surg 2007;23:89-92. Review.
4. Cairns G, McGhee CN. Orbscan computerized topography: attributes, applications, and limitations. J Cataract Refract Surg 2005;31:205-20. Review.

Non-Placido disc imaging (retinoscopy, keratometry, keratoscopy)

I. List the indications/contraindications

A. Indications

1. Preoperative management
 - a. Refractive surgery
 - b. Corneal surgery
 - c. Cataract IOL calculations
2. Postoperative management
 - a. Refractive surgery
 - b. Penetrating keratoplasty
3. Evaluation of corneal ectasia, including keratoconus
4. Irregular astigmatism
5. Contact lens fitting
6. Post-trauma
7. Evaluation of unexplained decreased vision

B. Contraindications

1. Inability to cooperate with testing

II. Describe the instrumentation and technique

A. Retinoscopy

1. Takes advantage of the eye's natural optics to determine refractive error and to assess corneal curvature
2. Shine retinoscope in patient's eye while patient fixates on distance target
3. Reflex is neutralized using appropriate lens powers yielding information on sphere and astigmatism
4. Quality of reflex is noted and is useful in assessing for irregular astigmatism
 - a. Non-linear or multiple reflexes are seen in irregular astigmatism
5. Decreased light reflex may also indicate cataract or other optic pathway obstruction (i.e. vitreous hemorrhage)

B. Keratometry

1. Measures central corneal curvature when the cornea is symmetrical
2. Takes advantage of the reflective qualities of the front of the corneal surface
3. The front of the cornea acts as a convex mirror whose reflection generates a virtual image of a target
4. Keratometer empirically estimates corneal power by reading four points of the central 2.8-4.0 mm zone

C. Keratotomy

1. Presents an illuminated series of concentric rings and views the reflection from the corneal surface (handheld Placido disc, collimating keratoscopes)
2. Allows measurement of central cornea and parts of cornea more peripheral (which can't be measured with a keratometer that doesn't have a topographer attachment)
3. Images can be stored on film (photokeratotomy) or video (videokeratotomy)

III. Describe the considerations in interpretation for this diagnostic procedure

A. Retinoscopy

1. Useful in detecting irregular astigmatism or multifocal corneas- irregular corneal reflex, scissoring reflex
2. Useful for:
 - a. Children
 - b. Non-cooperative patients
 - c. Mentally challenged patients
 - d. Patients with significant language barrier
3. More qualitative than quantitative

B. Keratometry

1. Useful for contact lens fitting and intraocular lens power calculation
2. Useful in IOL calculation formulas
3. Useful in detecting irregular astigmatism - irregular keratometric images
4. Most useful for central cornea measurements
5. Not useful for changes outside the central cornea (radial keratotomy, keratoconus)

C. Keratotomy

1. Has all of the uses discussed above
2. Gives readings of peripheral cornea
3. Requires skill to interpret test
4. Dependent on tear film

5. Its use has been superseded by computerized corneal topography

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Scanning-slit topography, 3-D imaging, wavefront analysis, and anterior segment optical coherence tomography, corneal aberrometry

I. List the indications/contraindications

A. Indications

1. Preoperative management
 - a. Refractive surgery
 - b. Corneal surgery
 - c. Preoperative cataract surgery planning
 - d. Intacs surgery
 - e. Phakic intraocular lens (IOL) surgery
2. Postoperative management
 - a. Refractive surgery
 - b. Penetrating keratoplasty
 - c. Lamellar corneal procedures affecting cornea curvature
3. Evaluation of corneal ectasia, including keratoconus
4. Evaluation of cornea scars (trauma or previous infection)
5. Irregular astigmatism
6. Contact lens fitting
7. Evaluation of unexplained decreased vision

B. Contraindications

1. Inability to cooperate with testing

II. Describe the instrumentation and technique

A. Computerized corneal topography: scanning-slit

1. Computerized corneal mapping device
2. Maps created
 - a. Anterior corneal elevation map

- b. Posterior corneal elevation map
- c. Simulated keratometry map
- d. Corneal pachymetry map

B. 3-D imaging: Computerized corneal topography/Scheimpflug camera

1. Computerized cornea mapping device and anterior segment camera
 - a. The cornea is imaged e.g., by a rotating Scheimpflug camera which measures thousands of elevation points to create a 3D image of the anterior segment
2. Multipurpose instrument
 - a. Anterior and posterior corneal elevation maps and topography
 - b. Corneal pachymetry maps (limbus to limbus)
 - c. 3-D anterior chamber analysis (AC depth/chamber angle, chamber volume)
 - d. Lens density (quantification of light transmittance of crystalline lens and IOL's)
 - i. IOL calculation software for post LASIK, PRK and RK patients

C. Wavefront analysis

1. Optical aberrations produced by each individual's eye are as distinct as fingerprints and wavefront imaging allows the physician to measure aberrations beyond sphere, cylinder, and axis
2. Wavefront sensing devices measure the cumulative sum of optical aberrations induced by each structure in the visual pathway
3. The most common wavefront sensing devices utilize the Hartmann-Schack method (Autonomous, VISX, Bausch and Lomb)
4. Light rays from a single (safe) laser beam are aimed into the eye and the light rays reflect back from the retina in parallel rays
5. Aberrations inside the eye cause the light rays to change directions and a wavefront sensor collects this information in front of the cornea
6. Other methods for wavefront sensing: Tscherning and Tracy - measure wavefront as light goes into the eye
7. All wavefront systems give detailed report of higher order aberrations mathematically, the aberrated wavefront can be described by Zernicke polynomials to quantify spherical aberration, coma, etc. or using Fourier analysis can be isolated into individual components of a compound waveform, concentrating them for easier detection or use

D. Anterior segment optical coherence tomography (OCT)

1. Measures the delay of light (typically infrared) reflected from tissue structures
2. Its principle is similar to that of ultrasound in which the round trip delay time of the reflected wave is used to probe the target structure depth
3. Because light travels fast, it is not possible to measure the delay at a micron resolution, so a low-coherence interferometry is employed to compare the delay of tissue reflections against a reference reflection

4. Images are obtained by use a light beam laterally, creating a series of axial scans (A-scans), after which it combines these A-scans into a composite image
5. Each A-scan contains information on the strength of a reflected signal as a function of depth
6. OCT resolution is very high, ranging from 2 to 20mm, making it ideal for imaging and measuring small eye structures

E. Wavefront corneal aberrometry

1. Pre-operative assessment
 - a. Determines origin optical aberrations (corneal or lenticular)
 - b. Provides the ability to follow aberrations in scotopic and photopic conditions
 - c. Evaluate the effects of cataracts and internal aberrations
2. Intra-operative assessment
 - a. Analysis is taking during surgery
 - b. Measures optical aberration in aphakic or pseudophakic state
 - c. Assists in intraocular lens (IOL) selection or position

III. Describe the considerations in interpretation for this diagnostic procedure

A. Scanning-slit corneal topography: (Orbiscan)

1. Identifies regular and irregular astigmatism
2. Anterior elevation maps useful for evaluating anterior ectasias, guiding astigmatism treatment, glare symptoms, haze symptoms, unexplained decreased vision, central islands
3. Posterior elevation maps useful for evaluating posterior ectasias, glare symptoms, haze symptoms, unexplained decreased vision
4. Pachymetry map useful in giving measurement of corneal thickness throughout the cornea
5. Identifies changes in astigmatism over time or after surgery
6. Identifies contact lens induced warpage
7. Useful in postoperative management of corneal transplant patients
8. Critical screening tool for refractive surgery
9. Allows clinicians to detect subtle variations in power distributions of the anterior corneal surface
10. Helpful in determining etiology for unexplained decreased vision
11. Helpful in explaining unexpected post-surgical results including: undercorrection, aberrations, induced astigmatism, decentered ablations, etc.
12. Reproducible data
13. Operator dependent and misalignment may lead to sampling error
14. Non-standardized data maps; can manipulate appearance of data by changing scales; colors may

be absolute or varied (normalized)

15. Tear film dependent
16. Higher cost compared with Placido based computerized corneal topography
17. Pachymetry requires an acoustic adjustment factor

B. 3-D imaging: Computerized corneal topography/Scheimpflug camera (Pentacam, Galilei, others)

1. Provides similar functions as listed in scanning-slit corneal topography (items 1-12)
2. Rotating image process helps better identify central cornea and correct for eye movements
3. Higher cost compared with Placido based computerized corneal topography and scanning-slit corneal topography
4. Provides equivalent K readings for IOL calculations and includes formulas to calculate IOL powers in post RK and post-laser surgery patients
5. Helps plan phakic IOL surgery by imaging and calculating the anterior chamber dimensions
6. Keratoconus detection program useful in determining what size penetrating keratoplasty button to use due to peripheral corneal thinning
7. Scheimpflug images can be use to evaluate placement of INTAC segments, evaluate DSAEK lenticle apposition to the cornea, and document relative depth of cornea scars
8. Densitometry software provides cataract grading system

C. Wavefront analysis

1. Only technology currently available which is able to measure and quantitate higher order aberrations
2. Information from the wavefront is fed directly into the excimer laser computer to treat patient's refractive errors and higher order aberrations ("custom cornea," wavefront guided laser ablations)
3. Should be useful for all situations where computerized corneal topography is helpful (see above)
4. Currently, the ideal wavefront for optimal vision is not known.
 - a. Current systems attempt to eliminate all higher order aberrations
5. Clinical uses for wavefront technology are currently being defined
6. Expensive instrumentation

D. Anterior segment OCT

1. Anterior chamber angle assessment
2. Accurately maps corneal thickness in clear and opacified corneas
3. Allows precise depth measurements of corneal opacities, LASIK flap thickness, and the degree of epithelial hyperplasia
4. Images corneal degenerations, scars and dystrophies allowing for pre-operative planning (ablative procedures versus lamellar or full thickness procedures)
5. Images anterior segment tumors, and monitor iris cysts, iris nevi, and iris melanomas

6. Images intrastromal corneal ring segments (INTACS), providing accurate positioning and depth assessment
7. Images post-operative DSAEK patients and can provide information on dislocations, partial detachments, retained Descemet membrane, and other anterior segment abnormalities which may not be clearly visible in post-operative corneas that are edematous
8. Provides objective measurements of donor and host corneal thickness after DSAEK which can be used as markers for clinical improvement
9. In PK with femtosecond laser applications, can identify top hat, mushroom, and zigzag-shaped incisions, alignment of donor and host cornea and depth of sutures

E. Wavefront corneal aberrometry

1. Measuring solely corneal aberrations may assist in improving refractive procedure selection
2. Preoperative knowledge of corneal aberrations assists in optimal IOL selection and calculations
3. Intra-operative analysis aids with implantation of presbyopia-correcting IOLs to achieve emmetropia
4. Intra-operative analysis demonstrates proper axis placement of astigmatism correcting IOLs
5. Intra-operative analysis on patients with previous laser vision correction aides in IOL selection making it less of a challenge

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Cairns G, McGhee CN. Orbscan computerized topography: attributes, applications, and limitations. J Cataract Refract Surg 2005;31:205-20.
3. AAO, Focal Points: Wavefront Analysis, Module #10, 2005.
4. Lawless MA, Hodge C. Wavefront's role in corneal refractive surgery. Clin Experiment Ophthalmol. 2005 Apr;33(2):199-209.
5. Ramos JL, Li Y. Huang D. Clinical and research applications of anterior segment optical coherence tomography-a review. Clin Experiment Ophthalmol 2009;37:81-9.
6. Konstantopoulos A, Hossain P, Anderson DF. Recent advances in ophthalmic anterior segment imaging: a new era for ophthalmic diagnosis? Br J Ophthalmol. 2007 Apr;91(4):551-7.

Universal precautions for minimizing transmission of infectious agents

I. Handwashing

- A. Single most effective means of avoiding risk of transmitting infections
- B. Wash hands between patient exams and after procedure involving contact with tears
- C. Methods
 - 1. Alcohol-based hand rubs
 - 2. Soap and water, with complete drying

II. Gloves

- A. Use gloves if blood or blood-contaminated fluid is present
- B. Use gloves if examiner's hand have cuts, scratches or open sores
- C. Change gloves after contact with each patient
- D. Use cotton-tipped applicators to minimize direct contact

III. Eyedropper bottles

- A. Avoid direct contact of bottle tip with tears or conjunctiva
- B. Discard bottle if tip does contact the ocular surface
- C. Date bottles when opened
- D. Consider individual sterile strips impregnated with dye if available

IV. Disinfection of instruments and lenses

- A. Tonometer prisms
 - 1. Wipe clean and then disinfect in diluted bleach, hydrogen peroxide, ethanol, or isopropanol
 - 2. After soaking, rinse tip and wipe dry before re-use to avoid corneal de-epithelialization that might be caused by residual disinfectant
- B. Contact lenses
 - 1. For rigid gas-permeable or hard contact lenses, use hydrogen peroxide or chlorhexidine-containing disinfectant system
 - 2. For soft contact lenses, use hydrogen peroxide or heat disinfection system or multipurpose solution

3. For diagnostic lenses (e.g., gonioleus), wipe with alcohol or immerse in diluted bleach then irrigate and dry before re-use

C. Surgical instruments

1. When there is contact with high-infectivity tissues in patients with confirmed or suspected Creutzfeldt-Jakob disease, use single-use instruments or decontaminate or destroy reusable instruments

V. Recommendations for infections among health care personnel

- A. Health care personnel with viral keratoconjunctivitis or purulent conjunctivitis should avoid providing direct patient care for the duration of symptoms**
- B. Personnel with draining skin lesions infected with *Staphylococcus aureus* or infections with group A streptococci should be restricted from direct patient care until they have received appropriate therapy**

Additional Resources

1. Basic and Clinical Science Course. Section 8. External Disease and Cornea, American Academy of Ophthalmology, San Francisco, 2013-2014.
2. Boyce JM, Pittet D. Guideline for hand hygiene in health-care settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. MMWR 2002;51(RR16):1-44. <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5116a1.htm> (<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5116a1.htm>)
3. Information Statement: Infection Prevention in Eye Care Services and Operating Areas and Operating Rooms. American Academy of Ophthalmology, San Francisco, August 2012. <http://one.aao.org/clinical-statement/infection-prevention-in-eye-care-services-operatin> (<http://one.aao.org/clinical-statement/infection-prevention-in-eye-care-services-operatin>)
4. World Health Organization Infection Control Guidelines for Transmissible Spongiform Encephalopathies Report of a WHO Consultation 1999. <http://www.who.int/csr/resources/publications/bse/whocdscsraph2003.pdf> (<http://www.who.int/csr/resources/publications/bse/whocdscsraph2003.pdf>)
5. Centers for Disease Control: Guidelines for Infection Control in Health Care Personnel: 1998. <http://www.cdc.gov/ncidod/dhqp/pdf/guidelines/InfectControl98.pdf> (<http://www.cdc.gov/ncidod/dhqp/pdf/guidelines/InfectControl98.pdf>)

Conjunctivochalasis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Age related process
2. Thought to be due to elastotic degeneration and collagenolysis that leads to laxity of the adherence of the conjunctiva to the underlying connective tissue
3. Suggested that enzyme accumulation in the tear film due to delayed tear clearance may lead to degradation of the conjunctiva

B. Define the relevant aspects of epidemiology of the disease

1. Occurs more frequently with age
2. Prevalence low prior to age 30
3. Prevalence may be higher in patients with autoimmune thyroid disease

C. List the pertinent elements of the history

1. Tearing
2. Tired feeling eyes
3. Pain
4. Blurred vision
5. Foreign body sensation
6. Irritation

D. Describe pertinent clinical features

1. Loose conjunctival folds interposed between the inferior globe and the lid margin of the lower eyelid
 - a. Folds may be located temporally, centrally, and/or nasally
 - b. If the chalasis is nasally located it may cause punctal occlusion and delayed tear clearance
2. Folds may be single or multiple, and may be lower than, equal to, or higher than the tear meniscus
3. Localized injection of the redundant conjunctiva may be seen

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Slit lamp examination
2. With fluorescein or Rose Bengal stain discrete areas of staining may be present on the redundant bulbar conjunctiva, the adjacent lid margin, and tarsal conjunctiva. These features may help distinguish symptoms due to conjunctivochalasis from other causes

II. Define the risk factors

- A. Age**
- B. Thyroid disease**

III. List the differential diagnosis

- A. Entropion**
- B. Ectropion**
- C. Punctal stenosis**
- D. Nasolacrimal obstruction**
- E. Lid laxity**
- F. Tear film abnormalities**
- G. Aqueous tear deficiency**
- H. Meibomian gland dysfunction**
- I. Conjunctival edema, chemosis, lymphangiectasis**
- J. Superior limbic keratoconjunctivitis**

IV. Describe patient management in terms of treatment and follow-up

A. Describe the natural history, outcome and prognosis

1. Conjunctivochalasis is common with age
2. It may be asymptomatic in which case no treatment is required
3. Symptoms such as intermittent epiphora, dry eye type symptoms, and exposure related pain and irritation can occur and require treatment
4. Medical therapy may improve symptoms. If not, surgical intervention may be indicated

B. Describe medical therapy options

1. Ocular lubricants
2. Topical corticosteroids
3. Topical antihistamines
4. Patching at bedtime with ointment to protect the exposed conjunctiva

C. Describe surgical therapy options

1. Most surgical methods include excision of the area of conjunctivochalasis
2. A crescentic excision of the inferior bulbar conjunctiva 5mm away from the limbus followed by closure with absorbable sutures may be performed
 - a. Fibrin glue can be used in lieu of sutures to reduce suture related granuloma formation and inflammation

- b. Amniotic membrane can be placed over the defect created after the crescentic excision of conjunctiva. This can be sutured or glued into place
3. Suture can be placed to tighten the conjunctiva
4. Transconjunctival cautery can be applied

V. List the complications of treatment, their prevention and management

A. Complications

1. Recurrence
2. Conjunctival scarring
3. Cicatricial entropion
4. Retraction of the lower fornix
5. Motility restriction
6. Corneal complications

B. Prevention and management

1. Conjunctival area of excision should be limited as much as possible to avoid these complications
2. Use of amniotic membrane may reduce the likelihood of these complications

VI. Describe disease-related complications

A. Delayed tear clearance may lead to an increase in ocular surface irritation, inflammation and pain

B. Epiphora secondary to blocking access to lid puncta

VII. Describe appropriate patient instructions

A. Appropriate use of topical therapy

B. If indicated, proper instruction on patching at bedtime

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Erdogan-Poyraz C et al. Delayed Tear Clearance in Patients with Conjunctivochalasis Is Associated With Punctal Occlusion. *Cornea* 26:290-293, 2007.
3. Yokoi N. Clinical Impact of Conjunctivochalasis on the Ocular Surface. *Cornea* 24(Suppl. 1):S24-S31, 2005.
4. Meller D, Tseng SCG. Conjunctivochalasis: Literature Review and Possible Pathophysiology. *Survey of Ophthalmology* 43(3): 225-32, Nov-Dec 1998.

5. Meller D et al. Amniotic Membrane transplantation for symptomatic conjunctivochalasis refractory to medical treatments. *Cornea* 19(6): 796-803, 2000.

Aqueous tear deficiency, Sjögren syndrome and Mucin deficiency

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Decreased aqueous tear production due to
 - a. Localized lacrimal gland disease
 - i. Idiopathic inflammation
 - ii. Trauma
 - iii. Infiltrative disorders
 - i) Lymphoma
 - ii) Amyloidosis
 - iii) Sarcoidosis
 - iv. Scarring with obliteration of lacrimal ducts and atrophy of lacrimal gland
 - i) Mucous membrane pemphigoid
 - ii) Stevens-Johnson syndrome
 - iii) Trachoma
 - iv) Radiotherapy
 - v. Absence of the lacrimal gland: congenital or surgical
 - b. Autoimmune disorders affecting the lacrimal glands
 - i. Primary Sjögren syndrome
 - i) Aqueous tear deficiency (keratoconjunctivitis sicca) and/or,
 - ii) Decreased salivary gland flow (xerostomia), and/or
 - iii) Lymphocytic infiltration of lacrimal and salivary glands, and/or
 - iv) Presence of serum autoantibodies.
 - ii. Secondary Sjögren syndrome, associated with systemic autoimmune disease (e.g., rheumatoid arthritis, others)
 - i) Aqueous tear deficiency (keratoconjunctivitis sicca) and/or,
 - ii) Decreased salivary gland flow (xerostomia), and/or
 - iii) Lymphocytic infiltration of lacrimal and salivary glands, and/or
 - iv) Presence of serum autoantibodies.
 - v) Systemic autoimmune disease (e.g. rheumatoid arthritis, systemic lupus

erythematosus, progressive systemic sclerosis, and chronic hepatobiliary cirrhosis)

- c. Medications with anticholinergic effects (e.g., tricyclic antidepressants)
- d. Decreased corneal sensation
 - i. Trigeminal nerve dysfunction
 - ii. Contact lens wear
 - iii. Post-surgical (e.g., laser in situ keratomileusis)
- 2. Excessive tear evaporation
 - a. Meibomian gland dysfunction
 - b. Lid/globe congruity disorders
 - c. Lid closure and blinking disorders
 - i. Bell's palsy and other disorders of cranial nerve VII
 - ii. Parkinson disease
 - iii. Cicatricial, post surgical and other traumatic causes
- 3. Decreased mucin production from chemical or inflammatory destruction of conjunctival goblet cells, conjunctiva
 - a. Goblet cell destruction from conjunctival scarring
 - i. Mucous membrane pemphigoid (MMP) (ocular cicatricial pemphigoid (OCP))
 - ii. Stevens-Johnson syndrome
 - iii. Trachoma
 - iv. Chemical alkali burn
 - v. Erythema multiforme major
 - b. Goblet cell dysfunction
 - i. Vitamin A deficiency
 - c. Drug induced mucin deficiency
 - i. Prochlorolol
 - ii. Echothiophate iodide
 - d. Goblet cell loss from surgical trauma, such as suction for microkeratome use with LASIK

B. Define the relevant aspects of epidemiology of this disease

- 1. Dry eye syndrome is common, and more common in women
- 2. Prevalence increases with age
- 3. More common among people with arthritis

C. List the pertinent elements of the history

- 1. Dryness

2. Irritation
3. Foreign body sensation
4. Burning
5. Light sensitivity
6. Blurred or fluctuating vision
7. Excessive tearing
8. Symptoms may increase as the day progresses or wax and wane
9. Dry mouth
10. Medication use

D. Describe pertinent clinical features

1. Tear film
 - a. Decreased tear meniscus
 - b. Rapid tear film breakup time
 - c. Reduced Schirmer test
 - d. Hyperosmolarity
2. Ocular surface
 - a. Interpalpebral conjunctival staining
 - b. Interpalpebral and/or inferior corneal staining, using fluorescein, rose bengal, or lissamine green
 - c. Relative mucous excess, filaments, and plaques

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Tear film break up time less than 10 seconds (See Tear film evaluation: static and dynamic assessments; tear break-up time, Schirmer)
2. Schirmer Test
3. Aqueous tear deficiency: laboratory testing usually not necessary, although tear assays (e.g., tear osmolarity, lysozyme and lactoferrin) are available
4. Sjögren syndrome (e.g., dry eye and dry mouth)
 - a. Anti-Ro (SS-A) antibody
 - b. Anti-La (SS-B) antibody
 - c. Antinuclear antibody
 - d. Rheumatoid factor
5. Consider salivary or lacrimal gland biopsy if abnormal glandular enlargement
6. Impression cytology of the conjunctiva
 - a. Look for decreased conjunctival goblet cell density

II. Define the risk factors

- A. Hormonal effects (e.g. menopause in women)**
- B. HIV infection**
- C. Certain human leukocyte antigen (HLA) types**
- D. Connective tissue disease**
- E. Conjunctival scarring**

III. List the differential diagnosis

- A. Neurotrophic keratopathy**
- B. Exposure keratopathy**
- C. Toxicity of topical medications/preservatives**
- D. Factitious keratoconjunctivitis**
- E. Aqueous tear deficiency**
- F. Mucin tear deficiency**
- G. Lipid tear deficiency**
- H. Blepharitis**

IV. Describe patient management in terms of treatment and follow-up

A. Define medical therapy options

1. Tear replacement therapy
 - a. Preserved artificial tears in milder cases
 - b. Preservative-free artificial tears when frequent application is necessary
 - c. Gel or ointment in severe cases
 - d. Artificial tear pellet , prescription lubrication
 - e. Oral secretagogues
 - f. Autologous serum tears
2. Reduce medications contributing to dry eye or ocular surface irritation
3. Reduce evaporation
 - a. Room humidification
 - b. Side shields to eyeglasses, moisture chamber goggles
 - c. Avoid drafts
 - d. Adjust work tasks (e.g. lower computer screen to reduce interpalpebral fissure width)

4. Suppress ocular surface inflammation
 - a. Topical cyclosporine
 - b. Topical corticosteroid
5. Vitamin A deficiency treatment
 - a. Adults and children older than one year
 - i. 200,000 international units (IU) (oral or IM) daily for 2 days, repeat in two weeks
 - ii. 100,000 IU (oral or IM) every 4-6 months
 - b. Pregnant women and children less than one year
 - iii. 100,000 IU every 4 to 6 months
 - c. Infants
 - iv. 50,000 IU prophylactic dose
6. Oral immunosuppression for active MMP, Sjögren, autoimmune disorders

B. Define surgical therapy options

1. Increase tear retention
 - a. Punctal occlusion: plugs or cauterization
2. Decrease tear evaporation
 - a. Correction of eyelid position abnormalities or lagophthalmos
 - b. Tarsorrhaphy

V. Describe disease-related complications

- A. Loss of epithelial integrity: punctate epithelial erosions or large epithelial defect
- B. Microbial keratitis
- C. Sterile corneal ulceration
- D. Corneal thinning, neovascularization, scarring, or perforation
- E. Corneal calcific deposits and band keratopathy
- F. Fornix shortening, symblepharon, lid malposition
- G. Loss of vision

VI. Describe appropriate patient instructions

- A. Proper administration of topical medications
- B. Appropriate frequency and timing for use of topical lubricants
- C. Advantages/disadvantages of different lubricants
 1. Preserved vs. non-preserved

2. Viscosity, retention on the ocular surface, and blurring

D. Obtain care for dry mouth and oral complications of xerostomia

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 11: Lens and Cataract, 2013-2014.

Filamentary keratopathy

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Filaments are composed of degenerated epithelial cells and mucus in variable proportions
2. Seen in various corneal conditions which have in common an abnormality of the ocular surface and altered tear composition

B. List the pertinent elements of the history

1. Common symptoms include: foreign body sensation, ocular pain (may be severe), photophobia, blepharospasm, increased blink frequency, and epiphora
2. Symptoms tend to be most prominent with blinking and alleviated when the eyes are closed

C. Describe pertinent clinical features

1. Filaments stain with fluorescein and rose bengal dyes, facilitating identification
2. Filaments range in length from 0.5 to several millimeters, and are relatively strongly attached to the cornea
3. Often a small, gray, subepithelial opacity will be present beneath the site of corneal attachment
4. Any underlying epithelial defect will stain with fluorescein prominently
5. The location of the filaments may provide a clue as to the cause
 - a. Superior cornea
 - i. Associated with superior limbic keratoconjunctivitis, ptosis, or other causes of prolonged lid closure
 - b. Interpalpebral distribution
 - i. Associated with keratoconjunctivitis sicca, pharmacologic dry eye, or exposure keratopathy
 - ii. After cataract extraction, filaments may be found superiorly
 - c. Graft-host junction
 - i. Filaments after cornea transplantation typically reside on the graft or at the graft-host interface or at the base of the suture on donor side
6. Evidence of a predisposing condition
 - a. Ptosis
 - b. Lid lag
 - c. Incomplete lid closure
 - d. Punctate epithelial erosions associated with dry eye syndrome
 - e. Epithelial irregularity or epithelial defect

II. Define the risk factors

A. Any condition associated with irregularity (including desiccation) of the ocular surface

1. Dry eye syndrome
 - a. Keratoconjunctivitis sicca
 - b. Medication-induced
 - c. Posterior blepharitis (tear film instability)
2. Exposure keratopathy
 - a. Cranial Nerve (CN) VII palsy
 - b. Altered mental status with decreased blink rates
3. Ocular trauma (including surgery)
 - a. Epithelial abrasion/erosion
 - b. Contact lens overwear
 - c. Cataract extraction
 - d. Penetrating keratoplasty
 - e. Glaucoma filtering surgery
4. Prolonged occlusion
 - a. Ptosis
 - b. Prolonged patching
5. Ophthalmic disorders
 - a. Superior limbic keratoconjunctivitis
 - b. Epithelial keratitis (e.g., herpes simplex virus (HSV) keratitis) and epithelial erosions (e.g., toxicity)

III. List the differential diagnosis

- A. Dendritic lesions, such as HSV dendritic epithelial keratitis**
- B. Loosened sutures**
- C. Corneal abrasion**
- D. Non-adherent mucus or foam**

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Mechanical removal of filaments
2. Bandage contact lens (for relief of discomfort; may increase number of filaments)
3. Management of dry eye syndrome
 - a. Preservative free artificial tears
 - b. Punctal occlusion
 - c. Topical cyclosporine
 - d. Autologous serum drops
4. Mucolytics
 - a. N-Acetylcysteine
5. Topical sodium chloride (e.g. Muro 128 drops and ointment)

B. Describe surgical therapy options

1. Repair of contributory lid malposition
2. Tarsorrhaphy if secondary to severe dry eye syndrome
3. Superior conjunctival resection or cauterization if secondary to superior limbic keratoconjunctivitis

V. List the complications of treatment, their prevention and management

A. Mechanical removal of filaments - epithelial defect with secondary infection

1. Prescribe topical antibiotics after filament removal

B. Mucolytic treatment - toxic keratopathy

1. Discontinue use

VI. Describe disease-related complications

A. Major symptoms are ocular surface irritation and pain, and decreased vision

B. Filaments are an indicator of ocular surface disease

1. Complications are not typically secondary to the filaments, but the underlying disease process

VII. Describe appropriate patient instructions

A. Once underlying process is effectively treated, filaments will resolve

B. Removal of filaments/use of mucolytics may be successfully employed when filaments present, but are not definitive treatments, as filaments will recur

C. Continue with aggressive topical lubrication (if not possible to eliminate underlying process)

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Meibomian gland dysfunction, rosacea, and seborrheic blepharitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Meibomian gland dysfunction is a result of progressive obstruction and inflammation of the gland orifices
2. Seborrheic blepharitis is a chronic inflammation of the eyelid, eyelashes, forehead and scalp skin
3. Rosacea is a skin disease characterized by dysfunction of meibomian glands and/or other cutaneous sebaceous glands of the skin of the face and chest

B. Define the relevant aspects of epidemiology of the disease

1. The prevalence increases with increasing age. It mainly develops in patients between ages 30 and 60 years but can affect all age groups including children
2. Slight female preponderance

C. List the pertinent elements of the history

1. Burning, gritty, sandy, foreign body sensation
2. Crusting of the eyelids (especially in seborrheic blepharitis)
3. Chronic eyelid margin redness
4. Conjunctival injection
5. Blurred (occasionally) or unstable vision from tear-film disturbances
6. Eye pain and photophobia (occasionally)
7. Recurrent chalazia
8. In rosacea, additional elements may be reported
 - a. Facial rash
 - b. Flushing episodes

D. Describe pertinent clinical features

1. Meibomian gland dysfunction
 - a. Affects posterior eyelid margin
 - b. Increased opaque secretion in meibomian glands
 - c. Foamy secretions
 - d. Pouting, metaplastic meibomian gland orifices
 - e. Telangiectasias of the eyelid margin

- f. Meibomian gland drop out (meimography)
- g. Abnormal meibum after expression of glands (with slight pressure on lid margin with Q tip or finger)
- h. Bulbar and tarsal conjunctival injection
- i. Papillary conjunctival reaction
- j. Atrophy of Meibomian gland acini
- k. Episcleritis
- l. Corneal punctate epithelial erosions
- m. Corneal marginal infiltrates
- n. Corneal vascularization
- o. Evidence of systemic rosacea in some individuals
- p. Lipid-tear deficiency

2. Rosacea

- a. Malar rash and telangiectasias of facial skin and eyelid margin
- b. Papules, pustules, hypertrophic sebaceous glands
- c. Rhinophyma
- d. Meibomian gland dysfunction, distortion
- e. Excessive sebum secretion
- f. Bulbar and tarsal conjunctival injection
- g. Marginal corneal infiltrates and sterile ulceration of cornea
- h. Episcleritis
- i. Iridocyclitis
- j. Corneal neovascularization and scarring
- k. Atrophy of meibomian glands late in disease
- l. Lipid tear deficiency and aqueous tear deficiency

3. Seborrheic blepharitis

- a. Affects primarily anterior eyelid margin
- b. Oily or greasy eyelid crusting
- c. Increased and turbid meibomian gland secretions
- d. Mild conjunctival injection
- e. Corneal punctate epithelial erosions
- f. Aqueous tear deficiency
- g. May have evidence of seborrhea elsewhere on the body

- h. May be associated with staphylococcal blepharitis or meibomianitis

II. List the differential diagnosis

- A. Staphylococcal blepharitis
- B. Lice infestation
- C. Masquerade syndrome (eyelid neoplasm - rare, but should be considered in chronic unilateral blepharitis)
- D. Discoid lupus
- E. Demodex blepharitis

III. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Daily eyelid hygiene (warm compresses, eyelid massage, and eyelid scrubbing) with commercially available pads, using clean washcloth or Q-tip soaked in warm water +/- dilute baby shampoo
2. Artificial tears
 - a. If aqueous tear deficiency or lipid-induced tear film instability present
3. Topical corticosteroids
 - a. For acute exacerbations
 - b. If marginal corneal infiltrates or progressive corneal neovascularization
4. Antibiotics
 - a. Oral tetracyclines e.g. doxycycline, minocycline, tetracycline in adults
 - b. Oral erythromycin in children
 - c. Topical macrolides e.g. azithromycin
5. Topical metronidazole for skin involvement

IV. List the complications of treatment, their prevention and management

- A. Complications of topical corticosteroids, if used (including glaucoma and cataract)
- B. Corneal toxicity and allergic reactions to topical antibiotics, if used
- C. Side effects related to systemic tetracyclines, if used

V. Describe disease-related complications

- A. Corneal ulceration
- B. Corneal vascularization

- C. Corneal scarring
- D. Corneal thinning and perforation (rare)
- E. Eyelid ulceration, trichiasis, madarosis
- F. Atrophy of Meibomian glands and lipid-layer tear deficiency

VI. Describe appropriate patient instructions

- A. Chronic nature of these conditions
- B. Importance of daily eyelid hygiene
- C. Instruction on proper eyelid hygiene
- D. Instruction on medications and their side effects
- E. Instructions regarding follow-up

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
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Benign conjunctival masses

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Benign lesions occur as a result of over proliferation of cells
2. Others may occur due to accumulation or deposition of substances in the conjunctiva
3. There can be changes in lymphatic channels of the conjunctiva
4. And infection and inflammation may result in benign lesions

B. Define the relevant aspects of epidemiology of the disease

1. May occur at various ages
2. No sex predilection

C. List the pertinent elements of the history

1. Length of time the lesion has been present
2. Color, location, topography of lesion
3. Single or multiple lesions
4. Unilateral or bilateral
5. Other lesions in non ocular locations
6. Presence of systemic disease
7. Presence of pain, swelling, ptosis, discharge, redness, tearing, irritation
8. History of prior lesion removal, either benign or malignant
9. History of prior ocular surgery
10. Recent changes in the appearance of the lesion(s)
11. Pertinent family history

D. Describe pertinent clinical features

1. Benign Nevi
 - a. Focal unilateral lesion may be flat or elevated
 - b. Most commonly brown, may be tan, amelanotic
 - c. Intralesional cysts in 50%
 - d. Occur near the limbus, bulbar conjunctiva, plica, caruncle Rarely in the fornix or tarsal conjunctiva
 - e. Typically noted in the first two decades of life, stable, unlikely to develop into malignancy
 - i. May increase in size and pigmentation at puberty and during pregnancy

- f. May be junctional (intraepithelial), subepithelial, compound
2. Conjunctival papilloma
 - a. Pedunculated
 - i. Seen in children and younger patients
 - ii. Associated with Human papilloma virus (HPV 6, 16)
 - iii. Fleshy, multilobular growth with fibrovascular core
 - iv. Typically arises in the inferior fornix, may develop on the tarsal or bulbar conjunctiva, or the semilunar fold
 - v. Unilateral or bilateral
 - vi. Multiple lesions may occur and may be extensive in immunocompromised patients
 - b. Sessile
 - i. Seen in adults
 - ii. Usually located at limbus
 - iii. Flat base, glistening with red dots (strawberry-like)
 - iv. Unilateral, solitary
 - v. May spread onto cornea
 - vi. Possibly related to UV exposure
 - c. Pyogenic granuloma
 - d. Red, raised lesion often pedunculated
 - e. Develops rapidly over days to weeks
 - f. May result from inflammation, ocular surface surgery, infection, chalazion, foreign body
 3. Capillary hemangioma
 - a. Red, protuberant vascular growth
 - b. May occur in infancy associated with cutaneous or orbital lesion
 - c. Adults can develop a primary conjunctival hemangioma
 - i. Thought to be a variant of pyogenic granuloma
 - ii. Similar to cherry hemangiomas found in the skin
 4. Lymphangiectasia
 - a. Dilated lymph channels seen as sausage like clear or hemorrhagic conjunctival cystic lesions
 - b. Chemosis, focal or diffuse
 - c. May have history of eye irritation, tearing
 - d. Associated with local venous hypertension (thyroid eye disease, orbital apex syndrome,

cavernous sinus thrombosis, carotid-cavernous fistula), increased vascular permeability (allergy), local lymphatic scarring

5. Lymphangioma
 - a. Prominent mass of lymphatic channels
 - i. Lymphangiectasia of tumorous proportions
 - ii. May be continuous with orbital lesion
 - b. Can be clear or have intralesional hemorrhage (chocolate cysts)
 - c. Multiloculated, cystic in appearance
 - d. Unilateral
 - e. Clinically apparent in first decade
 - f. Consists of irregular cyst like channels with clear fluid or blood
6. Benign reactive lymphoid hyperplasia
 - a. Salmon-pink colored lesion
 - b. Typically found in adults
 - c. Rarely reported in children (associated with Epstein-Barr virus)
 - d. Irritative (periocular inflammation, chalazia, conjunctivitis, chemical injury) or antigenic stimulus (from microorganisms, allergens, drugs)
 - e. 15-25% associated with development of systemic lymphoma
7. Primary localized conjunctival amyloidosis
 - a. Avascular, non-inflamed, soft yellow or salmon colored deposits
 - b. Nodular, fusiform or polypoid in shape
 - c. Palpebral conjunctiva, superior fornix and tarsus most commonly involved
 - d. Ptosis, ophthalmoplegia may occur.
 - e. May be asymptomatic or have pain, swelling, recurrent hemorrhages
 - f. Young to middle aged adults
 - g. Amyloidosis may be localized to one organ or may be systemic.
 - i. It may be primary (idiopathic) or secondary (to some chronic disease) and familial or nonfamilial
8. Epithelial Inclusion cyst
 - a. Single cystic mass or multiple cysts may be seen
 - b. Bulbar, fornix
 - c. May occur spontaneously, following inflammation, trauma, surgery
9. Inflammatory granulomatous lesions

- a. Nodule of the bulbar or palpebral conjunctiva
 - b. Single or multiple small tan, yellow nodules can resemble follicles
 - c. Conjunctival injection
 - d. Infectious (parasitic, fungal, cat scratch disease) or non infectious (foreign bodies, rheumatoid arthritis, sarcoidosis)
- 10. Juvenile Xanthogranuloma
 - a. Unilateral, yellow mass, may be vitelliform
 - b. More commonly located at limbus
 - c. Typically seen in children, may present in adults
- 11. Dermoid
 - a. Well circumscribed solid yellow-white lesion (choristoma)
 - b. Present at birth
 - c. Usually located at inferotemporal limbus
 - d. Fine hairs may be present
 - e. Can be associated with Goldenhar syndrome
 - f. Dense fibrous tissue, may contain hair, sebaceous glands
- 12. Dermolipoma
 - a. Occurs superotemporally
 - b. Pale yellow dermoid
 - c. Contains adipose tissue
 - d. Differentiate from orbital fat prolapse
- 13. (See Pterygium and pinguecula)
- E. Describe appropriate testing and evaluation for establishing the diagnosis**
 - 1. Most lesions can be diagnosed based on clinical appearance
 - 2. In cases where it is unclear, biopsy (excisional in small lesions, incisional in larger lesions) is performed

II. Define the risk factors

- A. Varies by lesion**

III. List the differential diagnosis

- A. Malignant lesions such as melanoma, lymphoma, leukemia, squamous cell carcinoma, sebaceous cell carcinoma, Kaposi's sarcoma**

- B. These benign lesions make up their own unique differential diagnosis**
- C. Allergic conjunctivitis, episcleritis, conjunctivochalasis**
- D. Conjunctival pigmentation: Associated with skin complexion (also called benign epithelial melanosis or racial melanosis); Primary acquired melanosis; Secondary acquired melanosis; melanoma**

IV. Describe patient management in terms of treatment and follow-up

A. Describe the natural history, outcome and prognosis

- 1. Varies by lesion
 - a. Some lesions may regress, some may remain stationary, and others may progress to malignancy. There may be systemic associations, systemic evaluation should be performed when indicated

B. Describe medical therapy options

- 1. Some lesions can be observed
 - a. Observation with slit lamp drawings and/or slit lamp photos every 6-12 months as indicated. (ex. Nevus, dermoid, pinguecula, inclusion cysts)
- 2. Some may respond to topical corticosteroid
 - a. Lymphangiectasia, pyogenic granuloma
- 3. Papilloma
 - a. May be treated with topical interferon
 - b. Oral Cimetidine may reduce recurrence with Papilloma

C. Describe surgical therapy options

- 1. Excisional biopsy is performed for small and intermediate sized lesions that may be symptomatic or suspected to be malignant.
 - a. Examples: Steroid-resistant pyogenic granuloma, limbal dermoid, epibulbar osseous choristoma, lymphangiectasia, Molluscum contagiosum, and because they are rare, pigmented nevi of the fornix and tarsal conjunctiva should be biopsied
 - b. Excisional biopsy should be performed on lesions that exhibit a change in appearance
 - c. If the defect cannot be closed primarily, an amniotic membrane graft may be inserted, or a pressure patch used until the epithelial defect is healed
 - d. If malignancy is suspected and with papilloma (due to its high rate of recurrence), a 'no-touch' technique should be performed with a wide excision around the lesion. Cryotherapy may be indicated as well (nevi, papilloma). Cautery may be indicated for lesions such as lymphangioma.
 - i. Caution should be taken when excising pedunculated papilloma due to possibility of virus dissemination with multiple recurrences

V. List the complications of treatment, their prevention and management

A. Complications of topical corticosteroid

B. Surgical excision

1. Infection, bleeding, scarring, recurrence
2. Prevention and management complications
 - a. Meticulous surgical technique
 - b. Treat infection with topical antibiotics

VI. Describe disease-related complications

A. Minimal in most benign lesions

B. Some may grow over the cornea and reduce vision

C. There may be malignant transformation

D. Complications related to the systemic disease process

VII. Describe appropriate patient instructions

A. Return for an evaluation if the lesion changes in appearance or new symptoms occur

B. When indicated, advise that systemic evaluation be performed

C. Review complications of medical and surgical treatment

D. Review postoperative instructions as indicated

Additional Resources

1. AAO, Basic and Clinical Science Course. External Disease and Cornea: Section 8, 2013-2014.

Hordeolum and chalazion

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Hordeolum
 - a. Inspissation and infection of sebaceous glands
 - b. Anterior lid (glands of Zeis, lash follicles): external hordeolum or sty
 - c. Posterior lid (Meibomian glands): internal hordeolum
 - d. *Staphylococcus aureus* is most common pathogen
2. Chalazion
 - a. Inspissation of Meibomian or Zeis gland
 - b. Extrusion of sebum into adjacent tissues produces sterile granulomatous inflammation

B. List the pertinent elements of the history

1. Hordeolum
 - a. Rapid onset, painful, tender
 - b. Typically resolve in 1-2 weeks
 - c. May produce purulent discharge with rupture
2. Chalazion
 - a. Slow onset or previous hordeolum
 - b. Either painless or mild soreness
 - c. Resolution in weeks to months or no resolution
 - d. May drain externally
 - e. Occasional blurred vision due to astigmatism from pressure on globe

C. Describe pertinent clinical features

1. Hordeolum
 - a. Tender, red nodules near lid margin
 - b. Surrounding edema, erythema may indicate preseptal cellulitis
2. Chalazion
 - a. Nontender nodules at lid margin or in region of tarsus
 - b. Redness of overlying skin

D. Describe appropriate laboratory testing for establishing the diagnosis

1. Cultures unnecessary in most cases

2. Histopathologic examination of material from recurrent chalazia to rule out neoplasia

II. Define the risk factors

- A. Rosacea
- B. Chronic blepharitis

III. List the differential diagnosis

- A. Preseptal cellulitis
- B. Basal cell carcinoma
- C. Squamous cell carcinoma
- D. Sebaceous carcinoma
- E. Keratoacanthoma
- F. Papilloma
- G. Inclusion cyst

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Warm compresses and massage of lesions
2. Topical antibiotics ineffective in treating hordeola and chalazia, but may be of value in treating accompanying staphylococcal blepharitis
3. Systemic antibiotics active against *Staphylococcus aureus* for accompanying preseptal cellulitis
4. Systemic tetracyclines for treatment of chronic accompanying meibomitis, rosacea

B. Describe surgical therapy options

1. Intralesional corticosteroid injection (0.1-0.2 mL Triamcinolone 10mg/mL)
2. Incision/excision and drainage
 - a. Curettage for larger lesions

V. List the complications of treatment, their prevention and management

A. Medication

1. Allergy
 - a. Prevention
 - i. Obtain history of medication allergies
 - b. Management

- i. Cessation of medication, corticosteroids if necessary

B. Incision/excision and drainage

1. Horizontal scarring of tarsal plate
 - a. Prevention
 - i. Vertical incision along Meibomian gland
 - b. Management
 - i. Plastic repair of tarsal plate
2. Infection
 - a. Prevention
 - i. Aseptic technique
 - ii. Prophylactic antibiotics
 - b. Management
 - i. Topical, systemic antibiotics
3. Damage to lacrimal drainage apparatus
 - a. Prevention
 - i. Careful attention to technique, avoid excising lesions overlying punctum, canaliculus

C. Intralesional corticosteroid injection

1. Skin depigmentation

VI. Describe disease-related complications

- A. Distortion of lid margin, with secondary exposure keratopathy
- B. Pressure on globe, with secondary astigmatism
- C. Preseptal cellulitis
- D. Rarely, orbital cellulitis (higher risk in children)

VII. Describe appropriate patient instructions

- A. Proper use of medications, warm compresses
- B. When to seek further care

Additional Resources

1. AAO. Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Exposure keratopathy

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Inadequate eyelid closure (lagophthalmos)
 - a. Cranial Nerve (CN) VII palsy, including Bells palsy
 - b. Decreased blinking (e.g., Parkinson disease)
 - c. Ectropion
 - d. Eyelid deformity
 - i. Congenital
 - ii. Acquired
 - i) Mucous membrane pemphigoid
 - ii) Stevens-Johnson syndrome
 - e. Trachoma
 - f. Blepharoplasty
 - g. Altered mental status
 - h. Drug abuse
 - i. Unconsciousness
2. Proptosis
 - a. Thyroid eye disease (thyroid orbitopathy)
 - b. Orbital pseudotumor
 - c. Retrobulbar tumor

B. List the pertinent elements of the history

1. Dryness, irritation, foreign body sensation, burning
2. Tearing
3. Blurred vision
4. Photophobia
5. Redness
6. Symptoms worse on awakening (nocturnal lagophthalmos)
7. History of eyelid surgery

C. Describe pertinent clinical features

1. Incomplete eyelid closure and/or proptosis

2. Dilated conjunctival vasculature
3. Punctate epithelial erosions
4. Epithelial defects of varying size
5. Lesions preferentially involving inferior third of cornea and conjunctiva, in exposure area and usually conjunctiva below the limbus
6. Bells phenomenon

II. Define the risk factors

- A. Decreased blinking associated with visually attentive tasks**
- B. Low humidity**

III. List the differential diagnosis

- A. Neurotrophic keratopathy**
- B. Keratoconjunctivitis sicca**
- C. Toxicity of topical medications/preservatives**
- D. Factitious keratoconjunctivitis**

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Treatment of underlying disease
2. Tear supplementation with frequent preservative-free lubricants
3. Ointment at bedtime
4. Reduce evaporative tear loss
 - a. Goggles, moisture shields
 - b. Taping lid shut at bedtime
 - c. Humidifier
5. Treatment of any concomitant dry eye (See Aqueous tear deficiency, Sjögren syndrome and Mucin deficiency)

B. Describe surgical therapy options

1. Punctal occlusion
2. Surgical correction of eyelid position, such as tarsorrhaphy, lateral canthal sling, medial canthoplasty or gold weight insertion
3. Orbital decompression for proptosis

V. List the complications of treatment, their prevention and management

A. Topical lubricants

1. Complications: epithelial toxicity of preservatives
2. Prevention and management: preservative-free lubricants

B. Surgical

1. (See Punctal occlusion, Tarsorrhaphy)
2. Gold weight: infection, shifting, extrusion, inflammation response to gold, induced astigmatism.
Prevention and management: Use sterile technique. Remove gold weight. Treat infection

VI. Describe disease-related complications

A. Corneal scarring

B. Microbial keratitis

C. Sterile corneal ulceration

D. Corneal perforation

VII. Describe appropriate patient instructions

A. Proper administration of topical medications

B. Use of moisture shields, taping of lids

C. Advantages/disadvantages of different lubricants

D. When to seek further care

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Floppy eyelid syndrome

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Laxity of upper, or less commonly, lower eyelid and tarsus
2. Upper eyelid everts with minimal manipulation
3. Chronic ocular irritation and inflammation, which may result from ocular contact with the pillow or bedding or exposure during sleep
4. Chronic eye rubbing with secondary lid laxity

B. List the pertinent elements of the history

1. Ocular discomfort and redness
2. Symptoms may be worse upon waking

C. Describe pertinent clinical features

1. Papillae on the upper palpebral conjunctiva
2. Mucous discharge
3. Mild to severe punctate corneal epitheliopathy
4. Severe cases may demonstrate corneal vascularization
5. Symptoms and clinical findings may be asymmetric or unilateral if the individual sleeps in one position

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Manually test ease of upper lid eversion
2. Manually test upper lid lateral laxity

II. Define the risk factors

- A. Obesity
- B. Obstructive sleep apnea
- C. Face down sleep position

III. List the differential diagnosis

- A. Vernal conjunctivitis
- B. Giant papillary conjunctivitis
- C. Atopic keratoconjunctivitis
- D. Infectious conjunctivitis

E. Toxic keratopathy

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Tape eyelid closed at bedtime
2. Wear eye shields or goggles while sleeping
3. Sleep upright in recliner

B. Describe surgical therapy options

1. Eyelid tightening procedure

V. List the complications of treatment, their prevention and management

A. Tape allergy

1. Change type of tape used
2. Discontinue use
3. Use goggles with elastic band

B. Postsurgical infection

1. Aseptic technique
2. Antibiotics

C. Postsurgical corneal exposure

1. Lubricants
2. Surgical revision

D. Recurrences common unless underlying disease/obesity addressed

VI. Describe disease-related complications

A. Ocular surface irritation

B. Corneal vascularization

C. Secondary infection

D. Corneal scarring

E. Decreased vision

VII. Describe appropriate patient instructions

A. Explain etiology of upper eyelid eversion leading to ocular surface exposure and how to prevent

B. Describe how to use tape or goggles at bedtime

C. Describe surgical option of eyelid tightening procedure

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Kersten RC. *Cornea*. 2nd ed. Philadelphia, PA: Elsevier Mosby; 2005: Chapter 34.

Recurrent erosion

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Poor adhesion of the corneal epithelium because of underlying abnormalities in the corneal epithelial basement membrane and its associated filament network
2. Predisposing condition
 - a. Previous corneal trauma, such as a fingernail scratch
 - b. Corneal epithelial basement membrane disease
 - c. Stromal dystrophy, such as lattice corneal dystrophy
 - d. Irregular corneal surface, such as Salzmann nodular degeneration
 - e. Previous corneal surgery, such as photorefractive keratectomy

B. List the pertinent elements of the history

1. Prior history of a traumatic corneal abrasion
2. Prior history of corneal epithelial basement membrane disease
3. Prior history of ocular surface or corneal disorder (e.g., dry eye, exposure, corneal edema, corneal dystrophy, or corneal degeneration)
4. Symptoms: sudden onset of eye pain, usually at night or upon first awakening, accompanied by redness, photophobia, and tearing; episodes vary from 30 minutes to several days

C. Describe the pertinent clinical features

1. The cornea will show areas of positive or negative staining if the last episode was recent. The patient may have an intact epithelial surface by the time of exam or present with frank corneal epithelial defect
2. Pooling of fluorescein over the affected area even with no frank epithelial defect
3. Subtle corneal changes such as epithelial cysts
4. Loosely attached corneal epithelium to the underlying basement membrane in either eye
5. Heaped up or edematous epithelium in area of erosion
6. May have signs of corneal epithelial basement membrane dystrophy (map-dot-fingerprint dystrophy)

D. Define the risk factors

E. Previous sudden, sharp, abrading injury (fingernail, paper cut, organic material) to the corneal surface which has not been treated aggressively at the time of initial occurrence

F. Preexisting corneal epithelial basement membrane dystrophy (See Corneal epithelial basement membrane dystrophy/degeneration)

G. Corneal edema

H. Corneal dystrophy or degeneration

II. List the differential diagnosis

- A. Corneal abrasion (See Traumatic corneal abrasion)**
- B. Corneal epithelial erosion associated with other corneal dystrophies**
- C. Exposure keratopathy (See Exposure keratopathy)**
- D. Neurotrophic keratopathy (See Neurotrophic keratopathy)**
- E. Nocturnal lagophthalmos**
- F. Herpes simplex virus epithelial keratitis (See Herpes simplex virus epithelial keratitis)**
- G. Keratoconjunctivitis sicca (See Aqueous tear deficiency, Sjögren syndrome and Mucin deficiency)**

III. Describe patient management in terms of treatment and follow up

A. Management of epithelial defect

- 1. Pain control
 - a. Cycloplegic agent, topical nonsteroidal antiinflammatory drug, and oral analgesics may have some role
- 2. Encourage epithelial healing
 - a. Patching and topical antibiotic until epithelium healed
 - b. Bandage contact lenses and antibiotic eyedrops until epithelium healed

B. Prevention of subsequent erosion

- 1. Lubrication
 - a. Petrolatum, mineral oil or hypertonic ointments (5%NaCl or dextran) or drops while asleep
 - b. Artificial tears 4-6 times each day
- 2. Protection by bandage soft contact lens has been used
- 3. Reduction of proinflammatory medications
 - a. Possible benefit of topical corticosteroid and/or oral doxycycline
- 4. Control of concomitant ocular surface condition, if present, such as:
 - a. Dry eye syndrome
 - b. Rosacea blepharitis
 - c. Neurotrophic keratopathy
 - d. Corneal dystrophy or degeneration

C. Surgical interventions

- 1. Anterior stromal micropuncture (See Anterior stromal puncture)
- 2. Corneal epithelial debridement with polishing of Bowman's layer (diamond burr) (See Corneal epithelial debridement)

3. Excimer laser phototherapeutic keratectomy

D. Follow-up

1. Acute phase
 - a. Close follow-up depending on clinical response
2. Chronic phase
 - a. Follow-up in 1-2 months

IV. List the complications of treatment, their prevention and management

A. Medical treatment

1. Topical irritation and persistent discomfort
2. Blurred vision

B. Surgical treatment

1. Change in refractive error or induced astigmatism
2. Increased discomfort

V. Describe disease-related complications

- A. Eye pain
- B. Sterile keratitis
- C. Microbial keratitis
- D. Corneal scarring
- E. Salzmann nodule

VI. Describe appropriate patient instructions

- A. Proper use of topical antibiotics in the acute stage
- B. Chronic nature of the disease which can be controlled medically, and in more severe forms surgically

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8, External Disease and Cornea, 2013-2014.
2. Aldave AJ, Sonmez B. Elucidating the molecular genetic basis of the corneal dystrophies: are we there yet? *Arch Ophthalmol*. 2007 Feb;125(2):177-86.
3. Weiss JS, Møller HU, Lisch W, et al. The IC3D classification of corneal dystrophies. *Cornea*. 2008;27:S1-S42
4. Hykin PG, Foss AE, Pavesio C, et al. The natural history and management of recurrent corneal

erosion: a prospective randomised trial. *Eye* 1994;8:35-40.

5. Ohman L, Fagerholm P. The influence of excimer laser ablation on recurrent corneal erosions: a prospective randomized study. *Cornea* 1998;17:349-52.
6. Hykin PG, Foss AE, Pavesio C, et al. The natural history and management of recurrent corneal erosion: a prospective randomised trial. *Eye* 1994;8:35-40.
7. Ramamurthi S, Rahman MQ, Dutton GN, et al. Pathogenesis, clinical features and management of recurrent corneal erosions. *Eye* 2006;20:635-44. Review.
8. AAO, Focal Points: Surgical Techniques for Ocular Surface Reconstruction, Module #12, 2006.
9. AAO, Focal Points: Therapy of Recurrent Erosion and Persistent Defects of the Corneal Epithelium, Module #9, 1991, p.3-4.

Persistent corneal epithelial defect

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Generally related to some underlying disease process that compromises epithelial regeneration and/or the reformation of a normal basement membrane complex
2. Common causes
 - a. Neurotrophic keratopathy
 - i. Herpes simplex virus (HSV) epithelial keratopathy
 - ii. Herpes zoster ophthalmicus (HZO)
 - iii. Diabetes mellitus
 - b. Limbal stem cell insufficiency
 - i. Chemical injury
 - ii. Congenital aniridia
 - c. Chronic cicatricial keratitis (ocular mucous membrane pemphigoid, Stevens Johnson Syndrome)
 - d. Exposure keratopathy
 - i. Eyelid malposition
 - ii. Proptosis
 - e. Toxic keratopathy
 - f. Anesthetic abuse
 - g. Neuroparalytic disease
 - i. Cranial nerve (CN) VII palsy
 - ii. Cerebellar pontine angle neoplasia
3. Medications (e.g., topical aminoglycoside antibiotics, antiviral agents, NSAIDs) and preservatives (e.g., benzalkonium chloride) that impair epithelial healing

B. Define the pertinent elements of the history

1. Nonhealing epithelial defect despite treatment
2. Key to determine underlying cause
3. Review ophthalmic medications with particular attention to preservatives
4. Infection
5. Allergic conditions

6. Trauma
7. Ocular surgery
8. Eyelid conditions
9. Dry eye symptoms
10. Equally important to elicit history of non-ocular conditions such as:
 - a. Dermatologic disorders
 - b. Neurological disorders
 - c. Systemic disorders (e.g., collagen vascular disease and nutritional disorders)

C. Describe pertinent clinical features

1. Often a round or oval epithelial defect located in inferior half of cornea
2. Frequently have elevated, rounded edge or scalloped borders
3. May be associated with underlying stromal inflammation
4. Frequently have corneal hypesthesia
5. If left untreated
 - a. Can progress to vascularization and corneal opacification or scarring
 - b. May progress to necrosis and thinning of the stroma, leading to perforation

II. Define the risk factors

- A. Undiagnosed, untreated, or undertreated ocular or systemic conditions**
- B. Poor medication or treatment compliance**
- C. Presence of any of the causes listed above**

III. List the differential diagnosis

A. Local, non-immune-mediated

1. Postinfectious (bacterial, viral, fungal, amoebic)
2. Traumatic (chemical, thermal, radiation burn)
3. Postsurgical (diabetes patient, refractive procedure, anterior segment ischemia)
4. Epithelial and basement membrane complex disorders (e.g., epithelial basement membrane dystrophy)
5. Abnormal eyelids or eyelashes
 - a. Ectropion/entropion/trichiasis
 - b. Exposure/lagophthalmos/floppy eyelid syndrome
6. Neurological disorders

- a. Neurotrophic keratitis (HSV)
 - b. Neuroparalytic keratitis (Bells palsy)
- 7. Dermatologic disorders
 - a. Acne rosacea
 - b. Psoriasis

B. Local, immune-mediated

- 1. Vernal conjunctivitis
- 2. Mooren ulcer
- 3. Marginal keratitis
- 4. Postsurgical
 - a. Suture reaction

C. Systemic, non-immune-mediated

- 1. Nutritional disorders (e.g., keratomalacia)
- 2. Psychiatric disorders (e.g., mucous fishing syndrome)

D. Systemic, immune-mediated

- 1. Lacrimal disorders
 - a. Keratoconjunctivitis sicca
 - b. Sjögren syndrome
 - c. Graft-versus-host disease
- 2. Collagen vascular disorders
 - a. Mucous membrane pemphigoid
 - b. Stevens-Johnson syndrome
 - c. Relapsing polychondritis
 - d. Rheumatoid arthritis
 - e. Systemic lupus erythematosus
 - f. Polyarteritis nodosa
 - g. Wegener granulomatosis

E. Allergic disorders

- 1. Atopic keratoconjunctivitis

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Remove the offending stimulus or aggravating drugs
2. Treat the underlying condition
3. Culture (as indicated)
4. Lubricants, hypertonics, ophthalmic viscosurgical devices (viscoelastics) (avoid preservatives)
5. Pressure patch
6. Bandage contact lens
7. Anti collagenolytics
 - a. Sodium citrate/medroxyprogesterone/tetracycline
8. Immunosuppression (e.g. cyclophosphamide)
9. Autologous serum tears
10. Epidermal and nerve growth factors and retinoids (off label use)

B. Describe surgical therapy options

1. Debridement of devitalized tissue
2. Punctal occlusion
3. Tissue adhesive
4. Tarsorrhaphy
5. Conjunctival resection
6. Tenon-plasty
7. Mucous membrane graft
8. Amniotic membrane graft/patch
9. Keratoepithelioplasty or limbal allograft
10. Limbal autograft
11. Conjunctival flap
12. Lamellar or penetrating keratoplasty
13. Keratoprosthesis

V. List the complications of treatment, their prevention and management

A. Topical corticosteroids

1. May exacerbate underlying or undiagnosed infectious process
 - a. Differentiation based primarily on history and clinical findings
 - b. May exclude other viral or bacterial processes with appropriate cultures
2. May limit repair processes and permit collagenolytic debridement of the stroma

- a. Continued intensive use of corticosteroid should be continued beyond 10 to 14 days only with close observation until reepithelialization is complete

B. Immunosuppressives

- 1. Adverse reactions include but are not limited to:
 - a. Bone marrow suppression
 - b. Nephrotoxicity
 - c. Hepatotoxicity
 - d. Secondary infections and malignancies
 - e. Hemolytic anemia

VI. Describe disease-related complications

- A. Progressive, and sometimes rapid, stromal thinning**
- B. Vascularization and scar formation**
- C. Superinfection**
- D. Corneal perforation**

VII. Describe appropriate patient instructions

- A. Treatment compliance and close follow-up are key to successful treatments**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
- 2. Focal Points: Therapy of Recurrent Erosion and Persistent Defects of the Corneal Epithelium, September 1991.

Neurotrophic keratopathy

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Dysfunction of the ophthalmic (first) division of the trigeminal (fifth) cranial nerve (CN):
 - a. Trauma, including surgical injury (e.g., trigeminal rhizotomy)
 - b. Neoplasm
 - c. Herpes zoster ophthalmicus (HZO)
 - d. Herpes simplex virus (HSV) keratitis
2. Topical ophthalmic medications
 - a. Chronic topical anesthetic use/abuse
 - b. Beta blockers
3. Central nervous system compromise of trigeminal nerve function (rare)
 - a. Cerebrovascular accident
 - b. Aneurysm
 - c. Demyelinating disease (multiple sclerosis)
 - d. Dysautonomias
 - e. Congenital insensitivity to pain

B. Define the relevant aspects of epidemiology of this disease

1. Varies with etiology

C. List the pertinent elements of the history

1. Age at onset (infancy in familial dysautonomia)
2. Past medical history
3. Past ocular history (chronic-recurrent HSV keratitis)
4. Family history (familial dysautonomia)
5. Blurred vision

D. Describe pertinent clinical features

1. Decreased corneal sensation
2. Decreased tearing
3. Punctate epithelial erosions
4. Non-healing epithelial defects, sterile ulceration
5. Poorly responsive to topical lubricants

6. Central, inferior paracentral cornea most often involved
7. HSV keratitis
 - a. Punctate epithelial erosions with fluorescein staining
 - b. Chronic epithelial regeneration lines
 - c. Trophic ulcers
 - d. Thickened, rolled, gray edges, oval shape
 - e. Minimal rose bengal staining of edges
 - f. Intense fluorescein staining/pooling in base
8. HZO
9. Zosteriform rash

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Neuroimaging if suspected tumor, cerebrovascular accident, demyelinating disease

II. Define the risk factors

- A. Decreased blinking associated with visually attentive tasks**
- B. Previous HSV or HZO**
- C. Low humidity**
- D. Topical ophthalmic medications**
 1. Preservatives, especially benzalkonium chloride
 2. Trifluridine
- E. Beta-adrenergic antagonists**
- F. Diabetes mellitus**

III. List the differential diagnosis

- A. Aqueous tear deficiency**
- B. Exposure keratopathy**
- C. Toxicity of topical medications/preservatives (toxic ulcerative keratopathy)**
- D. Factitious keratopathy**
- E. Anesthetic abuse**

IV. Describe patient management in terms of treatment and follow-up

- A. Describe medical therapy options**
 1. Treatment of underlying disease

2. Tear supplementation with frequent preservative-free lubricants
3. Reduce evaporative tear loss
 - a. Goggles, moisture shields
 - b. Humidifiers
4. Treatment of any concomitant dry eye (See Aqueous tear deficiency, Sjögren syndrome and Mucin deficiency)
5. Autologous serum tears
6. Anti collagenolytic agents (such as tetracyclines, medroxyprogesterone) in more severe cases

B. Describe surgical therapy options

1. Punctal occlusion
2. Lateral or medial tarsorrhaphy
3. Correction of eyelid abnormalities, lagophthalmos
4. Amniotic membrane graft/patch

V. List the complications of treatment, their prevention and management

A. Topical lubricants

1. Complications: epithelial toxicity of preservatives
2. Prevention and management: preservative-free lubricants

B. Surgical (See Punctal occlusion, Tarsorrhaphy)

VI. Describe disease-related complications

- A. Corneal scarring**
- B. Infectious keratitis**
- C. Sterile corneal ulceration**
- D. Corneal thinning, perforation**

VII. Describe appropriate patient instructions

- A. Careful avoidance of trauma, risk factors**
- B. Proper administration of topical medications**
- C. Proper frequency and timing for use of topical lubricants**
- D. Advantages/disadvantages of different lubricants**
- E. When to seek further care**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Neurotrophic Keratitis, Module #2, 2003.

Trichiasis and distichiasis

I. Describe the approach for establishing the diagnosis

A. Describe the etiology of this disease

1. Trichiasis
 - a. Acquired misdirection of eyelashes that curve toward the ocular surface
2. Distichiasis
 - a. Accessory eyelashes growing posterior to the normal row of eyelashes
 - i. Acquired distichiasis
 - i) Extra eyelashes emerge from meibomian glands
 - ii) Aberrant eyelashes emerge from tarsus
 - ii. Congenital distichiasis
 - i) Extra row of eyelashes emerge from meibomian glands

B. List the pertinent elements of the history

1. Presence and severity of foreign-body sensation and discomfort
2. Previous treatment for abnormal eyelashes and previous eyelid surgery
3. Previous ocular surface inflammation or disease

C. Describe the pertinent clinical features

1. Location and number of misdirected eyelashes
2. Ocular surface erosion and inflammation

II. Define the risk factors

A. Chronic inflammatory conditions of the eyelid and conjunctiva

1. Mucous membrane pemphigoid
2. Stevens-Johnson syndrome
3. Chemical burn
4. Rosacea blepharoconjunctivitis
5. Trachoma
6. Staphylococcal blepharitis

B. Distichiasis can be familial or part of a hereditary syndrome

III. List the differential diagnosis

- A. Entropion**
- B. Epiblepharon**
- C. Ectodermal dysplasia**

IV. Describe patient management in terms of treatment and follow up

A. Describe medical therapy options

- 1. Lubricants
- 2. Bandage soft contact lens to protect ocular surface
- 3. Treatment of associated ocular surface disorder

B. Describe surgical therapy options

- 1. Mechanical epilation of misdirected eyelashes
- 2. Electrolysis or electrocautery (hyfrecation) or laser destruction of eyelash follicles
- 3. Cryotherapy
- 4. Incisional procedure
 - a. Eyelid splitting along the gray line with excision, electrocauterization, or cryotherapy of the hair follicles
 - b. Resection of abnormal eyelash follicles without or with mucous membrane grafting and without or with tarsal rotation and tarsotomy
 - c. Surgical correction of concomitant entropion or other abnormal eyelid position

V. List the complications of treatment, their prevention and management

A. Mechanical removal

- 1. Broken eyelashes
- 2. Regrowth of aberrant eyelashes

B. Electrolysis

- 1. Treated eyelash may not fall out
- 2. Regrowth of aberrant eyelashes

C. Cryotherapy

- 1. Loss of adjacent, normal eyelashes
- 2. Eyelid margin thinning and hypopigmentation
- 3. Regrowth of aberrant eyelashes

D. Surgical incision

1. Eyelid notching

VI. Describe disease-related complications

- A. Conjunctivitis**
- B. Punctate epithelial erosions**
- C. Corneal neovascularization, inflammation, and opacity**
- D. Bacterial keratitis**

VII. Describe appropriate patient instructions

- A. Eyelash regrowth may occur**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: The Management of Trichiasis, Module #4, 2001.
3. AAO, Focal Points: Management of Cicatricial Entropion, Trichiasis, and Distichiasis, Module #12, 1993.

Ocular surface problems related to contact lens

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease (See Contact lens-induced conjunctivitis)

1. Direct mechanical trauma from contact lens
2. Immune-mediated response to mechanical trauma
3. Hypersensitivity reaction, allergic reaction (i.e., thimerosal)
4. Hypoxic response with metabolic epithelial damage
5. Toxicity from contact lens solution (i.e., hydrogen peroxide, benzalkonium chloride, etc.)
6. Limbal stem cell deficiency

B. List the pertinent elements of the history

1. Redness
2. Itching, irritation, mucoid discharge
3. Pain
4. Blurred vision

C. Describe pertinent clinical features

1. Conjunctival changes
 - a. Papillary reaction on the superior tarsal conjunctiva, giant papillary reaction, conjunctival injection
2. Corneal changes
 - a. Peripheral corneal neovascularization
 - b. Corneal infiltrates
 - c. Subepithelial infiltrates
 - d. Corneal haze
 - e. Central epithelial edema (Sattler veil) - more commonly with hard contact lenses
 - f. Epithelial erosions
 - g. Microcystic epitheliopathy - most commonly with extended-wear soft contact lenses
 - h. Superior epithelial arcuate lesion
 - i. Advancing wavelike epitheliopathy
 - j. Dimple veil - air bubble beneath gas permeable lens may cause indentation of cornea

- k. Corneal scarring, especially apical in keratoconus
- 3. Mild iritis

II. Define the risk factors

- A. Extended contact lens wear
- B. Overnight contact lens wear
- C. Lower oxygen permeability
- D. Poor compliance with lens hygiene, wearing schedule
- E. Smoking while wearing contact lenses

III. List the differential diagnosis

- A. Viral conjunctivitis
- B. Bacterial conjunctivitis, including chlamydia
- C. Allergic conjunctivitis/keratitis
- D. Toxic conjunctivitis
- E. Staphylococcal marginal keratitis
- F. Microbial keratitis, especially bacterial

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

- 1. Acute
 - a. Stop contact lens wear
 - b. Topical antibiotics (typically topical fluoroquinolone), if infection suspected (See Bacterial keratitis)
 - c. Consider topical corticosteroids, usually low dose (if significant corneal inflammation present) and there is no evidence of infection
 - d. Refit with a flatter contact lens in a patient with tight lens syndrome after acute symptoms resolve
- 2. Chronic
 - a. Decrease contact lens wearing time
 - b. Refit patient with a different type of contact lens (i.e., daily disposable soft contact lens or a rigid gas permeable contact lens)
 - c. Improved contact lens hygiene
 - d. Rarely, treatment for significant contact lens induced stem cell deficiency may require

surgical intervention (i.e. limbal stem cell graft)

3. Follow-up in 3-7 days depending on severity of presentation

V. List the complications of treatment, their prevention and management

A. Complications of topical corticosteroids

1. Glaucoma
2. Cataract
3. Worsening of infection

B. Complications of topical antibiotics

1. Allergy
2. Resistance

C. Prevention and management

1. Use topical corticosteroids judiciously
2. Use corticosteroids concurrently with antibiotics

VI. Describe disease-related complications

A. Microbial keratitis

B. Loss of vision

C. Corneal scarring

D. Contact lens intolerance

E. Corneal warpage

VII. Describe appropriate patient instructions

A. Emphasize importance of compliance with therapy and follow-up

B. Patients should be counseled to call if increasing pain develops or the vision changes

C. Importance of proper contact lens hygiene should be stressed

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Corneal Complications of Contact Lens, Module #2, 1993.
3. Sankarigurg PR, Sweeney DF, Holden BA, et al. Comparison of adverse events with daily disposable hydrogels and eyeglass wear: results from a 12-month prospective clinical trial. *Ophthalmology*. 2003;110:2327-34.

4. Nilsson SE. Seven-day extended wear and 30-day continuous wear of high oxygen transmissibility soft silicone hydrogel contact lenses: a randomized 1-year study of 504 patients. *CLAO J.* 2001;27:125-36.
5. Polse KA, Graham AD, Fusaro RE, et al. The Berkeley Contact Lens Extended Wear Study. Part II: Clinical results. *Ophthalmology.* 2001;108:1389-99.
6. Fusaro RE, Polse KA, Graham AD, et al. The Berkeley Contact Lens Extended Wear Study. Part I: Study design and conduct. *Ophthalmology.* 2001;108:1381-8.
7. AAO, Focal Points: Surgical Techniques for Ocular Surface Reconstruction, Module #12, 2006.

Limbal stem-cell deficiency

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Aniridia
2. Congenital erythrokeratoderma or ectodermal dysplasia
3. Keratitis associated with multiple endocrine deficiencies
4. Neurotrophic (neural and ischemic) keratopathy
5. Chronic limbal inflammation
6. Dysplastic, neoplastic lesions of the limbus
7. Rosacea blepharitis
8. Atopic disease
9. Chemical injuries, including toxic topical medications, preservatives
10. Thermal injuries
11. Mechanical (surgical) injuries
12. Immunologic destruction (chronic graft vs. host disease)
13. Cicatricial conjunctivitis (Stevens-Johnson Syndrome, Trachoma, mucous membrane pemphigoid)
14. Contact lens related

B. Define the relevant aspects of epidemiology of the disease

1. Varies with etiology
2. Uncommon disease except in patients with chronic inflammatory, neurotrophic, or genetic conditions causing loss or absence of corneal stem cells

C. List the pertinent elements of the history

1. Decreased vision
2. Photophobia
3. Tearing
4. Blepharospasm
5. Recurrent episodes of pain (epithelial breakdown)
6. History of chronic inflammation with redness

D. Describe pertinent clinical features

1. Dull and irregular reflex of the corneal epithelium which varies in thickness and transparency, late fluorescein staining

2. Chronic conjunctival hyperemia
3. Chronic keratitis with chronic staining
4. Conjunctivalization/vascularization of the corneal surface
5. Demarcation line visible between corneal and conjunctival epithelial cell phenotype (conjunctival epithelial cells stain with fluorescein)
6. Persistent epithelial defects
7. Melting and perforation of the cornea in advanced and severe cases

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Careful clinical and slit-lamp biomicroscopic examination
2. Additional testing may include
 - a. Impression cytology - Examination for goblet cells, indicating presence of conjunctival epithelium on the corneal surface
 - b. Epithelial debridement - Examination for goblet cells and immuno histochemistry looking for presence of cytologic markers associated with conjunctival epithelial cells (cytokeratin 13 and 19)
 - c. In vivo laser scanning confocal microscopy: alterations in normal anatomic findings

II. Define the risk factors

A. Intrinsic diseases that can be associated with partial or total stem cell deficiency include

1. Pterygium
2. Limbal tumors
3. Aniridia
4. Mucous membrane pemphigoid (ocular cicatricial pemphigoid)
5. Chronic limbitis
6. Chronic herpes simplex epithelial disease
7. Stevens-Johnson syndrome
8. Congenital erythrokeratoderma or ectodermal dysplasia
9. Neuroparalytic keratitis
10. Atopic disease

B. Chemical or thermal exposure

C. Multiple surgeries or cryotherapies

D. Contact lens wear

E. Extensive microbial infection

F. Chronic use of topical medication

- G. Dry eye
- H. Systemic chemotherapy
- I. Allogenic bone marrow transplant

III. List the differential diagnosis

- A. Keratoconjunctivitis sicca
- B. Medication induced toxic keratitis
- C. Allergic reactions
- D. Acute herpetic eye disease
- E. Contact lens induced toxic keratitis

IV. Describe patient management in terms of treatment and follow-up

A. Describe the natural history, outcome and prognosis

1. Patients with partial stem cell deficiency
 - a. If underlying disease process is halted prior to severe corneal conjunctivalization, visual outcome is quite good
2. Patients with total stem cell failure
 - a. Progressive conjunctivalization of the cornea with loss of transparency
 - b. Possible corneal thinning, melting, perforation

B. Describe medical therapy options

1. Patients with partial stem cell deficiency
 - a. Asymptomatic patients with partial and peripheral conjunctivalization of the corneal surface may not require intervention except close follow-up for progression
 - b. Treatment of the underlying problem (e.g., dry eye, blepharitis, rosacea)
2. Patients with total stem cell deficiency
 - a. Surgical therapy options as described below
3. Treatment of associated conditions (e.g., dry eye, meibomian gland dysfunction, corneal exposure)
 - a. Nonpreserved artificial tears and ointment
 - b. Punctal plugs
 - c. Autologous serum tears

C. Describe surgical therapy options

1. Patients with partial stem cell deficiency
 - a. If the visual axis or most of the corneal surface covered with conjunctival epithelium,

mechanical debridement of conjunctival epithelium may allow adequate corneal epithelial healing to occur from the remaining functioning limbal epithelium

- b. Amniotic membrane transplantation and mechanical debridement
- 2. Patients with total stem cell deficiency
 - a. Conjunctival limbal autograft if only one eye is affected and the fellow eye is completely normal
 - b. Conjunctival limbal or keratolimbal allograft when both eyes are affected; aggressive systemic immunosuppression for at least 12 months is essential
 - i. This may be followed by keratoplasty
 - c. Oral mucosal autograft
 - d. Keratoprosthesis
- 3. Correction of any lid abnormality or ocular surface issue that may contribute to ocular surface failure (Trichiasis, entropion, symblepharon)

V. List the complications of treatment, their prevention and management

A. Complications of systemic immunosuppression

- 1. Susceptibility to infection
- 2. Renal and hepatic toxicity
- 3. Cardiovascular events (myocardial infarction and cerebrovascular accident)
- 4. Prevention and management
 - a. Involvement of transplant specialists in management of these patients

VI. Describe disease-related complications

- A. Discomfort, photophobia, and chronic inflammation
- B. Corneal neovascularization and loss of corneal transparency
- C. Corneal melt
- D. Corneal perforations

VII. Describe appropriate patient instructions

- A. Chronic nature of the disease with limited treatment options needs to be explained to patient
- B. In patients on systemic immunosuppression due to allografts, possible complications associated with the therapy as well as the importance of regular follow-up with transplant specialists to monitor for signs of toxicity is essential

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Dua HS, Saini JS, Azuara-Blanco A, Gupta P. Limbal stem cell deficiency: concept, aetiology, clinical presentation, diagnosis and management. *Indian J Ophthalmol* 2000 Jun;48(2):83-92. Review.
3. Puangsricharern V, Tseng SC. Cytologic evidence of corneal diseases with limbal stem cell deficiency. *Ophthalmology* 1995 Oct;102(10):1476-85.
4. Tseng SC. Significant impact of limbal epithelial stem cells. *Indian J Ophthalmol* 2000 Jun;48(2):79-81.

Acute conjunctivitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Person-to-person
 - a. Direct
 - i. contact with eye secretions from the infected individual
 - ii. Sexual transmission
 - b. Indirect
 - i. Contact with fomites contaminated with infectious secretions
2. Auto-inoculation
 - a. From organisms colonizing patient's own nasal and sinus mucosa
 - b. Acute conjunctivitis associated with chronic inflammatory lid disease i.e., dermatoblepharitis and/or staphylococcal marginal blepharitis
3. Environmental
 - a. Seasonal allergies
 - b. Toxic/allergic conjunctivitis triggered by topical medication or other substance

B. Define the relevant aspects of epidemiology of the disease

1. Viral and bacterial conjunctivitis preferentially affects populations living in close quarters, such as schools, nursing homes, military housing and summer camps
2. Infectious conjunctivitis generally more common in children and young adults
3. Epidemic viral keratoconjunctivitis may also be contracted in eye care providers' offices

C. List the pertinent elements of the history

1. Watery, purulent, mucoid, or stringy discharge
2. Epiphora
3. Crusting and matting of eyelids and eyelashes
4. Eye redness
5. Eyelid swelling
6. Blurry vision
7. Foreign body sensation
8. Recent upper respiratory infection
9. Recent exposure to individual with red eye

10. Recent visit to eye care provider

11. Contact lens use

D. Describe pertinent clinical features

1. Conjunctiva

a. Bulbar

i. hyperemia with or without chemosis

ii. petechiae or hemorrhage

b. Tarsal

i. papillae or follicles may develop depending upon cause

ii. pseudomembranes and membranes in severe infections

2. Cornea

a. Punctate epithelial erosions

3. Watery, serous, mucoid, or purulent discharge depending upon cause

4. Preauricular adenopathy

5. Periocular dermatitis or lid vesicles

II. List the differential diagnosis

A. Viral conjunctivitis or blepharoconjunctivitis

B. Bacterial conjunctivitis

C. Allergic conjunctivitis

D. Toxic conjunctivitis

E. Exacerbation of lid disease with spillover conjunctival inflammation

III. Describe patient management in terms of treatment and follow-up

A. Supportive treatment with cool compresses and artificial tears

B. Determine need for collection of conjunctival scraping for cytology, culture or PCR amplification

C. Topical antibacterial agent for suspected bacterial conjunctivitis

D. Systemic antibacterial agent for gonococcal conjunctivitis or chlamydial conjunctivitis

E. Topical or oral antiviral agent for suspected herpes simplex virus conjunctivitis

F. Topical corticosteroids only for severe conjunctival membranes or subepithelial corneal infiltrates decreasing vision during adenovirus conjunctivitis

G. Infectious precautions

IV. List the complications of treatment, their prevention, and management

- A. Ocular surface toxicity from topical antibiotics, antivirals, and preservatives**
- B. Antibiotics (topical and systemic)**
 - 1. Allergic reaction
 - 2. Bacterial resistance
- C. Topical corticosteroids**
 - 1. Potentiation of infection, elevated IOP, cataract formation

V. Describe disease-related complications

- A. Conjunctival scarring and symblepharon formation**
- B. Corneal infiltrates and corneal scarring**
- C. Peripheral corneal vascularization**

VI. Describe appropriate patient instructions

- A. Precautions to avoid spreading the infection to the fellow eye or other people**
 - 1. Frequent hand washing
 - 2. Avoid touching the eyes
 - 3. Use separate towels and washcloths
- B. Instructions to discontinue contact lens wear until conjunctivitis resolves**
- C. Instructions as to when to return to school or work (usually after at least 24 hours of treatment with topical antibiotics in bacterial conjunctivitis, and longer in viral conjunctivitis, which may be contagious for 10-14 days)**
- D. Instructions as to when to expect resolution of symptoms**
- E. Discard contact lenses, case, and contact lens solution**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
- 2. AAO, Preferred Practice Patterns Committee, Cornea and External Disease Panel. Conjunctivitis Preferred Practice Pattern, 2008.

Chronic conjunctivitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Inflammation of the conjunctiva lasting longer than four weeks
2. May be subdivided into
 - a. Chronic papillary conjunctivitis
 - i. Bacterial blepharoconjunctivitis
 - ii. Keratoconjunctivitis sicca
 - iii. Floppy eyelid syndrome
 - iv. Superior limbic conjunctivitis
 - v. Chronic dacryocystitis or canaliculitis
 - vi. Foreign body (unilateral)
 - vii. Toxic conjunctivitis
 - viii. Mucus-fishing syndrome
 - ix. Allergic conjunctivitis
 - i) Hay fever
 - ii) Perennial conjunctivitis
 - iii) Vernal conjunctivitis
 - iv) Atopic conjunctivitis
 - x. Giant papillary conjunctivitis (GPC) (See Contact-lens induced conjunctivitis)
 - b. Chronic follicular conjunctivitis
 - i. Chlamydial conjunctivitis
 - ii. Molluscum contagiosum
 - iii. Toxic conjunctivitis
 - iv. Trachoma
 - c. Membranous conjunctivitis
 - i. Ligneous - systemic plasminogen deficiency
 - d. Cicatrizing conjunctivitis
 - i. Mucous membrane pemphigoid (See Ocular mucous membrane pemphigoid)
 - ii. Stevens-Johnson syndrome (See Stevens-Johnson syndrome (erythema multiforme major))

- iii. Chemical burn (See Chemical (alkali and acid) injury of the conjunctiva and cornea)
 - iv. Trachoma
 - v. Chronic glaucoma medication use
- e. Granulomatous conjunctivitis
 - i. Cat-scratch disease and other causes of Parinaud oculoglandular syndrome
 - ii. Sarcoidosis
- f. Masquerade syndrome (unilateral)
 - i. Meibomian gland carcinoma

B. List the pertinent elements of the history

- 1. Watery, purulent or mucoid discharge
- 2. Itching, burning, foreign body sensation, ocular discomfort
- 3. Blurry vision
- 4. Matting of the eyelashes and crusting of eyelids
- 5. Eye redness
- 6. Eyelid swelling

C. Describe pertinent clinical features

- 1. Chronic papillary conjunctivitis
 - a. Variable features depending on the cause
 - b. Mild to moderate purulent or mucopurulent discharge
 - c. Eyelid edema or ulceration
 - d. Conjunctival chemosis and injection
 - e. Tarsal conjunctival papillae
 - f. Punctate epithelial keratopathy
 - g. Corneal stromal infiltrates (rare)
 - h. May have associated blepharitis or eyelid lesion in masquerade syndrome
 - i. Corneal phlyctenules
- 2. Allergic conjunctivitis
 - a. Small to giant conjunctival papillae
 - b. Mucoid or ropy discharge
 - c. Conjunctival injection and chemosis
 - d. Punctate epithelial keratopathy and vascularization
 - e. Corneal ulceration (shield ulcers) and scarring

3. Chronic follicular conjunctivitis
 - a. Tarsal conjunctival follicles
 - b. Watery or mucoid discharge
 - c. Preauricular adenopathy with chlamydia
 - d. Conjunctival injection
 - e. Punctate epithelial keratopathy
 - f. Subepithelial corneal infiltrates and corneal vascularization with chlamydia
4. Membranous conjunctivitis (ligneous)
 - a. "Woody" conjunctival membranes
 - b. Conjunctival injection
 - c. Eyelid edema and ptosis
 - d. Persistence and progression after surgical removal
5. Cicatrizing conjunctivitis
 - a. Symblepharon, subconjunctival fibrosis, and foreshortening of the fornices
 - b. Entropion, distichiasis and trichiasis
 - c. Mucoid discharge and conjunctival pseudomembranes
 - d. Conjunctival injection
 - e. Punctate epithelial keratopathy
 - f. Corneal vascularization and scarring
 - g. Keratinization of the ocular surface
 - h. Limbal stem cell deficiency
 - i. Systemic findings in mucous membrane pemphigoid and Stevens-Johnson syndrome
 - j. Altered tear film
6. Granulomatous conjunctivitis
 - a. Conjunctival nodules that progress to pustules and large vegetations
 - b. Conjunctival injection
 - c. Mild conjunctival discharge
 - d. Preauricular, cervical and submaxillary adenopathy
 - e. Associated systemic symptoms: fever, malaise, etc.

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Conjunctival scraping for
 - a. Giemsa stain (intracytoplasmic inclusions in Chlamydia and eosinophils in allergic conjunctivitis)

- b. Immunofluorescent antibody test (Chlamydia)
 - c. Bacterial culture and susceptibility
 - d. Viral cultures
- 2. Conjunctival biopsy for
 - a. Complement and Ig deposition along BMZ (mucous membrane pemphigoid)
 - b. Histopathology (masquerade syndrome, granulomatous conjunctivitis)
- 3. Serology for
 - a. Antibodies to *Bartonella henselae* (Cat scratch disease)
 - b. Plasminogen antigen and activity (membranous conjunctivitis)

II. Define risk factors

- A. Variable depending on cause**
- B. Direct contact with infected individual eye secretions in bacterial and viral conjunctivitis**
- C. Sexual transmission in chlamydial disease**
- D. Zoonosis exposure: cat contact in cat-scratch disease, etc.**
- E. Personal or family history of atopy in atopic keratoconjunctivitis**
- F. Use of topical or systemic medications in cicatrizing disease**
- G. History of sleep apnea for floppy eyelid syndrome**
- H. Contact lens wear (GPC)**

III. List the differential diagnosis

- A. Staphylococcal blepharitis**
- B. Meibomian gland dysfunction and rosacea**
- C. Factitious conjunctivitis**
 - 1. Anesthetic abuse
 - 2. Foreign objects: feces, dental plaque
 - 3. Secondary gain/ malingering/ psychiatric disorders
- D. Episcleritis/ scleritis**
- E. Exposure**
- F. Benign folliculosis of childhood**
- G. Thyroid eye disease**

IV. Describe the management in terms of treatment and follow-up

- A. Treatment depends upon underlying cause
- B. Oral antichlamydial agent for adult chlamydial conjunctivitis
- C. Topical antibacterial agent for bacterial blepharoconjunctivitis
- D. Eyelid lesion excision for molluscum or other inflammatory nodule
- E. Topical antihistamine, mast-cell stabilizer, corticosteroid, and/or cyclosporine for ocular allergy
- F. Topical plasminogen (ligneous conjunctivitis)
- G. Systemic medications for zoonoses
- H. Systemic immunosuppressants for immune-mediated cicatrizing diseases
- I. Discontinuing topical medications in case of medicamentosa
- J. List complications of the disease
- K. Conjunctival scarring and symblepharon
- L. Trichiasis and tear deficiency
- M. Corneal vascularization
- N. Corneal ulceration and scarring

V. List complications of treatment, prevention, and management

- A. Corneal toxicity from topical antibiotics
- B. Allergic reaction to topical antibiotics
- C. Bacterial resistance to topical antibiotics
- D. Complications of topical corticosteroids, if used (cataract, glaucoma)
- E. Side effects related to systemic medications

VI. Describe appropriate patient instructions

- A. Precautions to avoid spreading the infection to the other eye or other people, if conjunctivitis infectious in etiology
 - 1. Avoid touching the eyes
 - 2. Use separate towels and washcloths, and wash hands frequently
 - 3. Duration and mode of contagion
- B. Instructions to discontinue contact lens wear until conjunctivitis resolves
- C. Instructions as to when to expect resolution of symptoms
- D. Instruction on medications and their side effects
- E. Instructions regarding follow-up
- F. Treatment of partner in sexually transmitted diseases

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Antibiotic Use in Corneal and External Eye Infections, Module #10, 1997, p.11.
3. Watts P, Suresh P, Mezer E. Effective treatment of ligneous conjunctivitis with topical plasminogen. *Am J Ophthalmol.* 2002;133:451-455.
4. Heidemann DG, Williams GA, Hartzler M. Treatment of ligneous conjunctivitis with topical plasmin and topical plasminogen. *Cornea.* 2003;22:760-762.

Herpes simplex virus blepharitis, conjunctivitis, and blepharoconjunctivitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Usually secondary to herpes simplex virus (HSV)-1
2. Initial infection in naive individuals occurs due to exposure, often in childhood, through contact with oral secretions containing virus
3. Initial infection is followed by centripetal migration to sensory ganglia resulting in latency state (ciliary or trigeminal ganglion)
4. Replication may occur in the ganglion and travel through the sensory nerves to present as a primary infection - usually subclinical
5. Also presents as recurrent ocular infection years after the initial infection due to reactivation of latent disease in the ganglion

B. Define the relevant aspects of epidemiology of this disease

1. 33% of world population infected
2. 99% of trigeminal ganglia affected by age 60
3. HSV-1 and HSV-2 reside in ganglia
 - a. Local factors control expression
4. Primary HSV infections usually unrecognized
5. Asymptomatic viral shedding in secretions is usual mode of transmission
6. Symptomatic patients are more infectious due to greater viral load
7. Increasing role of HSV-2 in ocular disease

C. List the pertinent elements of the history

1. History of previous ocular herpes or cold sores
2. Triggers for reactivation including
 - a. Sun exposure
 - b. Recent illness
 - c. Recent ocular surgery
 - d. Stress
3. Red eye
4. Skin lesions

D. Describe the pertinent clinical features

1. Primary HSV blepharoconjunctivitis if clinically manifest is clinically indistinguishable from recurrent disease
2. Vesicles on skin or eyelid margin
 - a. Raised clear vesicles
 - b. Progress to blistered, crusted lesions
3. Follicular conjunctivitis
4. Bulbar conjunctival ulceration
5. Presence of a pre-auricular lymphadenopathy
6. Can be bilateral in 10% of cases

E. Describe appropriate testing and evaluation for establishing a diagnosis

1. Clinical signs and symptoms usually establish diagnosis as testing may have poor sensitivity as well as increased expense
2. Cytology
 - a. Scrapings from active skin vesicles or conjunctiva demonstrate intranuclear eosinophilic inclusion bodies and giant cells
3. Antigen detection tests
 - a. Immunofluorescence
 - b. Enzyme-linked immunosorbent assay (ELISA)
4. Tissue culture
 - a. Swab from vesicle, conjunctiva, or cornea
 - b. Requires viral transport media (chill with ice)
5. Polymerase chain reaction (PCR) detection of HSV DNA collected from fluid or scraping (vesicle base or conjunctiva)
6. Serologic testing
 - a. Of very little use

II. Define the risk factors (primary disease as well as recurrence)

- A. Possible genetic predisposition**
- B. Environmental triggers such as sun exposure, recent illness, recent ocular surgery**
- C. Virulent strain of HSV-1**
- D. Immunocompromised patient**

III. List the differential diagnosis

- A. Varicella zoster virus (VZV)**

- B. Adenovirus**
- C. Other causes of recurrent follicular conjunctivitis (e.g., chlamydia, molluscum)**

IV. Describe patient management in terms of treatment and follow-up

A. Define medical therapy options - shorten course of disease

1. Topical antiviral, such as trifluridine 1% solution, or ganciclovir 0.15% gel
2. Oral antivirals
 - a. Acyclovir
 - b. Valacyclovir
 - c. Famciclovir

V. List the complications of treatment, their prevention and management

A. Complications of treatment

1. Topical agents
 - a. Epithelial toxicity
 - b. Follicular conjunctivitis
 - c. Contact dermatitis
2. Oral agents - avoid use in patients with renal impairment

B. Prevention and management

1. Limit use of topical antiviral to treatment of active disease
2. Consider use of oral antivirals - tolerated well

C. Treatment of children can be complicated by tearing which dilutes the drops and can render treatment ineffective

VI. Describe disease related complications

- A. Recurrence with keratouveitis - epithelial or stromal keratitis (concurrent or sequential)**
- B. Autoinoculation resulting in herpetic whitlow due to herpetic infection of a break in the skin surface (e.g. from thumb sucking with a herpetic oral infection)**
- C. Risk of transmission to others**

VII. Describe appropriate patient instructions

- A. Stress importance of compliance and need for follow up**
- B. Awareness of symptoms that may represent toxicity**

- C. Awareness of symptoms that may represent worsening of disease**
- D. Many times a self-limited condition**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Applications of New Laboratory Diagnostic Techniques in Cornea and External Disease, Module #9, 2002.
3. AAO, Preferred Practice Patterns Committee, Cornea and External Disease Panel. Conjunctivitis Preferred Practice Pattern, 2008.
4. Acyclovir for the prevention of recurrent herpes simplex virus eye disease. Herpetic Eye Disease Study Group. N Engl J Med. 1998;339:300-6.

Herpes simplex virus epithelial keratitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Usually secondary to herpes simplex virus (HSV)-1, sometimes HSV 2
2. Initial exposure often in childhood through contact with oral lesions and secretions - primarily subclinical
3. Centripetal migration to sensory ganglia resulting in latency state (ciliary or trigeminal ganglia)
4. Reactivation of latent virus periodically
5. Centrifugal migration to the cornea via sensory nerves
 - a. Replication of viral DNA and viral proteins in the epithelial cells, followed by viral reassembly and release, resulting in cell-to-cell spread and producing characteristic dendritic epithelial keratitis.

B. Define the relevant aspects of epidemiology of this disease

1. 33% of world population infected
2. Approximately 500,000 people in the U.S. with a history of herpes simplex eye disease
3. Approximately 20,000 new cases of ocular herpes occur in the U.S. annually, and more than 28,000 reactivations occur in the U.S. annually
4. HSV latent in nearly 100% of trigeminal ganglia by age 60
5. Primary HSV infections usually unrecognized
6. Asymptomatic viral shedding is usual mode of transmission.
7. Symptomatic patients are more infectious due to greater viral load.
8. Epithelial keratitis accounts for 59% of herpetic eye disease
9. Usually unilateral, but can be bilateral in 1-10%. Bilaterally more common with risk factors of immunosuppression or atopy
10. Stress is suspected but not proven underlying factor for activation

C. List the pertinent elements of the history

1. History of previous ocular herpes or cold sores
2. Close family member with a history of frequent cold sores
3. Risk factors for HSV epithelial reactivation include sun exposure, recent illness, recent ocular surgery with topical steroid use, immunosuppression
4. Photophobia, throbbing pain, lack of foreign body sensation

D. Describe the pertinent clinical features

1. Punctate epithelial keratitis

- a. Often seen in early stages of recurrence
- 2. Dendritic epithelial keratitis
 - a. Linear lesion with dichotomous branching and terminal bulbs at the ends of branches as opposed to feathered or tapered ends in pseudodendrites
 - b. Characteristic staining with rose bengal or lissamine green
- 3. Geographic epithelial keratitis
 - a. Scalloped, pleomorphic epithelial ulceration
 - b. May have peripheral branches similar to dendrites
 - c. Borders stain with rose Bengal or lissamine green
 - d. Often associated with use of topical corticosteroids or seen in immunocompromised host
- 4. Conjunctivitis
 - a. Unilateral follicular conjunctivitis that differentiates it from adenoviral conjunctivitis as that is usually bilateral
 - b. May be associated with periocular vesicles that make the diagnosis straightforward
- 5. HSV ocular infections in children present special problems
 - a. Children are difficult to examine
 - b. Crying may dilute the drops
 - c. Corneal scarring may lead to amblyopia

E. Describe appropriate testing and evaluation for establishing a diagnosis

- 1. Clinical signs and symptoms usually establish diagnosis as testing may have poor sensitivity as well as increased expense
- 2. Cytology
 - a. Scrapings from active skin vesicles
 - b. Intranuclear eosinophilic inclusion bodies and giant cells
- 3. Tissue culture
 - a. Swab from vesicle, conjunctiva, or cornea
 - b. Requires viral transport media (chill with ice)
- 4. Fluorescent antibody testing of corneal swab
 - a. Smear on slide
- 5. Polymerase chain reaction (PCR) detection of HSV DNA from fluid or scrapings
- 6. Serology not especially helpful

II. Define the risk factors (primary disease as well as recurrence)

- A. Possible genetic predisposition**
- B. Environmental triggers such as sun exposure, recent illness, recent ocular surgery**
- C. Virulent strain of HSV-1**
- D. Previous episodes of HSV keratitis**

III. List the differential diagnosis

- A. Varicella zoster virus (VZV) epithelial keratitis**
- B. Toxic epitheliopathy**
 - 1. Topical medications
 - 2. Preservatives
- C. Acanthamoeba keratitis (early stage)**
- D. Epithelial regeneration lines**
 - 1. Corneal abrasion and erosions
- E. Other rare causes of dendrites or dendritiform lesions include**
 - 1. Thygeson superficial punctate keratitis
 - 2. Adenovirus keratoconjunctivitis
 - 3. Epstein-Barr virus epithelial keratitis
 - 4. Tyrosinemia type II
 - 5. Drug deposits

IV. Describe patient management in terms of treatment and follow-up

- A. Describe medical therapy options**
 - 1. Topical antivirals
 - a. Trifluridine drops 5-9x/day for 10 days until reassessed for improvement. Watch for toxicity
 - b. Gentle wiping debridement (cotton-tipped applicator)
 - c. Ganciclovir gel 5 times a day
 - 2. Oral antivirals - acyclovir, valacyclovir, famciclovir
 - a. Oral antivirals have efficacy equivalent to topical agents
 - b. The Herpetic Eye Disease Study showed no benefit from adding oral acyclovir for 3 weeks in improving outcome of epithelial disease or preventing stromal disease when used concurrently with topical trifluridine
 - 3. An active epithelial corneal infection (dendritic or geographic ulcer) is a relative contraindication for topical corticosteroid use
- B. Describe follow-up**

1. Patients are often seen at 1 week interval for assessment
2. Active keratitis should resolve in 7-14 days - residual punctate epithelial erosions can remain for weeks
3. If keratitis appears active
 - a. Consider further debridement with culture
 - b. Consider switching medications

V. List the complications of treatment, their prevention and management

A. Complications of topical treatment

1. Epithelial toxicity
2. Follicular conjunctivitis
3. Lacrimal punctal occlusion
4. Contact dermatitis

B. Prevention and management

1. Limit use of topical antiviral drops to treatment of active epithelial keratitis
2. No evidence to suggest treatment should be continued in the presence of inactive keratitis or with taper
3. Toxicity from topical drops is related to duration of treatment
4. Consider use of oral antivirals in cases of significant toxicity

VI. Describe disease-related complications

- A. Delayed epithelial healing**
- B. Stromal scarring**
- C. Stromal keratitis**
- D. Neurotrophic cornea**

VII. Describe appropriate patient instructions

- A. Stress importance of compliance and need for follow up**
- B. Awareness of symptoms that may represent toxicity**
- C. Awareness of symptoms that may represent worsening of disease (stromal keratitis)**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

2. AAO, Focal Points: Applications of New Laboratory Diagnostic Techniques in Cornea and External Disease, Module #9, 2002, p.5-7.
3. AAO, Focal Points: Herpes Simplex Virus Eye Disease, Module #2, 1997.
4. Predictors of recurrent herpes simplex virus keratitis. Herpetic Eye Disease Study Group. Cornea 2001;20:123-8.
5. Oral acyclovir for herpes simplex virus eye disease: effect on prevention of epithelial keratitis and stromal keratitis. Herpetic Eye Disease Study Group. Arch Ophthalmol 2000;118:1030-6.
6. A controlled trial of oral acyclovir for the prevention of stromal keratitis or iritis in patients with herpes simplex virus epithelial keratitis. The Epithelial Keratitis Trial. Herpetic Eye Disease Study Group. Arch Ophthalmol 1997 Jun;115:703-12.
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Herpes simplex virus stromal keratitis and endotheliitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Usually secondary to herpes simplex virus (HSV)-1, sometimes HSV 2
2. Non-necrotizing (interstitial) stromal keratitis and endotheliitis (disciform keratitis)
 - a. Likely represents humoral immunologic response to viral antigens resulting in cytotoxicity
 - b. The role of live virus and latent infection is not well-defined although HSV has been isolated from aqueous humor during HSV stromal keratouveitis
3. Necrotizing stromal keratitis
 - a. Likely represents live viral infection of keratocytes with concomitant severe immune response, occasionally with granulomatous inflammation around Descemet's membrane

B. Define the relevant aspects of epidemiology of this disease

1. Primary HSV infections usually unrecognized
2. Asymptomatic viral shedding occurs sporadically with no clearly defined stimulus
3. Approximately 20% of patients with epithelial disease develop stromal keratitis

C. List the pertinent elements of the history

1. History of previous ocular herpes, particularly previous stromal keratitis
2. Triggers for reactivation may include
 - a. Sun exposure
 - b. Fever
 - c. Recent illness
 - d. Ocular surgery
 - e. Stress
3. Duration and severity of symptoms: photophobia, pain, decreased vision

D. Describe pertinent clinical features

1. Non-necrotizing stromal keratitis
 - a. Stromal inflammation, often with associated stromal edema and endothelial pseudoguttata
 - b. May be focal or multifocal
 - c. Overlying epithelium intact
 - d. May be accompanied by anterior chamber reaction with keratic precipitates

2. Endotheliitis
 - a. Granulomatous keratic precipitates with associated overlying corneal edema
 - b. Minimal stromal inflammation
 - c. May be associated with mild anterior chamber reaction
 - d. May have increased intraocular pressure (IOP) presumed due to associated trabeculitis
3. Necrotizing stromal keratitis
 - a. Dense stromal inflammation with necrosis and occasional ulceration that can resemble microbial keratitis
 - b. Variable anterior chamber reaction that may be intense with hypopyon
 - c. May be complicated by HSV geographic epithelial keratitis or neurotrophic epithelial defect

II. Define the risk factors

- A. Atopy, immunosuppression, and malnutrition may predispose to bilateral and/or chronic HSV keratitis**
- B. Role of modifiable environmental triggers uncertain**
- C. Strain of HSV-may play a role in keratitis severity**
- D. Prior stromal keratitis is a predictor of recurrent stromal keratitis**
- E. Epithelial keratitis**

III. List the differential diagnosis

- A. Viral keratitis due to varicella zoster virus, Epstein-Barr virus, mumps, measles or vaccinia**
- B. Infection-related keratitis associated with stromal inflammation due to syphilis or Lyme disease**
- C. Inflammatory keratitis associated with Cogan syndrome or connective tissue disease**
- D. Microbial keratitis, including bacterial keratitis, fungal keratitis, and Acanthamebic keratitis**

IV. Describe patient management in terms of treatment and follow-up

- A. Define medical therapy options**
 1. Topical corticosteroids
 - a. Initial frequency and dosage according to keratitis severity
 - b. Taper very gradually over weeks to months as indicated
 - c. Some patients may need a minimal dose of steroids indefinitely to keep the keratitis quiescent
 2. Antiviral
 - a. Oral agents are used concurrently as prophylaxis against epithelial keratitis

- b. Oral agents should be considered in therapeutic doses for necrotizing keratitis prior to initiation of steroids
- c. Duration of treatment has not been standardized

B. Define surgical therapy options

1. Indicated in the following disease-related complications
 - a. Persistent epithelial defect
 - i. Tarsorrhaphy
 - ii. Amniotic membrane graft
 - iii. Conjunctival flap - consider in eyes with poor visual potential
 - b. Corneal perforation
 - i. Cyanoacrylate gluing
 - ii. Tectonic penetrating keratoplasty
 - c. Secondary scarring, lipid keratopathy, or persistent edema
 - i. Penetrating keratoplasty
 - ii. Deep anterior lamellar keratoplasty

C. Define follow-up

1. Patients are seen periodically depending on keratitis severity
2. Taper topical steroid therapy as patient shows clinical improvement
3. HSV ocular infections in children present special problems
 - a. Children are difficult to examine
 - b. Crying may dilute drops, and oral medications may be preferred
 - c. Corneal scarring may lead to amblyopia
4. Role of long-term prophylactic oral acyclovir in patients with severe or recurrent HSV keratitis

V. List the complications of treatment, their prevention and management

A. Complications of corticosteroid treatment

1. Exacerbation of active epithelial keratitis
2. Progressive corneal thinning
3. Secondary superinfection (microbial keratitis)
4. Elevated IOP
5. Cataract formation

VI. Describe disease-related complications

- A. Persistent epithelial defect**
- B. Stromal scarring**
- C. Lipid keratopathy**
- D. Corneal neovascularization**
- E. Corneal thinning and perforation**
- F. Endothelial dysfunction and corneal edema**
- G. Elevated IOP**
- H. Neurotrophic keratopathy**
- I. Keratoconjunctivitis sicca**

VII. Describe appropriate patient instructions

- A. Stress importance of compliance and need for follow up**
- B. Awareness of symptoms that may represent worsening of disease**
- C. Importance of prophylactic oral antiviral in patient with a known history of HSV ocular disease who undergoes ocular surgery**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Herpetic Eye Disease Study Group. Predictors of recurrent herpes simplex virus keratitis. *Cornea*. 2001;20:123-8.
3. Herpetic Eye Disease Study Group. Oral acyclovir for herpes simplex virus eye disease: effect on prevention of epithelial keratitis and stromal keratitis. *Arch Ophthalmol*. 2000;118:1030-6.
4. Herpetic Eye Disease Study Group. A controlled trial of oral acyclovir for iridocyclitis caused by herpes simplex virus. *Arch Ophthalmol*. 1996;1065-72.
5. Wilhelmus RK, Gee L, Hauck WW. Herpetic Eye Disease Study. A controlled trial of topical corticosteroids for herpes simplex stromal keratitis. *Ophthalmology* 1994;101:1871-82.
6. Barron BA, Gee L, Hauck WW. Herpetic Eye Disease Study. A controlled trial of oral acyclovir for herpes simplex stromal keratitis. *Ophthalmology* 1994;101:1871-82.
7. Predictors of recurrent herpes simplex virus keratitis. Herpetic Eye Disease Study Group. *Cornea* 2001;20:123-8.
8. Oral acyclovir for herpes simplex virus eye disease: effect on prevention of epithelial keratitis and stromal keratitis. Herpetic Eye Disease Study Group. *Arch Ophthalmol* 2000;118:1030-6.
9. Young RC, Hodge DO, Liesegang TJ, Baratz KH. The Incidence, Recurrence and Outcomes of Herpes Simplex Virus Eye Disease in Olmsted County, Minnesota, 1976 through 2007: The Impact of Oral Antiviral Prophylaxis *Arch Ophthalmol*. 2010; 128: 1178-1183.

Varicella zoster virus dermatoblepharitis and conjunctivitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Varicella (chickenpox)
 - a. Results from varicella zoster virus (VZV) transmission from respiratory secretions and cutaneous lesions (more common)
2. Zoster
 - a. Reactivation of latent VZV (in sensory neural ganglia)
 - b. Due to endogenous reactivation in patients with declining cell-mediated immunity to varicella zoster virus
 - c. Complications of shingles due to a combination of:
 - i. Viral infection
 - ii. Immune reaction
 - iii. Vasculitis
 - iv. Neural involvement
 - v. Scarring

B. Define the relevant aspects of epidemiology of the disease

1. Approximately 90% of individuals over 15 have been infected with VZV (typically before the age of 3)
2. Approximately 20% of adults experience zoster at some point in life
3. Zoster most frequently affects the following dermatomes:
 - a. Lower thoracic and upper lumbar distribution: most common dermatome
 - b. Ophthalmic branch of cranial nerve V is the site of recurrence in 15% of all cases of zoster (herpes zoster ophthalmicus)
4. No sexual, seasonal, or racial predilection
5. Ocular involvement in about 50-70% of patients with herpes zoster ophthalmicus
6. The widespread, recent use of the varicella vaccine for children over 12 months of age (recommended by the American Academy of Pediatrics) may have a significant impact on the future development of varicella and zoster
7. If administered prior to the onset of infection, the zoster vaccine reduces the incidence, severity, and duration of subsequent herpes zoster and reduces the incidence of postzoster neuralgia (also called postherpetic neuralgia) among older adults

8. The zoster vaccine is recommended for all immunocompetent patients over 60 years old.

C. List the pertinent elements of the history

1. Prior history of chickenpox
2. Viral prodrome (fever, malaise)
3. Tingling (pain and burning) in area supplied by the trigeminal nerve
4. Vesicular rash on face
5. Lid edema
6. Acute neuralgia

D. Describe pertinent clinical features

1. Varicella (chicken pox)
 - a. Typically develops during childhood
 - b. Usually, mild, self-limited disease, does not recur
 - c. Fever, malaise, cutaneous exanthem that lasts 7-10 days
 - d. Rash begins as macules and progresses to papules, vesicles, and pustules, mild ocular involvement
 - e. Rash is generalized
 - f. Lesions more frequent on face and trunk
 - g. Follicular conjunctivitis
 - h. Vesicles on eyelid margin or bulbar conjunctiva
 - i. Punctate or dendritic epithelial keratitis may occur concurrently with the skin lesions
 - j. Stromal keratitis, endotheliitis, uveitis, and elevated intraocular pressure are rare, but may cause significant morbidity if they occur
2. Zoster
 - a. Cranial Nerve (CN) V branches into the following nerves: ophthalmic (most commonly involved), maxillary, mandibular
 - b. Ophthalmic nerve branches into the following: frontal (most commonly affected in herpes zoster ophthalmicus), nasociliary, and lacrimal nerves (least commonly affected)
 - c. Hutchinson sign
 - i. Vesicles on the tip of the nose (nasociliary involvement, 76% chance of ocular involvement)
 - d. Painful, vesicular dermatitis localized to one dermatome, respecting the midline
 - e. Zoster dermatitis involves deeper layers of the skin than does chickenpox
 - f. Eyelid involvement may result in
 - i. Scarring

- ii. Notching of the margin
 - iii. Loss of lashes or trichiasis
 - iv. Punctal occlusion
- g. Conjunctival changes
 - i. Chronic hyperemia
 - ii. Follicular reaction
 - iii. Conjunctival scarring and symblepharon possible
- h. Corneal changes in about 66% of patients with ocular involvement in herpes zoster ophthalmicus (See Varicella zoster virus epithelial keratitis, and Varicella zoster virus stromal keratitis)
 - i. Keratouveitis
 - j. Sectoral iris atrophy
 - k. Episcleritis or scleritis
 - l. Cranial nerve involvement
 - m. Retinal involvement

E. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Clinical diagnosis primarily
- 2. Can culture vesicular lesions
- 3. Tzanck smear of vesicular fluid
- 4. Polymerase chain reaction to detect HZV DNA
- 5. Serology
- 6. Consider screening for immunosuppression in younger patients

II. Define the risk factors

A. Varicella

- 1. No prior infection or immunization
- 2. Direct or airborne exposure to secretions from person with active chickenpox or shingles

B. Zoster

- 1. Increasing age, most patients are 60-90 years old
- 2. Immunosuppressed patients (human immunodeficiency virus (HIV), chemotherapy, chronic debilitated)
- 3. Patients with malignancy
- 4. Patients undergoing chemotherapy or radiation therapy

5. VZV reactivated by unknown stimuli

III. List the differential diagnosis

- A. Impetigo
- B. Contact dermatitis
- C. Atopic dermatitis
- D. Primary HSV infection

IV. Describe patient management in terms of treatment and follow-up

A. Systemic antiviral therapy

1. Best if begun within 72 hours of onset of skin rash
 - a. Some efficacy if therapy started after 72 hours
2. For acute VZV dermatoblepharitis
 - a. Acyclovir 800 mg, 5x/day, 7-10 days
 - b. Valacyclovir 1 gram, 3 times a day (TID), 7-10 days
 - c. Famciclovir 500mg, 3 times a day (TID), 7-10 days
3. No benefit to using topical antivirals

B. Topical antibacterial therapy to prevent superinfection may help, but controversial

C. Warm compresses to skin lesions

D. Consider oral corticosteroids in specific situations

1. Optic neuritis
2. Cerebral angiitis
3. Large, hemorrhagic skin bullae
4. Progressive proptosis with ophthalmoplegia (orbital apex syndrome)
5. Acute retinal necrosis

E. Seek consultation from internist or pain specialist for management of post-herpetic neuralgia (if develops)

F. Follow-up in 3-7 days depending on severity of presentation

V. List the complications of treatment, their prevention and management

A. Systemic antiviral therapy is generally very well tolerated

1. Rarely, hepatotoxicity
2. Systemic dosage should be lowered in patients with impaired renal function

VI. Describe disease-related complications

- A. Postherpetic neuralgia**
- B. Conjunctival scarring**
- C. Trichiasis**
- D. Neurotrophic keratopathy (See Varicella zoster virus epithelial keratitis, and Varicella zoster virus stromal keratitis)**

VII. Describe appropriate patient instructions

- A. Emphasize importance of compliance with therapy and follow-up**
- B. Patients should be counseled to call if increasing pain develops or the vision changes**
- C. Avoid contact with susceptible individuals**
 - 1. Avoid contact with pregnant women who have not had chickenpox

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
- 2. AAO, Focal Points: Applications of New Laboratory Diagnostic Techniques in Cornea and External Disease, Module #9, 2002.
- 3. Colin J, Prisant O, Cochener B, et al. Comparison of the efficacy and safety of valacyclovir and acyclovir for the treatment of herpes zoster ophthalmicus. *Ophthalmology*. 2000;107:1507-11.
- 4. Neoh C, Harding SP, Saunders D, et al. Comparison of topical and oral acyclovir in early herpes zoster ophthalmicus. *Eye*. 1994;8:688-91.
- 5. Oxman MN, Levin MJ, Johnson GR, Schmader KE, Straus SE, Gelb LD, et al. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. *N Engl J Med*. 2005;352:2271-84
- 6. Tyring S, Engst R, Corriveau C, et al. Famciclovir for ophthalmic zoster: a randomized acyclovir controlled study. *Br J Ophthalmol*. 2001;85:576-81.

Varicella zoster virus epithelial keratitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Viral infection of conjunctiva and corneal epithelium after reactivation of latent varicella zoster virus (VZV) in trigeminal ganglion and viral shedding
2. Innate and adaptive immune response to VZV affect viral reactivation and shedding
 - a. Chronic infectious keratitis may occur in patients with human immunodeficiency virus (HIV) infection

B. Define the relevant aspects of epidemiology of the disease

1. Punctate epithelial keratitis and/or pseudodendrite
2. Epithelial keratitis occurs in approximately 50% of individuals with ophthalmic zoster

C. List the pertinent elements of the history

1. Prior history of chickenpox (patients may not remember)
2. Viral prodrome (fever, malaise)
3. Tingling (pain and burning) in affected dermatome
4. Vesicular rash on face
5. Lid edema
6. Acute neuralgia (93% of patients)

D. Describe pertinent clinical features

1. Varicella (chicken pox)
 - a. Usually, mild, self limited disease, does not recur
 - b. Punctate or dendritic epithelial keratitis may occur concurrently with the skin lesions
 - c. Other: subepithelial infiltrates, stromal keratitis, disciform keratitis
 - d. Corneal scarring is rare (See Varicella zoster virus dermatoblepharitis and conjunctivitis)
2. Zoster (See Varicella zoster virus dermatoblepharitis and conjunctivitis)
 - a. Punctate epithelial keratitis (occurs early)
 - i. Peripheral, multiple, raised, lesions
 - ii. Associated with conjunctivitis
 - iii. VZV has been cultured from these lesions
 - b. Pseudodendrites (occurs after 4-6 days)
 - i. Swollen, raised epithelial cells

- ii. VZV has been cultured from these lesions
- c. Corneal mucous plaques (2-3 months after presentation)
 - i. VZV has not been cultured from these lesions
 - ii. Polymerase chain reaction has shown VZV DNA
 - iii. Possible immune mediated mechanism
- d. Neurotrophic keratopathy
 - i. 25-50% of patients with corneal involvement develop some degree of neurotrophic keratopathy

E. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Primarily a clinical diagnosis (See Varicella zoster virus dermatoblepharitis and conjunctivitis)

II. Define the risk factors

A. Varicella

- 1. Non-immunized status

B. Zoster

- 1. Increasing age (#1 risk factor for herpes zoster ophthalmicus), most patients are 60-90 years old
- 2. Immunosuppression (HIV, chemotherapy, radiation therapy)
- 3. Malignancy
- 4. VZV reactivated by unknown stimuli
- 5. Non-immunized status

III. List the differential diagnosis

- A. Herpes simplex virus (HSV) epithelial keratitis**
- B. Epstein-Barr virus (EBV) epithelial keratitis**
- C. Healing corneal abrasion**
- D. Toxic keratopathy**
- E. Acanthamoeba keratitis**
- F. Thygeson superficial punctate keratitis**
- G. Unusual causes of dendritiform lesions**

IV. Describe patient management in terms of treatment and follow-up

A. Systemic antiviral therapy

- 1. Give within 72 hours of the onset of skin lesions, some effect if therapy begun within 7 days of

onset of skin lesions

2. Oral acyclovir (800 mg 5x/day), valacyclovir (1000 mg tid) or famciclovir (500 mg tid) for 7 to 10 days with dosing reduced as necessary for impaired renal function
 - a. Valacyclovir may be contraindicated in immunocompromised patients as it has been associated with thrombotic thrombocytopenic purpura and hemolytic uremic syndrome in doses above 8 g a day in these patients

B. Consider topical antibacterial therapy to prevent superinfection

C. Consider topical corticosteroids to decrease inflammation and immune reaction

1. May predispose to prolonged treatment and recurrences
2. Concomitant antiviral therapy is unnecessary
3. Taper must be very slow to prevent recurrences

D. Consider oral corticosteroids in specific situations (See Varicella zoster virus dermatoblepharitis and conjunctivitis)

E. Debridement of corneal epithelial lesions

F. Recurrent epithelial lesions may benefit from topical antiviral treatment

G. Preservative free ophthalmic lubricants

H. Hypertonic saline ointment or bandage contact lenses may be needed in refractory disease

I. Follow-up in 3-7 days depending on severity of presentation

V. List the complications of treatment, their prevention and management

A. Systemic antiviral therapy is very well tolerated

1. Rarely, hepatotoxicity and nephrotoxicity

B. Topical corticosteroids

1. May lead to prolonged need for treatment and more frequent recurrences
2. Cataracts
3. Glaucoma

C. Prevention and management

1. Limit use of corticosteroids
2. Taper medications as appropriate

VI. Describe disease-related complications

A. Corneal scarring and vascularization

B. Neurotrophic keratopathy

C. Glaucoma

D. Sectoral iris atrophy

- E. Rarely, corneal perforation**
- F. Rarely, vasculitis leading to retinal, orbital, or cranial nerve involvement**

VII. Describe appropriate patient instructions

- A. Emphasize importance of compliance with therapy and follow-up**
- B. Patients should be counseled to call if increasing pain develops or the vision changes**
- C. Avoid contact with susceptible individuals**
 - 1. Avoid contact with pregnant women who have not had chickenpox

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
- 2. AAO, Focal Points: Applications of New Laboratory Diagnostic Techniques in Cornea and External Disease, Module #9, 2002.
- 3. Marsh RJ, Cooper M. Double-masked trial of topical acyclovir and steroids in the treatment of herpes zoster ocular inflammation. British Journal of Ophthalmology, 1991,75,542-546.

Varicella zoster virus stromal keratitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Delayed hypersensitivity reaction in corneal stroma producing infiltrates and/or edema
2. Loss of corneal sensation with neurotrophic keratopathy may exacerbate or prolong stromal keratitis

B. List the pertinent elements of the history

1. Prior history of chickenpox (may not be present if mild)
2. Viral prodrome (fever, malaise)
3. Tingling (pain and burning) in effected dermatome
4. Vesicular rash on face
5. Lid edema
6. Acute neuralgia

C. Describe pertinent clinical features

1. Varicella (chicken pox)
 - a. Usually, mild, self limited disease, does not recur
 - b. Subepithelial infiltrates, stromal keratitis, disciform keratitis may occur but are rare
 - c. Corneal scarring is rare
2. Zoster (See Varicella zoster virus dermatoblepharitis and conjunctivitis)
 - a. Hutchinson sign
 - i. Vesicles on the tip of the nose (nasociliary involvement, 76% chance of ocular involvement)
 - b. Corneal changes in about 66% of patients with ocular involvement in herpes zoster ophthalmicus
 - c. Anterior stromal infiltrates- isolated or multiple, granular, dry (occurs later than 10 days after disease onset)
 - i. Stromal reaction to soluble viral antigen diffusing into the anterior stroma
 - ii. May represent direct viral cytotoxicity
 - iii. Classically described as nummular keratitis
 - iv. May result in nummular corneal scars but often resolve without scarring if treated with steroids
 - d. Stromal keratouveitis/ endotheliitis (around 2-3 months after onset)

- i. May represent direct viral invasion into the endothelium with resulting immune response
 - ii. Manifests as overlying corneal edema (disciform keratitis)
 - iii. Indistinguishable from HSV keratouveitis
- e. Neurotrophic keratopathy
 - i. Zoster ophthalmicus can result in profound corneal anesthesia
 - ii. 25-50% of patients with corneal involvement get some degree of neurotrophic keratopathy
- f. Lipid keratopathy (very late)
 - i. Leakage from corneal vessels that develop due to chronic keratitis
- g. Sclerokeratitis

D. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Clinical diagnosis primarily (See Varicella zoster virus dermatoblepharitis and conjunctivitis)

II. List the differential diagnosis

- A. Herpes simplex virus (HSV) stromal keratitis**
- B. Adenovirus keratoconjunctivitis**
- C. Epstein-Barr virus (EBV) stromal keratitis**
- D. Corneal transplant rejection**
- E. Contact lens overwear**
- F. Interstitial keratitis secondary to other causes**

III. Describe patient management in terms of treatment and follow-up

- A. Topical corticosteroid eyedrops**
- B. No need for oral or topical antiviral "cover" unlike HSV keratitis**
- C. Oral antiviral therapy for acute varicella zoster virus (VZV) blepharitis may be of benefit in decreasing incidence of stromal keratitis**
- D. Periodic follow-up is necessary to monitor the response to therapy**

IV. List the complications of treatment, their prevention and management

- A. Systemic antiviral therapy is very well tolerated**
 - 1. Rarely, hepatotoxicity
 - 2. Lower systemic dose in patients with impaired renal function
- B. Topical corticosteroids**

1. May lead to prolonged need for treatment and more frequent recurrences
2. Cataracts
3. Glaucoma

C. Prevention and management

1. Limit use of corticosteroids
2. Taper medications as appropriate

V. Describe disease-related complications

- A. Loss of vision
- B. Corneal scarring
- C. Rarely, corneal perforation
- D. Neurotrophic keratopathy
- E. Glaucoma

VI. Describe appropriate patient instructions

- A. Emphasize importance of compliance with therapy and follow-up
- B. Patients should be counseled to call if increasing pain develops or the vision changes
- C. Avoid contact with susceptible individuals
 1. Avoid contact with pregnant women who have not had chicken pox

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Applications of New Laboratory Diagnostic Techniques in Cornea and External Disease, Module #9, 2002.

Adenovirus conjunctivitis and keratoconjunctivitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Adenoviridae
 - a. Simple follicular conjunctivitis without or with punctate epithelial keratitis
 - b. Pharyngoconjunctival fever
 - c. Epidemic keratoconjunctivitis

B. Define the relevant aspects of epidemiology of the disease

1. Epidemic outbreaks
 - a. Transmission via close contact with infected persons (ocular or respiratory secretions) or contaminated fomites
 - i. Populations living in close quarters
 - ii. Contaminated instrument/supplies in physicians' offices and physicians waiting rooms
2. Sporadic cases

C. List the pertinent elements of the history

1. Simple follicular conjunctivitis
 - a. Self limited
 - b. Transient
 - c. Mild if any epithelial keratitis symptoms
2. Pharyngoconjunctival fever
 - a. Fever
 - b. Headache
 - c. Pharyngitis
 - d. Follicular conjunctivitis
 - e. Preauricular adenopathy
 - f. Mild if any epithelial keratitis symptoms
3. Epidemic keratoconjunctivitis
 - a. Majority bilateral
 - b. Possible preceding upper respiratory infection

- c. Ocular symptoms 7 to 10 days after exposure to infected person/contaminated fomite
- d. Photophobia, epiphora, foreign body sensation possibly reduced visual acuity (associated with subepithelial infiltrates)

D. Describe pertinent clinical features

- 1. Acute conjunctivitis
 - a. Follicular conjunctivitis: tarsal conjunctival follicles
 - b. Bulbar conjunctival hyperemia and chemosis
 - c. Petechial hemorrhages
 - d. Pseudomembranes/membranes
- 2. Epithelial keratitis
 - a. First week of infection
 - i. Minute punctate epithelial opacities
 - ii. Fine punctate epithelial keratitis
 - b. Second week of infection
 - i. Coarse deep epithelial granular infiltrates
 - ii. Punctate epithelial keratitis resolves
 - iii. Possible central geographic erosions
 - iv. Subepithelial infiltrates
- 3. Extraocular
 - a. Preauricular adenopathy

E. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. The diagnosis of adenovirus conjunctivitis is usually based on clinical findings
- 2. Laboratory testing may be used as an adjunct to clinical diagnoses when the physician needs to differentiate adenovirus conjunctivitis from other causes of acute conjunctivitis
 - a. Laboratory tests with good sensitivity and specificity include the detection of infectious virus by cell culture and detection of viral antigen by commercially available immunoassay kit

II. Define the risk factors

A. Exposure to infected individual or contaminated fomite

III. List the differential diagnosis

A. Non-adenoviral viral conjunctivitis

- 1. Herpes simplex virus (HSV) blepharokeratoconjunctivitis

2. Varicella zoster virus (VZV) blepharokeratoconjunctivitis
3. Molluscum contagiosum-associated blepharoconjunctivitis

- B. Bacterial conjunctivitis**
- C. Allergic conjunctivitis**
- D. Toxic keratoconjunctivitis**

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Supportive
 - a. Cool compresses
 - b. Artificial tears
 - c. Topical vasoconstrictor
2. Pseudomembranes/membranes
 - a. Mechanical removal every 2-3 days
 - b. Topical corticosteroid
3. Subepithelial infiltrates
 - a. Topical corticosteroid
 - b. Topical cyclosporine

V. List the complications of treatment, their prevention and management

A. Topical corticosteroid

1. May exacerbate herpetic keratoconjunctivitis or bacterial conjunctivitis in case of misdiagnosis or coinfection
 - a. Differentiation based primarily on history and clinical findings
 - i. May exclude other viral or bacterial processes with appropriate cultures
2. May prolong shedding of adenovirus
 - a. Use only for visually significant (photophobia/reduced visual activity) subepithelial opacities and conjunctival membranes
 - b. May use topical cyclosporine in place of topical corticosteroid
 - c. May use topical nonsteroidal anti-inflammatory drugs (NSAIDs) instead of topical corticosteroids for discomfort, if vision unaffected or to wean off topical corticosteroids

VI. Describe disease-related complications

A. Following pseudomembrane/membrane formation

1. Conjunctival scarring
2. Forniceal foreshortening (more likely to get lacy scar of tarsal conjunctiva)
3. Symblepharon formation
4. Aqueous tear deficiency secondary to scarring of lacrimal ductules (very rare)

B. Following chronic recurrent subepithelial infiltrates

1. Photophobia or glare
2. Reduced visual acuity

VII. Describe appropriate patient instructions

A. Avoidance of transmission during period of viral shedding (7-10 days after onset of clinical signs and symptoms)

1. Avoidance of direct transmission
 - a. Frequent handwashing
 - b. Not touching eyes
 - c. Leave from work or school while shedding
2. Avoidance of indirect transmission
 - a. Cleaning linens
 - b. Not sharing objects with others

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Update on Ocular Allergy, Module #5, 1994.
3. AAO, Preferred Practice Patterns Committee, Cornea and External Disease Panel. Conjunctivitis Preferred Practice Pattern, 2008.

Staphylococcal blepharitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Bacterial infection of the eyelids caused usually by *Staphylococcus aureus*, but occasionally by coagulase-negative staphylococci

B. List the pertinent elements of the history

1. Burning, itching, foreign body sensation
2. Crusting of the eyelids, particularly on awakening
3. Blurred vision (occasionally)
4. Eye pain and photophobia (occasionally)

C. Describe pertinent clinical features

1. Hard, brittle, fibrinous scales and hard, matted crusts surrounding individual eyelashes
2. Eyelid ulceration, injection and telangiectases of the anterior and posterior eyelid margins
3. Poliosis (whitening of lashes), madarosis (loss of lashes) and trichiasis
4. Papillary conjunctivitis, occasionally with mucopurulent discharge
5. Corneal punctate epithelial erosions

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Eyelid culture and susceptibility
2. Conjunctival culture and susceptibility, if conjunctivitis present

II. Define risk factors

A. Younger age

B. Certain systemic conditions

1. Down syndrome

III. List the differential diagnosis

A. Seborrheic blepharitis

B. Meibomian gland dysfunction and rosacea

C. Infectious blepharitis secondary to other pathogens

1. *Moraxella*
2. *Corynebacterium* spp

3. *Demodex*
4. *Phthirus pubis*
- D. **Contact allergy**
- E. **Atopic dermatoblepharitis**
- F. **Discoid lupus**
- G. **Sebaceous cell carcinoma**

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Daily eyelid hygiene (warm compresses, eyelid massage, and eyelid scrubbing) with commercially available pads or using clean washcloth, soaked in warm water +/- dilute shampoo
2. Topical antibiotic ointment application
 - a. Treatment usually empirical, but cultures should be taken in cases that fail to respond to initial antibiotic therapy
 - b. Antibiotic modification depends on sensitivity testing, if cultures performed e.g. MRSA (See Bacterial keratitis)
3. Topical antibiotic solution application
 - a. If conjunctivitis present
4. Artificial tears
 - a. If aqueous tear deficiency or lipid-induced tear film instability present
5. Topical corticosteroids
 - a. If marginal corneal infiltrates or corneal vascularization or phlyctenulosis present
6. Consider systemic tetracyclines (doxycycline, minocycline), azithromycin or erythromycin for extensive or persistent disease

V. List the complications of treatment, their prevention and management

- A. **Complications of topical corticosteroids, if used (glaucoma, cataract, etc.)**
- B. **Corneal toxicity from topical antibiotics**
- C. **Allergic reactions to topical antibiotics**
- D. **Bacterial resistance from chronic use of topical antibiotic ointments and solutions**
- E. **Potential adverse effects of tetracycline and doxycycline (gastrointestinal upset, photosensitivity, contraindication in children less than 8 years, contraindication in pregnancy)**

VI. Describe disease-related complications

- A. Aqueous or lipid tear deficiency**
- B. Corneal phlyctenulosis**
- C. Corneal marginal infiltrates and ulceration**
- D. Corneal vascularization**
- E. Corneal scarring**
- F. Corneal thinning and perforation (rare)**

VII. Describe appropriate patient instructions

- A. Possible recurrent or chronic nature of this condition**
- B. Importance of daily eyelid hygiene**
- C. Instruction on proper eyelid hygiene**
- D. Instruction on medications and their side effects**
- E. Instructions regarding follow-up**

Additional Resources

1. AAO. Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Antibiotic Use in Corneal and External Eye Infections, Module #10, 1997, p.9-13.

Chronic blepharitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Chronic inflammatory condition of the eyelid margins
2. May be subdivided into
 - a. Anterior
 - i. Staphylococcal blepharitis
 - ii. Seborrheic blepharitis
 - b. Posterior
 - i. Meibomian gland dysfunction
 - c. Mixed type
 - d. Parasitic blepharitis
 - i. Demodex
 - ii. Phthiriasis/pediculosis

B. List the pertinent elements of the history

1. Burning, itching, foreign body sensation (gritty, foreign body sensation)
2. Crusting of the eyelids, particularly on awakening
3. Chronic eyelid margin redness
4. Blurred vision (occasionally)
5. Eye pain and photophobia (occasionally)
6. Diurnal variation in symptoms in some conditions
 - a. Worse in the am in staphylococcal blepharitis
 - b. Worse in the pm in meibomian blepharitis

C. Describe pertinent clinical features

1. Anterior blepharitis
 - a. Scales and crusts on eyelids
 - b. Collarettes at base of lashes
 - c. Misdirected lashes
 - d. Madarosis and poliosis
 - e. Eyelid ulceration
2. Posterior blepharitis

- a. Telangiectasias of the eyelid margin
 - b. Abnormal tear film, including rapid tear break-up time and increased debris in tear film
 - c. Meibomian gland inspissation and distortion
 - d. Foamy debris on eyelid margin
3. Anterior and posterior blepharitis
- a. Corneal punctate epithelial erosions
 - b. Papillary conjunctivitis
 - c. Corneal marginal infiltrates
 - d. Corneal vascularization
 - e. Phlyctenulosis
 - f. Tear deficiency
4. Parasitic blepharitis
- a. Demodex blepharitis
 - i. Sleeve-like encasement of the eyelash base
 - ii. Organisms demonstrable by simple light microscopy of epilated lashes
 - iii. Variable ocular surface signs of chronic blepharitis including marginal infiltrates, keratitis possibly leading to scarring and neovascularization
 - b. Phthiriasis/pediculosis
 - i. Nits on the shafts of lashes
 - ii. Pubic lice at the base of lashes
 - iii. Intense pruritus
 - iv. Occasional preauricular lymphadenopathy
 - v. Follicular conjunctivitis
 - vi. Usually sexually transmitted from pubic infestation but may rarely occur from extension of head lice

II. List the differential diagnosis

- A. Masquerade syndrome (eyelid neoplasm - rare, but should be considered in chronic unilateral blepharitis)**
- B. Allergic or atopic dermatoblepharitis**
- C. Toxic blepharoconjunctivitis**

III. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Daily eyelid hygiene (warm compresses, eyelid massage, and eyelid scrubbing) with commercially available pads or using clean washcloth, soaked in warm water +/- dilute shampoo
2. Topical antibiotic ointment or solution for staphylococcal blepharitis
3. Artificial tears, if aqueous tear deficiency or lipid-induced tear film instability present
4. Topical corticosteroid for acute exacerbations or if marginal corneal infiltrates or corneal vascularization or phlyctenulosis are present
5. Topical azithromycin drops for antibiotic and meibomian gland therapy
6. Systemic tetracycline or doxycycline for meibomian gland dysfunction or rosacea (erythromycin in children)
7. Tea Tree Oil scrubs and treatment for Demodex infestation
8. Mechanical removal and/or topical ophthalmic ointment to smother the parasites for phthiriasis

IV. List the complications of treatment, their prevention and management

- A. Complications of topical corticosteroids (glaucoma and cataract)
- B. Corneal toxicity from topical antibiotics
- C. Allergic reactions to topical antibiotics
- D. Bacterial resistance from chronic use of topical antibiotic ointments and solutions
- E. Side effects related to systemic antibiotics

V. Describe disease-related complications

- A. Corneal ulceration
- B. Corneal vascularization
- C. Corneal scarring and thinning
- D. Eyelid irregularity or notch
- E. Trichiasis
- F. Madarosis
- G. Tear deficiency

VI. Describe appropriate patient instructions

- A. Chronic nature of condition
- B. Role of daily eyelid hygiene
- C. Instruction on proper eyelid cleansing
- D. Instruction on medications and their side effects

E. Instructions regarding follow-up

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Bacterial conjunctivitis in children and adults

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Transmission by direct contact with secretions from a contaminated source or an infected individual or spread from microorganisms colonizing patient's own nasal or sinus mucosa or other sites, including genital mucosa
2. Bacteria infiltrate the conjunctival epithelial layer and sometimes the substantia propria
3. Alterations in ocular surface defense mechanisms or in the ocular flora can lead to clinical infection
4. May be subdivided into:
 - a. Hyperacute onset (<24 hrs)
 - i. *Neisseria gonorrhoeae*
 - ii. *Neisseria meningitidis*
 - b. Acute or subacute onset (days)
 - i. *Staphylococcus aureus*
 - ii. *Streptococcus pneumoniae*
 - iii. *Haemophilus influenzae*
 - c. Delayed onset (days to weeks)
 - i. *Staphylococcus aureus*
 - ii. *Moraxella sp.*

B. List the pertinent elements of the history

1. Purulent or mucopurulent discharge
2. Matting of the eyelashes and crusting of eyelids
3. Eye redness
4. Eyelid swelling
5. Eye discomfort

C. Describe pertinent clinical features

1. Acute purulent conjunctivitis
 - a. Pneumococcal and *Haemophilus* conjunctivitis
 - i. Moderate purulent discharge

- ii. Eyelid edema
 - iii. Conjunctival chemosis and injection
 - iv. Conjunctival papillary reaction
 - v. Subconjunctival hemorrhage (sometimes)
- b. Staphylococcal conjunctivitis
 - i. Usually less severe discharge
 - ii. May be associated with blepharoconjunctivitis or systemic dermatologic disease.
- 2. Gonococcal conjunctivitis
 - a. Transmitted sexually (direct genital-to-hand-to-eye transmission) or from mother to baby during vaginal delivery
 - b. Severe, rapidly progressing conjunctivitis
 - c. Massive exudation and purulent discharge
 - d. Conjunctival injection and chemosis
 - e. Conjunctival inflammatory membrane
 - f. Corneal marginal infiltrates, ulceration, and perforation
 - g. Enlarged preauricular lymph node
- 3. Chlamydial conjunctivitis (See Adult chlamydial keratoconjunctivitis)

D. Describe appropriate testing and evaluation to establish the diagnosis

- 1. Culture of the conjunctiva
 - a. Immunocompromised host
 - b. Severe purulent discharge
 - c. Cases unresponsive to initial therapy
- 2. Consider nasal and throat swab if pharyngitis is present or nasolacrimal system evaluation when recurrent conjunctivitis is present
- 3. Obtain Giemsa stain and/or immunofluorescent antibody tests of the conjunctiva to rule out chlamydial conjunctivitis in chronic cases

II. List the differential diagnosis

- A. Viral conjunctivitis**
- B. Toxic conjunctivitis**
- C. Allergic conjunctivitis**
- D. Exposure keratopathy**
- E. Cat-scratch disease and other causes of Parinaud oculoglandular syndrome**
- F. Rosacea blepharoconjunctivitis**

- G. Episcleritis
- H. Dacryocystitis
- I. Preseptal cellulitis

III. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options for acute purulent conjunctivitis

1. Mild conjunctivitis may be self-limiting, but a topical antibiotic speeds clinical improvement and microbiologic remission.
2. Empiric broad-spectrum topical antibiotics four times a day for 5-7 days
 - i. Choices include
 - ii. Aminoglycoside (gentamicin or tobramycin)
 - iii. Combination antibiotic (gramicidin-polymyxin B-neomycin)
 - iv. Fluoroquinolone (ciprofloxacin, ofloxacin, levofloxacin, gatifloxacin, or moxifloxacin)
 - v. Erythromycin or bacitracin ointment.
3. If a compromised host, severe purulence, or refractory case, then obtain culture
4. In refractory case with MRSA culture positive non-responsive to the above empiric antibiotics consider fortified vancomycin four times daily for 5-7 days (See Bacterial keratitis)
5. Systemic antibiotics reserved for acute purulent conjunctivitis with pharyngitis, for conjunctivitis-otitis syndrome, and for *Haemophilus* conjunctivitis in children
 - a. Referral to a primary care physician may be necessary if other tissues or organ systems are involved
6. Consider the possibility of sexually transmitted diseases caused by *N. gonorrhoeae* or *Chlamydia trachomatis* in sexually active age groups

B. Describe medical therapy options for gonococcal conjunctivitis

1. Systemic antibiotics are necessary
2. May need to adjust systemic dose for child dosing
3. If no corneal ulceration, treat with intramuscular ceftriaxone (1 g IM), oral cefixime, or oral ciprofloxacin on outpatient basis and examine periodically until conjunctivitis is resolved
4. Due to risk of corneal ulceration and systemic spread, consider treating with IV ceftriaxone for 3 to 7 days
 - a. If penicillin allergy present, consider oral fluoroquinolone for 5 days
5. Consider topical erythromycin, bacitracin, gentamicin, tobramycin or a fluoroquinolone for conjunctivitis
6. Irrigation of the eye with normal saline can remove inflammatory material that may contribute to corneal melting

7. Follow up until conjunctivitis and corneal ulceration resolve.
8. If gonococcal conjunctivitis confirmed, treat for chlamydial infection (up to a third of patients may have concomitant Chlamydial infection)
 - a. Use oral doxycycline, or erythromycin, or tetracycline for 1 week, or one-time dose of azithromycin
9. Advise sexual partner(s) to seek treatment
10. Need to ensure that gonococcal infection and other sexually transmitted diseases are reported to the local health department

IV. List the complications of treatment, their prevention, and management

- A. Ocular surface toxicity from topical antibiotics**
- B. Allergic reaction from topical antibiotics**
- C. Side effects related to systemic antibiotics**

V. Describe appropriate patient instructions

- A. Precautions to avoid spreading the infection to the fellow eye or other people**
 1. Avoid touching the eyes
 2. Use separate towels and washcloths and wash or discard after use
 3. Wash hands frequently
- B. Instructions to discontinue contact lens wear until conjunctivitis resolves**
- C. Instructions as to when to return to school or work (usually after at least 24 hours of treatment with topical antibiotics)**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Antibiotic Use in Corneal and External Eye Infections, October 1997, p.10-11.
3. Hwang DG, Schanzlin DJ, Rotberg MH, et al. A phase III, placebo controlled clinical trial of 0.5% levofloxacin ophthalmic solution for the treatment of bacterial conjunctivitis. Br J Ophthalmol 2003;87:1004-9.
4. Sheikh A, Hurwitz B. Antibiotics versus placebo for acute bacterial conjunctivitis. Cochrane Database Syst Rev. 2006;CD001211.
5. Epling J, Smucny J. Bacterial conjunctivitis. Clin Evid 2005;756-61. Review.

Bacterial conjunctivitis of neonates

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Infection of the conjunctiva, usually transmitted from the mother to neonate during vaginal delivery
2. May be subdivided into
 - a. Neonatal gonococcal conjunctivitis
 - b. Neonatal chlamydial conjunctivitis
 - c. Other causes of bacterial conjunctivitis in neonates:
 - i. Streptococci, including viridans group streptococci
 - ii. *Staphylococcus aureus*
 - iii. *Haemophilus influenzae*
 - iv. *Moraxella catarrhalis*
 - v. *Escherichia coli* and other gram negative rods

B. Define the relevant aspects of epidemiology of the disease

1. Affects infants in the first several days to weeks of life
2. Gonococcal conjunctivitis accounts for less than 1% of the cases
3. Chlamydial conjunctivitis is the most common cause of infectious neonatal conjunctivitis

C. List the pertinent elements of the history

1. Initially, watery, bloody drainage from the infant's eyes
2. Subsequently, thick, copious purulent drainage may develop
3. Swollen, red eyelids
4. Maternal history of sexually transmitted disease (sometimes)

D. Describe the pertinent clinical features

1. Neonatal gonococcal conjunctivitis
 - a. Usually bilateral conjunctival injection and discharge 2-5 days after parturition
 - b. Serosanguineous discharge for the first several days
 - c. Copious purulent exudates may develop later
 - d. Corneal ulceration and possibly corneal perforation
 - e. Endophthalmitis (rare)
 - f. May have other sites of infection such as rhinitis and proctitis
 - g. Signs of systemic illness (meningitis, pneumonitis, arthritis-rarely)

2. Neonatal chlamydial conjunctivitis
 - a. Onset of symptoms 5 to 14 days after parturition
 - b. Copious mucopurulent discharge
 - c. Conjunctival injection and membrane formation
 - d. No follicular conjunctival reaction
 - e. Pneumonitis and otitis media (sometimes)
3. Other non-gonococcal causes of bacterial conjunctivitis
 - a. Onset of symptoms 5 to 8 days after parturition
 - b. Conjunctival injection
 - c. Purulent or mucopurulent discharge

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Recommend Gram and Giemsa stain and culture of conjunctival scrapings in all cases of neonatal conjunctivitis
 - a. Gram negative diplococci in Gonococcal disease
 - b. Giemsa stain will demonstrate basophilic, intracytoplasmic inclusion bodies in chlamydia
2. If clinical diagnosis is not confirmed on culture or scrapings, immunofluorescent antibody tests on scrapings can aid in confirming diagnosis
3. Pediatrics consultation for evaluation and management of associated systemic complications

II. List the differential diagnosis

- A. Toxic chemical conjunctivitis from silver nitrate or topical antibiotic applied at birth
- B. Viral conjunctivitis, including herpes simplex virus keratoconjunctivitis
- C. Nasolacrimal duct obstruction

III. Describe patient management in terms of treatment and follow-up for gonococcal conjunctivitis

- A. Hospital admission and infectious disease consult
- B. For nondisseminated disease
 1. Ceftriaxone injection (25-50 mg/kg) or cefotaxime (100 mg/kg) IM or IV
 2. Systemic antibiotics if mother has gonorrhea, even if no conjunctivitis present in the neonate
- C. For disseminated disease
 1. Treatment per infectious disease specialist recommendations
- D. Topical erythromycin or broad-spectrum antibiotic several times per day until conjunctivitis resolves

- E. Frequent lavage of conjunctival discharge with normal saline to reduce proteases, debris, inflammatory cells which may increase the risk of corneal ulceration
- F. Follow-up until conjunctivitis resolves
- G. May need to treat at risk contacts

IV. Describe patient management in terms of treatment and follow-up for chlamydial conjunctivitis

- A. Topical erythromycin or sulfacetamide several times a day until conjunctivitis resolves is usually adequate for treatment
- B. Treat systemically with erythromycin to prevent pneumonitis and otitis media
- C. Consult pediatrician for evaluation and management of systemic complications
- D. Follow up until the conjunctivitis is resolved

V. List the complications of treatment, their prevention, and management

- A. Corneal toxicity from topical antibiotics
- B. Allergic reaction to topical antibiotics
- C. Bacterial resistance to topical or systemic antibiotics
- D. Side effects related to systemic antibiotics

VI. Describe disease-related complications

- A. Corneal ulceration, perforation, and scarring secondary to gonococcal conjunctivitis
- B. Blindness secondary to gonococcal endophthalmitis (rare)
- C. Otitis media and pneumonitis secondary to chlamydia
- D. Disseminated gonococcal disease: arthritis, meningitis, pneumonia, and sepsis (rarely)

VII. Describe appropriate patient instructions

- A. Precautions to avoid spreading the infection to the fellow eye or other contacts
 - 1. Caregivers should use separate towels and washcloths
- B. Caregivers should wash hands frequently and wear disposable gloves when cleaning the discharge from the eye
- C. Instructions on importance of follow-up
- D. Instructions on the expected timeline for resolution of the symptoms
- E. Treatment of mother and her sexual contacts

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Antibiotic Use in Corneal and External Eye Infections, Module #10, 1997, p.11.

Adult chlamydial keratoconjunctivitis

I. Describe the approach for establishing the diagnosis

A. Describe the etiology of this disease

1. *Chlamydia trachomatis*
 - a. Obligate intracellular bacterium
2. Sexually transmitted disease
 - a. Ocular infection via direct or indirect contact with infected genital secretions

B. List the pertinent elements of the history

1. Chronic red eye (over 4 weeks in duration)
2. History of previous sexually transmitted disease
3. History of sexual activity
4. History of topical medication use

C. Describe the pertinent clinical features

1. Preauricular lymphadenopathy
2. Follicular conjunctivitis
3. Follicles in the bulbar conjunctiva and semilunar fold often seen
4. May develop mild keratitis with fine epithelial and subepithelial infiltrates and micropannus
5. Mucopurulent discharge

D. Describe appropriate testing and evaluation for establishing a diagnosis

1. Antigen detection tests
 - a. Enzyme immunoassay detects antigens in conjunctival smears
 - b. Fluorescent antibody staining
 - i. Smears
2. Cytology
 - a. Conjunctiva (Giemsa staining)
 - i. Look for intracytoplasmic basophilic inclusion bodies within epithelial cells
3. Tissue culture

II. Define the risk factors

A. History of previous sexually transmitted disease

B. History of sexual activity

III. List the differential diagnosis

- A. Adenovirus conjunctivitis**
- B. Herpes simplex conjunctivitis**
- C. Molluscum contagiosum blepharoconjunctivitis**
- D. Ocular surface drug reaction to topical agent(s)/Medicamentosa**
- E. Allergic conjunctivitis**

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Azithromycin 1 g as a single dose (may need to be repeated in 1 week)
2. Tetracycline 250 mg qid for 3 weeks
3. Doxycycline 100 mg bid for 3 weeks
4. Erythromycin 500 mg qid for 3 weeks
5. Retreatment may be needed
6. Treat sexual partners concomitantly

V. List the complications of treatment, their prevention and management

A. Complications of treatment - associated with medication

1. Drug allergy
2. Gastrointestinal distress
3. Photosensitivity
4. Vaginal yeast infection in women

B. Prevention and management

1. Take medication with food
2. Limit sun exposure

VI. Describe disease-related complications

- A. Often resolves spontaneously over several months**
- B. May result in corneal pannus and subepithelial scarring**
- C. Recurrence with subsequent re-infection**

VII. Describe appropriate patient instructions

- A. Stress importance of further evaluation to look for co-infection with other sexually transmitted diseases**
- B. Contact sexual partners**
 - 1. Should be treated and be assessed for sexually transmitted diseases as well
- C. Awareness of symptoms that may represent drug reaction**
- D. Need to report sexually transmitted diseases to the Health Department**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
- 2. AAO, Preferred Practice Pattern Committee, Cornea and External Disease Panel. Conjunctivitis Preferred Practice Pattern, 2008.
- 3. Katusic D, Petricek I, Mandic Z, et al. Azithromycin vs doxycycline in the treatment of inclusion conjunctivitis. *Am J Ophthalmol*. 2003;135:447-51.
- 4. Diamant J, Benis R, Schachter J, et al. Pooling of Chlamydia laboratory tests to determine the prevalence of ocular Chlamydia trachomatis infection. *Ophthalmic Epidemiol*. 2001;8:109-17.

Bacterial keratitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Disruption of epithelial integrity
2. Bacterial adherence, replication, and stromal invasion
3. Polymorphonuclear leukocytes (PMN) initiate inflammatory cascade and release other inflammatory mediators and recruit other inflammatory cells
4. Production of matrix metalloproteinases and collagenases
5. Common etiological agents: *Pseudomonas* species, other Gram-negative rods (*Serratia marcescens*), *Staphylococcal* species, *Streptococcal* species, non-tuberculosis mycobacteria, and anaerobes

B. Define the relevant aspects of epidemiology of the disease

1. People of all ages and both sexes
2. Increased risk with contact lens (CL) wear
3. Gram negative organisms in refractive CL population
4. Gram positive organisms in therapeutic CL population

C. List the pertinent elements of the history

1. Ocular symptoms
 - a. Erythema
 - b. Ocular pain
 - c. Blurred or decreased vision
 - d. Purulent discharge
 - e. Photophobia
 - f. Lid swelling
2. Duration of symptoms
3. Identification of risk factors
4. Prior ocular history, including:
 - a. Prior corneal surgery
 - b. Corneal trauma
 - c. Preexisting ocular surface disease
5. Systemic medical problems including
 - a. Immunosuppression

- b. Diabetes mellitus
- 6. Current ocular medications
- 7. History of CL use
 - a. Type (daily, 2-week, monthly disposable)
 - b. Overnight wear of CL
 - c. Poor hygiene and lens care

D. Describe pertinent clinical features

- 1. Epithelial defect
- 2. Stromal infiltrate
 - a. Severity
 - i. Edema with mild-moderate polymorphonuclear neutrophil infiltration to dense white opacity
 - b. Dimensions of ulcer
 - c. Depth
 - d. Location (central, pericentral, peripheral)
- 3. Stromal ulceration
- 4. Iritis
- 5. Hypopyon
- 6. Infectious crystalline keratopathy
 - a. Persistent bacterial infection with minimal inflammation may produce intrastromal branching pattern

E. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Indications for corneal smears and cultures
 - a. Aid in selecting antimicrobial therapy, especially if severe or sight-threatening keratitis
 - b. History suggestive of atypical pathogen (e.g., trauma with vegetable matter, immunosuppression, ocular surface disease)
 - c. Findings suggestive of unusual pathogen (e.g., raised gray ulcer, satellite or multiple lesions, feathered edge, keratoneuritis, multifocal infiltrates)
 - d. Poor responsiveness to broad-spectrum antimicrobial therapy
- 2. Corneal specimen collection
 - a. Corneal scrapings or swabbing
 - b. Corneal biopsy if scrapings negative in face of progressive disease or deep infiltrate with overlying normal tissue
 - c. Contact lenses, contact lens cases, or solutions can be cultured as they may provide useful

- information when the corneal cultures are negative
- d. Prepare smears on glass slides
- e. Inoculate directly to culture media or use transport medium to send to laboratory
- 3. Corneal smears
 - a. Chromogenic stains: gram, acid-fast (mycobacteria, *Nocardia* species), Gomori-methenamine-silver (fungi, *Acanthamoeba*)
 - b. Fluorescent stains: acridine orange (bacteria, fungi, *acanthamoeba*), calcofluor white (*acanthamoeba*, fungi)
- 4. Corneal cultures
 - a. Standard culture media
 - i. Blood agar x 2 (one anaerobic and one aerobic) (most bacteria)
 - ii. Chocolate agar (most bacteria, especially *Neisseria gonorrhoeae* and *Haemophilus* species)
 - iii. Thioglycolate broth (aerobic and anaerobic bacteria)
 - iv. Sabouraud's dextrose agar (fungi)
 - b. Special culture medium
 - i. Lowenstein-Jensen medium (mycobacteria, *Nocardia* species)
 - ii. Middlebrook agar (non-tuberculous mycobacteria)
 - iii. Buffered charcoal-yeast extract agar or non-nutrient agar with bacterial overlay (*Acanthamoeba*)

II. Define the risk factors

A. Exogenous factors

1. CL wear (especially extended-wear use)
2. Ocular trauma (including corneal foreign body)
3. Previous ocular and eyelid surgery
4. Previous corneal surgery (including refractive surgery and penetrating keratoplasty) including loose corneal sutures

B. Ocular surface disease

1. Trichiasis
2. Exposure and related eyelid malposition
3. Dry eye syndrome and related tear film deficiency states
4. Adjacent infections (blepharitis, conjunctivitis, dacryocystitis, or canaliculitis)
5. Atopic dermatitis/blepharoconjunctivitis

6. Rosacea

C. Corneal epithelial abnormalities

1. Neurotrophic keratopathy
2. Recurrent erosion syndrome
3. Herpes simplex virus keratitis
4. Corneal edema (bullous keratopathy)
5. Persistent corneal epithelial defect

D. Systemic conditions

1. Diabetes mellitus
2. Malnourishment, including vitamin A deficiency
3. Obtunded, hospitalized patient
4. Substance abuse
5. Mucous membrane disorders
 - a. Stevens-Johnson syndrome
 - b. Mucous membrane pemphigoid
6. Immunocompromise
7. Rheumatoid arthritis

III. List the differential diagnosis

- A. Herpes simplex virus necrotizing stromal keratitis**
- B. Fungal keratitis**
- C. Immune (non-microbial) keratitis**
- D. Staphylococcal marginal keratitis**
- E. *Acanthamoeba* keratitis**

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Commercially available antibiotics
 - a. Fluoroquinolones (including ciprofloxacin, ofloxacin, levofloxacin, moxifloxacin, gatifloxacin, besifloxacin)
 - i. Excellent against many gram-negative organisms
 - ii. Susceptibility gaps against some gram-positive organisms (streptococcal species (a-strep, methicillin resistant staphylococcal species (MRSA))

2. Formulated or fortified antibiotics
 - a. Gram-positive activity
 - i. Cefazolin (50 mg/ml)
 - ii. Vancomycin (25-50 mg/ml) for multiresistant strains
 - b. Gram-negative activity
 - i. Aminoglycosides (tobramycin, gentamicin) (9-14 mg/ml)
 - ii. Extended spectrum cephalosporins (ceftazidime or cefepime) (50 mg/ml)
3. Recommended initial topical broad-spectrum therapy
 - a. Fortified antibiotics with gram positive activity (Cefazolin or Vancomycin) and fortified antibiotic with gram negative activity (aminoglycoside or extended spectrum cephalosporin)
 - b. Monotherapy with fluoroquinolone (only for small, non-vision threatening ulcers)
4. Adjuvant therapy
 - a. Cycloplegic agents (e.g. cyclopentolate 1% or scopolamine 0.25%)
 - b. Role of topical corticosteroids
 - i. Avoid if causative microorganism is uncertain and effective antibacterial therapy is not assured
 - ii. Consider if individual risk-benefit assessment suggests possible value in:
 - i) Reducing corneal inflammation
 - ii) Preventing further stromal ulceration
 - iii) Decreasing risk of corneal graft rejection
 - iv) Minimizing corneal neovascularization and opacification
 - v) Improving reepithelialization
 - iii. SCUT study evaluated the effect of steroids in bacterial keratitis
 - i) Overall no benefit with steroids but no increased risk either
 - ii) Ulcers with baseline visual acuity \leq count fingers and central ulcers had better visual outcomes with steroids
 - c. Pain control
5. Frequency of topical application
 - a. Start with frequent dosing (and/or loading dose) and taper depending on clinical response
6. Frequency of follow-up visits
 - a. Depends on initial severity and on therapeutic response
 - b. Monitor for signs of improvement
 - i. Decreased pain

- ii. Consolidation and sharper demarcation of the perimeter of the infiltrate (with cessation of progression)
 - iii. Decreased density of the infiltrate
 - iv. Decreased stromal edema
 - v. Resolution of hypopyon
 - vi. Decreased anterior chamber inflammation
 - vii. Re-epithelialization
7. Modification of therapy
- a. Consider additional or alternative antibacterial agent if insufficient response or stabilization
 - b. Targeted therapy in non-responsive cases when culture results available
 - c. Individual decision-making may be guided by results of sensitivity testing
 - i. Methicillin Resistant *Staphylococcus Aureus*
 - i) Two forms
 - (i) Hospital-Acquired
 - (a) Found commonly in health care workers or chronically hospitalized, institutionalized or immunocompromised patients
 - (b) More commonly multi-drug resistant
 - (ii) Community-Acquired
 - (a) Increasing percentage of community acquired ocular infections e.g. perioperative (cataract and refractive surgery), infectious keratitis, etc.
 - ii) Diagnosis
 - (i) Suspect in at risk individuals, communities with a high proportion of clinical MRSA isolates or in infections responding poorly to therapy
 - (ii) Culture if responding poorly to empiric therapy
 - (iii) Consider culturing nares in high risk patients to identify asymptomatic carriers (as part of pre-operative evaluation)
 - iii) Treatment
 - (i) High rate of laboratory resistance to common ophthalmic antibiotics including fluoroquinolones
 - (ii) Topical or intracameral vancomycin is the preferred therapy depending on the site of infection
 - (iii) Alternative systemic drugs include linezolid, daptomycin, tigecycline
 - (iv) Alternative topical ophthalmic medications include polymyxin B/trimethoprim, chloramphenicol, bacitracin

- (v) Consider alternative perioperative antibiotics and/or Infectious Disease consultation
 - iv) Pre-operative prophylaxis for high risk patients for ocular surgery
 - (i) Polytrim or Vancomycin topically
 - (ii) Bacitracin at night
 - (iii) Consider ID consult
 - (iv) Good draping of lids/lashes
 - ii. Nontuberculous mycobacteria
 - i) Amikacin
 - ii) Clarithromycin
 - iii) Moxifloxacin, Gatifloxacin
 - iii. Fluoroquinolone resistant pseudomonas
 - i) Aminoglycosides
 - ii) Anti-pseudomonal penicillins (ticarcillin)
- 8. Describe surgical therapy options
 - a. Reconstructive penetrating keratoplasty
 - b. Corneal glue for small perforation
 - c. Tarsorrhaphy for non-healing sterile ulceration

V. List the complications of treatment, their prevention and management

A. Complications of antibiotics

- 1. Ocular surface toxicity
- 2. Allergy
- 3. Drug deposition (ciprofloxacin)

B. Complications of corticosteroids

- 1. Exacerbation of corneal infection
- 2. Elevated intraocular pressure
- 3. Cataract
- 4. Tissue loss

C. Complications of therapeutic or tectonic penetrating keratoplasty (See Penetrating keratoplasty)

- 1. Endophthalmitis
- 2. Rejection

VI. Describe disease-related complications

- A. Persistent corneal epithelial defect**
- B. Corneal thinning and perforation**
- C. Endophthalmitis**
- D. Corneal opacification and neovascularization**
- E. Irregular astigmatism with loss of vision**
- F. Cataract**

VII. Describe appropriate patient instructions

- A. Medication instruction**
 - 1. Frequency of use and duration of therapy
- B. Avoid or correct predisposing factors**
 - 1. Appropriate CL hygiene
 - a. Advise regarding increased risks associated with extended wear contact lens
 - 2. Protective eyewear if occupational or sports hazard

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
- 2. AAO, Focal Points: Antibiotic Use in Corneal and External Eye Infections, Module #10, 1997, p.11-13.
- 3. AAO, Preferred Practice Patterns Committee, Cornea and External Disease Panel. Bacterial Keratitis Preferred Practice Pattern, 2008.
- 4. Keay L, Stapleton F, Schein O. Epidemiology of contact lens-related inflammation and microbial keratitis: a 20-year perspective. *Eye Contact Lens*. 2007 Nov;33(6 Pt 2):346-53, discussion 362-3. Review.
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Fungal keratitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Filamentary fungi
 - a. *Fusarium*
 - b. *Aspergillus*
 - c. *Acremonium*
 - d. *Curvularia*
 - e. *Alternaria*
2. Yeast
 - a. *Candida*

B. Define the relevant aspects of epidemiology of the disease

1. Climate specific
 - a. In warmer and more humid regions, filamentary fungi predominate
 - b. *Candida* species, as part of the indigenous human flora, are present worldwide
 - i. Its relative frequency as a cause of keratomycosis increases in temperate zones

C. List the pertinent elements of the history

1. History of trauma with vegetative matter or contact lens wear
 - a. Agricultural workers
2. Dirt exposure in the eye
3. Foreign body sensation, conjunctival injection, photophobia and decreased vision
4. More insidious onset than with bacterial keratitis with gradually increasing pain
5. Fungal keratitis tends to have fewer inflammatory signs and symptoms during initial periods compared to bacterial keratitis
6. Need to have clinical suspicion to make the diagnosis

D. Describe pertinent clinical features

1. Filamentary fungal keratitis
 - a. Frequently a gray-white, dry-appearing infiltrate with delicate filamentous or feathery, edge
 - b. Multifocal or satellite infiltrates may be present
 - c. Endothelial plaque
 - d. Hypopyon

- a. Occasionally gray or brown pigmentation
- e. Penetration of fungus through intact Descemet membrane and results in progressive anterior chamber inflammation
- 2. Yeast keratitis
 - a. Focal dense, creamy suppuration that may resemble keratitis induced by gram-positive bacteria
- 3. Progression of either filamentous or yeast fungal keratitis
 - a. Occasional invasion of the iris tissue and posterior chamber
 - b. May result in a dense fibrinoid response in the anterior chamber
 - c. May be associated with secondary glaucoma

E. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Corneal scraping for smears and cultures
 - a. Potassium hydroxide
 - b. Gram, Giemsa, Gomori-methenamine silver, acridine orange, and calcofluor white stains
 - c. Sabouraud's agar in addition to blood agar, chocolate agar and thioglycollate broth; incubation of media at room temperature can facilitate fungal recovery
 - d. Polymerase chain reaction
- 2. Corneal biopsy if clinical suspicion with negative smear/culture or if vision threatening keratitis with lack of clinical improvement
 - a. Histopathological examination
 - b. Homogenization and culture
 - c. Superior yield to scraping
- 3. Confocal microscopy, looking for filamentous forms or spores in the corneal stroma
- 4. Anterior chamber paracentesis, if strong clinical suspicion of fungal invasion into eye and negative smear/culture of corneal specimen
- 5. Sensitivities of isolated fungi to various antifungal agents only available at few centers
 - a. Unfortunately, there is poor correlation between in vitro sensitivity and in vivo response to the antifungals

II. Define the risk factors

- A. Trauma to the cornea with plant material commonly associated with filamentary fungal keratitis**
- B. Contact lens wear**
- C. Corticosteroid therapy- appears to reduce the resistance of the cornea to fungal infection and potentiate existing fungal keratitis**
- D. Compromised immune status (e.g., patients with diabetes mellitus, chronic illness) commonly**

associated with yeast keratitis

- E. **Compromised ocular surface (e.g., chronic keratitis, persistent epithelial defect) commonly associated with yeast keratitis**
- F. **Use of broad spectrum antibiotics- provides a noncompetitive environment for fungus**
- G. **Previous corneal surgery**

III. List the differential diagnosis

- A. **Bacterial keratitis**
- B. **Acanthamoeba keratitis**
- C. **Mycobacterial keratitis**
- D. **Herpes simplex virus keratitis**
- E. **Sterile posttraumatic keratitis, including corneal burns**

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Antifungal agents are mostly fungistatic (except for amphotericin B at high doses). Prolonged topical and systemic treatment is often necessary
 - a. Problems with antifungal treatment
 - i. Local toxicity
 - ii. Poor penetration
 - iii. Lack of correlation with in vitro sensitivities and clinical response
 - iv. Expense
 - b. Yeast keratitis
 - i. First line
 - i) Topical amphotericin or voriconazole
 - ii) Add oral fluconazole or voriconazole if severe, unresponsive candidal keratitis
 - ii. Second line
 - i) Topical fluconazole or rarely miconazole
 - ii) Poor response of candidal keratitis to topical natamycin
 - c. Filamentous fungal keratitis
 - i. First line
 - i) Topical natamycin
 - ii) Add oral itraconazole, voriconazole or posaconazole if deep, progressive keratitis,

- ii. Second line
 - i) Topical voriconazole, clotrimazole, fluconazole, or amphotericin B
 - iii. Beware of natamycin-resistant isolates, including *Scedosporium*, *Paecilomyces*, and *Colletotrichum*
- 2. Corticosteroid
 - a. Not recommended for patients with fungal keratitis, early or late in the disease.

B. Describe surgical therapy options

- 1. Mechanical debridement or superficial keratectomy, especially for superficial fungal keratitis and for exophytic proliferation during therapy
 - a. Debridement increases the penetration of topical antifungals but may increase scarring
- 2. Therapeutic penetrating keratoplasty for progressive keratitis despite antifungal therapy
 - a. To prevent scleral or intraocular extension
 - b. To reconstruct structurally damaged cornea
- 3. Anterior chamber washout with antifungal medication if penetration/extension suspected
- 4. Partial conjunctival flap, with or without a debulking lamellar keratoplasty
- 5. Cryotherapy

V. List the complications of treatment, their prevention and management

A. Antifungal toxicity, with conjunctivitis and persistent corneal epithelial defect

- 1. Reduce frequency and/or concentration

B. Recurrence of fungal keratitis following penetrating keratoplasty

- 1. Continue antifungal therapy following surgery
- 2. Minimize use of corticosteroid; consider cyclosporine as adjunctive agent following keratoplasty
- 3. May consider an optical graft if initial therapeutic graft fails

VI. Describe disease-related complications

- A. Intraocular and scleral extension, with fungal endophthalmitis or fungal keratoscleritis**
- B. Corneal perforation**
- C. Residual corneal scarring and vascularization**
- D. Glaucoma**

VII. Describe appropriate patient instructions

- A. Treatment compliance and close follow-up are key to successful treatments**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Diagnosis and Management of Fungal Keratitis, Module #6, 2002.
3. AAO, Focal Points: Infectious Keratitis, Module #8, 1992, p.2-4, 10-11.
4. Bron AJ, Seal DV, Hay J. Ocular Infection: Investigation and Treatment in Practice. St Louis: Mosby; 1998.
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6. O'Day DM. Fungal keratitis. In: Leibowitz HM, Waring GO III, eds. *Corneal Disorders: Clinical Diagnosis and Management.* 2nd ed. Philadelphia: Saunders; 1998:711-718.
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Acanthamoeba keratitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Free-living pathogenic protozoa of the order *Amoeba* and genus *Acanthamoeba*
2. Microbial co-infection may be associated

B. Define the relevant aspects of epidemiology of the disease

1. Low incidence but severe morbidity
2. Pathogen widespread in nature and in tap water, swimming pools, hot tubs, contact lens cases

C. List the pertinent elements of the history

1. Contact lens wear or trauma with soil contamination
2. Variable symptoms and protracted course
 - a. Severe pain, often out of proportion to the clinical signs
 - b. May be misdiagnosed and treated as herpes simplex virus (HSV) keratitis

D. Describe pertinent clinical features

1. Early stage
 - a. Punctate epithelial granularity
 - b. Raised epithelial lines
 - c. Dendriform epitheliopathy
2. Intermediate stage
 - a. Patchy anterior stromal infiltrates
 - b. Radial perineuritis
 - c. Minimal or no stromal neovascularization
3. Advanced stage
 - a. Deep stromal infiltrates
 - b. Annular or crescentic infiltrate
 - c. Ulcerative keratitis, descemetocoele, and corneal perforation
 - d. Scleritis
 - e. Iritis and hypopyon

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Smears of corneal scrapings (cysts easier to recognize than trophozoites, which may resemble mononuclear leukocytes)

- a. Giemsa, silver, gram or acridine orange stain
 - b. Calcofluor white (cyst wall fluoresces) stain
- 2. Cultures of corneal scrapings
 - a. Non-nutrient agar plate with bacterial overlay
 - b. Blood agar plate
- 3. Corneal biopsy for culture and histopathological examination, especially if smears and cultures are negative and suspicion is high
- 4. Confocal microscopy
 - a. May identify cysts and trophozoites in vivo

II. Define the risk factors

A. Contact lens wear

- 1. Soft daily-wear > soft extended-wear > rigid gas-permeable

B. Exposure to contaminated water or soil

III. List the differential diagnosis

A. Microbial or viral keratitis

- 1. HSV keratitis
- 2. Bacterial or mycobacterial keratitis
- 3. Fungal keratitis

B. Toxic or traumatic keratitis

- 1. Abuse of local anesthetics (e.g., proparacaine)
- 2. Medication toxicity
- 3. Factitious keratitis
- 4. Posttraumatic sterile stromal keratitis

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

- 1. Medical - usually requires prolonged therapy for six months or longer
 - a. Standard therapy
 - i. Topical biguanides
 - i) Chlorhexidine digluconate 0.02%

- ii) Polyhexamethylene biguanide (PHMB, PHBG, polyhexanide) 0.02%
 - ii. Topical diamidines
 - i) Propamidine isethionate 0.1% solution (Brolene)
 - ii) Hexamidine diisethionate 0.1% (Desomedine)
- b. Adjunct therapy - Antifungal azoles
 - i. Oral
 - i) Itraconazole
 - ii) Fluconazole
 - iii) Voriconazole
 - ii. Topical
 - i) Clotrimazole
 - ii) Fluconazole
 - iii) Voriconazole

B. Describe surgical therapy options

1. Epithelial debridement, during early infection
2. Penetrating keratoplasty
 - a. Optical keratoplasty (for corneal scarring)
 - b. Tectonic keratoplasty (for corneal perforation)
 - c. Therapeutic keratoplasty (but high risk of recurrent *Acanthamoeba* keratitis in corneal graft)

C. Describe patient follow-up

1. Patients with active, infectious keratitis should be followed closely during treatment (every day to once a week, depending on clinical features and clinical course).

V. List the complications of treatment, their prevention and management

A. Topical biguanides: chlorhexidine or polyhexamethylene biguanide

1. Stinging and limited epithelial toxicity (reduce frequency of applications or discontinue)
2. Severe toxic keratoconjunctivitis (avoid higher concentration; avoid preparations containing detergent)

B. Topical diamidines: propamidine or hexamidine

1. Stinging with conjunctivitis and punctate epithelial erosions (reduce frequency)
2. Contact hypersensitivity (reduce or discontinue)

C. Topical azoles

1. Irritation (reduce frequency)

2. Drug precipitation on eyelid margin and within epithelial defect (cleanse)

D. Oral azoles

1. Drug-induced hepatotoxicity (discontinue)
2. Other adverse drug reactions, including nausea, and drug interactions, (alter dosage or discontinue)

E. Penetrating keratoplasty

1. Graft failure
2. Graft rejection
3. Recurrence of infection

VI. Describe disease-related complications

- A. Permanent corneal scarring**
- B. Corneal perforation**
- C. Progressive infection**
- D. Scleritis**
- E. Globe atrophy**

VII. Describe appropriate patient instructions

A. Good contact lens hygiene

1. Use appropriate solutions; heat disinfection and two-step hydrogen peroxide are most effective systems for eradicating amoebic contaminants
2. Avoid contact lens wear while swimming, showering or bathing in hot tubs
3. Discontinue contact lens wear if persistent irritation develops and seek medical attention
4. Always use clean contact lens case, replace case as necessary

Additional Resources

1. AAO, Focal Points: and External Disease, Module #9, 2002, p.8.
2. AAO, Focal Points: Applications of New Laboratory Diagnostic Techniques in Cornea Infectious Keratitis, Module #8, 1992, p.1-2.
3. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
4. Bron AJ, Seal DV, Hay J. Ocular Infection: Investigation and Treatment in Practice. St Louis: Mosby; 1998.
5. Murray PR, Baron EJ, Pfaller MA, et al, eds. Manual of Clinical Microbiology. 7th ed. Washington, DC: ASM Press; 1999:1413-1420.

6. Wilkins JH, Joshi N, Margolis TP. Microsporidial keratoconjunctivitis treated successfully with a short course of fumagillin. *Eye* 1994;8:703-704.
7. Hammersmith KM. Diagnosis and management of *Acanthamoeba* keratitis. *Curr Opin Ophthalmol* 2006;17:327-31.

Microbial scleritis and sclerokeratitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Important causes of infectious scleritis:
 - a. Bacteria
 - i. Pseudomonas - most common bacterial cause of scleritis
 - ii. Staphylococcus
 - iii. Streptococcus
 - iv. Nocardia
 - v. Mycobacterium tuberculosis
 - vi. Other Mycobacteria
 - vii. Treponema pallidum
 - viii. Scleritis secondary to tuberculosis and syphilis is usually associated with systemic disease
 - b. Fungi
 - i. Many different species
 - c. Viruses
 - i. Herpes simplex, virus (HSV)
 - ii. Varicella zoster virus (VZV)
 - iii. Scleritis secondary to HSV or VZV may be immune mediated (i.e., not an active or infection), or may sometimes represent an active virus infection
2. Infectious scleritis occurs more rarely than scleritis associated with systemic immune-mediated disease
3. Most common source of scleral infection is the cornea

B. List the pertinent elements of the history

1. Symptoms usually more acute (compared with immune-mediated scleritis)
2. Symptoms may be similar to bacterial keratitis
3. Very severe pain is typical feature

C. Describe pertinent clinical features

1. In cases of microbial scleritis, the cause is usually readily apparent
 - a. Adjacent corneal ulcer, scleral buckle, wound infection, foreign body
 - b. History of trauma or immunocompromise

- c. Necrosis, conjunctival defect, purulent discharge, acute pain
- d. Scleritis associated with systemic disease (tuberculosis, syphilis, varicella zoster) may appear identical to "immune-mediated" scleritis
 - i. Careful history and systemic evaluation indicated
 - ii. Scleritis secondary to tuberculosis and syphilis is usually less acute, non-suppurative, and non-necrotizing
- 2. Mucopurulent discharge may be present
- 3. Subconjunctival abscess may be present

D. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Culture material from the involved sclera, cornea, vitreous, or other obviously infected tissues (See Bacterial keratitis)

II. Define the risk factors

A. Postsurgical

- 1. Pterygium excision - risk is higher if patient had Mitomycin C, or beta-irradiation
- 2. Scleral buckle
 - a. Infections may occur immediately or years after surgery
 - b. May have extruded buckle, conjunctival abscess or pain
 - c. May be present as uveitis or choroidal abscess
- 3. Less common
 - a. Cataract surgery (scleral tunnel infection)
 - b. Glaucoma surgery
 - c. Strabismus surgery
 - d. Scleral suture abscess after any surgery

B. Posttraumatic

- 1. Fingernail
- 2. Foreign body
- 3. Any other trauma (branch, vegetable matter, etc.)
- 4. Risk is higher if immunocompromised

C. Local extension from adjacent tissues

- 1. Most commonly from the cornea to the sclera (cornea (keratitis) - most common cause of infectious scleritis
 - a. Usually bacterial (Pseudomonas most common)
 - b. Infiltrate spreads to limbus, resulting in limbal inflammation and conjunctival necrosis, and

thereafter to sclera

2. May complicate infected scleral buckle
3. Other structures (less common)
 - a. Choroid
 - b. Retina
 - c. Conjunctiva (conjunctivitis)
 - d. Orbit (cellulitis, sinusitis)
 - e. Lacrimal sac (dacryocystitis)

D. Endophthalmitis leading to panophthalmitis

E. Endogenous (rare, in general less acute and suppurative)

1. Endogenous (septic emboli, endocarditis)
2. Includes scleritis secondary to syphilis and tuberculosis

F. Secondary infection of patients with immune-mediated scleritis (superinfection)

1. An additional risk factor may be immunosuppression as part of therapy for the underlying disease

III. List the differential diagnosis

- A. Immune-mediated scleritis**
- B. Episcleritis**
- C. Scleral extension of intraocular inflammation or neoplasm**
- D. Orbital cellulitis**

IV. Describe patient management in terms of treatment and follow-up

A. Therapy is directed at the causative organism

1. Topical antimicrobial agents typically used
 - a. Base on cultures and smears
2. Subconjunctival antimicrobial injections often used
3. Systemic antimicrobial agents usually necessary to achieve adequate medication levels
 - a. Specific etiologies (i.e. tuberculosis and syphilis) require systemic therapy
4. Prolonged therapy may be necessary

B. Adjuvant systemic corticosteroids may be necessary (depending on inflammation, usually contraindicated if *Pseudomonas* or fungi are causative organisms)

C. Adjuvant cryotherapy may be used for *Pseudomonas*

D. Remove any foreign bodies or foreign material (sutures, scleral buckles)

1. May also require debridement of necrotic scleral tissue

E. Follow-up in 1-7 days depending on severity of presentation

V. List the complications of treatment, their prevention, and management

A. Prevention and management (See Bacterial keratitis)

1. Taper medications as appropriate
2. Know toxicities of topical and systemic medications and monitor appropriately

VI. Describe disease-related complications

A. Endophthalmitis

B. Scleral necrosis, ulceration, thinning, and perforation (possible role of scleral grafting)

VII. Describe appropriate patient instructions

A. Emphasize importance of close follow-up

B. Discuss possible systemic side effects of medications

C. Discuss natural history of disease

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Scleritis and Episcleritis: Diagnosis and Management, Module #9, 1995.

Conjunctival inflammation with scarring

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease (See Ocular mucous membrane pemphigoid, Atopic keratoconjunctivitis, and Stevens-Johnson syndrome)

1. Underlying or predisposing disorder
 - a. Autoimmune process (e.g., mucous membrane pemphigoid, paraneoplastic pemphigus, linear immunoglobulin A dermatosis, Stevens-Johnson syndrome, atopic blepharoconjunctivitis, chronic ocular graft vs. host disease (GVHD), and lichen planus)
 - b. Infection (e.g., trachoma, adult chlamydial conjunctivitis, adenovirus keratoconjunctivitis, herpetic keratoconjunctivitis, and streptococcal conjunctivitis)
 - c. Ocular surface inflammatory condition (e.g., rosacea blepharoconjunctivitis)
 - d. Toxicity (topical medications)
 - e. Trauma, including chemical injury
 - f. History of radiation to the eye area
 - g. Genetic disorder (e.g., ligneous conjunctivitis)

B. List the pertinent elements of the history

1. Preceding pseudomembranous or membranous conjunctivitis, occasionally with previous conjunctival ulceration,
2. Environmental allergies, including asthma and eczema
3. Use of topical drugs associated with conjunctival scarring, including glaucoma medications, allergy and adverse reactions to oral medications
4. Current or previous skin rash
5. Mucosal symptoms, including mouth or gum inflammation, difficulty swallowing, hoarseness, obstructive sleep apnea, dysuria, and anogenital lesions
6. History of allogeneic transplantation or treatment with radiation to the ocular area.
7. Chronic or recurrent blepharoconjunctivitis, including dry or irritated sensation
8. History of fever, arthralgia, malaise, and respiratory symptoms associated with conjunctivitis
9. Living in a tropical, trachoma-endemic area

C. Describe the pertinent clinical features

1. Conjunctivitis, may show papillary or giant papillary conjunctivitis
2. Subepithelial fibrosis, often beginning in the inferomedial fornix and semilunar fold areas, leading to progressive conjunctival shrinkage and symblepharon
 - a. Conjunctival scar formation observed as lacy subconjunctival cicatrization, often linear, paralleling the eyelid margin, associated with trichiasis

- b. With progression, shortening of conjunctival fornix with symblepharon between the bulbar and palpebral conjunctiva
 - c. Severe cases include cicatricial entropion and ankyloblepharon
- 3. Conjunctival keratinization, hyperkeratosis
- 4. Aqueous tear deficiency
- 5. Mucin tear deficiency
- 6. Dilated tortuous conjunctival vascular changes
- 7. Lagophthalmos with exposure of the ocular surface; abnormal position of the eyelids and eyelashes including entropion, trichiasis, madarosis, and distichiasis
- 8. Corneal findings, may include punctate epithelial erosions, pannus, neurotrophic keratopathy, and subepithelial opacification
- 9. Pertinent nonocular findings
 - a. Skin lesions: non-scarring skin bullae of extremities and groin, or as erythematous plaques of the head; hyper or hypopigmentation
 - b. Oral lesions, including bullae of the mouth, nose, pharynx, or larynx; desquamative gingivitis; and esophageal strictures

D. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Accurate record keeping of sequential slit-lamp biomicroscopic examinations to evaluate presence, extent, and progression of subconjunctival scarring, fornix foreshortening, and symblepharon
- 2. Schirmer test
- 3. Culture
- 4. Histopathological evaluation
 - a. Cytological evaluation of conjunctival scraping or swabbing
 - b. Conjunctival biopsy for severe or progressive disease (See Conjunctival biopsy), including examination of cellular histopathology and immunopathology (linear deposition of immunoglobulin G, immunoglobulin A, and/or complement along epithelial base membrane)
 - c. Impression cytology of ocular surface
 - d. Biopsy of skin lesion or oral lesion

II. Define the risk factors

- A. Severe or progressive conjunctival inflammation from autoimmune or infectious disease**
- B. Exogenous exposure to inciting agent, including allergen, topical medication, or noxious chemical reagent**
- A. Possible genetic predisposition**

III. Patient Management

A. Medical therapy

1. Aggressive lubrication with drops and ointments
2. Topical corticosteroids
3. For immune-mediated diseases, topical and systemic immunosuppressive therapy when indicated
4. For infectious etiology, aggressive topical or oral antibiotic or antiviral therapy

B. Surgical interventions

1. Punctal occlusion
2. Daily lysis of symblepharon formation during active phase of the disease but remains controversial
3. Epilation of trichiasis
4. Repair of eyelid deformities
5. Ocular surface reconstruction with amniotic membrane grafting or mucous membrane grafting

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Allergic conjunctivitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Hypersensitivity reaction
2. Immunoglobulin E mediated mast cell degranulation triggering inflammatory cascade with the release of histamine and other mediators, including prostaglandins, thromboxanes, and leukotrienes
3. These various inflammatory agents, in conjunction with chemotactic factors, increase vascular permeability and result in the migration of eosinophils and neutrophils

B. List the pertinent elements of the history

1. Ocular itching, redness, and tearing
2. History of concomitant allergic rhinitis
3. Seasonal variation
4. Personal or family history of atopy, including asthma, eczema or seasonal allergies

C. Describe pertinent clinical features

1. Conjunctival injection
2. Chemosis
3. Eyelid edema
4. Papillary conjunctivitis
5. Subepithelial infiltrates may be present

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. History and clinical findings typically establish diagnosis
 - a. Superficial conjunctival scraping
 - i. Presence of eosinophils confirms diagnosis, although absence of eosinophils does not exclude it (for vernal and atopy, eosinophils very rare in epithelial scrapings)
2. Skin testing by an allergist may provide definitive diagnosis and identify the offending allergen(s)

II. Define the risk factors

A. History of atopy including allergic rhinitis

B. Seasonal variation

1. Exposure to the offending antigen

C. Awareness of common triggers

III. List the differential diagnosis

- A. Toxic conjunctivitis**
- B. Infectious conjunctivitis**
 - 1. Bacterial
 - 2. Viral

IV. Describe patient management in terms of treatment and follow-up

- A. Describe medical therapy options**
 - 1. Cool compresses
 - 2. Refrigerated artificial tears
 - 3. Topical histamine receptor antagonist
 - 4. Topical mast cell stabilizers: inhibit mast cell degranulation
 - 5. Combination agents (antihistamine, mast cell stabilizer, inhibition of inflammatory mediators)
 - 6. Mild topical corticosteroids for a limited time
 - 7. Topical vasoconstrictors
 - 8. Topical nonsteroidal anti-inflammatory drugs (NSAIDs)
 - 9. Oral antihistamines
 - 10. Avoid allergen
 - 11. De-sensitization with Allergist

V. List the complications of treatment, their prevention and management

- A. Possible reaction to medication or preservative (benzalkonium chloride)**
- B. Awareness of drug toxicity/contact allergy**
 - 1. Discontinuation of treatment as indicated
- C. Rebound from vasoconstrictor use may occur**
- D. Corticosteroids**
 - 1. Elevation of intraocular pressure
 - 2. Cataract with chronic use of steroids
 - 3. Increased risk of infection

VI. Describe disease-related complications

- A. Rarely associated with severe vision-threatening complications**
- B. Itching, tearing, and injection can be very frustrating resulting in marked discomfort and decrease in quality of life**

VII. Describe appropriate patient instructions

- A. Stress awareness of common offending antigens and avoidance of potential triggers**
- B. Educate patient regarding chronic nature of disease and reassure patient regarding long term visual prognosis**
- C. Discuss therapeutic options and outline appropriate management**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Update on Ocular Allergy, Module #5, 1994
3. AAO, Focal Points: Nonsteroidal Anti-Inflammatory Drugs, Module #6, 1997, p. 4.
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7. Daniell M, Constantinou M, Vu HT, et al. Randomised controlled trial of topical ciclosporin A in steroid dependent allergic conjunctivitis. *Br J Ophthalmol* 2006;90:461-4.
8. Butrus S, Portela R. Ocular allergy: diagnosis and treatment. *Ophthalmol Clin North Am* 2005;18:485-92.
9. Bielory B, O'Brien TP, Bielory L. Management of seasonal allergic conjunctivitis: guide to therapy. *Acta Ophthalmol* 2011:1-9.

Vernal keratoconjunctivitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Immune-mediated atopic eye disease of children
2. Hypersensitivity reaction affecting predisposed individuals during childhood until early adolescence

B. Define the relevant aspects of epidemiology of the disease

1. More prevalent in dry, hot climate countries
 - a. Common in Mediterranean area, central and West Africa, South America, Japan, and India
 - b. Less common in North America and Western Europe
2. Young males before 10 years of age more commonly affected
 - a. Disease typically lasts 2 to 10 years

C. List the pertinent elements of the history

1. History of other atopic manifestation
 - a. Eczema or asthma in three quarters of patients
 - b. A family history of atopy is found in two thirds of patients
2. Bilateral symmetrical disease
3. Seasonal exacerbations
4. Symptoms
 - a. Itching (most specific)
 - b. Photophobia
 - c. Tearing
 - d. Hyperemia
 - e. Discharge

A. Describe pertinent clinical features

5. Conjunctival
 - a. Papillae (2 forms)
 - i. Upper tarsal, classic "cobblestone papillae" frequent in Europeans and North Americans
 - ii. Limbal, gelatinous and confluent more common in African Americans and West Indian patients
 - b. Ropy mucous (associated with tarsal papillae)

- c. Horner-Trantas dots
- 6. Corneal (more common in tarsal form)
 - a. Punctate epithelial keratitis
 - b. Shield ulcer
 - c. Pseudogerontoxon - indicative of previous episode of limbal involvement

D. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Diagnosis is most commonly made clinically, without need for laboratory testing
- 2. Conjunctival biopsy or scraping may reveal presence of eosinophils

II. Define the risk factors

A. Family history (genetic predisposition)

B. Habitant of hot dry climate places

C. Patient characteristics

- 1. Young age
- 2. Male (but the disease also occurs in females)

III. List the differential diagnosis

A. Other forms of allergic conjunctivitis

- 1. Atopic keratoconjunctivitis
- 2. Seasonal allergic conjunctivitis
- 3. Perennial allergic conjunctivitis
- 4. Giant papillary conjunctivitis

B. Infectious conjunctivitis

- 1. Bacterial

C. Viral

D. Toxic keratoconjunctivitis

E. Infectious keratitis

IV. Describe patient management in terms of treatment and follow-up

A. Avoidance of allergens

- 1. Seasonal removal of affected children from their homes to a reduced allergen climate (not practical for the majority of families)
- 2. Avoid exposure to nonspecific triggering factors (sun, dust, salt water, wind)

B. Describe medical therapy options

1. Supportive
 - a. Cool compresses
 - b. Artificial tears (to dilute allergen)
2. Topical
 - a. Mast cell stabilizer/antihistamine
 - i. Mast cell stabilizer (cromolyn sodium, lodoxamide, nedocromil, and pemirolast)
 - ii. Antihistamines (levocabastine and emedastine)
 - iii. Combined mast cell stabilizer and antihistamine (azelastine, olopatadine, and ketotifen)
 - b. Anti-inflammatory
 - i. Nonsteroidal antiinflammatory drug (NSAID) (ketorolac and diclofenac)
 - ii. Topical corticosteroids
 - i) Lower absorption (fluorometholone, loteprednol, and rimexolone)
 - ii) Higher absorption: prednisolone and dexamethasone
 - iii. Topical cyclosporine
3. Systemic
 - a. Oral antihistamine (useful if other manifestations of atopic disease are present)
 - b. Oral NSAID
 - c. Oral corticosteroid in immunosuppressant doses (for vision-threatening disease)
 - d. Systemic immunomodulator (e.g., cyclosporine, for vision-threatening disease)
4. Local
 - a. Supratarsal corticosteroid injection

C. Describe surgical therapy options

1. Superior tarsal scarring producing entropion, trichiasis and corneal scarring
 - a. Buccal mucous membrane graft
2. Shield ulcer
 - a. Amniotic membrane graft

V. List the complications of treatment, their prevention and management

A. Topical mast cell stabilizers

1. May cause irritation and toxic reactions (replace or discontinue)

B. Topical antihistamine

1. Headache, burning, dry eyes, dry mouth, somnolence (replace or discontinue)

C. Topical corticosteroids

1. May induce cataract, glaucoma and infection
2. Clinician must pay close attention to initial signs and symptoms, in order to provide early treatment for these conditions

D. Topical cyclosporine

1. May cause irritation and burning

E. Systemic antihistamine

1. Somnolence, dry mouth, anorexia, or constipation

F. Oral NSAID

1. Gastrointestinal bleeding, acute renal failure

G. Oral corticosteroids

1. Major problems
 - a. Adrenal insufficiency
 - b. Peptic ulcer disease
 - c. Psychosis
 - d. Cushingoid features
 - e. Secondary infection
 - f. Aseptic necrosis of the femoral head
 - g. Hyperglycemia

H. Systemic immunomodulators

1. Internist assistance

VI. Describe disease-related complications

A. Superior tarsal papillae

1. Pseudoptosis
2. Conjunctival scarring with entropion and trichiasis, or corneal scarring

B. Limbal papillae

1. Corneal scarring, neovascularization, secondary infection

C. Shield ulcers

1. Corneal scarring, secondary infection

VII. Describe appropriate patient instructions

A. Avoidance of allergens

1. Seasonal removal of affected children from their homes to a reduced allergen climate (not practical for the majority of families)
2. Avoid exposure to nonspecific triggering factors (sun, dust, salt water, wind)

B. Compliance with treatment

C. Understand the natural history of the disease and its potential vision threatening complications

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Atopic and Vernal Keratoconjunctivitis, Module #1, 2001.
3. AAO, Focal Points: Update on Ocular Allergy, Module #5, 1994, p.2-3.
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Atopic keratoconjunctivitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Present in individuals with other, non-ocular manifestations of atopy: hay fever rhinitis, asthma, atopic dermatitis and eczema
2. Immunoglobulin (Ig) E mediated hypersensitivity reaction
3. Depressed systemic cell-mediated immunity
 - a. Increased prevalence of unilateral, bilateral, and recalcitrant herpes simplex virus (HSV) keratitis and HSV blepharitis

B. List the pertinent elements of the history

1. Non-ocular atopic disorders
2. Severe ocular itching
3. Stringy ocular discharge
4. Perennial symptoms with exacerbations and remissions

C. Describe the pertinent clinical features

1. Symptoms
 - a. Itching
 - b. Tearing
 - c. Burning
 - d. Photophobia
 - e. Decreased vision
2. Signs
 - a. Lichenification of skin of the face
 - b. Lids
 - i. Thickening (tylosis)
 - ii. Crusting
 - iii. Edema
 - iv. Ptosis
 - v. Blepharitis
 - c. Conjunctiva
 - i. Small, medium or giant papillae

- ii. Hyperemia
 - iii. "Milky" edema of tarsal conjunctiva
 - iv. Stringy discharge
 - v. Horner-Trantas dots at limbus
 - vi. Cicatrization and symblepharon in advanced disease
- d. Cornea
 - i. Punctate epitheliopathy
 - ii. Persistent epithelial defect
 - iii. Shield ulcer
 - iv. Micropannus
 - v. Subepithelial scarring
 - vi. Increased incidence of keratoconus and HSV keratitis (unilateral, bilateral or recalcitrant)
 - vii. Pannus
- e. Lens
 - i. Anterior or posterior subcapsular cataracts

II. Define the risk factors

- A. Presence of atopic disease**
- B. Exposure to environmental precipitants**

III. List the differential diagnosis

- A. Vernal keratoconjunctivitis**
- B. Allergic conjunctivitis**
- C. Contact lens-associated giant papillary conjunctivitis**
- D. Infectious conjunctivitis**
 - 1. Viral
 - 2. Bacterial
- E. Rosacea-associated blepharokeratoconjunctivitis**
- F. Medication-associated toxic conjunctivitis**

IV. Describe patient management in terms of treatment and follow-up

- A. Describe medical therapy options**

1. Topical therapy
 - a. Antihistamines
 - b. Corticosteroids
 - c. Cyclosporine
 - d. Tacrolimus or pimecrolimus for eyelid skin
2. Oral therapy
 - a. Corticosteroids
 - b. Immunosuppressants
 - i. Cyclosporine
 - c. Systemic antihistamines

B. Similar to management as vernal keratoconjunctivitis with additional monitoring for secondary infection

V. List the complications of treatment, their prevention and management

A. Complications of treatment

1. Medical
 - a. Corticosteroids
 - i. Cataracts
 - ii. Glaucoma
 - iii. Predisposition to corneal infections, reactivation of herpetic infection
2. Prevention
 - a. Limit use of topical corticosteroids
3. Management
 - a. Cataract extraction
 - b. Glaucoma drops/surgery

VI. Describe disease-related complications

A. Conjunctivitis

1. Cicatrization
2. Symblepharon

B. Cornea

1. Vascularization
2. Scarring

3. Ulceration

C. Lens

1. Anterior and posterior subcapsular opacities may develop

VII. Describe appropriate patient instructions

A. Avoid environmental precipitants

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Atopic and Vernal Keratoconjunctivitis, Module #1 2001.
3. AAO, Focal Points: Update on Ocular Allergy, Module #5, 1994, p.3.
4. Abelson MB, Udell IJ. Allergic and toxic reactions. The immune response. In: Albert DM, Jakobiec FA, eds. Principles and Practice of Ophthalmology.. 3rd ed. Philadelphia: Saunders, 2008:1:611-624
5. AAO, Preferred Practice Patterns Committee, Cornea and External Disease Panel. Conjunctivitis Preferred Practice Pattern, 2008.
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Contact lens-induced conjunctivitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Chronic conjunctival inflammation related to contact lens wear
2. More common with soft contact lens wear than with rigid gas permeable contacts
3. Immune-related response to mechanical trauma of the superior tarsus by the rough surface of a contact lens or hypersensitivity reaction to the contact lens polymer to the antigens associated with the contact lenses, or to other foreign material adhering to the contact lens polymer itself or to other foreign material, such as surface deposits, adhering to contact lenses

B. List the pertinent elements of the history

1. Decreased tolerance or inability to wear contact lenses (common)
2. Redness, itching, irritation, mucoid discharge from the eye
3. Blurred vision (occasionally)
4. Contact lens decentration, excessive movement, bloody tears, ptosis (rarely)

C. Describe pertinent clinical features

1. Papillary reaction on the superior tarsal conjunctiva
2. Papillary hypertrophy (papillae larger than 0.3 mm); in severe cases, referred to as giant papillary conjunctivitis (papillae > 1 mm)
3. Conjunctival injection and mucoid conjunctival discharge
4. Punctate epithelial erosions on the cornea
5. Peripheral corneal infiltrates
6. Corneal neovascularization (initially superiorly and then extending 360 degrees)

II. List the differential diagnosis

- A. Allergic conjunctivitis: seasonal, vernal, atopic
- B. Viral conjunctivitis
- C. Bacterial conjunctivitis, including chlamydia
- D. Toxic conjunctivitis
- E. Giant papillary conjunctivitis secondary to exposed suture, foreign body or ocular prosthesis
- F. Other causes of superior tarsal papillary conjunctivitis, such as superior limbic keratoconjunctivitis (SLK) or floppy eyelid syndrome

III. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Reduce the amount of or discontinue entirely contact lens wear. Discourage overnight use of contact lenses
2. Refit the patient with a different type of contact lens such as a daily disposable soft contact lens or a rigid gas permeable contact lens
3. Improve lens hygiene
 - a. Use hydrogen peroxide systems for disinfection
 - b. Use enzymatic treatment regularly to remove contact lens deposits
 - c. Clean and replace contact lens cases on regular basis
4. Topical mast cell stabilizers and/or antihistamines in mild cases
5. Brief course of topical corticosteroids in severe cases
6. Consider refractive surgery in patients intolerant to contact lens wear
7. Follow-up in 1-6 weeks depending on severity of presentation

IV. List the complications of treatment, their prevention and management

- A. Complications of topical corticosteroids, if used (glaucoma, cataract, etc)**
- B. Sensitivity to ophthalmic meds and preservatives**

V. Describe disease-related complications

- A. Scarring of superior tarsal conjunctiva**
- B. Ptosis**
- C. Contact lens intolerance**
- D. Corneal opacity**

VI. Describe appropriate patient instructions

- A. Chronic nature of this condition in some cases**
- B. Importance of proper lens hygiene**
- C. Importance of discontinuation of contact lens wear in persistent cases**
- D. Importance of regular follow-up**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Update on Ocular Allergy, Module #5, 1994, p.9.

3. AAO, Preferred Practice Patterns Committee. Cornea and External Disease Panel. Conjunctivitis Preferred Practice Pattern, 2008.
4. Friedlaender MH. Contact lens induced conjunctivitis: a model of human ocular inflammation. CLAO J. 1996;22:205-8.

Stevens-Johnson syndrome

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Immune-complex deposition in the dermis and conjunctival stroma
 - a. Common inciting agents
 - i. Medications including:
 - i) Sulfonamides
 - ii) Anticonvulsants
 - iii) Salicylates
 - iv) Penicillin
 - v) Ampicillin
 - vi) Isoniazid
 - ii. Infectious organisms including:
 - i) Herpes simplex virus (HSV)
 - ii) Streptococci
 - iii) Adenovirus
 - iv) Mycoplasma
 - v) *Pneumocystis carinii*
2. Pathologic changes include subepithelial bullae with subsequent scarring
3. Erythema multiforme major (Stevens-Johnson syndrome) refers to an acute vesiculobullous reaction of the skin and mucous membranes, and occurs in 20% of patients with erythema multiforme
 - a. Minor only involves skin

B. List pertinent elements of the history and define the risk factors

1. More common in
 - a. Children and young adults
 - b. Females more than males
 - c. Patients with acquired immune deficiency syndrome (AIDS), especially if treated for *Pneumocystis carinii* pneumonia
2. History of sudden onset of fever, arthralgia, malaise, and upper and lower respiratory symptoms
3. History of use or exposure to inciting agent prior to flu-like symptoms

C. List pertinent clinical features

1. Appearance of skin eruption with target lesions (red center surrounded by a pale ring and then a red ring)
 - a. Can also have maculopapular or bullous lesions
2. Mucous membranes of eyes, mouth and genitalia may be affected by bullous lesions with membrane or pseudomembrane formation
3. New lesions appear over 4-6 weeks with a 2-week cycle
4. Primary ocular finding is mucopurulent conjunctivitis; bullae and necrosis may develop
5. Late ocular complications are caused by cicatrization causing trichiasis, forniceal shrinkage, symblepharon, tear deficiency, limbal stem cell deficiency, and epithelial compromise

II. List the differential diagnosis

- A. Mucous membrane pemphigoid**
- B. Atopic keratoconjunctivitis**
- C. Acute Graft-versus-host disease**
- D. Chemical burn**
- E. Rosacea blepharoconjunctivitis**
- F. Pseudopemphigoid**

III. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Ocular lubrication with drops and ointments
2. Close surveillance for early signs of ocular infections
3. Systemic corticosteroids reduce the mortality rate and topical cyclosporine and corticosteroids may reduce surface inflammation

B. Describe surgical therapy options

1. Early
 - a. Application amniotic membrane and topical steroid to the ocular surface
 - b. Daily lysis of symblepharons controversial during acute phase because further scarring may result
2. Late
 - a. Late reconstruction of eyelid sequelae including entropion, trichiasis, fornix foreshortening
 - b. Lamellar keratoplasty, tectonic patch graft, and penetrating keratoplasty have poor prognosis but can be used in progressive thinning and perforation
 - c. Keratoprosthesis
 - d. Ocular surface reconstruction with amniotic membrane

- e. Limbal stem cell replacement

IV. List the complications of treatment, their prevention and management

A. Systemic corticosteroids may increase the risk of systemic and ocular infection, and are associated with numerous systemic complications including:

1. Gastrointestinal hemorrhage
2. Electrolyte imbalance
3. Sudden death

B. Topical corticosteroids:

1. Infection
2. Corneal thinning and perforation (See Bacterial keratitis, Corneal perforation)
3. Increased intraocular pressure

V. Describe disease-related complications

A. Conjunctival cicatrization resulting in:

1. Conjunctival shrinkage, fornix foreshortening, symblepharons
2. Trichiasis, entropion
3. Tear deficiency

B. Loss of epithelial barrier

C. Microbial keratitis

D. Corneal thinning or perforation

E. Altered ocular surface and ocular surface disease resulting in

1. Corneal neovascularization and/or superficial scarring
2. Corneal thinning

F. Limbal stem cell deficiency

VI. Describe appropriate patient instructions

A. Severe cases result in lifelong ocular morbidity

B. Close monitoring for signs of infection and thinning

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Foster CS. Immunologic disorders of the conjunctiva, cornea, and sclera. In: Albert DM, Jakobiec

FA, eds. Principles and Practice of Ophthalmology. Vol 2. 2nd ed. Philadelphia: Saunders; 2000:803-829.

3. Holland EJ, Hardten DR. Stevens-Johnson syndrome. In: Pepose JS, Holland GN, Wilhelmus KR, eds. Ocular Infection and Immunity. St Louis: Mosby; 1996:416-425.
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5. AAO, Focal Points: Surgical Techniques for Ocular Surface Reconstruction, Module #12, 2006.
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7. Shamma MC, Lai EC, Sarkar JS et al. Management of acute Stevens-Johnson syndrome and toxic epidermal necrolysis utilizing amniotic membrane and topical corticosteroid. Am J Ophthalmol. 2010;149(2):203-213.

Ocular mucous membrane pemphigoid

I. Describe the approach for establishing the diagnosis

A. Describe the etiology of this disease (also known as ocular cicatricial pemphigoid)

1. Autoimmune reaction to the conjunctival epithelial basement membrane

B. List the pertinent elements of the history

1. Chronic or recurrent blepharoconjunctivitis
2. Use of glaucoma medications and other drugs associated with conjunctival scarring
3. Skin rash or blisters
4. Mucosal symptoms affecting mouth or gums, difficulty swallowing, hoarseness, obstructive sleep apnea, dysuria, or anogenital lesions
5. Can be exacerbated by ocular or adnexal surgery

C. Describe the pertinent clinical features

1. Conjunctival and ocular surface lesions, usually bilateral
 - a. Inflammatory changes may include papillary conjunctivitis and conjunctival erosions
 - b. Conjunctival subepithelial fibrosis, that may lead to progressive conjunctival shrinkage and symblepharon
 - c. Tear deficiency
 - d. Lagophthalmos with exposure of the ocular surface and conjunctival keratinization
 - e. Abnormal position of the eyelids and eyelashes, including entropion, trichiasis, and distichiasis
2. Skin lesions (uncommon): recurrent skin bullae of extremities or groin; and erythematous plaques of the head
3. Oral or respiratory lesions (uncommon): bullae of the mouth, nose, pharynx, or larynx; desquamative gingivitis; and esophageal strictures

D. Describe appropriate testing and evaluation for establishing a diagnosis

1. Sequential examinations to evaluate progression of subconjunctival scarring, fornix foreshortening, and symblepharon
2. Conjunctival biopsy (See Conjunctival biopsy) to evaluate immunoglobulin linear deposits along the basement membrane

II. Define the risk factors

A. More common among patients older than 60 years

B. Possible response to topical medication, such as glaucoma medication

III. List the differential diagnosis

- A. Stevens-Johnson syndrome (erythema multiforme major)**
- B. Medication toxicity or allergy, including drug-induced scarring (sometimes called pseudopemphigoid)**
- C. Residual scarring following chronic conjunctival inflammation**
 - 1. Atopic conjunctivitis
 - 2. Rosacea blepharoconjunctivitis
 - 3. Graft vs. host disease

IV. Describe patient management in terms of treatment and follow-up

- A. Define medical therapy options**
 - 1. Agents to suppress inflammation and progressive cicatrization
 - a. Dapsone
 - b. Immunosuppressive agent, including cyclophosphamide, azathioprine, mycophenolate mofetil, methotrexate, or cyclosporine
 - c. Oral corticosteroid, often used as an adjunctive agent rather than as sole treatment
 - d. Immunotherapy, such as intravenous immunoglobulin and rituximab
 - 2. Lubricants and other means to control dry eye
- B. Define surgical therapy options**
 - 1. Punctal occlusion
 - 2. Correction of lid and lash malposition
 - 3. Fornix reconstruction
 - 4. Surgical repair of entropion and trichiasis
 - 5. Ocular surface reconstruction including:
 - a. Amniotic membrane transplantation
 - b. Limbal allografting
 - c. Mucous membrane grafting
 - d. Keratoplasty
 - e. Keratoprosthesis

V. List the complications of treatment, their prevention and management

- A. Bone marrow suppression, including anemia, leukopenia, and thrombocytopenia**

- B. Toxic effects on gastrointestinal tract, liver, or urinary tract**
- C. Infection**
- D. Dapsone should be used cautiously in patients with glucose-6-phosphate dehydrogenase deficiency or sulfa allergy**
- E. Corticosteroid-related effects, including osteoporosis, bone fracture, and weight change**
- F. Prevention and management of treatment-related complications (See Scleritis)**

VI. Describe disease-related complications

- A. Progressive conjunctival scarring**
 - 1. Conjunctival biopsy or other conjunctival surgery may exacerbate conjunctival scarring
 - 2. Symblepharon that may progress to obliterated conjunctival fornix and ankyloblepharon
- B. Exposure and xerosis of the ocular surface**
 - 1. Conjunctival keratinization
 - 2. Corneal neovascularization, opacification, ulceration, or perforation
 - 3. Secondary infection, including bacterial conjunctivitis and microbial keratitis
- C. Manifestations affecting other mucous membranes, including oral mucosa or respiratory tract**

VII. Describe appropriate patient instructions

- A. Awareness of symptoms that may represent secondary infection**
- B. Need for monitoring systemic side effects of immunosuppressive therapy**
- C. Methods to control dry eye syndrome (See Aqueous tear deficiency, Sjögren syndrome and Mucin deficiency)**
- D. Education regarding chronic nature of the disease with remission and exacerbation**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
- 2. Foster CS. Immunologic disorders of the conjunctiva, cornea, and sclera. In: Albert DM, Miller JW et al, eds. Principles and Practice of Ophthalmology. 3rd ed. Philadelphia: Saunders; 2008
- 3. Ross AH, Jaycoo P, Cook SD et al. The use of rituximab in refractory mucous membrane pemphigoid with severe ocular involvement. Br J Ophthalmol 2009;93(4):421-2.

Thygeson superficial punctate keratitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disorder

1. Unknown
2. Although a viral immune response is suspected, an etiological agent has not been confirmed.

B. Describe the relevant epidemiology of the disorder

1. Infrequent disorder
2. No gender predilection
3. Affects all age groups, probably most frequent in the second and third decades

C. List the pertinent elements of the history

1. Intermittent photophobia
2. Tearing
3. Mild blurring of vision
4. Burning, foreign body sensation
5. Usually without ocular redness
6. Spontaneously resolves to be followed by later exacerbations
7. Usually bilateral
8. Untreated episodes may last for weeks to 1-2 months

D. Describe pertinent clinical features

1. Scattered clumps of fine epithelial lesions which are round, oval, or stellate
2. Lesions are slightly elevated and may have mild punctate staining over them and subepithelial infiltrates beneath them
3. The lesions may be few or number up to 50 or more in each cornea
4. Minimal or no conjunctival reaction
5. Lesions change in location over time

II. List the differential diagnosis

A. Staphylococcal toxic keratitis

B. Rosacea

C. Herpes simplex virus (HSV) keratitis

D. Dry eye

E. Molluscum contagiosum

F. Epidemic keratoconjunctivitis

1. May be confused but has florid conjunctival involvement

III. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Topical corticosteroids
 - a. Usually exquisitely sensitive to low dose steroids tapered over several days
2. Topical cyclosporine tapered over many months may be of benefit
3. Topical trifluridine has been suggested by some authors but others have been disappointed with this treatment
4. Bandage soft contact lenses provide temporary relief of symptoms and may lead to temporary resolution of the lesions

B. Describe surgical therapy options

1. Scraping of the lesions is not beneficial
2. Phototherapeutic keratectomy has been reported to decrease recurrences in the area of treatment but has also been reported to induce recurrences
 - a. Remains controversial
 - b. Recurrence after laser assisted in situ keratomileusis (LASIK) has been reported.

IV. List the complications of treatment, their prevention and management

- A. Corticosteroid toxicity and steroid dependence are significant risks with prolonged topical use, so using the lowest dose for the shortest time that is effective is important in this chronic and recurrent disease**
- B. Corneal scarring generally is not seen with this disorder although anterior stromal haze may occur but resolves over time**

V. Describe disease-related complications

- A. Persistent or recurrent discomfort**
- B. Blurred vision**

VI. Describe appropriate patient instructions

- A. Use the lowest amount of corticosteroids for the shortest time necessary to relieve symptoms**
- B. Seek ophthalmic care if symptoms persist despite treatment**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Corneal Complications of Contact Lens, Module #2, 1993, p.4.
3. Schwab IR, Thygeson P. Thygeson superficial punctate keratopathy. in: Pepose JS, Holland GN, Wilhelmus KR, eds. Ocular Infection and Immunity. St. Louis: Mosby; 1996:403-407.

Marginal corneal infiltrates associated with blepharoconjunctivitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Toxic/immune response to staphylococcal antigens from lid margin organisms

B. List the pertinent elements of the history

1. Acute onset
2. Photophobia
3. May have history of preexisting blepharitis, lid crusting, chalazia, but not essential
4. Often history of prior episodes

C. Describe pertinent clinical features

1. Usually round infiltrate in peripheral anterior stroma
 - a. May at times be elongated concentric with the limbus
 - b. Occur typically where lid margins cross the limbus at 2, 4, 8, and 10 o'clock
2. Relative clear zone between lesion and the limbus
3. Punctate overlying staining may develop and may become a frank epithelial defect that is usually smaller than the infiltrate
4. Conjunctival injection, diffuse or localized
5. Often lid margins shows changes of staphylococcal blepharitis

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. None for classic presentation
 - a. By definition the lesion is not infected

II. Define risk factors

A. Staphylococcal blepharitis

III. List the differential diagnosis

A. Microbial keratitis

1. Bacterial
2. Herpes simplex virus (HSV)

- B. Contact lens associated peripheral corneal infiltrates
- C. Peripheral ulcerative keratitis associated with rheumatoid disease, Wegener granulomatosis
- D. Phlyctenulosis
- E. Rosacea keratitis
- F. Atopic keratoconjunctivitis
- G. Toxic/ allergic reaction (e.g., marginal infiltrates due to Neosporin)
- H. Sterile limbal infiltrates during bacterial conjunctivitis

IV. Describe patient management in terms of treatment and follow-up

A. Define medical therapy options

1. Therapy of blepharitis with warm compresses, lid scrubs, antibiotic ointment to lid margins or topical antibiotic
2. Topical corticosteroids or corticosteroid/antibiotic combination
3. Oral tetracyclines or erythromycin may be considered

V. List the complications of treatment, their prevention and management

- A. Exacerbation of active microbial keratitis if inaccurate diagnosis
- B. Culture of lids, conjunctiva or cornea may be considered if diagnosis is uncertain
- C. Photosensitivity of skin with oral tetracycline
- D. Corticosteroid-induced elevation of intraocular pressure
 1. Limit duration of treatment with corticosteroids
 2. Usually there is a rapid response and they may be tapered after 5 to 7 days

VI. Describe disease-related complications

- A. Peripheral corneal scarring, occasionally thinning

VII. Describe appropriate patient instructions

- A. Warm compress to the lids (long-term, daily therapy)
- B. Lid scrubs
- C. Antibiotic ointment to lid margins after lid hygiene
- D. Consider long-term use of oral systemic tetracyclines as a prophylactic measure, although there is limited evidence on their efficacy.
- E. Consider oral omega-3-fatty acids such as flaxseed oil, although there is limited evidence on their efficacy.

- F. Advise patients to seek care if develop redness or pain in eye**
- G. Patients should be advised not to self-treat with topical corticosteroids**
- H. Patients should be aware that problem may reoccur**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Peripheral keratitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of these diseases

1. The close anatomic relationship between the avascular peripheral cornea and the potentially immune-responsive vascular limbal conjunctiva makes the peripheral cornea a common site for inflammatory corneal disease
2. Immune reactants from the limbus may react with antigens from the cornea in the corneal periphery
3. Nutrition to the peripheral cornea comes in part from the limbal vessels, and disorders involving the limbal vessels may affect the peripheral cornea
4. Substances may diffuse from the vascular system into the peripheral cornea where they may accumulate or induce inflammation
5. Limbal stem cells for the corneal epithelium reside along the margins of the cornea
 - a. Abnormalities in these cells may lead to changes in the peripheral corneal surface.

B. Describe the relevant aspects of epidemiology of these diseases

1. There are numerous disorders in this category ranging from the infrequent (neoplasms) to the more common (staphylococcal marginal keratitis) (These individual entities are discussed in their specific outlines)

C. List the pertinent elements of history

1. Symptoms depend on the specific entity
2. Complaints of ocular irritation and redness are most common
3. Evaluate for systemic diseases, such as connective-tissue diseases

D. Describe pertinent clinical features

1. Vary with the disorder, may include
 - a. Ulceration
 - b. Thinning
 - c. Edema
 - d. Vascularization
 - e. Infiltration with inflammatory cells
 - f. Lipid deposition
 - g. Irregular epithelium and mucous plaques or filaments
 - h. Elevated mass

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Depends on the entity being considered
 - a. Microbial or viral assays
 - b. Serologic testing

II. List the differential diagnosis

A. Infection-related conditions

1. Microbial keratitis
2. Stromal (interstitial) keratitis, including Herpes simplex virus (HSV) stromal keratitis and syphilitic interstitial keratitis

B. Marginal keratitis associated with blepharitis, including staphylococcal blepharitis and rosacea

C. Collagen-vascular diseases

1. Rheumatoid arthritis
2. Wegener granulomatosis
3. Polyarteritis nodosa
4. Systemic lupus erythematosus
5. Relapsing polychondritis

D. Allergic keratoconjunctivitis including limbal vernal and drug reaction

E. Degenerative and/or inflammatory disorders

1. Terrien marginal corneal degeneration
2. Dellen
3. Superior limbic keratoconjunctivitis
4. Mooren ulcer
5. Contact lens peripheral infiltrate

F. Neoplastic

1. Corneal intraepithelial neoplasia may mimic peripheral keratitis

G. Limbal stem cell deficiency

1. Congenital
 - a. Aniridia
 - b. Ectodermal dysplasia
2. Acquired
 - a. Toxic
 - b. Post-inflammatory
 - c. Postsurgical

- d. Traumatic (i.e., contact lens-induced)

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Nonulcerative keratitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Humoral and cellular immune reaction to antigens (including viral glycoproteins and other microbial substances) in the corneal stroma resulting in cellular infiltration and inflammation

B. List the pertinent elements of the history

1. Previous ocular herpes, particularly previous herpes simplex virus (HSV) stromal keratitis
2. Previous chickenpox or shingles (herpes zoster virus)
3. Previous congenital syphilis with dental deformities, bone and cartilage deformities, or hearing loss
4. Systemic illness including infectious mononucleosis, measles, and Lyme disease
5. Recent upper respiratory infection with ear-related symptoms such as dizziness and reduced hearing (Cogan syndrome)

C. Describe the pertinent clinical features

1. Stromal inflammation with stromal edema; may be focal or disciform, multifocal, or diffuse; endothelial pseudoguttata
2. Corneal epithelium intact
3. Keratitis often accompanied by iritis and keratic precipitates: stromal keratouveitis/ endotheliitis
4. Presence and extent of stromal neovascularization
5. Presence and extent of corneal scarring
6. Interstitial keratitis associated with infectious diseases
7. Subepithelial infiltrates and multifocal posterior corneal nodular infiltrates associated with Cogan syndrome

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Serological testing, depending upon history and clinical findings
 - a. Fluorescent treponemal antibody absorption or similar treponemal test
 - b. HSV antibody
 - c. Varicella zoster virus (VZV) antibody
 - d. Epstein-Barr virus (EBV) antibodies

II. Define the risk factors

A. HSV stromal keratitis

1. Possible genetic predisposition

2. Environmental triggers such as sun exposure, recent illness, recent ocular surgery
3. Virulent strain of HSV - 1
4. Prior stromal keratitis is a strong predictor of recurrent disease

B. VZV stromal keratitis

1. Increasing age
2. Immunosuppression and malignancy

C. Interstitial keratitis associated with infectious diseases

1. Exposure to
 - a. *Treponema pallidum*
 - b. *Mycobacterium tuberculosis*
 - c. *Mycobacterium leprae*
 - d. *Borrelia burgdorferi* (Lyme disease)
 - e. Rubeola (measles)
 - f. EBV (infectious mononucleosis)
 - g. Other systemic microorganisms

III. List the differential diagnosis

- A. Microbial keratitis**
- B. Corneal transplant rejection**
- C. Contact lens-related corneal infiltrate**
- D. Diffuse lamellar keratitis following keratorefractive surgery**
- E. Rosacea keratitis**
- F. Atopic keratoconjunctivitis**
- G. Corneal edema**
- H. Sterile keratitis following trauma**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Kaufman SC. Peripheral Corneal Disease, In Cornea. Krachmer, Mannis, Holland, Editors. 3rd Ed. 2011, Elsevier inc.

Ulcerative keratitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease (corneal epithelial defect and stromal inflammation, without or with stromal ulceration)

1. Epithelial defect from delayed epithelial replication, migration, and/or adherence
2. Stromal inflammation from innate immune response
3. Stromal ulceration from keratocyte destruction and apoptosis and from proteolysis of stromal collagen and proteoglycans
 - a. Microbial enzymes (e.g., bacterial proteinases)
 - b. Phagocyte (neutrophil) enzymes (e.g., lysosomal proteinases)
 - c. Corneal degradative mechanisms, including matrix metalloproteinases and the plasminogen-dependent pathway

B. List the pertinent elements of the history

1. Onset and evolution of ocular inflammation
 - a. Exacerbating and alleviating factors
2. Contact lens wear
 - a. Contact lens care (e.g., products, frequency of cleansing and disinfection, and lens case)
3. Ocular trauma
 - a. Foreign body
4. Exposure to fluids (water and chemicals)
5. Prior ocular surgery, including keratorefractive procedure
6. Prior ocular disease
 - a. Recurrent erosion
 - b. Herpes simplex virus (HSV) keratitis
 - c. Varicella zoster virus (VZV) keratitis
7. Recent topical ophthalmic medications
 - a. Anesthetics
 - b. Antibacterials
 - c. Antivirals
 - d. Corticosteroids
 - e. Nonsteroidal anti-inflammatory drugs (NSAIDs)
 - f. BAK preserved drops- frequent use

8. Systemic disease
 - a. Diabetes mellitus
 - b. Connective tissue disorder
 - c. Immunosuppression
9. Nutritional status, including alcohol use
10. Recent exposure to others with "red eye"
11. Effect of eye condition on quality of life, including level and duration of pain
12. Duration and level of symptoms
 - a. Pain
 - b. Redness
 - c. Light sensitivity
 - d. Tearing
 - e. Decreased vision
13. General medical health
 - a. Fever
 - b. Fatigue
 - c. Headache
 - d. Weight change
 - e. Appetite
 - f. Upper respiratory tract symptoms
 - g. Joint aches
 - h. Reason for any recent hospitalization
 - i. History of "fever blisters" or shingle

C. Describe pertinent clinical features

1. Status of ocular adnexa, skin, and extremities
2. Presence of palpable preauricular and other regional lymph node(s)
3. Position of eyelids and eyelashes
4. Presence of exposure
5. Status of tear film and lacrimal system
6. Status of conjunctiva, including presence of symblepharon and scarring
7. Corneal sensation
8. Size and shape of corneal epithelial defect

9. Status of remaining corneal epithelium and corneal epithelial basement membrane
10. Type of stromal inflammation: suppurative or nonsuppurative
11. Area and depth of stromal inflammation, including location, number of separate infiltrates, and appearance of border of any focal infiltrate
12. Presence and extent of stromal thinning or ulceration
13. Presence and extent of corneal vascularization
14. Area and extent of corneal edema and pseudoguttata
15. Presence or absence of iritis, including iris synechiae, inflammatory endothelial plaque, or hypopyon
16. Status of contralateral eye

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Infectious ulcerative keratitis (See Diagnostic techniques for infectious diseases of the cornea and conjunctiva, including specimen collection methods for microbiologic testing and diagnostic assessment of the normal ocular flora)
2. Immune-mediated ulcerative keratitis
 - a. Biopsy for suspected autoimmune disease
 - b. Serological tests such as
 - i. Rheumatoid factor
 - ii. Antinuclear antibodies (ANA)
 - iii. Anti-neutrophil cytoplasmic antibodies (ANCA)
 - iv. Hepatitis C antibodies

II. Define the risk factors

A. Viral epithelial keratitis

1. Adenovirus keratoconjunctivitis
 - a. Exposure to infected individual or contaminated fomite
2. HSV epithelial keratitis
 - a. Environmental triggers such as sun exposure, recent illness, or recent ocular surgery
3. VZV epithelial keratitis
 - a. Increasing age
 - b. Immunosuppression
 - c. Malignancy
 - d. Chemotherapy/radiotherapy

B. Suppurative microbial keratitis

1. Contact lens use (especially extended-wear use)
2. Ocular trauma (corneal foreign bodies, chemical and thermal injuries)
3. Previous ocular and eyelid surgery
4. Loose sutures
5. Previous corneal surgery (including refractive surgery and penetrating keratoplasty)
6. Medication toxicity (medicamentosa)
7. Immunosuppression (systemic and local)
8. Anesthetic abuse
9. Ocular surface disease (trichiasis, exposure/lid abnormalities, tear film abnormalities)
10. Adjacent infections (blepharitis, conjunctivitis, dacryocystitis, canaliculitis)

C. Nonsuppurative keratitis

1. Ocular surface disorders (e.g., neurotrophic keratitis, recurrent erosion, previous corneal infections, viral keratitis, bullous keratopathy, keratoconjunctivitis sicca, blepharoconjunctivitis)
2. Systemic conditions (e.g., diabetes mellitus, malnourishment, connective-tissue disorders, substance abuse, dermatological/mucous membrane disorders, Stevens-Johnson syndrome, mucous membrane pemphigoid, immunocompromise, atopic dermatitis/ blepharoconjunctivitis, vitamin A deficiency)

III. List the differential diagnosis

A. Ulcerative keratitis (corneal epithelial defect and stromal inflammation)

1. Punctate and dendritic epithelial keratitis and epithelial erosions with stromal infiltrate
 - a. Viral infections
 - i. Adenovirus keratoconjunctivitis
 - ii. HSV epithelial keratitis
 - iii. VZV epithelial keratitis
 - b. Thygeson superficial punctate keratitis
 - c. Toxicity
 - d. Dry eye syndrome
 - e. Contact lens reaction
2. Suppurative or necrotizing ulcerative keratitis
 - a. Microbial infections
 - i. Bacterial keratitis
 - ii. Fungal keratitis

- iii. Acanthamebic keratitis
 - b. Herpetic keratitis (persistent corneal epithelial defect with necrotizing herpes simplex virus stromal keratitis)
 - c. Zoster-associated neurotrophic keratopathy
- 3. Nonsuppurative ulcerative keratitis
 - a. Marginal corneal infiltrate associated with blepharoconjunctivitis
 - b. Sterile infiltrate due to contact lens wear or corneal trauma
 - c. Peripheral ulcerative keratitis associated with systemic immune-mediated disease
 - d. Mooren ulcer
- B. Corneal epithelial defect without stromal inflammation**
 - 1. Traumatic corneal abrasion
 - 2. Toxic keratopathy
 - 3. Neurotrophic keratopathy
 - 4. Exposure keratopathy
- C. Nonulcerative keratitis: stromal inflammation without epithelial defect**
 - 1. Phlyctenulosis and rosacea keratitis
 - 2. Vernal and atopic keratoconjunctivitis
 - 3. Various forms of nonulcerative keratitis (HSV stromal keratitis, VZV stromal keratitis, Epstein-Barr virus keratitis, interstitial keratitis associated with infectious diseases such as congenital syphilis, Cogan syndrome)
- D. Nonulcerative opacity: stromal opacification with corneal thinning but intact corneal epithelium**
 - 1. Terrien marginal corneal degeneration
 - 2. Senile furrow degeneration
 - 3. Postinfectious and posttraumatic corneal scarring

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
- 2. AAO, Focal Points: Infectious Keratitis, Module #8, 1992, p.1-2.

Peripheral ulcerative keratitis associated with systemic immune-mediated diseases

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Vasculitis and immune complex deposition
2. Contiguous with adjacent scleritis

B. Describe the relevant epidemiology of this disease

1. Epidemiology is that of the systemic disease

C. List the pertinent elements of the history

1. Rheumatoid arthritis
 - a. History of erythematous, hot, tender, swollen joints
 - b. May also have history of dry eyes, nose, and mouth
2. Wegener granulomatosis
 - a. May have history of pulmonary, sinus, ear, or renal disease
 - b. Conjunctivitis or scleritis at presentation or in the past
 - c. Ocular disease may be present alone (limited form) or prior to the onset of systemic disease
3. Systemic lupus erythematosus
 - a. Fatigue
 - b. Fever
 - c. Anorexia
 - d. Weight loss
 - e. Arthralgias and myalgias
 - f. Skin rash and photosensitivity
 - g. Renal disease
 - h. Neurologic symptoms
 - i. Pleuritis
4. Inflammatory bowel disease
 - a. Rectal bleeding
 - b. Diarrhea
 - c. Abdominal pain

- d. Anorexia
 - e. Weight loss
 - f. Fever
 - g. None may be present as ocular disease may precede symptomatic bowel disease
5. Ocular symptoms
- a. May vary
 - b. Foreign body sensation
 - c. Tearing
 - d. Pain may or may not be present.
 - e. Photophobia
 - f. Decreased vision
 - g. Associated symptoms such as pain related to scleritis if present

D. Describe pertinent clinical features

- 1. Peripheral ulcerative keratitis
 - a. Peripheral epithelial defect, infiltration of the corneal stroma, and thinning
 - b. Rheumatoid arthritis
 - i. Peripheral stromal opacities with overlying epithelial defect, thinning, may be adjacent to necrotizing scleritis
 - ii. Stromal melting without clinical evidence of inflammation may occur peripherally or centrally, more commonly in patients with concurrent keratoconjunctivitis sicca
 - c. Wegener granulomatosis
 - i. Peripheral corneal subepithelial infiltrates
 - ii. Anterior grainy stromal opacities
 - iii. Peripheral guttering with adjacent scleritis
 - d. Systemic lupus erythematosus
 - i. Corneal ulceration is uncommon
 - e. Inflammatory bowel disease
 - i. Peripheral subepithelial infiltrates and nebulae
 - ii. Malabsorption may lead to vitamin A deficiency and its corneal complications

II. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

- 1. Treat systemic disorder to suppress systemically mediated inflammation and vaso-occlusive

disease

- a. Systemic corticosteroids
 - b. Cytotoxic agents
 - c. Immunosuppressive/immunomodulatory agents
 - d. Tumor necrosis factors (TNF)-alpha antagonists
2. Maintain adequate lubrication of the ocular surface
 3. Promote corneal re-epithelialization

B. Describe surgical therapy options

1. Perforation or impending perforation of the cornea may require treatment with tissue adhesive, amniotic membrane graft, perilimbal conjunctival resection, and/or lamellar or penetrating keratoplasty, often performed as a crescentic or circular peripheral graft. When possible, intraocular surgery should be avoided until systemic immunosuppression has commenced

III. List the complications of treatment, their prevention and management

A. Systemic side effects of corticosteroids, cytotoxic and immunosuppressive agents including

1. Secondary infection
2. Gastrointestinal symptoms
3. Secondary neoplasms

B. Surgical complications

1. Graft rejection
2. Infection
3. Recurrent corneal ulceration and perforation

IV. Describe disease-related complications

A. Disease related complications are diverse and include

1. Articular disease
2. Pulmonary disease
3. Renal disease
4. Death

B. Ocular complications include

1. Uveitis
2. Dry eye
3. Cataract

4. Retinal vasculitis
5. Conjunctivitis
6. Scleritis
7. Eyelid involvement
8. Corneal melt/perforation
9. Loss of vision

V. Describe appropriate patient instructions

- A. These patients must be managed in concert with the appropriate medical specialist, especially the rheumatologist or gastroenterologist but at times also the nephrologist, pulmonologist, or dermatologist**
 1. Patients must be strongly impressed with the importance of maintaining these relationships

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Virasch VV, Brasington RD, Lubniewski AJ. Corneal Disease in Rheumatoid Arthritis. In Cornea. ed. Krachmer, Mannis, Holland, 3rd Ed. 2011, Elsevier inc.
3. Sugar J, Cortina MS. Corneal Disease Associated with nonrheumatoid Collagen-Vascular Disease, In Cornea. ed. Krachmer, Mannis, Holland, 3rd Ed. 2011, Elsevier inc.

Mooren ulcer

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Appears to be an immunologic disorder with autoimmunity to corneal antigens of unknown etiology. Precipitating factors may include:
 - a. Idiopathic
 - b. Secondary to previous corneal insults such as trauma, chemical injury, surgery, or infection
 - c. Hepatitis C, intestinal parasites, and other infections have been found in some patients, but causal association remains uncertain

B. Define the relevant aspects of epidemiology of this disease

1. Infrequent disorder
2. Two populations have been described although some reports have disputed this:
 - a. Older people with a more benign, often unilateral disease
 - b. More aggressive bilateral painful disease, often in younger patients

C. List the pertinent elements of the history

1. Pain, often severe, chronic, progressive
2. Conjunctival injection
3. Photophobia
4. Decreased visual acuity

D. Describe pertinent clinical features

1. Peripheral gray to white stromal infiltrate, usually in the interpalpebral zone
2. Overlying epithelial defect
3. Associated stromal thinning
4. Undermined leading edge progresses centrally and circumferentially
5. Peripheral corneal reepithelialization as the ulcer moves centrally
6. Injection and chemosis of adjacent conjunctiva

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Serologic testing to rule out collagen-vascular diseases (antinuclear antibody (ANA) panel, perinuclear-staining anti-neutrophil cytoplasmic antibodies (p-ANCA), cytoplasmic-staining anti-neutrophil cytoplasmic antibody (c-ANCA), rheumatoid factor)
2. Hepatitis C antibodies

II. Define the risk factors

- A. Unknown, associated with some human leukocyte antigen subtypes, trauma, hepatitis C**

III. List the differential diagnosis

A. Inflammatory

1. Peripheral ulcerative keratitis and/or scleritis secondary to collagen vascular disease (rheumatoid arthritis, Wegener granulomatosis, systemic lupus erythematosus, polyarteritis nodosa)
2. Marginal keratitis (staphylococcal)

B. Infectious

1. Peripheral keratitis (bacterial, herpes simplex virus)

C. Degenerative

1. Terrien marginal corneal degeneration - peripheral, more slowly progressive, usually intact epithelium
2. Senile furrow degeneration

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Topical corticosteroids, especially in milder cases
2. Systemic immunosuppression
 - a. Oral corticosteroids
 - i. Prednisone
 - b. Antimetabolites
 - i. Methotrexate
 - ii. Azathioprine
 - c. Immunomodulatory agents
 - i. Cyclosporine
 - ii. Mycophenolate mofetil
 - d. Alkylating agents
 - i. Cyclophosphamide
3. Systemic interferon (if associated with hepatitis c)

B. Describe surgical therapy options

1. Conjunctival resection - adjacent to ulcer
2. Superficial keratectomy - for isolated de-epithelialized central corneal islands

3. Corneal/scleral patch grafting for perforations
4. Corneal gluing may be helpful occasionally for very small perforations

V. List the complications of treatment, their prevention and management

- A. Side effects of systemic immunosuppressives including secondary infections, gastrointestinal symptoms, secondary neoplasms**
- B. Side effects of topical corticosteroids- glaucoma, cataract, secondary infection**

VI. Describe disease-related complications

- A. Corneal opacification**
- B. Cataract**
- C. Glaucoma**
- D. Exacerbation of disease with surgical interventions**
- E. Corneal Perforation**
- F. Vision loss**

VII. Describe appropriate patient instructions

- A. Disease may reactivate after periods of quiescence**
 1. Patients must be warned to return promptly if there is any activation of symptoms
- B. For systemic immunosuppressive treatment, co-management with a medical specialist (rheumatologist, etc.) is essential**
- C. Avoid even minor trauma given the risk of perforation**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Garg P, Sangwan VR. Mooren's Ulcer. In Cornea. ed. Krachmer, Mannis, Holland, 3rd Ed. 2011, Elsevier inc.
3. Gottsch JD, Stark WJ, Liu SH. Cloning and sequence analysis of human and bovine corneal antigen (CO-Ag) cDNA: identification of host-parasite protein calgranulin C. Trans Am Ophthalmol Soc. 1997;95:111-125.

Episcleritis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Idiopathic (most common)
2. Post-traumatic, post-surgical
3. Associated with underlying systemic condition
 - a. Connective tissue disorders
 - i. Rheumatoid arthritis
 - ii. Systemic lupus erythematosus
 - iii. Polyarteritis nodosa
 - iv. Sjögren syndrome
 - b. Infectious diseases
 - i. Bacteria
 - i) Tuberculosis
 - ii) Syphilis
 - ii. Virus
 - i) Herpes simplex virus (HSV)
 - ii) Varicella zoster virus (VZV)
 - c. Miscellaneous
 - i. Gout
 - ii. Atopy
 - iii. Rosacea
 - iv. Inflammatory bowel diseases
 - v. Sarcoidosis

B. List the pertinent elements of history

1. Acute onset or recurrence of mild ocular discomfort
2. Localized or diffuse conjunctival injection

C. Describe pertinent clinical features

1. Localized injection of the bulbar conjunctival and episcleral vessels is more common than diffuse involvement
2. Blanching with topical (2.5% or 10%) phenylephrine

3. Excessive tearing
4. Conjunctival nodule (in nodular form)
5. Small peripheral corneal opacities
6. Mild anterior chamber cell and flare

D. Describe the appropriate testing and evaluation for establishing the diagnosis

1. If recurrent or if history suggests an underlying associated systemic disorder
2. Serum uric acid
3. Complete blood count with differential count
4. Antinuclear antibody (ANA)
5. Rheumatoid factor
6. Erythrocyte sedimentation rate (ESR)
7. Fluorescent treponemal antibody-absorption test, Venereal Disease Research Laboratory (VDRL) test
8. Chest X-ray

II. List the differential diagnosis

- A. Viral conjunctivitis
- B. Superior limbic keratoconjunctivitis
- C. Anterior scleritis
- D. Conjunctival abrasion
- E. Allergic conjunctivitis
- F. Pingueculitis
- G. Iritis
- H. Staphylococcal blepharoconjunctivitis

III. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Treat underlying disorder, if present
2. Judicious use of vasoconstrictors
3. Mild
 - a. Artificial tears
4. Moderate
 - a. Topical nonsteroidal anti-inflammatory drug (NSAID) or mild corticosteroid

5. Severe, recalcitrant, or recurrent
 - a. Stronger topical corticosteroid +/- oral NSAID

IV. List the complications of treatment, their prevention and management

A. Topical corticosteroids

1. Complications
 - a. Potentiation of ocular infection
 - b. Glaucoma
 - c. Cataract
 - d. Prolong time to natural resolution
2. Prevention
 - a. Limit use of topical corticosteroids (lowest effective potency for shortest duration)
3. Management
 - a. Control intraocular pressure (IOP) with topical therapy/surgery if necessary
 - b. Cataract surgery if indicated

B. Topical NSAID

1. Complications
 - a. Corneal melt
 - b. Medicamentosa
2. Prevention
 - a. Limit use
3. Management
 - a. Cessation of use
 - b. Topical lubricants (See Management of descemetocoe and corneal perforation by bandage contact lens, tissue adhesive or reconstructive graft)

C. Topical vasoconstrictors

1. Complications
 - a. Rebound vasoconstriction
2. Prevention
 - a. Limit use
3. Treatment
 - a. Cessation

V. Describe disease-related complications

- A. No visually significant sequelae**
- B. Persistent dilation of conjunctival or episcleral vessels may be of cosmetic concern**

VI. Describe appropriate patient instructions

- A. Self-limiting disease**
- B. Relapses may occur, in the same or contralateral eye**
- C. No visually significant sequelae**
- D. Use of topical corticosteroids should be limited to decrease incidence of associated side effects**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Scleritis and Episcleritis: Diagnosis and Management, Module #9, 1995.
3. Williams CP, Browning AC, Sleep TJ, et al. A randomised, double-blind trial of topical ketorolac vs artificial tears for the treatment of episcleritis. *Eye* 2005;19:739-42.
4. Pearlstein ES. Episcleritis. In *Cornea*. ed. Krachmer, Mannis, Holland, 3rd Ed. 2011, Elsevier inc.

Scleritis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. 50-75% idiopathic
2. 25-50% have underlying systemic disease
 - a. More common: rheumatoid arthritis, Wegener granulomatosis, relapsing polychondritis
 - b. Less common: ankylosing spondylitis, systemic lupus erythematosus, polyarteritis nodosa, inflammatory bowel disease, gout, post-herpes zoster ophthalmicus, sarcoidosis, syphilis
3. Deposition of immune complexes in vessel walls appears to be important
4. Disordered immune response leads to tissue and blood vessel damage

B. List the pertinent elements of the history

1. Severe eye pain, boring quality
2. Red eye
3. Pain on movement of eye
4. Tearing
5. Slow onset
6. May be recurrent

C. Describe pertinent clinical features

1. Classification
 - a. Anterior
 - i. Diffuse - most common presentation, least severe
 - ii. Nodular
 - iii. Necrotizing with inflammation- most severe, greatest potential for visual loss
 - iv. Necrotizing without inflammation (scleromalacia perforans)- association with rheumatoid arthritis
 - b. Posterior
2. Signs
 - a. Anterior: pain on palpation, red-violet hue to sclera (seen best with natural lighting), non-blanching with 10% phenylephrine drops, inflammation of sclera and episclera, scleral nodules, uveitis, adjacent peripheral keratitis
 - b. Posterior: hyperopia, proptosis, lid edema, ophthalmoplegia, disc edema, exudative retinal detachment, macular edema, choroidal folds

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Medical workup
 - a. Complete blood count (CBC)
 - b. Erythrocyte sedimentation rate (ESR)
 - c. rapid plasma reagin test or Venereal Disease Research Laboratory (VDRL) test
 - d. Fluorescent treponemal antibody absorption test (FTA)
 - e. Rheumatoid factor
 - f. Antinuclear antibody (ANA) panel
 - g. Angiotensin converting enzyme (ACE) test
 - h. Cytoplasmic-staining anti-neutrophil cytoplasmic antibody (cANCA)
 - i. Perinuclear-staining anti-neutrophil cytoplasmic antibody (pANCA)
 - j. Chest radiograph
 - k. Purified protein derivative (PPD) (tuberculosis skin test)
 - l. Urinalysis
2. Ultrasound (if posterior scleritis is suspected)
3. Consider computed tomography scan (if posterior scleritis is suspected)

II. Define the risk factors

- A. Depends on etiology**
- B. May be idiopathic**
- C. Genetic factors**

1. Certain major histocompatibility antigens may predispose some individuals

III. List the differential diagnosis

- A. Episcleritis**
- B. Conjunctivitis**

IV. Describe patient management in terms of treatment and follow-up

- A. Oral nonsteroidal anti-inflammatory drugs**
- B. Systemic corticosteroids (start with 1 mg/kg/day and slowly taper)**
- C. Systemic immunosuppressive agents in consultation with internist, oncologist, rheumatologist**
 1. Cyclophosphamide particularly for systemic vasculitis, polyarteritis nodosa, Wegener granulomatosis

2. Methotrexate
 3. Azathioprine
 4. Cyclosporine
 5. Tumor Necrosis Factor (TNF) inhibitors such as Infliximab (Remicade®) and other immunomodulators
- D. Consider periocular steroid injection if no evidence of infection**
- E. Surgical management (i.e., scleral patch graft) may be required to maintain or re-establish the integrity of the globe**
- F. Follow-up in 2-7 days depending on severity of presentation**

V. List the complications of treatment, their prevention, and management

A. Nonsteroidal anti-inflammatory drugs

1. Gastrointestinal disturbance
2. Impaired renal function

B. Systemic corticosteroids

1. Hypertension
2. Elevated blood glucose
3. Weight gain
4. Cushingoid appearance

C. Systemic Immunosuppressive agents

1. Cyclophosphamide
 - a. Bone marrow suppression
 - b. Hemorrhagic cystitis
 - c. Secondary malignancies
2. Methotrexate
 - a. Hepatotoxicity
 - b. Interstitial pneumonitis
 - c. Bone marrow suppression
 - d. Gastrointestinal disturbance
 - e. Alopecia
 - f. Mouth sores
3. Azathioprine
 - a. Bone marrow depression

- b. Hepatotoxicity
 - c. Gastrointestinal disturbance
- 4. Cyclosporine
 - a. Renal toxicity
 - b. Hepatotoxicity
 - c. Hypertension
 - d. Secondary malignancy
 - e. Increased risk of infection
 - f. Growth of body hair
- 5. TNF inhibitors
 - a. Secondary malignancies, including solid tumors
 - b. Secondary infection

D. Prevention and management

- 1. Taper medications as appropriate
- 2. Know toxicities and monitor appropriately
- 3. Combination therapy may allow for tapering of systemic corticosteroids
- 4. Manage in concert with physician experienced in use of these medications (e.g., rheumatologist, oncologist, primary care physician)

VI. Describe disease-related complications

- A. Scleral melting**
- B. Scleral perforation**
- C. Cataract**
- D. Glaucoma**
- E. Cystoid macular edema**
- F. Ocular pain**

VII. Describe appropriate patient instructions

- A. Emphasize importance of close follow-up**
- B. Discuss possible systemic side effects of medications**
- C. Discuss natural history of disease**

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Scleritis and Episcleritis: Diagnosis and Management, Module #9, 1995.
3. Biber JM, Schwam B, Raizman MB. Scleritis. In Cornea. ed. Krachmer, Mannis, Holland, 3rd Ed. 2011, Elsevier inc.

Ocular surface squamous neoplasia: corneal intraepithelial neoplasia, conjunctival intraepithelial neoplasia, and squamous cell carcinoma

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Neoplasia of the epithelium of the limbal conjunctiva and/or cornea
2. Varies from partial thickness dysplasia to full thickness disease to invasive squamous cell carcinoma
3. Human papillomavirus found in some cases of conjunctival intraepithelial neoplasia

B. Define the relevant aspects of epidemiology of this disease

1. Higher prevalence with untreated acquired immune deficiency syndrome (AIDS)

C. List the pertinent elements of the history

1. Duration of lesion
2. Severity of foreign body sensation

D. Describe pertinent clinical features

1. Conjunctival intraepithelial neoplasia
 - a. Vascularized limbal lesion
 - b. Keratinization (e.g., leukoplakia) and inflammation may indicate increased risk of dysplasia
 - c. Conjunctiva may stain with Rose Bengal
2. Corneal intraepithelial neoplasia
 - a. Gray epithelium, often with fimbriated margin usually contiguous with limbus although free islands may occur
 - b. May slowly change size and shape
 - c. Adjacent limbus may appear clinically normal or corneal lesion may be associated with signs of conjunctival intraepithelial neoplasia
3. Squamous cell carcinoma of the conjunctiva
 - a. Limbal lesion may appear papilliform, gelatinous, or leukoplakic
 - b. Most often occurs in the interpalpebral fissure
 - c. Pigmentation of lesion may be present in dark-skinned individuals

- d. May be affixed to the underlying tissue

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Histopathological examination of incisional or excisional biopsy
2. Impression cytology

II. Define the risk factors

- A. Light complexion**
- B. Advancing age**
- C. Environmental risk factors such as cigarette smoking, sunlight exposure, and exposure to certain chemicals such as pesticides and petroleum products**
- D. Immunosuppression and human immunodeficiency virus (HIV) infection may increase incidence of conjunctival squamous neoplasia and/or potential for growth**
- E. Possible role of human papilloma virus 16 and 18**

III. List the differential diagnosis

A. Conjunctival intraepithelial neoplasia and squamous cell carcinoma of the conjunctiva

1. Pterygium
2. Pinguecula
3. Nodular episcleritis or scleritis
4. Foreign body reaction
5. Pyogenic granuloma
6. Epibulbar dermoid tumor or other choristoma
7. Melanoma of the conjunctiva
8. Sebaceous carcinoma of the conjunctiva
9. Conjunctival primary localized amyloidosis
10. Benign hereditary intraepithelial dyskeratosis

B. Corneal intraepithelial neoplasia

1. Limbal stem-cell failure or deficiency
2. Superior limbic keratoconjunctivitis
3. Vernal or atopic keratopathy
4. Rosacea keratopathy
5. Toxic epithelial keratopathy
6. Corneal epithelial basement membrane dystrophy

7. Spheroidal/Salzmann degeneration

IV. Describe patient management in terms of treatment and follow up

A. Describe medical therapy options

1. Topical interferon-alpha
 - a. Topical interferon, usually administered until tumor disappearance
 - b. Subconjunctival interferon-alpha, may be administered alone or as an adjunct with excisional biopsy
2. Topical mitomycin C (has risk to bare sclera)
3. Topical 5 fluorouracil (least common option)

B. Describe surgical therapy options

1. Conjunctival intraepithelial neoplasia: excisional conjunctival biopsy (See Conjunctival biopsy) with cryotherapy. and/or topical chemotherapy (interferon or antimetabolite)
2. Corneal intraepithelial neoplasia: chemical or mechanical debridement (See Corneal epithelial debridement) with limbal excision and cryotherapy.
3. Squamous cell carcinoma: excisional biopsy, usually with lamellar sclerectomy and adjunctive cryotherapy

V. List the complications of treatment, their prevention and management

A. Incomplete removal and destruction of lesion, recurrence

1. Take wide excision at time of surgery, use cryotherapy as adjunctive therapy

B. Conjunctival scarring

1. Use amniotic membrane or conjunctiva to reconstruct ocular surface
2. Use symblepharon ring in eye post operatively for large excisions

C. Ulceration, inflammation, punctal stenosis, or other adverse effect due to topical mitomycin C or other antimetabolite

1. Carefully monitor patients on topical antimetabolites

D. Limbal stem cell failure

1. Limit limbal treatment to involved areas
2. Treat with conservative measures if mild, amniotic membrane or limbal stem cell transplant when severe

VI. Describe disease-related complications

A. Conjunctival intraepithelial neoplasia and corneal intraepithelial neoplasia

1. Recurrence

B. Squamous cell carcinoma of the conjunctiva

1. Scleral and intraocular extension
2. Orbital invasion
3. Metastasis

VII. Describe appropriate patient instructions

- A. Awareness of possible recurrence, invasion, and metastasis that may lead to loss of vision, loss of eye, or death**
- B. Need for follow-up reevaluation**
- C. Consult internist/oncologist for invasive carcinoma**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Nonpigmented Lesions of the Ocular Surface, Module #9, 1996.
3. Poththullil AM, Colby KA. Topical medical therapies for ocular surface tumors. Semin Ophthalmol 2006;21:161-9.
4. Stone DU et al: Ocular surface squamous neoplasia: a standard of care survey. Cornea 2005;24:297.
5. Pe'er J. Ocular surface squamous neoplasia. Ophthalmol Clin North Am 2005;18:1-13,vii.
6. AAO, Focal Points: Ocular Surface Neoplasia, Module #1, 2007.

Sebaceous gland carcinoma of the eyelid margin and conjunctiva

I. Describe the approach for establishing the diagnosis

A. Describe the etiology of this disease

1. Sebaceous gland carcinoma, also called sebaceous cell carcinoma, arises by malignant transformation from one or more meibomian glands, or possibly from the glands of Zeis, sebaceous glands of the caruncle, or pilosebaceous glands of the eyelid margin

B. Define the relevant aspects of epidemiology of this disease

1. Less than 1% of eyelid tumors
2. Can masquerade as chalazion

C. List the pertinent elements of the history

1. Painless, slow-growing, firm nodule of the conjunctiva
2. Chronic unilateral conjunctivitis/blepharitis
3. Eyelid thickening and deformity, with focal loss of eyelashes (madarosis)

D. Describe the pertinent clinical features

1. Variable location, although upper lid more common than the lower
2. Subepithelial spread, often multicentric and inflammatory, that may resemble chronic papillary conjunctivitis
3. Non-mobile yellowish nodule, that may have features overlapping with the spreading form
4. Status of preauricular lymph node

E. Describe appropriate testing and evaluation for establishing a diagnosis

1. Biopsy, with attention to histopathologic characteristics, including presence of anaplastic cells, multiple mitoses, and lipid
2. Map biopsies to detect multicentric neoplasia

II. Define the risk factors

A. Advancing age

B. Prior radiation therapy

III. List the differential diagnosis

A. Blepharitis, blepharoconjunctivitis, and chalazion

B. Mucous membrane pemphigoid and other causes of cicatrizing conjunctivitis

- C. Ocular surface squamous neoplasia, including papilloma and squamous cell carcinoma of the conjunctiva
- D. Other neoplastic conditions, including basal cell carcinoma, lymphoma, and melanoma of the conjunctiva

IV. Describe patient management in terms of treatment and follow-up

- A. Excision of lesion with tumor-free margins, that may be done with wide excision, map biopsies, frozen-sections, or Mohs micrographic surgery
- B. Adjunctive cryotherapy, radiotherapy, or chemotherapy may be considered
- C. Know indications for orbital exenteration if invasive or recurrent neoplasia
- D. Follow for local recurrences and regional metastasis

V. List the complications of treatment, their prevention and management

- A. Local recurrence
- B. Conjunctival scarring
- C. Corneal exposure
- D. Need for eyelid reconstruction following excision

VI. Describe disease-related complications

- A. Orbital invasion
- B. Metastasis to preauricular, parotid, or cervical lymph nodes
- C. Death from distant metastasis, especially if duration longer than 6 months, extensive tumor invasion, or incomplete excision

VII. Describe appropriate patient instructions

- A. Be aware of possible complications, including local recurrence and metastases to other tissues and organs
- B. Need for follow up

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Management of Malignant Eyelid Tumors, Module #6, 1989.
3. AAO, Focal Points: Periorbital Skin Cancers: The Dermatologist's Perspective, Module #1, 2006.

Primary acquired melanosis of the conjunctiva

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Neoplasia of conjunctival melanocytes

B. Define the relevant aspects of epidemiology of this disease

1. Unilateral pigmentation in white race or light-skinned ethnicity more often affected
2. Racial melanosis is seen bilaterally in pigmented individuals, but conjunctival melanoma can occur in pigmented individuals

C. List the pertinent elements of the history

1. Appearance may remain stable or progress
2. Change in size or appearance may be associated with hormone changes such as puberty or pregnancy
3. Usually has little or no conjunctivitis

D. Describe pertinent clinical features

1. Flat, brown lesion of the conjunctival epithelium
2. Unilateral
3. May be single or multiple
4. Irregular margins
5. Note asymmetry between two eyes
6. Signs of malignant transformation
 - a. Enlargement
 - b. Increased pigmentation
 - c. Nodularity
 - d. Increased vascularity or inflammation
 - e. Conjunctival feeder vessel
7. Rare pigmentary variations
 - a. No visible pigmentation (amelanotic)
 - b. Eyelid margin pigmentation
 - c. Corneal epithelium may have fine pigmentation

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Periodic observation with photographic follow up
2. Biopsy with histopathological examination to determine malignant potential
 - a. Large or progressive lesion of bulbar conjunctiva should be removed or do map biopsies if inexcisable
 - b. Darkly pigmented lesion of palpebral conjunctiva, fornix, or caruncle
 - c. Multiple pigmented lesions

II. Define the risk factors

A. European ancestry

III. List the differential diagnosis

A. Congenital pigmented lesions of the conjunctiva or episclera

1. Benign racial melanosis of conjunctiva (complexion-associated conjunctival pigmentation)
2. Congenital conjunctival nevus
3. Ocular melanosis (melanosis oculi) and oculodermal melanosis (nevus of Ota)

B. Acquired pigmentation of the conjunctiva (See Pigmentation of the conjunctiva and cornea)

1. Acquired conjunctival nevus
2. Secondary acquired melanosis of conjunctiva
3. Melanoma of conjunctiva (See Melanoma of the conjunctiva)

IV. Describe patient management in terms of treatment and follow up

A. Describe surgical therapy options

1. Excisional biopsy
2. Adjunctive cryotherapy, such as double freeze-thaw at -20°C
3. Primary or adjunctive chemotherapy, such as mitomycin C for inexcisable disease

V. List the complications of treatment, their prevention and management

A. Incomplete excision

1. May justify further excisional surgery or adjunctive therapy
2. Follow-up to check for local recurrence or spread to preauricular or other regional lymph nodes

VI. Describe disease-related complications

A. Melanoma of the conjunctiva

1. Lower melanoma risk if no histopathological atypia
 - a. Hyperpigmentation and hyperplasia confined to basal epithelium
 - b. No hyperchromaticity
2. Higher melanoma risk if histopathological features associated with atypia
 - a. Intraepithelial spread
 - b. Epithelioid cells
 - c. Invasion into substantia propria

VII. Describe appropriate patient instructions

- A. Need for follow up**
- B. Awareness of change in morphology of lesion**
- C. Awareness of possible recurrence**
- D. Awareness of possible malignant melanoma**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Melanoma and Other Pigmented Lesions of the Ocular Surface, Module #11, 1996.
3. Chalasani R, Giblin M, Conway RM. Role of topical chemotherapy for primary acquired melanosis and malignant melanoma of the conjunctiva and cornea: review of the evidence and recommendations for treatment. Clin Experiment Ophthalmol 2006;34:708-14.
4. AAO, Focal Points: Ocular Surface Neoplasia, Module #1, 2007.
5. Hu DN, Yu G, McCormick SA, Finger PT. Population-based incidence of conjunctival melanoma in various races and ethnic groups and comparison with other melanomas. Am J Ophthalmol. 2008 Mar;145(3):418-423. Epub 2008 Jan 11.

Melanoma of the conjunctiva

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Malignancy of conjunctival melanocytes
2. Often arises from primary acquired melanosis of the conjunctiva, may evolve from preexisting conjunctival nevus or may appear de novo

B. List the pertinent elements of the history

1. Duration of lesion
2. Course of lesion, including changes of pigmentation, size, and inflammation
3. Bleeding from lesion
4. Previous melanoma affecting skin or uvea
5. Previous biopsy

C. Describe pertinent clinical features

1. Location of lesion (bulbar versus palpebral conjunctiva vs forniceal)
2. Size, thickness, number, and nodularity of lesion(s)
3. Check whether lesion is attached to the underlying sclera or is freely movable
4. Palpation of ipsilateral preauricular, submandibular, and cervical lymph nodes
5. Rule out uveal melanoma with dilated fundus examination, transillumination, or ultrasonography
6. Examine skin or recommend dermatology consult to look for cutaneous melanoma

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Excisional biopsy for suspicious lesion, such as large or nodular lesion or lesion having progressive increase in size or thickness
2. Histopathological examination to determine presence and severity of cellular atypia and prominent cell type: epithelioid, spindle, or mixed.
3. Consider ultrasonography for thick lesion or possible intraocular extension
4. Obtain imaging (e.g., PET scan, computerized tomography (CT) or magnetic resonance imaging (MRI)) of orbit and paranasal sinuses
5. Consider roles of orbital or sinus surgery and radiotherapy
6. Consider sentinel node biopsy although role of sentinel lymph node biopsy and lymphoscintigraphy are unclear
7. Consider screening for genetic testing for prognostic and therapeutic outcomes
8. Consult with oncologist to detect metastasis, which tends to involve lung, liver, brain, or skin

II. Define the risk factors

A. Risk factors for lesion

1. Middle-age or elderly
2. White race or light-skinned ethnicity (e.g., European and Eurasian descent) more common, but can rarely occur in darker-skinned races/ethnicities (Asian or African descent)
3. Previous primary acquired melanosis of the conjunctiva or conjunctival acquired nevus

B. Risk factors influencing outcome

1. Presence of cellular atypia on histopathology is primary association with progression to melanoma
2. Site of lesion on conjunctiva (lesions of limbal and bulbar conjunctiva may have less risk of post-excision recurrence than lesions of palpebral conjunctiva, fornix, or caruncle)
3. Number of pigmented lesions
4. Other histopathologic characteristics: tumor thickness, growth pattern and scleral invasion
5. Metastases

III. List the differential diagnosis

A. Conjunctival nevus

B. Primary acquired melanosis

C. Pigmented epithelial tumor, including squamous cell carcinoma

D. Ocular melanocytosis

E. Staphyloma

F. Implantation of foreign substances: calcium, medications, cosmetics

IV. Describe patient management in terms of treatment and follow up

A. Define surgical therapy options

1. Wide excisional biopsy
2. Adjunctive therapy to destroy residual tumor cells
 - a. Cryotherapy of conjunctival margins
 - b. Absolute alcohol to adjacent corneal epithelium (if limbal involvement) and scleral base
 - c. Topical mitomycin may have a role in chemotherapy
3. Orbital exenteration or radiotherapy may be considered for diffuse, multifocal, or extended melanoma

V. List the complications of treatment, their prevention and management

A. Local recurrence due to incomplete excision

1. Prevention
 - a. Perform complete excision
2. Management
 - a. Repeat excision with wide surgical margins

B. Structural alteration of ocular surface

1. Prevention
 - a. Avoid excessive use of cryotherapy or mitomycin C
2. Management
 - a. Reconstruct large defect with amniotic membrane graft or conjunctival autograft

C. Limbal stem cell deficiency

1. Prevention
 - a. Avoid excessive excision or mitomycin C
2. Management
 - a. Reconstruct large defect with amniotic membrane graft or limbal stem cell transplant

VI. Describe disease-related complications

A. Subconjunctival invasion into orbit

B. Lymphatic spread and distant metastasis with organ failure and death

VII. Describe appropriate patient instructions

A. Knowledge of possible recurrence, local invasion, metastasis, loss of vision, and death

B. Need for long-term follow up

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Seregard S. Conjunctival melanoma. *Surv Ophthalmol* 1998;42:321-350.
3. Shields CL, Shields JA, Gunduz K, et al. Conjunctival melanoma: risk factors for recurrence, exenteration, metastasis, and death in 150 consecutive patients. *Arch Ophthalmol* 2000;118:1497-1507.
4. AAO, Focal Points: Melanoma and Other Pigmented Lesions of the Ocular Surface, Module #11, 1996.

5. AAO, Focal Points: Ocular Surface Neoplasia, Module #1, 2007.

Conjunctival lymphoma

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Monoclonal proliferation of lymphocytes, most commonly B cells

B. Define the relevant aspects of epidemiology of the disease

1. Usually young to middle aged adults
2. Ocular involvement represents only 2% of extranodal lymphoma
3. Lymphoid tumors of the conjunctiva associated with systemic lymphoma in up to 31% of patients
4. Systemic lymphoma found more often in patients with forniceal or midbulbar conjunctival involvement and those with multiple conjunctival tumors, and bilateral disease
5. May have infectious etiology such as Chlamydia or H. pylori

C. List the pertinent elements of the history

1. History of chronic redness
2. Possible foreign body sensation
3. Painless

D. Describe pertinent clinical features

1. Diffuse; slightly elevated pink mass located in the stroma or deep to Tenon fascia
2. Color similar to salmon, hence the term "salmon patch"
3. Lesions are fleshy, often originate in fornix or adjacent to the limbus
4. May also present as a chronic follicular conjunctivitis

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Biopsy of lesion for histopathologic diagnosis, must send fresh tissue for flow cytometry and gene rearrangement
2. Evaluation for systemic lymphoma in conjunction with oncologist or hematologist if biopsy is positive
 - a. Tumor staging with complete blood count (CBC) and differential, imaging of the head, neck and abdomen

II. Define the risk factors

A. No specific risk factors except those associated with lymphomas in general including

1. Prolonged antigen stimulation, leading to loss of regulation of B-lymphocyte proliferation and differentiation

2. Human immunodeficiency virus (HIV)

III. List the differential diagnosis

- A. Benign lymphoid hyperplasia**
- B. Scleritis and episcleritis**
- C. Ectopic lacrimal gland**
- D. Amyloid deposition**
- E. Foreign body with pyogenic granuloma**
- F. Lymphangiectasia**
- G. Sarcoidosis**
- H. Cat Scratch Disease**
- I. Degenerative conjunctival changes (e.g., pinguecula, pterygium)**
- J. Other ocular surface tumors**
 1. Conjunctival intraepithelial neoplasia
 2. Squamous carcinoma
 3. Amelanotic melanoma
 4. Langerhans cell tumor

IV. Describe patient management in terms of treatment and follow-up

- A. Describe the natural history, outcome and prognosis**
 1. Worse prognosis with
 - a. Systemic disease
 - b. Non-mucosal associated lymphoid tissue (MALT) lymphomas
 2. Late manifestations of extra-ocular lymphoma occur up to 53 months after diagnosis, therefore repeat systemic evaluation every 6 months for 5 years
- B. Describe medical therapy options**
 1. Complete systemic evaluation
 2. Treatment options depend on the presence of systemic disease
 - a. Radiation considered for symptomatic lesions, especially if they threaten vision
 - b. Intralesional interferon alpha-2b
 - c. Chemotherapy for aggressive histological subtypes and for systemic diseased
 - d. Anti CD 20 immunotherapy (intralesional or systemic)
- C. Describe surgical therapy options**

1. Surgical biopsy for histopathologic diagnosis, rarely as a therapeutic modality

V. List the complications of treatment, their prevention and management

A. Radiation therapy

1. Complications
 - a. Xerophthalmia
 - b. Keratitis
 - c. Cataract formation
2. Prevention
 - a. Careful dosimetry by radiation oncologist

B. Chemotherapy varies with agent

1. Administration and management by oncologist with training to manage these complications

VI. Describe disease-related complications

A. Isolated ocular disease

1. Usually minimal complications

B. Complications associated with systemic lymphoma

VII. Describe appropriate patient instructions

A. Discuss association with systemic disease and importance of regular long-term follow-up and medical surveillance for development of systemic lymphoma

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Shields CL, Shields JA, Carvalho C, Rundle P, Smith AF. Conjunctival lymphoid tumors: clinical analysis of 117 cases and relationship to systemic lymphoma. *Ophthalmology* 2001 May;108(5):979-84.
3. Ross JJ, Tu KL, Damato BE. Systemic remission of non-Hodgkin's lymphoma after intralesional interferon alpha-2b to bilateral conjunctival lymphomas. *Am J Ophthalmol* 2004 Oct;138(4):672-3.
4. Takahira M, Okumura H, Minato H, et al. Primary conjunctival follicular lymphoma treated with the anti-CD20 antibody rituximab and low-dose involved-field radiotherapy. *Jpn J Ophthalmol* 2007 Mar-Apr;51(2):149-51.

Corneal epithelial basement membrane dystrophy/degeneration

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Abnormal corneal epithelial basement membrane, which is thickened, multilaminar, and misdirected into the epithelium
2. Altered epithelial turnover and maturation
3. Ineffective hemidesmosome formation by epithelial cells, resulting in poor adhesion

B. Define the relevant aspects of epidemiology of the disease

1. The most common anterior corneal dystrophy/degeneration
2. Increasing frequency over 50 years of age

C. List the pertinent elements of the history

1. Most patients are asymptomatic
2. Blurred vision
3. Monocular diplopia
4. Glare
5. Foreign body sensation
6. Photophobia
7. Eye pain and epiphora during sleep or upon awakening

D. Describe the pertinent clinical features

1. Gray patches, microcysts, and/or fine lines in the central epithelial layer
2. Fingerprint lines (or "putty marks")
 - a. Thin, hair like lines, often arranged in a concentric pattern
3. Map lines
 - a. Same as fingerprints but thicker, more irregular, surrounded by a faint haze, resembling geographic borders
4. Dots or microcysts
 - a. Intraepithelial spaces with debris of epithelial cells that have collapsed and degenerated before reaching the epithelial surface
5. Epithelial defects, loose epithelium or punctate epithelial erosions
6. Subepithelial haze or scarring

- E. Describe the appropriate testing and evaluation for establishing the diagnosis**
1. Slit-lamp biomicroscopic exam including fluorescein staining and retroillumination
 2. Corneal topography
 3. Keratometry

II. List the differential diagnosis

- A. Corneal scarring secondary to injury**
- B. Meesmann juvenile epithelial dystrophy**
- C. Reis-Bucklers dystrophy**
- D. Thiel-Behnke dystrophy**
- E. Corneal intraepithelial neoplasia**
- F. Herpes simplex virus (HSV) keratitis**
- G. Traumatic corneal abrasion**
- H. Keratoconjunctivitis sicca**
- I. Amiodarone deposits**

III. Describe patient management in terms of treatment and follow-up

- A. Describe medical therapy options**
1. Antibiotic drops for acute recurrent erosion
 2. Patching for acute recurrent erosion
 3. Topical nonsteroidal anti-inflammatory drugs (NSAIDs)
 4. Loose soft bandage contact lens for recurrent erosion
 5. Hypertonic saline drops and ointment for maintenance
 6. Lubricating eyedrops and ointment for maintenance
 7. Rigid gas-permeable contact lens to improve vision if irregular astigmatism present
- B. Describe surgical therapy options**
1. Epithelial debridement for recurrent erosion (See Corneal epithelial debridement)
 2. Anterior stromal puncture for recurrent erosion especially in identifiable localized noncentral disease in post-traumatic erosions.(See Anterior stromal puncture)
 3. Epithelial debridement for recurrent erosion with scraping or diamond burr polishing
 4. Excimer laser phototherapeutic keratectomy for recurrent erosion or scarring decreasing vision

IV. List the complications of treatment, their prevention and management

- A. Irritation from hypertonic saline eyedrops and ointment
- B. Corneal epithelial erosion or irritation related to bandage contact lenses
- C. Microbial keratitis secondary to bandage contact lens wear, patching, or surgical treatment
- D. Corneal scarring related to surgical treatment
- E. Irregular astigmatism related to surgical treatment

V. Describe disease related complications

- A. Corneal erosion
- B. Persistent corneal epithelial defect
- C. Microbial keratitis
- D. Corneal scarring
- E. Irregular astigmatism
- F. Loss of best-corrected visual acuity

VI. Describe appropriate patient instructions

- A. Advise of recurrent or chronic nature of this condition
- B. Instruction on medications and side effects
- C. Instruction on patching and bandage soft contact lenses, if used
- D. Education on medical and surgical treatment options for recurrent erosions
- E. Instruction on proper follow-up

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Weiss JS, Moller H, Lisch W, Kinoshita S, Aldave AJ, et al. The IC3D classification of the corneal dystrophies. *Cornea* 2008; 27 Suppl 2:S1-83.
3. Aldave AJ, Kamal KM, Vo RC, and Yu F. Epithelial debridement and Bowman's layer polishing for visually significant epithelial irregularity and recurrent corneal erosions. *Cornea* 2009; 28:1085-90.
4. AAO, Ophthalmology Monographs 18. A Compendium of Inherited Disorders and the Eye, 2006.

Corneal dystrophy of Bowman layer I (CDB I; Reis-Bücklers dystrophy) and corneal dystrophy of Bowman layer II (CDB II; Thiel-Behnke dystrophy)

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. CDB 1 - Autosomal dominant; secondary to a mutation in the transforming growth factor beta-induced gene (*TGFBI*). A spontaneous mutation has been reported in individuals without a family history
2. CDB 2 - Autosomal dominant; secondary to a mutation in *TGFBI* (different than the one that causes CDB 1). A spontaneous mutation has been reported in individuals without a family history

B. Define the relevant aspects of epidemiology of the disease

1. Uncommon dystrophy in countries in which prevalence of different corneal dystrophies has been reported
2. Clinical features and associated symptoms most commonly present in the first decade of life

C. List the pertinent elements of the history

1. Slow progressive decrease in vision
 - a. Progression is more rapid than other stromal dystrophies, affecting visual acuity by the second to third decade
2. Poor quality vision due to irregular astigmatism
3. Foreign body sensation
4. Halos and glare at night
5. Episodic pain from recurrent erosions developing in first or second decade, abating by third decade of life

D. Describe pertinent clinical features

1. Slit-lamp biomicroscopy: bilateral geographic or honeycomb, gray white, axially-distributed opacification involving Bowman layer that spares the peripheral cornea.
2. Anterior stromal scarring in advanced cases
3. Decreased corneal sensation

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Slit lamp evaluation
2. Family history - One parent and 50% of siblings and offspring typically affected.

3. Tissue diagnosis after corneal transplant or keratectomy
4. Histopathology: deposits in Bowman's layer
5. Molecular genetic analysis - Screening of *TGFBI* recommended in cases of atypical phenotype or absence of family history.

II. Define the risk factors

- A. Positive family history**

III. List the differential diagnosis

- A. Granular dystrophy**
- B. Combined granular lattice corneal dystrophy (Avellino corneal dystrophy)**
- C. Epithelial basement membrane corneal dystrophy**

IV. Describe patient management in terms of treatment and follow-up

- A. Describe the natural history, outcome and prognosis**

1. Slow progressive decrease in vision
2. Episodes of painful recurrent erosions

- B. Describe medical therapy options**

1. Bandage contact lenses for recurrent erosions
2. Lubricating ointment to decrease incidence of recurrent erosions
3. Rigid contact lens wear to improve visual acuity
 - a. Avoid in patients with recurrent erosions

- C. Describe surgical therapy options (see separate outlines for each procedure)**

1. Superficial keratectomy (See Superficial keratectomy)
2. Anterior lamellar keratoplasty (See Anterior lamellar keratoplasty)
 - a. Shallow
 - b. Deep
3. Phototherapeutic keratectomy
4. Penetrating keratoplasty (See Penetrating keratoplasty)

V. List the complications of treatment, their prevention and management

- A. Recurrence of disease after PTK, keratectomy, or corneal transplant**
- B. Corneal infection from contact lens wear or recurrent erosions - prophylactic antibiotics reduce**

risk

- C. Abrasion from rigid contact lens wear - discontinue if this occurs repeatedly
- D. Poor quality vision from lamellar keratoplasty
- E. Complications of phototherapeutic keratectomy
- F. Complications of lamellar, penetrating keratoplasty (See Anterior lamellar keratoplasty) (See Penetrating keratoplasty)

VI. Describe disease-related complications

- A. Painful recurrent erosions
- B. Corneal scarring
- C. Amblyopia from irregular astigmatism if present in early childhood

VII. Describe appropriate patient instructions

- A. Discuss progressive decrease in vision
- B. Discuss recurrent erosions, counsel on management
- C. Counsel regarding recurrence after surgical therapy
- D. Counsel patients regarding risk of transmission to offspring

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Weiss JS, Moller H, Lisch W, Kinoshita S, Aldave AJ, et al. The IC3D classification of the corneal dystrophies. Cornea 2008; 27 Suppl 2:S1-83.

Meesmann corneal dystrophy

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Autosomal dominant
2. Causative mutations have been identified in two different genes on two different chromosomes
 - a. The genes encode keratins that are expressed only in the cornea. This is why affected patients do not experience extra corneal manifestations

B. List the pertinent elements of the history

1. Mildly reduced vision
2. Glare
3. Foreign body sensation associated with infrequent epithelial erosion

C. Describe pertinent clinical features

1. Minute intraepithelial cysts, typically bilateral and most densely concentrated in the interpalpebral zone.

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Slit lamp evaluation
2. Family history - One parent and 50% of siblings and offspring typically affected.
3. Tissue diagnosis after corneal transplant or keratectomy
4. Transmission electron microscopy
5. Intracytoplasmic inclusions, representing aggregated keratin filaments
6. Molecular genetic analysis - Screening of the genes in which causative mutations have been identified may be performed in cases of an atypical phenotype or absence of a family history.

II. Define the risk factors

A. Positive family history

III. List the differential diagnosis

A. Band shaped, whorled microcystic corneal dystrophy

B. Diffuse punctate epithelial keratopathy from various causes

IV. Describe patient management in terms of treatment and follow-up

A. Describe the natural history, outcome and prognosis

1. Many patients remain asymptomatic
2. Some patients may note persistent glare or mild visual disturbances

B. Describe medical therapy options

1. Lubricating ointment may decrease incidence of recurrent erosions
2. Bandage contact lenses for management of ocular irritation associated with epithelial erosions

C. Describe surgical therapy options (see separate outlines for each procedure)

1. Note: epithelial changes would be expected to recur following any of the following procedures. Therefore, they should be reserved for the management of associated subepithelial fibrosis or scarring
 - a. Phototherapeutic keratectomy
 - b. Superficial keratectomy (See Superficial keratectomy)
 - c. Anterior lamellar keratoplasty (See Anterior lamellar keratoplasty)

V. List the complications of treatment, their prevention and management

- A. Recurrence of disease after PTK, superficial keratectomy, or anterior lamellar keratoplasty**
- B. Complications of phototherapeutic keratectomy**
- C. Complications of superficial keratectomy (See Superficial keratectomy)**
- D. Complications of anterior lamellar keratoplasty (See Anterior lamellar keratoplasty)**

VI. Describe disease-related complications

- A. Painful recurrent erosions**
- B. Glare symptoms**
- C. Subepithelial corneal scarring**

VII. Describe appropriate patient instructions

- A. Discuss implications of corneal epithelial adherence in terms of contact lens wear and refractive surgery**
- B. Counsel patients regarding risk of transmission to offspring**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Weiss JS, Moller H, Lisch W, Kinoshita S, Aldave AJ, et al. The IC3D classification of the corneal dystrophies. Cornea 2008; 27 Suppl 2:S1-83.

Granular and lattice corneal dystrophies

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Granular corneal dystrophy type 1
 - a. Autosomal dominant inheritance
 - b. Secondary to a conserved mutation in the transforming growth factor beta-induced gene (*TGFB1*)
2. Lattice corneal dystrophy
 - a. Classic (type 1; LCD1)
 - i. Autosomal dominant inheritance
 - ii. Secondary to a conserved mutation in the transforming growth factor beta-induced gene (*TGFB1*)
 - b. Variant
 - i. Autosomal dominant inheritance
 - ii. Secondary to a variety of rare mutations in the transforming growth factor beta-induced gene (*TGFB1*)
 - c. Gelsolin (type 2; LCD2)
 - i. Autosomal dominant inheritance
 - ii. Secondary to mutations in the gelsolin gene (*GSN*)
 - d. Granular corneal dystrophy type 2 (Avellino dystrophy; combined granular - lattice dystrophy)
 - i. Autosomal dominant inheritance
 - ii. Secondary to a conserved mutation in the transforming growth factor beta-induced gene (*TGFB1*)
 - iii. Initial reports of individuals with Italian ancestry but more common in other populations (Korea and Japan)

B. List the pertinent elements of the history

1. Family history of corneal stromal dystrophy
2. Progressive decrease of vision
3. Photophobia is often the initial symptom
4. Corneal epithelial recurrent erosions

C. Describe pertinent clinical features

1. Granular corneal dystrophy

- a. Discrete deposits in the central cornea noted in the first 2 decades of life
 - i. Intervening stroma typically clear
 - b. Decreased vision may result from stromal haze and epithelial surface irregularity
 - c. Recurrent epithelial erosions
 - d. Type I granular dystrophy
 - i. Early age onset with crumb like opacities that broaden into a disciform appearance in the teens
 - ii. Clear peripheral 1-2 mm of cornea
 - iii. Lesions can extend anteriorly through focal breaks in Bowman layer
 - iv. Slowly progressive
 - v. Vision rarely drops to 20/200 after age 40
 - vi. Onset during childhood with superficial granular deposits
2. Lattice dystrophy
- a. Broad spectrum of corneal changes including:
 - i. Refractile lines (lattice lines)
 - ii. Central and subepithelial ovoid white dots
 - iii. Diffuse anterior stromal haze
 - b. Decreased vision may result from lattice lines, stromal haze (ground glass appearance) or epithelial surface irregularity
 - c. Frequent recurrent epithelial erosions
 - d. Classic (type I) lattice corneal dystrophy
 - i. Thin, branching anterior stromal lattice lines
 - ii. Recurrent erosions and visual symptoms are common starting in the first decade but significant visual disturbance does not develop typically until the third or fourth decades
 - iii. No systemic amyloid deposition
 - e. Variant lattice corneal dystrophy
 - i. Significant phenotypic variability, with thicker and more posteriorly located lattice lines
 - ii. Late-onset (fifth to seventh decade) and unilateral variants reported
 - f. Gelsolin type (type 2) lattice corneal dystrophy
 - i. Associated with Meretoja syndrome (systemic amyloidosis with lattice dystrophy)
 - ii. Presents in third or fourth decades
 - iii. Characteristic facial mask (mask-like facies secondary to amyloid deposition in the facial nerves)

- iv. Blepharochalasis
 - v. Pendulous ears
 - vi. Cranial and peripheral nerve palsies
 - vii. Dry lax skin with amyloid deposition
 - viii. Corneal lattice lines are less numerous and more peripheral
3. Granular dystrophy type 2 (Avellino dystrophy, combined granular and lattice corneal dystrophy)
 - a. Often only granular phenotype observed; stellate deposits are characteristic
 - b. Lattice lines may develop late in life, if ever
 - c. Older patients have intervening stromal haze resulting in decreased visual acuity

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Granular dystrophy
 - a. Clinical diagnosis
 - b. Masson trichome stain of corneal button to reveal bright red eosinophilic hyaline deposits
 - c. Molecular genetic analysis (screening of *TGFB1*)
2. Lattice dystrophy
 - a. Clinical diagnosis
 - b. Congo red stain of corneal button to highlight orange-red deposits of amyloid
 - c. Crystal violets stains amyloid metachromatically
 - d. Amyloid exhibits dichroism and birefringence
 - e. Molecular genetic analysis (screening of *TGFB1*)

II. Define the risk factors

- A. Family history of corresponding stromal dystrophy**

III. List the differential diagnosis

- A. Corneal dystrophy of Bowmans I (Reis-Buckler dystrophy) and Corneal dystrophy of Bowmans II (Thiel-Behnke dystrophy)**
- B. Gelatinous droplike dystrophy (primary familial amyloidosis)**
- C. Schnyder crystalline corneal dystrophy**
- D. Fleck dystrophy**
- E. Central cloudy dystrophy of François**
- F. Corneal scar following stromal interstitial keratitis**
- G. Corneal ghost vessels**

- H. Corneal nerves
- I. Secondary, localized corneal amyloidosis
- J. Polymorphic amyloid degeneration
- K. Macular corneal dystrophy

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Therapeutic contact lens, lubrication for recurrent erosions

B. Describe the surgical therapy options

1. Phototherapeutic keratectomy, superficial keratectomy for recurrent erosions or visually significant anterior stromal deposits
2. Penetrating keratoplasty for reduction of visual acuity
3. Possible lamellar keratoplasty if only anterior stroma is involved with dystrophy

V. List the complications of treatment

- A. Keratitis following superficial keratectomy, phototherapeutic keratectomy, or therapeutic contact lens
- B. Corneal scarring following superficial keratectomy, phototherapeutic keratectomy, or therapeutic contact lens
- C. Complications of penetrating keratoplasty (See Penetrating keratoplasty)
- D. Recurrence of disease process in graft after penetrating keratoplasty or anterior lamellar keratoplasty

VI. Describe disease-related complications

- A. Decreased visual acuity
- B. Recurrent erosions
- C. Keratitis
- D. Corneal scarring
- E. Recurrence after keratoplasty

VII. Describe appropriate patient instructions

- A. Use of appropriate drops for recurrent erosions
- B. Risks of penetrating keratoplasty

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Weiss JS, Moller H, Lisch W, Kinoshita S, Aldave AJ, et al. The IC3D classification of the corneal dystrophies. *Cornea* 2008; 27 Suppl 2:S1-83.
3. AAO, Ophthalmology Monographs 18. A Compendium of Inherited Disorders and the Eye, 2006.

Macular corneal dystrophy

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Autosomal recessive transmission, associated with different mutations in the carbohydrate sulfotransferase gene located on chromosome 16q22
2. Accumulation of non-sulfated keratan sulfate in endoplasmic reticulum of keratocytes and endothelial cells, and extracellular stroma.

B. List the pertinent elements of the history

1. Family history of corneal stromal dystrophy
2. History of parental consanguinity
3. Progressive decrease of vision
4. Corneal epithelial recurrent erosions

C. Describe pertinent clinical features

1. Clear corneas at birth, clouding begins in first decade
2. Focal, gray-white superficial stromal opacities with indefinite edges, progress to involve full stromal thickness and corneal periphery
3. Intervening stroma is diffusely cloudy
4. Involvement of Descemet membrane and endothelium with guttata
5. Central corneal thinning in some
6. Visual acuity affected in the second to fourth decades of life
7. Type I more prevalent than type II but identical clinical presentation

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Clinical diagnosis
2. Alcian blue or colloidal iron stain on pathology specimens delineates macular mucopolysaccharides
3. Molecular genetic analysis (screening of *CHST6*)
4. Enzyme-linked immunosorbent assay (ELISA) to measure sulfated keratan sulfate in serum to help diagnose in preclinical forms

II. Define the risk factors

A. Family history of corresponding stromal dystrophy

III. List the differential diagnosis

- A. Central cloudy dystrophy of François**
- B. Fuchs endothelial dystrophy**
- C. Corneal scar following stromal interstitial keratitis**
- D. Secondary, localized corneal amyloidosis**
- E. Granular corneal dystrophy**
- F. Crocodile shagreen**

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Therapeutic contact lens, lubrication for recurrent erosions
2. Tinted contact lens for photophobia

B. Describe the surgical therapy options

1. Phototherapeutic keratectomy (PTK) for smoothing of anterior surface irregularities from symptomatic anterior macular dystrophy
2. Penetrating keratoplasty or deep anterior lamellar keratoplasty for reduction of visual acuity
3. Anterior lamellar keratoplasty if only anterior stroma is involved with dystrophy

V. List the complications of treatment, their prevention and management

- A. Keratitis following therapeutic contact lens**
- B. Corneal scarring following therapeutic contact lens**
- C. Infection, scarring, astigmatism, loss of vision following PTK**
- D. Complications of penetrating keratoplasty (See Penetrating keratoplasty)**
- E. Recurrence of disease process in graft after penetrating keratoplasty**

VI. Describe disease-related complications

- A. Decreased visual acuity**
- B. Recurrent erosion syndrome**

VII. Describe appropriate patient instructions

- A. Use of appropriate drops for recurrent erosions**
- B. Risks of penetrating keratoplasty**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Aldave AJ, Sonmez B. Elucidating the molecular genetic basis of the corneal dystrophies: are we there yet? *Arch Ophthalmol*. 2007 Feb;125(2):177-86.
3. Weiss JS, Møller HU, Lisch W, et al. The IC3D classification of corneal dystrophies. *Cornea*. 2008;27:S1-S42.
4. AAO, Ophthalmology Monographs 18. A Compendium of Inherited Disorders and the Eye, 2006.

Fuchs endothelial dystrophy

I. Describe the approach for establishing the diagnosis

A. Describe the etiology of this disease

1. Probable autosomal dominant inheritance pattern
2. Dysfunctional endothelial cell - primary etiology unknown
 - a. Abnormal production and thickening of Descemet membrane
 - b. Later in course, progressive loss of endothelial cells with associated loss of Na⁺/K⁺ ATPase endothelial pumps and subsequent corneal edema and decompensation

B. Define the relevant aspects of epidemiology of this disease

1. Occurs more frequently in women than men
2. Corneal decompensation more likely in females
3. Common indication for endothelial and penetrating keratoplasty

C. List the pertinent elements of the history

1. Family history of Fuchs dystrophy or corneal transplant
2. Onset of symptoms typically after age 50
3. Decreased vision - worse in the morning
4. Photophobia, pain and tearing in later stages associated with epithelial edema and bullae formation

D. Describe the pertinent clinical features

1. Corneal guttae
 - a. Nodular excrescences of Descemet membrane
 - b. Mottled appearance - posterior corneal surface, with variable pigmentation
 - c. Disrupt endothelial cell mosaic pattern
2. Corneal edema
 - a. Stromal edema begins posteriorly, progresses to Descemet folds, then to mid- and anterior-stromal edema, with progressive increases in corneal thickness
 - b. Subepithelial bullae and epithelial edema with progressive decompensation
 - c. Epithelial erosions - ruptured bullae
 - d. Subepithelial scarring secondary to repeated bulla formation and healing

II. List the differential diagnosis

- A. Bullous keratopathy - aphakic or pseudophakic**
- B. Herpetic disciform keratitis**
- C. Chandler syndrome**
- D. Pseudo guttae associated with infectious or inflammatory conditions**

III. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Topical hyperosmotic agents (5% sodium chloride) - used primarily for epithelial edema
 - a. Drops may be used during the day
 - b. Ointment at night may reduce edema upon awakening
2. Hair dryer
 - a. Cool setting applied to cornea may increase evaporation and temporarily improve vision
3. Bandage soft contact lens may be useful in the treatment of painful erosions and ruptured bullae, and may improve blurring due to corneal irregularity from microcystic edema or bullae in the visual axis

B. Describe surgical therapy options

1. Visual rehabilitation
 - a. Endothelial replacement (e.g., Descemet stripping with endothelial keratoplasty), with cataract extraction as indicated
 - b. Penetrating keratoplasty, with cataract extraction as indicated
 - c. In presence of cataract, assess cornea for signs of decompensation including pachymetry and endothelial cell count
 - d. Cataract extraction could lead to corneal decompensation and patients should be informed of this risk prior to surgery
2. Pain relief
 - a. Penetrating keratoplasty with preservation of visual potential
 - b. For patients with poor visual potential (e.g., retinal or optic nerve disease)
 - i. Conjunctival flap
 - ii. Amniotic membrane transplant
 - iii. Corneal cauterization

IV. List the complications of treatment

A. Complications of treatment (See Endothelial keratoplasty and Penetrating keratoplasty)

1. Epithelial toxicity - secondary to topical agents

B. Prevention and management

1. Limit use of topical agents (See Endothelial keratoplasty and Penetrating keratoplasty)

V. Describe disease-related complications

- A. Corneal decompensation with progressive visual loss
- B. Corneal decompensation following cataract surgery
- C. Recurrent erosions
- D. Epithelial breakdown resulting in secondary stromal scarring and risk of infectious corneal ulcer
- E. Visual loss, glare, halos around lights from guttae without corneal edema, pain, or other non-visual complications

VI. Describe appropriate patient instructions

- A. Stress education of disease process as well as implications of penetrating keratoplasty and endothelial keratoplasty
- B. Awareness of symptoms that may represent worsening of disease

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Anshu A, Price MO, Tan DTH, Price FW. Endothelial keratoplasty: a revolution in evolution
3. Survey of Ophthalmology 2012;57:236-52. Aldave AJ, Sonmez B. Elucidating the molecular genetic basis of the corneal dystrophies: are we there yet? *Arch Ophthalmol*. 2007 Feb;125(2):177-86.
4. Weiss JS, Møller HU, Lisch W, et al. The IC3D classification of corneal dystrophies. *Cornea*. 2008;27:S1-S42
5. Price MO, Gorovoy M, Benetz BA, et al. Descemet's stripping automated endothelial keratoplasty outcomes compared with penetrating keratoplasty from the cornea donor study. *Ophthalmology*. 2010; 117: 438-444.

Posterior polymorphous corneal dystrophy

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Autosomal dominant
2. Mutations in genes on two different chromosomes are responsible for causing posterior polymorphous corneal dystrophy

B. List the pertinent elements of the history

1. Family history may or may not be present as many affected individuals are asymptomatic
2. Blurred vision and painful bullae may be present in the minority of patients with corneal edema

C. Describe pertinent clinical features

1. Common features
 - a. Isolated and/or grouped endothelial vesicles - often appear in clusters with surrounding gray halo
 - b. Geographic-shaped gray endothelial lesions
 - c. Parallel endothelial bands with scalloped edges
2. Uncommon features
 - a. Corneal stromal edema
 - b. Iris abnormalities (corectopia, iridocorneal adhesions)
 - c. Elevated intraocular pressure

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Slit lamp examination for typical endothelial lesions
2. Specular microscopy: typical endothelial vesicles, bands
3. Confocal microscopy: Descemet membrane abnormalities
4. Family history - One parent and 50% of siblings and offspring typically affected.
5. Molecular genetic analysis - Genetic testing may be performed to confirm the diagnosis in cases of an atypical phenotype or absence of a family history.

II. List the differential diagnosis

A. Iridocorneal endothelial (ICE) syndrome

B. Fuchs corneal dystrophy

C. Congenital hereditary endothelial dystrophy

D. Descemet membrane tear (secondary to trauma or congenital glaucoma)

III. Describe patient management in terms of treatment and follow-up

A. Describe the natural history, outcome and prognosis

1. Most patients remain asymptomatic
2. Stromal edema may present at birth or later in life
3. Elevated intraocular pressure may present at birth or later in life

B. Describe medical therapy options

1. Corneal edema
 - a. Epithelial
 - i. Topical hyperosmotic agents (5% sodium chloride)
 - ii. Hair dryer - cool setting applied tangentially to cornea may increase evaporation and temporarily improve vision
 - iii. Bandage soft contact lens may relieve pain from ruptured bullae
 - b. Stromal
 - i. Reduction of elevated intraocular pressure may improve endothelial function

C. Describe surgical therapy options

1. Visual rehabilitation
 - a. Penetrating keratoplasty, with cataract extraction as indicated (See Penetrating keratoplasty)
 - b. Endothelial keratoplasty (e.g., Descemet stripping endothelial keratoplasty) (See Endothelial keratoplasty)
 - c. In presence of cataract, assess likelihood of corneal decompensation with pachymetry and endothelial cell count prior to cataract surgery
2. Pain relief
 - a. Penetrating or endothelial keratoplasty with preservation of visual potential
 - b. For patients with poor visual potential (e.g., retinal or optic nerve disease)
 - i. Conjunctival flap
 - ii. Amniotic membrane transplant (See Amniotic membrane transplantation)
 - iii. Anterior stromal micropuncture (See Anterior stromal puncture)

IV. List the complications of treatment, their prevention and management

A. Complications of treatment (See Anterior stromal puncture) (See Penetrating keratoplasty)

1. Epithelial toxicity from topical hyperosmotics

2. Potential of burning cornea or face from hair dryer

B. Prevention and management (See Anterior stromal puncture) (See Penetrating keratoplasty) (See Endothelial keratoplasty)

1. Cessation of topical hyperosmotics
2. Keep hair dryer on cool, at appropriate distance from face

V. Describe disease-related complications

- A. Corneal decompensation with progressive visual loss
- B. Corneal decompensation following cataract surgery
- C. Recurrent erosion symptoms from ruptured bullae
- D. Epithelial breakdown resulting in secondary stromal scarring and risk of infectious corneal ulcer
- E. Glaucoma

VI. Describe appropriate patient instructions

- A. Education of disease process, implications of penetrating keratoplasty and endothelial keratoplasty
- B. Awareness of symptoms that may represent worsening of disease

Additional Resources

1. AAO Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Anshu A, Price MO, Tan DTH, Price FW. Endothelial keratoplasty: a revolution in evolution. Survey of Ophthalmology 2012;57:236-52.
3. Weiss JS, Moller H, Lisch W, Kinoshita S, Aldave AJ, et al. The IC3D classification of the corneal dystrophies. Cornea 2008; 27 Suppl 2:S1-83.

Keratoconus

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Multifactorial/unknown

B. Define the relevant aspects of epidemiology of the disease

1. Affects all races
2. Onset in the second decade of life, but symptomatic at any age.
3. Prevalence 1 per 2,000, but 1 to 5% of patients screened for refractive surgery are excluded due to possible keratoconus
4. Family history of keratoconus in up to 5-10% of cases
5. Other family members may have known keratoconus or subclinical (forme fruste) keratoconus

C. List the pertinent elements of the history

1. Blurred vision not fully correctable with eyeglasses
2. Contact lenses can no longer be fit comfortably
3. Progressive change in eyeglasses into adulthood

D. Describe pertinent clinical features

1. Bilateral disease, may be highly asymmetric
2. Irregular, high or progressive astigmatism
3. Irregular retinoscopic reflex
4. Central or paracentral corneal thinning
5. Apical subepithelial cornea scarring
6. Posterior corneal stromal striae (Vogt's striae)
7. Descemet membrane breaks/ reduplication
8. Fleischer iron ring outlining the cone
9. Munson sign
 - a. Bulging of the lower lid when the patient looks
10. Corneal hydrops
 - a. Sudden loss of vision secondary to an acute tear in Descemet membrane resulting in the rapid development of corneal stromal edema

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Computerized corneal topography

- a. High keratometry values
 - b. Inferior or eccentric steepening
 - c. Inferior-superior dioptric asymmetry
2. Keratometry
 - a. High keratometry values- steeper in the periphery especially on upgaze
 - b. Irregular mires - inability to superimpose central keratometric rings
3. Pachymetry - increasing thinning of the cornea as corneal thickness is measured from the center to the inferior position of the cornea

II. Define risk factors

- A. Eye rubbing**
- B. Allergic or atopic conjunctivitis**
- C. Associated systemic diseases**
 1. Down syndrome
 2. Marfan syndrome
 3. Mitral valve prolapse
 4. Floppy eyelid syndrome
 5. Atopy
 6. Leber congenital hereditary optic neuropathy

III. List the differential diagnosis

- A. Pellucid marginal degeneration**
- B. Keratoglobus**
- C. Contact lens-induced irregular astigmatism**
- D. Dry eye-induced epithelial hypertrophy**

IV. Describe patient management in terms of treatment and follow-up

- A. Describe medical therapy options**
 1. Eyeglasses
 2. Rigid gas permeable contact lenses
 3. Scleral contact lens
- B. Describe surgical therapy options**
 1. Superficial keratectomy may be used to remove superficial scars that prevent contact lens wear

2. Deep anterior lamellar keratoplasty or penetrating keratoplasty, if contact lens wear unsuccessful
3. Intracorneal ring segments may improve acuity or contact lens tolerance and delay need for keratoplasty
4. Collagen cross linking performed for progression of corneal steepening

V. List the complications of treatment

- A. Complications of contact lens wear (giant papillary conjunctivitis, microbial keratitis, etc)
- B. Complications of keratoplasty (rejection, microbial keratitis, etc)

VI. Describe disease-related complications

- A. Hydrops
- B. Corneal scarring
- C. Corneal perforation (rare)

VII. Describe appropriate patient instructions

- A. Progressive nature of the disease
- B. Explain associated risk factors
- C. Importance of proper contact lens fit
- D. Instructions regarding follow-up, medications and rejection signs after penetrating keratoplasty

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Aldave AJ, Sonmez B. Elucidating the molecular genetic basis of the corneal dystrophies: are we there yet? *Arch Ophthalmol*. 2007 Feb;125(2):177-86.
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Pellucid marginal corneal degeneration

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Unknown
2. Very likely a variant of keratoconus

B. Describe the epidemiology of this disease

1. Uncommon disorder
2. May be seen in patients who also have more typical changes of keratoconus or relatives of keratoconus patients
3. Associated with allergy and atopy

C. List the pertinent elements of the history

1. Increasing against-the-rule astigmatism
2. Onset in the teens or later, may be seen in elderly patients
3. Acuity initially often correctable with eyeglasses

D. Describe pertinent clinical features

1. Corneal thinning and ectasia usually 1 to 2 mm central to the inferior limbus in an oval pattern from 4 to 8:00
2. Corneal ectasia is most prominent just superior (central) to the area of thinning
3. Usually no iron ring but there may be deep stromal striae
4. High against-the-rule astigmatism
5. Area of involvement is clear (pellucid) without vascularization or lipid deposition and with intact epithelium

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Keratometry confirms against-the-rule astigmatism which is often regular
2. Corneal topography shows peripheral steepening usually in or a crab's claw pattern

II. Define risk factors

A. Unknown

B. Atopy/allergy

C. Association with eye rubbing in some patients

III. List the differential diagnosis

- A. **Keratoconus**
- B. **Senile furrow degeneration** - which is usually not ectatic and is closer to and more concentric with the limbus
- C. **Terrien marginal corneal degeneration** - is often listed in the differential diagnosis but this is associated with vascularization and lipid deposition as well as at times inflammatory episodes
- D. **Post-laser assisted in-situ keratomileusis (LASIK) ectasia**

IV. Describe patient management in terms of treatment and follow-up

- A. **Describe medical therapy options**
 - 1. Contact lens fitting, often with a large rigid gas-permeable lens (or scleral lens)
- B. **Describe surgical therapy**
 - 1. Large eccentric penetrating keratoplasty or deep anterior lamellar keratoplasty
 - 2. Lamellar keratoplasty - total or crescentic
 - 3. Excision of stroma overlying the thinned area with oversewing of the tissue (corneal imbrication)
 - 4. Intrastromal corneal ring segments

V. List the complications of treatment

- A. **High rejection rate in large eccentric penetrating keratoplasty**

VI. Describe disease-related complications

- A. **Decreased vision**
- B. **Hydrops may occur**
- C. **Corneal ectasia can occur after excimer laser refractive surgery, making these patients poor candidates for this procedure**

VII. Describe appropriate patient instructions

- A. **Avoid eye rubbing**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
- 2. Weiss JS, Moller H, Lisch W, Kinoshita S, Aldave AJ, et al. The IC3D classification of the corneal dystrophies. *Cornea* 2008; 27 Suppl 2:S1-83.
- 3. Sridhar MS, Mahesh S, Bansal AK, Nutheti R, Rao GN. Pellucid marginal corneal degeneration. *Ophthalmology* 2004, 111:1102-7.

Corneal congenital syndromes and anomalies

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Anomalies of structure and clarity
 - a. Anterior displaced border of Schwalbe line
 - b. Absence of corneal endothelium and Descemet membrane
 - c. Scleralization of the cornea
 - d. Degeneration of endothelial cells
2. Congenital infection
3. Dysplasia of anterior chamber angle

B. List the pertinent elements of the history

1. Genetics
2. Laterality of ocular involvement
3. Corneal opacification/edema/vascularization
4. Epiphora
5. Photophobia
6. Blepharospasm
7. Nystagmus

C. Describe pertinent clinical features

1. Posterior embryotoxon
 - a. Inherited, autosomal dominant inheritance
 - b. Bilateral
 - c. Presence of irregular and opaque ring central to limbus
 - d. May be associated with other anomalies including iris hypoplasia, attached iris strands, and glaucoma
2. Peters anomaly
 - a. Most occur sporadically, however both autosomal dominant and recessive inheritance has been reported
 - b. Mostly bilateral, in 60% of cases
 - c. Central cornea opacity present since birth with iridocorneal adhesions

- d. May be associated with other anomalies including keratolenticular touch, cataract, congenital glaucoma, microcornea, aniridia, persistent fetal vasculature, and skeletal anomalies
 - e. Associated with skeletal anomalies
- 3. Congenital hereditary endothelial dystrophy (CHED)
 - a. Inherited, autosomal dominant and recessive inheritance
 - b. Bilateral
 - c. Diffuse stromal edema
 - d. May be associated with nystagmus
- 4. Sclerocornea
 - a. Sporadic, however both autosomal dominant and recessive inheritance has been reported
 - b. Bilateral, in 90% cases
 - c. Noninflammatory scleralization of cornea with ill-defined limbus, and vascularization which can affect partial or complete cornea
 - d. Commonly associated with cornea plana and angle structure malformation
- 5. Intrauterine keratitis
 - a. Sporadic
 - b. Unilateral or bilateral
 - c. Posterior corneal defect, with corneal infiltrates, vascularization, keratic precipitates, iris adhesions and uveitis
 - d. May be associated with teratogenic effects with ocular malformation
- 6. Congenital glaucoma
 - a. Sporadic or inherited
 - b. Unilateral or bilateral
 - c. Buphthalmos, increased corneal diameter greater than 12mm, with corneal edema, elevated intraocular pressure, and Haab striae (tears in Descemet membrane oriented horizontally)
 - d. No significant associated ocular anomalies

D. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Examination under anesthesia
- 2. Slit lamp examination of corneal edema and anterior segment anomalies
- 3. Measure intraocular pressure
- 4. Serial corneal diameter measurements
- 5. Immersion ultrasound

6. Attempt gonioscopy, examination of anterior and posterior segment if epithelial edema can be cleared with topical hyperosmotic agent (glycerin)
7. Molecular genetic analysis when indicated

II. Define the risk factors

- A. Positive family history**
- B. Genetic syndromes**

III. List the differential diagnosis

- A. Birth trauma**
- B. Sclerocornea**
- C. Peter anomaly**
- D. Cornea plana**
- E. CHED**
- F. Intrauterine keratitis**
- G. Congenital glaucoma**

IV. Describe patient management in terms of treatment and follow-up

A. Describe the natural history, outcome and prognosis

1. Persistent edema if untreated
2. Optic nerve cupping with severe visual loss if left untreated
3. Amblyopia likely to develop

B. Describe medical therapy options

1. Glaucoma medications
2. Antibiotics for intrauterine infection
3. Corneal edema
 - a. May be lessened by topical hyperosmotic agents (5% sodium chloride)
 - b. Stromal edema may be improved with reduction of intraocular pressure improving endothelial function

C. Describe surgical therapy options

1. Trabeculotomy
2. Goniotomy
3. Trabeculectomy

4. Glaucoma shunt surgery
5. Penetrating keratoplasty if cornea is permanently damaged

V. List the complications of treatment, their prevention and management

A. Glaucoma surgery

1. Choroidal effusions
2. Choroidal hemorrhage
3. Hypotony
4. Infection

B. Corneal transplant (See Penetrating keratoplasty) (See Allograft rejection)

VI. Describe disease-related complications

- A. Progressive optic nerve damage and visual field loss**
- B. Recurrent corneal edema (See Corneal edema)**
- C. Permanent corneal opacification**
- D. Amblyopia**

VII. Describe appropriate patient instructions

- A. Need for compliance with medical therapy and regular follow-up visits**
- B. Need for lifelong management**
- C. Counsel parents regarding risk of transmission to additional offspring**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Pterygium and pinguecula

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Related to ultraviolet B exposure
2. Microtrauma from a windy or sandy environment may play a role, in addition

B. Describe the relevant aspects of epidemiology of this disease

1. Prevalence higher closer to the equator - in hot, dry climates
2. Males and outdoor workers predominate

C. List the pertinent elements of the history

1. Onset typically in the 20's to 40's
2. Complaint of ocular redness, irritation
3. May be asymptomatic
4. Usually report childhood years in hot, dry climate
5. Pterygium
 - a. May note visual distortion or decreased acuity
 - b. May note diplopia, especially on lateral gaze
6. Pinguecula
 - a. May report yellowish elevated growth

D. Describe pertinent clinical features

1. Pterygium
 - a. Fibrovascular triangular mass extending onto the cornea in the horizontal meridian, most commonly nasally although may be nasal, temporal, or both
 - b. Usually bilateral
 - c. Lesion usually thick, vascular, has a leading edge (cap) with an iron line central to it on the cornea, a fleshy head from the cap to the limbus, and a fleshy body in the conjunctiva with discrete superior and inferior margins
 - d. May be quiescent with less dilated vessels and little growth or "active" with dilated vessels and progressive growth centrally on the cornea
 - e. Punctate staining or dellen formation may be present central to the cap on the cornea
 - f. Restriction of ocular mobility may occur, especially on lateral gaze with extensive lesions or lesions recurrent after prior surgeries
2. Pinguecula

- a. Yellow white conjunctival lesion
- b. Most commonly located nasally, may be temporal, in the interpalpebral space
- c. Adjacent to limbus
- d. Does not involve the cornea
- e. May be associated with an adjacent cataract

E. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Pterygium and pinguecula are clinically diagnosed
- 2. May be confirmed by histopathology after excision

II. Define the risk factors

- A. Ultraviolet light exposure, especially in the early years of life**
- B. Living closer to the equator**
- C. Possibly wind and sand exposure**
- D. Uncommonly familial**

III. List the differential diagnosis

A. Pterygium

- 1. Pseudopterygium
 - a. Occurs after focal corneal trauma or inflammation
 - b. May occur in any meridian and is non-adherent to the limbus so a probe can be passed beneath it
- 2. Symblepharon and subconjunctival fibrosis associated with:
 - a. Mucous membrane pemphigoid
 - b. Stevens-Johnson syndrome
 - c. Atopic disease
 - d. Chemical injury
- 3. Pinguecula
- 4. Pannus
 - a. Usually does not involve the conjunctiva peripheral to the limbus
 - b. Usually concentric with the limbus
- 5. Conjunctival/corneal intraepithelial neoplasia or other limbal tumors
 - a. Usually appears morphologically different, lacks radial orientation and vascular straightening associated with pterygium

B. Pinguecula

1. Dermoid
2. Pterygium
3. Nonpigmented nevus
4. Conjunctival intraepithelial neoplasm

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy

1. Artificial tears/ocular lubricants
2. Vasoconstrictors intermittently for redness
3. Topical corticosteroids briefly when lesion very inflamed
4. Ultraviolet B blocking eyeglasses or sunglasses may have a role in reducing the likelihood of progression or recurrence

B. Describe surgical therapy (See Pterygium excision)

1. Excision of pinguecula in rare cases when chronically inflamed, interfere with contact lens wear, or for cosmetic reasons.

V. List the complications of treatment, their prevention and management

A. Topical corticosteroid side effects

B. Pterygium

1. Recurrence after surgical treatment
 - a. This appears to be most frequent with simple excision leaving bare sclera, least frequent with primary closure, conjunctival grafting, amniotic membrane transplantation and/or mitomycin C application
 - b. There is a higher rate of recurrence with subsequent resections
 - c. Recurrence can be managed with post-operative 5-Fu or triamcinolone injections, conjunctival autograft, amniotic membrane transplantation, or mitomycin C
2. Fibrosis with restriction of ocular motility
3. Dellen formation related to inadequate smoothing at limbus, too thick a conjunctival graft at the limbus
4. Pyogenic granuloma formation
5. Irregular astigmatism - less likely with avulsion of the head from the cornea or blunt dissection
6. Corneal and/or scleral melting with mitomycin C or radiation

C. Pinguecula

1. Post-surgical recurrence
2. Pyogenic granuloma formation

VI. Describe appropriate patient instructions

A. Avoidance of ultraviolet light

1. Sunglasses, protective eyewear
2. Brimmed hat

B. Limit the use of topical corticosteroids

C. Frequent use of artificial tears

D. Discourage chronic vasoconstrictor use

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Surgical Treatment of Pterygium, Module #12, 1996.
3. Al Fayez MF. Limbal versus conjunctival autograft transplantation for advanced and recurrent pterygium. *Ophthalmology* 2002;109:1752-5.
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7. Mahar PS. Conjunctival autograft versus topical mitomycin C in treatment of pterygium. *Eye* 1997;11:790-2.
8. Panda A, Das GK, Tuli SW, et al. Randomized trial of intraoperative mitomycin C in surgery for pterygium. *Am J Ophthalmol* 1998;125:59-63.
9. Manning CA, Kloess PM, Diaz MD, et al. Intraoperative mitomycin in primary pterygium excision. A prospective, randomized trial. *Ophthalmology* 1997;104:844-8.
10. Hirst LW. The treatment of pterygium. *Surv Ophthalmol* 2003;48:145-180.
11. Tsai YY, Chang KC, Lin CL, et al. Expression in pterygium by immunohistochemical analysis: a series report of 127 cases and review of the literature. *Cornea* 2005;24:583-6.

Salzmann nodular degeneration

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Postinflammatory fibrosis of subepithelial cornea
2. Idiopathic, reason for nodule formation is often unclear

B. List the pertinent elements of the history

1. History of corneal trauma
2. History of trachoma
3. Previous corneal surgery
4. Recurrent corneal erosions
5. Episodes of conjunctival injection/photophobia
6. History of contact lens wear

C. Describe pertinent clinical features

1. Gray-white/blue-white subepithelial nodules
2. Adjacent to corneal scarring or corneal pannus, or vascularization
3. Often localized to the midperiphery
4. Often overlying incisions, subepithelial scarring (e.g., following recurrent corneal erosions)
5. Surrounded by iron line or ring in some cases
6. Can be unilateral or bilateral

II. Define the risk factors

A. Any of the associated predisposing conditions listed above

B. More commonly seen in women

C. Fibrotic response following keratitis

1. Phlyctenulosis
2. Trachoma
3. Interstitial keratitis

D. Fibrotic response following epithelial disruption

1. Recurrent corneal erosions
 - a. Corneal epithelial basement membrane dystrophy
 - b. Corneal dystrophy of Bowman's layer

- c. Pseudophakic bullous keratopathy
- 2. Persistent epithelial defect
- 3. Keratoconjunctivitis sicca

E. Fibrotic response at incision site following corneal surgery

- 1. Penetrating keratoplasty
- 2. Cataract extraction
- 3. Laser in situ keratomileusis

III. List the differential diagnosis

- A. Calcific band keratopathy**
- B. Spheroidal degeneration**
- C. Gelatinous, droplike corneal dystrophy**
- D. Corneal keloid**

IV. Describe patient management in terms of treatment and follow-up

A. Indications for treatment

- 1. Interference with contact lens wear
- 2. Visual disturbance
 - a. Direct obstruction of visual axis
 - b. Associated tear film instability
 - c. Associated irregular astigmatism

B. Define medical therapy options

- 1. Artificial tear replacement
- 2. Punctal occlusion
- 3. Bandage soft contact lens

C. Define surgical therapy options

- 1. Epithelial debridement/superficial keratectomy/
- 2. Phototherapeutic keratectomy

V. List the complications of treatment, their prevention and management

A. Contact lens

- 1. Predisposition to infection

- a. May decrease incidence with the use of prophylactic antibiotics

B. Epithelial debridement/superficial keratectomy

1. Subepithelial corneal haze
 - a. Judicious use of topical corticosteroids
 - b. Possible use of anti-fibrotic agent mitomycin C

C. Phototherapeutic keratectomy

1. Irregular astigmatism
 - a. Minimize depth of ablation
 - b. Use masking agent
2. Subepithelial corneal haze
 - a. Judicious use of topical corticosteroids
 - b. Possible use of anti-fibrotic agent mitomycin C
3. Hyperopic shift
 - a. Minimize depth of ablation

VI. Describe disease-related complications

- A. Visual disturbance, recurrent corneal erosions with secondary bacterial keratitis**

VII. Describe appropriate patient instructions

- A. Treatment only indicated if one of the criteria listed above is met**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Aldave AJ, Sonmez B. Elucidating the molecular genetic basis of the corneal dystrophies: are we there yet? *Arch Ophthalmol.* 2007 Feb;125(2):177-86.
3. Weiss JS, Møller HU, Lisch W, et al. The IC3D classification of corneal dystrophies. *Cornea.* 2008;27:S1-S42

Band keratopathy

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Calcium hydroxyapatite deposition
 - a. Chronic ocular disease
 - i. Uveitis in children
 - ii. Phthisis bulbi
 - iii. Prolonged corneal edema, including corneal graft failure
 - iv. Silicone oil in an aphakic eye
 - v. Chronic exposure to mercurial vapors or to mercurial preservatives in ophthalmic medications
 - vi. Prolonged superficial keratitis or keratopathy
 - b. Hyperphosphatemia, such as associated with renal failure
 - c. Hypercalcemia, such as associated with sarcoidosis or hyperparathyroidism
2. Urate deposition
 - a. Brown urate deposits may be associated with hyperuricemia during gout

B. List the pertinent elements of the history

1. History of one of the etiologic conditions
 - a. Chronic eye disease
 - b. Chronic exposure to environmental irritants
 - c. Systemic disorders
2. Decreased visual acuity
3. Ocular discomfort

C. Describe pertinent clinical features

1. Early changes
 - a. Fine, dust like deposits in Bowman layer in the horizontal interpalpebral fissure zone
 - i. Deposits associated with ocular surface disease usually begin near the limbus
 - ii. Deposits associated with anterior uveitis usually begin centrally
 - b. Peripheral clear zone between the limbus and the peripheral edge of the band keratopathy
2. Later changes
 - a. Horizontal band of dense calcific plaque across interpalpebral zone of the cornea, varying in

color from beige-gray to chalky white

- b. Small holes or clear areas in the plaque

D. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. If no localized ocular cause identified
 - a. Calcium, phosphorus, albumin, magnesium, blood urea nitrogen (BUN), and creatinine (if renal disease or other systemic disease suspected)
 - b. Uric acid (if gout suspected)

II. Define the risk factors

- A. Chronic ocular surface or corneal disorder**
- B. Chronic anterior segment inflammation**
- C. Abnormal level of serum calcium, phosphate, or uric acid**

III. List the differential diagnosis

- A. Medication precipitation**
- B. Epithelial disorders, including spheroidal degeneration**
- C. Subepithelial corneal opacification**
 - 1. Age-related changes such as limbal girdle of Vogt
 - 2. Posttraumatic changes such as Coats white ring
 - 3. Post-inflammatory lipid deposition
 - 4. Superficial stromal dystrophies such as corneal dystrophy of Bowman layer I and II

IV. Describe patient management in terms of treatment and follow-up

- A. Describe medical therapy options**
 - 1. Treatment of any precipitating ocular conditions
 - a. Artificial tears in keratoconjunctivitis sicca
 - b. Topical corticosteroids in chronic iritis
 - 2. Treatment of underlying systemic conditions
 - 3. Bandage contact lens
- B. Describe the surgical therapy options**
 - 1. Indications
 - a. Associated ocular discomfort
 - b. Chronic overlying epithelial defect

- c. Decreased visual acuity
 - d. Recurrent infection
- 2. Scraping (debridement) and chelation for calcific band keratopathy
 - a. Removal of overlying epithelium and loose calcium deposits with surgical blade
 - b. Application of 0.4% - 3.0% ethylenediaminetetraacetic acid [EDTA]
 - i. Solution poured inside optical zone marker, trephine, or similar reservoir that is held onto corneal surface, or applied to corneal surface with soaked cellulose sponge
 - ii. Repeated until most calcium phosphate is removed
 - c. Bandage soft contact lens can be placed until epithelium has healed
- 3. Phototherapeutic keratectomy
 - a. Considered for vision-limiting calcific deposits that remain after scraping and chelation
 - b. Transepithelial ablation or ablation after epithelium has been removed (with a masking agent)

V. List the complications of treatment, their prevention and management

A. Scraping and chelation

- 1. Bacterial keratitis
 - a. Prevention
 - i. Use of antiseptic technique during surgical removal
 - ii. Uncertain role of prophylactic antibiotics, although topical antibacterial agent could be considered until epithelial defect has resolved
 - b. Management: (See Bacterial keratitis)
- 2. Incomplete removal or recurrence
 - a. Management
 - i. No further treatment
 - ii. Additional debridement, chelation, or phototherapeutic keratectomy
- 3. Corneal scarring
 - a. Prevention
 - i. Minimize scraping of Bowman layer

B. Phototherapeutic keratectomy

- 1. Irregular corneal surface secondary to different rates of ablation between calcium and corneal stroma
 - a. Prevention

- i. Transepithelial ablation
 - ii. Use of masking agent
 - iii. Limiting depth of ablation
- 2. Corneal scarring
 - a. Prevention
 - i. Limiting depth of ablation
 - ii. Use of topical corticosteroids after treatment

VI. Describe disease-related complications

- A. Decreased visual acuity**
- B. Discomfort**
 - 1. Surface irregularity
 - 2. Recurrent corneal erosions
- C. Undesirable cosmetic appearance**

VII. Describe appropriate patient instructions

- A. Management of predisposing condition (if identified and if possible) important in prevention of recurrences**
- B. Serial treatments may be necessary**
 - 1. Probability of recurrence and necessity for repeat removals

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
- 2. Aldave AJ, Sonmez B. Elucidating the molecular genetic basis of the corneal dystrophies: are we there yet? *Arch Ophthalmol*. 2007 Feb;125(2):177-86.
- 3. Weiss JS, Møller HU, Lisch W, et al. The IC3D classification of corneal dystrophies. *Cornea*. 2008;27:S1-S42.

Pigmentation of the conjunctiva and cornea

I. Describe the approach to establishing the diagnosis

A. Define the pertinent elements of the history

1. Age of onset
2. Duration and progression
3. Medication use

B. Describe pertinent clinical features

1. Color
2. Location, distribution, and number of pigmented foci
3. Depth
 - a. Intraepithelial (conjunctival)
 - b. Subepithelial (episcleral)
4. Size, shape, and edges of lesion
5. Thickness and consistency
6. Growth and rate of change
7. Presence or absence of cysts, inflammation, ulceration, or bleeding
8. Status of cornea and adjacent tissues
9. Status of regional lymph nodes
10. Periocular skin pigmentation

II. List the differential diagnosis

A. Conjunctival pigmentation

1. Conjunctival pigmentation associated with skin complexion (also called benign epithelial melanosis or racial melanosis)
 - a. Typically bilateral
2. Conjunctival nevus
 - a. Usually small
 - b. Sometimes cystic
 - c. Very frequently stable in color and size

- d. Congenital melanocytic nevus
 - i. Pigmentation may increase with puberty or pregnancy
- e. Acquired melanocytic nevus
- 3. Primary acquired melanosis
 - a. Multiple or diffuse
 - b. Flat brown patches
- 4. Melanoma of the conjunctiva
- 5. Secondary acquired melanosis
 - a. Postinflammatory melanosis, following chronic conjunctivitis
 - b. Systemic conditions with flat pigmentary patches of conjunctiva:
 - i. Addison disease
 - ii. Peutz-Jeghers syndrome
 - iii. Von Recklinghausen disease
- 6. Brown, black, or gray deposits
 - a. Carbon or metal deposits
 - b. Adrenochrome (oxidized epinephrine) deposits
 - c. Argryrosis (silver deposition)
 - d. Oral medications: tetracyclines or phenothiazines

B. Episcleral or scleral pigmentation

- 1. Nerve loops of Axenfeld
- 2. Ocular melanocytosis (melanosis oculi) and oculodermal melanocytosis (nevus of Ota)
- 3. Extraocular extension of uveal melanoma
- 4. Alkaptonuric ochronosis
- 5. Senile scleral plaques
- 6. Foreign body

C. Corneal epithelial pigmentation

- 1. Striate melanokeratosis: melanin pigmentation extending from limbus
- 2. Iron line associated with uneven corneal topography or with aging
- 3. Pigmented band keratopathy
- 4. Spheroidal degeneration
- 5. Cornea verticillata
 - a. Fabry disease (X-linked lysosomal storage disease)

- b. Amiodarone medication use

D. Corneal stromal pigmentation

1. Intrastromal melanin following perforating corneal trauma or surgery
2. Deposits associated with systemic medications, such as phenothiazines or gold
3. Foreign bodies, including ocular siderosis
4. Corneal blood staining associated with hyphema
5. Kayser-Fleischer ring associated with copper deposition in Wilson disease

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Melanoma and Other Pigmented Lesions of the Ocular Surface, Module #11, 1996.
3. AAO, Focal Points: Ocular Surface Neoplasia, Module #1, 2007.

Postinflammatory, post-traumatic, and postsurgical corneal opacity

I. Describe the approach to establishing the diagnosis

A. List the pertinent elements of the history

1. History of previous ocular inflammation - "red eyes", "infection", or "keratitis"
2. History of orofacial herpes simplex
3. History of herpes zoster ophthalmicus
4. History of sexually transmitted disease
5. History of trauma including chemical injury
6. History of ocular surgery - type of procedure and complications encountered
7. Description of course and nature of visual loss and associated symptoms

B. Describe pertinent clinical features

1. Location and depth of corneal opacification
 - a. Bilateral versus unilateral
 - b. Focal versus multifocal
 - c. Central versus peripheral
2. Associated findings
 - a. Neovascularization and ghost vessels
 - b. Lipid deposition
 - c. Corneal thinning
 - d. Corneal edema
 - e. Epithelial defect
 - f. Corneal anesthesia
 - g. Associated intraocular findings - e.g., posterior synechiae, peripheral anterior synechiae, elevated intraocular pressure (IOP)

II. List the differential diagnosis

A. Corneal dystrophy

B. Congenital corneal opacity

C. Chronic stromal keratitis, such as herpes simplex virus (HSV) stromal keratitis or varicella zoster virus (VZV) keratitis

- D. Chronic microbial keratitis, including infectious crystalline keratopathy**
- E. Corneal deposits**

III. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Work up and treat any underlying medical condition causing the opacification
2. Improve visual function
 - a. Contact lenses
 - i. Correct irregular astigmatism
 - b. Topical hypertonic agents
 - i. Relieve superficial corneal edema
 - c. Alleviate discomfort or pain
 - d. Bandage contact lenses
 - e. Lubricants
 - f. Cycloplegic agents
3. Enhance cosmetic appearance
 - a. Custom designed eyeglasses
 - b. Cosmetic contact lens
 - c. Scleral shell

B. Describe surgical therapy options

1. Improve visual function
 - a. Superficial keratectomy
 - b. Phototherapeutic keratectomy
 - c. Anterior lamellar keratoplasty
 - d. Penetrating keratoplasty
 - e. Rotational autograft
2. Alleviate discomfort or pain if persistent corneal edema or epithelial defect
 - a. Bandage contact lens
 - b. Corneal cautery
 - c. Conjunctival flap
 - d. Amniotic membrane graft
 - e. Penetrating keratoplasty

- f. Retrobulbar alcohol if poor visual potential
- 3. Enhance cosmetic appearance
 - a. Penetrating or lamellar keratoplasty
 - b. Corneal tattoo

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Chemical (alkali and acid) injury of the conjunctiva and cornea

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Chemical agents alter the levels of highly reactive hydrogen and hydroxyl ions in affected tissues
2. Alkalis
 - a. Raise pH of tissues causing saponification of fatty acids in cell membranes and cellular disruption
 - b. Surface epithelial damage allows penetration of alkali into corneal stroma destroying proteoglycan ground substance and collagen fibers of stroma matrix
 - c. Leukocytic infiltration of corneal stroma
 - d. Secondary protease expression by corneal cells and leukocytes and penetration into anterior chamber can then occur causing tissue damage and inflammation
 - e. Damage to limbal stem cells can lead to disruption of normal repopulation of corneal epithelium, resulting in:
 - i. Conjunctivalization of the cornea with vascularization
 - ii. Goblet cells in the cornea
 - iii. Poor epithelial adhesion
 - iv. Recurrent epithelial breakdown
 - v. Stromal thinning, worse with persistent epithelial defect
 - vi. Chronic inflammation
3. Acids
 - a. Lower pH of tissues and cause denaturing and precipitation of proteins in tissues
 - b. Cause less injury than alkalis due to buffering capacity of tissues and barrier formed by precipitated proteins
 - c. Can cause severe inflammation leading to upregulation of protease expression resulting in damage to corneal matrix

B. List the pertinent elements of the history

1. Nature of the chemical substance
2. Method of exposure and quantity of chemical substance
3. Duration of exposure and time to treatment
4. Immediate measures taken including irrigation, removal of particulate material

5. Presence of a contact lens

C. List the pertinent clinical features

1. Extent of ocular surface injury
 - a. Amount of scleral and limbal ischemia or blanching (predictor of progression to limbal stem cell failure)
 - b. Percentage of epithelial defect
 - c. Presence of corneal edema and haze
 - d. Presence of stromal necrosis
 - e. Presence of intraocular inflammation
2. Presence and degree of skin and eyelid burns
3. pH of offending substance and of ocular surface
4. Residual chemical matter on the ocular surface

II. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Minimize ongoing exposure to offending agent
 - a. Immediate and copious irrigation of the ocular surface with water or normal saline or any nontoxic solution that is not grossly contaminated
 - i. Use of eyelid immobilization, topical anesthesia, and continuous irrigation with IV tubing, irrigating lid speculum, or irrigating contact lens (e.g., Medi-flow)
 - b. Irrigation should continue until pH of the conjunctival sac is normalized
 - c. Removal of contact lenses
 - d. Removal of particulate matter from the ocular surface with cotton-tip applicators and forceps
 - i. Double eversion of lids to look for matter
2. Decrease inflammation
 - a. Topical corticosteroids in the acute phase (inhibit leucocyte) (during first 2 weeks)
 - b. Oral tetracyclines, citric acid (chelate calcium in the plasma membrane of leucocytes)
 - c. Topical 1% medroxyprogesterone (suppresses collagen breakdown)
 - d. Topical cycloplegics in patients with significant anterior chamber reaction
 - e. Amniotic membrane grafts
 - f. Systemic corticosteroids
3. Control intraocular pressure
 - a. Oral carbonic anhydrase inhibitor to prevent ocular surface toxicity

- b. Topical therapies if epithelium is healing well
- 4. Promote healing
 - a. Stroma
 - i. Oral vitamin C (high dose, approximately 2 g per day) (ascorbic acid is a cofactor in collagen synthesis) (monitor renal status)
 - b. Epithelium
 - i. Intensive nonpreserved lubricants
 - ii. Bandage contact lens with topical antibiotic broad-spectrum prophylaxis
- 5. Inhibit collagenolysis
 - a. Topical agents
 - i. Medroxyprogesterone
 - ii. N-acetylcysteine
 - iii. Na-citrate
 - iv. Ethylenediaminetetraacetic acid (EDTA)
 - b. Oral agents
 - i. Doxycycline/tetracycline
 - ii. Vitamin C
 - iii. Oral corticosteroids

B. Describe surgical therapy options

- 1. Normalize pH
- 2. Promote healing
 - a. Tarsorrhaphy
- 3. Ocular surface reconstruction
 - a. Early
 - i. Amniotic membrane grafting to ocular surface (sutured or self retained)
 - b. Late
 - i. Autologous conjunctival or limbal transplant from the uninvolved eye
 - ii. Limbal stem cell replacement (cadaveric keratolimbal or living-donor conjunctival-limbal allograft)
 - iii. Amniotic membrane transplantation has limited effectiveness in the presence of severe limbal stem cell deficiency)
 - iv. Mucous membrane graft (reconstruct fornix)
 - v. Corneal transplantation has very poor prognosis if eye inflamed or if stem cells deficient

- vi. Keratoprosthesis
- 4. Eyelid reconstruction
 - a. Repair of ectropion, entropion, trichiasis, exposure

III. List the complications of treatment, their prevention and management

A. Corticosteroids

- 1. Infection
- 2. Predisposition to stromal thinning and perforation
- 3. Delayed reepithelialization

B. Bandage contact lens

- 1. Infection

C. Corneal transplantation

- 1. Rejection (See Allograft rejection)
- 2. Graft failure (See Penetrating keratoplasty)
- 3. Persistent epithelial defect (See Persistent corneal epithelial defect)
 - a. Stromal thinning
 - b. Perforation

IV. Describe disease-related complications

- A. Ocular surface disease/dry eye state
- B. Corneal stem cell deficiency
- C. Secondary super-infection
- D. Corneal stromal scarring and vascularization
- E. Corneal perforation
- F. Intraocular inflammation and synechiae formation
- G. Glaucoma
- H. Symblepharon formation and lid position abnormalities
- I. Phthisis bulbi

V. Describe appropriate patient instructions

- A. Immediate copious irrigation
- B. Use of topical and oral medications to promote healing and prevent complications
- C. Chronicity of injury in severe burns

D. Compliance with follow-up

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Wagoner MD, Kenyon KR. Chemical injuries of the eye. In: Albert DM, Jakobiec FA, eds. Principles and Practice of Ophthalmology. Vol 2. 2nd ed. Philadelphia: Saunders; 2000:943-959.
3. Letko E, Stechschulte SU, Kenyon KR, et al. Amniotic membrane inlay and overlay grafting for corneal epithelial defects and stromal ulcers. Arch Ophthalmol. 2001;119:659-663.

Toxic medication injury of the conjunctiva

I. Describe the approach to establishing the diagnosis

A. Provide mechanistic description

1. Direct toxicity to cell membranes of conjunctival epithelium producing cell loss and secondary inflammation
2. Irritant effect of specific agents on conjunctiva -associated lymphoid tissue

B. List the pertinent elements of the history

1. History of prolonged use of topical medication
2. History of topical anesthetic abuse

C. List the pertinent clinical features

1. Generalized injection of the bulbar and tarsal conjunctiva
2. Mild to severe papillary reaction of the tarsal conjunctiva
3. Mucopurulent discharge
4. Asymmetry between eyes
5. Chronic follicular conjunctivitis, more prominent on the inferior tarsus and fornix
6. Bulbar follicles
7. Subconjunctival fibrosis
8. Pseudomembranoid or drug-induced mucous membrane pemphigoid (progressive fibrosis)

II. Define the risk factors

A. Common topical therapeutic agents include

1. Atropine
2. Topical aminoglycosides
3. Antiviral agents
4. Miotics especially phospholine iodide
5. Sulfonamides
6. Epinephrine
7. Apraclonidine
8. Alpha2-adrenergic agonists
9. Vasoconstrictors
10. Topical antimetabolites

- B. Topical anesthetic agents

III. List the differential diagnosis

- A. Allergic conjunctivitis
- B. Vernal conjunctivitis
- C. Atopic conjunctivitis
- D. Viral conjunctivitis
- E. Contact-lens induced conjunctivitis
- F. Bacterial conjunctivitis
- G. Chlamydial conjunctivitis
- H. Mucous membrane pemphigoid
- I. Chemical injury
- J. Conjunctivochalasis
- K. Sequelae of Stevens-Johnson syndrome

IV. Describe patient management in terms of treatment and follow-up

- A. Define medical therapy options
 - 1. Discontinuation of offending topical medications
 - 2. Topical lubricants
 - 3. Chemotherapy (dapsone, cyclophosphamide, corticosteroids) for drug-induced mucous membrane pemphigoid

V. Describe the disease-related complications

- A. Symblepharon
- B. Trichiasis
- C. Entropion
- D. Superficial keratitis
- E. Corneal ulceration
- F. Corneal scarring

VI. Describe appropriate patient instructions

- A. Discontinuation of offending agents
- B. Resolution of signs and symptoms may take weeks to months
- C. Use of topical lubricants to optimize the ocular surface

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Grant WM, Schuman JS. Toxicology of the Eye. 4th ed. Springfield, IL: Thomas; 1993.
3. Liesegang TJ. Conjunctival changes associated with glaucoma therapy: implications for the external disease consultant and the treatment of glaucoma. *Cornea*. 1998;17:574-583.

Toxic medication injury of the cornea

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Dose-dependent cytotoxicity involving the corneal epithelium and corneal stem cells in some instances
2. Epithelial loss and breakdown can lead to stromal scarring and thinning associated with upregulation of matrix metalloproteinases
3. Irritant effect on conjunctiva
 - a. Associated lymphoid tissue hyperplasia may occur with specific agents

B. Describe the relevant aspects of epidemiology of the disease

1. Prolonged use of topical medications
2. Use of topical anesthetics
3. Aqueous tear deficiency and delayed tear clearance with use of topical medications

C. List the pertinent elements of the history

1. History of prolonged use of topical medication (common agents include anesthetics, aminoglycosides, antivirals, diclofenac, mitomycin, and drops preserved with benzalkonium chloride)
2. History of topical anesthetic abuse

D. List the pertinent clinical features

1. Punctate epithelial erosions of the inferior cornea
2. Diffuse punctate epitheliopathy
3. Vortex or hurricane keratopathy
4. Corneal epithelial defect of the inferior or central cornea
5. Stromal opacification
6. Dense stromal infiltrates or ring opacity
7. Corneal thinning
8. Corneal neovascularization
9. Limbal stem-cell deficiency
10. Peripheral corneal infiltrates with a limbal clear zone

II. Define the risk factors

A. Prolonged use of topical medications or use of topical anesthetics

- B. Aqueous tear deficiency**

III. List the differential diagnosis

- A. Dry eye syndrome**
- B. Microbial keratitis**
- C. Viral keratoconjunctivitis**
- D. Herpes simplex virus (HSV) keratitis**
- E. Amiodarone/Indomethacin vortex keratopathy**
- F. Neurotrophic keratopathy**
- G. Exposure keratopathy**
- H. Chronic blepharoconjunctivitis**

IV. Describe patient management in terms of treatment and follow-up

- A. Define medical therapy options**
 - 1. Discontinuation of offending topical medications
 - 2. Topical preservative free lubricants
 - 3. Topical corticosteroids
- B. Lateral tarsorrhaphy for severe cases**

V. List the complications of treatment, their prevention and management

- A. Topical corticosteroids can cause cataract, glaucoma, and predispose to infection**

VI. Describe disease-related complications

- A. Microbial keratitis**
- B. Corneal thinning with secondary irregular astigmatism**
- C. Corneal perforation**
- D. Corneal opacification**

VII. Describe appropriate patient instructions

- A. Discontinuation of offending agents**
- B. Resolution of signs and symptoms may take weeks to months**
- C. Use of topical lubricants for comfort**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Grant WM, Schuman JS. Toxicology of the Eye. 4th ed. Springfield, IL: Thomas; 1993.
3. Liesegang TJ. Conjunctival changes associated with glaucoma therapy: implications for the external disease consultant and the treatment of glaucoma. *Cornea* 1998;17:574-583.

Subconjunctival hemorrhage

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Direct injury to ocular surface
2. Sudden venous congestion (Valsalva maneuver)
 - a. Vomiting
 - b. Forceful coughing
 - c. Weight lifting
 - d. Straining to defecate or urinate
3. Vascular fragility (e.g., conjunctival amyloid deposition)
4. Thrombocytopenia and/or impaired clotting
5. Medications
 - a. Systemic (chemotherapy, anti-coagulants)
 - b. Topical (corticosteroids)
6. Uncontrolled hypertension
7. Idiopathic

B. List the pertinent elements of the history

1. Ocular or cranial trauma
2. History of Valsalva maneuver
3. History of hypertension
4. Use of oral anticoagulants (medications or vitamins)

C. Describe pertinent clinical features

1. Extravasated blood within and beneath the conjunctiva
 - a. May be localized or diffuse
 - b. Appearance not affected by vasoconstrictors

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. If patient has a history of recurrent subconjunctival hemorrhages, as well as features of a bleeding diathesis (easy bruising, bleeding from the gums, nose or bowels), may consider
 - a. Bleeding time
 - b. Complete blood count (CBC)
 - c. Prothrombin time (PT) and INR derived from the PT if patient is on warfarin (Coumadin)

- d. Activated partial thromboplastin time (aPTT)
- 2. Blood pressure

II. Define the risk factors

- A. Local trauma
- B. Increased venous or arterial blood pressure
- C. Bleeding diathesis

III. List the differential diagnosis

- A. Focal or diffuse conjunctival injection
 - 1. Episcleritis
 - 2. Pingueculitis
 - 3. Scleritis
 - 4. Conjunctival trauma
 - 5. Allergic or infectious conjunctivitis
 - 6. Localized corneal amyloid deposition

IV. Describe patient management in terms of treatment and follow-up

- A. Describe medical therapy options
 - 1. No treatment needed in most cases
 - 2. Topical lubricants if necessary for localized drying
 - 3. Address underlying systemic condition, if present
- B. Describe surgical therapy options in chronic recurrent disease
 - 1. Argon laser of feeding vessels if anatomic area is identified
 - 2. Conjunctival excision if anatomic area identified

V. List the complications of treatment, their prevention and management

- A. No treatment needed

VI. Describe disease-related complications

- A. No sequelae result from the subconjunctival hemorrhage itself
- B. Localized drying, dellen, or exposure keratopathy if large and protuberant

VII. Describe appropriate patient instructions

- A. Reassurance that no treatment is needed, and subconjunctival hemorrhage itself will not harm the eye**
- B. Spontaneous resolution expected in 7-14 days**
- C. Hemorrhage may enlarge before it resolves, and may appear to change colors during its resolution**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Conjunctival laceration

I. Describe the approach to establishing the diagnosis

A. List the pertinent elements of the history

1. History of trauma
 - a. Timing
 - b. Circumstances
 - i. Likelihood of foreign body
 - ii. Nature of foreign body
2. Pain
3. Foreign body sensation
4. Discomfort with blinking
5. Tearing
6. Loss of vision - suggestive of more extensive injury
7. Purulent discharge - suggestive of infection

B. Describe pertinent clinical features

1. Conjunctival erythema
2. Subconjunctival hemorrhage
3. Slit-lamp biomicroscopic examination with topical anesthesia (evaluate both eyes)
 - a. Determine extent of laceration
 - b. Explore margins, base with forceps or cotton-tip for
 - i. Foreign body
 - ii. Scleral laceration
 - c. Assess anterior segment for signs of globe penetration
 - d. Dilated fundus exam to examine for intraocular foreign body
 - e. Imaging study may be indicated
 - i. X-Ray and/or CT scan if intraorbital foreign body suspected
 - ii. Anterior segment ultrasound biomicroscopy if occult anterior segment foreign body suspected

II. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Topical antibiotic prophylaxis until laceration healed
2. Topical corticosteroids to control inflammation as needed
3. Topical lubricants for comfort as needed
4. Oral analgesics as needed
5. Regular follow-up until healed

B. Describe surgical therapy options

1. Peritomy for further exploration if possibility of globe penetration can not be ruled out with office examination
2. Foreign body removal that can not be accomplished at slit-lamp biomicroscope
3. Suture closure of laceration - rarely necessary, unless large flap of conjunctiva is dislocated and then close for patient comfort

III. List the complications of treatment, their prevention and management

A. Allergy to topical medications

1. Prevention
 - a. History
2. Management
 - a. Cessation of medication
 - b. Consider use of topical corticosteroids if clean and healing

B. Infection

1. Prevention
 - a. Antibiotic prophylaxis
2. Management
 - a. Culture and sensitivity
 - b. More intensive topical antibiotic therapy, directed at specific organisms once known
 - c. Systemic antibiotics if infectious scleritis develops

IV. Describe disease-related complications

A. Infection

B. Retained foreign body

C. Associated scleral laceration, globe penetration

V. Describe appropriate patient instructions

- A. Proper use of topical medications**
- B. When to seek further care**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Conjunctival foreign body

I. Describe the approach to establishing the diagnosis

A. List the pertinent elements of the history

1. History of trauma
 - a. Timing
 - b. Nature of injury, possible alkali exposure (e.g., cement)
2. Foreign body sensation
3. Discomfort with blinking
4. Tearing
5. Photophobia
6. Blurred vision

B. Describe pertinent clinical features

1. Conjunctival erythema and/or hemorrhage
2. Lid edema may be present
3. Visible foreign body
4. Secondary epithelial erosions
 - a. Linear pattern of fluorescein staining is highly suggestive of foreign body on corresponding tarsal conjunctiva

II. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Topical antibiotic prophylaxis, drops or ointments
2. Follow-up to evaluate healing if epithelial keratopathy or abrasion present

B. Describe surgical therapy options

1. Removal usually possible with slit lamp biomicroscope in office
 - a. Apply topical anesthesia
 - b. Always evert upper lids. May use Desmarres retractor or bent paper clip to visualize foreign body
 - c. Double-evert lid if multiple foreign bodies or particulate matter suspected
 - d. Wipe away superficial foreign body(ies) with cotton-tipped applicator
 - e. Remove embedded foreign body(ies) with jewelers forceps or needle tip

- f. If no foreign body visualized, or if multiple foreign bodies present or suggested by history, irrigate fornix and sweep with cotton-tipped applicator
2. Patients with multiple, extensive foreign bodies or who are uncooperative may need exploration in operating room
3. Take meticulous care in removal of all foreign bodies, particularly in cases of wet cement or other alkali-containing materials
4. Topical antibiotic prophylaxis, drops or ointments following removal

III. List the complications of treatment, their prevention and management

A. Allergy to topical medications

1. Prevention
 - a. History
2. Management
 - a. Cessation of medication, consider use of topical corticosteroids if clean and healing

B. Infection

1. Prevention
 - a. Antibiotic prophylaxis
2. Management
 - a. Culture and sensitivity
 - b. More intensive topical antibiotic therapy, directed at specific organisms once known
 - c. Systemic antibiotics if infectious scleritis develops

IV. Describe disease-related complications

- A. Secondary epithelial erosion**
- B. Microbial keratitis**
- C. Allergic conjunctivitis**
- D. Chemical burn if significant acid or alkali content**

V. Describe appropriate patient instructions

- A. Proper use of topical medications**
- B. When to seek further care**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Corneal foreign body

I. Describe the approach to establishing the diagnosis

A. List the pertinent elements of the history

1. History of trauma
 - a. Timing
 - b. High- or low-velocity injury
 - c. Nature of material
2. Foreign body sensation

B. Describe pertinent clinical features

1. Visualize foreign body location and depth
2. Evaluate chamber depth and perform Seidel test if deep corneal foreign body extends into inner eye

II. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Topical antibiotic prophylaxis
2. Systemic antibiotics for extension into anterior chamber
3. Topical cycloplegics for relief of ciliary spasm
4. Embedded glass foreign bodies without surface exposure are often inert and may be left in place, but must be followed carefully for evidence of infection or inflammation
5. Pressure patching or topical nonsteroidal anti-inflammatory drugs (NSAIDs) may aid in comfort
6. Initially, frequent evaluation for microbial keratitis, endophthalmitis, aqueous leak
7. Evaluate both eyes

B. Describe surgical therapy options

1. Remove all accessible foreign bodies
 - a. Topical anesthesia
 - b. Jeweler's forceps or needle tip to remove foreign body
 - c. Battery-powered drill with sterile dental burr for removal of rust resistant to removal with needle tip
2. Indications for sterile operating room environment
 - a. Foreign body inaccessible from corneal surface

- b. Extension into anterior chamber present or suspected
 - c. Multiple, extensive foreign bodies
 - d. Uncooperative patient
- 3. Surgical technique for deep, embedded foreign bodies
 - a. Topical or peribulbar anesthesia, sedation as needed
 - b. Surgical "cut-down" or placement of needle through uninvolved cornea at obtuse angle to foreign body, with manipulation to push foreign body back along entry track
 - c. Paracentesis, ophthalmic viscosurgical device (viscoelastic) if extension into anterior chamber
 - d. Corneal sutures if necessary (See Corneal and corneoscleral laceration)

III. List the complications of treatment, their prevention and management

A. Penetration into anterior chamber with aqueous leakage

- 1. Prevention
 - a. Avoid overly aggressive attempts to remove embedded foreign bodies at the slit-lamp biomicroscope
- 2. Management
 - a. Therapeutic contact lens
 - b. Tissue adhesive (See Application of corneal tissue adhesive, Corneal and corneoscleral laceration)
 - c. Surgical repair

IV. Describe disease-related complications

A. Microbial keratitis

B. Sterile keratitis

- 1. Immune
- 2. Chemical
 - a. Plant
 - b. Animal (e.g., envenomations)

C. Corneal scarring

D. Regular and irregular astigmatism

E. Endophthalmitis

- 1. Prevention
 - a. Avoid penetration of anterior chamber

- b. Prophylactic antibiotics

V. Describe appropriate patient instructions

- A. Proper use of topical medications**
- B. Avoid postoperative exposure to non-sterile tap water**
- C. Hand-washing, proper wound care as applied to ocular surface**
- D. When to seek further care**

Additional Resource

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Goyal R, Shankar J, Fone DL, et al. Randomised controlled trial of ketorolac in the management of corneal abrasions. *Acta Ophthalmol Scand*. 2001;79:177-9.
3. Kaiser PK. A comparison of pressure patching versus no patching for corneal abrasions due to trauma or foreign body removal. Corneal Abrasion Patching Study Group. *Ophthalmology*. 1995;102:1936-42.

Traumatic corneal abrasion

I. Describe the approach to establishing the diagnosis

A. List the pertinent elements of the history

1. History of trauma
 - a. Timing
 - b. Circumstances
 - i. Nature of injury
 - ii. Contact lens wear
 - c. Absence of symptoms suggestive of recurrent erosion or herpes simplex virus (HSV)
 - d. Work history (construction, plumbing, welder)
 - e. History of recent general anesthesia
2. Pain
3. Foreign body sensation
4. Discomfort with blinking
5. Tearing
6. Photophobia
7. Blurred vision if visual axis involved

B. Describe pertinent clinical features

1. Epithelial defect on slit-lamp biomicroscopic examination
 - a. Positive fluorescein staining
 - b. Size of defect may be measured to follow healing
2. Presence or absence of stromal edema or infiltrate
3. Loose epithelial tissue
4. Presence or absence of corneal or tarsal conjunctival foreign body
5. Note opacification or signs of infection

II. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Topical anti-infective drop or ointment often used
2. Pressure patching

- a. Does not accelerate healing, though theoretically reduces repetitive lid trauma from blinking
 - b. May be more comfortable for patients with large abrasion
 - c. Potential risk of exacerbating microbial keratitis in abrasions associated with contact lens wear
 - d. Patients unable to assess if vision worsens
3. Therapeutic contact lens for comfort
 4. Topical cycloplegic agent for comfort
 5. Topical nonsteroidal anti-inflammatory drugs (NSAIDs) for comfort
 6. Use 5% NaCl ointment q hs in cases of trauma from organic material to prevent recurrent erosions
 7. Frequent follow-up to evaluate for microbial keratitis
 - a. Initial follow up may be daily if:
 - i. Large abrasion
 - ii. Associated with contact lens
 - iii. Secondary to trauma with dirty or organic material

B. Define surgical therapy options

1. Rarely necessary, unless corneal abrasion is associated with:
 - a. Persistent corneal epithelial defect (See Persistent corneal epithelial defect)
 - b. Recurrent corneal erosion (See Recurrent erosion)
 - c. Tear deficiency (See Aqueous tear deficiency, Sjögren syndrome and Mucin deficiency)
 - d. Neurotrophic keratopathy (See Neurotrophic keratopathy)
 - e. Exposure keratopathy (See Exposure keratopathy)
 - f. Corneal melting or perforation (See Corneal perforation)
2. May include
 - a. Punctal occlusion
 - b. Corneal epithelial and/or basement membrane debridement
 - c. Anterior stromal puncture
 - d. Phototherapeutic keratectomy
 - e. Tarsorrhaphy

III. List the complications of treatment, their prevention and management

A. Allergy to topical medications

1. Prevention

- a. History
- 2. Management
 - a. Cessation of medication
 - b. Consider use of topical antihistamine, mast cell stabilizer, NSAID, and/or corticosteroid if abrasion clean and healing
- B. Epithelial toxicity, delayed healing (especially NSAIDs)**
 - 1. Prevention
 - a. Minimize use of topical medications
 - 2. Management
 - a. Cessation or dose reduction
- C. Therapeutic contact lens**
 - 1. Tight lens syndrome
 - a. Prevention
 - i. Good fit
 - b. Management
 - i. Discontinue lens
 - ii. Looser fit
 - 2. Bacterial keratitis (See Bacterial keratitis)
- D. Recurrent erosion**
 - a. Management
 - i. Lubricants and hypertonic solutions
 - ii. Stromal puncture/superficial keratectomy (see Recurrent erosion section)
- E. Superficial corneal scarring associated with delayed epithelial healing**

IV. Describe disease-related complications

- A. Microbial keratitis**
- B. Recurrent erosions especially in those caused by fingernail or paper cut injury, or by vegetative trauma**
- C. Persistent epithelial defect**
- D. Corneal scarring**

V. Describe appropriate patient instructions

- A. Proper use of topical medications**

B. When to seek further care

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Corneal Complications of Contact Lens, Module #2, 1993.
3. Goyal R, Shankar J, Fone DL, et al. Randomised controlled trial of ketorolac in the management of corneal abrasions. *Acta Ophthalmol Scand*. 2001;79:177-9.
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5. Morrison D, Eke T, Austin DJ. High prevalence of recurrent symptoms following uncomplicated traumatic corneal abrasion. *Br J Ophthalmol*. 1998;76:108-11.
6. Kaiser PK, Pineda R 2nd. A study of topical non steroidal anti-inflammatory drops and no pressure patching in the treatment of corneal abrasions. Corneal Abrasion Patching Study Group. *Ophthalmology*. 1997;104:1353-9.
7. Kaiser PK. A comparison of pressure patching versus no patching for corneal abrasions due to trauma or foreign body removal. Corneal Abrasion Patching Study Group. *Ophthalmology*. 1995;102:1936-42.

Corneal and corneoscleral laceration

I. Describe the approach for establishing the diagnosis

A. Describe the etiology of this disease

1. Occurs due to blunt or penetrating globe trauma

B. Define the relevant aspects of epidemiology of the disease

1. Incidence is common in industrial and farm workers, and in young males

C. List the pertinent elements of the history

1. Mechanism and nature of injury (specifically time and circumstances of injury, suspected composition of intraocular foreign body, high or low-velocity injury, use of eye protection)
2. Previous history of ocular trauma or surgery
3. Level of acuity prior to injury
4. Medications
5. Time of last oral intake
6. Status of tetanus prophylaxis

D. Describe pertinent clinical features

1. Clinically evident corneal, corneoscleral, or scleral laceration
2. Uveal prolapse
3. Flat or shallow anterior chamber
4. Hypotony
5. Aqueous humor efflux as detected by Seidel test
6. Iris defect, irregular pupil, or unilateral cataract after trauma may indicate occult corneal or scleral laceration and possibly an intraocular foreign body
7. Blood in anterior chamber (hypopyon)
8. Subconjunctival hemorrhage may hide underlying scleral laceration

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Assess extent of injury to formulate medical or surgical management
 - a. Partial thickness versus full thickness
 - b. Seidel testing for smaller lacerations
 - c. Length and depth of laceration
 - d. Iris prolapse
 - e. Lens injury

2. Perform ophthalmic evaluation to rule out concomitant ocular injury (e.g., traumatic optic neuropathy, intraocular foreign body)
3. Evaluate other eye
4. Determine need for radiologic imaging (x-ray or CT scan; MRI if metallic foreign body not suspected)

II. Describe patient management in terms of treatment

A. Define medical therapy options

1. Use protective shield
2. Bandage soft contact lens for small lacerations with minimal wound gape
3. Aqueous suppressant (e.g. carbonic anhydrase inhibitor)
4. Application of tissue adhesive has a role for pinpoint perforations

B. Define surgical therapy options:

1. Use protective shield
2. Avoid eating or drinking by patient during preoperative period
3. Consider facial nerve anesthesia to reduce eyelid squeezing until definitive repair
4. Consider obtaining cultures of external eye (See Repair of corneal laceration and suture closure of corneal wound)
5. Possible need for corneal tissue if portion of cornea is missing from wound

C. Medications

1. Consider systemic and/or subconjunctival and/or topical antimicrobial prophylaxis
2. Pain medication
3. Tetanus prophylaxis may be applicable depending on mechanism of laceration

III. List the complications of treatment, their prevention and management (See Repair of corneal laceration and suture closure of corneal wound)

IV. Describe disease related complications

- A. Wound leak**
- B. Infectious corneal ulcer**
- C. Endophthalmitis**
- D. Corneal scarring**
- E. Irregular astigmatism**
- F. Retinal detachment**

- G. Cataract**
- H. Iris damage**

V. Describe appropriate patient instructions

- A. Stress importance of compliance with medications**
- B. Recommend physical restrictions, importance of eye protection, and plans for further care**
- C. Discuss expectations for post-operative recovery and visual rehabilitation depending on nature and extent of the injury**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Repair of the Traumatized Anterior Segment, Module #1, 1992.

Corneal perforation

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Injury
 - a. Direct tissue destruction from mechanical or chemical trauma
 - b. Perforating foreign body
2. Ocular surface disorder
 - a. Breakdown of corneal epithelium with decreased barrier protection
3. Immune-mediated corneal ulceration
4. Corneal inflammation and necrosis
 - a. Microbial invasion and exotoxins
 - b. Infiltration of leukocytes
 - c. Corneal proteinases

B. List the pertinent elements of the history

1. Recent change in symptoms with "gush of fluid" or increased tearing
2. Presence and type of preexisting corneal or ocular surface disorder
3. Recent ocular trauma
4. Current ophthalmic and systemic medications

C. Describe the pertinent clinical features

1. Flat or shallow anterior chamber (compare with other eye)
2. Low intraocular pressure
3. Positive Seidel test
4. Size, configuration, and topographic location of corneal perforation
5. Folds in Descemet membrane emanating from the thinned area
6. Iris prolapse or plugging
7. Status of crystalline lens or intraocular lens

D. Describe the appropriate testing and evaluation for establishing the diagnosis

1. If suspect corneal infection, consider obtaining corneal specimen for cultures
2. If suspect systemic disease, obtain serological assessment for connective-tissue disease

II. Define the risk factors

- A. Infection (bacteria, fungi, protozoa, or viruses) is the most common cause of corneal perforation**
 - 1. Bacterial keratitis is most common infectious etiology, such as *Pseudomonas aeruginosa*
 - 2. Fungal keratitis may lead to corneal perforation by rapid progression (e.g., *Fusarium solani*) or slow necrosis (e.g., *Scedosporium apiospermum*)
 - 3. Corneal perforation may complicate course of Acanthamoeba keratitis
 - 4. Corneal perforation may occur during progressive herpes simplex virus stromal keratitis or following zoster keratitis with loss of corneal sensation
- B. Trauma (blunt, sharp, surgical, chemical, thermal)**
- C. Connective-tissue disorder or systemic ischemic vasculitis (rheumatoid arthritis, systemic lupus erythematosus, rosacea, atopic disease, Wegener granulomatosis)**
- D. Xerosis (Sjögren syndrome, Stevens-Johnson syndrome, mucous membrane pemphigoid, vitamin A deficiency)**
- E. Exposure keratopathy (cranial nerve (CN) VII palsy, thyroid ophthalmopathy, ectropion, lagophthalmos)**
- F. Neurotrophic keratopathy**
- G. Cornea degeneration (Terrien marginal degeneration, keratoconus, keratoglobus, pellucid marginal degeneration)**
- H. Mooren ulcer**
- I. Medication (topical corticosteroids, topical nonsteroidal antiinflammatory drugs, anesthetic)**

III. List the differential diagnosis

- A. Descemetocoele**
- B. Impending corneal perforation**
- C. Corneal melt**
- D. Corneal ulceration**
- E. Partial thickness defect in cornea**
- F. Dellen**

IV. Describe patient management in terms of treatment and follow-up

- A. Describe medical therapy options**
 - 1. Aqueous humor suppression
 - 2. Patch eye and shield orbit
 - 3. Bandage (therapeutic) soft contact lens
 - 4. Cycloplegia and mydriasis
- B. Describe surgical therapy options**
 - 1. Application of tissue cyanoacrylate glue to cornea

2. Corneal sutures
3. Corneal patch graft
 - a. Penetrating keratoplasty
 - b. Lamellar keratoplasty
4. Tarsorrhaphy for impending perforation associated with non-healing epithelial defects
5. Amniotic membrane patch graft (small perforation)

C. Patient follow-up

1. Follow patient closely until the integrity of the globe is re-established

V. List the complications of treatment, their prevention and management

A. Disease-related complication

1. Failure to seal wound
2. Progression of thinning
3. Progression or development of corneal infiltrate or endophthalmitis
 - a. Patients should receive antibiotic prophylaxis to prevent infection

B. Bandage contact lens

1. Corneal pannus formation
2. Corneal edema
3. Development of corneal infiltrate

C. Tissue adhesive

1. Loosening of glue
2. Corneal pannus formation
3. Development of corneal infiltrate
4. Effects of glue on adjacent ocular structures
 - a. Toxicity to endothelium
 - b. Toxicity to lens- cataract formation
 - c. Symblepharon
5. Corneal sutures
6. Loosening of sutures
7. Development of corneal infiltrate
8. Vascularization
9. Induced astigmatism

D. Lamellar keratoplasty

1. Graft rejection (epithelial rejection, subepithelial infiltrates, stromal rejection)
2. Interface opacities
3. Vascularization of the interface
4. Development of corneal infiltrate
5. Inflammatory necrosis of the flap

E. Penetrating keratoplasty- tectonic or optical, patch grafts

1. Graft rejection
2. Graft failure
3. Development of corneal infiltrate
4. Irregular astigmatism
5. Glaucoma

VI. Describe disease-related complications

- A. Loss of vision**
- B. Corneal scarring**
- C. Irregular astigmatism**
- D. Increasing size of the perforation**
- E. Endophthalmitis**
- F. Choroidal detachment**
- G. Cataract**

VII. Describe appropriate patient instructions

- A. Close follow-up until the tectonic integrity of the globe is re-established**
- B. Advise patients to call as soon as possible should they develop increasing pain, loss of vision, increasing tearing, increased redness or a gush of fluid**
- C. Shield/eye protection at all times**
- D. No eye rubbing**
- E. Minimize sneezing or coughing**
- F. Limited activity**
- G. Topical antibiotics may be considered**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

2. AAO, Focal Points: Scleritis and Episcleritis: Diagnosis and Management, Module #9, 1995, p.9.

Corneal edema

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Decreased corneal endothelial pump and/or barrier function
 - a. Trauma
 - i. Surgical (See Postsurgical corneal edema) (See Surgical injury of Descemet membrane and corneal endothelium)
 - ii. Nonsurgical
 - iii. Birth trauma
 - b. Infection
 - i. Keratitis
 - i) Viral
 - ii) Bacterial
 - iii) *Acanthamoeba*
 - iv) Fungal
 - ii. Endotheliitis (Herpes simplex)
 - iii. Endophthalmitis
 - c. Immune-mediated
 - i. Anterior uveitis
 - ii. Corneal endothelial graft rejection
 - d. Hypoxia
 - i. Contact lens wear
 - ii. Anterior segment ischemia
 - e. Spontaneous tears in Descemet membrane
 - i. Keratoconus with hydrops
 - ii. Congenital glaucoma
 - iii. (Haab striae)
 - f. Toxicity of topical or intraocular pharmacologic agents
 - g. Endothelial dystrophies and dysgeneses
 - i. Fuchs dystrophy
 - ii. Posterior polymorphous dystrophy

- iii. Congenital hereditary endothelial dystrophy
 - iv. Iridocorneal endothelial syndrome
- h. Systemic medications (e.g., Amantadine)
- 2. Disrupted corneal epithelial barrier function
 - a. Traumatic corneal abrasion
 - b. Recurrent erosion
 - c. Chronic corneal epithelial defect secondary to neurotrophic, exposure keratopathy
 - d. Chemical injury
 - e. Thermal injury
- 3. Increased intraocular pressure (IOP)

B. List the pertinent elements of the history

- 1. Decreased visual acuity
 - a. Duration
 - b. Laterality
 - i. Dystrophies, dysgeneses usually bilateral, except iridocorneal endothelial syndrome
 - c. Timing
 - i. Worse in morning in early stages of endothelial dysfunction, related to sleep hypoxia and decreased surface evaporation
- 2. Pain and foreign body sensation related to epithelial edema, bulla(e)
 - a. May subside over time with development of subepithelial fibrosis
- 3. Other specific symptoms vary with etiology

C. Describe pertinent clinical features

- 1. Corneal edema, with increasing corneal thickness
 - a. Endothelial dysfunction
 - i. Edema is first evident in the posterior stroma with Descemet folds, progresses to full-thickness stromal edema, then microcystic epithelial edema, and finally epithelial bullae
 - b. Epithelial barrier disruption
 - i. Edema develops first in the anterior stroma, may be full-thickness with large epithelial defects or in the presence of toxins or inflammatory mediators
 - c. Increased intraocular pressure (IOP)
 - i. Epithelial edema develops, stroma remains compact if endothelial function is intact
- 2. Epithelial bullae
- 3. Subepithelial opacification, fibrosis may develop secondary to chronic epithelial edema

4. Other specific findings vary with specific etiology

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Specular microscopy
 - a. Fuchs dystrophy
 - i. Cornea guttae
 - ii. Pleomorphism
 - iii. Polymegathism
 - b. Iridocorneal endothelial syndrome
 - i. Dark/light cell border/body reversal
 - ii. Abrupt border between normal and abnormal areas
 - c. Posterior polymorphous dystrophy
 - i. Vesicles
 - ii. Linear parallel tracks
2. Corneal pachymetry

II. Define the risk factors

- A. Increased IOP**
- B. Intraocular inflammation**
- C. Other risk factors vary according to etiology**

III. List the differential diagnosis

- A. Corneal stromal scarring**
 1. Prior trauma, infection, inflammation
- B. Corneal stromal inflammation, infiltrates**
 1. Microbial keratitis
 2. Immune-mediated keratitis
- C. Congenital corneal opacification**
 1. Peters anomaly
 2. Sclerocornea
 3. Congenital hereditary stromal dystrophy
 4. Intrauterine infection
 5. Inborn errors of metabolism

- a. Mucopolysaccharidoses
- b. Hyperlipoproteinemias
- c. Mucopolipidoses

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

- 1. Endothelial dysfunction
 - a. Topical hyperosmotic agents
 - i. 2% or 5% NaCl ointment at bedtime, drops during day (ointment during day if severe edema)
 - b. Gentle use of hair dryer to increase evaporation
 - c. Low water-content therapeutic contact lens for epithelial edema
 - d. Lowering IOP may reduce edema when endothelial dysfunction is the cause of corneal edema
- 2. Epithelial defects (See Traumatic corneal abrasion) (See Neurotrophic keratopathy) (See Exposure keratopathy)
- 3. Increased intraocular pressure - treat accordingly

B. Describe surgical therapy options

- 1. Endothelial dysfunction
 - a. Repair Descemet's detachment if present (See Surgical injury of Descemet membrane and corneal endothelium)
 - i. Endothelial keratoplasty
 - b. Pain relief without restoration of optical quality
 - i. Conjunctival flap
 - ii. Amniotic membrane transplantation
 - iii. Cautery of corneal surface
 - iv. Anterior stromal micropuncture
- 2. Epithelial defects (See Traumatic corneal abrasion) (See Neurotrophic keratopathy) (See Exposure keratopathy) (See Amniotic membrane transplantation)
- 3. Increased IOP - treat accordingly

V. List the complications of treatment, their prevention and management

A. Endothelial replacement (See Penetrating keratoplasty)

B. Conjunctival flap

1. Microbial keratitis
2. Flap or graft retraction
 - a. Prevention via careful suturing
 - b. Treatment via re-grafting or re-suturing

C. Cautery of corneal surface

1. Microbial keratitis
2. Corneal melting
3. Corneal perforation (See Corneal perforation)

VI. Describe disease-related complications

- A. Secondary infection, melting due to loss of epithelial barrier**
- B. Corneal scarring**

VII. Describe appropriate patient instructions

- A. Proper use of topical medications**
- B. Proper use of hairdryer to reduce corneal edema**
- C. When to seek further care**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Corneal Dystrophies & Degenerations: A Molecular Genetics Approach, 2003.

Postsurgical corneal edema

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Intraoperative compromise of endothelial pump and/or barrier function
 - a. Mechanical trauma - contact between endothelium and:
 - i. Surgical instruments
 - ii. Crystalline lens fragments
 - iii. Intraocular lens or haptics
 - iv. Phacoemulsification tip
 - v. Iris hooks
 - vi. Capsular tension rings (CTR)
 - b. Descemet's membrane detachment
 - c. Ultrasonic energy from phacoemulsification tip
 - d. Thermal burn from phacoemulsification tip
 - e. Hydrostatic pressure from copious irrigating solution or elevated bottle
 - f. Toxicity of pharmacologic agents, capsule staining solutions, irrigating solutions (toxic anterior segment syndrome) (TASS)
 - g. Gas bubble
 - h. Primary graft failure in corneal transplant recipients
2. Postoperative compromise of endothelial pump and barrier functions
 - a. Mechanical trauma - contact between endothelium and:
 - i. Vitreous
 - ii. Intraocular lens (IOL)
 - b. Intraocular inflammation
 - c. Endophthalmitis
 - d. Anterior segment ischemia after retina, strabismus surgery
 - e. Endothelial rejection in corneal transplant recipients
 - f. Preoperative history Fuchs' endothelial dystrophy
 - g. Preoperative history low endothelial cell count
3. Disrupted corneal epithelial barrier function
 - a. Intraoperative corneal abrasion

- b. Toxicity of irrigating solutions, pharmacologic agents
- 4. Increased intraocular pressure
 - a. Pupillary block
 - b. Retained ophthalmic viscosurgical device (OVD) (viscoelastic)
 - c. Retained lens material

B. Define the relevant aspects of epidemiology of this disease

- 1. Post-cataract surgery edema remains the leading indication for corneal transplant surgery in the United States
- 2. Infrequent clusters due to:
 - a. Toxicity of irrigating solutions, pharmacologic agents
 - b. Introduction of new surgical techniques, technologies
- 3. Diabetic patients may be more prone than non-diabetic patients to develop postsurgical corneal edema following vitrectomy surgery
- 4. Complicated cataract extraction

C. List the pertinent elements of the history

- 1. Pre-existing corneal endothelial disease or compromise
- 2. History of diabetes mellitus
- 3. Procedure performed
 - a. Length of procedure, phacoemulsification time and power
 - b. Density of lens nucleus
 - c. Type and volume of irrigating solution used
 - d. Topical and intracameral pharmacologic agents used
 - e. OVD use and removal technique
 - f. Re-usable cannulas or tubing
 - g. Iris hooks, CTRs
 - h. Complications encountered
 - i. Endothelial contact with instruments, IOL
 - ii. Vitrectomy
 - iii. Retained lens material
- 4. Postoperative course
 - a. Onset of edema
 - i. Immediate
 - i) Typical after cataract surgery

- ii) Typical following corneal transplant; may also indicate primary graft failure
- ii. Delayed
 - i) May occur after cataract surgery in patients with previous endothelial compromise or relatively mild intraoperative cell loss
 - ii) Endothelial rejection or late failure after corneal transplant
- b. Intraocular pressure (IOP)
- c. Intraocular inflammation

D. Describe pertinent clinical features

1. Endothelial dysfunction
 - a. Posterior stromal edema and Descemet folds in mild cases
 - b. Full-thickness stromal edema with increasing severity
 - c. Microcystic epithelial edema with greater severity
 - d. Epithelial bullae in most severe cases
2. Epithelial barrier disruption
 - a. Edema develops first in the anterior stroma
 - b. May be full-thickness with large epithelial defects or in the presence of toxins or inflammatory mediators
3. Increased IOP
 - a. Epithelial edema develops, stroma remains compact if endothelial function is intact
4. Findings specific to other possible etiologies listed above:
 - a. Descemet membrane detachment
 - b. Retained lens fragments
 - c. Pupillary block
 - d. Elevated IOP
 - e. Marked intraocular inflammation
 - f. Epithelial defect
 - g. Presence of thermal burn at site of incision
 - h. Iris atrophy or pupillary abnormalities (TASS)
 - i. Endophthalmitis - profound visual loss, hypopyon, pain

II. Define the risk factors

A. Preoperative

1. Preexisting endothelial disease or compromise

- a. Fuchs endothelial dystrophy or endothelial guttae
 - b. Posterior polymorphous dystrophy
 - c. Prior intraocular surgery
 - d. Corneal transplantation
 - e. Nonsurgical trauma
 - f. History of severe intraocular inflammation
- 2. Dense nuclear sclerosis
 - 3. Narrow anterior chamber depth
 - 4. Glaucoma
 - 5. Diabetes mellitus

B. Intraoperative

- 1. Irrigating solution additives
- 2. Intraocular delivery of pharmacologic agents
- 3. Reuse of cannulas, especially for OVD
- 4. Reuse of irrigation tubing
- 5. Mechanical trauma to endothelium
 - a. Inadequate OVD use
 - b. Prolonged ultrasound time during phacoemulsification
 - c. Significant air bubbles in anterior chamber during phacoemulsification
 - d. Contact with instruments, lens fragments, or IOL
- 6. Thermal burn during phacoemulsification
 - a. Tight incision
 - b. Inadequate irrigation fluid flow
- 7. Incomplete OVD removal

C. Postoperative

- 1. Excessive intraocular inflammation
- 2. Marked IOP elevation

III. Describe patient management in terms of treatment and follow-up

A. Define medical therapy options

- 1. Treat epithelial defects
- 2. Control inflammation with topical, rarely systemic, corticosteroids

3. Control IOP with topical and systemic pressure lowering agents
4. Topical 5% NaCl ointment at bedtime, drops during day (for epithelial edema)
5. Drying of ocular surface (hair dryer) for epithelial edema
6. Low water-content therapeutic contact lens for epithelial edema
7. Watchful waiting to see if edema clears over 3-4 months

B. Define surgical therapy options

1. Control IOP
 - a. Aqueous release via paracentesis (plus medications)
 - b. Filtering surgery if necessary
 - c. Peripheral iridotomy or iridectomy for pupillary block
 - d. YAG laser of vitreous face or pars plana vitrectomy for aqueous misdirection
2. Vitrectomy for broad-based vitreous/endothelial contact and retained lens material
3. Repair Descemet membrane detachment (See Surgical injury of Descemet membrane and corneal endothelium)
4. Endothelial replacement for optical correction of persistent edema
 - a. Penetrating keratoplasty (See Penetrating keratoplasty)
 - b. Endothelial Keratoplasty (See Endothelial keratoplasty)
5. Pain relief without restoration of optical clarity
 - a. Conjunctival flap
 - b. Amniotic membrane graft (oriented basement membrane side up) or patch (oriented basement membrane side down) may provide temporary relief of pain (See Amniotic membrane transplantation)
 - c. Cautery of corneal surface

IV. List the complications of treatment, their prevention and management

A. Endothelial replacement (See Penetrating keratoplasty)

B. Conjunctival flap, amniotic membrane graft

1. Microbial keratitis
2. Flap or graft retraction
 - a. Prevention via careful suturing
 - b. Treatment via re-grafting or re-suturing

C. Cautery of corneal surface

1. Microbial keratitis

2. Corneal melting, perforation (See Corneal perforation)

V. Describe disease-related complications

- A. Secondary infection, melting due to loss of epithelial barrier
- B. Pain secondary to ruptured bullae
- C. Corneal scarring

VI. Describe appropriate patient instructions

- A. Proper use of topical medications
- B. Proper use of hairdryer to reduce corneal edema
- C. When to seek further care

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Penetrating Keratoplasty, Module #6, 1992.

Surgical injury of Descemet membrane and corneal endothelium

I. Describe the approach for establishing the diagnosis

A. Describe the etiology of this disease

1. Descemet membrane detachment
 - a. Traumatic injury associated with tear and separation of Descemet membrane
 - b. Often associated with manipulation of wound
 - i. Injection of balanced salt solution
 - ii. Ophthalmic viscosurgical device (OVD) (viscoelastic)
 - iii. Insertion of instruments into the anterior chamber,
 - iv. Lens implantation
2. Endothelial damage
 - a. Mechanical trauma secondary to surgical instruments, lens fragments, and intraocular lens (IOL)
 - b. Ultrasonic energy from phacoemulsification tip
 - c. Thermal burn from phacoemulsification tip
 - d. Toxicity from pharmacologic agents and irrigating solutions

B. List the pertinent elements of the history

1. Preexisting corneal endothelial disease or compromise
2. Details of surgery
 - a. Length of procedure, phacoemulsification time and power
 - b. Density of lens nucleus
 - c. Type and volume of irrigating solution
 - d. Type and placement of IOL
 - e. Topical and intracameral pharmacologic agents
 - f. OVD use and removal technique
 - g. Reusable cannulas or tubing
 - h. Complications including endothelial contact with instruments or intraocular lens, vitrectomy, or retained lens material
3. Postoperative course
 - a. Immediate onset of edema

- b. Associated visual loss if central cornea involved

C. Describe the pertinent clinical features

1. Descemet membrane detachment
 - a. Sharply demarcated area of edema
 - b. Descemet scroll or tear often visible
 - c. Often found near entrance wound
 - d. Diagnosis and determining extent of detachment may be aided by UBM or OCT
2. Endothelial injury and dysfunction
 - a. Posterior stromal edema and Descemet folds in mild cases
 - b. Full-thickness stromal edema with increasing severity
 - c. Microcystic epithelial edema with greater severity
 - d. Epithelial bullae in most severe cases
3. Decreased vision
 - a. May have pain, tearing, and light sensitivity

II. Define the risk factors

A. Findings which may contribute to complicated cataract extraction

1. Shallow anterior chamber
2. Dense nuclear sclerosis

B. Surgical technique - mechanical trauma to Descemet membrane and endothelium

1. Inadequate OVD use
2. Prolonged phacoemulsification time
3. Contact with instruments, lens fragments, or IOL
4. Thermal burn from phacoemulsification tip

III. List the differential diagnosis

A. Toxic anterior segment syndrome (TASS)

1. Intense inflammatory reaction which may result in marked corneal edema
2. Often secondary to toxins or chemical residue on instruments or in irrigating solutions
3. Specific etiology should be established to avoid other cases

B. Corneal edema secondary to other factors

1. Elevated intraocular pressure (IOP)

2. Keratouveitis (i.e., herpetic disciform endotheliitis)

IV. Describe patient management in terms of treatment and follow-up

A. Define medical therapy options

1. Observation
 - a. May resolve spontaneously
2. Small 1-2 mm peripheral detachments can be observed and typically do not progress to involve the central cornea
3. Trial with intensive topical corticosteroids
4. Symptomatic trial of hypertonic saline drops (Muro 128 2% or 5%)

B. Define surgical therapy options

1. Descemet membrane detachment
 - a. Injection of air or gas (sulfur hexafluoride SF₆ or C₃F₈ perfluoropropane) to tamponade detachment and reposition membrane to the posterior corneal stroma
 - b. Face up positioning (lay on back)
 - c. Suture Descemet membrane - full-thickness suture
 - d. Penetrating keratoplasty or endothelial keratoplasty for recalcitrant detachments
2. Endothelial injury with subsequent persistent corneal edema and decompensation
 - a. Penetrating keratoplasty
 - b. Endothelial keratoplasty

V. List the complications of treatment, their prevention and management

A. Complications of treatment

1. Injection of gas
 - a. Elevated IOP from large bubble resulting from pupillary block
 - b. Minimal risk of endophthalmitis

B. Prevention and management

1. Limit size of gas bubble (60% fill)
2. Mydriasis (See Penetrating keratoplasty and Endothelial keratoplasty)

VI. Describe disease-related complications

A. Corneal decompensation with progressive visual loss

B. Subepithelial bullae with advanced corneal decompensation with secondary erosions and

epithelial breakdown resulting in secondary stromal scarring and risk of infectious corneal ulcer

C. Chronic pain

VII. Describe appropriate patient instructions

- A. Stress education of disease process as well implications of treatment options including intracameral gas injection and penetrating keratoplasty**
- B. Awareness of symptoms that may represent worsening of disease**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Clinical Evaluation of the Corneal Endothelium, Module #8, 1986.

Punctal occlusion

I. List the indications/contraindications

A. Indications

1. Treat ocular surface disorders associated with abnormal tear film
 - a. Keratoconjunctivitis sicca
 - b. Exposure keratopathy
 - c. Neurotrophic keratopathy
 - d. Contact lens intolerance related to tear insufficiency
2. Prolong retention and reduce systemic absorption of topically administered drugs

II. Describe the pre-procedure evaluation

- A. Slit-lamp biomicroscopic examination with dye staining**
- B. Schirmer testing (optional)**

III. List the alternatives to this procedure

- A. Topical therapy: lubricants and/or cyclosporine**
- B. Increase humidity: room humidifier, moisture shields, occlusive goggles**
- C. Bandage contact lenses**
- D. Tarsorrhaphy**

IV. Describe the instrumentation, anesthesia and technique

A. Temporary

1. Temporary intracanalicular plug
 - a. Dissolvable collagen plugs can be inserted into one or more puncta
 - b. Used to determine whether bothersome epiphora might occur in a patient with mild to moderate aqueous tear deficiency before proceeding to a non-dissolving plug or to punctal cauterization

B. Permanent

1. Reversible
 - a. Topical anesthesia
 - b. Insert silicone or polymer plugs into punctum with inserter

- c. Plug diameter should be judged according to the size of the punctum
- d. Used to treat aqueous tear deficiency and other chronic ocular surface disorders
- 2. Irreversible
 - a. Punctal cauterization
 - i. Topical anesthesia and/or infiltrative anesthesia
 - ii. Canaliculus and punctum cauterized with thermal cautery or radiofrequency unit
 - iii. Used to treat severe aqueous tear deficiency

V. List the complications of this procedure, their prevention and management

A. Epiphora

- 1. Prevention
 - a. Reversible procedure prior to permanent occlusion
 - b. Occlude 1 punctum at a time in each eye
- 2. Treatment
 - a. Removal of plug

B. Punctum re-opens

- 1. Prevention
 - a. Use of largest plug that will fit
 - b. Intracanalicular plugs
 - c. Avoidance of laser to occlude punctum (high failure rate)
- 2. Treatment
 - a. Larger plug
 - b. Cauterize punctum

C. Inflammation

- 1. Treatment
 - a. Removal of plug

D. Canaliculitis or dacryocystitis

- 1. Prevention
 - a. Risk of lacrimal sac infection may be higher with intracanalicular plug or occlusion of both puncta but still uncommon
- 2. Treatment
 - a. Removal of plug
 - b. Topical and/or oral antibiotics

VI. Describe the follow-up care

- A. Slit-lamp biomicroscopic evaluation several weeks after procedure**

VII. Describe appropriate patient instructions (post-op care, vision rehabilitation)

- A. Avoid rubbing inner canthus (if silicone plug with exposed head)**
- B. Instructions on continued lubrication use**
- C. Describe expectations for improved comfort**
- D. Instructions regarding contact lens use, if appropriate**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Ophthalmic Technology Assessment: Punctal Occlusion for the Dry Eye. *Ophthalmology* 1997;104:1521-1524.
3. Hamano T. Lacrimal duct occlusion for the treatment of dry eye. *Semin Ophthalmol* 2005;20:71-4. Review.
4. Altan-Yaycioglu R, Gencoglu EA, Akova YA, et al. Silicone versus collagen plugs for treating dry eye: results of a prospective randomized trial including lacrimal scintigraphy. *Am J Ophthalmol* 2005;140:88-93.
5. AAO, Focal Points: Ocular Surface Neoplasia, Module #1, 2007.

Tarsorrhaphy

I. List the indications/contraindications

A. Indications

1. Severe, recalcitrant keratopathy, persistent epithelial defect, or corneal thinning resulting from:
 - a. Neurogenic exposure keratopathy (Cranial Nerve (CN) VII palsy)
 - b. Neurotrophic corneal ulceration (CN V deficit, herpes simplex virus (HSV) or varicella zoster virus (VZV) keratitis)
 - c. Severe keratitis sicca
 - d. Progressive corneal thinning or descemetocoele
 - e. Limbal stem cell deficiency
 - f. Eyelid abnormalities (e.g., trauma, previous eyelid surgery, cicatricial disease, ectropion and floppy eyelid syndrome)
 - g. Exposure (thyroid eye disease, orbital tumors)

B. Contraindications

1. Active microbial (bacterial or fungal) keratitis (although tarsorrhaphy may be necessary in some cases after the infection is controlled)

II. Describe the pre procedure evaluation

A. Visual acuity testing to document vision

B. Slit-lamp biomicroscopic examination

1. Documenting keratopathy location
2. Examining palpebral conjunctiva for foreign bodies or keratinization
 - a. External examination to document eyelid abnormalities (e.g., lagophthalmos, eyelid retraction, and proptosis)
 - b. Assessment of corneal sensitivity
 - c. Determination of what type of tarsorrhaphy is necessary (permanent vs. temporary) and extent of tarsorrhaphy (lateral vs. medial vs. central vs. total)

III. List the alternatives to the procedure

A. Frequent lubrication with ointments and artificial tears

B. Bandage contact lens

C. Amniotic membrane grafting

- D. **Temporary eyelid taping**
- E. **Botulinum toxin injection to induce a temporary ptosis**
- F. **Moisture chambers or cellophane eye patching**
- G. **Other eyelid surgery as indicated to correct ectropion, lagophthalmos, or eyelid retraction, including tarsal strip procedure and gold eyelid weights**

IV. Describe the technique

A. Temporary suture

1. Local anesthesia
2. Place horizontal mattress sutures (at least 2) through upper and lower lids and tie over bolsters on skin

B. Temporary glue

1. Topical anesthesia
2. Manually oppose upper and lower eyelids with slight eversion and apply cyanoacrylate glue to lid margin and lashes

C. Permanent

1. Local anesthesia
2. De-epithelialize portion of eyelid margin for adherence
3. Place vertical incision in upper and lower tarsus
4. Place absorbable sutures in horizontal mattress fashion joining upper and lower lid tarsal grooves
5. Advanced tarsorrhaphy techniques (Oculoplastics referral): e.g. mobilization of tarsoconjunctival flaps

V. List the complications of the procedure, their prevention, and management

A. Temporary

1. Premature loosening of sutures
2. Suture infection
 - a. Prevention
 - i. Antibiotic ointment

B. Permanent

1. Tarsorrhaphy dehiscence (prevention: leave sutures for longer or use nonabsorbable sutures)
2. Wound infection
 - a. Prevention
 - i. Antibiotic prophylaxis

3. Trichiasis or eyelid abnormalities after tarsorrhaphy is severed
 - a. Prevention
 - i. Meticulous technique when performing tarsorrhaphy
4. Corneal epithelial defects or corneal ulceration from loose or inappropriately placed sutures or from misdirected eyelashes resulting from the procedure
 - a. Prevention
 - i. Removal of loose sutures
 - ii. Epilation of eyelashes

VI. Describe follow up care

- A. Regular follow-up to monitor corneal and tarsorrhaphy status**

VII. Describe appropriate patient instructions

- A. Instructions on the use of antibiotic ointment to the eyelids following tarsorrhaphy**
- B. Instruction on the use of lubricants and/or topical antibiotics, depending on the underlying problem**
- C. Instruction on importance of regular follow-up**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Management of Eyelid Burns, Module #2, 1990, p.3, 8.

Conjunctival biopsy

I. List the indications

A. For diagnosis not achieved by another means

1. Neoplasia affecting the conjunctiva
 - a. Ocular surface squamous neoplasia
 - b. Sebaceous carcinoma
 - c. Lymphoma or leukemia
 - d. Metastatic tumor
2. Chronic cicatrizing or ulcerative conjunctivitis
 - a. Mucous membrane pemphigoid
3. Conjunctival nodule or inflammation
 - a. Sarcoidosis
 - b. Foreign-body granuloma
 - c. Fungal or parasitic lesion
 - d. Cat scratch disease
 - e. Microsporidiosis
4. Abnormal conjunctival pigmentation
 - a. Primary acquired melanosis in Caucasians
 - b. Primary acquired melanosis in any individual with suspicious characteristics (See Primary acquired melanosis of the conjunctiva)
 - c. Melanoma (See Melanoma of the conjunctiva)
5. Inherited metabolic disorder
 - a. Fabry disease and other lysosomal storage disorders
 - b. Cystinosis

B. For management

1. Excisional biopsy of conjunctival lesion
2. Management of chronic conjunctivitis
 - a. Superior limbic keratoconjunctivitis
 - b. Conjunctivochalasis

II. Describe the pre-procedure evaluation

- A. Record conjunctival abnormalities, including dimensions of conjunctival mass
- B. Review available tests and radiographs if systemic disease is a reason to perform conjunctival biopsy

III. List the alternatives to this procedure

- A. Conjunctival scraping (exfoliative cytology) or impression cytology
- B. Biopsy of another site for systemic disorder
- C. Medical rather than surgical therapy for ocular surface lesion

IV. Describe the instrumentation and technique

- A. Consider preoperative antiseptic or antibiotic
- B. Provide topical or infiltrative anesthesia of planned biopsy site
- C. Use forceps and scissors to resect portion of conjunctiva that incorporates lesion, generally acquiring at least 3 mm²
- D. Place biopsy specimen in appropriate transport medium or fixative

V. List the complications of the procedure, their prevention and management

- A. Damage to adjacent tissues
- B. Conjunctival scarring or symblepharon

VI. Describe the considerations of interpretation of this diagnostic procedure

- A. Conjunctival tissue is thin and flimsy, often curling when placed into liquid, so lay specimen flat by placement onto absorbent paper and transfer mounted specimen into fixative
- B. If orientation is important, then identify margin and explain which edge is tagged
- C. Give laboratory sufficient information to determine the appropriate examination method

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Melanoma and Other Pigmented Lesions of the Ocular Surface, Module #11, 1996, p. 6, 10-11.
3. AAO, Focal Points: Nonpigmented Lesions of the Ocular Surface, Module #9, 1996, p.8-10, 12.

Pterygium excision

I. List the indications/contraindications

A. Indications

1. Decreased vision secondary to pterygium
 - a. Due to the lesion approaching the visual axis
 - b. Due to induced regular or irregular astigmatism
 - c. Due to disrupted tear film
2. Visual side effects such as glare and halos around lights or difficulty driving at night
3. Progression of the lesion toward the visual axis
4. Restriction of motility/diplopia
5. Persistent discomfort
6. Persistent/recurrent inflammation
7. Cosmesis
8. Interference with contact lens wear
9. To rule out malignant process if suspicious features are present

II. Describe the pre-procedure evaluation

- A. Refraction**
- B. Assessment of tear film**
- C. Motility evaluation**
- D. Slit-lamp biomicroscopy**
- E. Consider corneal topography**

III. List the alternatives to this procedure

- A. Observation**
- B. Ocular lubricants and anti-inflammatory agents to reduce discomfort and erythema**

IV. Describe the instrumentation, anesthesia and technique

A. Instrumentation

1. Standard anterior segment instruments are used under the operating microscope

2. A diamond burr may be of benefit in smoothing a rough corneal surface after lesion removal

B. Anesthesia

1. Anesthesia is partially dependent on the procedure chosen.
2. For simple excision with bare sclera (not recommended) or with conjunctival closure, topical and/or subconjunctival anesthetic may be sufficient
3. Peribulbar anesthetic injection helpful to reduce blepharospasm

C. Technique

1. The pterygium is resected by incising the body of the lesion and dissecting it at the limbus and by avulsion or superficial dissection of the head from the cornea
 - a. This can also be carried out in the reverse order by removing the corneal portion of the lesion first
 - b. Dissection should remove subconjunctival fibrovascular tissue while sparing as much of the conjunctiva as possible.
 - c. Repair of the defect left in the conjunctiva is the area of greatest variability. Options include:
 - i. Free conjunctival autograft
 - i) A thin free conjunctival piece is dissected from the superior bulbar area where it has been protected from sunlight exposure
 - ii) The dissection may be extended to include limbal tissue
 - iii) The free graft is then placed over the area of the resection of the body of the lesion and sutured in place
 - (i) Fibrin adhesive may be used to fixate the graft instead of sutures
 - iv) Suture repair of donor site is not necessary
 - ii. Sliding conjunctival pedicle flap
 - i) A thin flap of conjunctiva may be dissected from above the resected area and moved as a pedicle flap to the area of resection and sutured in place
 - d. Amniotic membrane may be used instead of conjunctiva although recurrence is more likely
2. At the time of the procedure, MMC may be placed over the resected area prior to covering with conjunctival tissue
 - a. Local beta irradiation has been used but has a significant risk of late scleral necrosis
 - b. The appropriate concentration and duration of MMC should be used to avoid complications of toxicity
 - c. The MMC should be irrigated off thoroughly

V. List the complications of the therapy

A. Recurrence

1. Most frequent complication is recurrence of pterygium
 - a. Frequency may range from over 50% for bare sclera techniques to 5 to 20% or more with conjunctival flaps and grafts
- B. Pyogenic granuloma formation**
- C. Infection and necrosis of the corneoscleral bed**
- D. Diplopia, strabismus**
- E. Dellen associated with swollen or excessively thick conjunctival or amniotic membrane graft at limbus**
- F. Corneal and/or scleral melting with MMC or radiation**
- G. Excision or lysis of medial rectus tendon if dissection of tenons is not performed carefully**

VI. Describe the follow-up care

- A. Postoperatively, topical corticosteroid-antibiotic combinations are used frequently and tapered over several weeks to months**
- B. Follow-up visits allow suture removal as grafted tissue becomes adherent**
- C. Observation for recurrence is carried out over progressively extended periods of time**
- D. Antibiotics can be discontinued once epithelial integrity has been re-established**
- E. Topical corticosteroids are often continued for a few months to reduce the risk of recurrence**
- F. Ocular lubrication**
- G. Protection of the eye from UV exposure with sunglasses**

VII. Describe appropriate patient instructions

- A. The eye may remain patched for the first day after surgery**
- B. Topical medications are then begun and slowly tapered**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Surgical Treatment of Pterygium, Module #12, 1996.
3. Hirst LW. The treatment of pterygium. *Surv Ophthalmol* 2003;48:145-180.
4. Mutlu FM, Sobaci G, Tatar T, et al. A comparative study of recurrent pterygium surgery: limbal conjunctival autograft transplantation versus mitomycin C with conjunctival flap. *Ophthalmology* 1999;106:817-21.
5. Chen PP, Ariyasu RG, Kaza V, et al. A randomized trial comparing mitomycin C and conjunctival autograft after excision of primary pterygium. *Am J Ophthalmol* 1995 Aug;120:151-60.
6. Frucht-Pery J, Siganos CS, Ilsar M. Intraoperative application of topical mitomycin C for pterygium surgery. *Ophthalmology* 1996 Apr;103:674-7.

7. Kucukerdonmez C, Akova YA, Altinors DD. Vascularization is more delayed in amniotic membrane graft than conjunctival autograft after pterygium excision. *Am J Ophthalmol* 2007;143:245-249.
8. Luanratanakorn P, Ratanapakorn T, Suwan-Apichon O, et al. Randomised controlled study of conjunctival autograft versus amniotic membrane graft in pterygium excision. *Br J Ophthalmol* 2006;90:1476-80.
9. Prabhasawat P, Tesavibul N, Leelapatranura K, et al. Efficacy of subconjunctival 5-fluorouracil and triamcinolone injection in impending recurrent pterygium. *Ophthalmology* 2006;113:1102-9.
10. Frucht-Pery J, Raiskup F, Ilisar M, et al. Conjunctival autografting combined with low-dose mitomycin C for prevention of primary pterygium recurrence. *Am J Ophthalmol* 2006;141:1044-1050.

Bandage contact lenses

I. List the indications/contraindications

A. Indications

1. Therapeutic
 - a. Pain relief
 - b. Promote epithelial healing
 - c. Act as a splint in the treatment of lacerations, perforations and ulcerations
 - d. Protect the cornea from mechanical damage secondary to abnormalities of the eyelid
 - e. Improve visual acuity by correcting irregular corneal surface
 - f. Deliver medications
2. Clinical
 - a. Corneal edema
 - b. Persistent epithelial defects
 - c. Noninfectious corneal ulcerations or small perforations especially those requiring cyanoacrylate glue
 - d. Recurrent corneal erosions
 - e. Filamentary keratitis
 - f. Keratitis sicca
 - g. Neurologic conditions leading to exposure
 - h. Irregular corneal surfaces secondary to anterior corneal dystrophies
 - i. Corneal scars or opacities
 - j. Cosmetic tinted and painted lenses
 - k. Post surgical (such as after Boston Keratoprosthesis)

B. Relative contraindications

1. Anatomical considerations leading to an inability to place or center a contact lens
2. Poor patient tolerance
3. Poor patient hygiene and lens care

II. Describe the pre-therapy evaluation

A. Complete comprehensive eye examination (including lids)

B. Determination of etiology of corneal pathology

- C. **Fluorescein/rose bengal staining when appropriate**
- D. **Evaluation of contact lens fit**

III. List the alternatives to this therapy

A. Non-surgical

- 1. Patching
- 2. Lubrication

B. Surgical

- 1. Suture tarsorrhaphy
- 2. Botox tarsorrhaphy
- 3. Amniotic membrane
- 4. Gunderson conjunctival flap
- 5. Corneal cautery for painful bullous keratopathy in blind eyes

IV. Describe the instrumentation, anesthesia and technique- fitting considerations

A. Base curves

- 1. Flatter fit- larger base curve

B. Lens thickness

C. Lens diameter

- 1. Bigger lens more stable but increases the area of tissue that depends on exchange of metabolic nutrients through the lens

D. Lens materials

- 1. Hydrogel
- 2. Silicone
- 3. Collagen

E. Dk/oxygen permeability and water content in Silicone Hydrogel lenses

- 1. Are important considerations for therapeutic contact lenses
- 2. The higher the Dk the more oxygen permeability yet the stiffer the contact lens.

F. Expense

G. Examples of some available lenses

- 1. Food and Drug Administration (FDA) approved - (examples)
 - a. Permalens Therapeutic (Cooper Vision)
 - b. Acuvue Oasys (Vistakon)

- c. Air Optix (Night & Day) (CIBA Vision)
 - d. Purevision (Bausch & Lomb)
 - e. Softform-55 EW (Unilens Corp.)
- 2. Non Food and Drug Administration (FDA) approved
 - a. Disposable lenses
 - i. Many examples
 - ii. Readily available
 - iii. Inexpensive

V. List the complications of the therapy, their prevention and management

- A. Infection (prophylactic antibiotics often prescribed)
- B. Decentration
- C. Loss of contact lens

VI. Describe the follow-up care

- A. The patient seen at slit-lamp biomicroscope within the first 24-48 hours after placement
- B. Seen at slit-lamp biomicroscope thereafter on a 1 to 2-week basis
- C. Prophylactic antibiotics
- D. Proper lens lubrication with preservative-free artificial tear drops and ointments
- E. Lens replacement schedule

VII. Describe appropriate patient instructions

- A. Therapeutic modality with possible complications
- B. If lens dislodges from eye, do not attempt to replace
- C. If lens decenters, seek proper care
- D. Use medications as directed
- E. Lens replacement on a regular basis

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
- 2. AAO, Focal Points: Postoperative Management of the PRK Patient, Module #10, 1998.
- 3. AAO, Focal Points: Surgical Techniques for Ocular Surface Reconstruction, Module #12, 2006.

Application of corneal tissue adhesive

I. List the indications/contraindications

A. Indications

1. Small corneal perforation - impending or frank (less than 1-2 mm)
2. Corneal thinning
3. Corneal melt
4. Wound leaks

B. Contraindications

1. Large corneal perforations (over 3 mm)
2. Severe corneal ulceration or corneal melting
3. Inability to re-establish anterior chamber

II. Describe the pre-procedure evaluation

A. Slit-lamp biomicroscopic examination

1. Measure degree of corneal thinning
2. Assess size of corneal perforation
3. Evaluation of corneal ulceration
4. Anterior chamber depth

III. List the alternatives to this procedure

- A. Observation
- B. Bandage contact lens
- C. Sutures
- D. Lamellar keratoplasty
- E. Tectonic penetrating keratoplasty

IV. Describe the instrumentation, anesthesia and technique

- A. Topical anesthesia
- B. Lid speculum
- C. Remove loose epithelium, necrotic tissue
- D. Keep corneal surface dry with micro-sponges

E. Available cyanoacrylate glue preparations

1. Indermil, butyl-2-cyanoacrylate, Sherwood, Davis, and Geck, St. Louis, MO
2. Histoacryl butyl-2-cyanoacrylate, Braun, Melsungen, Germany
3. Nexacryl, N-butyl-cyanoacrylate, Closure Medical, Raleigh, NC
4. Dermabond, 2-octyl-cyanoacrylate, Closure Medical, Raleigh, NC

F. Application of corneal glue

1. Device for delivery of appropriately small quantity of glue (e.g. tuberculin syringe with 25-30 gauge needle, butterfly needle, lacrimal probe, plastic micro-dropper)

G. Two or three mm disc punched from plastic surgical drape may be used along with glue as corneal patch for larger perforations

H. Application of adhesive then await polymerization

I. Bandage contact lens

V. List the complications of this procedure, their prevention and management

A. Failure to seal wound

B. Progression of thinning

C. Progression or development of corneal infiltrate

D. Pain

E. Decreased vision

F. Corneal scarring

G. Loosening of glue

H. Corneal neovascularization

I. Giant papillary conjunctivitis

J. Effects of glue on adjacent ocular structures

1. Toxicity to endothelium
2. Toxicity to lens
 - a. Cataract formation
3. Symblepharon
4. Adherent leukoma between iris and cornea

VI. Describe the follow-up care

A. Monitor status of glue

B. Monitor status of cornea

C. Monitor for corneal ulceration

- D. Remove glue when healed or allow it to fall off as epithelialization occurs under glue
- A. Re-glue if indicated

VII. Describe appropriate patient instructions (post-op care, vision rehabilitation)

- A. Not a Food and Drug Administration approved use
- B. No eye rubbing
- C. Protective eye shield
- D. Call if pain increases, contact lens falls out or a gush of fluid is noted

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Anterior stromal puncture

I. List the indications/contraindications

A. Indications

1. Post-traumatic localized corneal recurrent erosions
2. Recurrent erosions secondary to corneal epithelial basement membrane dystrophy
3. Chronic, painful corneal edema when corneal transplant is not indicated

B. Contraindications

1. Use with caution in the visual axis

II. Describe the pre-procedure evaluation

A. History

1. Symptoms of recurrent corneal erosions (sudden onset of eye pain, usually at night or upon first awakening, with redness, photophobia, and tearing)
 - a. Episodes lasting from 30 minutes to several days depending on severity
2. History of previous traumatic corneal abrasion, usually secondary to a sudden sharp, shearing injury (fingernail, paper cut, tree branch)
 - a. Interval from injury to recurrent erosions can vary from days to years

B. Slit-lamp biomicroscopy

1. Often intact epithelial surface at time of exam
 - a. May have pooling of fluorescein over affected area
2. If erosion present, epithelium in involved area appears heaped up and edematous
 - a. Epithelium is loosely attached to underlying Bowman layer
3. Retroillumination may reveal subtle corneal abnormalities
4. Corneal epithelial dots or "microcysts" in the other eye suggest a degenerative or dystrophic cause

III. List the alternatives to this procedure

A. Conservative therapy

1. Acute phase: frequent lubrication, antibiotic ointments, cycloplegia
2. Chronic phase: nonpreserved lubricants, hypertonic saline (5% NaCl) ointments; topical corticosteroids combined with systemic tetracyclines

B. Therapeutic bandage contact lens

- C. Epithelial debridement with or without polishing with burr/drill
- D. Excimer laser phototherapeutic keratectomy
- E. Neodymium: yttrium argon garnet (Nd:YAG) laser reinforcement
- F. Thermal cautery

IV. Describe the instrumentation, anesthesia and technique

- A. A bent (usually 21,23, or 25 gauge) needle tip (to reduce the risk of full-thickness penetration of the cornea) is used to make numerous superficial puncture wounds in the involved area and extending slightly beyond the borders of the previously observed erosions, allowing a firm adhesion to develop as the epithelium heals, under topical anesthesia at the slit-lamp biomicroscope
- B. Sterile precautions

V. List the complications of this procedure, their prevention and management

- A. Significant scarring, with increased risk from more aggressive/deeper punctures, may reduce best corrected visual acuity
 - 1. Caution should be used if working in the visual axis
 - 2. If scarring begins to appear, topical corticosteroids may help to decrease severity
- B. Infection
 - 1. Prophylactic antibiotic drops should be used postoperatively
 - 2. If microbial keratitis develops, cultures and scrapings should be performed and broad-spectrum topical antibiotic therapy should be initiated pending culture results
- C. Inadequate treatment of affected area
 - 1. Treatment may need to be repeated

VI. Describe the follow-up care

- A. Topical antibiotic prophylaxis to prevent infection
- B. Topical hyperosmotics and lubricants to promote healing
- C. Possible bandage contact lens for pain control
- D. Topical non-steroidal anti-inflammatory drugs (NSAIDs) for pain control

VII. Describe appropriate patient instructions (post-op care, vision rehabilitation)

- A. Postoperative medications and follow-up
- B. Discomfort similar to recurrent erosions may be experienced
- C. Explanation as to likelihood of the procedure to be effective and the possible need for retreatment

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Aldave AJ, Sonmez B. Elucidating the molecular genetic basis of the corneal dystrophies: are we there yet? Arch Ophthalmol. 2007 Feb;125(2):177-86.
3. Weiss JS, Møller HU, Lisch W, et al. The IC3D classification of corneal dystrophies. Cornea. 2008;27:S1-S42
4. AAO, Focal Points: Therapy of Recurrent Erosion and Persistent Defects of the Corneal Epithelium, Module #9, 1991, p.4.

Corneal epithelial debridement

I. List the indications/contraindications

A. Indications

1. Recurrent erosions (See Recurrent erosion)
2. Corneal epithelial basement membrane dystrophy (for decreased vision due to epithelial irregularities) (See Corneal epithelial basement membrane dystrophy/degeneration)
3. Microbial keratitis (to decrease pathogen load in fungal and acanthamoeba keratitis and to enhance corneal penetration of the topical medications)
4. Ocular surface disease (debridement of necrotic epithelium in chemical corneal burns, corneal intraepithelial neoplasia)
5. Irregular or heaped-up traumatic corneal abrasion (See Traumatic corneal abrasion)
6. Phototherapeutic keratectomy and photorefractive keratectomy

B. Contraindications/cautions

1. Conditions predisposing to persistent epithelial defects
 - a. Limbal stem cell deficiency
 - b. Neurotrophic keratopathy
 - c. Ocular surface disease

II. Describe the pre-procedure evaluation

- A. Assess for risk factors for poor epithelial healing
- B. Slit-lamp biomicroscopic examination with vital dye staining
- C. Corneal topography or keratometry (to detect irregular astigmatism in some cases)
- D. Identify areas of epithelial and subepithelial involvement

III. List the alternatives to this procedure

- A. Hypertonic saline or lubricating ointment for recurrent erosions
- B. Pressure patch, bandage contact lens, lubrication, topical antibiotic for recurrent erosion or traumatic corneal abrasion
- C. Anterior stromal puncture for recurrent erosions
- D. Superficial keratectomy with or without the use of diamond burr for recurrent erosions
- E. Phototherapeutic keratectomy for recurrent erosions or visual disturbance secondary to epithelial irregularity associated with corneal epithelial basement membrane dystrophy

IV. Describe the instrumentation, anesthesia and technique

- A. Performed at the slit-lamp biomicroscope or under the operating microscope**
- B. Topical anesthesia**
- C. Insert eyelid speculum, if needed**
- D. Remove the loosely adherent epithelium using a cotton swab, surgical sponge, spatula, blade, or forceps while avoiding trauma to Bowmans layer**
- E. Leave the perilimbal cells intact**
- F. Instill antibiotic, nonsteroidal anti-inflammatory drug, and cycloplegic eyedrops. Limit use of topical NSAIDs to 1-3 days due to possible delay in reepithelialization**
- G. Patch the eye or place a bandage contact lens**
- H. Oral analgesics (over the counter and/or narcotics)**

V. List the complications of the procedure, their prevention and management

A. Microbial keratitis

- 1. Prevention
 - a. Follow sterile technique and maintain the patient on topical antibiotic until epithelium heals
- 2. Treatment
 - a. Culture the infiltrate and treat with the appropriate topical antibiotics

B. Non-healing epithelial defect

- 1. Prevention
 - a. Screen patients for dry eyes and other predisposing conditions such as neurotrophic keratopathy
- 2. Treatment
 - a. Increased lubrication
 - b. Bandage soft contact lens
 - c. Patching of the eye
 - d. Autologous serum drops
 - e. Tarsorrhaphy

C. Corneal scarring

- 1. Prevention
 - a. Avoid traumatizing Bowman layer when using a surgical blade to perform debridement
- 2. Treatment
 - a. Topical corticosteroids may limit amount of scarring

VI. Describe the follow-up care

- A. Slit-lamp biomicroscopic evaluation frequently until epithelium heals and later as needed depending on the underlying condition**

VII. Describe appropriate patient instructions (post-op care, vision rehabilitation)

- A. Instructions on topical medication use**
- B. Instructions regarding contact lens use, if appropriate**
- C. Instructions on importance of follow-up**
- D. Describe expectations for postoperative pain and slow, gradual improvement of comfort and visual acuity**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Therapy of Recurrent Erosion and Persistent Defects of the Corneal Epithelium, Module #9, 1991, p.2.

Corneal biopsy

I. List the indications/contraindications

A. Indications

1. Infectious corneal processes
 - a. Deep suppurative stromal keratitis without involvement of anterior stroma
 - b. Sight-threatening or progressive corneal infiltrate exhibiting one or more of the following:
 - i. Inadequate response to appropriate antimicrobial therapy
 - ii. Culture negative on superficial scrapings
 - iii. An atypical clinical course
 - c. Infectious crystalline keratopathy if cultures not easily obtained with superficial scraping
2. Neoplastic limbal processes
 - a. Suspected conjunctival neoplasms with corneal extension

B. Contraindications

- a. Corneal infiltrate in a region of the cornea that is very thin, making risk of perforation during biopsy excessively high
- b. Intracameral infiltrate that is located on posterior aspect of the cornea, without posterior stromal involvement

II. Describe the pre-procedure evaluation

A. Slit-lamp biomicroscopic examination

1. Depth of the infiltrate and overlying corneal thickness should be evaluated (pachymetry may be useful)
2. Confocal microscopic examination, if strongly suggestive of the presence or absence of infectious organisms, may obviate the need for a corneal biopsy

B. Topically applied antimicrobial should be stopped approximately 24 hours prior to performance of the biopsy if culture is planned

III. List the alternatives to this procedure

- A. Continued empiric broad-spectrum antimicrobial therapy
- B. Superficial corneal scrapings for culture and/or cytology
- C. Anterior chamber paracentesis and aspiration of infiltrate on posterior surface of the cornea
- D. Corneal imaging, including confocal microscopy or confocal scanning laser ophthalmoscopy

IV. Describe the instrumentation, anesthesia and technique

A. Setting

1. Patient lying supine under operating microscope
2. If patient is very cooperative, all techniques except trap door may be performed with patient seated at the slit-lamp biomicroscope
3. Operative eye can be prepared and draped in sterile fashion for ocular surgery
4. Speculum inserted into operative eye if necessary

B. Anesthesia

1. Preservative-free tetracaine drops or similar anesthetic agent
2. If needed, a cotton tip applicator soaked in lidocaine may be held at limbal position where forceps fixation performed

C. Techniques for collecting material for microbial culture

1. Cut-down
 - a. Supersharp blade may be used to create a vertical or oblique incision to allow sampling using sterile needle or spatula
2. Suture
 - a. Braided silk suture can be passed through the infiltrate; then cut into pieces for inoculation
3. Trap door
 - a. A flap (either triangular or rectangular) of anterior stroma is created overlying the active edge of the deep stromal infiltrate with a supersharp or #69 blade, reflected, and the underlying tissue is excised using forceps and a surgical blade
 - b. The flap is then sutured into position with an interrupted 10-0 nylon suture
4. Trephination
 - a. A 2 or 3 mm corneal or dermatologic trephine is used to perform a partial-thickness trephination overlying the active edge of the deep stromal infiltrate
 - b. The edge of the partially trephinated disc is carefully grasped with .12 forceps, and the base is undermined using a blade or microscissors
 - c. The stromal base may be scraped and plated onto culture media

D. Specimen handling and processing

1. Corneal scrapings plated onto culture media as well as glass slides for staining
2. Corneal tissue specimens divided and sent in fixative to histopathology laboratory and in sterile saline to microbiology laboratory
3. Discuss case with pathology laboratory prior to submitting specimen to alert them as to small specimen size and to ensure use of proper container

V. List the complications of the procedure, their prevention and management

A. Complications and management

1. Perforation
 - a. May result in aqueous humor leakage and/or introduction of infectious organisms into anterior chamber
 - i. Cut-down technique
 - i) A simple incision made in cornea, should be closed with single 10-0 nylon suture
 - ii. Suture technique
 - i) Should not require suture closure
 - iii. Trap door technique
 - i) Additional 10-0 nylon sutures may be placed in flap
 - ii) If not able to maintain deep anterior chamber, may place thin application of cyanoacrylate tissue adhesive over flap, followed by bandage contact lens placement
 - iv. Trephination technique
 - i) If perforation occurs during trephination, trephinated tissue can be secured to surrounding stroma with 10-0 nylon sutures
 - ii) If perforation occurs during lamellar dissection of base, may either secure trephinated tissue to surrounding stroma or perform more superficial lamellar dissection, and apply tissue adhesive to base after trephinated tissue removed
 - iii) If tissue is necrotic and closure is not possible with sutures and/or tissue adhesive, a corneal or scleral patch graft or Tutoplast may be needed for closure
 - iv) If no tissue is immediately available, temporary closure of the globe may be performed using a piece of sterile material, such as the surgical drape,
 - v) The material may be cut with a trephine, placed over the defect, and secured to the globe using tissue adhesive or sutures

B. Prevention of perforation

1. Perform thorough slit-lamp biomicroscopic examination prior to procedure to estimate local corneal thickness and depth of infiltrate
2. Ultrasonic corneal pachymetry when possible before lamellar dissection
3. Corneal imaging with optical coherence tomography or ultrasonography to determine depth of lesion and corneal thickness prior to dissection

VI. Describe the follow-up care

- A. Antimicrobial therapy restarted after the biopsy**
- B. Treatment modified according to results of microbiologic and histopathologic investigations**

VII. Describe appropriate patient instructions

- A. Precautions against rubbing the operated eye**
- B. Need for medical therapy**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Superficial keratectomy

I. List the indications/contraindications

A. Indications

1. Pterygium/pseudopterygium
 - a. Reduced visual acuity
 - b. Chronic inflammation
 - c. Interference with contact lens wear
 - d. Rule out malignant process
2. Anterior corneal dystrophies, either primary or recurrent after penetrating keratoplasty, (corneal epithelial basement membrane dystrophy, corneal dystrophy of Bowman layers I and II, etc.)
 - a. Reduced visual acuity
 - b. Recurrent corneal erosions
3. Anterior corneal degenerations (Salzmann nodular degeneration, band keratopathy, etc.)
 - a. Reduced visual acuity
 - b. Discomfort
4. Pannus
 - a. Reduced visual acuity
 - b. Interference with contact lens wear
5. Conjunctival neoplasm with superficial corneal involvement

B. Contraindications

1. Corneal dystrophy or degeneration producing visual loss via stromal opacification

II. Describe the pre-procedure evaluation

A. Complete slit-lamp biomicroscopic examination to ensure:

1. Opacification epithelial/subepithelial (amenable to treatment with superficial keratectomy)

III. List the alternatives to this procedure

- A. Observation
- B. Fitting with a rigid contact lens (for visually significant corneal epithelial irregularity)
- C. Phototherapeutic keratectomy
- D. Lamellar or penetrating keratoplasty

IV. Describe the instrumentation, anesthesia and technique

A. Setting

1. Minor procedure room with patient lying supine under operating microscope
2. May be performed at the slit lamp with a cooperative patient.
3. Preparation
4. Operative eye prepped and draped in standard sterile fashion for ocular surgery
5. Speculum inserted into operative eye

B. Anesthesia (for all techniques)

1. Proparacaine or preservative free tetracaine drops
2. If needed, a cotton tip applicator soaked in 4% lidocaine may be held to limbal positions where forceps fixation performed

C. Technique

1. Fixation of the globe at the limbus with .12 forceps
2. Removal of corneal epithelium over involved area with Weck-cel sponge or surgical blade
3. Dissection of abnormal tissue from Bowman layer using:
 - a. Forceps to peel tissue
 - b. Surgical blade to dissect abnormal tissue
4. Diamond-dusted burr may be used to polish Bowman layer to:
 - a. Decrease incidence of recurrent erosions
 - b. Produce smoother ocular surface

D. Specimen handling and processing

1. Excised tissue placed on a piece of paper and then placed in formalin and submitted for histopathologic examination

V. List the complications of the procedure, their prevention and management

A. Persistent corneal epithelial defect

1. Management
 - a. Treat with bandage soft contact lens, lubricating ointment and drops, tarsorrhaphy, amniotic membrane graft/patch

B. Microbial keratitis

1. Prevention
 - a. Topical antibiotics while bandage soft contact lens in place, or until epithelial defect has resolved

2. Management
 - a. Corneal cultures/smears and intensive topical antibiotic therapy

C. Corneal scarring

1. Prevention
 - a. Avoid lamellar dissection into Bowman layer or anterior stroma
2. Management
 - a. Topical corticosteroids
 - b. Optical keratoplasty if visually limiting

D. Recurrence of the primary disease process

1. Prevention
 - a. Treat underlying disease process (if possible) that led to need for superficial keratectomy
2. Management
 - a. Repeat superficial keratectomy
 - a. Lamellar or penetrating keratoplasty

E. Corneal perforation

1. Prevention
 - a. Evaluate corneal thickness carefully preoperatively
 - b. Consider penetrating keratoplasty in cases of very thin, scarred corneas
2. Management
 - a. Tissue adhesive or suture closure of defect if small or linear
 - b. Corneal graft for perforations not amenable to closure with sutures or glue

VI. Describe the follow-up care

- A. Bandage soft contact lens while epithelium is healing**
- B. Topical antibiotics and corticosteroids**

VII. Describe appropriate patient instructions

- A. Compliance with postoperative topical medication regimen**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Amniotic membrane transplantation

I. List the indications/contraindications

A. General indications

1. Cover defects of ocular surface
2. Amniotic membrane may be used as a substrate for epithelial growth on the ocular surface
3. It may reduce inflammation and scarring.

B. Specific indications

1. Covering ocular surface defects
 - a. Conjunctival loss
 - i. Surgery (pterygium, tumors, lysis of symblepharon)
 - ii. Chemical injuries
 - b. Cornea
 - i. Descemetocoele or small corneal perforation (Layered approach)
2. Substrate for epithelial growth
 - a. For persistent corneal epithelial defects
 - b. Limbus- may be of benefit in conjunction with limbal stem cell grafts or to allow limbal stem cell expansion in partial limbal stem cell deficiency
3. Decreasing Inflammation and scarring
 - a. Acute Stevens Johnson Syndrome/Toxic Epidermal Necrolysis with significant ocular involvement
 - b. Acute chemical injuries

II. Describe the pre-procedure evaluation

A. History and slit-lamp biomicroscopic examination to determine

1. Prognosis, based on preexisting conditions and underlying disease
 - a. Etiology
 - b. Extent
 - c. Stability
2. Surgical planning

B. Identify and correct anatomical abnormalities of lids (may occur simultaneously with amniotic membrane transplantation)

C. Identify and treat systemic conditions contributing to ocular disease

- D. Identify and treat keratoconjunctivitis sicca and Meibomian gland disease (blepharitis, rosacea)**
 - 1. Lubricants
 - 2. Punctal occlusion
 - 3. Tetracyclines, azithromycin

III. List the alternatives to this procedure

- A. Alternatives to amniotic membrane transplantation may be indicated or contraindicated depending on the underlying disease.**
- B. Medical therapy of underlying disease**
- C. Therapeutic bandage contact lens**
- D. Conjunctival flap or free graft**
- E. Limbal stem cell graft(s)**
 - 1. Conjunctival limbal autograft(s)
 - 2. Keratolimbal allograft(s) (cadaveric or living related)
 - 3. *Ex-vivo* expanded auto- or allograft(s)
- F. Mucous membrane graft(s)**
- G. Temporary or permanent tarsorrhaphy**
- H. Lamellar or penetrating keratoplasty**

IV. Describe the instrumentation, anesthesia and technique

- A. Operating room with operating microscope.**
- B. Standard sterile preparation and draping for ocular surgery**
- C. Topical, sub-Tenons, peri- or retrobulbar, or general anesthesia depending on extent of accompanying surgical procedures and American Society of Anesthesiology classification**
- D. Instruments**
 - 1. Lid speculum
 - 2. 0.12 mm forceps for globe fixation
 - 3. Smooth tying forceps for handling amniotic membrane
 - 4. 10-0 nylon suture for cornea
 - 5. 8-0 or 9-0 absorbable suture for conjunctiva, sclera
- E. Preparation of ocular surface based on underlying disease**
 - 1. Pterygium excision (See Pterygium excision)
 - 2. Tumor excision with adjunctive therapy as indicated
 - 3. Symblepharon release

4. Corneal epithelial debridement

F. Amniotic membrane may be obtained fresh, frozen on a filter paper sheet with the stromal side adherent to the sheet, or in a lyophilized form

1. The best preparation has not yet been established in comparative studies

G. Placement and fixation

1. When used as a graft to promote epithelialization, it is placed with the basement membrane (non-sticky) side up

2. As a patch, it is placed with the stromal (sticky) side up or in multiple layers

3. The tissue is trimmed to fit the area to be covered and sutured in place with interrupted or continuous sutures

H. The placement of a bandage lens and/or use of temporary tarsorrhaphy (depending on the clinical situation) may be useful in preventing early dehiscence of the amniotic membrane graft

I. Amniotic membrane fused to symblepharon ring is alternative and can be placed outside the operating room

V. List the complications of the procedure, their prevention and management

A. Failure to suppress underlying disease process with resultant corneal scarring, thinning, perforation, or progressive conjunctival scarring and forniceal shrinkage

B. Early dissolution of amniotic membrane transplant (less than 1 week)

1. Prevention

a. Adequate suture fixation of graft

b. Preoperative treatment of exposure and dry eye

c. Treat exposure prior to or at time of amniotic membrane grafting

2. Management

a. Correct exposure and treat tear insufficiency

i. Lubricants, autologous serum

ii. Punctum plugs

iii. Therapeutic contact lens

iv. Tarsorrhaphy

VI. Describe the follow-up care

A. Topical antibiotics and corticosteroids

B. Therapeutic soft contact lens is optional in some cases

C. Weekly follow-up

D. Consider removal of amniotic membrane if it is still present after underlying disease process

resolved

- E. Suture removal once amniotic membrane has dissolved

VII. Describe appropriate patient instructions

- A. Compliance with postoperative topical medication regimen
- B. Avoid eye rubbing
- C. When to seek further care

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Tseng SC. Amniotic Membrane Transplantation for Ocular Surface Reconstruction. Biosci Rep. 2001 Aug;21(4):481-9. Mannis, Springer, New York, 2002.
3. Aldave AJ, Sonmez B. Elucidating the molecular genetic basis of the corneal dystrophies: are we there yet? Arch Ophthalmol. 2007 Feb;125(2):177-86.
4. Weiss JS, Møller HU, Lisch W, et al. The IC3D classification of corneal dystrophies. Cornea. 2008;27:S1-S42.
5. Gruterich M, Espana EM, Tseng SC. Ex vivo expansion of limbal epithelial stem cells: amniotic membrane serving as stem cell niche. Surv Ophthalmol 2003;48:631-46.
6. AAO, Focal Points: Surgical Techniques for Ocular Surface Reconstruction, Module #12, 2006.

Repair of corneal laceration and suture closure of corneal wound

I. List the indications/contraindications

A. Indications

1. Penetrating injury
2. Perforating injury

B. Contraindications

1. Perforations with significant tissue loss
 - a. Perforation from microbial keratitis
 - b. Perforation from immune melt
 - c. Perforation with traumatic tissue avulsion
 - d. These conditions may not be amenable to primary closure and often require removal of adjacent involved tissue and corneal grafting

II. Describe the pre-procedure evaluation

A. Complete history

1. Mechanism and nature of injury
2. Previous history of ocular trauma and surgery
3. Level of visual acuity prior to injury
4. Medications
5. Time of last food intake
6. Status of tetanus prophylaxis

B. Physical examination

1. Visual acuity of both eyes
2. External examination to assess orbital trauma with inspection of involved eye and other eye
3. Pupils
 - a. Check for afferent pupillary defect
4. Slit-lamp biomicroscopic examination with Seidel testing if indicated
 - a. Partial vs. full-thickness injury
 - b. The presence of foreign bodies in cornea, anterior chamber (AC) angle (which may require gonioscopy)

- c. Lens status (i.e. presence of cataract or anterior capsule rupture)
- 5. Dilated fundus examination unless iris plugging the wound, foreign body in or extending into the anterior chamber from the cornea, or complete hyphema
- C. Diagnostic imaging - localization of foreign body if suspected**
 - 1. Plain film
 - 2. Computed tomography
 - 3. Ultrasound

III. List the alternatives to this procedure

- A. Application of tissue adhesive for perforations less than 2 mm diameter**
- B. Bandage soft contact lens for small partial-thickness lacerations with minimal wound gape or shelved, self-sealing lacerations**

IV. Describe the instrumentation, anesthesia and technique

- A. General anesthesia (avoid agents that cause contraction of the extra-ocular muscle such as succinylcholine, use nondepolarizing muscle relaxants instead) and perioperative antibiotics**
- B. Prep, drape, and insert eyelid speculum avoiding pressure to the globe**
- C. Inspect for iris prolapse and incarceration**
 - 1. May need to excise necrotic or epithelialized tissue
- D. Ophthalmic viscosurgical device (viscoelastic) introduced via a paracentesis**
 - 1. Can be used to deepen the chamber and relieve iris incarceration
- E. Align wound at limbus first**
- F. Use 9-0 nylon for limbus and 10-0 nylon for clear cornea with spatulated needle**
- G. Use large, compressive sutures to close the peripheral aspects of the wound and smaller bites to close the central cornea**
 - 1. This flattens the peripheral cornea and steepens the central cornea, resulting in some reduction of astigmatism
 - 2. Suture placement should avoid posterior wound gape
- H. Orient suture bites 90 degrees to wound with 90% stromal thickness s**
- I. Stellate lacerations may require a purse string suture for closure**
- J. Remove the lens if anterior capsule disrupted**
- K. Anterior vitrectomy if indicated**
- L. Conjunctival peritomy when scleral laceration suspected**
- M. Inspect carefully to insure watertight globe**
- N. Subconjunctival antibiotics**

- O. Topical antibiotics, corticosteroids, and cycloplegics**
- P. Consider cephalosporin, fluoroquinolone, aminoglycoside**
- Q. Pain medications**

V. List the complications of this procedure, their prevention and management

A. Post-operative infection including keratitis and endophthalmitis

- 1. Prevention
 - a. Follow sterile technique
 - b. Maintain the patient on topical antibiotics and systemic antibiotics as indicated
- 2. Treatment
 - a. Culture and treat with the appropriate antibiotics

B. Wound leak

- 1. Prevention
 - a. Careful inspection of wound intra-operatively to insure watertight globe
 - b. Apply mild pressure on wound edges and look for leak
 - c. Seidel testing
- 2. Treatment
 - a. Return to operating room for closure of large leaks (flat chamber). If fistula suspected, remove epithelium from inner aspect of wound.
 - b. Trial with pressure patching or bandage soft contact lens and aqueous suppressants if leak is minimal

C. Elevated intraocular pressure (IOP)

- 1. Treat as indicated with topical agents

D. Hyphema

- 1. Corticosteroids and cycloplegics
 - a. May need wash-out

E. Corneal scarring and opacification

- 1. Prevention
 - a. Minimize suture placement in central visual axis
- 2. Treatment
 - a. May require penetrating or rotational keratoplasty

F. Postoperative irregular astigmatism

- 1. Prevention

- a. Difficult
- b. Attempt to maintain corneal architecture

G. Treatment

- 1. Rigid gas permeable lens may be indicated

H. Describe the follow-up care

I. Frequency of postoperative visits is a function of epithelial healing and control of intraocular pressure and inflammation

J. Essential components of the postoperative exam include:

- 1. Interval history
- 2. Measurement of visual acuity
- 3. Slit-lamp biomicroscopy
- 4. IOP assessment

K. Discontinue antibiotics as epithelium heals

L. Taper corticosteroids as inflammation resolves

M. Sequential suture removal in 6-12 weeks before sutures vascularize and loosen

VI. Describe appropriate patient instructions (post-op care, vision rehabilitation)

- A. Stress importance of compliance with medications and need for regular postoperative care to ensure optimum visual rehabilitation**
- B. Discuss physical restrictions, importance of eye protection, and details for emergency care**
- C. Discuss expectations for postoperative recovery depending on the nature and extent of the injury**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
- 2. AAO, Focal Points: Repair of the Traumatized Anterior Segment, Module #1, 1992.

Management of descemetocoele and corneal perforation by bandage contact lens, tissue adhesive or reconstructive graft

I. List the indications/contraindications

A. Indications

1. Corneal perforation - impending or frank
2. Descemetocoele
3. Corneal thinning
4. Corneal melt
5. Wound leaks
6. Contraindications
7. Severe corneal ulceration or corneal melting in an eye with no or very limited visual potential
8. Blind, painful eye

II. Describe the pre-procedure evaluation

A. Slit-lamp biomicroscopic examination

1. Measure degree of corneal thinning (pathology)
2. Seidel test
3. Assess size of corneal perforation
4. Evaluate wound configuration
5. Evaluation of corneal ulceration
6. Evaluate whether any tissue was lost
7. Anterior chamber depth
8. Determine reason for descemetocoele or corneal thinning
9. Evaluate lens status

B. Identify and correct any anatomical abnormalities leading to corneal thinning (exposure, entropion, ectropion, trichiasis, etc.)

1. May occur simultaneously with corneal intervention

C. Identify and treat any contributing systemic conditions

1. May occur simultaneously with corneal intervention (i.e., rheumatoid arthritis, Wegener granulomatosis, systemic lupus erythematosus, gout, Crohn disease)

D. Consider tetanus prophylaxis

E. Consider systemic antibiotics

F. Optimize the ocular surface

1. May occur simultaneously with corneal intervention
 - a. Treat keratoconjunctivitis sicca (i.e. preservative free lubricants)
 - b. Treat any lid disease (rosacea, blepharitis)
 - c. Punctal occlusion

III. List the alternatives to this procedure

A. Observation

B. Lubrication

C. Patching

D. Pharmacological aqueous suppression

E. Bandage contact lens for small leaks with well opposed wound margins

F. Tarsorrhaphy (temporary or permanent) as adjuvant therapy or for descemetoceles due to exposure or neurotrophic disease

G. Cyanoacrylate adhesive for small wounds (under 2 mm)

H. Corneal sutures (if no loss of tissue)

I. Amniotic membrane (small perforation or descemetocoele)

J. Ophthalmic viscosurgical device (viscoelastic) injection for reforming the anterior chamber if indicated (especially if patient is phakic)

K. The use of collagenase inhibitors (i.e., acetylcysteine, medroxyprogesterone)

L. Lamellar keratoplasty (if wound is not full-thickness)

M. Penetrating keratoplasty

1. Full size graft may have to be large and eccentric, depending on the size and location of the thinned area
2. Patch graft (under 5 mm)

N. Enucleation or evisceration

IV. Describe the instrumentation, anesthesia and technique

A. Bandage contact lens

1. Topical antibacterial prophylaxis

B. Tarsorrhaphy

1. Lidocaine 1% or 2% with epinephrine injected subcutaneously into the upper and lower eyelids
2. Apposition of the eyelid margins using one of the following: Frost suture, tarsal pillar, cyanoacrylate adhesive, intermarginal adhesion, Botox tarsorrhaphy

C. Cyanoacrylate adhesive - (See Application of corneal tissue adhesive)

D. Corneal sutures - (See Repair of corneal laceration and suture closure of corneal wound)

E. Amniotic membrane- requires multiple layers

F. Lamellar keratoplasty

1. Recipient cornea is dissected first (may be necessary to convert to full thickness penetrating keratoplasty)
2. Donor lamellar graft from whole globe or from donor cornea-scleral rim of 16 mm or more (with use of an artificial anterior chamber)
3. Microkeratome may be helpful with the dissection
4. Remove Descemet membrane from donor button
5. Meticulous irrigation, cleaning, and smoothing of the interface (See Penetrating keratoplasty)

G. Patch graft

1. Even if the area to be repaired is small, if the patch graft would interfere with vision, full-sized penetrating keratoplasty is preferable
2. Full-size graft may have to be large and eccentric, depending on the size and location of the thinned area
3. Ulcerated (or thinned) area is outlined with a small trephine (See Penetrating keratoplasty)

H. Penetrating keratoplasty (See Penetrating keratoplasty)

V. List the complications of this procedure, their prevention and management

A. Common to all

1. Failure to seal wound
2. Progression of thinning
3. Progression or development of corneal infiltrate
4. Pain
5. Decreased vision
6. Corneal scarring
7. Corneal neovascularization
8. Endophthalmitis
9. Giant papillary conjunctivitis
10. Shallow/flat anterior chamber

11. Cataract formation
12. Anterior synechiae formation leading to glaucoma

B. Bandage contact lens

1. Corneal pannus formation
2. Corneal edema
3. Development of corneal infiltrate

C. Tarsorrhaphy

1. Trichiasis
2. Entropion
3. Corneal abrasion

D. Cyanoacrylate adhesive

1. Loosening of glue
2. Corneal pannus formation
3. Effects of glue on adjacent ocular structures
 - a. Toxicity to endothelium
 - b. Toxicity to lens - cataract formation
 - c. Symblepharon

E. Corneal sutures

1. Loosening of sutures
2. Development of corneal infiltrate/suture abscess
3. Induced astigmatism

F. Lamellar keratoplasty

1. Graft rejection (epithelial rejection, subepithelial infiltrates, stromal rejection)
2. Interface opacities
3. Vascularization of the interface
4. Inflammatory necrosis of the flap
5. Corneal perforation

G. Penetrating keratoplasty - tectonic or optical, patch grafts

1. Graft rejection
2. Graft failure
3. Development of corneal infiltrate
4. Irregular astigmatism
5. Glaucoma

H. Prevention and management

1. Select appropriate therapy for situation
2. Careful surgical technique
3. Careful follow-up

VI. Describe the follow-up care

- A. Monitor status of glue or sutures or transplant
- B. Monitor status of cornea
- C. Monitor for the development of new corneal ulceration or progression of corneal ulceration
- D. Remove glue or sutures when healing noted
- E. Use topical antibiotics to prevent superinfection
- F. Follow-up every 1-3 days depending on clinical response

VII. Describe appropriate patient instructions (post-op care, vision rehabilitation)

- A. No eye rubbing
- B. Eye protection at all times/eye shield
- C. No coughing or sneezing
- D. Limited activities
- E. Use medications as directed (topical antibiotics, aqueous suppressants, cycloplegics, collagenase inhibitors)
- F. Call physician if pain increases, vision changes, increased tearing, or a gush of fluid is noted

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.

Donor selection criteria contraindicating donor cornea use for corneal transplantation

I. List the contraindications

A. Donor evaluation must include

1. Serologic testing for hepatitis B (hepatitis B surface antigen (HBsAg), hepatitis C (anti-HCV), and human immunodeficiency virus (anti-HIV1, anti-HIV2 [or combination test])
2. Physical assessment of the donor
 - a. Physical signs of human immunodeficiency virus (HIV) disease
 - b. Infectious hepatitis
 - c. Injection drug use
3. Tissue evaluation
 - a. Gross evaluation
 - b. Slit-lamp biomicroscopic evaluation
 - c. Specular microscopy
 - i. Generally, corneas with endothelial cell counts of $<2000\text{cells/mm}^2$ are not used for endothelial keratoplasty or penetrating keratoplasty
 - ii. Lower cell counts are acceptable for lamellar keratoplasty
 - d. Death to preservation time (optimal range <12 hours)
 - e. Donor age (more important indicator of tissue elasticity than graft survival)
4. Donor history evaluation including donor's name and donor information obtained from at least one of the following
 - a. Pathologist or medical examiner physical assessment of death report
 - b. Police investigation report
 - c. Medical examiner's investigative report
 - d. Family interview
 - e. Medical record or hospital chart
 - f. Treating physician interview

B. Contraindications for human transplantation

1. Penetrating keratoplasty
 - a. Death of unknown cause

- b. Creutzfeldt-Jakob disease, variant Creutzfeldt-Jakob disease, or family member with Creutzfeldt-Jakob disease
- c. Death with neurologic disease of unestablished diagnosis
- d. Dementia, unless due to cerebrovascular disease, brain tumor, or head trauma
 - i. Donor with toxic or metabolic-induced dementia may be acceptable pending documentation of consultation with the medical director. The approval of the medical director is required
- e. Subacute sclerosing panencephalitis
- f. Progressive multifocal leukoencephalopathy
- g. Congenital rubella
- h. Reyes syndrome
- i. Active viral encephalitis or encephalitis of unknown origin or progressive encephalopathy
- j. Active septicemia (bacteremia, fungemia, viremia)
- k. Active bacterial or fungal endocarditis
- l. Active viral hepatitis
- m. Rabies
- n. Intrinsic eye disease
 - i. Retinoblastoma
 - ii. Malignant tumors of the anterior segment or known adenocarcinoma in the eye of primary or metastatic origin
 - iii. Active ocular or intraocular inflammation: conjunctivitis, keratitis, scleritis, iritis, uveitis, vitritis, choroiditis, retinitis
 - iv. Congenital or acquired disorders of the eye that would preclude a successful outcome for the intended use
 - i) Central donor corneal scar for an intended penetrating keratoplasty, keratoconus and keratoglobus
 - v. Pterygia or other superficial disorders of the conjunctiva or corneal surface involving the central optical area of the corneal button that would preclude a successful outcome for penetrating keratoplasty.
 - i) May be used for posterior lamellar grafts
- o. Prior intraocular or anterior segment surgery is a relative contraindication depending on the use of the tissue. Donor's status post LASIK and PRK are acceptable for DMEK. Eyes that have had prior cataract surgery can be used for all grafts if the cell count is adequate and the wounds do not enter the area of the planned trephination
- p. Leukemias
- q. Active disseminated lymphomas

- r. Hepatitis B surface antigen positive donors
 - s. Recipients of human pituitary-derived growth hormone (pit-hGH) during the years from 1963-1985
 - t. Human T-Lymphotropic virus (HTLV)-I or HTLV-II infection.
 - u. Recipients of non-synthetic dura mater graft
 - v. Hepatitis C seropositive donors
 - w. HIV or high risk for HIV, HIV seropositive donors
 - x. Positive syphilis serology as defined as a contraindication by Food and Drug Administration (FDA) guidance
2. Lamellar or patch grafts
 - a. Criteria are the same as listed for penetrating keratoplasty
 - i. Except that the endothelial cell count does not matter as long as the corneal tissue is clear
 3. Endothelial keratoplasty
 - a. Criteria are the same as listed for penetrating keratoplasty
 - i. Except that tissue with non-infectious anterior pathology that does not affect the posterior stroma and endothelium is acceptable.
 - ii. Surgeons must be notified of any prior pathology prior to placing tissue for transplant
 4. Scleral tissue
 - a. Criteria are the same as for penetrating keratoplasty except that tissue with local eye disease affecting the cornea is acceptable for use. Death to preservation time may be extended

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Eye Bank Association of America Medical Standards. June 2012. EBAA. Washington D.C.
3. AAO, Focal Points: Penetrating Keratoplasty, Module #6, 1992, p.1-2.

Penetrating keratoplasty

I. List the indications/contraindications

A. Indications

1. Pseudophakic or aphakic corneal edema
2. Endothelial dystrophies: Fuchs and posterior polymorphous corneal dystrophy
3. Regraft related to allograft rejection
4. Regraft unrelated to allograft rejection
5. Stromal dystrophies: lattice, granular, Avellino,
6. Keratoconus and other ectasias
7. Viral/postviral keratitis/keratopathy
8. Microbial/post microbial keratitis/keratopathy
9. Noninfectious ulcerative keratitis or perforation
10. Corneal degenerations
11. Chemical injury
12. Mechanical trauma, nonsurgical
13. Congenital opacity
14. Iridocorneal endothelial syndrome
15. Corneal degeneration
16. Other causes of corneal opacification or distortion, including surgical trauma

B. Contraindications

1. Active uveitis
2. Active keratitis, except when necessary for tectonic support or for removal of infectious material in progressive microbial keratitis
3. Severe ocular surface disease
 - a. Marked 360 degrees, limbal stem cell deficiency
 - b. Neurotrophic cornea
4. Preexisting conditions that limit visual potential, including amblyopia, macular or retinal disease and optic nerve damage
 - a. Surgery may be considered in this situation if visualization of the posterior pole is necessary and as a means of treating pain from bullous keratopathy
 - b. Penetrating keratoplasty is contraindicated in individuals with complete loss of vision

5. Multiple graft rejections
6. Stromal neovascularization
 - a. If not severe, transplantation may be successful with intensive steroid treatments, but prognosis is more guarded
7. Poorly controlled glaucoma
 - a. May benefit from combined glaucoma filtering procedure or placement of tube
8. Eyelid abnormality
 - a. Address lid malposition first
 - b. May benefit from combined tarsorrhaphy
 - i. Poor blink due to facial nerve paresis
 - ii. Lagophthalmos
 - iii. Ectropion
 - iv. Entropion
9. Dry eye
 - a. Address prior to surgery
 - i. Topical cyclosporine
 - ii. Punctal plugs
 - iii. Aggressive lubrication

II. Describe the pre-procedure evaluation

- A. Performing a complete ophthalmic history and examination is essential to assess whether the corneal abnormality is a cause of decreased visual acuity and whether a corneal graft would be expected to survive in the recipient's ocular environment**
- B. Patient history**
 1. Assessment of past ocular history including previous vision and disorders of the involved eye
 2. Cause and course of visual loss
 3. Other medical conditions
 4. Previous and current medications
- C. Clinical examination**
 1. Best corrected visual acuity including rigid contact lens over-refraction if indicated
 2. External examination of ocular adnexa
 3. Ocular surface, including eyelids, conjunctiva, tears, and corneal sensation
 4. Corneal and anterior segment status, including extent of corneal vascularization, inflammation, and thinning

5. Intraocular pressure (IOP) assessment
6. Evaluation of the lens to determine need for combined cataract extraction
7. Posterior segment evaluation and/or B-scan ultrasound

D. Preoperative assessment

1. Evaluate prognosis of corneal graft based on history and examination
 - a. Identify and counsel individuals at greater risk for allograft rejection
 - b. May benefit from intensive topical corticosteroids (See Allograft rejection)
2. Aim for stable medical health, including conditions such as diabetes mellitus, hypertension, cardiopulmonary disease, and endocrine disorders
3. Control abnormal IOP
4. Suppress ocular inflammation and treat ocular surface disease
1. Interface with eye bank and evaluate donor cornea
5. Consider perioperative antimicrobial or antiseptic prophylaxis
6. Consider systemic immunosuppression in the preoperative assessment (especially for high risk grafts)

III. List the alternatives to this procedure

A. Based on depth of corneal opacity and visual potential

1. Endothelial keratoplasty for endothelial dysfunction
2. Ethylenediaminetetraacetic acid (EDTA) chelation for band keratopathy
3. Superficial keratectomy
4. Phototherapeutic keratectomy
5. Lamellar keratectomy
6. Lamellar keratoplasty
7. Keratoprosthesis
8. Thermocautery
9. Conjunctival flap

IV. Describe the instrumentation, anesthesia and technique

- A. General versus retrobulbar anesthesia**
- B. Donor cornea**
- C. Donor corneal trephine**
- D. Flieringa ring for scleral support**

- E. Recipient corneal trephine**
- F. Corneal scissors and knife**
- G. Instruments for cataract extraction, intraocular lens exchange or insertion, anterior vitrectomy, and/or iridectomy, as indicated**
- H. Suturing techniques: interrupted, continuous, and combined**

V. List the complications of the procedure, their prevention and management

A. Intraoperative

1. Damage to the lens or iris
2. Vitreous loss
3. Retained Descemet membrane
4. Poor graft centration
5. Poor tissue apposition and wound leak
6. Suturing problems
7. Problems reforming the anterior chamber
8. Hyphema
9. Choroidal hemorrhage or effusion and suprachoroidal hemorrhage

B. Postoperative

1. Wound leak
 - a. Patching
 - b. Bandage soft contact lens
 - c. Aqueous suppressants
 - d. May need resuturing
2. Flat chamber/iris incarceration
 - a. Indicative of poor wound integrity or posterior pressure
 - b. Early surgical intervention often necessary
3. Elevated IOP
 - a. Treat with medical, laser surgery, or surgical intervention as indicated
4. Endophthalmitis
 - a. Urgent, aggressive intervention with consultation with retina specialist for anterior chamber tap, vitreous biopsy and intravitreal antibiotics
5. Severe inflammation including formation of fibrin
 - a. Treat aggressively with corticosteroids

- b. Tissue plasminogen activator may have a role in fibrinolysis
- 6. Microbial or viral keratitis
 - a. Scrape and culture as indicated
 - b. Initiate treatment promptly as indicated
- 7. Persistent epithelial defect
 - a. Identify and treat concomitant ocular surface disease
 - b. Aggressive lubrication, patching, bandage soft contact lens, autologous serum, and tarsorrhaphy may be indicated
- 8. Primary endothelial failure
 - a. Consider regrant if edema is significant and fails to resolve after several weeks
- 9. Recurrence of primary disease
 - a. Treat as indicated in cases of microbial keratitis
 - b. Regraft may be required for recurrent dystrophy
- 10. Suture-related problems
 - a. Remove broken or loose sutures
 - b. Treat suture abscesses aggressively
- 11. Postoperative astigmatism
 - a. Selective suture removal based on corneal topography
 - b. Consider relaxing incisions and placement of additional sutures
- 12. Allograft rejection
 - a. Recognize early and treat aggressively with corticosteroids
 - b. Cyclosporine may have a role as an adjuvant therapy in the prevention and treatment of allograft rejection (See Allograft rejection)
- 13. Anterior synechiae
 - a. Release existing synechiae during surgery
 - b. Aggressive control of inflammation
- 14. Posterior synechiae
 - a. Use postoperative mydriatics
- 15. Pupillary block
 - a. Attempt medical management
 - b. Will likely need peripheral iridotomy
- 16. Choroidal detachment
 - a. Likely due to choroidal effusion

- b. Usually self-limiting, observe closely for resolution
- 17. Corneal vascularization
 - a. Remove adjacent sutures
 - b. Associated with increased risk of graft rejection
- 18. Epithelial ingrowth
 - a. Treat aggressively with complete surgical excision and cryotherapy
- 19. Transmission of donor disease
- 20. Traumatic wound rupture
- 21. Graft failure
 - a. Higher probability in eyes with tube shunts
 - b. Patients should be advised of higher likelihood of re graft within 5 years if a tube is present
 - c. Management of failed penetrating keratoplasty
 - i. Determine cause of graft failure (e.g. ocular surface disease, immunologic graft rejection, graft failure without rejection, uncontrolled glaucoma, etc)
 - ii. Assess if regrafting would be helpful and have realistic chance of success
 - iii. If chance of success poor, consider conjunctival flap, cautery to corneal surface, or keratoprosthesis
 - iv. If realistic chance of success, address problems that led to graft failure (e.g. ocular surface disease, glaucoma, etc)
 - v. If replacing graft and previous refractive result acceptable, and graft-host interface well apposed posteriorly, consider endothelial keratoplasty as it provides more rapid visual recovery and maintains ocular surface.
 - vi. If refractive results was not acceptable prior to failed PK, proceed with repeat PK

VI. Describe the follow-up care

- A. Frequency of postoperative visits is a function of epithelial healing and control of IOP and inflammation**
- B. Visits are indicated more frequently in the first 90 days**
- C. Essential components of the postoperative exam include:**
 - 1. Interval history
 - 2. Measurement of visual acuity
 - 3. Slit-lamp biomicroscopy
 - 4. IOP assessment
- D. Topical corticosteroid and other ophthalmic medications**
- E. Suture removal**

VII. Describe appropriate patient instructions

- A. **Stress importance of compliance with medications and need for regular postoperative care to ensure optimum visual rehabilitation, which may take up to a year**
- B. **Discuss symptoms of corneal transplant rejection and need for immediate attention (redness, sensitivity to light, visual changes, pain)**
- C. **Discuss physical restrictions, importance of eye protection, and details for emergency care**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. AAO, Focal Points: Penetrating Keratoplasty, Module #6, 1992.
3. AAO, Preferred Practice Patterns Committee, Cornea and External Disease Panel. Corneal Opacification and Ectasia Preferred Practice Patterns, 2000.
4. Shimazaki J, Shimmura S, Ishioka M, et al. Randomized clinical trial of deep lamellar keratoplasty vs penetrating keratoplasty. *Am J Ophthalmol* 2002;134:159-65.
5. Karabatsas CH, Cook SD, Figueiredo FC, et al. Combined interrupted and continuous versus single continuous adjustable suturing in penetrating keratoplasty: a prospective, randomized study of induced astigmatism during the first postoperative year. *Ophthalmology* 1998;105:1991-8.
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Endothelial keratoplasty

I. List the indications/contraindications

A. Indications

1. Persistent corneal endothelial dysfunction, with corneal surgery aiming to improve vision, to alleviate bullous keratopathy or to allow visualization of posterior pole
 - a. Pseudophakic or aphakic corneal edema
 - b. Fuchs endothelial dystrophy
 - c. Corneal graft failure
 - d. Other endothelial disorders e.g. posterior polymorphous corneal dystrophy, iridocorneal endothelial syndrome, congenital hereditary endothelial dystrophy, post traumatic endothelial failure

B. Relative Contraindications

1. Limited visual potential from amblyopia, macular disease or optic nerve damage, unless visualization of the posterior pole is necessary or surgery is needed to control pain from bullous keratopathy
2. Active keratitis
3. Active uveitis
4. Corneal stromal scarring
5. Resolved keratitis with significant irregular astigmatism
6. Multiple graft rejections
7. Uncontrolled glaucoma
8. Shallow anterior chamber with significant peripheral anterior synechiae and/or anterior chamber intraocular lens (ACIOL)

II. Describe the pre-procedure evaluation

A. Performing a complete ophthalmic history and examination is essential to assess whether the guttae and corneal edema from endothelial dysfunction are the cause of decreased visual acuity and whether the graft would offer visual rehabilitation and/or patient comfort from bullous keratopathy

B. Patient history

1. Assessment of past ocular history including previous vision and disorders of the involved eye
2. Cause and course of visual loss
3. Assessment of pain level with current condition
4. Other medical conditions

5. Previous and current medications

C. Clinical examination

1. Best corrected visual acuity including contact lens over-refraction if indicated
2. External examination of ocular adnexa
3. Status of ocular surface, including eyelids, conjunctiva, and tear film
4. Corneal and anterior segment status, including extent of corneal decompensation and presence of corneal scarring
5. Intraocular pressure (IOP) assessment
6. Evaluation of the lens to determine need for cataract extraction
7. Posterior segment evaluation, possibly including B-scan ultrasound if inadequate visualization

D. Preoperative assessment

1. Evaluate patient and identify contraindications and risk factors which may affect the prognosis and long term viability of corneal graft
 - a. Presence of AC IOL
 - b. Presence of glaucoma drainage device
 - c. Shallow anterior chamber and/or PAS
 - d. Aphakia
2. Counsel individuals at greater risk for allograft rejection (See Allograft rejection)
3. Consider cataract removal prior to endothelial keratoplasty (EK) (staged procedure) or at time of EK (combined procedure).
4. If ACIOL, consider IOL exchange (either staged or combined procedure) prior to EK. Note presence and location of peripheral iridectomy
5. Note presence of peripheral anterior synechiae, and if extensive, counsel against EK
6. Achieve control of abnormal IOP
7. Suppress ocular inflammation and treat ocular surface disease
8. Interface with eye bank to discuss plans for endothelial graft that may be pre-cut by eye bank or prepared by surgeon

III. List the alternatives to this procedure

A. Penetrating keratoplasty

1. Advantages
 - a. In cases of subepithelial haze with chronic bullous changes, this will be removed
2. Disadvantages
 - a. Higher risk of intraoperative vision loss

- b. Longer healing and time for suture removal, therefore longer time for visual rehabilitation
- c. Potential for high surgically-induced postoperative astigmatism and ametropia
- d. Higher potential for suture related complications and/or infection
- e. Theoretical higher risk of rejection
- f. Less tectonic strength of globe long-term

B. Other treatments of symptomatic endothelial dysfunction in an eye with poor visual potential

- 1. Bandage contact lens application
- 2. Anterior stromal micropuncture +/- amniotic membrane transplantation
- 3. Conjunctival (Gunderson) flap for painful bullous keratopathy

IV. Describe the instrumentation, anesthesia and technique

A. Anesthesia

- 1. Topical, peribulbar, or retrobulbar with monitored intravenous anesthesia

B. Techniques and instrumentation for EK

- 1. Size and centration of donor disc determined
- 2. Incision is either clear corneal or scleral tunnel ranging from 3-5mm in diameter for DSEK or 2.8mm clear corneal incision for DMEK
- 3. Donor tissue can be pre-cut or donor preparation carried out on back bench by surgeon utilizing artificial anterior chamber and microkeratome
- 4. Appropriate trephine punch used to create posterior lamellar graft
- 5. Descemet membrane is scored
- 6. Descemet membrane may be stripped under viscoelastic or under balanced salt solution.. If viscoelastic is used, it must be completely removed following this step
- 7. Peripheral recipient full-thickness venting incisions and/or peripheral stromal roughening to increase chance of graft adherence in DSEK cases
- 8. In DSEK cases, the posterior lamellar graft can be inserted with tissue insertion forceps, or a tissue inserter such as a glide or retractable platform inserter, or the suture pull through technique. In DMEK, the donor membrane is inserted with a glass pipette or IOL injector.
- 9. Anterior chamber is filled with a 100% air bubble to allow for proper centration and adherence of posterior lamellar graft
- 10. After adherence in OR, air bubble is partially removed to allow for a mobile air bubble over the pupil, and cycloplegic drops placed (unless inferior peripheral iridotomy is present)
- 11. The patient remains supine for a period of time so that the air bubble ensures that the endothelial graft stays in position

V. List the complications of the procedure, their prevention and management

A. Intraoperative

1. Damage to the lens or iris
2. Damage to the donor cornea during preparation

B. Postoperative

1. Dislocation of endothelial graft
 - a. Management
 - i. Reposition graft with air bubble
 - ii. Caution patient to avoid eye rubbing post operatively
2. Pupillary block from air bubble
 - a. Management
 - i. Remove air via paracentesis
 - ii. Consider pre-op laser PI or intra-op peripheral iridectomy
3. Elevated IOP
 - a. Management
 - i. Treat with medical, laser surgery, or surgical intervention as indicated
4. Wound leak
 - a. Management
 - i. Suture
 - ii. Patching
 - iii. Bandage soft contact lens
 - iv. Aqueous suppressants
5. Endophthalmitis
 - a. Management
 - i. Urgent, aggressive intervention with consultation with retina specialist for anterior chamber tap, vitreous biopsy and intravitreal antibiotics
6. Primary endothelial failure
 - a. Management
 - i. Consider re graft if edema is significant and fails to resolve after several weeks
7. Allograft rejection
 - a. Management
 - i. Treat aggressively with corticosteroids. (See Allograft rejection)

8. Late interface infectious keratitis

VI. Describe the follow-up care

- A. Frequency of postoperative visits related to graft attachment and control of intraocular pressure and inflammation**
 1. Patients are often seen the next day, at one week and at one month, then regularly
 2. In DMEK cases, patients are often also seen 4-5 days post-operatively before air bubble is totally gone to see if reinjection of air to push up detaching areas is indicated
- B. Essential components of the postoperative exam include:**
 1. Interval history
 2. Measurement of visual acuity
 3. Slit-lamp biomicroscopy
 4. IOP assessment
 5. Manifest refraction is typically stable 4-6 weeks post-op
- C. Topical corticosteroid and other ophthalmic medications**
 1. Topical corticosteroids in endothelial keratoplasty are administered similarly to those given after penetrating keratoplasty

VII. Describe appropriate patient instructions

- A. Stress importance of compliance with medications and need for regular postoperative care to ensure visual rehabilitation.**
- B. Discuss symptoms of graft rejection and need for immediate attention (redness, sensitivity to light, visual changes, pain)**
- C. Discuss physical restrictions, importance of eye protection, avoid eye rubbing and details for emergency care**
- D. Patients can achieve good visual acuity although interface haze may occur between the recipient cornea and the donor endothelial graft**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Price FW Jr, Price MO. Descemet's stripping with endothelial keratoplasty in 200 eyes: Early challenges and techniques to enhance donor adherence. *J Cat Refract Surg* 2006;32:411.
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4. Terry MA, Ousley PJ. Deep lamellar endothelial keratoplasty: early complications and their management. *Cornea* 2006;25:37.
5. Culbertson WW. Descemet stripping endothelial keratoplasty. *Int Ophthalmol Clin* 2006;46:155.

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Anterior lamellar keratoplasty

I. List the indications/contraindications

A. Indications

1. Corneal stromal opacities with healthy endothelium
 - a. Corneal stromal dystrophies
 - b. Corneal stromal degenerations
 - c. Corneal opacities from non-perforating trauma
 - d. Corneal opacities from resolved infectious keratitis
 - e. Corneal opacities from resolved inflammatory/immunologic conditions
 - f. Alternative to penetrating keratectomy (PK) in high risk patients
 - i. Atopy
 - ii. Herpes simplex
 - iii. Down syndrome
2. Corneal irregular astigmatism with healthy endothelium
 - a. Keratoconus with contact lens intolerance
 - b. Pellucid marginal degeneration with contact lens intolerance
 - c. Resolved infectious keratitis (Herpes simplex, Herpes zoster, bacterial, fungal) with surface scar and irregular astigmatism
 - d. Post-refractive surgery (photo refractive keratectomy (PRK), laser in situ keratomileusis (LASIK)) with irregular astigmatism and/or ectasia
 - e. Resolved ulcerative keratopathy from autoimmune or neurotrophic corneal melting
3. Tectonic reconstruction of the cornea
 - a. Corneal thinning disorders such as Terrien marginal degeneration, pellucid marginal degeneration, Mooren ulcer, or any ulcerative disorder from autoimmune or resolved infectious etiology
 - b. Thinned corneas following trauma or surgical excision of dermoids, pterygium, or neoplasm
 - c. Non-infectious corneal descemetoceles
 - d. Corneal perforations less than 2 mm in size

B. Contraindications

1. Optical rehabilitation
 - a. Abnormal endothelium
 - b. Limited visual potential from amblyopia, macular disease or optic nerve damage, unless

visualization of the posterior pole is necessary or surgery is needed to control pain

- c. Uncontrolled glaucoma
- 2. Tectonic rehabilitation
 - a. Abnormal endothelium, unless surgery in an emergency setting to preserve the globe
 - b. Corneal perforations greater than 3 mm in size

II. Describe the pre-procedure evaluation

A. Patient history

- 1. Assessment of past ocular history including previous vision and disorders of the involved eye, especially previous ocular surgery history
- 2. Cause and course of visual loss; chronic or acute
- 3. Assessment of pain level with current condition
- 4. Other medical conditions, especially autoimmune disorders
- 5. Family history of eye disease
- 6. Previous and current medications

B. Clinical examination

- 1. Best corrected visual acuity including contact lens over-refraction if indicated
- 2. External examination of ocular adnexa
- 3. Status of ocular surface, including eyelids, conjunctiva, and tear film
- 4. Corneal and anterior segment status, including extent and location of any corneal thinning, degree of any corneal opacity, depth of opacity
- 5. Corneal topography assessment to determine location and extent of irregular astigmatism
- 6. Corneal endothelial health assessment by slit lamp examination, pachymetry, and specular microscopy if possible
- 7. Determination of depth, location and area of any corneal melt and decision making as to urgency of any tectonic repair
- 8. Intraocular pressure (IOP) assessment
- 9. Evaluation of the lens to determine need for later cataract extraction
- 10. Posterior segment evaluation, possibly including B-scan ultrasound if inadequate visualization

C. Preoperative assessment

- 1. Evaluate patient and identify contraindications and risk factors which may affect the prognosis and long term viability of corneal graft
- 2. Assess whether the patient is a candidate for an anterior lamellar keratoplasty, endothelial keratoplasty, or penetrating keratoplasty

3. Treat and eliminate acute infectious keratitis prior to surgery
4. Achieve control of abnormal IOP
5. Suppress ocular inflammation and treat ocular surface disease
6. Treat autoimmune causes of corneal melting (e.g. rheumatoid disease) with systemic immunosuppression
7. Consult with internal medicine colleagues (e.g. rheumatologist) for management of acute and long term systemic immunosuppression of appropriate autoimmune diseases
8. Counsel individuals at greater risk for continued melting due to systemic disease, inform them of imperfect visual outcome even in ideal circumstances due to interface image degradation
9. Determine additional procedures that may need to be done at time of anterior lamellar keratoplasty such as: amniotic membrane overlay, tarsorrhaphy, punctal cautery, lid reconstruction, bandage contact lens application, etc.

III. List the alternatives to this procedure (based on presence of corneal opacification and visual potential)

A. Penetrating keratoplasty

1. Advantages
 - a. Potential for better acuity due to lack of interface irregularity
2. Disadvantages
 - a. Higher risk of rejections
 - b. Higher short and long term endothelial cell loss
 - c. Higher risk of intra-operative vision loss (e.g. suprachoroidal hemorrhage, retinal detachment)
 - d. Longer time to suture removal, visual rehabilitation
 - e. Longer exposure to topical steroids and their potential complications
 - f. Less tectonic strength of globe long-term

B. Laser phototherapeutic keratoplasty (PTK)

1. Advantages
 - a. Surface ablation for superficial opacities and irregular astigmatism is faster, easier and less traumatic
2. Disadvantages
 - a. Potential for ectasia
 - b. Induced hyperopia, residual irregular astigmatism or opacities

C. Intrastromal corneal rings

1. May reduce irregular astigmatism, stabilize topography, defer corneal transplantation in cases of

keratoconus, post-LASIK ectasia and other corneal warpage conditions

D. Other treatments for corneal melting, Descemetocoele, and perforations

1. Corneal glue with bandage contact lens application for small perforations and Descemetocoeles
2. Conjunctival flaps for neurotrophic ulcerations and melts
3. Amniotic membrane placement for neurotrophic ulcerations and melts
4. Tarsorrhaphy for stabilized neurotrophic ulcerations

IV. Describe the instrumentation, anesthesia and technique

A. Anesthesia

1. Usually retrobulbar, may be topical if using femtosecond laser or microkeratome for anterior lamellar grafts
2. General anesthesia if perforation or uncooperative patient

B. Techniques and instrumentation

1. Standard anterior lamellar keratoplasty - Optical procedure
 - a. Central trephination performed down to desired depth
 - b. Lamellar dissection performed to remove anterior stromal tissue
 - c. Donor prepared to similar thickness stabilized on artificial anterior chamber or sutured to gauze-wrapped sphere
 - d. Donor sutured into recipient bed
 - e. Suture tension adjusted for astigmatism
2. Standard anterior lamellar keratoplasty - tectonic
 - a. Area of melt and/or perforation determined
 - b. Anterior chamber filled with viscoelastic to stabilize anatomy and pressure
 - c. Smallest possible diameter trephine used to encompass area of thinning, and trephination taken to 80% depth or more, anterior tissue removed, and donor prepared and placed as described above
 - d. If melt cannot be surrounded by trephine (e.g. limbal area and extensive), then freehand keratotomy performed (preferably with diamond knife) in adjacent healthy tissue surrounding thinned area to depth of 80% and the anterior tissue removed. Filter paper can be placed over the recipient bed and then cut to form and used as a template for preparation of the proper shape for the donor tissue. The donor can then be prepared and placed as described above
3. Automated lamellar therapeutic keratoplasty (ALTK)
 - a. Microkeratome cuts pre-set depth and diameter of recipient and donor, utilizing artificial anterior chamber for preparation of the donor
 - b. Donor tissue secured with sutures or fibrin glue

- c. No sutures required if graft less than 200 microns thick (place bandage contact lens over graft)
- 4. Femtosecond laser assisted lamellar keratoplasty
 - a. Femtosecond laser cuts pre-set depth and diameter of recipient and donor utilizing artificial anterior chamber for preparation of the donor
 - b. Donor tissue secured with sutures or fibrin glue
 - c. Superficial dissections can be secured with a bandage contact lens
- 5. Deep anterior lamellar keratoplasty (DALK) - Limbal approach (Melles technique)
 - a. Incision , usually 5 mm in length, is made at the scleral limbus
 - b. An air bubble in anterior chamber used to judge the depth of stromal dissection by using the reflection of the tip of the dissection instrument seen on the air bubble. Maximum depth is desirable without perforation
 - c. Specialized stromal dissectors are used to create a total stromal pocket, limbus to limbus, just above Descemet membrane
 - d. Intraocular pressure lowered as much as possible by air-fluid exchange through paracentesis
 - e. Cohesive viscoelastic is injected into the pocket to detach Descemet membrane into anterior chamber
 - f. Trephination from corneal surface down into the viscoelastic pocket
 - g. Anterior tissue removed, leaving bare Descemet or Descemet and minimal posterior stromal fibers
 - h. The viscoelastic thoroughly washed off the recipient bed
 - i. Remove Descemet membrane from donor with forceps or sponge
 - j. Donor is sutured into position, sutures adjusted for astigmatism
- 6. DALK - corneal surface approach (big bubble technique)
 - a. Trephination of central cornea performed to 80% depth
 - b. Descemet membrane detached from the stroma into the anterior chamber using forced injection of either air (Anwar Big Bubble technique) or fluid (hydrodissection technique of Sugita) using a 27 gauge needle with bevel down or a rounded cannula. Tip needs to be deeper than 80% depth, but does not need to be immediately above Descemet membrane to achieve detachment
 - c. Limbal paracentesis made to reduce pressure and allow room for intrastromal air bubble or fluid to expand and further detach Descemet membrane
 - d. Anterior 80% of stromal tissue removed
 - e. Cohesive viscoelastic placed into space between detached Descemet membrane and overlying residual posterior stromal tissue
 - f. Blunt spatula placed into space and blade used to cut down from surface to spatula to enter

space and divide posterior tissue into halves or quadrants

- g. Standard corneal scissors used to cut a trephination circle and excise posterior tissue, leaving 8.0 mm diameter or larger area of bare Descemet
 - h. Viscoelastic thoroughly washed off recipient bed
 - i. Remove Descemet membrane from donor with forceps or sponge
 - j. Donor is sutured into position, sutures adjusted for astigmatism
7. DALK anterior surface approach with manual dissection
- a. Used in cases where a big bubble cannot be attained or do not want to attempt due to scarring involving Descemet's membrane (risk of perforation)
 - b. Trephination of central cornea performed to 80% depth
 - c. Create deep dissection plane 50-80 microns above Descemet's membrane and dissect across corneal surface by peeling back stroma and excising at base. Multiple layers may be excised in this manner going deeper each time. Scissors are used to excise stroma along trephination edge.
 - d. Remove Descemet's membrane from donor with forceps or sponge
 - e. Donor is sutured into position, sutures adjusted for astigmatism

V. List the complications of the procedure, their prevention and management

A. Intraoperative

- 1. Perforation of Descemet membrane with loss of chamber
- 2. Inadequate depth of dissection
- 3. Inability to achieve "Big Bubble" or detachment of Descemet in DALK
- 4. Damage to intraocular structures with collapse of chamber

B. Postoperative

- 1. Interface fluid ("double anterior chamber") due to break in Descemet membrane with separation of recipient Descemet membrane from overlying swollen graft
 - a. Management: place large enough air bubble into anterior chamber to cover defect in Descemet membrane and position head to allow contact of air bubble with defect
- 2. Pupillary block from residual air bubble: remove air via paracentesis, or place inferior iridotomy to prevent pupillary block
- 3. Elevated IOP: treat with medical therapy, laser surgery, or surgical intervention as indicated
- 4. Interface haze
 - a. In DALK surgery: usually resolves over several months. If vision unacceptable at 1 year, perform PK
 - b. In traditional anterior lamellar keratoplasty, ALTK and femtosecond laser assisted anterior

lamellar keratoplasty: interface haze is variable and can get better or worsen over time. Increased risk of vascularization compared to DALK. If vision unacceptable at 1 year, perform PK

5. Interface infection: if suspected interface bacterial or fungal infection, treat aggressively with topical antibiotics and schedule PK as urgent case. Alternatively, graft could be removed, infection cleared, and then new graft placed after the eye no longer inflamed.
6. Endophthalmitis: urgent, aggressive intervention with consultation with retina specialist for anterior chamber tap, vitreous biopsy and intravitreal antibiotics
7. Irregular corneal surface due to poor epithelial healing and dry eye
 - a. Treat with aggressive lubrication with drops and ointment, punctal plugs, autologous serum and topical cyclosporine.
8. High degrees of surgically induced regular or irregular astigmatism, hyperopia, or myopia
 - a. Treat in same manner as penetrating keratoplasty with selective suture removal or adjustment, relaxing incisions, laser refractive surgery, etc.

VI. Describe the follow-up care

- A. Frequency of postoperative visits related to Descemet membrane attachment, interface haze, surface topography and control of intraocular pressure and inflammation**
 1. Patients routinely seen one day, one week and one month, and then every 2 months until sutures are removed and/or topography is stable for glasses or contacts
- B. Essential components of the postoperative exam include:**
 1. Interval history
 2. Measurement of visual acuity
 3. Slit-lamp biomicroscopy
 4. IOP assessment
 5. Suture removal may begin as early as 1 to 2 months
- C. Topical corticosteroid and other ophthalmic medications**
 1. Topical prednisolone acetate 1% 4 times a day initially, tapered over 3-6 months, and discontinued
 2. Stromal rejection and vascular invasion of the stroma and/or interface is less likely with steroid therapy

VII. Describe appropriate patient instructions

- A. Stress importance of compliance with medications and need for regular postoperative care to ensure visual rehabilitation**
- B. Discuss symptoms of infection and need for immediate attention (redness, sensitivity to light, visual changes, pain)**
- C. Discuss physical restrictions, importance of eye protection, and details for emergency care**

D. Patients can achieve good visual acuity although interface haze may occur between the recipient cornea and the donor tissue

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
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4. Shimmura S, Tsubota K. Deep anterior lamellar keratoplasty. Curr Opin Ophthalmol. 2006;17:349-55.
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Allograft rejection

I. Describe the approach for establishing the diagnosis

A. Describe the etiology of this disease

1. Complex cascade of events initiated by recognition of foreign donor corneal antigens by the recipient
2. Cell surface markers - human leukocyte antigens present on donor corneal epithelial, stromal, and endothelial cells interact with recipient cytotoxic T cells resulting in local inflammation, cellular destruction and corneal graft rejection

B. Define the relevant aspects of epidemiology of the disease

1. Leading cause of secondary graft failure
2. 2 year cumulative fraction of eyes with a rejection episode:
 - a. DMEK: <1%
 - b. DSEK: 10-14%
 - c. PKP: 18%

C. List the pertinent elements of the history

1. History of previous graft rejection and failure
2. Visual loss, photophobia, conjunctival hyperemia, and may experience pain
3. Patients may be asymptomatic

D. Describe the pertinent clinical features

1. Epithelial rejection
 - a. Linear rejection line - stains with fluorescein
 - b. Progresses across corneal surface over several days
 - c. Typically self limited
2. Stromal rejection
 - a. Subepithelial infiltrates (rare)
 - i. Small focal areas of leukocyte aggregation
 - ii. Similar in appearance to adenoviral keratitis
 - b. Corneal thickening and focal inflammation
 - i. Usually in conjunction with endothelial rejection
 - ii. May appear similar to herpes simplex keratitis
 - iii. May be associated with neovascularization
 - c. Predisposing factors (broken suture, focal corneal neovascularization, suture infiltrate)

3. Endothelial rejection (most common type of rejection in PKP)
 - a. Focal or generalized corneal edema
 - b. Keratic precipitates - may aggregate to form endothelial rejection line (Khodadoust line)
 - c. Progresses across graft with subsequent endothelial cell destruction
 - d. Associated anterior chamber cellular reaction (may be very mild and unnoticed)
 - e. Predisposing factors (broken suture, focal corneal neovascularization, suture infiltrate)

II. Define the risk factors

- A. Previous graft failure**
- B. Corneal neovascularization**
- C. Large or eccentric grafts**
- D. Active ocular inflammation**
- E. Active microbial keratitis**
- F. In EK, transplanting stroma**

III. List the differential diagnosis

- A. Herpetic keratouveitis (herpes simplex virus (HSV), varicella zoster virus (VZV))**
- B. Epithelial downgrowth**
 1. May mimic endothelial rejection line
- C. Indolent microbial keratitis**
 1. Fungal or infectious crystalline keratopathy
- D. Early graft failure**
 1. May result in focal edema, nonresponsive to topical corticosteroids
- E. Endothelial decompensation secondary to low endothelial cell count**

IV. Describe patient management of endothelial rejection in terms of treatment and follow-up

- A. Define medical therapy options**
 1. Corticosteroids
 - a. Prompt and frequent (e.g., hourly) administration of topical corticosteroid (e.g. prednisolone acetate 1% or difluprednate)
 - b. Periocular injections or oral corticosteroids may have a role in severe rejection episodes or in patients with poor compliance
 - c. IV corticosteroids may be of benefit when administered early in the course of a rejection

episode

2. Removal of loose suture if present
3. Treatment of coexistent microbial keratitis, if present
4. Central corneal pachymetry measurements allow detection of early immunologic reactions as well as gradual return to normal function after treating rejection episodes.
5. Initially followed weekly or more and decreased based on clinical response

V. List the complications of treatment, their prevention and management

A. Complications of corticosteroid treatment

1. Elevated intraocular pressure (IOP)
2. Cataract development with prolonged corticosteroid use
3. Worsening of underlying condition (e.g., herpetic keratitis)

B. Prevention and management

1. Follow closely to monitor inflammatory response and assess IOP
2. Taper corticosteroids as indicated
3. Prophylactic oral antiviral in individuals with history of herpetic keratitis
4. Consider topical cyclosporine 2% (in patients who are steroid responders or patients grafted for recent fungal keratitis)

VI. Describe disease related complications

A. Secondary corneal graft failure (See Postsurgical corneal edema)

B. Corneal endothelial cell compromise with secondary corneal edema (ranging from visually insignificant to significant stromal and epithelial edema with microcyst and bullae formation)

VII. Describe appropriate patient instructions

A. Stress importance of compliance and need for follow up

B. Awareness of symptoms that may represent worsening of disease

C. African-Americans have been shown to have 5 times the risk of immunologic graft rejection compared to Caucasians after DSEK

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Chiou AG, Kaufman SC, Kaz K. Characterization of epithelial downgrowth by confocal microscopy. J Cataract Refract Surg 1999;25:1172-4.

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4. Karabatsas CH, Hoh HB, Easty DL. Epithelial downgrowth following penetrating keratoplasty with a running adjustable suture. *J Cataract Refract Surg* 1996;22:1242-4.
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12. Jordan CS, Price MO, Trespalacios R, Price FW. Graft Rejection Episodes after Descemet's Stripping with Endothelial Keratoplasty: Part One: Clinical Signs and Symptoms. *Br J Ophthalmol* 2009;93:387-90.

Conjunctival limbal autograft

I. List the indications/contraindications

A. Indications

1. Stem cell deficiency
 - a. Alkali burn
 - b. Chemotherapeutic burn
 - c. Thermal burn
 - d. Ultraviolet exposure/pterygium
 - e. Asymmetric contact lens keratopathy
 - f. Postcryodestructive therapy or lesional excision with stem cell depletion

B. Contraindications

1. Pemphigoid (frequently bilateral, asymmetric)
2. Bilateral surface burns (risks both eyes)
3. Borderline stem cell supply or early deficiency in donor eye

II. Describe the pre procedure evaluation

A. Determine laterality and degree of stem cell deficiency

B. Decide if donor needs to cover single or multiple recipient sites

1. Large areas may require a donor to be split to supply four quadrants
2. Proportionately less sites for smaller areas of deficiency

III. List the alternatives to the procedure

A. Aggressive supportive care

1. Tear replacement
2. Withdrawal of preservatives
3. Topical nonpreserved corticosteroids
4. Amniotic membrane transplant
5. Tarsorrhaphy
6. Topical cyclosporine
7. Topical retinoic acid

B. Conjunctival allograft

1. Last resort due to need for lifelong systemic/topical immunosuppression
2. Generally only to save a monocular individual

IV. Describe the technique

- A. Prepare the recipient bed by dissecting the conjunctiva, use minimal cautery (allows better vascularization, reduces inflammation)**
- B. Measure/mark/dissect a trapezoid of conjunctival tissue with a short side of the trapezoid at the limbus**
- C. Make a scratch incision just anterior to the vascular arcade/palisades of Vogt**
- D. Carry a lamellar dissection from the underside of the conjunctiva to the limbus**
- E. Divide the graft if necessary**
- F. Use tissue adhesive or suture to fixate the donor graft(s)**
- G. Consider the use of amniotic membrane as a substrate for the graft or as a bandage covering to promote healing, or both**

V. List the complications of the procedure, their prevention, and management

- A. Graft loss**
 1. Due to poor fixation
 2. Suture more securely, assure glue adherence, have patient wear shield continuously to avoid rubbing graft off
 3. Re-graft if necessary
- B. Recurrence of pathology (e.g., pterygium)**
 1. Decide if size of graft inadequate or pathology too aggressive for autograft
 2. Consider regrafting
 3. Consider regrafting with chemoadjuvantive therapy (mitomycin), amniotic membrane and/or more aggressive postoperative corticosteroid therapy in cases of recurrent pterygium (not limbal stem cell dysfunction).

VI. Describe follow up care

- A. Observe for recurrence of pathology**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
2. Kim JY, Djalilian AR, Schwartz GS, Holland EJ. Ocular surface reconstruction: limbal stem cell

transplantation. *Ophthalmol Clin North Am* 2003;16(1):67-77.

Keratolimbal allograft (KLAL) - cadaveric donor, living-related conjunctival limbal allograft (lr-CLAL) - living related donor

I. List the indications and contraindications

A. Indications

1. Bilateral total corneal limbal stem cell deficiency
2. Unilateral total corneal limbal stem cell deficiency and partial corneal stem cell deficiency in the fellow eye
3. Unilateral total corneal stem cell deficiency and normal fellow eye where the patient does not want any surgical procedure on the good eye

B. Contraindications

1. Ocular contraindications
 - a. Total corneal and conjunctival cell failure with complete keratinization of the ocular surface
 - b. Poor visual potential secondary to posterior segment pathology such as total chronic retinal detachment, etc.
 - c. Uncontrolled or poorly controlled glaucoma
 - d. Severe tear film insufficiency
2. Non-ocular contraindications
 - a. Any systemic disease precluding systemic immunosuppression such as liver, and renal disease.
 - b. Other chronic poorly controlled systemic disease which can be worsened by postoperative systemic immunosuppression such as poorly controlled diabetes mellitus
 - c. Lack of ability for regular follow-up for management of immunosuppressive therapy

II. Describe the pre-procedure evaluation

A. Thorough and detailed history to establish the etiology of the disease such as

1. External etiology (e.g., chemical and thermal burns)
2. Intrinsic etiologies (e.g. ocular mucous membrane pemphigoid, Stevens Johnson syndrome, aniridia)

B. Complete ocular examination with emphasis on

1. Anterior segment examination
2. Measurement of tear production

3. Intraocular pressure measurement
 4. Examination of the posterior segment when possible by ophthalmoscopy and, if not possible, by performing ultrasound
- C. Establish the diagnosis of stem cell deficiency**
1. Dull and irregular reflex of the corneal epithelium which varies in thickness and transparency
 2. Ingrowth of thickened fibrovascular pannus
 3. Chronic keratitis
 4. Scarring and calcification
 5. Stippled late staining pattern with fluorescein
 6. Impression cytology which can detect goblet cells containing conjunctival epithelium on the corneal surface
- D. Determination of patient's expectations and ability for chronic follow-up**
- E. Determination of any living relatives who may be willing to donate tissue**
- F. Consultation with rheumatologist, hematologist/oncologist or transplant service for preoperative evaluation of general health as well the management of postoperative immunosuppression**

III. List the alternatives to this procedure

- A. Keratoprosthesis**
- B. Use of ex-vivo expanded corneal stem cells**
1. Ex vivo cultivated limbal autograft (EVLAU) if stem cells are from recipient eye
 2. Ex vivo cultivated cadaveric limbal allograft (EVc-LAL) if stem cells are from cadaver
 3. Ex vivo cultivated living-related limbal allograft (EVlr-LAL) if source of donor cells is living relative
 4. Ex vivo cultivated living nonrelated limbal allograft (EVlnr-LAL) if donor is living nonrelative
- C. Use of patient's own buccal mucosa as a source of stem cells (experimental): Ex vivo cultivated oral mucosa autograft (EVOMAU)**

IV. Describe the instrumentation, anesthesia and technique

- A. Instrumentation**
1. Instrumentation includes standard instruments normally used for corneal transplantation including trephines, fine needle holders, etc.
- B. Anesthesia**
1. General or retrobulbar
- C. Technique**
1. Variable techniques depending on whether a cadaver eye is used or cells from a living related donor tissue is utilized

- a. Living related donor
 - i. If living relatives are potential donors, an HLA-matched tissue is preferred if possible
 - ii. Donor
 - i) Harvest two conjunctival corneal scleral specimens of approximately two clock hours each, in circumferential length, from the superior and inferior limbal zones of the donor eye
 - ii) Each graft extending approximately 2 mm into bulbar conjunctiva, 1 mm into limbus, and 2 mm into peripheral clear cornea
 - iii. Recipient
 - i) Strip off abnormal corneal epithelium and superficial vascularized scar by blunt dissection
 - ii) Incise conjunctiva to expose limbus and perilimbal sclera where donor tissue will be grafted
 - iii) Prepare bed to receive donor tissue
 - iv) Suture donor tissue to recipient site with interrupted 10-0 nylon sutures at corneal and scleral margin
- b. Stem cell transplant from cadaveric tissue
 - i. Fresh eyes preferred because success depends on the transplantation of healthy limbal stem cells
 - ii. Tissue is harvested from whole globe or donor corneoscleral rim
 - iii. Recipient bed is prepared as described above 360 degrees
 - iv. 360° cadaveric donor cornea-limbal ring graft trephined from a corneoscleral button
 - v. Secure harvested ring to surrounding conjunctival edge with 9-0 or 10-0 interrupted absorbable sutures and to the denuded corneal surface with a running 10-0 nylon suture

V. List the complications of the procedure, their prevention and management

A. Intraoperative

1. Perforation of globe with potential for
 - a. Endophthalmitis
 - b. Suprachoroidal hemorrhage
 - c. Damage to intraocular structures

B. Postoperative

1. Possible complications to the living related donor
 - a. Relative stem cell deficiency

- b. Infection
- 2. Complications related to the recipient
 - a. Ocular complications
 - i. Areas of epithelial loss at donor site
 - ii. Conjunctival epithelial growth over the graft and onto the corneal surface
 - iii. Delayed epithelial healing
 - iv. Immunological destruction of the transplanted limbal stem cells
 - b. Systemic complications
 - i. Complications related to systemic immunosuppression such as susceptibility to infections, renal, and hepatic toxicity

C. Prevention of complications

- 1. Living related donor
 - a. Careful examination of the donor for any signs of ocular disease and any signs of stem cell disease
 - b. Harvesting the minimal amount of tissue possible; no more than 4 clock hours of tissue
- 2. Recipient related complications
 - a. Careful surgical technique
 - b. Careful patient selection (e.g., prognosis better for aniridia than for bilateral severe chemical burns)
 - c. Management of inflammation and immunological response with immune modulating agents

D. Management of complications

- 1. Management of ocular surface complications includes aggressive lubrication with preservative free artificial tears, possible autologous serum, application of amniotic membrane, and aggressive topical and systemic immunosuppression
- 2. Management of systemic complications related to systemic immunosuppression should be handled by the appropriate specialist and not the ophthalmologist

VI. Describe the follow-up care

- A. Topical antibiotics until corneal epithelial defect completely healed**
- B. Topical corticosteroids**
- C. Preservative free artificial tears**
- D. Consider autologous serum in selected patients**
- E. Effective systemic immunosuppression is considered essential for at least 12 months after surgery when non HLA matched limbal allografts are used**
 - 1. In some instances, permanent systemic immunosuppression may be needed

VII. Describe appropriate patient instructions (post-operative care)

- A. Management of patient expectations**
- B. Chronic nature of the disease with limited success rate of allografts**
- C. Importance of follow-up with both ophthalmologist and physician monitoring systemic immunosuppression needs to be emphasized**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 8: External Disease and Cornea, 2013-2014.
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Keratoprosthesis

I. Indications and contraindications

A. Indications

1. Boston keratoprosthesis type I (must have adequate eyelid and tear function)
 - a. Repeated allograft rejection
 - b. Corneal opacity with significant corneal vascularization after
 - i. Herpes simplex virus keratitis
 - ii. Varicella zoster virus reactivation (shingles)
 - iii. Microbial keratitis
 - iv. Trauma
 - c. Limbal stem cell failure
 - i. Multiple ophthalmic surgeries
 - ii. Aniridia
 - iii. Moderate chemical injury
 - iv. Others
 - d. Congenital corneal opacity
2. Boston keratoprosthesis type II
 - a. Stevens Johnson syndrome
 - b. Mucous membrane pemphigoid
 - c. Severe autoimmune dry eye
 - d. Severe chemical injury
3. Osteo-odonto-keratoprosthesis (OOKP)
 - a. Stevens Johnson syndrome
 - b. Mucous membrane pemphigoid
 - c. Severe autoimmune dry eye
 - d. Severe chemical injury

B. Contraindications

1. Boston keratoprosthesis type I
 - a. Uncontrolled glaucoma
 - b. Severe ocular inflammation

- c. Severe dry eye syndrome (associated with keratinization of the ocular surface)
- 2. Boston keratoprosthesis type II
 - a. Low likelihood of compliance with medications and follow-up care
 - b. Any condition that can be safely treated with Boston keratoprosthesis type I
 - c. Uncontrolled glaucoma
 - d. Sighted contralateral eye
 - e. Phthisis
- 3. Osteo-odonto-keratoprosthesis (OOKP)
 - a. Children
 - b. Low likelihood of compliance with medications and follow-up care
 - c. Any condition that can be safely treated with Boston keratoprosthesis type I
 - d. Uncontrolled glaucoma
 - e. Sighted contralateral eye
 - f. Phthisis

II. Describe the pre-procedure evaluation

A. Visual potential

- 1. Acuity
- 2. Visual field
- 3. Color perception
- 4. Light projection

B. Pupil responses

- 1. Afferent papillary defect

C. Eyelids

- 1. Closure
- 2. Blepharitis

D. Intraocular pressure

E. Slit lamp examination

- 1. Cornea
- 2. Conjunctival fornices
- 3. Lens status (phakic, pseudophakic, aphakic)

F. Schirmer test

G. Fundus

1. Macula
 2. Optic nerve
 3. B scan if necessary
- H. **Axial length (Boston keratoprosthesis, if aphakic, and all patients with OOKP)**
- I. **Psychological assessment (Boston keratoprosthesis type II and OOKP)**

III. List the alternatives to this procedure

- A. **Corneal transplantation**
- B. **Limbal stem cell transplant**

IV. Describe the instrumentation, anesthesia and technique

A. Instrumentation

1. Boston keratoprosthesis type I
 - a. Request either pseudophakic or aphakic version (need axial length for latter)
 - b. Standard instrumentation for corneal transplantation and lateral tarsorrhaphy
2. Boston keratoprosthesis type II
 - a. Boston keratoprosthesis type II device (pseudophakic or aphakic)
 - b. Standard instrumentation for corneal transplantation and lateral tarsorrhaphy
3. Osteo-odonto-keratoprosthesis (OOKP)
 - a. OOKP optical cylinder
 - b. Instrumentation for dental procedure
 - c. Instrumentation for oral mucous membrane graft
 - d. Instrumentation for automated vitrectomy

B. Anesthesia

1. Boston keratoprosthesis type I
 - a. Local or general
2. Boston keratoprosthesis type II
 - a. General
3. Osteo-odonto-keratoprosthesis (OOKP)
 - a. General

C. Technique

1. Boston keratoprosthesis type I

- a. Prosthesis is constructed around a corneal donor or the patient's own cornea
 - i. 3 mm trephination of center of donor cornea
 - ii. 8.5 mm (or greater) trephination of corneal donor to accommodate 8.5 mm back plate (regular size), or 7.0 mm (or greater) trephination of corneal donor to accommodate 7.0 mm back plate (pediatric size)
 - iii. Insertion of optic stem with attached front plate through hole in cornea
 - iv. Snap in back plate secured
 - v. Titanium locking ring secured
 - b. Trephination and removal of host cornea at 0.5 mm smaller than donor cornea (8 mm if donor cornea is 8.5mm)
 - c. Extracapsular lens extraction if phakic
 - d. Corneal donor / prosthesis construct sutured to the eye as with any corneal transplant
 - e. Bandage contact lens placed at conclusion of surgery
2. Boston keratoprosthesis type II
- a. Construction around donor cornea and implantation same as with type I
 - b. Division of any symblepharon
 - c. Removal of all conjunctiva and limbus
 - d. Excision of eyelid margins
 - e. Construction of lateral and medial tarsorrhaphies to completely close lids around the stem of the device
 - f. No contact lens
3. Osteo-odonto-keratoprosthesis (OOKP)
- a. Stage 1
 - i. Removal of tooth and anchoring bone in conjunction with oral surgeon
 - ii. Placement of keratoprosthesis optic through drilled hole in tooth
 - iii. Implantation of OOKP in tooth in submuscular layer of lower eyelid
 - iv. Oral mucous membrane graft to ocular surface
 - b. Stage 2 (2-4 months later)
 - i. Removal of OOKP from implantation site
 - ii. Lifting of mucous membrane ocular surface graft as a flap
 - iii. 5.5 mm Trephination of cornea to accommodate the posterior aspect of OOKP optic
 - iv. Total iridodialysis, lensectomy subtotal vitrectomy
 - v. Placement of keratoprosthesis optic through the cornea with tooth and lamina sutured to surface of the eye

- vi. Replacement of mucous membrane graft over the device
- vii. Opening of central hole in mucous membrane graft to accommodate OOKP optic

V. List the complications of the procedure, their prevention and management

A. Intraoperative

1. Boston keratoprosthesis type I
 - a. Same as with corneal transplant
 - b. Inability to construct the device around the corneal donor
2. Boston keratoprosthesis type II
 - a. Same as with corneal transplant
 - b. Inability to construct the device around the corneal donor
3. Osteo-odonto-keratoprosthesis (OOKP)
 - a. Jaw injury, oral infection
 - b. Same as with corneal transplant

B. Postoperative

1. Boston keratoprosthesis type I
 - a. Glaucoma
 - b. Microbial infection
 - i. Keratitis
 - ii. Endophthalmitis
 - c. Difficulty with contact lens retention
 - d. Sterile vitritis
 - e. Retroprosthetic membrane
2. Boston keratoprosthesis type II
 - a. Same as type I (except no contact lens related complications)
 - b. Corneal melt and extrusion of device
 - c. Retinal detachment
3. Osteo-odonto-keratoprosthesis (OOKP)
 - a. Glaucoma
 - b. Extrusion of device
 - c. Endophthalmitis
 - d. Retinal detachment

- e. Retroprosthetic membrane

C. Prevention of complications

1. Boston keratoprosthesis type I
 - a. Close observation of all patients
 - b. Annual visual field examination
 - c. Timely replacement of contact lens
 - d. Topical antibiotics
 - i. Fluoroquinolone
 - ii. Vancomycin
2. Boston keratoprosthesis type II
 - a. Same as for type I
 - b. Oral carbonic anhydrase inhibitor if history of glaucoma
3. Osteo-odonto-keratoprosthesis (OOKP)
 - a. Close observation of all patients
 - b. Antibiotic ointment
 - c. Oral carbonic anhydrase inhibitor if history of glaucoma
 - d. Chlorhexidine mouth wash

D. Management of complications

1. Extrusion: revision or replacement of device
2. Glaucoma
 - a. Topical aqueous suppressants and outflow facilitators
 - b. Drainage tube device (may be considered before keratoprosthesis or concurrent to keratoprosthesis implantation in patients with pre-existing glaucoma)
 - c. Cyclophotocoagulation
 - d. Cyclodialysis
3. Microbial infection
 - a. Topical antibiotics or antifungals
 - b. Subconjunctival antibiotics or antifungals
 - c. Systemic antibiotics or antifungals
 - d. Replacement if recalcitrant to medical therapy
 - e. Pars plana vitreous aspiration for smear, culture, and sensitivities followed by injection of intraocular antibiotics if endophthalmitis suspected
4. Sterile vitritis

- a. Assume infectious if any external or orbital signs of infection
 - b. Sub-tenons triamcinolone
- 5. Retroprosthetic membrane
 - a. Yag laser capsulotomy
 - b. Surgical excision if too thick for laser capsulotomy or if vascularized
- 6. Retinal detachment treated with pars plana vitrectomy

VI. Describe the follow-up care

A. Boston keratoprosthesis type I

- 1. Topical prednisolone acetate 1% tapered from 4 times a day to once a day over 4-6 weeks after surgery
- 2. Topical fluoroquinolone tapered from 4 times a day to once a day over 4-6 weeks after surgery, (can be replaced by other broad-spectrum topical antibiotic such as polymyxin B/trimethoprim)
- 3. Topical vancomycin 14 mg/ml with benzalkonium chloride preservative once a day in selected patients (autoimmune, monocular, chemical burns)
- 4. Topical glaucoma medications as necessary

B. Boston keratoprosthesis type II

- 1. same as for type I
- 2. oral carbonic anhydrase inhibitor if needed

C. Osteo-odonto-keratoprosthesis (OOKP)

- 1. Requires hospital admission and multiple medications

VII. Describe appropriate patient instructions (post-operative care)

A. Boston keratoprosthesis type I

- 1. Call and be seen immediately for
 - a. Change in vision
 - b. Redness
 - c. Discharge
 - d. Pain
 - e. Lost contact lens

B. Boston keratoprosthesis type II

- 1. Call and be seen immediately for
 - a. Change in vision

- b. Redness or swelling of eyelids
- c. Discharge
- d. Clear fluid from eye
- e. Pain

C. Osteo-odonto-keratoprosthesis (OOKP)

- 1. Call and be seen immediately for
 - a. Change in vision
 - b. Discharge
 - c. Pain

Additional Resources

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Clinical trials in cornea external disease

I. Multi-centered randomized controlled trials

A. Herpetic Eye Disease Study I (HEDS-I)

1. Purpose
 - a. To assess the efficacy of topical corticosteroids and oral Acyclovir in treating HSV stromal keratitis and iridocyclitis
2. Trials: Three randomized, placebo-controlled studies
 - a. Herpes Stromal Keratitis, Not on Steroid Trial (HEDS-SKN):
 - i. Treatment Group: 106 patients treated with topical steroids and topical trifluridine were followed for 26 weeks
 - ii. Control Group: Topical trifluridine only
 - iii. Results: Treatment group had faster resolution of the stromal keratitis and fewer treatment failures. However, delaying the initiation of corticosteroid treatment did not affect the eventual outcome of the disease, in that visual acuity was similar in the two groups at 26 weeks
 - b. Herpes Stromal Keratitis, on Steroid Treatment (HEDS-SKS):
 - i. Treatment Group: 104 patients were treated with topical steroids, topical trifluridine and oral Acyclovir
 - ii. Control Group: Topical trifluridine and topical steroids only
 - iii. Results: There was no difference in the rate of treatment failure between the two groups so no apparent benefit from adding acyclovir. However, visual acuity improved in more patients in the treatment group at 6 months but was not statistically significant
 - c. Herpes Simplex Virus Iridocyclitis, Receiving Topical Steroids (HEDS-IRT):
 - i. Treatment Group: Only 50 of the planned 104 patients could be recruited over 4 years and were treated with topical steroids, topical trifluridine and oral Acyclovir
 - ii. Control Group: Topical trifluridine and topical steroids only
 - iii. Results: Recruitment was too low to achieve statistical significance but there was a trend towards lower treatment failures in Acyclovir group
 - d. Meta-analysis of the three trials to determine the risk of epithelial disease in patients with stromal keratitis
 - i. Groups compared
 - i) Trifluridine alone
 - ii) Trifluridine and steroids

- iii) Trifluridine, steroids and acyclovir
- ii. Results:
 - i) No difference in risk of epithelial disease between groups
 - ii) Previous epithelial disease or non-whites were at increased risk

B. Herpetic Eye Disease Study II (HEDS-II)

1. Purpose
 - a. To assess the role of oral Acyclovir in the management of HSV keratitis
 - b. To investigate risk factors, including stress, for the development of ocular recurrences of the disease
2. Trials: Two randomized, placebo-controlled trials and one epidemiologic study
 - a. Herpes Simplex Virus Epithelial Keratitis Trial (HEDS-EKT):
 - i. Recruitment ended November 1995
 - ii. Treatment Group: 287 patients were treated with topical trifluridine and oral Acyclovir
 - iii. Control Group: Topical trifluridine only
 - iv. Results: in the treatment of acute HSV epithelial keratitis, there was no benefit from the addition of oral acyclovir to treatment with topical trifluridine in preventing the development of stromal keratitis or iritis. Incidentally, the risk was lower than published literature
 - b. Acyclovir Prevention Trial (HEDS-APT):
 - i. Recruitment began September 1992 and was completed December 1996
 - ii. Treatment Group: 357 patients were treated with oral Acyclovir at 400 mg twice a day for one year and followed for an additional six months
 - iii. Control Group: 346 patients were treated with a placebo
 - iv. Results: Oral acyclovir reduced the recurrence rate of HSV epithelial keratitis by 41 percent and a reduction in the recurrence rate of stromal keratitis by 50 percent in patients who had an infection with epithelial or stromal keratitis, respectively, in the previous year. However, the effect did not persist after discontinuing the Acyclovir
 - c. Ocular HSV Recurrence Factor Study (HEDS-RFS):
 - i. Cohort: 308 immunocompetent adults, aged 18 years or older, with a documented history of ocular HSV disease in the prior year and observed for up to 15 months.
 - ii. Exposure variables: Psychological stress, systemic infection, sunlight exposure, menstrual period, contact lens wear, and eye injury were recorded on a weekly log.
 - iii. Results: No association was found between any of the exposure variables and recurrence

C. Cornea Donor Study (CDS)

1. Purpose

- a. To determine whether the graft-failure rate over a 5-year follow-up period following corneal transplantation is the same when using corneal tissue from donors older than 65 years of age compared with tissue from younger donors.
 - b. To assess the relationship between donor/recipient ABO blood type compatibility and graft failure due to rejection.
 - c. To assess corneal endothelial cell density as an indicator of the health of the cornea and as a surrogate outcome measure
- 2. Design
 - a. Multi-center prospective, double-masked, controlled clinical trial
- 3. Participants
 - a. Recruitment began in January 2000 and was completed August 2002
 - b. 1090 subjects undergoing corneal transplantation for moderate risk conditions (principally Fuchs dystrophy or pseudophakic corneal edema) were enrolled by 105 surgeons at 80 sites
 - c. Donors were in the age range of 12 to 75 year old with endothelial cell densities of 2300 to 3300 cells/mm²
- 4. Results
 - a. Five-year survival was similar using corneas from donors ≥ 66 years or < 66 years and there was no difference in the causes of graft failure
 - b. The five-year incidence for a rejection episode, irrespective of whether graft failure ultimately occurred, was 12% for ABO compatible compared with 8% for ABO incompatible cases and the percent loss of endothelial cells was similar in the two groups
 - c. There was a substantial loss of endothelial cells 5 years after corneal transplantation in all participants. The median cell loss in corneas from donors < 66 years was 69% compared to 75% in corneas from donors ≥ 66 years. Additionally, there was a weak negative correlation between donor age and endothelial cell density at 5 years

D. Collaborative Corneal Transplantation Studies (CCTS)

- 1. Purpose
 - a. To determine whether histocompatibility matching of corneal transplant donors and recipients can reduce the incidence of graft rejection in high-risk patients
- 2. Design
 - a. Two controlled, double-masked studies
 - i. The Antigen Matching Study (AMS) was a prospective, double-masked, observational study of the effectiveness of HLA-A, -B, and -DR donor-recipient matching in high-risk corneal transplants
 - ii. The Crossmatch Study (CMS) was a randomized study assessing the effectiveness of crossmatching in preventing graft rejection among high-risk patients with lymphocytotoxic antibodies

3. Participants
 - a. Recruitment began in May 1986 and was completed September 1989
 - b. AMS: 419 patients with no lymphocytotoxic antibodies were allocated corneas with varying degrees of HLA matching and followed for 3 years. ABO blood group compatibility was determined but not used for recipient selection
 - c. CMS: 37 patients with lymphotoxic antibodies were randomly assigned to receive a cornea from either a positively or negatively crossmatched donor and followed for 3 years
4. Results
 - a. Matching for HLA-A, -B and -DR antigens had no effect on overall graft survival, the incidence of irreversible rejection, or the incidence of rejection episodes
 - b. The positively crossmatched group in the CMS had fewer graft failures, rejection failures, and rejection episodes than the negatively crossmatched group; however, these differences were not statistically significant
 - c. Patients with ABO compatibility had lower rates of graft failure and rejection than those with ABO incompatibility
 - d. Incidentally noted that the rate of rejection was lower than reported and concluded that it likely was related to aggressive steroid use in the postoperative period, good patient compliance with medication, and close patient follow-up

E. Mycotic Ulcer Treatment Trial I (MUTT I)

1. Purpose
 - a. To compare topical natamycin vs topical voriconazole in the treatment of fungal keratitis
2. Design
 - a. Randomized, active comparator-controlled, double-masked, multicenter clinical trial
3. Participants
 - a. Recruitment began April 2010 and was completed December 2011
 - b. 323 patients with a smear and/or culture positive fungal corneal ulcers with visual acuity between 20/40 and 20/400 were randomized to receive either topical 5% Natamycin or 1% Voriconazole and followed for 3 months
4. Results
 - a. Natamycin treated cases had significantly better 3-month best spectacle-corrected visual acuity than voriconazole-treated cases
 - b. Natamycin-treated cases were significantly less likely to have perforation or require therapeutic penetrating keratoplasty compared to voriconazole-treated cases
 - c. The difference between the treatment groups was secondary to improved outcomes in Fusarium keratitis; other fungal organisms had comparable outcomes with the two medications

F. Steroids for Corneal Ulcers Trial (SCUT)

1. Purpose
 - a. To determine whether there is a benefit in clinical outcomes with the use of topical corticosteroids as adjunctive therapy in the treatment of bacterial corneal ulcers.
 - b. Primary outcome was best corrected visual acuity at 3 months from enrollment
 - c. Secondary outcomes include BSCVA at 3 weeks from enrollment; infiltrate/scar size at 3 weeks and 3 months, and rate of adverse events, including corneal perforation and time to re-epithelialization
2. Design
 - a. Randomized, placebo-controlled, double-masked, multicenter clinical trial
3. Participants
 - a. Recruitment began in September 2006 and was completed February 2010
 - b. 500 patients with a culture-positive bacterial corneal ulcer who received topical moxifloxacin for at least 48 hours were randomized to receive either prednisolone sodium phosphate 1.0% or placebo and followed for 3 months
 - c. Results
 - d. There was no difference overall in the visual acuity at 3 months (primary outcome variable), scar size, time to re-epithelialization, or rate of perforation
 - e. In patients with presenting vision of Count Fingers or worse, or with central ulcers at baseline, the steroid group had significantly greater improvement in vision at 3 months compared to the control group
 - f. Subgroup analysis of pseudomonas ulcers showed that there was no difference between the response of these ulcers to steroids compared to other bacterial ulcers

Additional Resources

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