Retinoblastoma

- Most common primary intraocular malignancy of childhood (3% of all childhood cancer)
- Results from malignant transformation of primitive retinal cells before final differentiation
- Seldom seen after 3 years of age
- May be heritable (40% and bilateral) or non-heritable (60% and unilateral)
- Siblings should be screened soon after birth until age 4 or 5 years
- Present within 1st year in bilateral cases and around 2 years if unilateral
- Leukocoria present in 60%; strabismus 20%

Retinoblastoma (continued)

- If undetected, metastatic spread to regional nodes, lung, brain, and bone
- Signs:
  - Intraretinal tumor - homogenous, dome-shaped white lesion often with white flecks of calcification
  - Endophytic tumor - white mass projecting into vitreous
  - Exophytic tumor - multilobular white subretinal masses with overlying RD
- Treatment:
  - Small Tumors 1 photocoagulation and cryotherapy
  - Medium Tumors 1 brachytherapy or chemotherapy
  - Large tumors 1 chemotherapy or enucleation

Bacterial Conjunctivitis

- Unilateral or bilateral red eye(s) with purulent or mucopurulent discharge of varying degree
- In subtle cases, carefully examine the lacrimal lake under high magnification and look for microparticulate debris which can be evidence of bacterial infection.
- Preauricular lymphadenopathy is uncommon, but can be present in hyperacute cases
- Chemosis may be present in more severe cases
- SPK can be present, especially if staphylococcal etiology. This is usually the result of staph exotoxin chemotoxicity, and tends to be seen mostly inferionasally because of tear film dynamics
- Common etiology:  
  - Adults: Staph aureus, Staph epidermidis, Strep pneumoniae
  - Children: Strep pneumoniae, Haemophilus
- Therapy:  
  - Adults: Tobramycin, Polynyn, or Fluoroquinolone
  - Children: Polynyn or AzaSite solution or Polysporin ung
- Treat for five to seven days as a rule

Superior Limbic Keratoconjunctivitis

- Both sexes affected, women more
- Main symptoms: distressingly irritated eyes
- Dry eyes common companion finding
- Symptoms disproportionate to clinical findings
- Spontaneous exacerbations and remissions
- 25-40% have some thyroid dysfunction
- Tx: difficult -.5% AgNO3, optimum lubrication, pressure patching, therapeutic soft lenses, surgical resection, cryotherapy
### Adenoviral Infections
- Common cause of “red eyes”
- Assume adenovirus until proven otherwise
- Often have pre-auricular node
- Non-purulent watery discharge
- Usually starts in one eye and spreads to fellow eye in a few days
- Always evert lids to survey tarsal conjunctiva
- With EKC, spotty sub-epithelial infiltration in 50 to 75% of untreated cases

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### Povidone - Iodine 5% ophthalmic solution
- Broad spectrum microbicide
- Indicated for “irrigation of the ocular surface”
- “Off label” use: Tx adenoviral keratoconjunctivitis
  - Anesthetize with proparacaine
  - Instill 1 or 2 drops of NSAID
  - Instill several drops Betadine 5% in eye(s), close eye(s)
  - Swab or rub excess over eyelid margin
  - After 1 minute, irrigate with sterile saline
  - Instill 1 or 2 drops of NSAID
  - Rx steroid qid x 4 days
- No reports in clinical trials of adverse reactions.
- Avoid use if patient is allergic to iodine
- Marketed as Betadine 5% ophthalmic prep solution (30 ml opaque bottle) by Alcon surgical
- CPT 99070 supply code

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### Literature on Adenoviral Keratoconjunctivitis
- Pseudo membranes are a frequent complication of EKC
- In untreated cases, 50% of corneas develop subepithelial infiltrates i.e. a cellular immune reaction against viral antigens
- AdenoPlus® is highly sensitive, specific, simple and inexpensive
- Bacterial superinfection is rare
- Topical steroids relieve symptoms, and 5% betadine kills the virus in tears, thus reducing the risk of disease spread.
- Restasis does not affect the natural course of the disease.

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### Acute Conjunctivitis and Antibiotic Use
- “Conjunctivitis is the most common cause of red or pink eye, but most (up to 80%) are viral.”
- “Topical antibiotics (for bacterial infection) provide only a very modest beneficial effect on clinical remission.”

<table>
<thead>
<tr>
<th>Antibiotic Rx</th>
<th>Combo Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>ODâ‘ 44%</td>
<td>ODâ‘ 30%</td>
</tr>
<tr>
<td>MDâ‘ 36%</td>
<td>MDâ‘ 23%</td>
</tr>
<tr>
<td>Non-Eye Drâ‘ 68%</td>
<td>Non-Eye Drâ‘ 8%</td>
</tr>
</tbody>
</table>
- One-fifth of all Rx’s were for a combination antibiotic-steroid “which are contra-indicated in acute cases of conjunctivitis.” (Not True!)
- Use of AdenoPlus may reduce diagnostic uncertainty and increase comfort with deferring antibiotic therapy.

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### Hypochlorous Acid
- Pure hypochlorous acid (HOCl) is released from neutrophils
  - Essential part of body’s immune response
- In the body, HOCl:
  - Kills microorganisms
  - Neutralizes inflammatory toxins released from pathogens
  - Helps suppress the body’s inflammatory response
  - Prevents biofilm formation
- Ophthalmic strength HOCl has comparable microbial spectrum to Betadine (povidone iodine 5%)
- Covers some bacterial strains missed by Betadine (Serratia marcescens)
- Onset of activity twice as fast as Betadine (1 min vs 2 min)
- Remains active with a toxicity level 1000x lower than Betadine
- 2013 Adenoviral Acuity: Comparison of Pure Hypochlorous Acid (0.01) with other Wound and Skin Cleansers at Non-Toxic Concentrations. Ren, Rei. *Wound, Int. Ped. Wang, D.A.* SAWC Spring 2013
- 2013 Kuzin, MS et al. Time-Kill Comparison of Povidone Iodine to Hypochlorous Acid Against Endophthalmitis Isolates of *Staphylococcus*. ARVO Annual Meeting 2016 Abstract Number 5861

### Herpes Gladiatorum
- Occurs most commonly among young wrestlers, or in other sports where there is very close skin contact.
- First described in the 1960’s in NEJM
- It is an expression of HSV-1
- Lymph nodes (preauricular and/or submandibular) are commonly present on one or both sides
- Treated with oral antiviral for a week
- Like all HSV infections, can become recurrent in nature.
- Temporary isolation from sports while being treated is key to breaking cycle of perpetuation
**Eczema Herpeticum**
- Opportunistic non-unilateral expression usually of the face and neck
- These patients have atopy, of which eczema is the typical association — get a good history
- Seen mostly in people in their teens and 20’s
- Primary expression of HSV
  - Globe is rarely involved
- Because of potential for a more virulent expression, use Zoster dosage of 800 mg of ACV 5X5D, or 1,000 mg of VCV TID X 7-10 days
- Usually seen primarily by dermatology, but if periocular involvement, eye doctor consultation is common practice.

**Primary HSV Infection**
- Vesicular eruptions on the eyelid skin and/or eyelid margin
- Can be limited to the skin or can also result in follicular conjunctivitis and/or corneal epithelial disease
- Treatment: PO ACV 400 mg 5 x D x 1W
  - PO Valtrex 500 mg tid x 1W
- Vesicles resolve without scarring

**Non-ophthalmic steroid: ointment/cream/lotion**
- Triamcinolone - moderate potency steroid
- Available in cream, ointment and lotion (0.5%, 0.1%, 0.025%)
- Our favorite: the 0.1% cream
  - Reference: Drug Facts and Comparisons

**Anti-inflammatory Effects of 0.1% Tacrolimus**
- The topical calcineurin inhibitor, tacrolimus, has good anti-inflammatory properties.
- 0.1% tacrolimus eye drops can be highly effective in treating severe allergic conjunctival diseases.
- Tacrolimus eye drops often cause a stinging sensation or conjunctival redness, especially in the beginning of treatment of severely inflamed eyes. This can be avoided by topical steroid pretreatment.
- Tacrolimus eye drops did not have an immediate effect and required 1-2 weeks to be effective.
- In contrast, topical steroids are fast acting and can immediately relieve allergic symptoms. Although treatments eventually can be conducted without topical steroids, prompt relief of symptoms merits topical steroids.

**Systemic Prednisone**
- Most common Rx’d systemic corticosteroid
- Common initial dosage 40-60 mg
- Available generically in both tablets and DosePaks (5 or 10 mg at 6 or 12 day course)
- Questions to ask before prescribing?
  - Diabetic?
  - Peptic Ulcer Disease?
  - Tuberculosis?
  - Pregnant?

**Choroidal Melanoma Data**
- Risk of Malignant Transformation of a Choroidal Nevus: “If it is assumed that all choroidal melanomas arise from preexisting nevi, then the published data suggest a low rate (1/8845) of malignant transformation of a choroidal nevus in the U.S. white population.” (Ophthalmology, Oct 2005)
- Incidence of Uveal Melanoma: “The annual age-adjusted incidence (per million population) of uveal melanoma was 0.31 (black), 0.38 (Asian), 1.67 (Hispanic), and 6.02 (non-Hispanic white) (AOJ, Oct 2005)
Epidemiological Perspective on Choroidal Nevi

- “White race” is the only known risk factor
- No association with skin melanomas, or other CA
- Prevalence increases with age, especially among Hispanics
- Overall prevalence:
  - 14-28% in Whites
  - 1.5-3% in Blacks
  - 7-14% in Hispanics
  - Very low in Asians / Indians

Perspective on Posterior Vitreous Detachment

- Occurs mostly between ages 50 and 70 (peak incidence 62)
- No association with refractive error, except patients with -3.00D or more go to P.V.D. 5-10 years earlier
- 80-90% of breaks associated with P.V.D. are in the superior quadrants

Treatment of Vitreous Floaters

- Treatment options:
  - Live with them
  - Vitrectomy
  - YAG laser - angle of focus can be changed to reach floaters; special vitreous lenses allow the laser beam to focus on floater
- Advantages: simple, noninvasive, no pain or discomfort
- Disadvantages: healthy eyes getting elective surgery, risk of retinal detachment
- Clear visualization of floaters key to successful surgery
- Treatment may require more than one laser session; symptomatic vitreous opacifications (SVO) only treated if SVO’s > 4mm from retina treated
- Patient decision on benefits vs risks

Timing and RD Repair: Is there a hurry?

- Preoperative VA is the strongest predictor of postoperative VA
- When control vision is affected, about 30% of patients ultimately achieve 20/40 or better
- “There is no difference in VA outcomes among patients who underwent within the first week of onset”
- VA can improve for months to years after surgical repair
- There was no association between duration of macular detachment and postoperative VA
- “Clinical evidence suggests that the duration of macular detachment has a minor, if any, effect on visual outcome when repair is performed within about one week. Similarly, many fovea-sparing RD’s can likely be deferred for a short period without affecting visual outcomes.”

Phlyctenular Keratoconjunctivitis

- Nodular inflammation of paralimbal tissues
- Mainly in children and young adults (females); allergic hypersensitivity response to some antigen to which the tissue has become sensitized (staphylococcal most common; TB rare)
- Symptoms: photophobia and FB sensation (worse in corneal involvement)
- Signs: pinkish-white elevations; +fl stain
- Tx: antibiotic/steroid along with lid scrubs
- If TB suspected, Tine or PPD(skin); chest x-ray

Differential Diagnosis of Corneal Ulcers vs. Infiltrates

<table>
<thead>
<tr>
<th>Ulcer (UK)</th>
<th>Infiltrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Usually painful</td>
<td>Mild pain</td>
</tr>
<tr>
<td>Tend to be central</td>
<td>Tend to be peripheral</td>
</tr>
<tr>
<td>1 to 1 staining defect to lesion ratio</td>
<td>Staining defect size relatively small</td>
</tr>
<tr>
<td>Cells in anterior chamber</td>
<td>Rare cells in anterior chamber</td>
</tr>
<tr>
<td>Generalized conjunctival injection</td>
<td>Sector skewed injection pattern</td>
</tr>
<tr>
<td>Usually solitary lesion</td>
<td>Can be multiple lesions</td>
</tr>
<tr>
<td>Possible tear lake debris</td>
<td>Clear tear lake</td>
</tr>
</tbody>
</table>
Usually bilateral, punctate epithelial keratopathy of unknown etiology

More common in women under 40; exacerbations and remissions over 1-2 decades possible

Symptoms: fb sensation, lacrimation, and photophobia with minimal conjunctival injection

Signs: coarsely scattered (4-20) intraepithelial granular opacities; stain lightly with fluorescein

Tx: responds dramatically to topical steroids

DDX with HSK, if unilateral

Thygeson’s eye:
- Mild injection
- Relatively abrupt onset
- Crushed bread crumb morphology

Vitamin K quickly reverses warfarin, a vitamin K antagonist

Newer anticoagulants: Pradaxa, Xarelto, Eliquis, and Savaysa

Praxbind reverses Pradaxa

The Xa-inhibitors; Xarelto, Eliquis, and Savaysa are inhibited by Andexanet within minutes

Andexanet is a major enhancement to the clinical usefulness of these newer anticoagulants!

90% of adults harbor the Herpes Virus

Strain-specific expression of the disease

Unilateral red eye with serous discharge

Affected cornea has decreased sensitivity

Males more commonly affected; recur more often

40% chance of recurrence within 5 years

Fellow eye not at risk of involvement (1’ and 2’)

Cause of recurrence: trauma, stress, adrenergic and prostaglandin eyedrops, fever, menstruation, climate, UV light

Treatment: topical or systemic anti-viral

Topical
- Trifluridine (Viroptic)
- Ganciclovir (Zirgan)

Oral
- Acyclovir (Zovirax)
- Valacyclovir (Valtrex)

- These are anti-herpetic drugs and are ineffective against the various adenoviral serotypes -

Direct thrombin inhibitor
- Pradaxa (dabigatran)

Oral factor Xa inhibitor
- Xarelto (rivaroxaban)
- Eliquis (apixaban)
- Savaysa (edoxaban)

Herpes Simplex Keratitis

Anti-Viral Medicines

Topical
- Trifluridine (Viroptic)
- Ganciclovir (Zirgan)

Oral
- Acyclovir (Zovirax)
- Valacyclovir (Valtrex)

Topical Antiviral Options

Trifluridine
- Old drug
- Indiscriminate expression
- Potentially toxic
- More frequent dosing
- Refrigerate until opened
- Thimerisol preserved
- Solution (7.5 ml bottle)
- Viropic and generic

Ganciclovir
- New drug
- Infected cell-specific
- Minimally toxic
- Less frequent dosing
- No refrigeration needed
- ABAK preserved
- Gel (5 gram tube)
- Zirgan by B+L
Study on Stromal HSK

- OD response rate, 6% - MD response rate 15%
- ALL: 95% treated epithelial keratitis correctly
- For stromal immune keratitis
  - 54% OD correct
  - 74% MD correct
  - 82% corneal subspecialist correct
- Correct = topical steroids with antiviral cover
- Correct use of oral antiviral prophylaxis for recurrences
  - 51% - OD, 60% - MD, 62% corneal subspecialist
- “Training” was most significant determining factor

Reference: Letters – Arch. Oph., December 2010

Preventing HSV Disease Recurrences

- Patients being treated with oral antiviral therapy were 9 times less likely than untreated patients to develop recurrent keratitis
- Recurrence rates: 27% at 1 year, 50% by 5 years, 57% by 10 years, 63% by 20 years
- Stromal disease is more likely to recur than epithelial disease
- Length of prophylaxis: Generally 5 disease-free years