DRUG ERUPTION

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INTERNAL MEDICINE BOARD REVIEW COURSE
Disclosures

- No Relevant Financial Relationships
DRUG ERUPTIONS
Drug Reactions
3 things you need to know

1. Type of drug reaction

2. Statistics
   ▶ What drugs are most likely to cause that type of reaction?

3. Timing
   ▶ How long after the drug was started did the reaction begin?
Clinical Pearls

- Drug eruptions are extremely common
- Tend to be generalized/symmetric
  - Maculopapular/morbilliform are most common
- Best Intervention: Stop the Drug!
  - Do not dose reduce
  - Completely remove the exposure
- How to spot the culprit?
  - Drug started within days to a week prior to rash
  - Can be difficult and take time
  - Tip: can generally exclude all drugs started after onset of rash
- Drug eruptions can continue for 1-2 weeks after stopping culprit drug
LITT’s drug eruption database
Drug Eruptions

- Skin is one of the most common targets
- Antibiotics and anticonvulsants are most common
  - 1-5% of patients
- 2% of all drug eruptions are “serious”
  - TEN, DRESS
- More common in adult females and boys < 3 y/o
- Not all drugs cause eruptions at same rate:
  - Aminopenicillins: 1.2-8% of exposures
  - TMP-SMX: 2.8-3.7%
  - NSAIDs: 1 in 200
  - Lamotrigine: 10%
Drug Eruptions

Three basic rules

1. **Stop** any unnecessary medications
2. Ask about **non-prescription medications**
   - Eye drops, suppositories, implants, injections, patches, vitamin and health supplements, friend’s medications
3. **ALWAYS consider medications as possible cause** (no matter how atypical)
Note confluence of lesions on trunk
Morbilliform reaction to ampicillin-amoxicillin
<table>
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<tr>
<th>Clinical presentation</th>
<th>Percentage that are drug-induced (%)</th>
<th>Time interval</th>
<th>Mortality (%)</th>
<th>Selected responsible drugs</th>
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<tr>
<td>Exanthematous eruption</td>
<td>Child: 10–20 Adult: 50–70</td>
<td>4–14 days</td>
<td>0</td>
<td>Aminopenicillins Sulfonamides Cephalosporins Anticonvulsants Allopurinol</td>
</tr>
<tr>
<td>Urticaria Anaphylaxis</td>
<td>&lt;10 30</td>
<td>Min-hours Min-hours</td>
<td>0</td>
<td>Penicillins Cephalosporins NSAIDs Monoclonal Abs Contrast media</td>
</tr>
<tr>
<td>Fixed drug eruption</td>
<td>100</td>
<td>First exposure: 1–2 weeks Re-exposure: &lt;48 hours, usually within 24 hours</td>
<td>0</td>
<td>TMP-SMX NSAIDs Tetracyclines Pseudoephedrine</td>
</tr>
<tr>
<td>Acute generalized exanthematous pustulosis (AGEP)</td>
<td>70-90</td>
<td>&lt;4 days</td>
<td>1-2</td>
<td>β-Lactam antibiotics Macrolides Calcium channel block.</td>
</tr>
<tr>
<td>Drug reaction with eosinophilia and systemic symptoms (DRESS)</td>
<td>70-90</td>
<td>15-40 days</td>
<td>5-10</td>
<td>Anticonvulsants Sulfonamides Allopurinol Minocycline Lamotrigine</td>
</tr>
<tr>
<td>Stevens–Johnson syndrome (SJS) Toxic epidermal necrolysis (TEN)</td>
<td>70-90</td>
<td>7-21 days</td>
<td>5 30</td>
<td>Sulfa Anticonvulsants NSAIDS Allopurinol</td>
</tr>
</tbody>
</table>
Vasculitis
Drug Induced Vasculitis

- Palpable Purpura
  - Dependent area
  - **Symmetrical distribution**
  - Urticaria-like lesions, ulcers, nodules, hemorrhagic blisters, pustules and digital necrosis
- Typically small vessels
- 7 to 10 days after drug administration and < 3 days following rechallenge
- Medications associated:
  - PCNs, NSAIDs (oral and topical), sulfonamides and cephalosporins
  - Propylthiouracil, thiazide diuretics, furosemide, allopurinol, phenytoin
  - Fluoroquinolones and biologic agents [G-CSF, GM-CSF], interferons
- Treatment
  - Stop offending agent
  - Supportive care
  - NSAIDS, antihistamines
Fixed Drug Eruption
Fixed Drug Eruptions

• Lesions reoccur at the same site with each exposure to medication
  – 1 to 2 weeks after first exposure
  – Within 24 hours, after subsequent exposures

• Clinically:
  – One or a few, round, sharply demarcated erythematous & edematous plaques
  – Dusky, violaceous hue, central blister or detached epidermis

• Anywhere on the body,

• Favor the lips, face, hands, feet and genitalia
  – 50% on oral or genital mucosa
  – 2% of all genital ulcers (especially young boys)

• Treatment
  – Lesions fade, leaving a residual postinflammatory brown pigmentation
Fixed Drug Eruptions

- Usually intermittent drugs:
  - NSAIDs
  - Sulfonamides (TMP) → majority of genital fixed drug eruptions
  - Barbiturates, TCNs, phenolphthalein, acetaminophen, cetirizine, celecoxib, dextromethorphan, hydroxyzine, lamotrigine, phenylpropanolamine, erythromycin, herbs
Acneiform Eruption

• Epidermal growth factor receptor (EGFR)
  – Treatment of advanced lung, pancreatic, colorectal, and head and neck cancers
    • Monoclonal antibodies
      – Cetuximab, panitumumab
    • Small-molecule tyrosine kinase inhibitors
      – Gefitinib, erlotinib, lapatinib
  – Cutaneous adverse events to EGFR inhibitors are frequent
    • Abundant expression of EGFR in the skin and adnexal structures.
Acneiform
This lung cancer patient who has been receiving radiation therapy is on a tea and toast diet and complains of myalgias. History is positive for soft tissue bleeding. Hb is 8 gm. He is deficient in vitamin:
A. B6
B. A
C. D
D. E
E. C

Gingival hyperplasia

"Corkscrew hairs"
NUTRITIONAL DISORDERS

- Vitamin K Deficiency
- Vitamin B3 Deficiency
- Vitamin C Deficiency
- Zinc Deficiency
- Iron Deficiency
Vitamin K Deficiency

- **Infants**
  - Premature, uncolonized GI tract

- **Adults**
  - Malabsorption; liver dz

- **Clinical:**
  - Purpura
  - Massive hemorrhage

- **Dx:** elevated PT and PTT

- **Tx:**
  - Adults = Vitamin K 5-10 mg/day IM x several days
  - Kids = 2 mg/day (0.5 to 1mg in newborns)
  - Acute crisis = Fresh Frozen Plasma (FFP)
Vitamin B3 Deficiency - Pellagra

- *Skin manifestations may be the 1st sign*
- **Glossitis**: inflammation of the tongue
- The 4 D’s: **diarrhea, dementia, dermatitis → DEATH**
  - **Diarrhea**
    - Acute inflammation of the small intestine and colon
  - **Dementia**
    - Patchy demyelination and degeneration of the affected nervous system
  - **Dermatitis**
    - Four types of dermatitis
      - **Photosensitive eruptions**
      - **Perineal lesions**
      - Thickening and pigmentation over bony prominences
      - Seborrheic-like dermatitis of the face
Pellagra

**Casal’s necklace**: Photosensitive eruption on face, neck, and upper chest
Pellagra

- Additional manifestations:
  - Depression, apathy, psychosis, coma
  - Death in 4-5 yrs if untreated
- Dx: clinical
  - Low serum niacin, tryptophan
- Tx: Niacin 50-300mg/day PO (rapid reversal of pellagra)
  - 100mg/day IV for malnourished
VITAMIN C DEFICIENCY

Scurvy

- Water-soluble vitamin found in fresh fruits, vegetables
- Roles:
  - Collagen & ground substance formation
  - Synthesis of epinephrine & carnitine
  - Leukocyte function, iron absorption, folic acid metabolism
- Reducing agent:
  - Cofactor for hydroxylation of procollagen → collagen
- Elderly male alcoholics (MC), psych patients on restrictive diets, children 6-24mo
Scurvy

- **Four Hs:**
  - Hemorrhage
    - Hemorrhagic gingivitis
    - Epistaxis
    - Perifollicular petechiae
    - Subungual, IM, and intraarticular hemorrhage
    - Subperiosteal hemorrhage leading to pseudoparalysis
  - Hyperkeratosis of the hair follicles
  - Hypochondriasis
  - Hematologic abnormalities
• Clinical
  – Woody edema
  – **Corkscrew hairs** → plugging of hair follicles by curled hairs
    – Forearms, abdomen, thighs
  – Delayed wound healing
    – due to secondary defect in collagen formation
  – **Depression**
  – **ANEMIA** (secondary to bleeding)
• Tx:
  – Ascorbic acid 1000 mg/day
  – Maintenance dose of 100 mg/day should be considered
Zinc Deficiency

Functions of Zinc:
- Wound healing
- Immune/reproductive/neuropsychiatric function

Inc. zinc requirements:
- infections, post-surgery, pregnancy, cancer

Largely dependent on food intake
- Nuts, whole grains, green leafy vegetables, shellfish, human milk

Presents most commonly in infancy
- Premature
  - suboptimal absorption, high zinc requirements, inadequate body stores
  - Breast milk generally provides adequate zinc
  - Occurs at the time of weaning from breast milk to cow’s milk
Genetic Acquired

Zinc Deficiency

“acrodermatitis enteropathica”

zinc transporter mutation

Acquired

alcoholics, malnourished, CRF, malignancies, pregnancy, drugs, HIV
Zinc Deficiency

- Triad: *Dermatitis, diarrhea* and *alopecia*
  - **Dermatitis:**
    - Acral and periorificial distribution
    - Patchy, red, dry scaling with exudation and crusting
    - Angular cheilitis and stomatitis; drooling
  - **Diarrhea:** *suspect in infant with chronic diaper rash & diarrhea*
  - **Alopecia:** generalized

- **Additional Sx:**
  - Growth retardation
  - Impaired wound healing
  - CNS findings
  - Emotional lability & irritability
Zinc Deficiency

**Dx:**
- Low serum zinc levels but not diagnostic
- **LOW** alkaline phos (zinc-dependent enzyme)

**Tx:**
- Zinc sulfate PO 1 to 2 mg/kg/day
- **Acrodermatitis enteropathica:** 3 mg/kg/day lifelong
- Warm compresses and petroleum applied TID to areas of weeping or crusted dermatitis to support reepithelialization
Iron Deficiency

- Decreased total-body iron content
- Common
  - Menstruating women
  - Diet low in red meat or diminished absorbable dietary iron
- **Iron balance**: achieved by regulation of iron absorption in the proximal small intestine
- **Dx**: check serum iron, TIBC and ferritin
- **Tx**: Iron sulfate 325 mg PO TID
- **Plummer-Vinson**: middle-aged women
  - Microcytic anemia
  - Dysphagia/esophageal webs
  - Thin lips with small inelastic opening of the mouth
Iron Deficiency

Clinical Manifestations

- koilonychia
  - “spoon nails”
  - 40-50%
  - *physiologic in kids*
- Glossitis
- Angular cheilitis
- Pruritus
- Telogen effluvium
Case

- 84 y.o. obese, caucasian female
- Multiple enlarging, necrotic, ulcerated plaques on the lower extremities
- Rapidly expanding up to 15 cm over several weeks
- Painful upon palpation, indurated
Initial Presentation
Initial Presentation
Patient History

- Past medical history
  - Atrial fibrillation, hypercholesterolemia, lower extremity edema
- Past dermatological history
  - none
- Medications
  - Warfarin, simvastatin, spironolactone, torsemide
Plan

- Biopsy
  - A punch biopsy and incisional biopsy were performed in the office

- Labs
  - CBC, CMP, phosphorus, PT/PTT/INR, protein C & S, antithrombin III, anticardiolipin antibody, lupus anticoagulant, factor V leiden, serum cryoglobulins, hepatitis C antibody, vitamin D, parathyroid hormone

- Hospital admission
  - Further evaluation and treatment
Incisional Biopsy
Pathology Report

- Punch biopsy and incisional biopsy revealed fibrin thrombi with a broad ddx
  - Protein C & S deficiency
  - Warfarin induced necrosis
  - DIC
  - Purpura fulminans
  - Cryoglobulinemia
  - Antiphospholipid syndrome
  - Factor V leiden deficiency
Labs

- Significant for:
  - Increased: serum creatinine, alk phos, PT, anticardiolipin IgM antibody, lupus anticoagulant
  - Normal: calcium, phosphorus, INR, parathyroid hormone, factor V leiden, cryoglobulins
  - Decreased: GFR (29), protein C & S
Hospital Course

- Excisional biopsy performed by general surgery on one of the ulcerated, necrotic plaques
  - Consistent with calciphylaxis
- Patient was started on sodium thiosulfate 25g IV daily
- Patient deferred further treatment and was discharged to a nursing home for palliative care
- Patient died within 1 month of initial visit
Excisional Biopsy
Calciphylaxis

- AKA *calcific uremic arteriolopathy*
- Rare and serious disorder that features systemic medial calcification of arterioles that causes ischemia and subcutaneous necrosis
- Most commonly occurs in ESRD patients on hemodialysis
- Pathogenesis
  - Poorly understood, multifactorial
  - Vascular calcification
- Risk factors
  - ESRD, female sex, obesity, hyperparathyroidism, hypercoaguable states, hyperphosphatemia, medications
    - *warfarin*, vit D analogs, systemic glucocorticosteroids
      - *warfarin*: 10 fold increased risk of calciphylaxis
Discussion Cont

- Treatment
  - Evidence based guidelines have yet to be determined
  - IV Sodium thiosulfate - calcium binder and antioxidant
  - Wound care and pain management
  - Oxygen therapy
  - Correct any underlying lab abnormalities
Calciphylaxis Conclusion

- Elderly, obese female with an acute onset of calciphylaxis
- Multiple cofactors that might have contributed to the pathogenesis
- Treatments range from case report experience to the correction of underlying etiologies
- Calciphylaxis is an aggressive and poorly prognostic diagnosis that still leaves a lot to be learned
HELP!

- I am Red and Scaly From Head to Toe!
Erythroderma

What is it?
- Exfoliative dermatitis that involves >90% surface area

Causes
- Psoriasis
- Seborrheic Dermatitis
- Drug Eruptions
- Pityriasis rubra pilaris
- Lymphoma
- Eczema
- Infection
  - Bacterial
  - Fungal
  - Viral
- Autoimmune bullous dz
Psoriasis
Seborrheic Dermatitis
Drug Eruption
Pityriasis Rubra Pilaris

[Image of skin lesions with red patches and scales]
Lymphoma
Case 1: 65 y/o Female presents w/ “tender skin all over” which began after few days of coughing and fever and chills
Case 1: Continued...

- **ROS:** Photophobia & dysphagia/odynophagia
- **Recently Rx** an antibiotic for a “large boil on her leg”
- **PMHx:** seizure disorder
- **Meds:** Trimethoprim/sulfamethoxazole, Lamotrigine
Stevens-Johnson (SJS) & Toxic Epidermal Necrolysis (TEN)

Characteristic dusky red color of the early macular eruption
Erythema Multiforme, Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis

- **Spectrum of Disease**
  - Histologically indistinguishable
  - *More severe reactions are likely to be drug induced (50% of SJS, 80% of TEN)*

- **Definitions**
  - SJS = less than 10% BSA
  - SJS/TEN overlap = 10-30% BSA
  - TEN = greater than 30% BSA
SPECTRUM OF DISEASE BASED UPON SURFACE AREA OF EPIDERMAL DETACHMENT

SJS

SJS-TEN overlap

TEN

<10%

10-30%

>30%

= Surface area of epidermal detachment

= detached epidermis

SJS = Stevens-Johnson syndrome

TEN = Toxic epidermal necrolysis
### Associated Medications SJS/TEN

<table>
<thead>
<tr>
<th>Medications Most Frequenty Associated with SJS and TEN</th>
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<tr>
<td>Allopurinol</td>
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<tr>
<td>Aminopenicillins</td>
</tr>
<tr>
<td>Amithiozone (thioacetazine)*,¹</td>
</tr>
<tr>
<td>Barbiturates</td>
</tr>
<tr>
<td>Carbamazepine</td>
</tr>
<tr>
<td>Chlormezanone*,²</td>
</tr>
<tr>
<td>Phenytoin antiepileptic</td>
</tr>
<tr>
<td>Lamotrigine</td>
</tr>
<tr>
<td>Phenylbutazone*,³</td>
</tr>
<tr>
<td>Piroxicam</td>
</tr>
<tr>
<td>Sulfadiazine*,¹</td>
</tr>
<tr>
<td>Sulfadoxine*,¹</td>
</tr>
<tr>
<td>Sulfasalazine</td>
</tr>
<tr>
<td>Trimethoprim–sulfamethoxazole</td>
</tr>
</tbody>
</table>
Infections

Mycoplasma common cause of SJS in kids
EM, SJS, TEN

- Fever, flu-like symptoms *precede* eruption by a few days

- SJS & TEN: Involvement of 2 or more mucosal surfaces
  - Oral mucosa and conjunctivae most common
  - May be present before rash

- Stop drug promptly
  - Decreases mortality rate (from 26% to 5%) in drugs with short half lives
SJS/TEN

- Treatment: burn unit
  - Supportive
    - Fluids, nutrient, electrolyte replacement, infection control
  - IVIG:
    - Stops keratinocyte apoptosis, blocks death receptor FAS (CD95)
  - Immunosuppressive therapy
    - Controversial
    - May increase morbidity/mortality
  - Systemic steroids - early short trial, rapid taper

- Outcome Measures:
  - Age, severity of underlying disease & extent of skin loss
  - Epidermal regrowth – 3 weeks
  - Ocular scarring and vision loss, nail abnormalities, transient widespread verrucous hyperplasia, confluent SKs

- Mortality rates: SJS 5%, TEN 30%
TEN (50% body surface area involvement) before (A) and 3 weeks after (B) treatment with IVlg (0.75 g/kg/day for 4 days)
Erythema Multiforme
What is the most common infectious cause of erythema multiforme?
What is the most common infectious cause of erythema multiforme?

- Herpes Virus
Infectious
Staphylococcal Infections

- Cutaneous manifestations of endocarditis
- Impetigo of Bockhart
- Sycosis Barbae
- Folliculitis
- Furunculosis
- Pyogenic Paronychia
- Botryomycosis
- Pyomyositis
- Impetigo
- Staph Scalded Skin Syndrome
- Toxic Shock Syndrome
Skin lesions: pustules, furuncles, erosions with honey-colored crusts, bullae, erythema and desquamation, or vegetating pyoderma

Staph is the most common bacterial infection in children
- Extremely contagious
- Person-to-person contact

Endocarditis:
- Osler node: painful, erythematous nodule pale center located on fingertips, thenar, and hypothenar eminences
- Janeway lesions: non-tender, angular hemorrhagic lesions on palms
Osler nodes

- Both Janeway lesions & Osler nodes are due to septic emboli
- Osler nodes are painful
  - Osler=Ouch
Janeway lesions
Community Acquired MRSA

- First appeared in isolates of *S. aureus* in 1961
- Risk factors:
  - Age > 65
  - Exposure to MRSA
  - Prior Abx therapy
  - Recent hospitalization or chronic illness—IV Vancomycin or Linezolid
- If MRSA suspected:
  - Clindamycin
  - Trimethoprim/sulfamethoxazole (alone or with rifampin)
  - Minocycline/Doxycycline
  - Oral linezolid (very expensive)
  - Empiric Vancomycin in all pts w/ severe, life-threatening infection
- Colonized Pts of anterior nares with MRSA or with localized impetigo → mupirocin
IMPETIGO CONTAGIOSA

DDx:

- Tinea corporis (circinate lesions)
- Toxicodendron/rhus dermatitis
- Varicella (small, discrete vesicles)
- Ecthyma (crusted ulcers, not erosions)
Impetigo Contagiosa

- **Presentation:** 2mm erythematous papule develops into vesicles and bullae. Upon rupture a straw colored seropurulent discharge dries to form yellow, friable crust.

- **Etiology:** S. Aureus > S. Pyogenes.

- **Lesions located on exposed parts of body.**

- **Group A Strep can cause AGN**
  - Children <6 yrs old
  - 2% to 5% of infections
  - Serotypes 49, 55, 57, 60 strain M2 most associated
  - Good prognosis in children
Toxic Shock Syndrome

Presentation:
- Acute, febrile, multi-system disease
- S. Aureus:
  - Cervical mucosa historically in early 1980’s
  - Also seen with: wounds, catheters, nasal packing. Mortality 12%
- Group A Strep:
  - Necrotizing fasciitis. Mortality 30%
Toxic Shock Syndrome (TSS)

- *S. aureus* exotoxin (TSST-1) isolated in 90% of cases
- *Strep M* types 1 and 3 (80% produce exotoxin A)
- Acute, febrile, multi-system illness characterized by:
  - Myalgias, n/v/d, HA, pharyngitis
  - Rapid progression to shock
  - Diffuse *scarlatiniform* exanthem starts on trunk & spreads centripetally
  - Erythema + edema of palms, soles, and mucous membranes
  - Beau’s lines in nails after recovery + Telogen Effluvium
Toxic Shock Syndrome (TSS)

- CDC diagnostic guidelines...
- Diffuse macular erythrodermic rash
- Bulbar conjunctival hyperemia and palmar erythema
- Temp 38.9 or higher
- 3 or more organ systems (GI, renal, hepatic, heme, CNS)
- Desquamation of palms, soles 1-2 weeks after onset (vs SSSS)
- Negative RMSF, leptospira, rubeola titers
- Negative blood, urine, CSF cultures
- Hypotension
Toxic Shock Syndrome (TSS)
Toxic Shock Syndrome (TSS)

- Initially isolated from cervical mucosa in menstruating women, but recently from wounds, catheters, diaphragms, nasal packing
- Mortality of non-menstrual cases higher (12%) compared with menstrual (5%)
- Rapidly progressive type...
  - Usually secondary to group A or group B *strep* (strep *M* types 1 and 3, 80% produce exotoxin A)
  - Similarities to staph TSS, except rapidly progressive, soft-tissue destruction... necrotizing fasciitis; case fatality rate of 30%
Toxic Shock Syndrome (TSS)

TSS (Staph)
- TSST-1 toxin
- Staph enterotoxins
- Superantigens that promote TNF-a, IL-1, IL-6
- Clinical:
  - Perineal erythema, desquamation, strawberry tongue
  - Tampons (5% mortality rate)
  - Nonmenstrual cases (surgical packing, catheters, meshes, abscesses); higher mortality (12%)

TSS (Strep)
- Group A strep (M types 1,3)
- SPE = pyrogenic
- Exotoxins A,B,C = superantigens
- Clinical:
  - Preceded by soft tissue infection (localized extremity pain) 80% of time
  - High mortality
Folliculitis

Superficial (follicle ostium) or deep infection of the hair follicle
- Common in AIDS, frequent cause of pruritus
- Can occur on eyelashes, pubis (sexual contact, STD), thighs
- S. aureus most common infectious cause
- Pseudomonas assoc. with swimming pools + jacuzzis
  - Alkaline water & low chlorine content
  - Bathing suit distribution
- Other Gram-negatives (*Klebsiella, E. coli, Enterobacter, Proteus*) = implicated in pts on long-term abx therapy for Tx of acne/roacea
Scarlet Fever

- Group A β hemolytic strep produces exotoxin
- Diffuse erythematous exanthem marked by erythematous, (tiny 1-2mm) papular eruption, with a rough, sandpaper quality
- Occurs during course of strep pharyngitis, 24-48 hrs after onset of pharyngeal symptoms
  - Also headache, malaise, chills, anorexia, nausea, high fevers
- Check ASO titer, throat swab
- Strawberry tongue, with enlarged, exudative tonsils
- MC between 1-10 years of age
White: early

Red: 4-5<sup>th</sup> day

Strawberry tongue, with enlarged, exudative tonsils
Scarlet Fever

Rash with circumoral pallor
Scarlet Fever
Erythema Marginatum

- Two skin signs among diagnostic criteria for rheumatic fever
  - Erythema marginatum (early)
  - Subcutaneous nodules (late)
  - (carditis, chorea, polyarthritis)
- Spreading patchy erythema spreads peripherally, polycyclic; evanescent lasting hours to days
- Lesions asymptomatic
Staphylococcal Scalded Skin Syndrome
*Ritter’s disease, Pemphigus neonatorum*

- Primarily children < 6 y/o
- Characterized by red, blistering skin 2° a *staph* infection from distant foci
- Localized toxigenic strain of *S. aureus*
  - Naso-oropharynx or conjunctiva
  - Tender, flaccid, *sterile bullae* (culture negative)
  - *Not at the DEJ as in TEN which exhibits ‘full thickness necrosis’*
Staphylococcal Scalded Skin Syndrome
*Ritter’s disease, Pemphigus neonatorum*

- Prodrome of malaise, fever, irritability, sore throat, & severe tenderness of the skin → Purulent rhinorrhea or conjunctivitis

- **Erythema** 1st appears on head, then generalized in 48 hours
  - Skin develops wrinkled appearance due to flaccid bullae in superficial epidermis → *spares palms, soles, mucous membranes*
  - Perioral crusting, mild facial edema

- Scaling & desquamation continue for 3-5 days w/ re-epithelialization in 10-14 days
  - Mortality rates: 3% in children, over 50% in adults, 100% in adults w/underlying disease
Staphylococcal Scalded Skin Syndrome

- **Diagnosis:**
  - Cultures from intact bullae are negative (sterile bullae)
  - Culture instead from conjunctiva, nasopharynx, perineum, or pyogenic foci on the skin

- **Treatment:**
  - Inpatient IV penicillinase-resistant antibiotic agents
    - Nafillin
    - If penicillin-allergic → macrolides or aminoglycosides
  - Supportive care such as fluid and electrolyte replacement and local wound care
<table>
<thead>
<tr>
<th></th>
<th>TEN</th>
<th>SSSS</th>
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</thead>
<tbody>
<tr>
<td><strong>Cause</strong></td>
<td>Usu. Drug induced</td>
<td>Toxin-producing <em>S. aureus</em> infection</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>Adults</td>
<td>Infants and young kids</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td>D-E separation; dermis w/ variable inflammatory infiltrate</td>
<td>Granular layer split in epidermis; dermis lacks inflammatory infiltrate</td>
</tr>
<tr>
<td><strong>Distribution of rash</strong></td>
<td>Areas of sparing</td>
<td>Generalized w/ flexural accentuation</td>
</tr>
<tr>
<td><strong>Mucous Membranes</strong></td>
<td>Involved; erosions</td>
<td>Uninvolved</td>
</tr>
<tr>
<td><strong>Nikolsky’s sign</strong></td>
<td>In some areas; difficult to elicit</td>
<td>Present in seemingly uninvolved skin</td>
</tr>
<tr>
<td><strong>Face</strong></td>
<td>Vermilion lip redness; edema, erosions</td>
<td>Perioral crusting and radial fissuring with mild facial swelling</td>
</tr>
<tr>
<td><strong>Tx</strong></td>
<td>Standard burn Tx; IVIg, CSt. (controversial)</td>
<td>Abx (B-lactamase resistant) and supportive care</td>
</tr>
</tbody>
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Erysipelas

*St. Anthony’s Fire, Ignis sacer*

- **Group A β-hemolytic strep**
- **Group B strep** in newborns
- **Acute infection of dermis & superficial dermal lymphatics**
  - Local redness, heat, swelling
  - Raised, indurated border that spreads
  - Legs and face MC sites (scalp barrier to extension)
- **Prodromal constitutional Sx:**
  - Lymphadenopathy
  - Leukocytosis > 20,000
Erysipelas

Complications:
- Septicemia, deep cellulitis, necrotizing fasciitis

Differential diagnosis:
- Contact derm (plants, drugs, dyes) although not assoc. w/ f/c, pain
- Lupus erythematosus butterfly pattern

Treatment:
- PCN, erythromycin at least 10 days
- Ice compresses
- Inpatient and IV Abx
Cellulitis

- Deep dermal & SQ infection of mainly *Staph. aureus* or *Strep. pyogenes*
- Suppurative inflammation usually following a wound
  - **MC port-of-entry is due to T. pedis**
  - Purulent and necrotic material will drain
  - Local erythema, tenderness, malaise
- Erythema becomes intense rapidly and spreads → Streaks of lymphangitis
- Risk factors:
  - DM, Alcoholism, lymphedema, IVDA, PVD
  - Damage to lymphatic system (vein stripping)
Cellulitis

- Cellulitis is almost always unilateral, if bilateral, think stasis dermatitis
- Complications (rare in immunocompetent hosts)
  - Gangrene
  - Metastatic abscesses
  - Septicemia
- Initial therapy cover *staph* and *strep*:
  - 1\(^{st}\) gen ceph or pcn’ase resistant pcn
  - Suspect MRSA if unresponsive
Pseudomonas aeruginosa

- Obligate aerobe, Gram(-) bacillus
- Can produce blue pigment (**pyocyanin**) or yellow-green pigment (**fluorescein**)
- Produces exotoxin A (role unclear)
- Widely distributed: water, soil, plant life, animal carriers, dust, sewage
- Intertriginous areas and moist areas most prone to infection
- GI reservoir of infection in ICU patients
- Disease spectrum: paronychia, folliculitis (w/ Abx tx for acne), toe web space maceration, ecthyma gangrenosum, burn superinfections
Pseudomonas aeruginosa

- **Ecchyma gangrenosum**
  - Bacteremia with skin conditions
  - Debilitated patients (leukemia, burns, chronic granulomatous diz, Ca, neutropenia)
  - Healthy infants after Abx therapy + macerated diaper area
  - Starts as a vesicle → hemorrhagic pustule → necrotic ulcers
  - **MUST** assume pseudomonal sepsis
- **DDX:** pyoderma gangrenosum, necrotizing vasculitis, and cryoglobulinemia
- **Tx:** double coverage
  - Amioglycoside + piperacillin
  - +/- GM-CSF
Pseudomonas aeruginosa

- **Green nail syndrome**
  - Greenish discoloration in areas of onycholysis is due to pigment production:
    - Pyocyanin: blue
    - Flourescein: yellow/green
    - Pyomelinin: black
  - Seen in people who *chronically* have their hands in water
  - DDX: subungual hematoma, melanocytic nevus, melanoma, Aspergillus infection
  - Benzoyl peroxide; 1% acetic acid soaks, debridement
Gram-negative toe web infection

- **Toe-web infection**
  - **Pseudomonas**
  - Occurs in chronically moist areas i.e. wet feet
  - Tx - dry area, vinegar soaks, ciprofloxacin
Pseudomonas aeruginosa

- **Hot tub folliculitis**
  - 1-4 days after exposure
  - Maintain chlorination of water 7.2-7.4
  - Apocrine areas (breast, axilla)
  - *Risk for malignant external otitis* (facial nerve palsy in 30%)
  - Folliculitis self-limiting (7-14 days)
  - Cipro for systemic symptoms

*Otitis externa*
Meningococcemia

- *N. meningitidis*
  - gram-negative diplococcus
- Virulence related to polysaccharide capsule (gonorrhea does not have)
- Endotoxin → inflammation
- Serogroups A, B, C, W135, X, Y and Z
  - Vaccines cover A, C, Y, W-135
- Transmitted from person to person via respiratory secretions
- Complement deficiencies components C5 to C9
  - Properdin or immunoglobulin deficiency, asplenia, and HIV infection
Meningococcemia
Meningococcemia

- Flu-like s/s that RAPIDLY progress
- Acute: Fever, chills, hypotension, meningitis, 50-60% have petechiae (trunk, ext)
- *Angular infarcts with erythematous rim and gun-metal gray interior
- *Waterhouse-Friderichsen Syndrome” (adrenal hemorrhage/ infarct) may occur
  - 2* hypotension
  - Nasal carriage in 5-10%
  - Chronic form, very rare

DDX: Acute-- septic vasculitis due to acute bacteremias and endocarditis, acute hypersensitivity vasculitides, enteroviral infections, RMSF, TSS, purpura fulminans and leptospirosis. Chronic-- subacute bacterial endocarditis, Sweet's syndrome, Henoch–Schönlein purpura, rat-bite fever, erythema multiforme and chronic gonococcemia
Case  35 y/o postal worker presents for evaluation of a painless, necrotic lesion on his forearm that is mildly pruritic
Anthrax “Woolsorter’s disease”

- Re-emergence with bioterrorism
  - Occupation-related disease
  - Exposure to infected animals/carcass
- Wool-sorters, cattlemen, ranchers, butchers
- *Bacillus anthracis* (gram +, spore forming rod)
  - Polyglutamic acid capsule -- inhibits phagocytosis
  - Edema toxin -- transport protein (*protective Ag*)
  - Lethal toxin -- lethal factor + protective Ag
- Cutaneous anthrax is uncommon in most of world
- Most human infections are result from infected animals/hides (zoonotic)
Anthrax: 3 forms

- Cutaneous (MC)
  - Necrotizing **painless carbuncle 3-5 days after inoculation**
  - Bulla, edema, ruptures, **eschar** forms on hot, indurated area
  - NON-tender
  - Tender regional nodes → **suppurative adenitis**

- Inhalation (Wool sorter’s disease)
  - Necrotizing, hemorrhagic mediastinal infection
  - Hemorrhagic meningitis almost always resulting in death
  - High fevers, more necrotic lesions, death w/in a few days (20%)

- GI infection
  - Secondary to ingestion; necrotic ulcerative lesion may lead to hemorrhage
Anthrax

- **Diagnosis**
  - Biopsy for PCR, culture & Gram stain
  - ELISA titer for Abs to protective Ag or capsular Ag

- **Differential diagnosis:** Staph carbuncle, recluse spider bite, tularemia

- **Treatment (curative for cutaneous forms) → Do not I&D**
  - Ciprofloxacin 500 mg BID x 60 days
  - Doxycycline 100 mg BID x 60 days
  - If lesion on head or neck, age < 2 yrs, or systemic involvement
  - Refer to CDC guidelines for IV therapy

- **Asymptomatic exposed**
  - Prophylaxis with 6 week course of cipro or doxy
  - Vaccine - postexposure prophylaxis in person at risk
Necrotizing Fasciitis
“Flesh-eating bacteria” syndrome

- 500-1500 US cases reported/year
- Mortality rate = 20-40%
- Etiology:
  - Majority are mixed infection
  - Beta-hemolytic strep (10%)
  - Pseudomonas, Bacteroides
- Rapidly progressing necrosis of subcutaneous fat & fascia
  -Usu. follows surgery, perforating trauma, de novo (DM, IVDA, PVD, psoriasis)
  - Complication of childhood varicella
  - Within 24-48 hrs, pain, erythema, edema progress to patches of dusky blue discoloration, +/- serosanguinuous blisters
- Anesthesia of involved skin
  - Suggests deep involvement & nerve destruction

Necrosis of SQ fat and fascia of inner arm in a pt. with DM
Necrotizing Fasciitis

- Probe test: 2cm incision, probe with finger... lack of bleeding, murky discharge and lack of resistance = ominous signs
- Early surgical debridement is essential for successful therapy and IV Abx (broad spectrum & then more focused)
- Poor prognostic factors: age > 50, Diabetes, atherosclerosis, delay of > 7 days in Dx/Sx, on trunk
- In neonates, abdominal wall is common location
  - Higher mortality rate
Necrotizing Fasciitis

- 3 types of NF
  - Type I - polymicrobial
  - Type II - group A streptococcal
  - Type III - gas gangrene or clostridial myonecrosis
- Fournier’s gangrene - Localized variant of type I NF involving scrotum & penis
Thank You

Questions?

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