Objectives
- Describe and discuss clinical presentations of several dangerous dermatologic rashes
- Understand clinical clues that can aid in diagnosis and treatment
- Explain current work-up and treatments for several eruptions
- Expand differential diagnosis of dangerous rashes based on clinical exams

Eruptions
- Stevens-Johnson Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN)
- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
- Meningococcemia
- Eczema Herpeticum
- Staph Scalded Skin Syndrome
- Serum Sickness-Like Reaction
- *Not covered: Kawasaki disease, vasculitides
Stevens-Johnson Syndrome (SJS)
- Rare, potentially fatal, acute reaction
- Meds implicated in majority of causes
- Characterized by mucosal and skin lesions
- Due to extensive keratinocyte death
- Average mortality rate of 1 to 5%
- Higher in elderly adults
- Immunosuppression (HIV, lymphoma) is a risk factor

SJS Clinical Features
- Prodrome of fever, URI symptoms, painful skin, dysphagia.
  - 1 to 3 days before cutaneous signs
- Skin lesions:
  - Started as pink macules > dusky red or purpuric > gray > then vesicles/bulla > irregular erosions
  - Appears on trunk and spreads to arms, neck, face
  - +Nikolsky sign
  - May take hours to a few days
  - <10% BSA

SJS Clinical Features (cont.)
- Mucosal Lesions (present in 90%):
  - Painful erosions that coalesce
  - Lips, mouth, throat, esophagus
  - Nose
  - Eyes
  - Genitalia
- Other features
  - Lymphadenopathy
  - Hepatitis
  - Cytopenias

Pathogenesis
- Not well understood
- Impaired capacity to detoxify certain intermediate drug metabolites
- Antigenic response to complex of metabolites and certain tissues
- Typically presents 1 to 3 weeks after onset of drug therapy

Offending Agents
- >100 medications have been reported
- Allopurinol
- Antibiotics (sulfa*, penicillins, tetracyclines, quinolones, cephalosporins)
- NSAIDs
- Anticonvulsants (carbamazepine, lamotrigine, phenytoin)
- Antiretrovirals (especially NNRTIs)
- Barbiturates
Treatment
- Stop offending agent(s)
- Treat like patients with severe burns (admit to ICU)
  - Fluids/electrolytes
  - Caloric replacement
  - Protect from secondary infections
  - Ophthalmology consult
  - Urology consult
  - Mouth care
  - Consider biologic dressings for skin

Systemic Treatment
- No treatment to date has shown efficacy in prospective clinical trials
- Case reports and small uncontrolled series
- Recent meta-analysis showed IVIG + steroid accelerated improvement
- Intravenous immunoglobulins (IVIG)
  - > 2g/kg total dose, over 3 to 4 days
- Systemic immunosuppressives
  - Cyclosporine
  - Cyclophosphamide
  - TNF-α antagonists
  - Plasmapheresis
  - Steroids*

Toxic Epidermal Necrolysis (TEN)
- Exists on spectrum with SJS
- > 30% BSA
- Mortality rate approaches 25 to 35% of patients
- Typically due to systemic infection
- Risk of developing TEN is 1000-fold higher if you have AIDS
- Several factors correlated with poor outcome

<table>
<thead>
<tr>
<th>SCORTEN</th>
<th>Prognostic factors</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Age &gt;60 yrs</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Heart rate &lt;50 bpm</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>Cancer or hematologic malignancy</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>Risk involved on day 1 &gt; 10%</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>Serum lactic acid (LAD) &gt; 4 mmol/L</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>Serum glucose level (GLU) &gt; 14 mmol/L</td>
<td>1</td>
</tr>
</tbody>
</table>

SCORTEN mortality rate (%)

<table>
<thead>
<tr>
<th>SCORTEN</th>
<th>Mortality rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.2</td>
</tr>
<tr>
<td>1</td>
<td>12.3</td>
</tr>
<tr>
<td>2</td>
<td>35.8</td>
</tr>
<tr>
<td>3</td>
<td>58.3</td>
</tr>
<tr>
<td>4</td>
<td>79.3</td>
</tr>
<tr>
<td>5</td>
<td>99.6</td>
</tr>
</tbody>
</table>

* © 2003 Boucher - Bolognia, Jorizzo and Rapini Dermatology - www.dermhub.com
**Mycoplasma pneumoniae**-induced mucositis
- Distinct entity from SJS/TEN
- More extensive mucosal involvement; less skin involvement
- Preceding respiratory symptoms
- Mycoplasma PCR is typically positive
  - Does not have to be if symptoms c/w mycoplasma infection
- Treatment
  - Marcolides
  - Prednisone or IVIG

**Elementary lesion**

**True** target – Erythema multiforme

**Atypical** target - Stevens Johnson Syndrome (SJS)

**Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)**
- Eruption that develops in setting of eosinophilia and multiple systemic symptoms
- Later than most drug reactions (2-6 weeks)
- Fever (85%)
- Rash (75%)
  - Morbilliform, edema, vesicles, erythroderma, purpura, targets, bullae
- Edema of acral extremities and face
Orbital edema and scale
Facial edema and morbilliform exanthem

Orbital edema
Facial edema

Purpuric exanthem
Peeling exanthem

DRESS Clinical Features
- Rash typically involves face and upper body
- Usually morbilliform and pruritic
- Can have mucosal crusting
- Fever precedes the eruption by several days
- Most affected visceral organ: liver (transaminitis)
- LAD in 75%
- Marked leukocytosis up to 50K
- 30% with eosinophilia > 2K (can be delayed)
- Early atypical lymphocytes (mono-like)

DRESS Clinical Features (cont.)
- Multiple organs can be affected
  - Kidneys (interstitial nephritis)
  - Lungs (interstitial pneumonitis)
  - Heart (myocarditis)
  - Brain (encephalitis)
  - GI tract (esp. allopurinol)
  - Thyroid and other endocrine
  - Joints (arthralgias & arthritis)
- Can persist for weeks to months
- Late thyroiditis and diabetes as complications
- Overall mortality 5-10%, usually due to fulminant hepatitis
**Offending Meds**

- Aromatic anticonvulsants (phenobarbital, carbamazepine, phenytoin)
- Lamotrigine
- Sulfonamides
- Minocycline
- Allopurinol (full doses + renal dysfunction)
- Gold Salts
- Dapsone
- HIV meds - abacavir
**Treatment**
- Stop offending agent
- Systemic steroids (1 to 2 mg/kg)
  - Often for several months
  - Relapses can happen with tapering of steroids
- Monitor labs for late onset symptoms
- Thyroid
- Liver
- Kidneys

**Meningococcemia**
- Etiology - Neisseria meningitidis
  - Commensal organism of nasopharynx (8-25%)
  - Devastating pathogen
- Gram-negative diplococcus
- Transmission
  - respiratory droplets
  - Incubation 1-10 days
  - Children < 5 years of age and adolescents/young adults

**Pathogenesis**
- Lipo-oligosaccharide activates various immune cells
  - Activates nuclear factor KB (NFkB)
  - Other cytokines
- Disseminated intravascular coagulation (DIC)
  - Excessive activation of coagulation system
  - Concomitant decrease of fibrolytic system
  - Antithrombin and Protein C are low

**Clinical Presentations**
- Meningitis (60%)
- Upper respiratory symptoms
- Headache
- Myalgias
- Pneumonia
- Rashes
  - Petechial eruption
  - Retiform purpura; ischemic necrosis
  - Blanchable morbilliform eruption (minority of patients)

**Clinical Features - Skin**
- Seen in up to 77% of patients with invasive disease
- Macules
- Petechiae
- Retiform purpura, with jagged, geographic borders
  - “Gun-metal gray”
  - Vesicles may form
- Gangrene
- Digits
### Treatment
- High dose IV penicillin
- Third generation cephalosporin (cefotaxime or ceftriaxone)
- Chloramphenicol is alternative in severely allergic
- Isolation
- Intravascular support (fluids, vasopressors)
- Activated protein C and other anticoagulants*  
  - Not proven to improve outcome
- Monitor for adrenal hemorrhage

### Prevention for Close Contacts
- Prophylaxis with rifampin, ceftriaxone, or ciprofloxacin
- Prophylaxis recommended for:
  - Household contacts (esp. young children)
  - Child care or nursery school contacts in days prior to onset of the illness
  - Health care workers giving mouth-to-mouth

### Mimicker – Levamisole contaminated cocaine
- Transient:
  - pANCA +
  - antiphospholipid panel +  
    (often lupus anticoagulant)
  - Agranulocytosis +/-  
  - ANA +/-  
  - Combination vasculitis/thrombo-occlusive
  - Common but not necessary locations - ears

### Eczema Herpeticum
- HSV in atopic dermatitis
- AKA: “Kaposi varicelliform eruption”
- Rapid cutaneous dissemination
- Fevers and malaise are common
Eczema Herpeticum
- Often superinfected with *S. aureus*
- 1/3 of patients, in one study
- Should consider bacterial culture and treatment
- Ok to start topical steroids for eczema, as long as they are on antivirals

Work Up & Treatment
- HSV PCR or viral culture
- Bacterial culture (often secondarily infected)
- Acyclovir or Valacyclovir
- Antibiotics (if suspicious for bacterial infection)
- Then topical steroids

Staph Scalded Skin Syndrome (SSSS)
- Caused by *Staph aureus*
- Carries Exfoliative Toxin (ET-A and ET-B)
  - Phage Group II, Types 55 and 71
  - Targets Desmoglein 1, found in granular layer of epidermis
- Interaction of toxin with skin causes desquamation
Staph-Scalded Skin Syndrome

- Typically affects neonates and young children < 5
- Due to reduced immunity
- Imperfect renal clearance of toxin
- Can affect adults (worse prognosis)
- Renal failure or immunocompromise
- Transferred to skin and enters body through microabrasions in skin, orifices

Treatment

- Culture – skin, urine, nose, throat, blood*
- IV Antibiotics to cover Staph
  - Penicillinase-resistant anti-staph antibiotic
  - Clindamycin
- Can switch to oral once improving
- Symptomatic care
  - Fluids
  - Monitor electrolytes
  - Topical ointment to moisturize/protect skin

Sequelae

- Secondary infection (strep)
- Glomerulonephritis, particularly in adults
  - Rare in children

Serum Sickness-Like Reaction

- Hypersensitivity Reaction
  - 1 to 3 weeks after exposure to antibiotics
  - Usually in conjunction with URI
- Cutaneous eruption – urticarial or purpuric
- Malaise
- Fever
- Arthralgias and joint swelling

- Self-limiting; resolves in 2 to 3 weeks
Cutaneous eruption

- Large urticarial and purpuric plaques
- Tend to be annular and polycyclic
- Lilac-colored center
- Facial involvement is common

Medications Implicated

- Cefaclor (classic)
- Penicillins
- Tetracyclines
- Cephalosporins
- Sulfonamides
- Itraconazole
- Fluoxetine
- Bupropion

Treatment

- Stop offending medication (often is already completed)
- Antihistamines
  - Scheduled and usually twice to three times daily
- NSAIDs
- If severe, may use oral steroids
  - Thought to prolong the course
- Risk of cross-reaction to other antibiotics is low
  - May be able to give offender in future

Final Pearls

- Look at eyes
  - Can help you differentiate SJS/TEN from Staph Scalded Skin Syndrome
  - Kawasaki disease usually shows eye involvement too
- Look at the oral mucosa and genitalia
- SJS/TEN will have involvement
- SSSS and Serum-Sickness Like Reaction won't
- Take a good history
Objectives

- Describe and discuss clinical presentations of several dangerous dermatologic rashes
- Understand clinical clues that can aid in diagnosis and treatment
- Explain current work-up and treatments for several eruptions
- Expand differential diagnosis of dangerous rashes based on clinical exams

Acknowledgement

- Dr. Beth Drolet
- Dr. Barb Wilson

Questions?

- shumphre@mcw.edu

Bibliography