Management of Viral Eye Disease

J. James Thimons, O.D., FAAO
Chairman, National Cornea Society

ANTI-VIRALS

- ACYCLOVIR
- ZOVIRAX
- FAMVIR
- VALTREX

HSK

- OPHTHALMIC INDICATIONS
  - DENDRITIC KERATITIS
  - SURGICAL PROPHYLAXIS
  - STROMAL KERATITIS
  - IMMUNOCOMPROMISED PATIENTS

Famvir (famciclovir)

- Pharmacology:
  - Synthetic nucleoside (guanine) analog, prodrug of penciclovir.
  - Penciclovir conversion into acyclovir triphosphate inhibits herpes virus-specific polymerases & produces viral DNA termination.

- Formulation:
  - 125, 250 and 500 mg tablets.

- Usual Dosage:
  - Adults: 500 mg q8h x 7 days (HZV)
  - Children: Safety not fully evaluated.

- Indications:
  - HZV ophthalmicus, suppression of recurrent HSV keratitis.
  - Safety/efficacy of long-term HSV suppressive tx not fully established.

- Contraindications:
  - Known famciclovir or penciclovir (Denavir) hypersensitivity.

- Pregnancy
  - Category B: No adequate studies.

- Nursing
  - Contraindicated in nursing patients or requires cessation of breast feeding.

- Cautions/Warnings:
  - Caution in patients w/ impaired renal function.

- Adverse Reactions:
  - Common: headache, nausea, diarrhea, vomiting, fatigue, pruritus, paresthesias, etc.
  - Severe (extremely low incidence): anaphylaxis.
  - No reported severe reactions to famciclovir to date.

- Cost
  - #30 (125 mg) = $92; #30 (250 mg) = $100;
  - #30 (500 mg) = $206.
Valtrex (valacyclovir)

**Pharmacology:**
- Synthetic purine (guanosine) nucleoside analog, prodrug of acyclovir.
  - Valacyclovir is almost completely converted to acyclovir by first pass intestinal and/or hepatic metabolism.

**Formulation:**
- 500 and 1000 mg tablets.

**Usual Dosage:**
- Adults: 1000 mg q8h x 7 days (HZV).
- Children: Safety not fully evaluated.

**Indications:**
- HZV ophthalmicus, suppression of recurrent HSV keratitis.
  - Safety/efficacy of long-term HSV suppressive tx not fully established, but likely comparable to acyclovir.

**Contraindications:**
- Known valacyclovir or acyclovir hypersensitivity.

**Pregnancy**
- Category B: No adequate studies. Should be used only if potential benefit justifies potential fetal risk.

**Nursing**
- Safety in nursing infants unknown. Inadequate studies.

**Cautions/Warnings:**
- Caution in patients w/ renal insufficiency/disease.

**Adverse Reactions:**
- Common:
  - Nausea, headache, vomiting, dizziness, diarrhea, abdominal pain.
- Serious (extremely rare):
  - Anaphylaxis, anemia, thrombocytopenia, leukopenia, renal failure, aplastic anemia, ophthalmia.

**Cost:**
- #30 (1000 mg) = $137
- #30 (500 mg) = $39

Zovirax (acyclovir)

**Pharmacology:**
- Synthetic purine (guanosine) nucleoside analog.
  - Acyclovir is phosphorylated by the enzyme thymidine kinase which is encoded by herpes viruses (HSV-1, HSV-2, HZV). Acyclovir triphosphate selectively inhibits herpes-specific polymerase which, in tum, produces viral DNA termination.

**Formulation:**
- 400 and 800 mg tablets.

**Usual Dosage:**
- Adults: 800 mg 5x qd x 7 days (acute HZV).
- Children: Safety and efficacy not fully evaluated in ocular disease mgmt.

**Indications:**
- HZV ophthalmicus, suppression of recurrent HSV keratitis.
  - 400 mg bid for up to 1 yr. for chronic suppressive tx. (greatest benefit in recurrent, vision threatening stromal HSV keratitis or cases where vision loss from HSV epith. keratitis is a concern).

**Contraindications:**
- Known hypersensitivity to acyclovir or formulation hypersensitivity.

**Pregnancy**
- Category B: No adequate studies. Should be used only if potential benefit justifies potential fetal risk.

**Nursing**
- Safety in nursing infants unknown. Inadequate studies.

**Cautions/Warnings:**
- Caution in patients w/ renal insufficiency/disease or the elderly.
  - Reduced dosages may be needed.

**Adverse Reactions:**
- Common:
  - Nausea, headache, vomiting, dizziness, diarrhea, abdominal pain, malaise, arthralgia, lethargy.
- Serious (extremely rare):
  - Anaphylaxis, angioedema, anemia, coma, seizures, thrombocytopenia, leukopenia, renal failure/dysfunction, hepatitis, encephalopathy.

**Cost:**
- #30 (800 mg) = $170 ($25 if generic)
- #30 (500 mg) = $39 ($15if generic)
ANTI-VIRALS

- CLINICAL APPLICATIONS
  - ACUTE VS CHRONIC INFECTION
  - PRIMARY LESIONS
  - EPITHELIAL HERPES SIMPLEX
  - STROMAL HERPES SIMPLEX
  - HERPES ZOSTER
  - HERPETIC IRIDOCYCLITIS

HSK

- PREVENTION /TRIGGER FACTORS
  - FEVER
  - UV LIGHT
  - TARUMA
  - EPINEPHRINE
  - STRESS

ANTI-VIRALS

- SIDE EFFECTS
  - RENAL FAILURE/ IMPAIRMENT
  - HYPERSENSITIVITY REACTIONS
  - FACIAL EDEMA
  - VISUAL HALLUCINATIONS

Epidemic Keratoconjunctivitis

- EKC
  - Serotypes 8,19 most typical
  - Seasonal
  - Primarily bilateral
  - Atypical serotypes; Enterovirus 70

Clinical Presentation

- Chemosis
- Injection
- Infiltrates
- Ac/reaction?
- FRS

Treatments

- Palliative
  - Cold compress
  - Tears
- Interventional
  - Anti-inflammatory agents
  - Decongestants
  - Combination agents
  - Cidofovir
  - Zigan?
EKC
- Treatments
  - Betadine wash
  - Surgical Debridement

HERPES SIMPLEX
- ENDEMIC VIRUS
  - 65% AGE 5
  - 95% AGE 15
- PUNCTATE EPITHELIAL DISEASE
  - UNILATERAL
  - NON-SPECIFIC PUNTATE KERATITS
  - SEROUS FOLLICULAR CONJUNCTIVITIS
  - BLEPHAROCONJUNCTIVITIS
  - SKIN OR LID VESICLES
DENDRITIC KERATITIS

WITH OR WITHOUT DENDRITE

DIFFERENTIAL Dx

VARICELLA-ZOSTAR

EPSTEIN-BARR

VACCINIA

THYGESON'S

IMPAIRED EPITHELIAL HEALING

ANTIVIRALS

ANTIBIOTICS

PRESERVATIVES

POST INFECTIOUS

SCL's
HSK

- **CLINICAL FINDINGS**
  - *Acanthamoeba*
  - Epithelial Deposits
  - Mucous Plaques
  - Geographic Keratitis
  - Stromal Keratitis
  - Necrotizing Keratitis

- **DIAGNOSIS**
  - CYTOLOGY
    - SCRAPE - ACTIVE VESSELS
    - PAPANICOLAOU STAIN
    - MULTINUCLEATED GIANT CELLS
  - ANTIGEN DETECTION TESTS
    - IMMUNOFLOURESCENCE
    - IMMUNOPEROXIDASE
    - ENZYME IMMUNOASSAY
    - DNA PROBE
    - PCR

- **MANAGEMENT/EPITHELIAL DISEASE**
  - DEBRIDEMENT
  - ROSE BENGAL / LISSAMINE GREEN
  - DRUG THERAPY
    - TRIFLURIDINE
    - IDOXURIDINE
    - VIDARABINE
    - ORAL AGENTS
    - CIDOFIR
    - TREATMENT

- **STROMAL KERATITIS**
  - RULE OUT MICROBIAL DISEASE
  - VIROPTIC
  - ORAL AGENTS
  - CORTICOSTEROIDS
  - CYCLOSPORINE A
  - SURGERY
    - PKP
    - CONJUNCTIVAL FLAPS
    - TISSUE ADHESIVES
The Antiviral for the 21st Century

- Ziran 0.15% Gel
- Sirion Pharmaceuticals
- HSK 2 years and older
- Ganciclovir: Selectively targets replication of HSV DNA within corneal cells
- Dose: 5 x / day till lesion resolves then tid for one week
- Toxicity:
  - 60% blur
  - 20% irritation
  - 5% Hyperemia
VARICELLA ZOSTAR-KERATITIS

- PRIMARY INFECTION
  - CHICKEN POX
  - VACCINATION RECOMMENDED BY AMERICAN ACAD of PEDIATRICS

- RECURRENT INFECTION
  - OPHTHALMIC INVOLVEMENT 10-255
  - OPHTHALMIC ZOSTAR > OVER AGE 60
  - UNDER 40 50% IMMUNOCOMPRIMISED

HZK

- HZK
  - V1, V2, V3
  - CONJUNCTIVA
  - CORNEA
  - MUCOUS PLAQUE
  - DECREASED CORNEAL SENSATION
  - ENDOTHELEITIS
HZK

- STROMAL KERATITIS
  - BASIC FEATURES
  - IMMUNOGENIC RESPONSE
  - CLINICAL FEATURES
    - DISCIFORM
    - SUPPERATIVE
    - MIXED
    - TREATMENT

- TREATMENT
  - ORAL AGENTS
    - ACYCLOVIR 800 mg
    - FAMVIR 500 mg
    - VALTREX 1000 mg
    - SORIVUDINE
    - VRIVUDIN

- HZK
  - V1, V2, V3
  - CONJUNCTIVA
  - CORNEA
  - MUCOUS PLAQUE
  - DECREASED CORNEAL SENSATION
  - ENDOTHELEITIS