STEVENS-JOHNSON SYNDROME

Background
1. Definition
   o Epidermal detachment of <10% of body surface area
   o Toxic Epidermal Necrolysis (TEN): >30% of body surface area involvement
   o Mucous membrane involvement: oral, genital, anal, nasal, conjunctival

Pathophysiology
1. Pathology of Disease
   o Drug hypersensitivity leads to Major Histocompatibility Complex-I (MHC-1) restricted drug presentation and is followed by an expansion of cytotoxic T-lymphocytes leading to infiltration of skin lesions with cytotoxic T-lymphocytes and Null Killer (NK) cells.
   o Keratinocyte apoptosis due to Fas and Fas ligand (CD95)\(^1\)
   o Reaction to underlying infection
2. Incidence, Prevalence
   o 1 to 7 cases per million person-years
3. Risk Factors:
   o 74-94% of cases triggered by preceding medication or URI infection\(^1\)
     - Trimethoprim-sulfamethoxazole and other sulfonamides most common.
     - Less common: cephalosporin, quinolones, aminopenicillins
     - Cross reactivity among beta lactams and cephalosporins
   o Mycoplasma pneumonia, HIV, herpesvirus - more common in Erythema Multiform, hepatitis A
   o HLA-B1502 gene presence in Chinese patients with use of carbamazepine\(^1\)
4. Morbidity / Mortality
   o 1-3% a year
   o Less in children then adults
   o Sepsis major cause of death

Diagnostics
1. History
   o Fever and influenza like symptoms, occurring 1-3 weeks after use of offending agent
   o Rash
   o Erosive changes on the lips, mouth, conjunctivae, genital area
2. Physical Examination
   o 90% of cases involve mucous membranes, including eyes, mouth, nose and genitalia
   o Skin lesions: generalized macules with purpuric centers.
• Macules progress to large blisters which then cause epidermal detachment.
• 3-5 days later separation of epidermis progresses
  o Ulcerative stomatitis
  o Labored breathing if tracheobronchial involvement
  o Large wound areas cause pain, protein/ fluid loss, bleeding
  o Nikolsky sign: light pressure causing detachment of full thickness epidermis
  o Hyper-/hypo-pigmentation of skin
  o Esophageal ulceration
  o Ocular: swollen, erythematous eyelids, conjunctivitis, keratitis, endophthalmitis; can cause loss of vision

3. Diagnostic Testing
  o Skin biopsy: shows separation of epidermis at the dermal-epidermal junction.
  o Mycoplasma PCR, IgG, IgM

4. Laboratory evaluation
  o Bun, creatinine, lytes, CBC, glucose, skin swabs for erosions, blood cultures

5. Diagnostic imaging
  o CXR

6. Other studies
  o Direct immunofluorescence

**Differential Diagnosis**

1. Key Differential Diagnoses
  o Erythema multiforme
  o Bullous pemphigoid
  o Staphylococcal scalded skin syndrome
  o Linear IgA dermatosis
  o Behcet’s syndrome
  o Kawasaki disease
  o Toxic shock syndrome
  o Toxic epidermal necrolysis >30% of body involvement

**Therapeutics**

1. Acute Treatment
  o Immediate drug discontinuation
  o Transfer to burn unit improves mortality\(^1\)
  o 600 calories or 22% less per day than burn patients \(^1\)
  o Provide analgesia: swish and swallow
  o Prevent dehydration; monitor lytes
  o Mycoplasma treatment: \(^3\)
    • Macrolides
      • Macrolide resistance common: fluoroquinolones can be used or tetracyclines, but use of either not currently recommended for children

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\(^1\)
\(^3\)
Skin lesion treatment with copper sulfate, silver nitrate or sulfadiazine cream (can cause cross reactivity if a sulfa was predisposing drug)¹
- Acticoat, Aquacel Ag, supathel: synthetic materials containing nanocrystalline silver; can be changed weekly¹
- Bland emollients better choice⁵

Avoid skin trauma

Corticosteroid treatment: shorter duration of illness¹
- Some showed slower time to recovery
- May cause underlying infection to flare
- Can have more medical complications, administering steroids for greater than 48 hours showed high rate of infection¹
- No consensus reached for treatment, but trend - more complications without significant benefit…esp. >48 hrs Tx

Corticosteroids vs IVIG vs supportive care: no significant effect on mortality¹

IVIG: in severe cases can prevent further skin manifestations

Plasmapharesis can be used safely for extensive cases

### 2. Further Management (24 hrs)

#### Ocular

- Long term steroid treatment for ocular complications¹
  - Pulsed topical steroid treatment for 4 days (In adults, 2mg/kg per day) → minimal ocular manifestations,
    - Note: if significant skin sloughing has already occurred, then would cause more systemic complications
- Lubrication of eyes
- Amniotic membrane transplantation²
  - Must occur within 10 days of disease
  - Used in severe cases of ocular involvement: large areas of epithelial sloughing of conjunctiva, cornea and lid margins
  - Used alone (without steroids) show most benefit
  - Used locally, so no systemic effects

### 3. Long-Term Care

- Chronic ophthalmic complications: corneal inflammation¹
  - 30% in surviving children
  - Up to 74% in adults
  - Severe in 25%

#### Follow-Up

1. Return to Office
   - 2-3 days for close follow-up
If clinical symptoms worsen then seek immediate medical attention

2. Refer to Specialist
   - Dermatology: excessive skin peeling, ulcerations, alopecia, lack of nail growth
   - Ophthalmology:
     - Ocular manifestations; photophobia, keratitis, corneal abrasions, visual impairment and dry eye.

3. Admit to Hospital
   - Severe skin sloughing greater then 10 percent of body surface, ocular manifestations, respiratory compromise

Prognosis
1. Recurrence rate: 20% of affected children up to 7 years after first episode
2. Long term ocular complications

Prevention
1. Avoid eliciting drugs/medications

Patient Education

References
5. Treat J. Stevens Johnson Syndrome and Toxic Epidermal Necrolysis. Pediatric Anals 2010; 39:10

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