DRUG ERUPTION

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Disclosures

- No Relevant Financial Relationships

DRUG ERUPTIONS

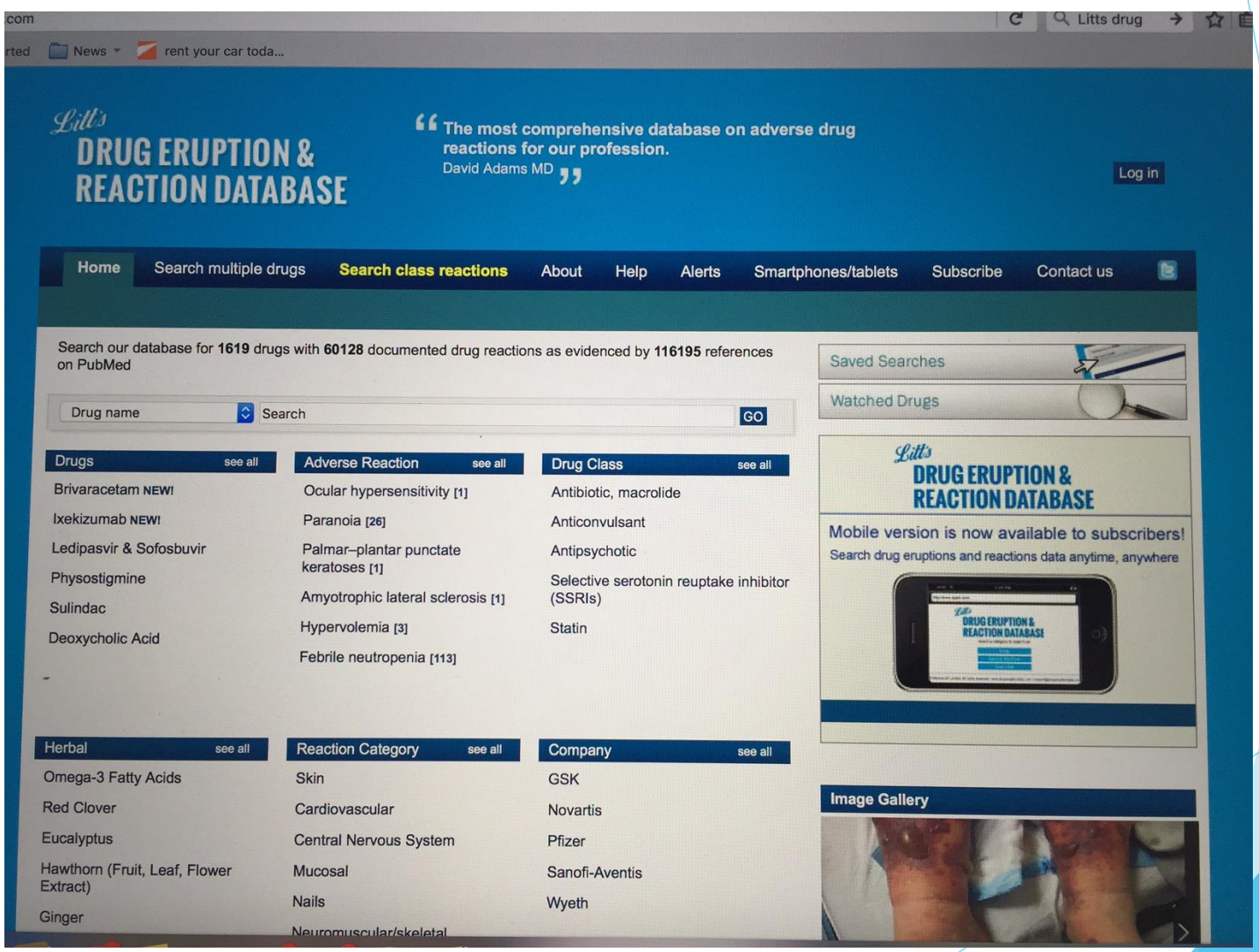
Drug Reactions
3 things you need to know

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

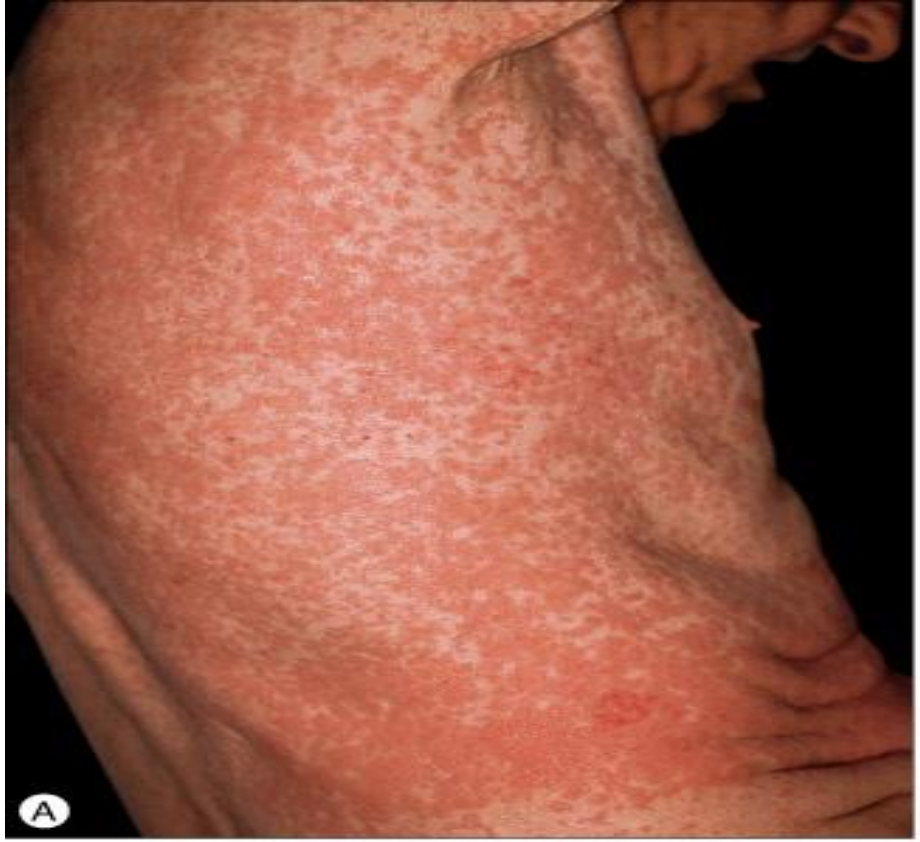


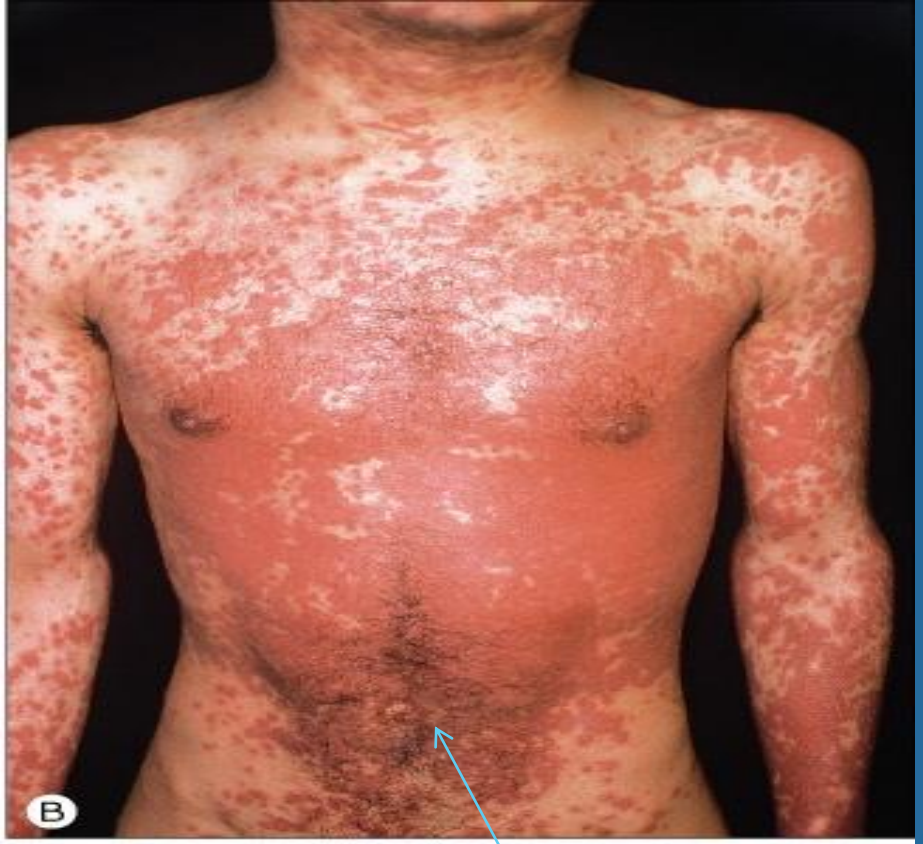
Drug Eruptions

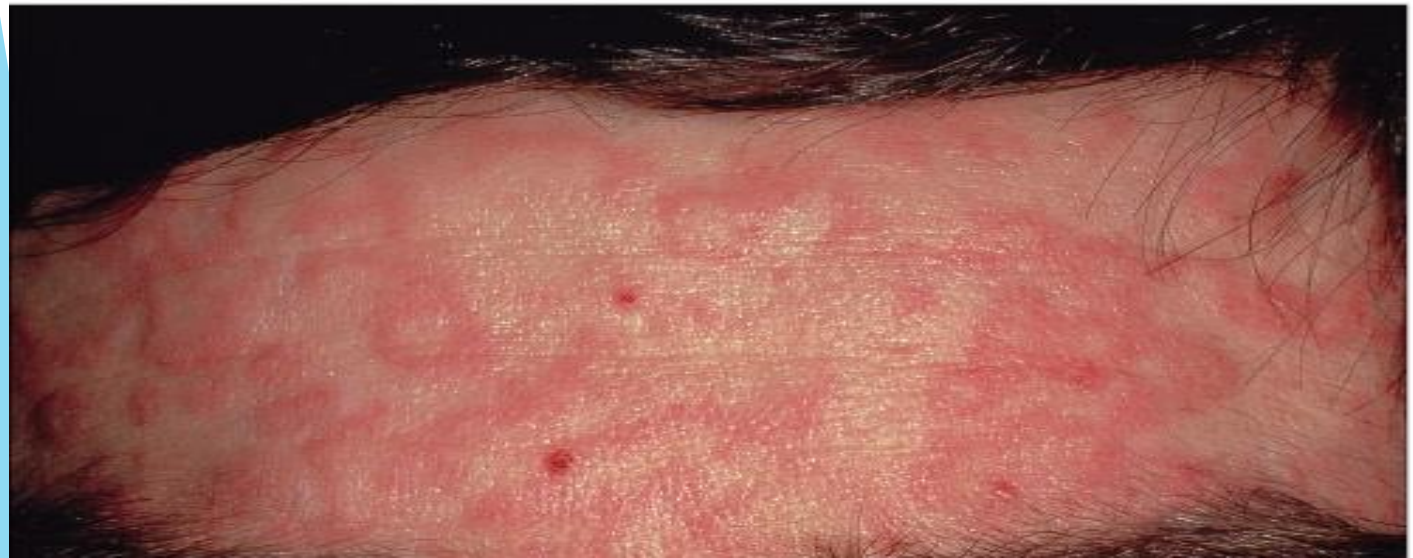
- Skin is one of the most common targets
- **Antibiotics** and **anticonvulsants are most common**
  - 1-5% of patients
- 2% of all drug eruptions are "serious"
  - TEN, DRESS
- More common in adult females and boys < 3 y/o
- Not all drugs cause eruptions at same rate:
  - Aminopenicillins: 1.2-8% of 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)

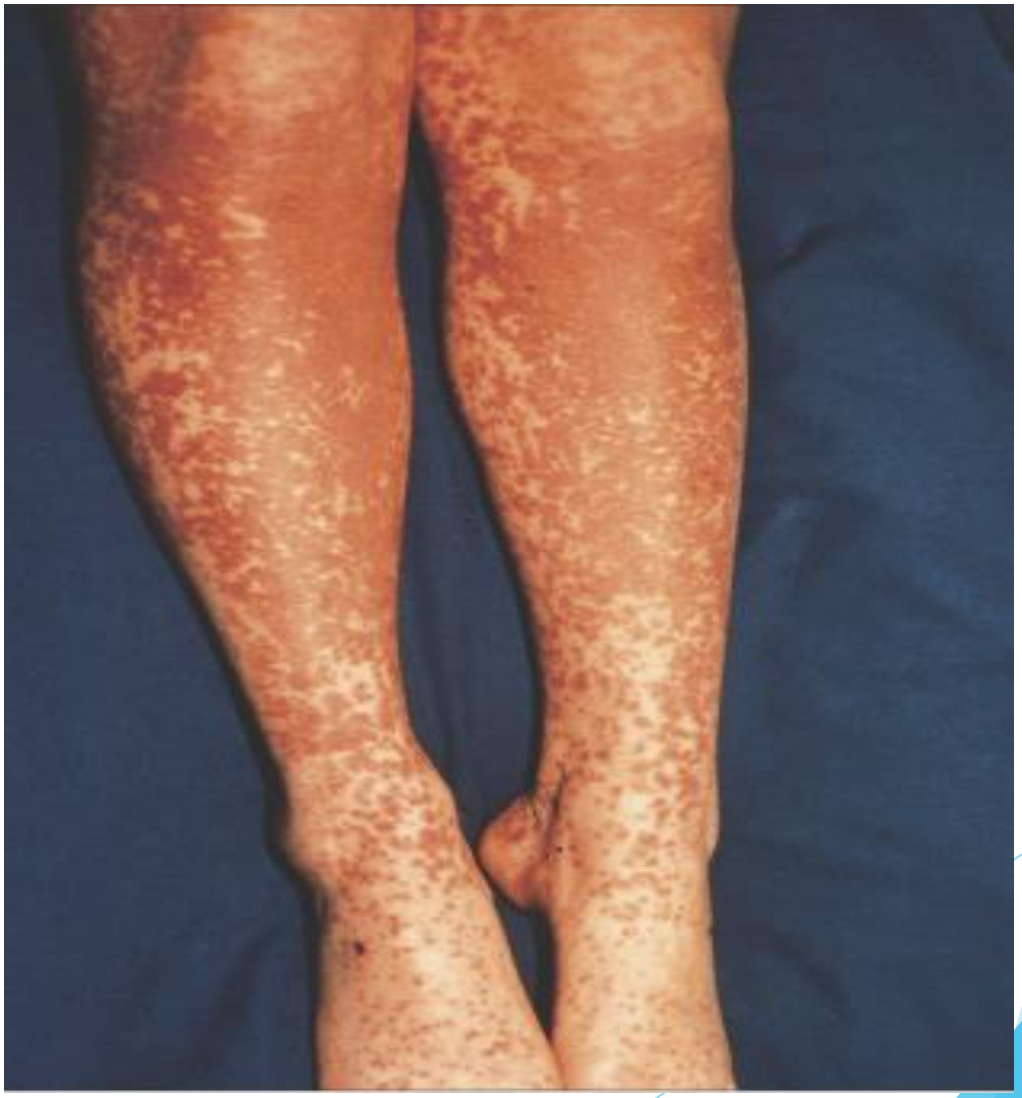




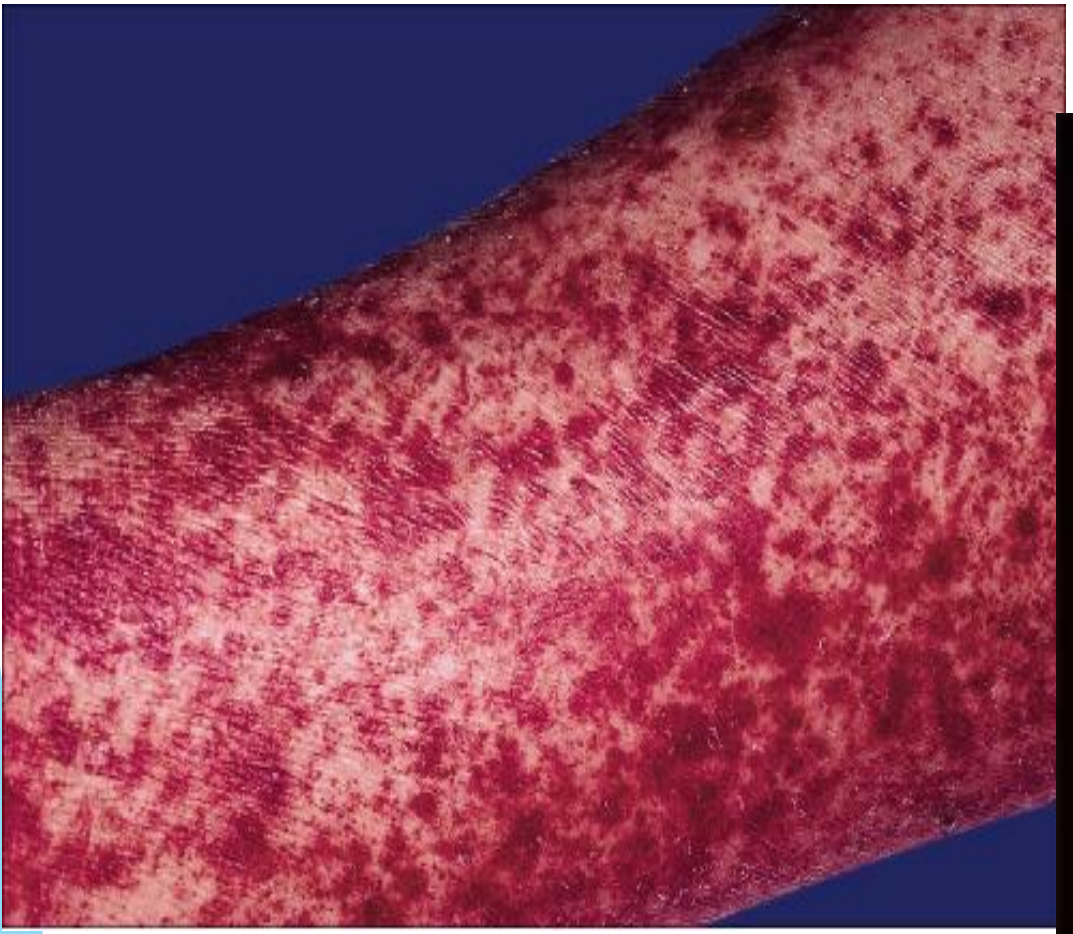


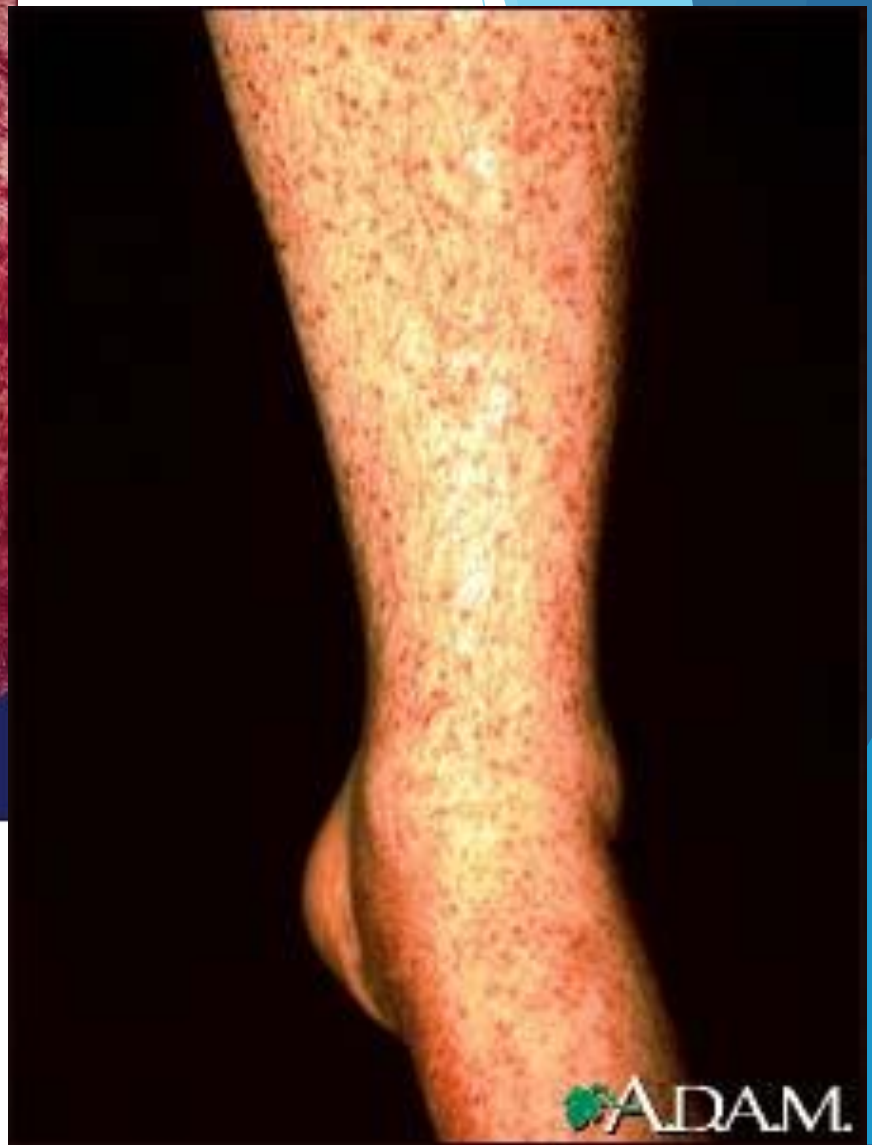
Note confluence of lesions on trunk

Morbilliform reaction to ampicillin-amoxicillin



Clinical presentation	Percentage that are drug-induced (%)	Time interval	Mortality (%)	Selected responsible drugs
Exanthematous eruption	Child: 10–20 Adult: 50–70	4–14 days	0	Aminopenicillins Sulfonamides Cephalosporins Anticonvulsants Allopurinol
Urticaria Anaphylaxis	<10 30	Min-hours Min-hours	0 5	Penicillins Cephalosporins NSAIDs Monoclonal Abs Contrast media
Fixed drug eruption	100	First exposure: 1–2 weeks Re-exposure: <48 hours, usually within 24 hours	0	TMP-SMX NSAIDs Tetracyclines Pseudoephedrine
Acute generalized exanthematous pustulosis (AGEP)	70-90	<4 days	1-2	β-Lactam antibiotics Macrolides Calcium channel block.
Drug reaction with eosinophilia and systemic symptoms (DRESS)	70-90	15-40 days	5-10	Anticonvulsants Sulfonamides Allopurinol Minocycline Lamotrigine
Stevens–Johnson syndrome (SJS) Toxic epidermal necrolysis (TEN)	70-90	7-21 days	5 30	Sulfa Anticonvulsants NSAIDS Allopurinol

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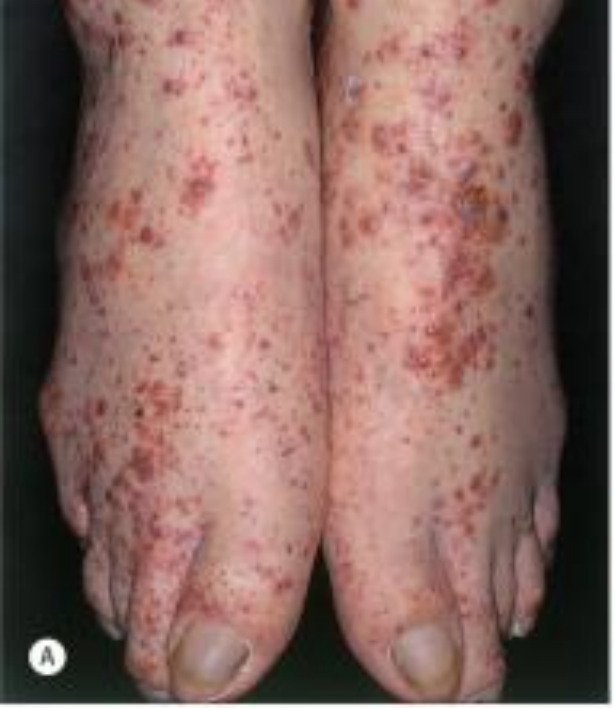
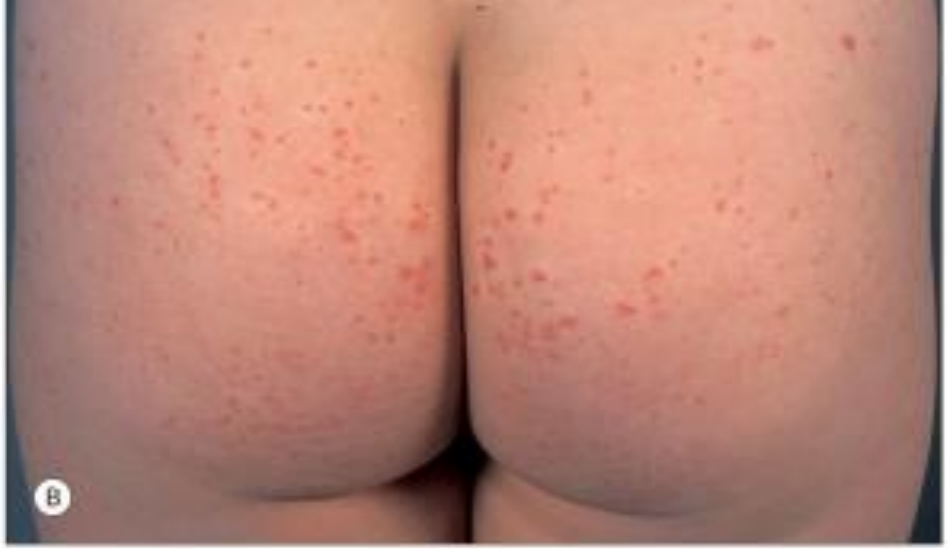
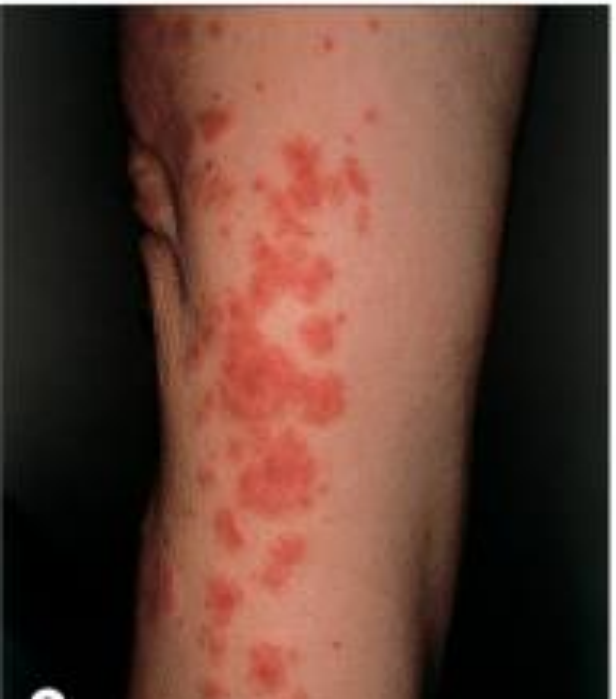
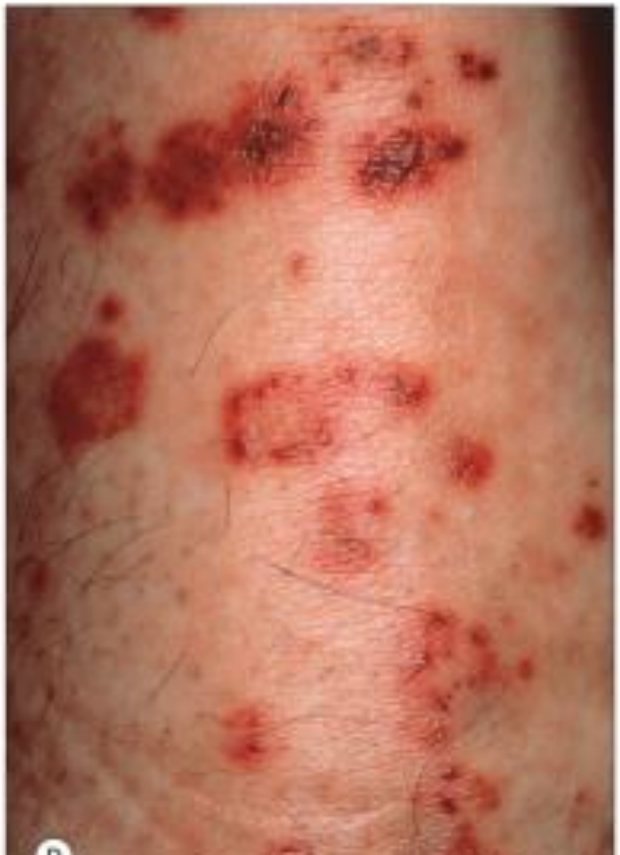
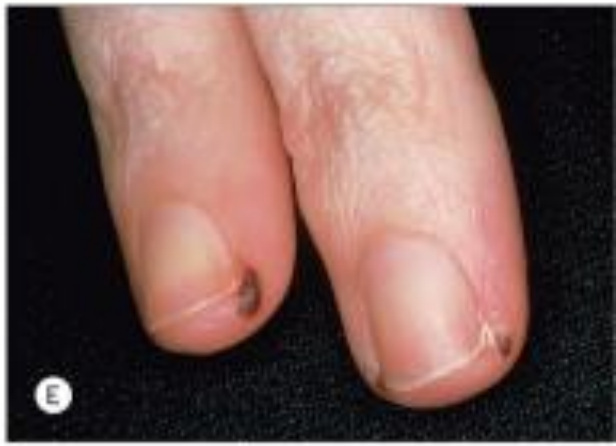






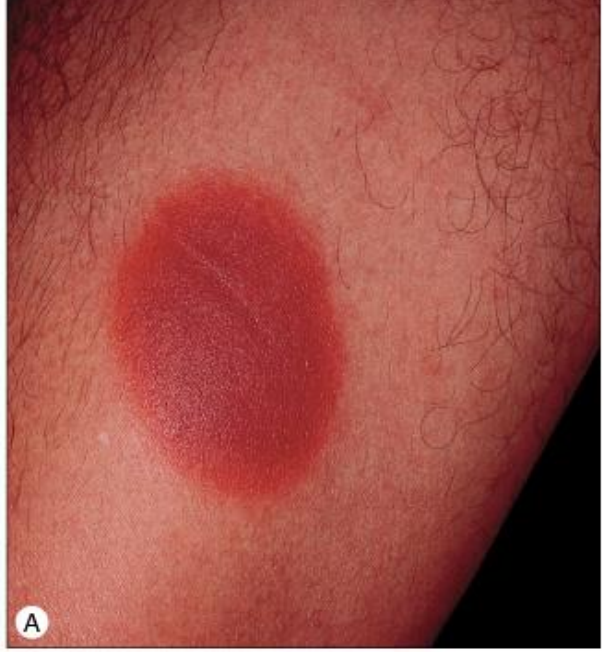


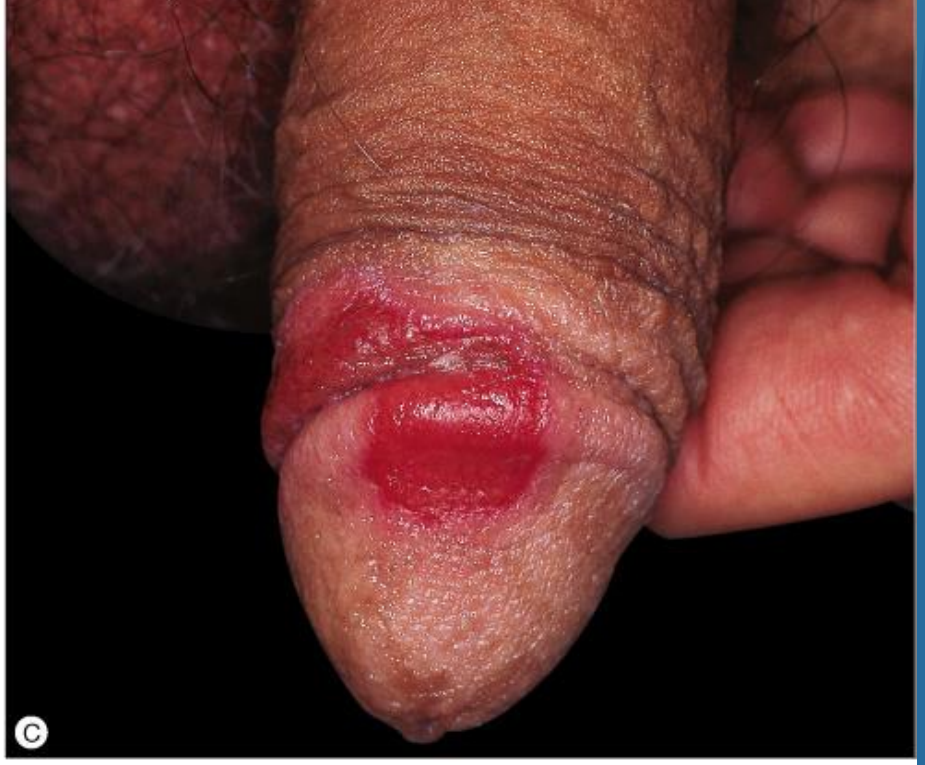


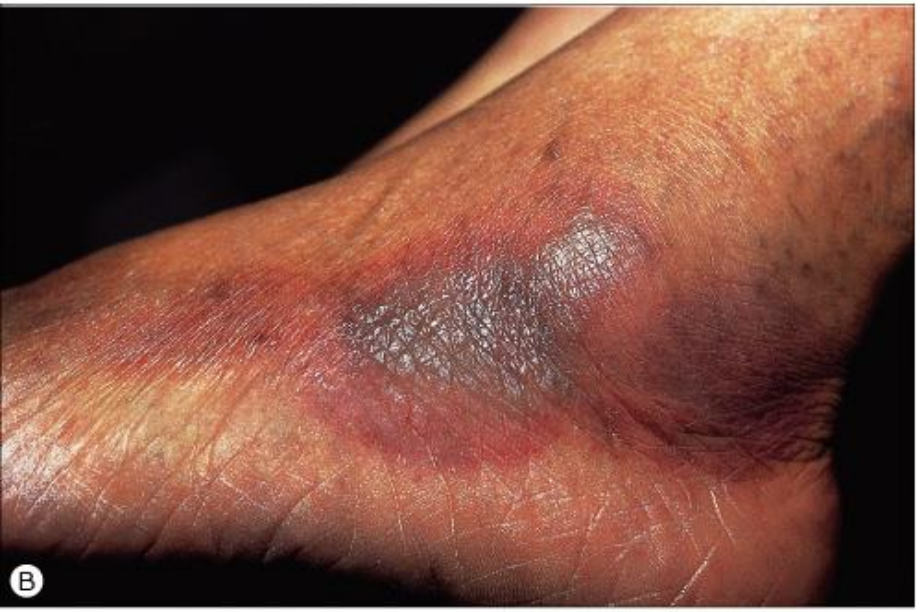
Vasculitis

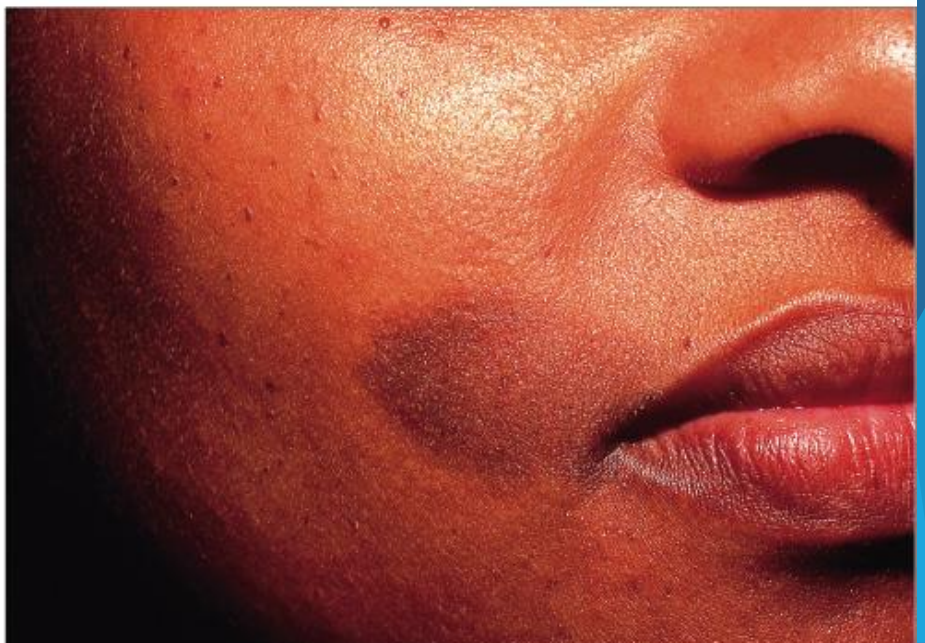
Drug Induced Vasculitis

- 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

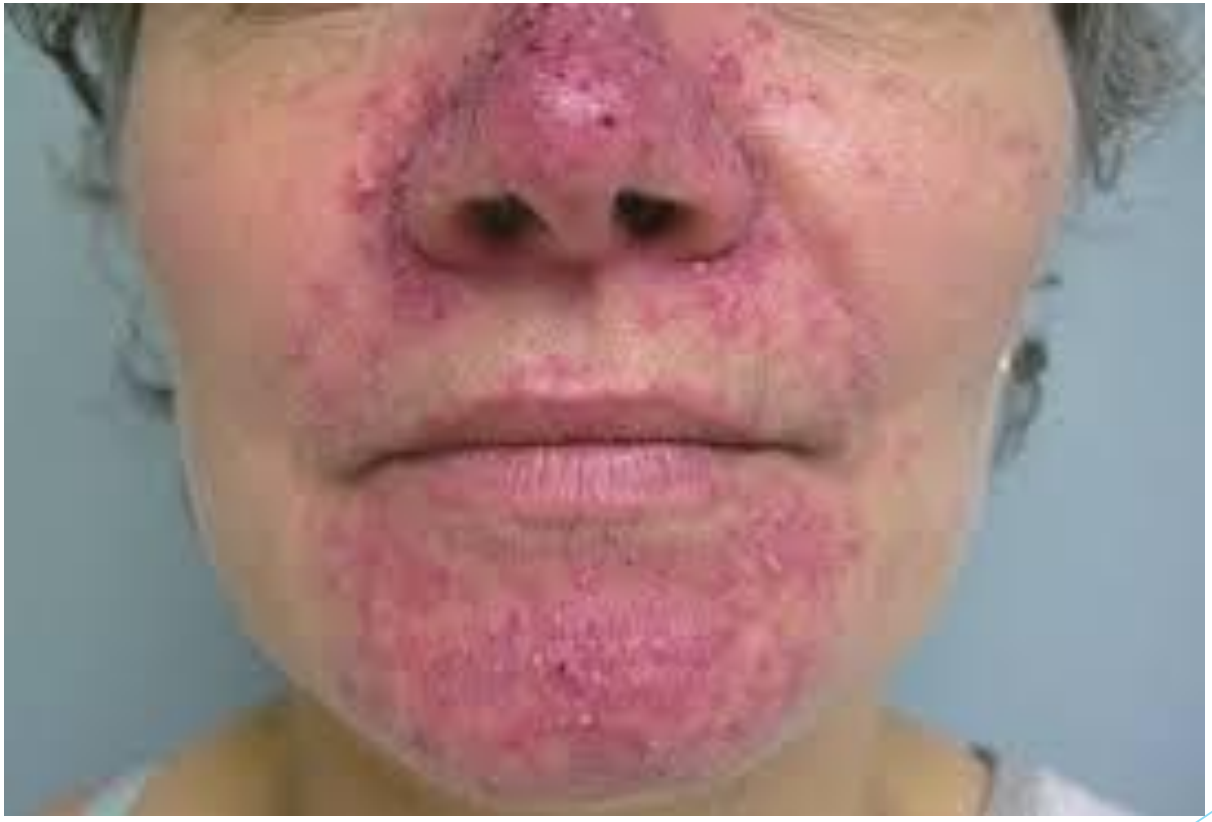
Fixed Drug Eruptions

- 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

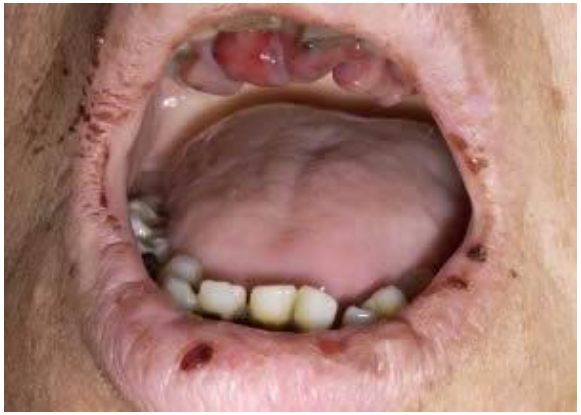
- Epidermal growth factor receptor (EGFR)
  - Treatment of advanced lung, pancreatic, colorectal, and head and neck cancers
    - Monoclonal antibodies
      - Cetuximab, panitumumab
    - Small-molecule tyrosine kinase inhibitors
      - Gefitinib, erlotinib, lapatinib
  - Cutaneous adverse events to 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
- <u>Clinical:</u>
  - 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)

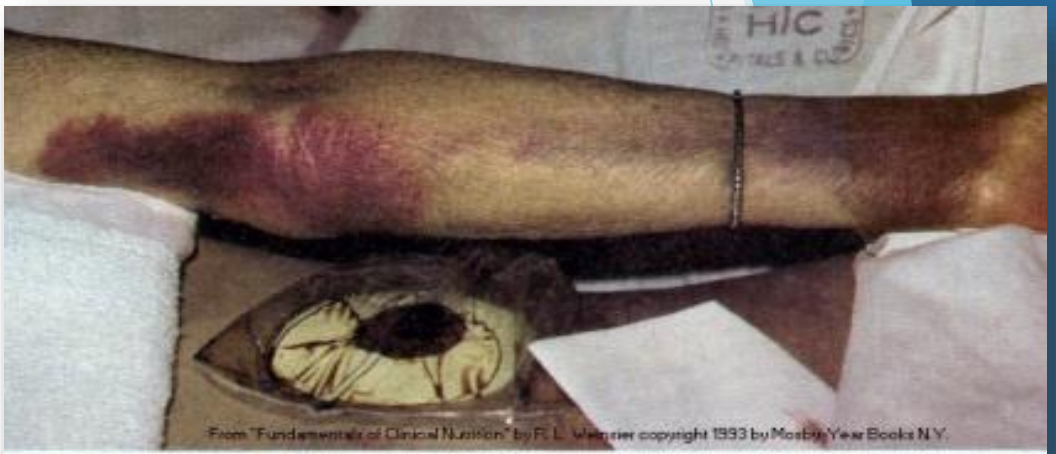
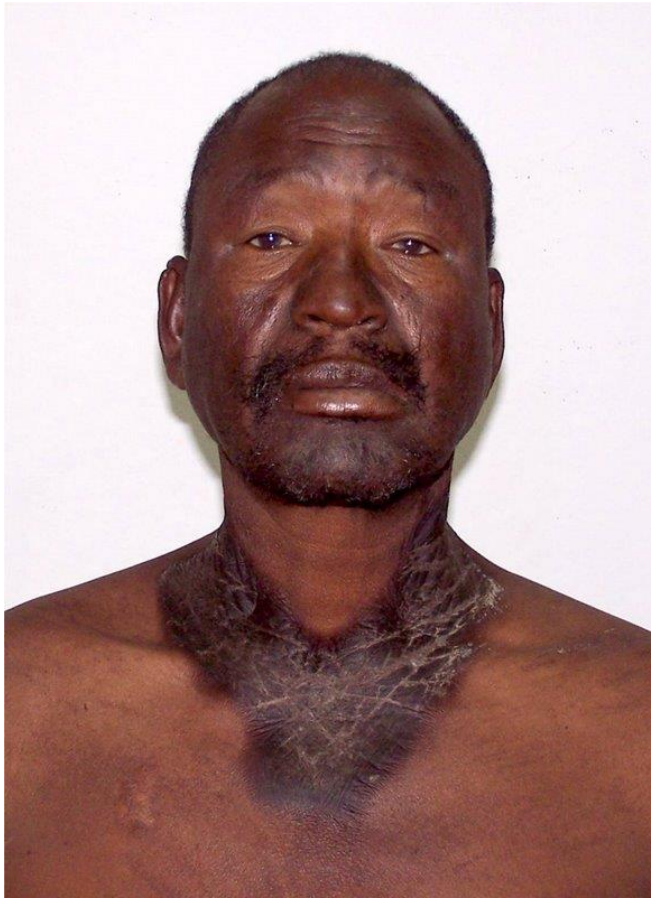


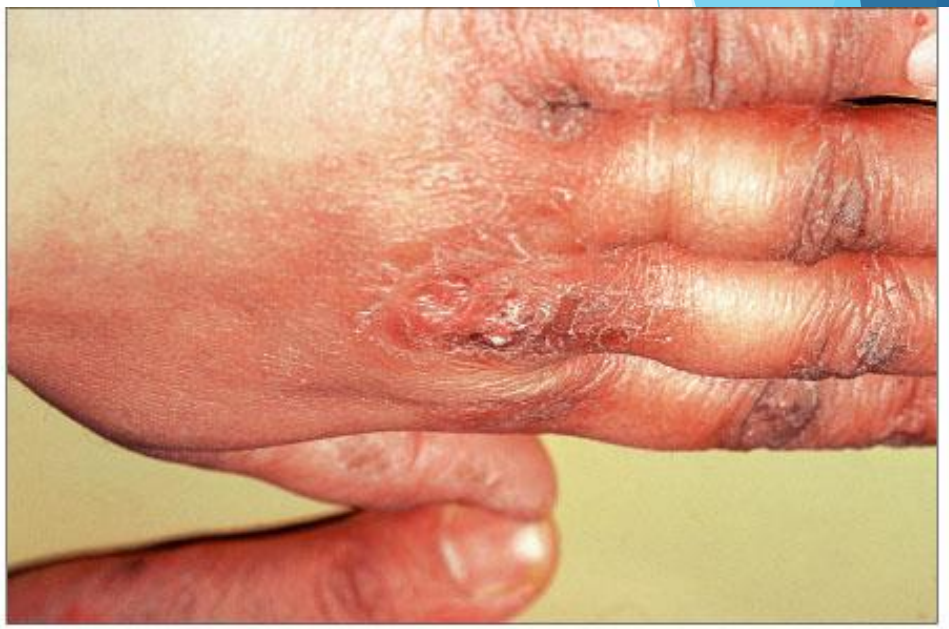
Fig. 6-5 Easy bruisability in vitamin K deficiency.

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 demyelinization 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

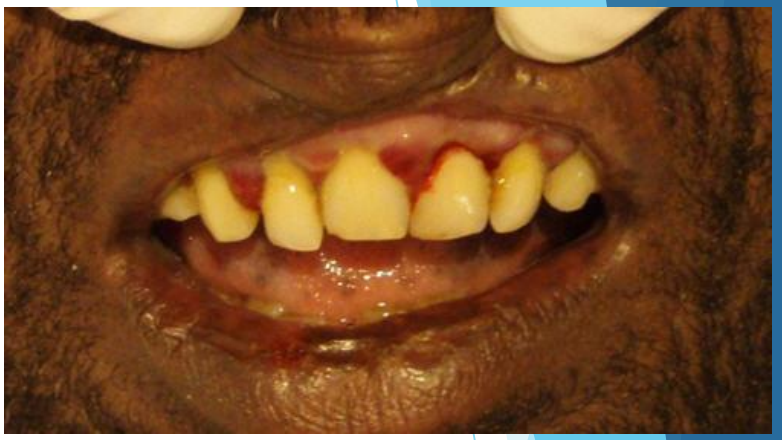
Pellagra

- 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

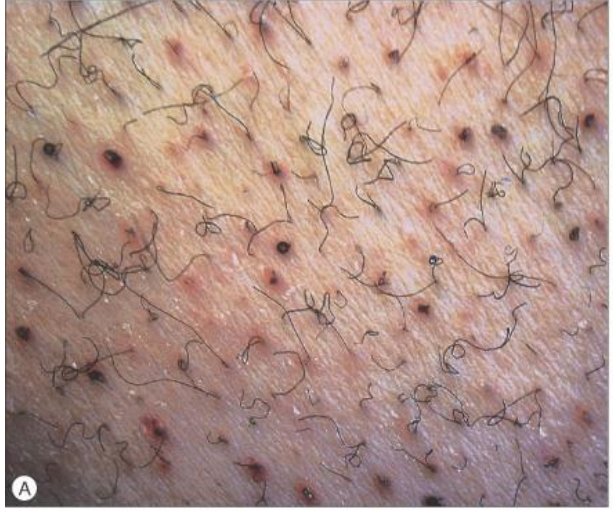
VITAMIN C DEFICIENCY
Scurvy

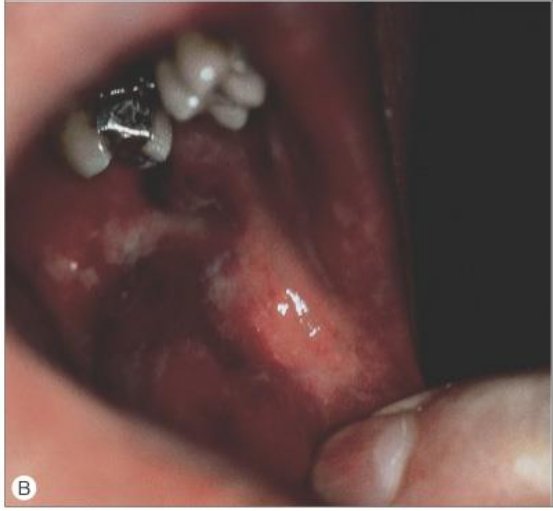
- Water-soluble vitamin found in fresh fruits, vegetables
- Roles:
  - Collagen & ground substance formation
  - Synthesis of epinephrine & carnitine
  - Leukocyte function, iron absorption, folic acid metabolism
- Reducing agent:
  - **Cofactor for hydroxylation of procollagen → collagen**
- **Elderly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

Scurvy



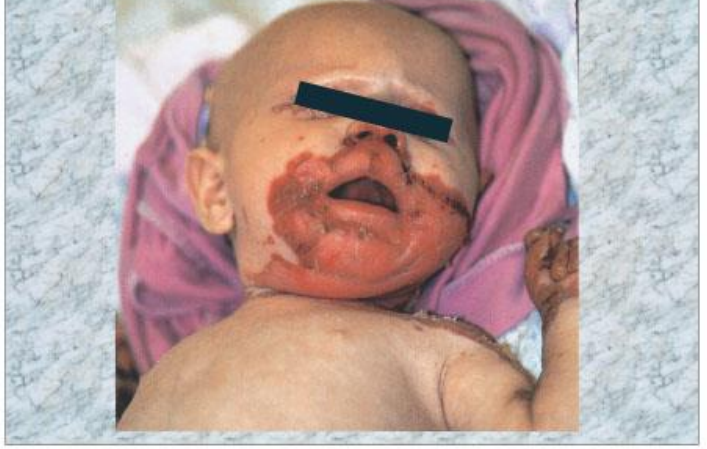
- Four Hs:
  - Hemorrhage
    - Hemorrhagic gingivitis
    - Epistaxis
    - Perifollicular petechiae
    - Subungual, IM, and intraarticular hemorrhage
    - Subperiosteal hemorrhage leading to pseudoparalysis
  - Hyperkeratosis of the hair follicles
  - Hypochondriasis
  - Hematologic abnormalities



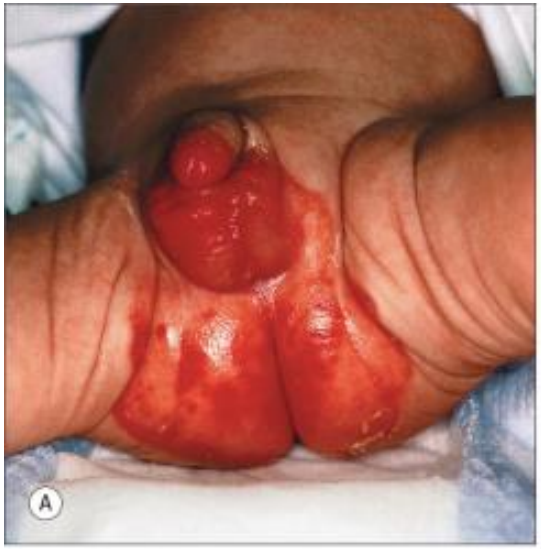


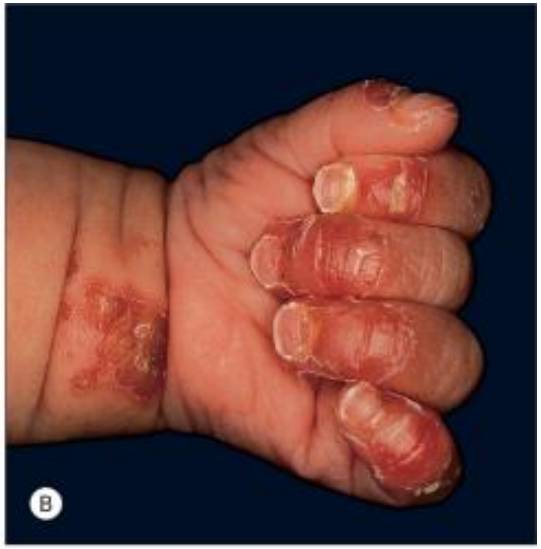
- Clinical
  - Woody edema
  - **Corkscrew hairs** → plugging of hair follicles by curled hairs
    - Forearms, abdomen, thighs
  - Delayed wound healing
    - due to secondary defect in collagen formation
  - ***Depression***
  - **ANEMIA** (secondary to bleeding)
- Tx:
  - Ascorbic acid 1000 mg/day
  - Maintenance dose of 100 mg/day should be considered

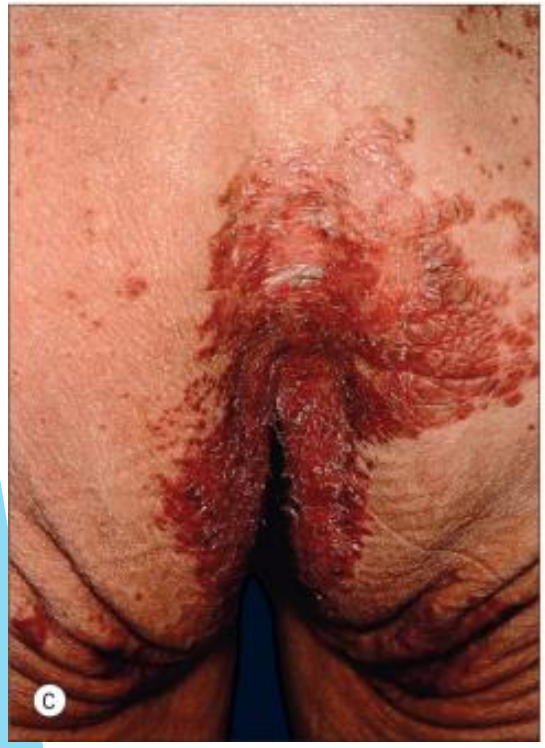
Zinc Deficiency

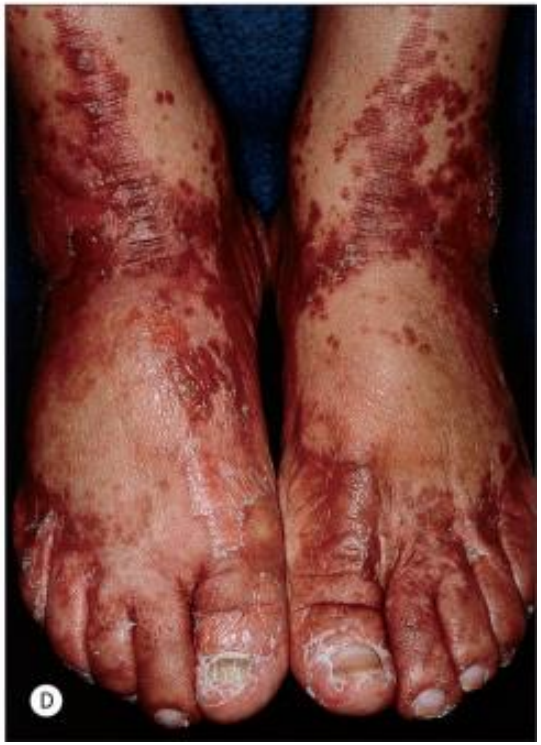


- Functions of Zinc:
  - **Wound healing**
  - Immune/reproductive/neuropsychiatric function
- Inc. zinc requirements:
  - infections, post-surgery, pregnancy, cancer
- *Largely dependent on food intake*
  - Nuts, whole grains, green leafy vegetables, shellfish, human milk
- **Presents most commonly 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









Zinc Deficiency

Genetic

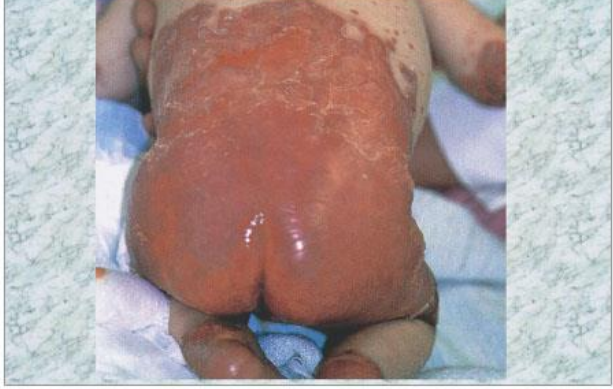
“acrodermatitis enteropathica”

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 chelitis 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

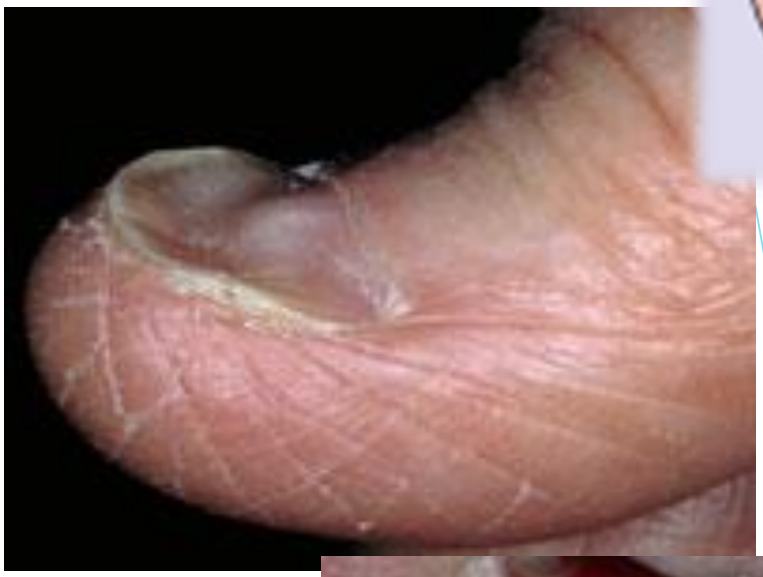
- Dx:
  - Low serum zinc levels but not diagnostic
  - **LOW alkaline phos** (zinc-dependent enzyme)
- Tx:
  - Zinc sulfate PO 1 to 2 mg/kg/day
  - **Acrodermatitis enteropathica**: 3 mg/kg/day **lifelong**
  - Warm compresses and petroleum applied TID to areas of weeping or crusted dermatitis to support reepithelialization

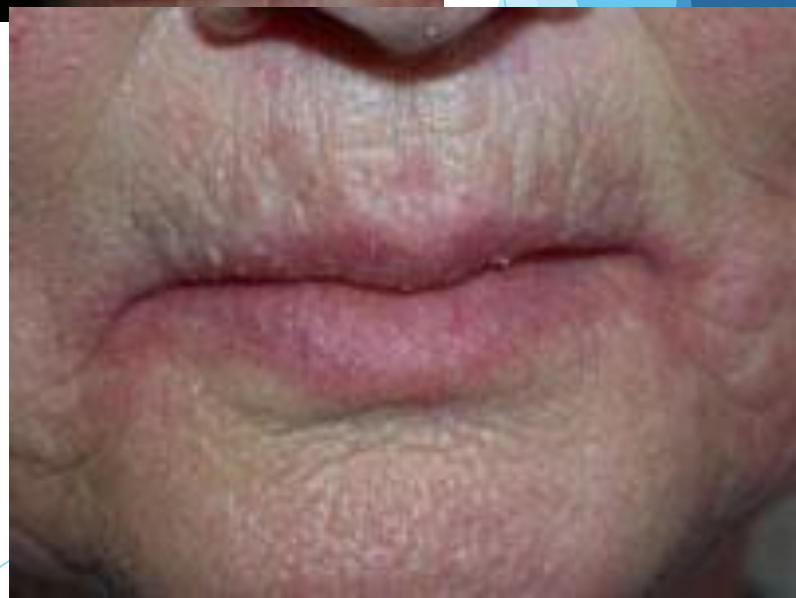
Iron Deficiency

- 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

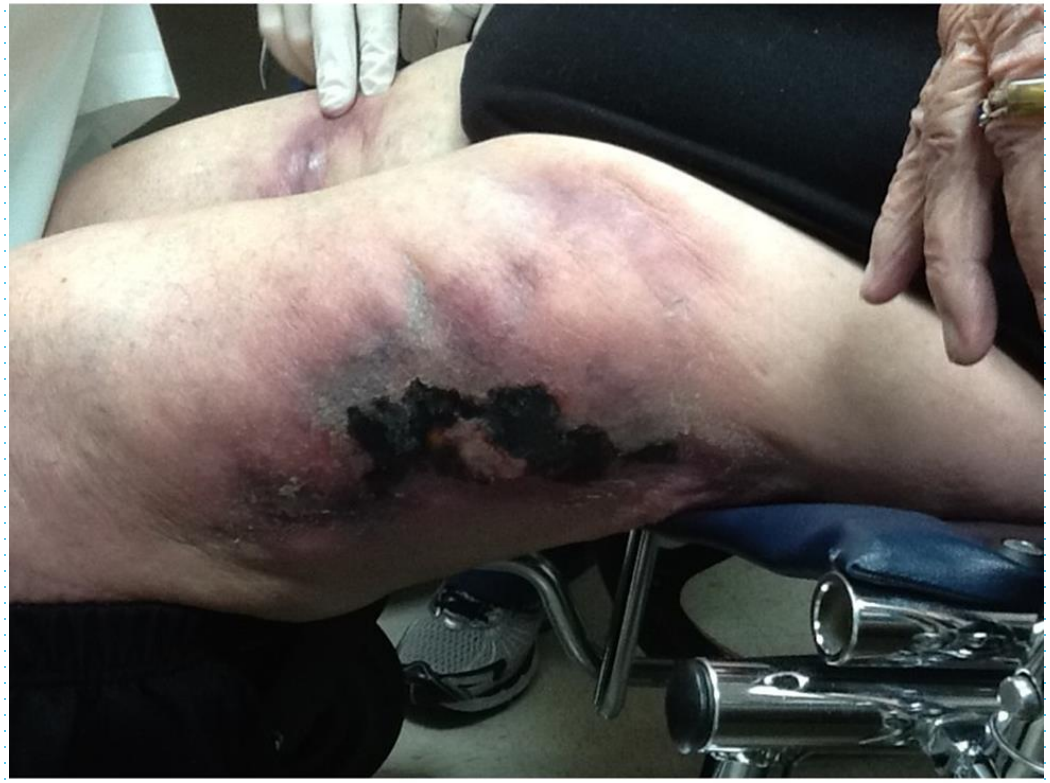




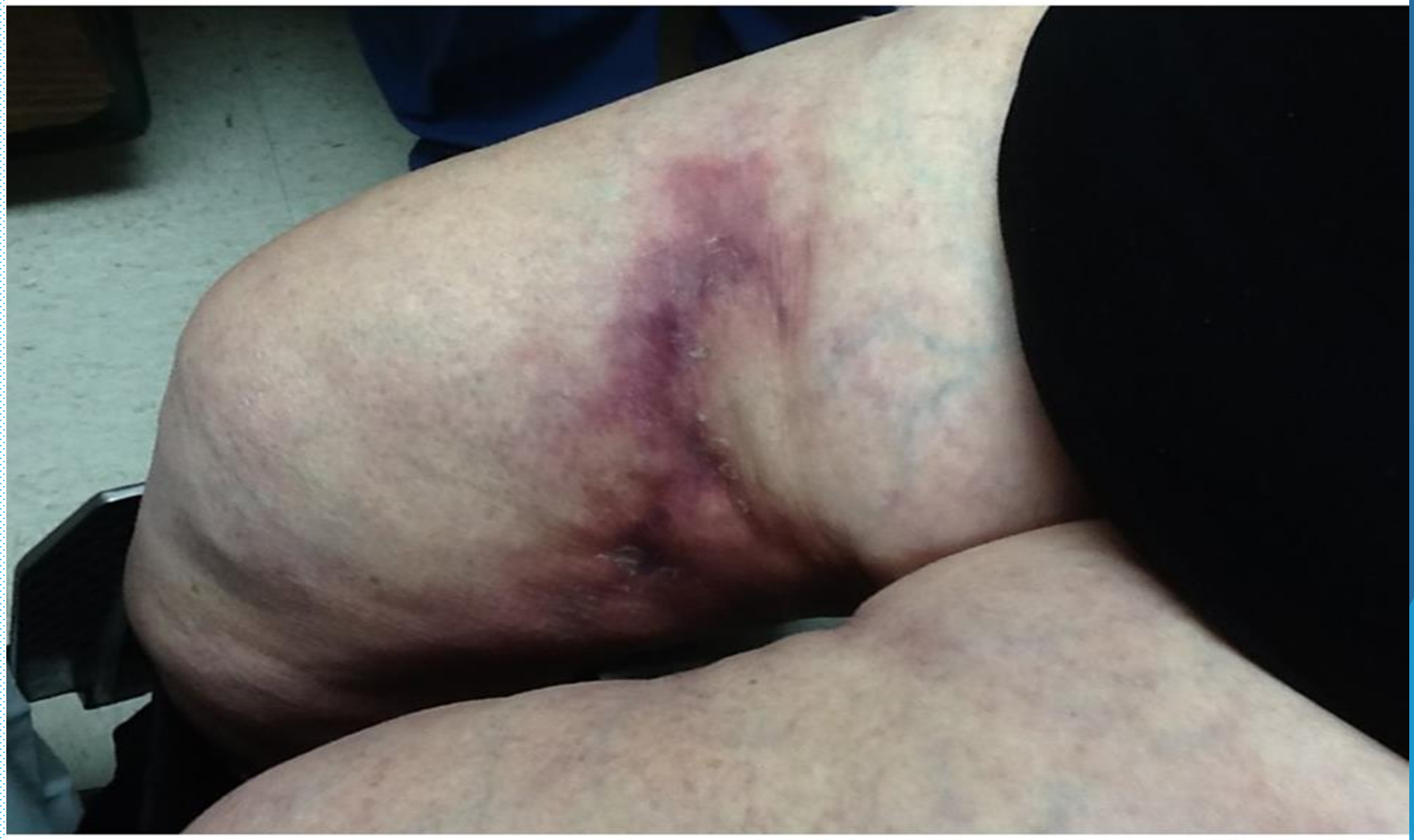
Case

- 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



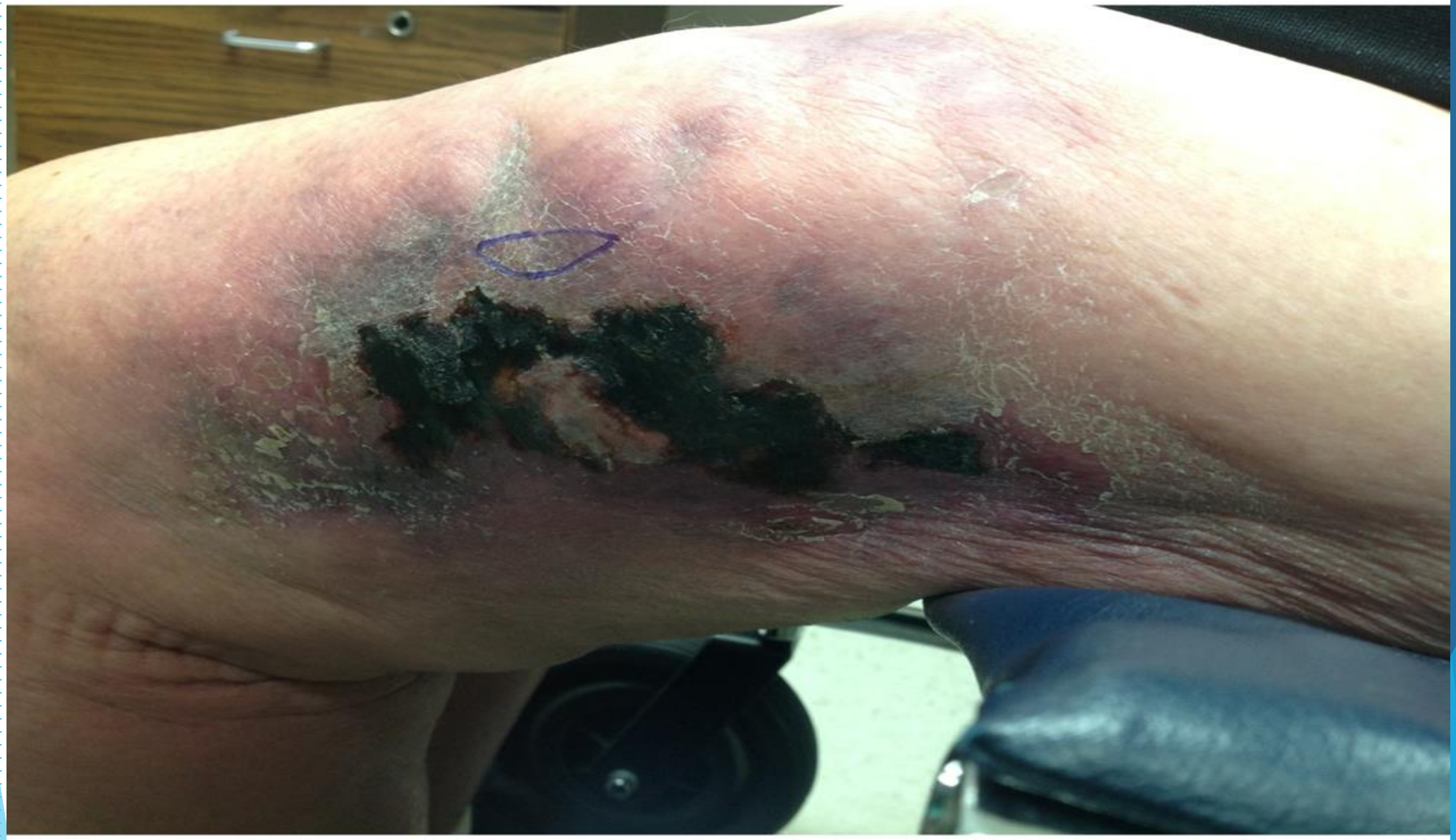
Patient History

- 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

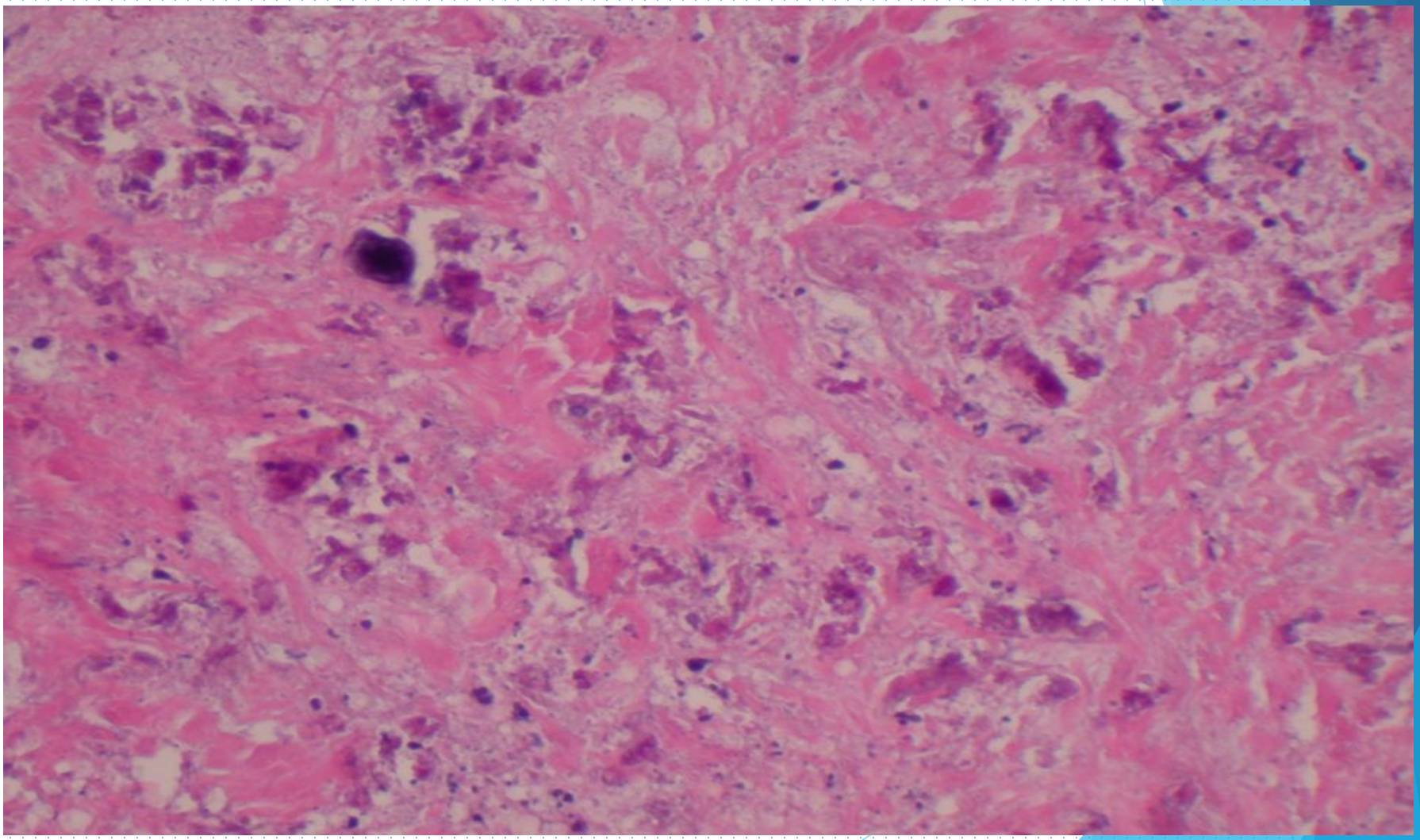
Labs

- 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

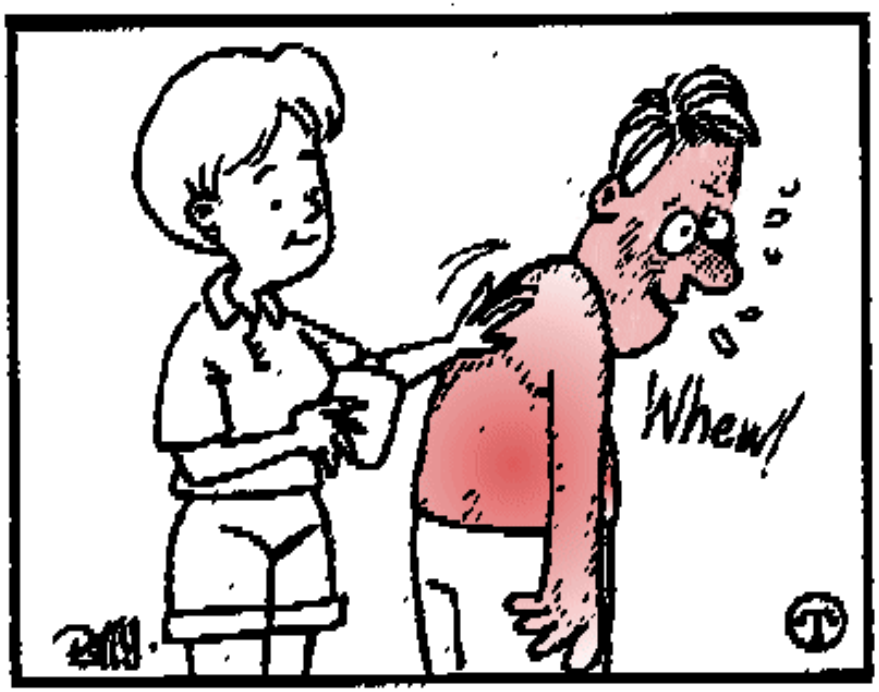
- Treatment
  - Evidence based guidelines have yet to be determined
  - IV Sodium thiosulfate – calcium binder and antioxidant
  - Wound care and pain management
  - Oxygen therapy
  - Correct any underlying lab abnormalities

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

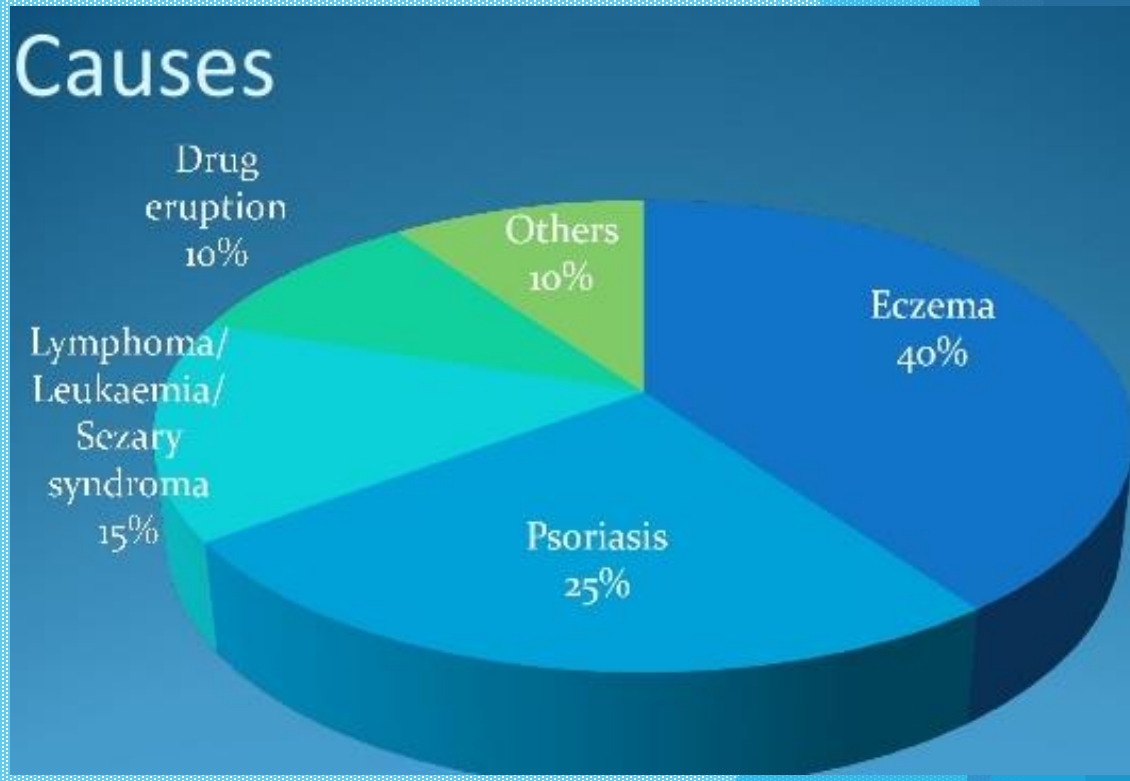
HELP!

- I am Red and Scaly From Head to Toe!

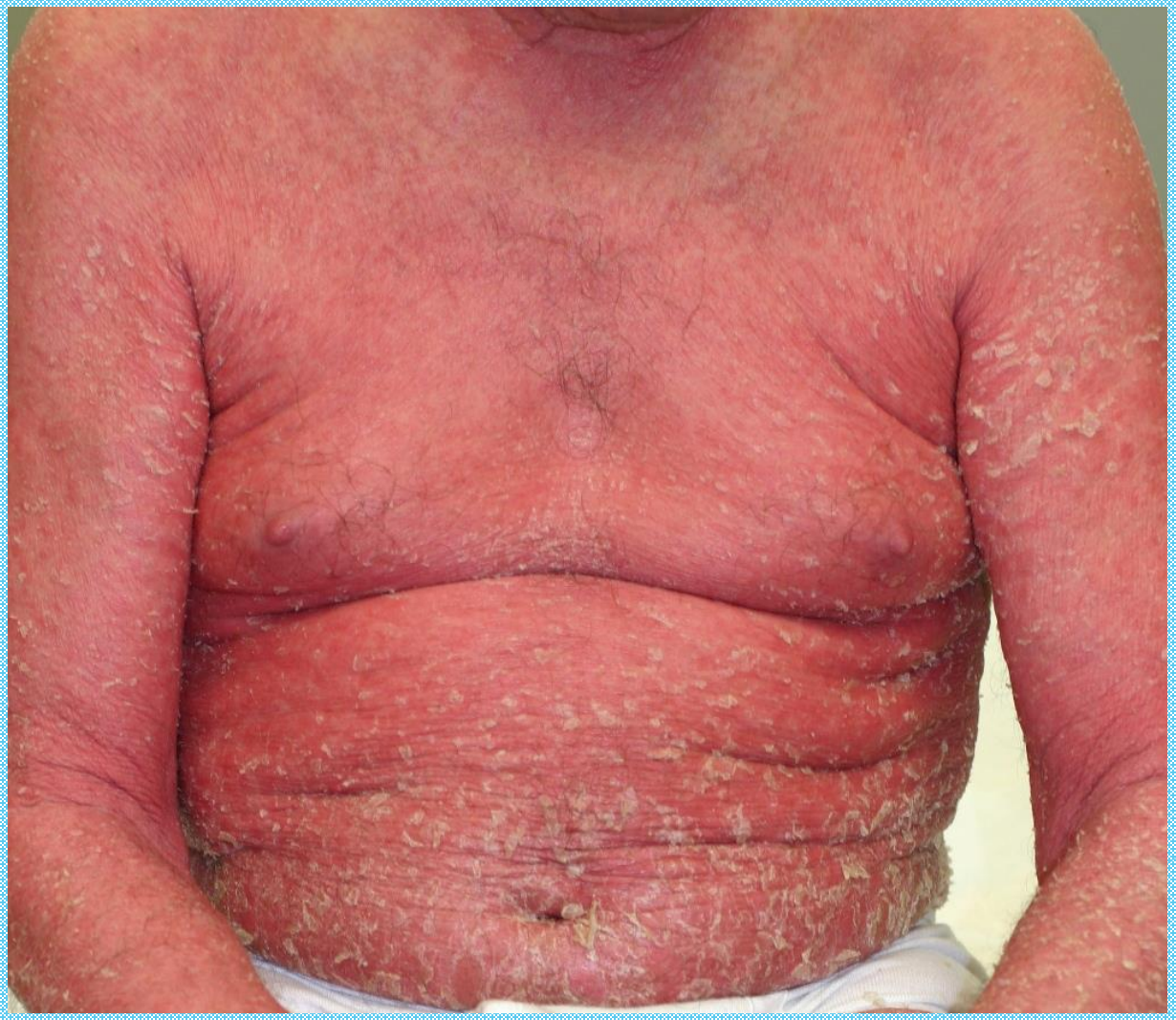


Erythroderma

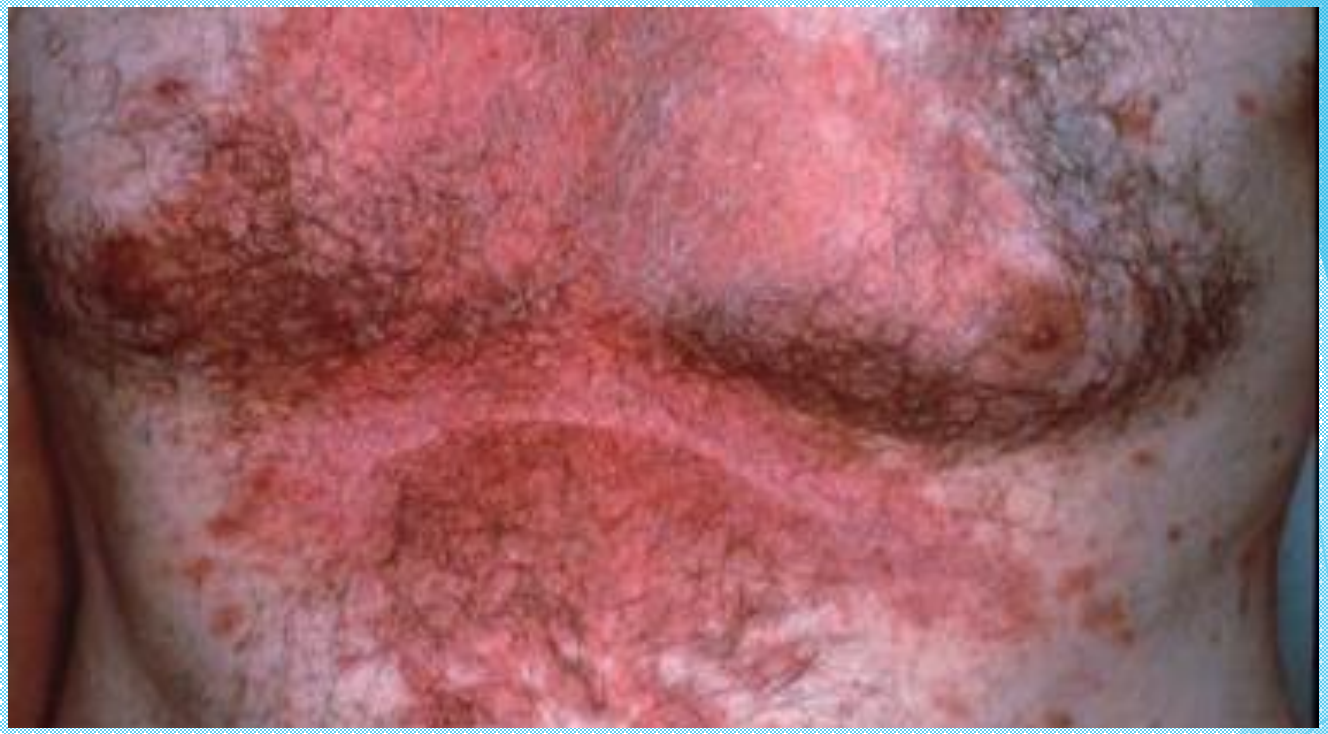
- What is it?
  - Exfoliative dermatitis that involves >90% surface area
- Causes
  - Psoriasis
  - Seborrheic Dermatitis
  - Drug Eruptions
  - Pityriasis rubra pilaris
  - Lymphoma
  - Eczema
  - Infection
    - Bacterial
    - Fungal
    - Viral
  - Autoimmune bullous dz



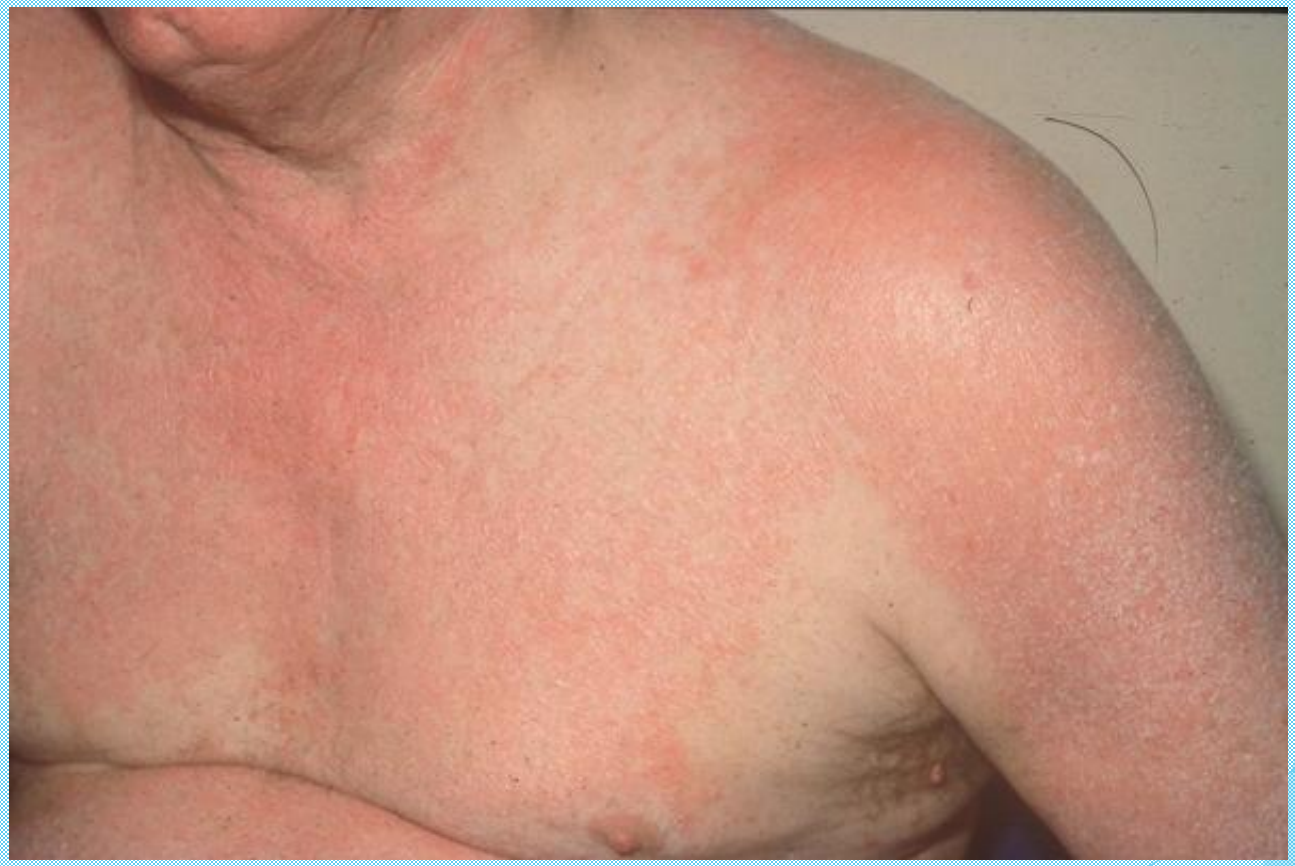
Psoriasis



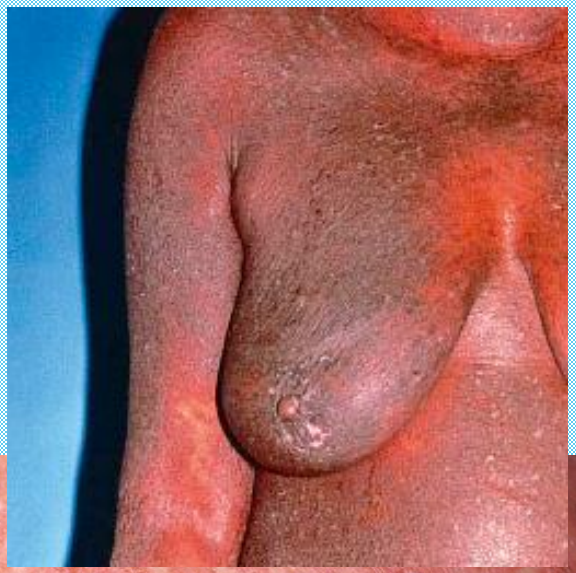
Seborrheic Dermatitis

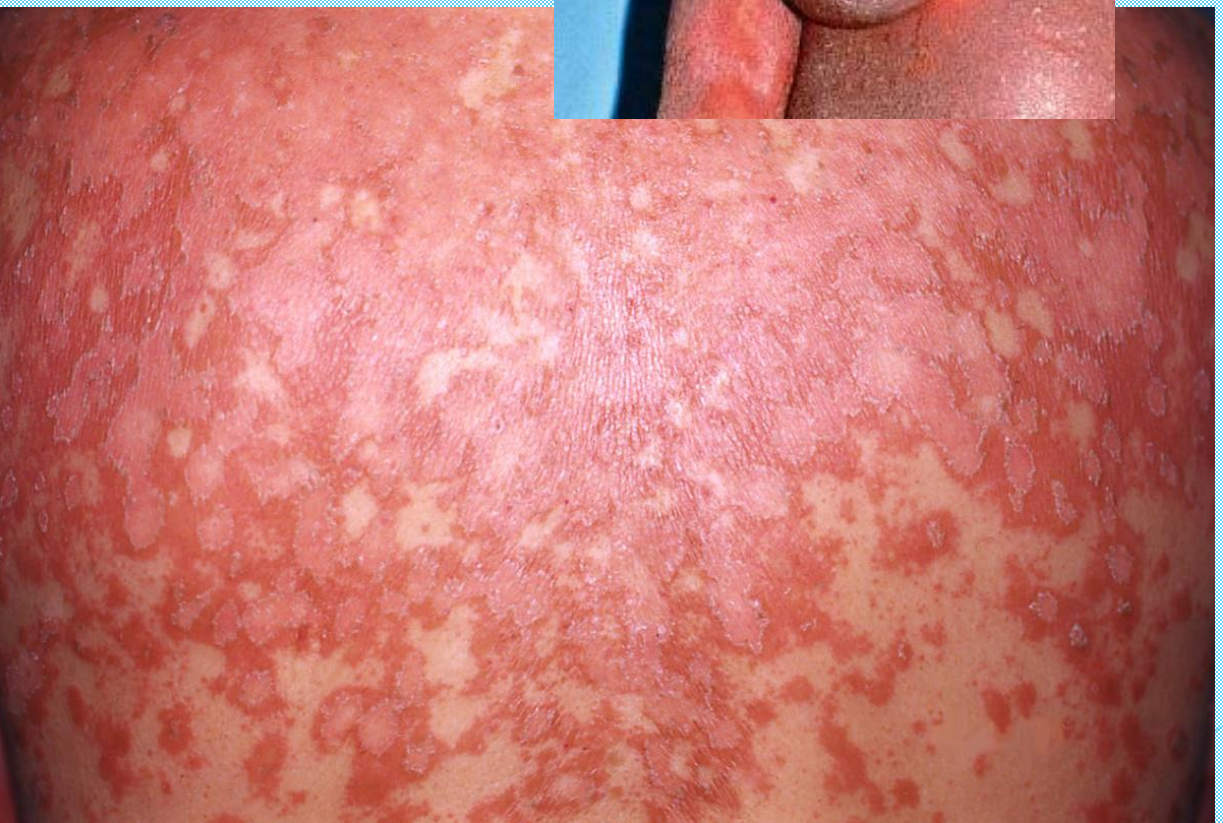


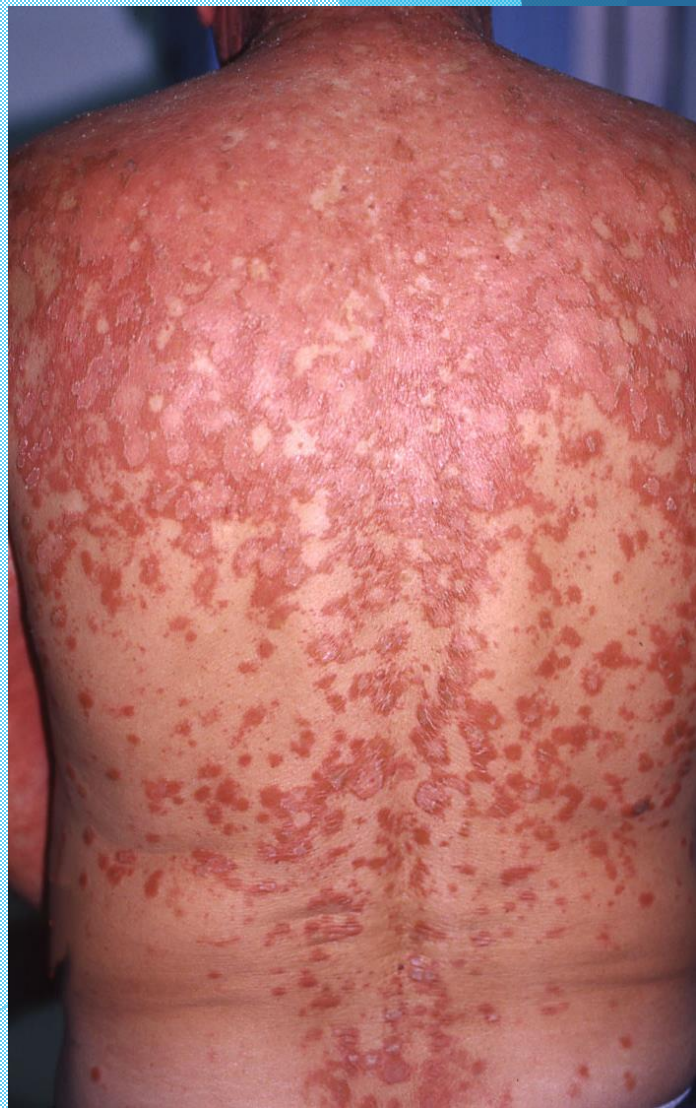
Drug Eruption



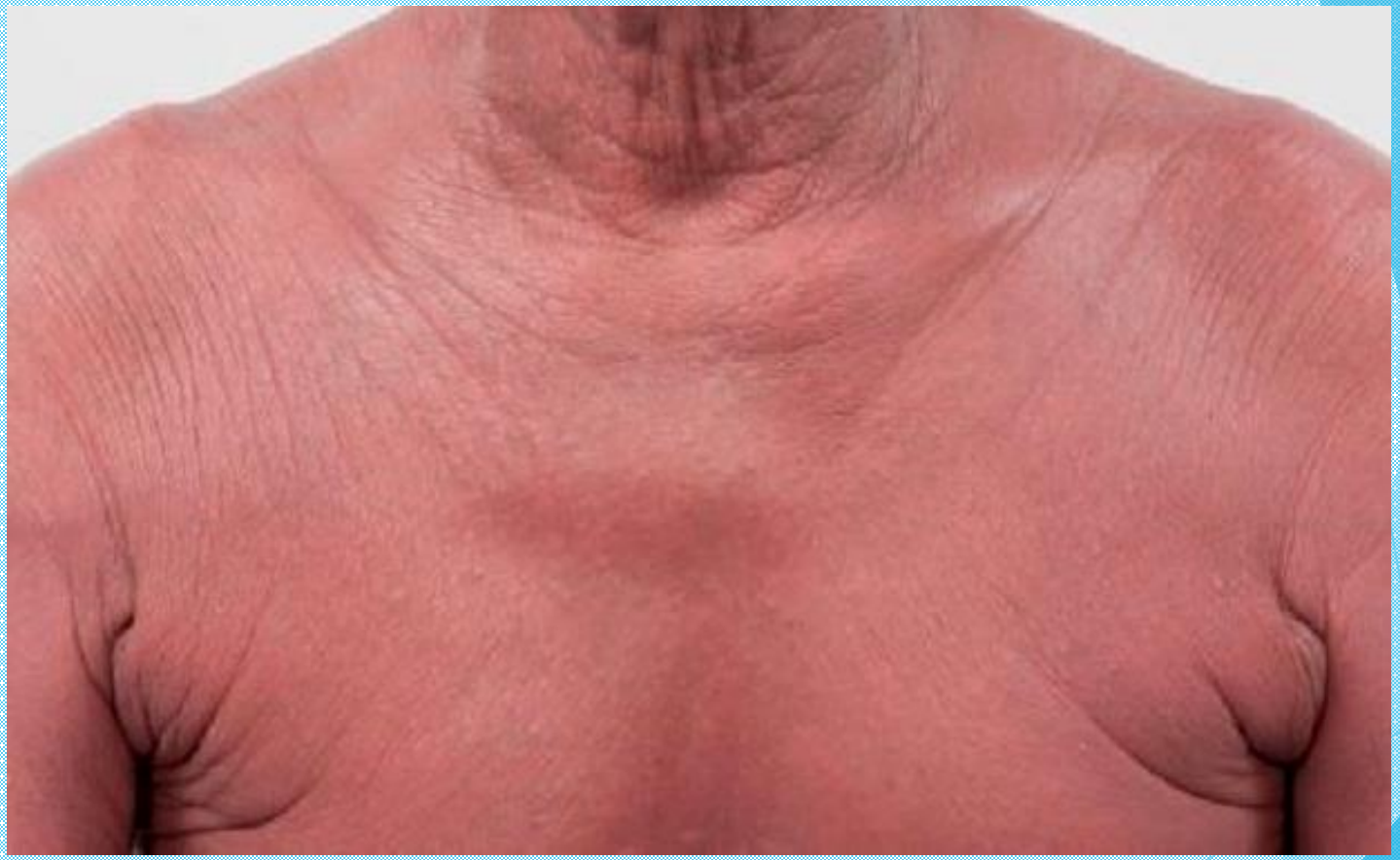
Pityriasis Rubra Pilaris



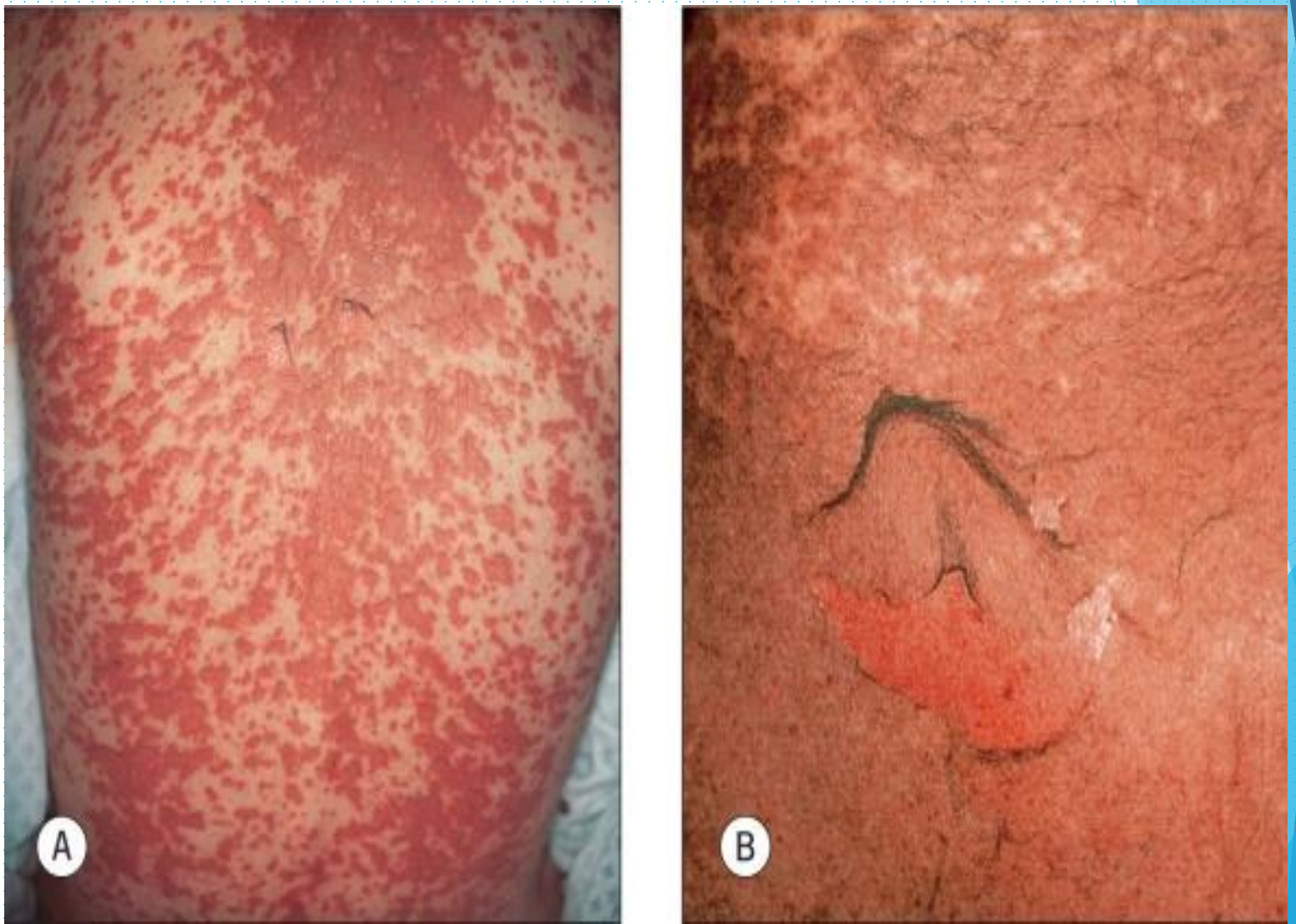




Lymphoma

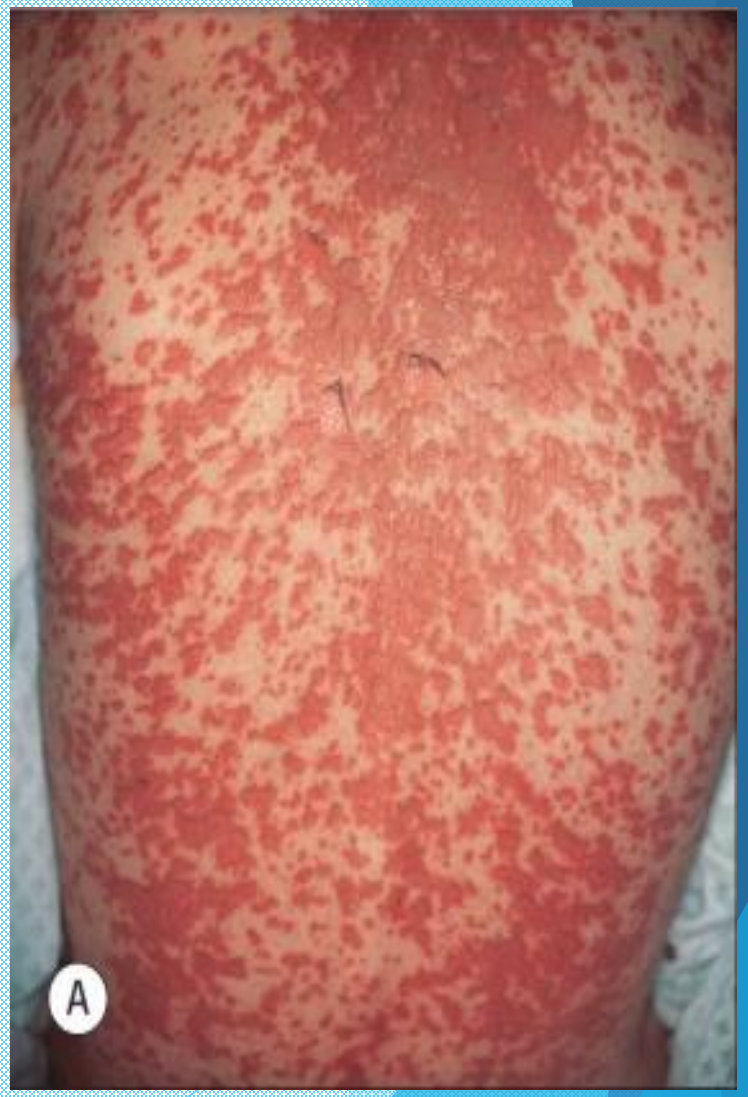


Case 1: 65 y/o Female presents w/ “tender skin all over” which began after few days of coughing and fever and chills

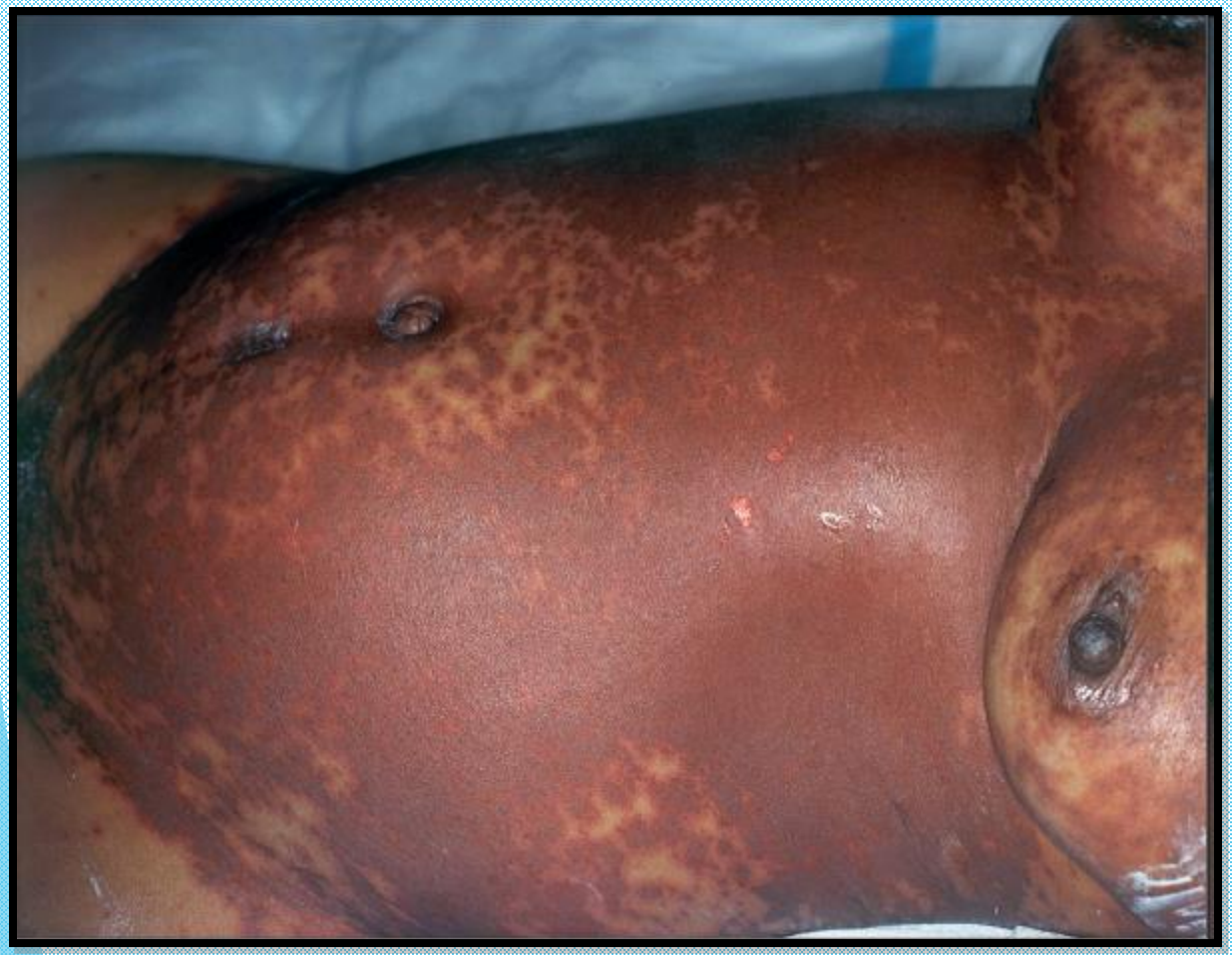


Case 1: Continued…

- 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)

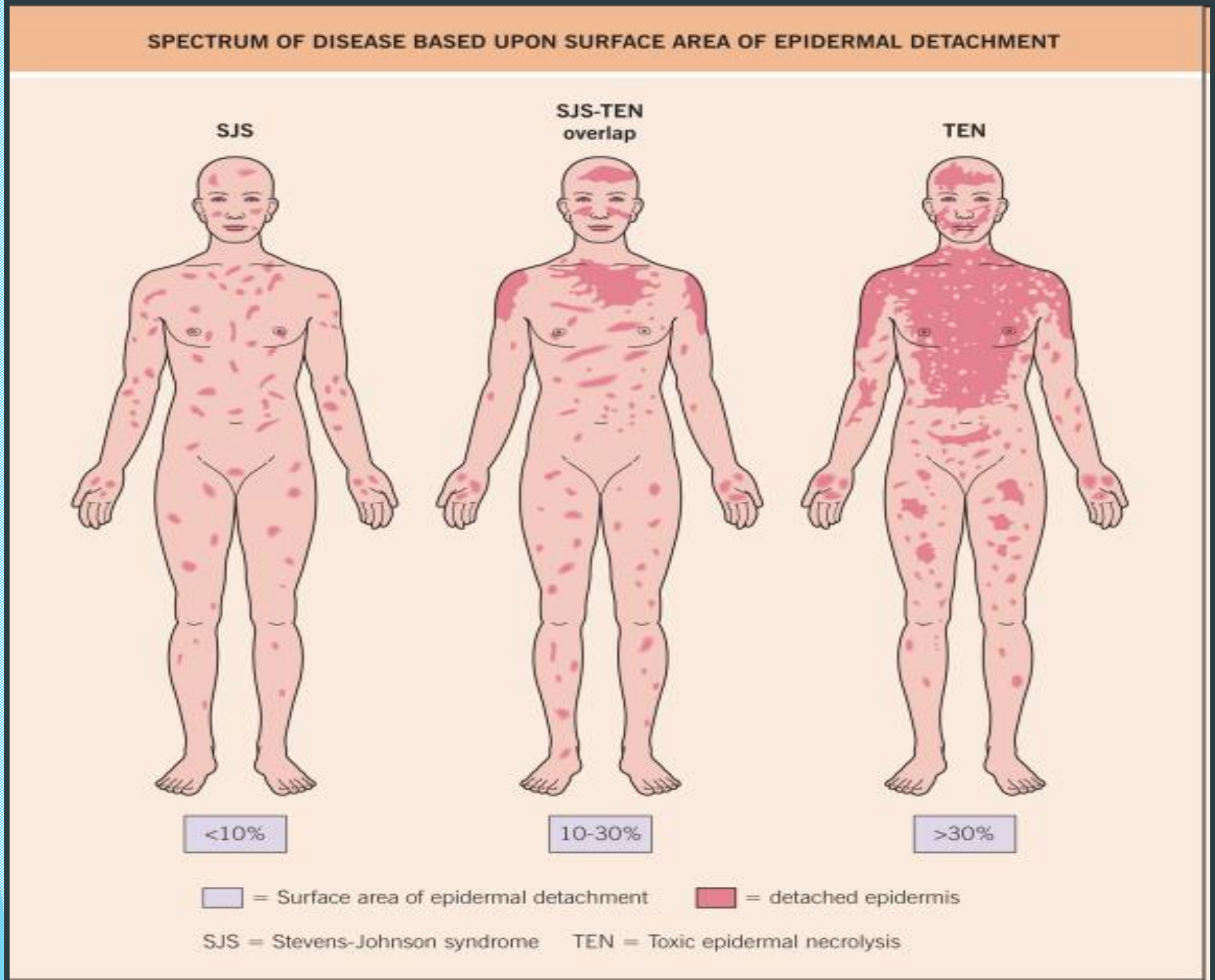


Characteristic dusky red color of the early macular eruption

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)**

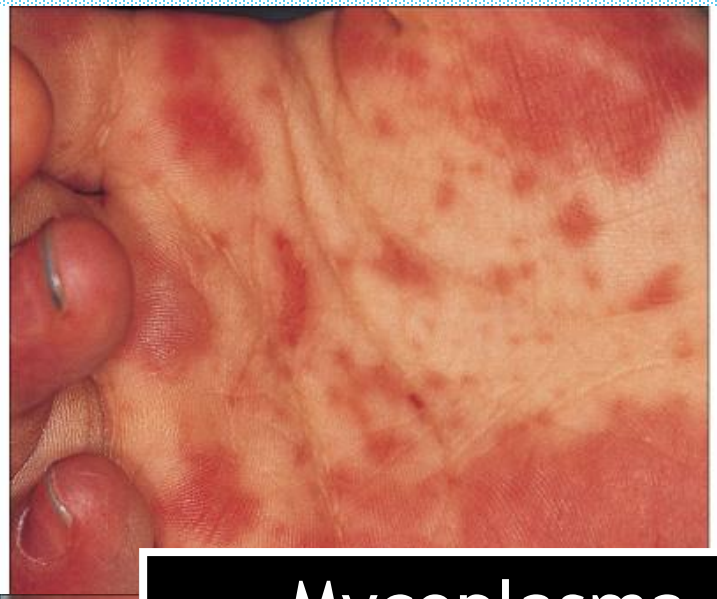
- **Definitions**
  - **SJS = less than 10% BSA**
  - **SJS/TEN overlap = 10-30% BSA**
  - **TEN = greater than 30% BSA**

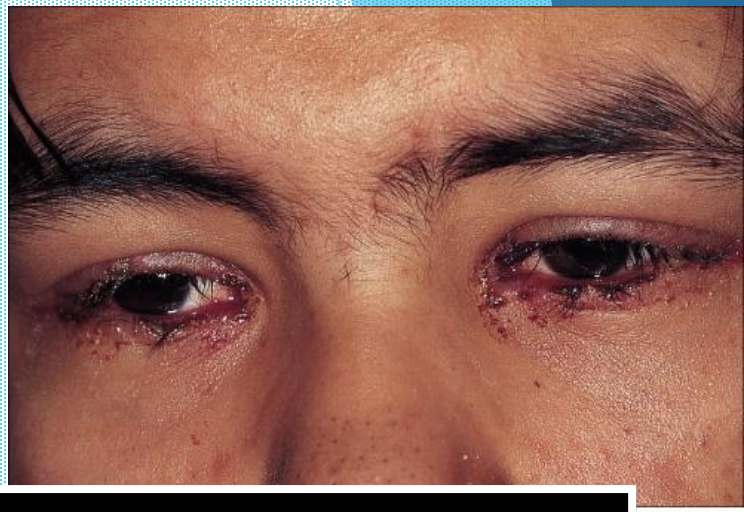

SPECTRUM OF DISEASE BASED UPON SURFACE AREA OF EPIDERMAL DETACHMENT
SJS
SJS-TEN overlap
TEN
<10%
10-30%
>30%
= Surface area of epidermal detachment
= detached epidermis
SJS = Stevens-Johnson syndrome
TEN = Toxic epidermal necrolysis

Associated Medications SJS/TEN

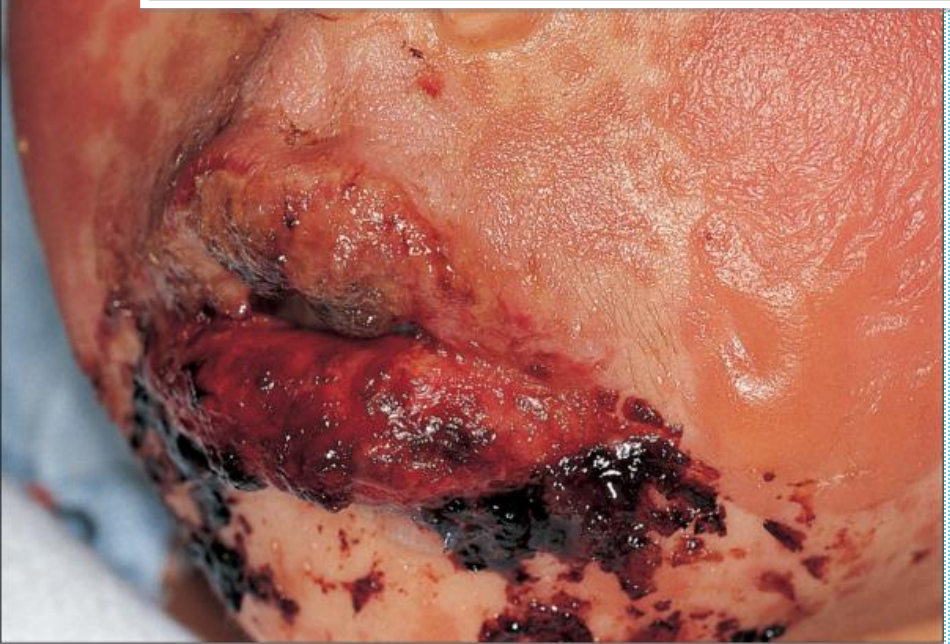
MEDICATIONS MOST FREQUENTLY ASSOCIATED WITH SJS AND TEN	
Allopurinol	Lamotrigine
Aminopenicillins	Phenylbutazone*,[3]
Amithiozone (thioacetazone)*,[1]	Piroxicam
Barbiturates	Sulfadiazine*,[1]
Carbamazepine	Sulfadoxine*,[1]
Chlormezanone*,[2]	Sulfasalazine
Phenytoin antiepileptic	Trimethoprim–sulfamethoxazole

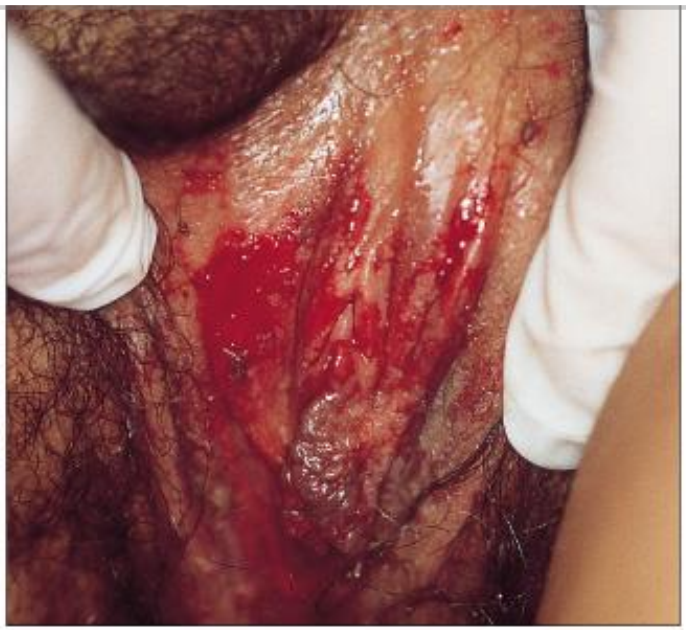
Infections





Mycoplasma common cause of SJS in kids

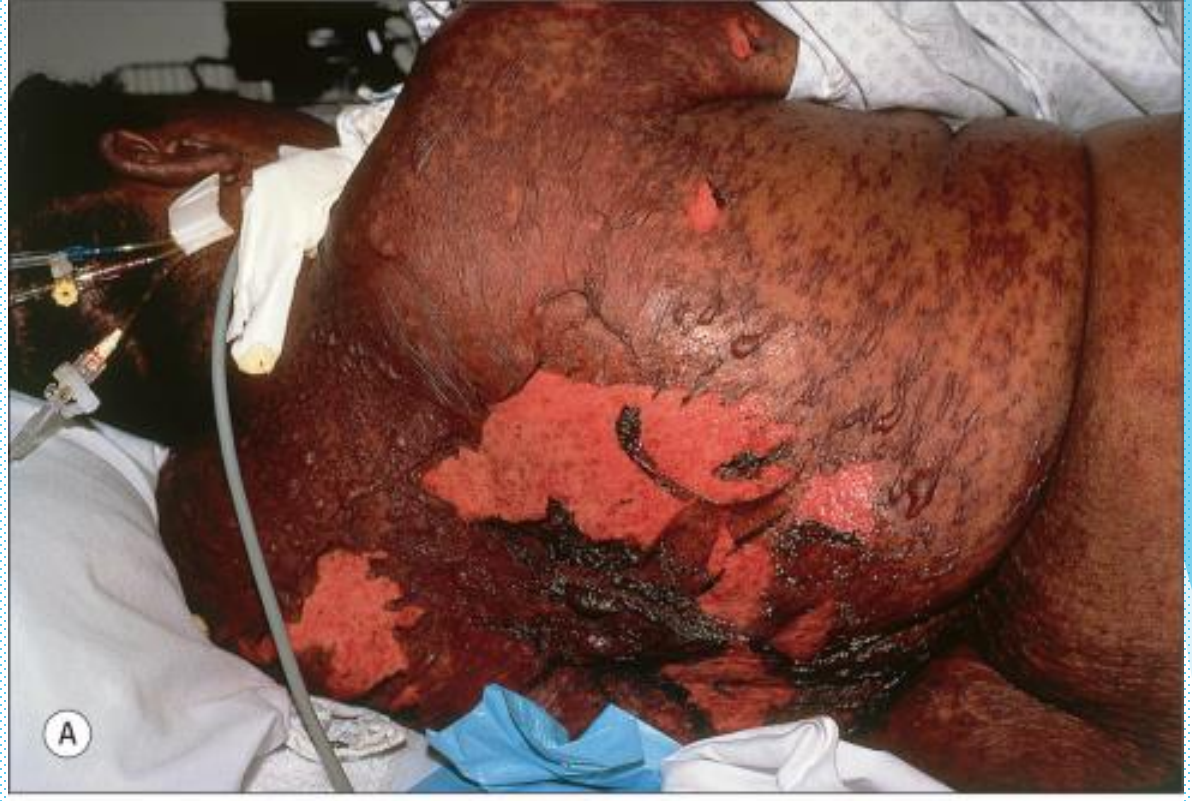


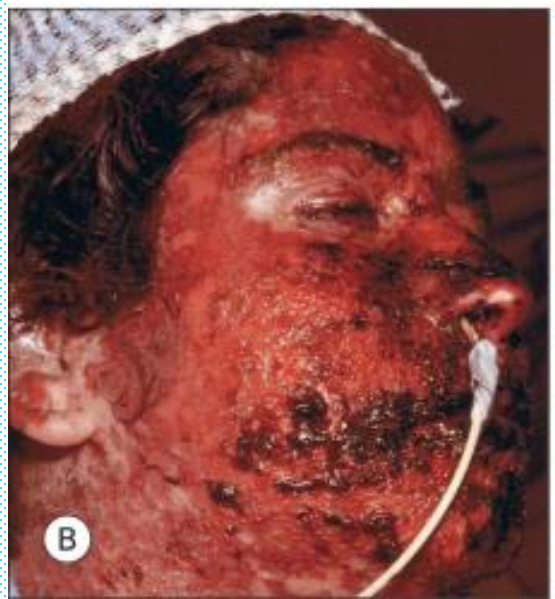


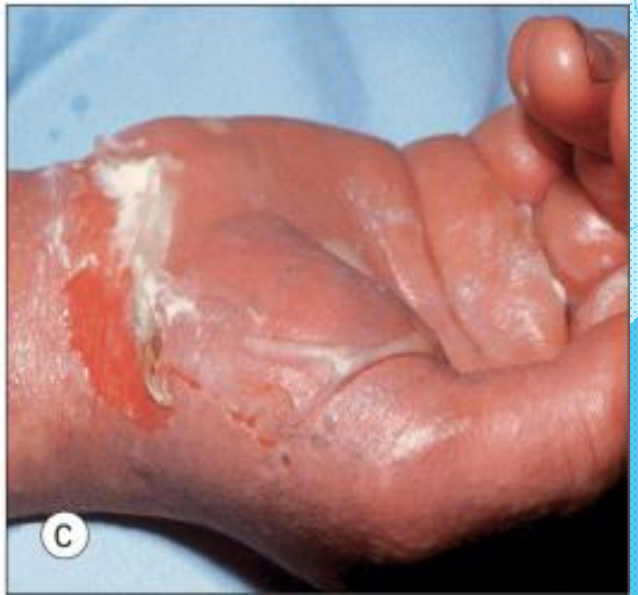
EM, SJS, TEN

- 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

TEN





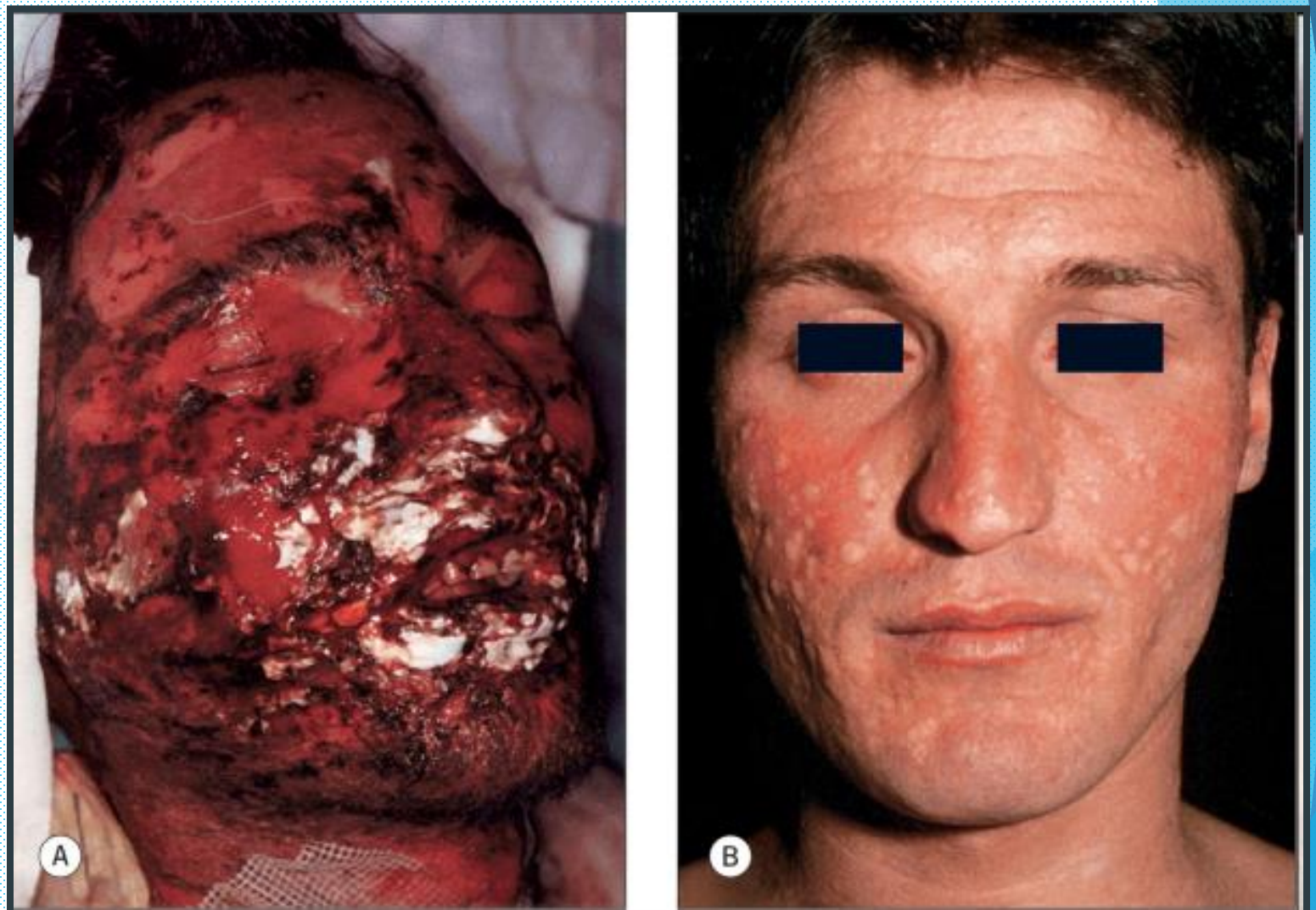


SJS/TEN

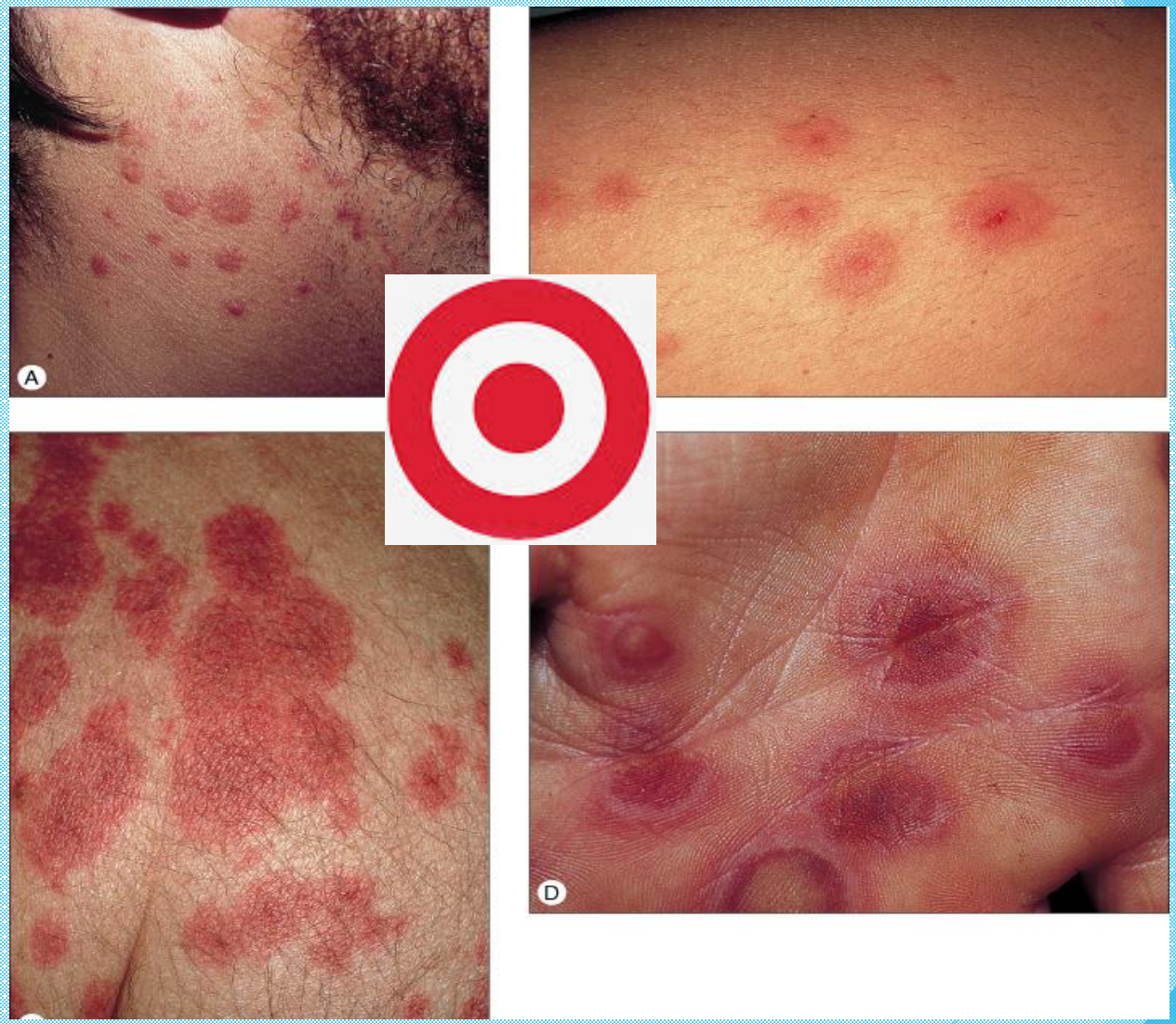
- Treatment: burn unit
  - **Supportive**
    - Fluids, nutrient, electrolyte replacement, infection control
  - **IVIG:**
    - Stops keratinocyte apoptosis, blocks death receptor FAS (CD95)
  - **Immunosuppressive therapy**
    - Controversial
    - May increase morbidity/mortality
  - **Systemic steroids** – 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 IVIg (0.75 g/kg/day for 4 days)



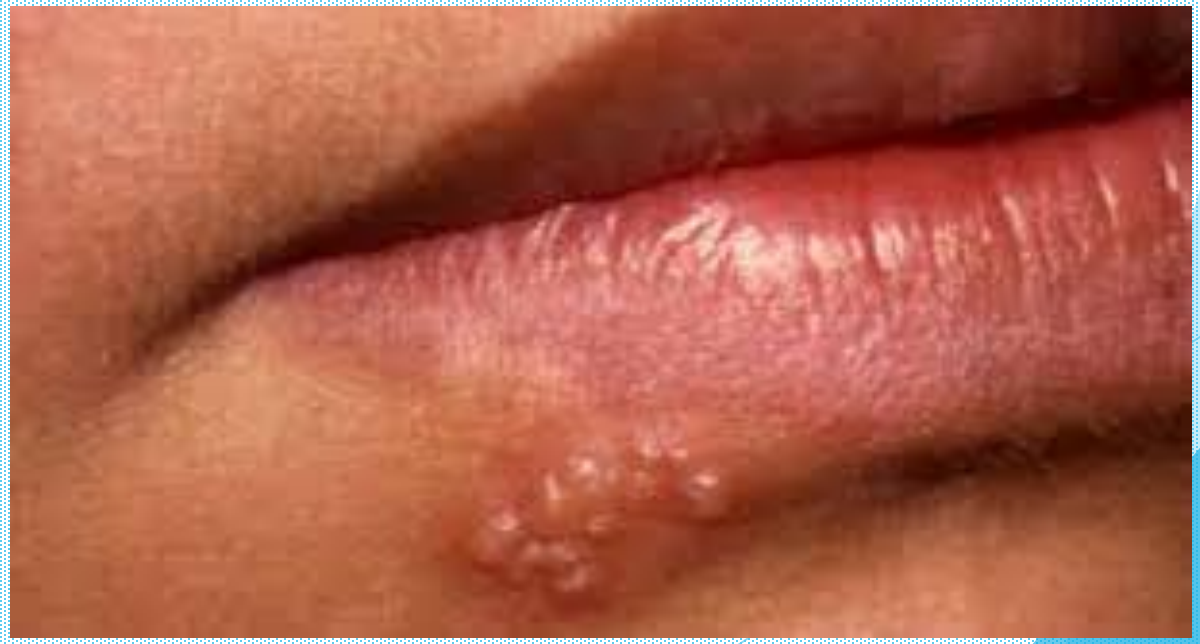
Erythema Multiforme



What is the most common infectious cause of erythema multiforme?

What is the most common infectious cause of erythema multiforme?

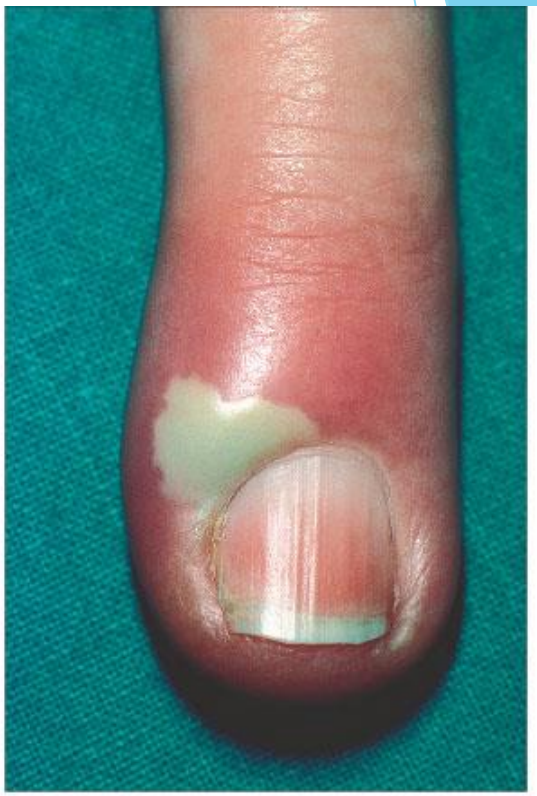
- Herpes Virus



Infectious

Staphylococcal Infections

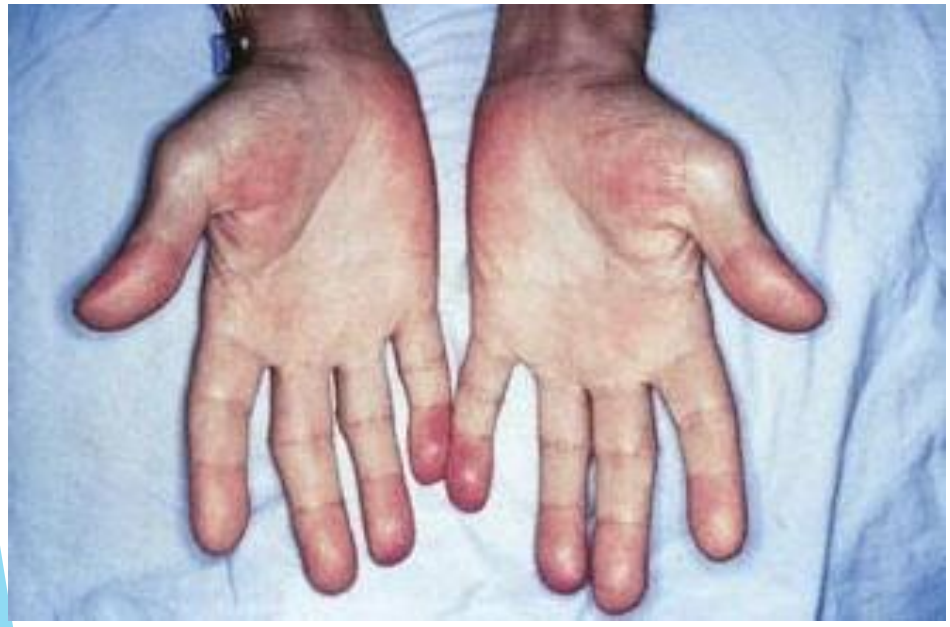
- Cutaneous manifestations of endocarditis
- Impetigo of Bockhart
- Sycosis Barbae
- Folliculitis
- Furunculosis
- Pyogenic Paronychia
- Botryomycosis
- Pyomyositis
- Impetigo
- Staph Scalded Skin Syndrome
- Toxic Shock Syndrome



Staphylococcal Infections

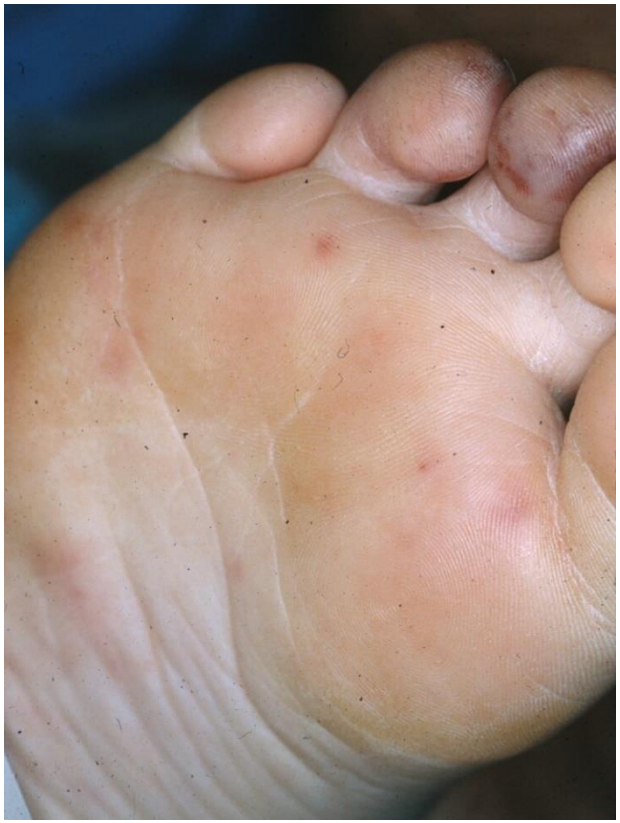
- Skin lesions: pustules, furuncles, erosions with honey-colored crusts, bullae, erythema and desquamation, or vegetating pyodermas
- Staph is the most common bacterial infection in children
  - Extremely contagious
  - Person-to-person contact
- Endocarditis:
  - Osler node: painful, erythematous nodule pale center located on fingertips, thenar, and hypothenar eminences
  - Janeway lesions: non-tender, angular hemorrhagic lesions on palms

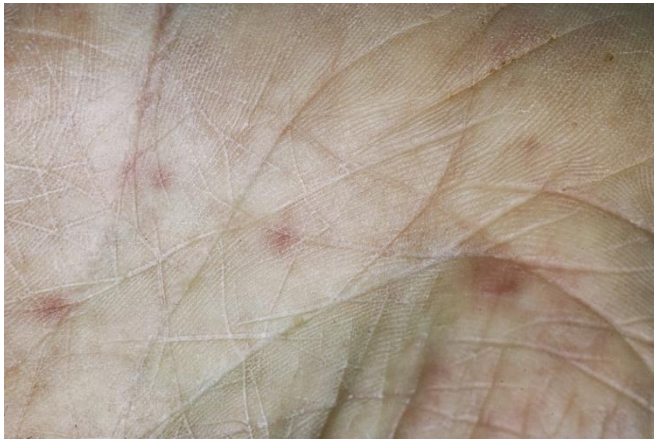
Osler nodes



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

Janeway lesions





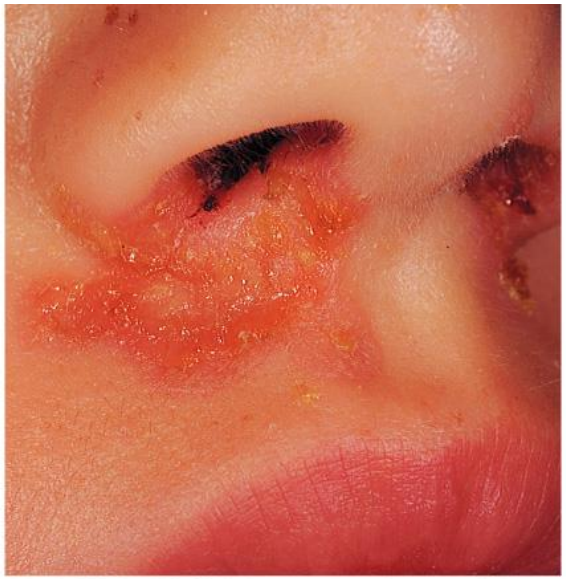
Community Acquired MRSA

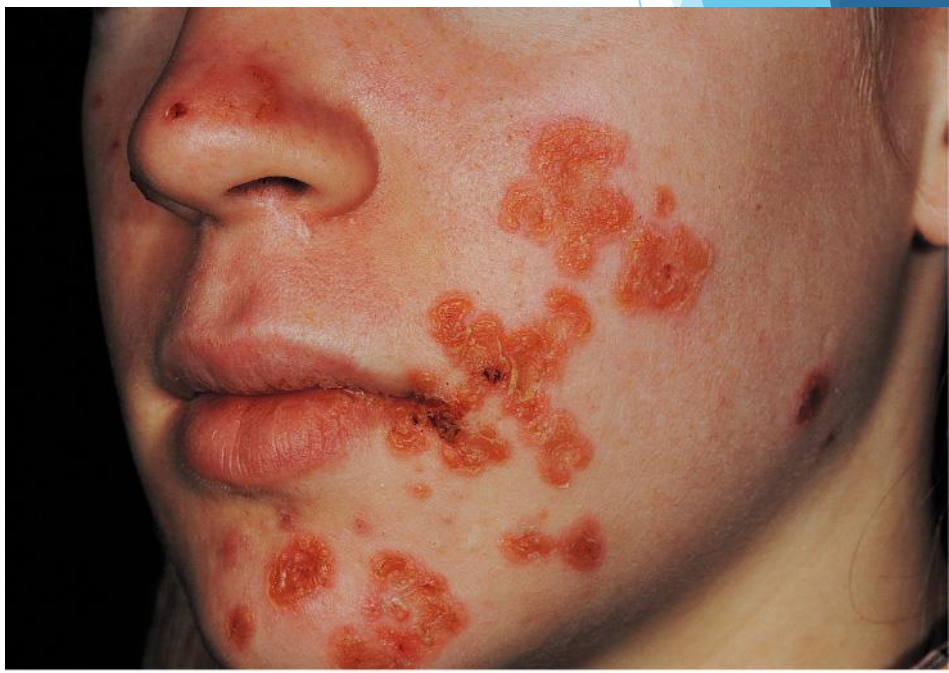
- First appeared in isolates of *S.aureus* in 1961
- Risk factors:
  - Age > 65
  - Exposure to MRSA
  - Prior Abx therapy
  - Recent hospitalization or chronic illness—IV Vancomycin or Linezolid
- If MRSA suspected:
  - Clindamycin
  - Trimethoprim/sulfamethoxazole (alone or with rifampin)
  - Minocycline/Doxycycline
  - 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

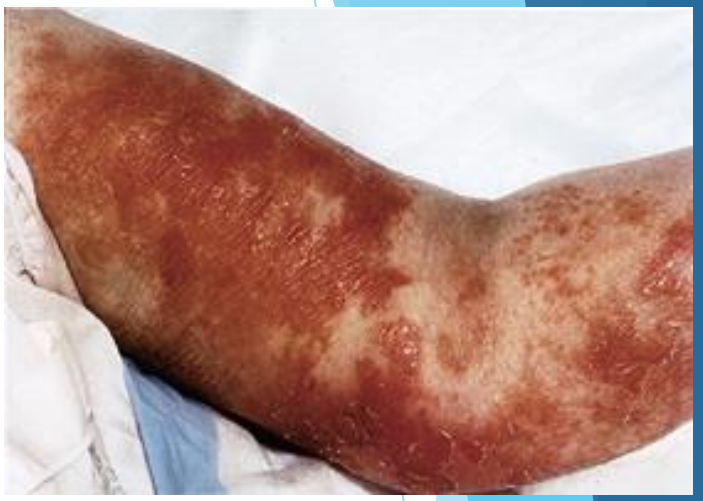
- Presentation: 2mm erythematous papule develops into vesicles and bullae. Upon rupture a straw colored seropurulent discharge dries to form yellow, friable crust.
- Etiology: S. Aureus > S. Pyogenes.
- Lesions located on exposed parts of body.
- Group A Strep can cause AGN
  - Children <6 yrs old
  - 2% to 5% of infections
  - Serotytpes 49, 55, 57, 60 strain M2 most associated
  - Good prognosis in children

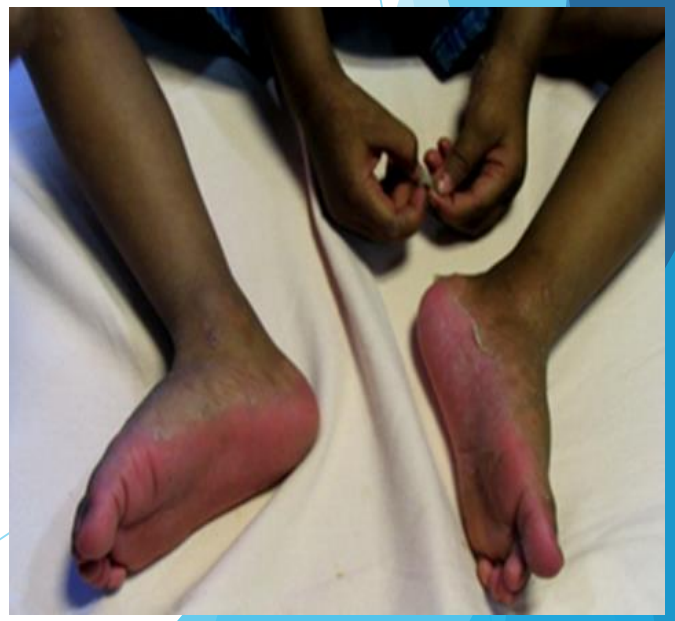
Toxic Shock Syndrome

- 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. Mortality30%

Toxic Shock Syndrome (TSS)

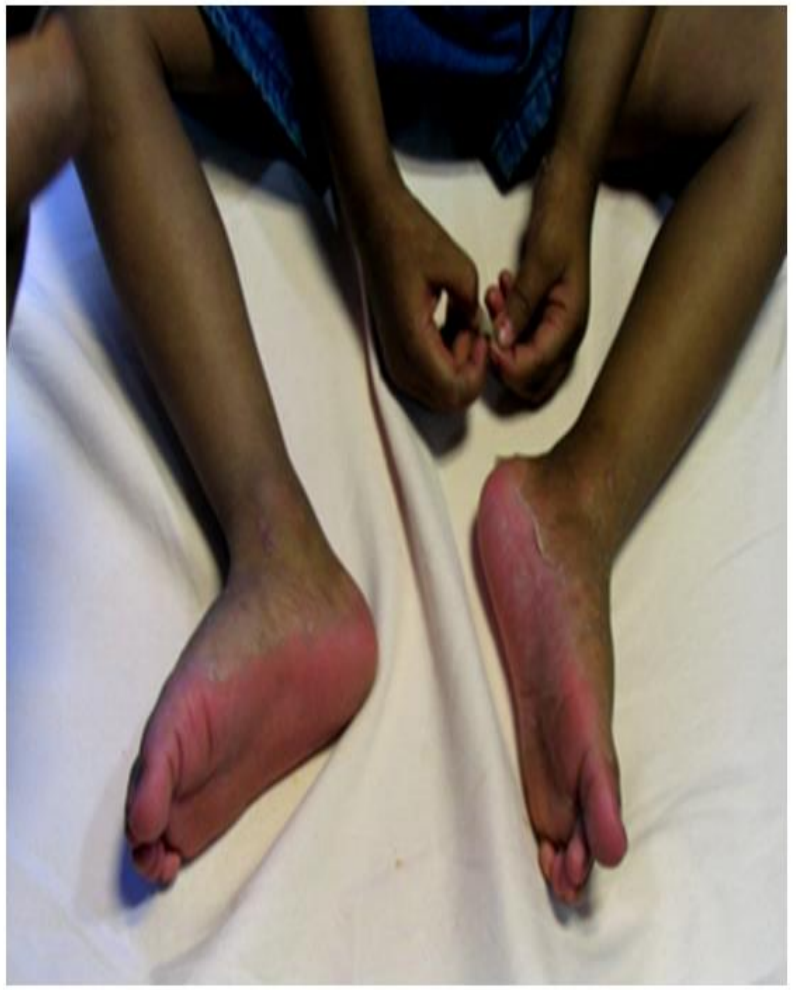
- *S. aureus* exotoxin (TSST-1) isolated in 90% of cases
- *Strep* M types 1 and 3 (80% produce exotoxin A)
- Acute, febrile, multi-system illness characterized by:
  - Myalgias, n/v/d, HA, pharyngitis
  - Rapid progression to shock
  - Diffuse *scarlatiniform* exanthem starts on trunk & spreads centripetally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



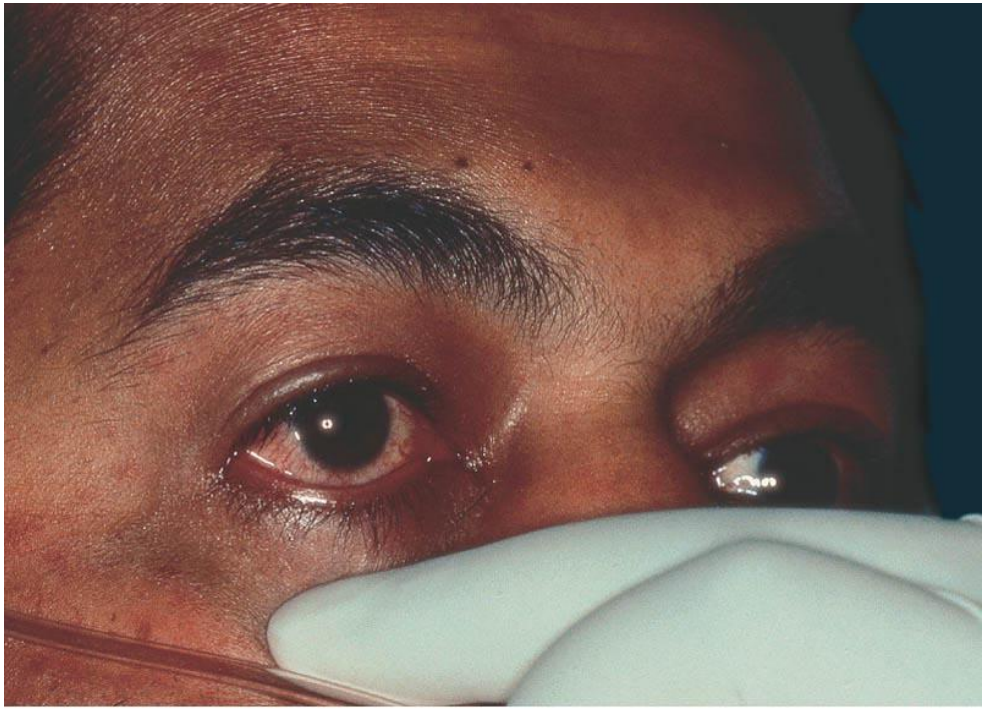


Toxic Shock Syndrome (TSS)

- 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)

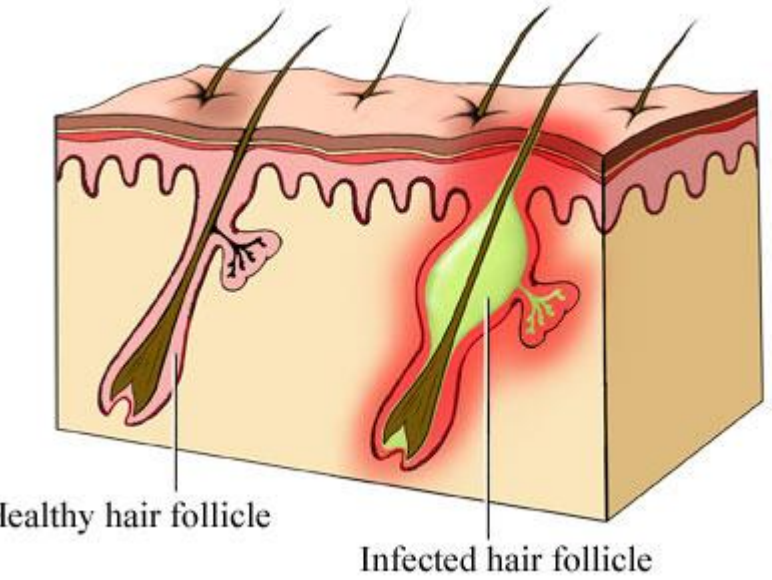
TSS (Staph)

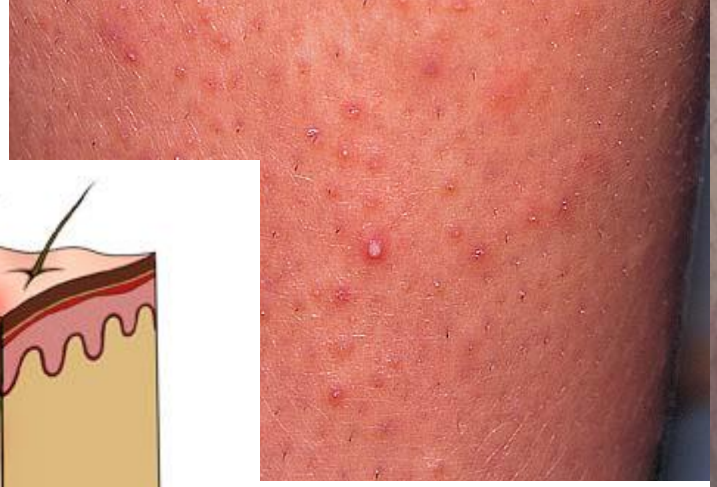
- TSST-1 toxin
- Staph enterotoxins
- Superantigens that promote TNF-a, IL-1, IL-6
- Clinical:
  - Perineal erythema, desquamation, strawberry tongue
  - Tampons (5% mortality rate)
  - Nonmenstrual cases (surgical packing, catheters, meshes, abscesses); higher mortality (12%)

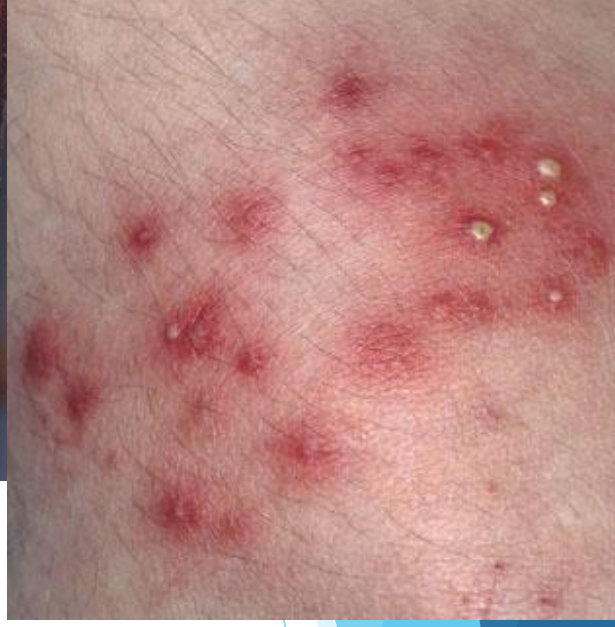
TSS (Strep)

- 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



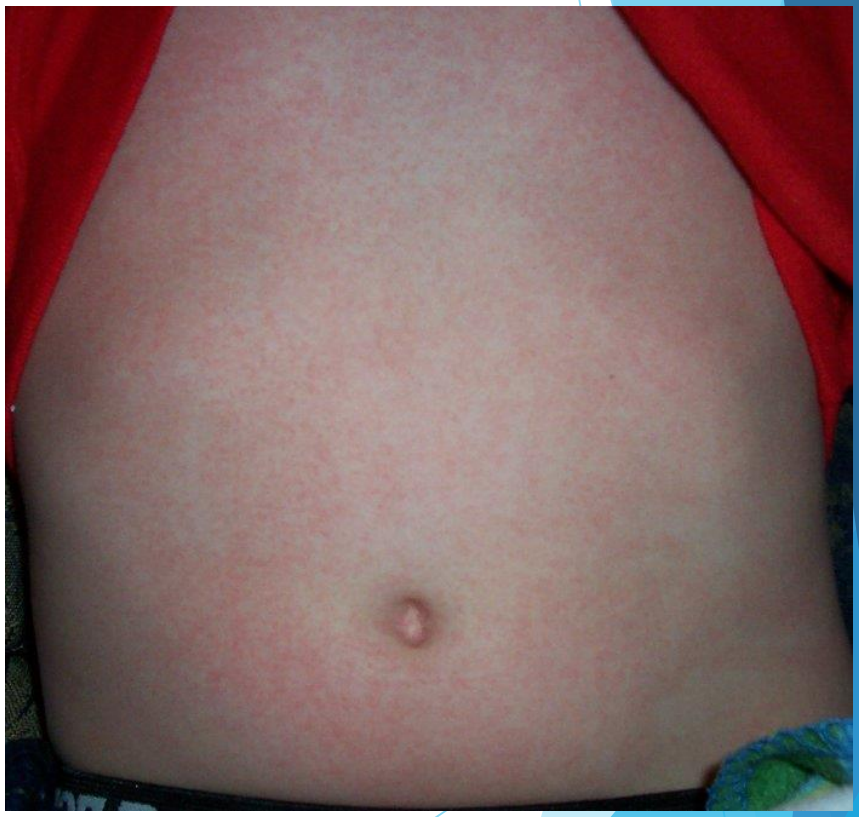




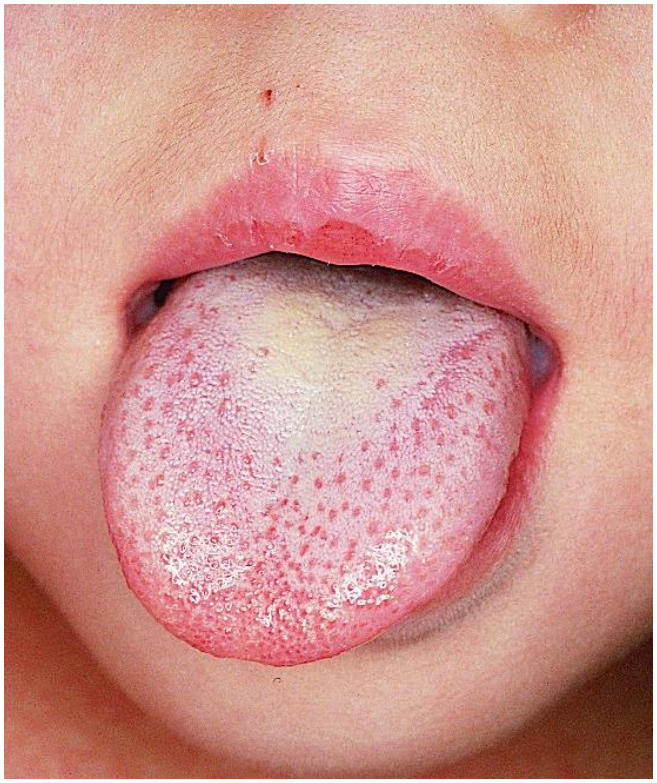
- Superficial (follicle ostium) or deep infection of the hair follicle
  - Common in AIDS, frequent cause of pruritus
  - Can occur on eyelashes, pubis (sexual contact, STD), thighs
- *S. aureus* most common infectious cause
- *Pseudomonas* assoc. with swimming pools + jacuzzis
  - Alkaline water & low 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/rosacea

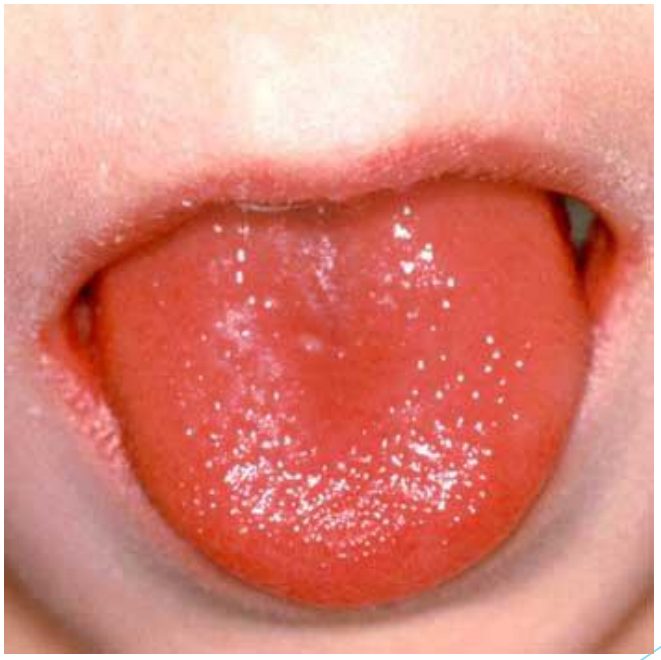
Scarlet Fever

- 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



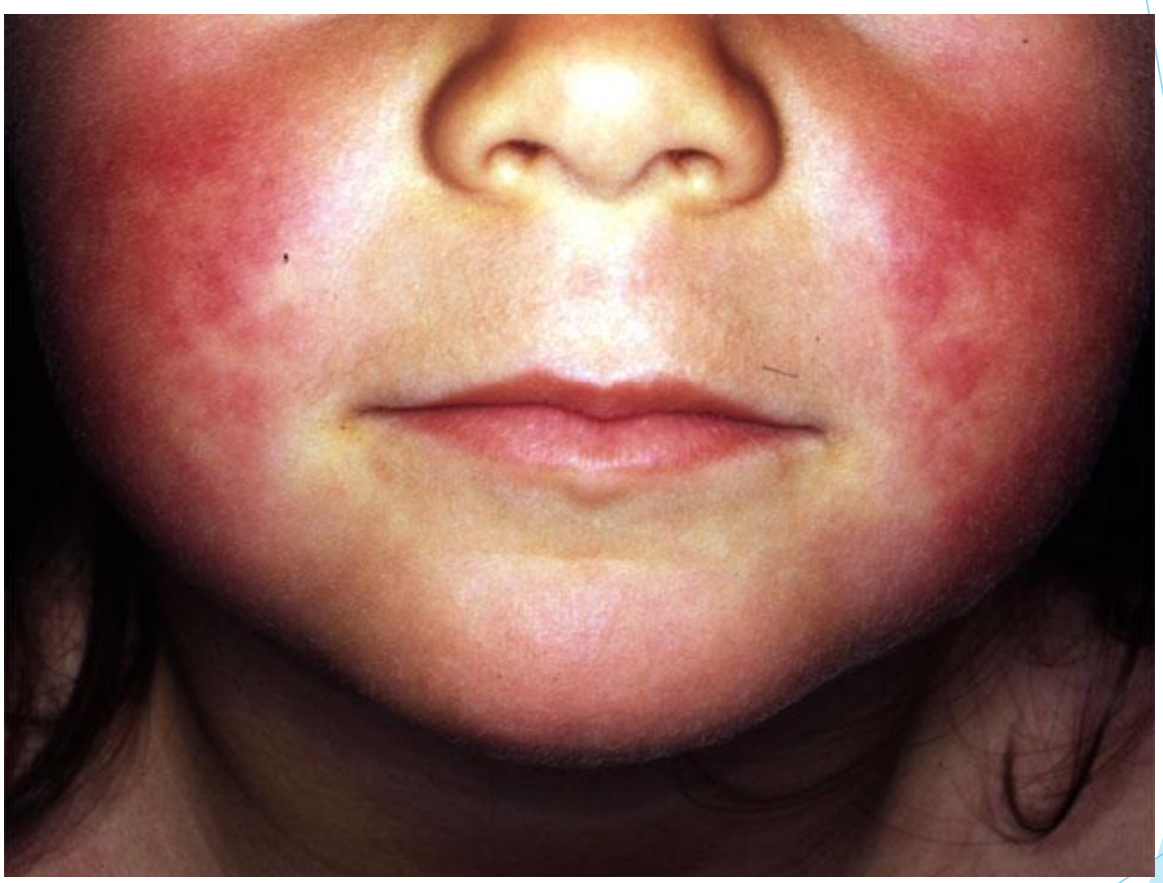
White: early Red: 4-5th day





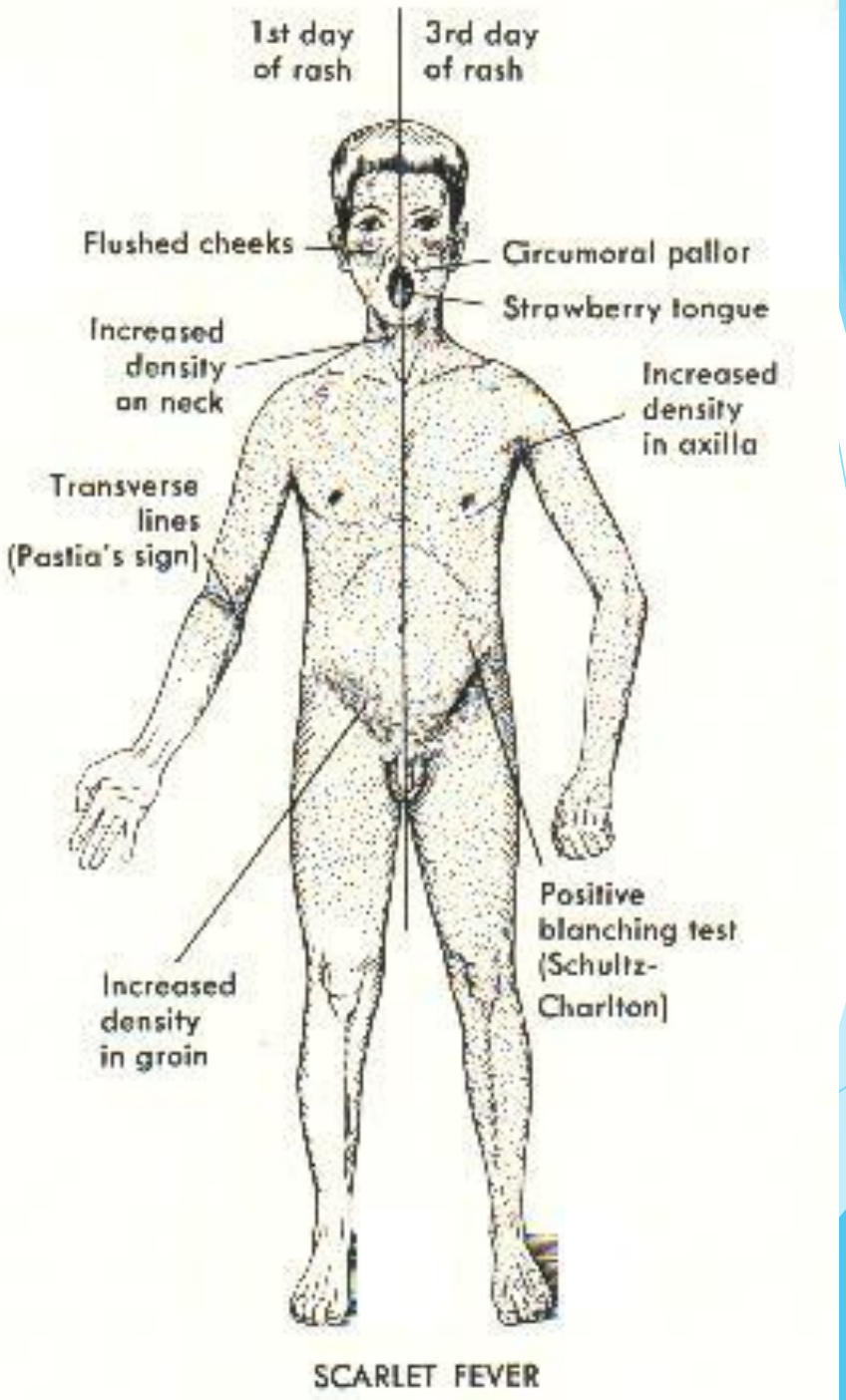
Strawberry tongue, with enlarged, exudative tonsils

Scarlet Fever



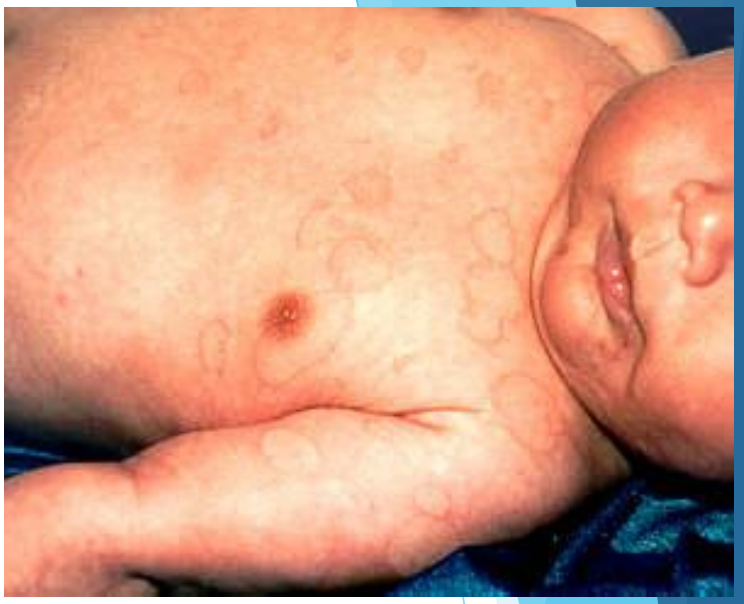
Rash with circumoral pallor

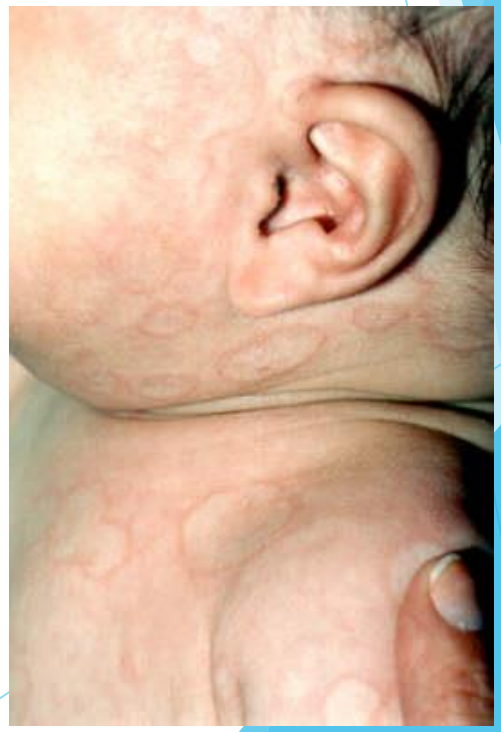
Scarlet Fever



Erythema Marginatum

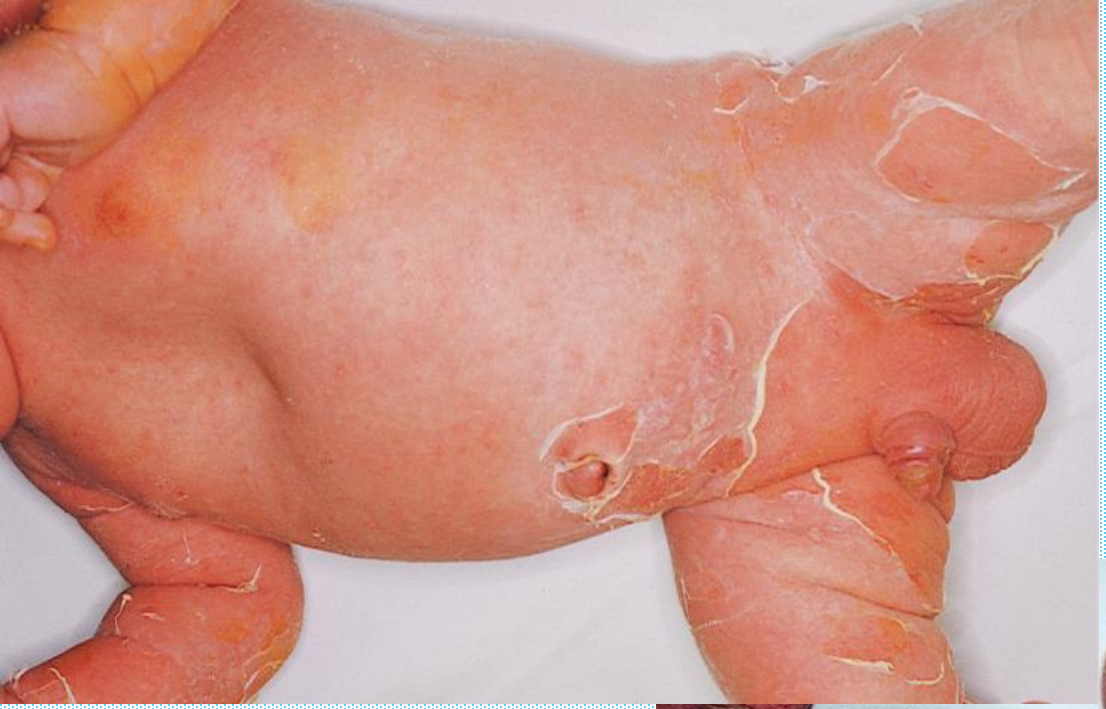
- Two skin signs among diagnostic criteria for rheumatic fever
  - Erythema marginatum (early)
  - Subcutaneous nodules (late)
  - (carditis, chorea, polyarthritis)
- Spreading patchy erythema spreads peripherally, polycyclic; evanescent lasting hours to days
- Lesions asymptomatic

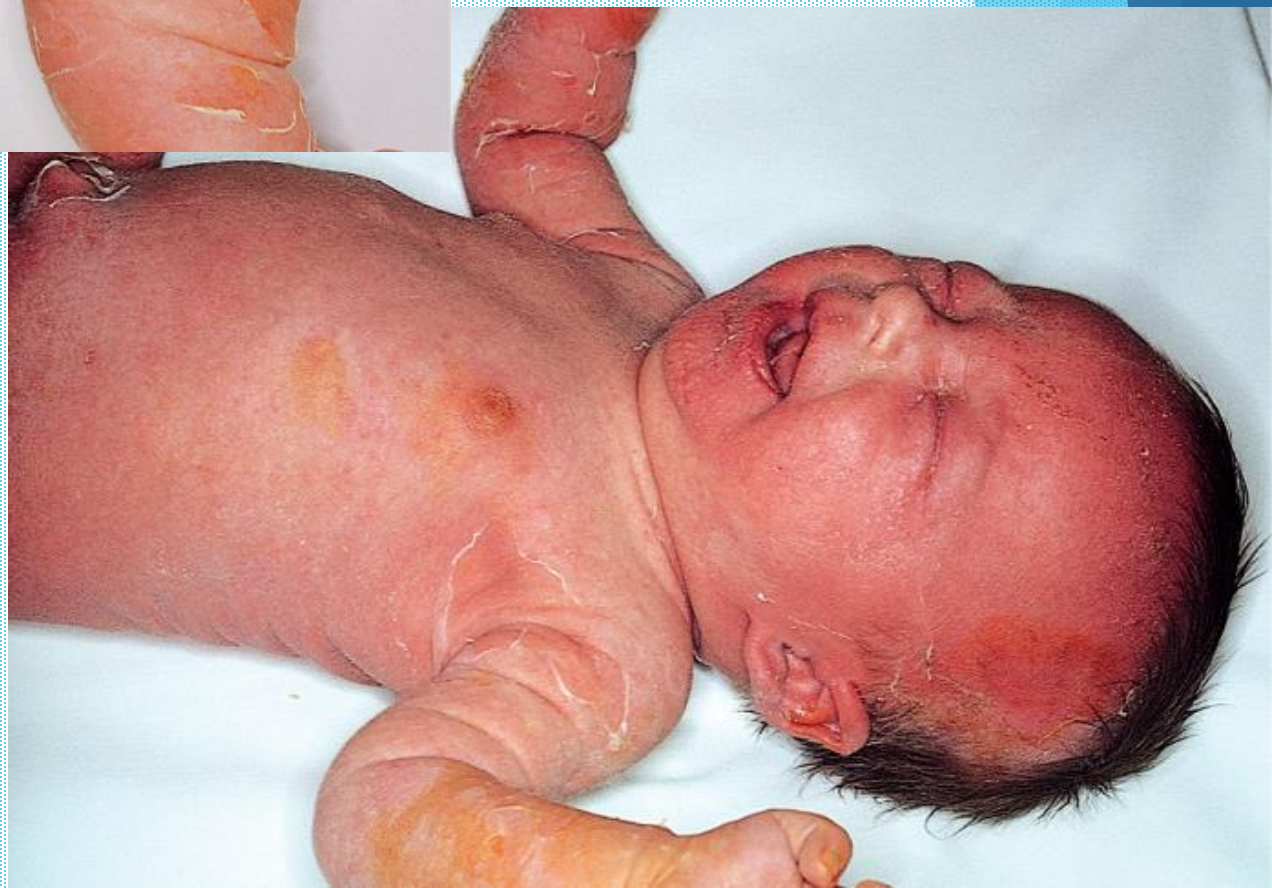




Staphylococcal Scalded Skin Syndrome
Ritter's disease, Pemphigus neonatorum

- 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

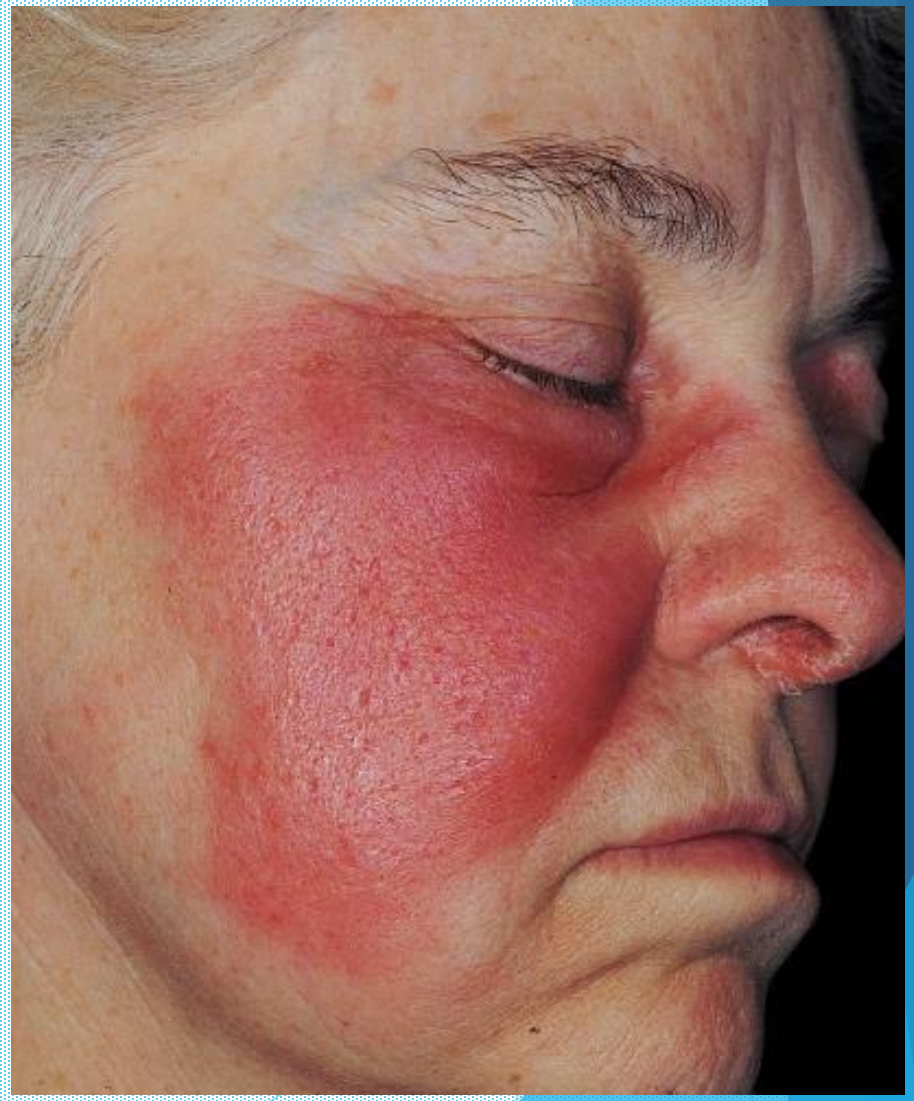
- **Diagnosis:**
  - Cultures from intact bullae are negative (sterile bullae)
  - Culture instead from conjunctiva, nasopharynx, perineum, or pyogenic foci on the skin
- **Treatment:**
  - Inpatient IV penicillinase-resistant antibiotic agents
    - Nafcillin
    - If penicillin-allergic → macrolides or aminoglycosides
  - Supportive care such as fluid and electrolyte replacement and local wound care

Comparison of TEN and SSSS		
	TEN	SSSS
Cause	Usu. Drug induced	Toxin-producing *S. aureus* infection
Age	Adults	Infants and young kids
Histology	D-E separation; dermis w/ variable inflammatory infiltrate	Granular layer split in epidermis; dermis lacks inflammatory infiltrate
Distribution of rash	Areas of sparing	Generalized w/ flexural accentuation
Mucous Membranes	Involved; erosions	Uninvolved
Nikolsky's sign	In some areas; difficult to elicit	Present in seemingly uninvolved skin
Face	Vermilion lip redness; edema, erosions	Perioral crusting and radial fissuring with mild facial swelling
Tx	Standard burn Tx; IVIg, CSt. (controversial)	Abx (B-lactamase resistant) and supportive care

Erysipelas

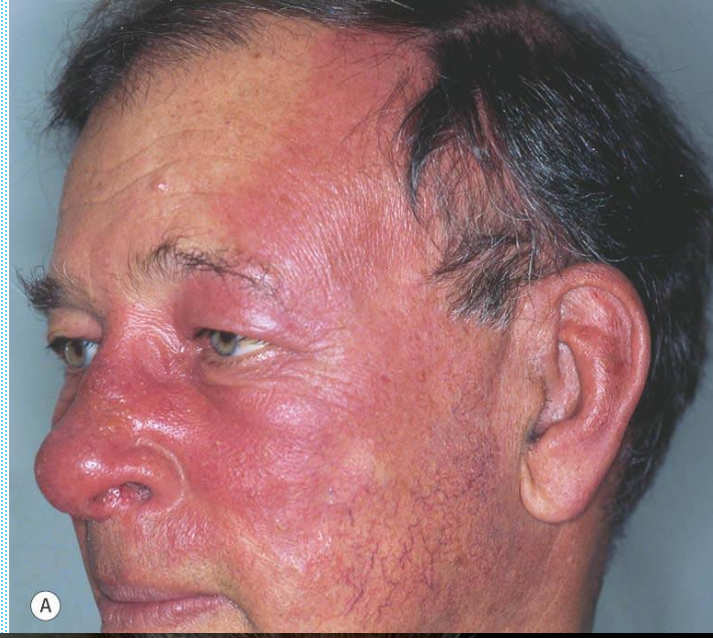
St. Anthony's Fire, Ignis sacer

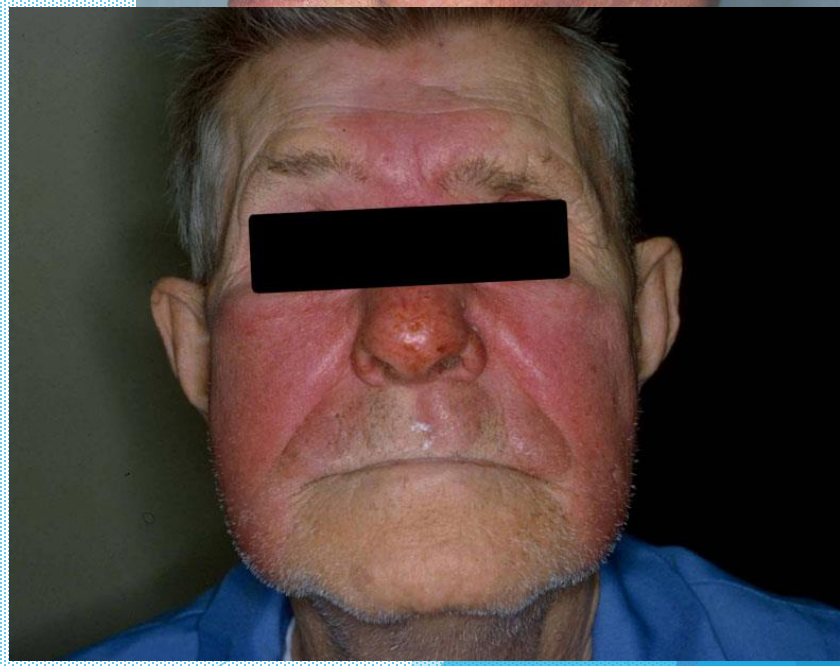
- **Group A β-hemolytic *strep***
- Group B *strep* in newborns
- Acute infection of dermis & superficial dermal lymphatics
  - Local redness, heat, swelling
  - Raised, indurated border that spreads
  - Legs and face MC sites (scalp barrier to extension)
- Prodromal constitutional Sx:
  - Lymphadenopathy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



Erysipelas

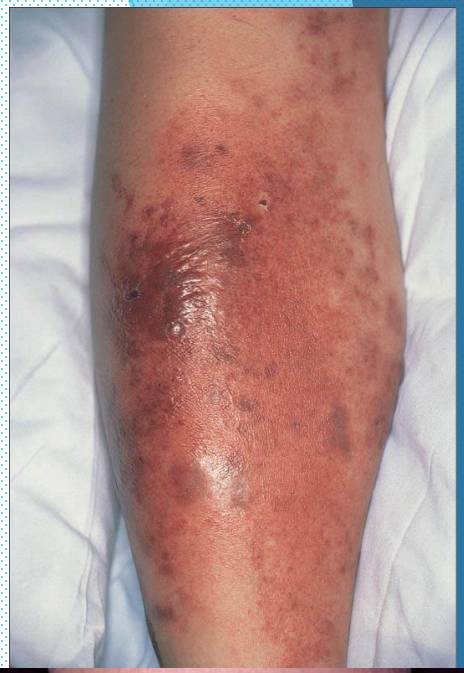
- Complications:
  - Septicemia, deep cellulitis, necrotizing fasciitis
- Differential diagnosis:
  - Contact derm (plants, drugs, dyes) although not assoc. w/ f/c, pain
  - Lupus erythematosus butterfly pattern
- Treatment:
  - PCN, erythromycin at least 10 days
  - Ice compresses
  - Inpatient and IV Abx

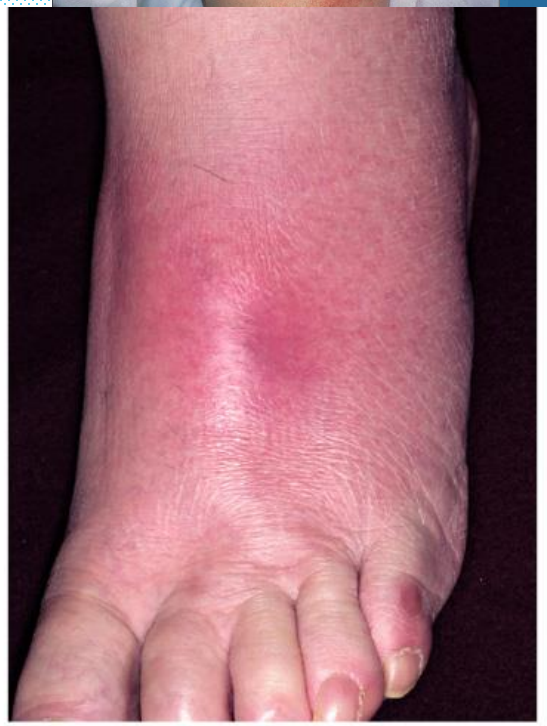




Cellulitis

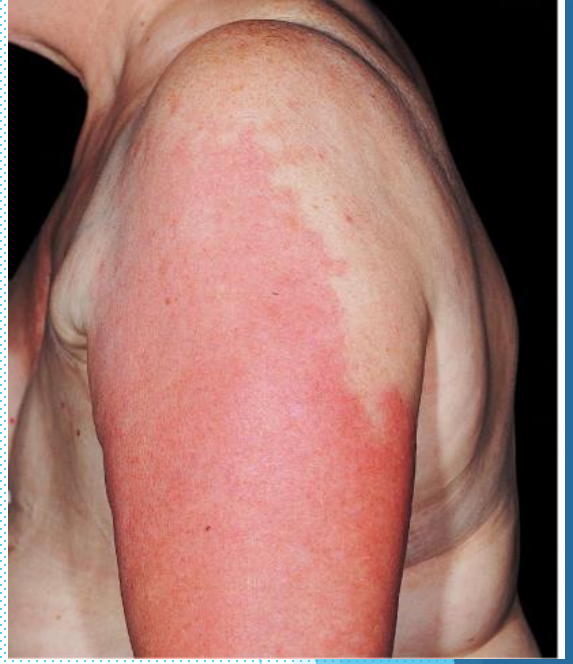
- Deep dermal & SQ infection of mainly
  Staph. aureus or *Strep. pyogenes*
- Suppurative inflammation usually following a wound
  - **MC port-of-entry is due to T. pedis**
  - Purulent and necrotic material will drain
  - Local erythema, tenderness, malaise
- Erythema becomes intense rapidly and spreads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

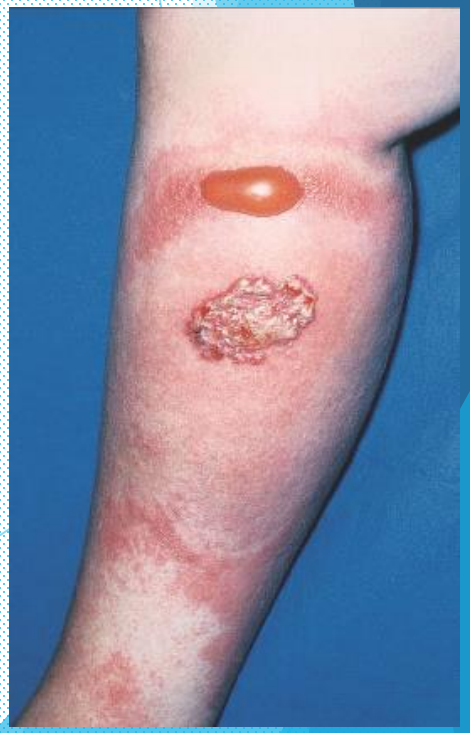




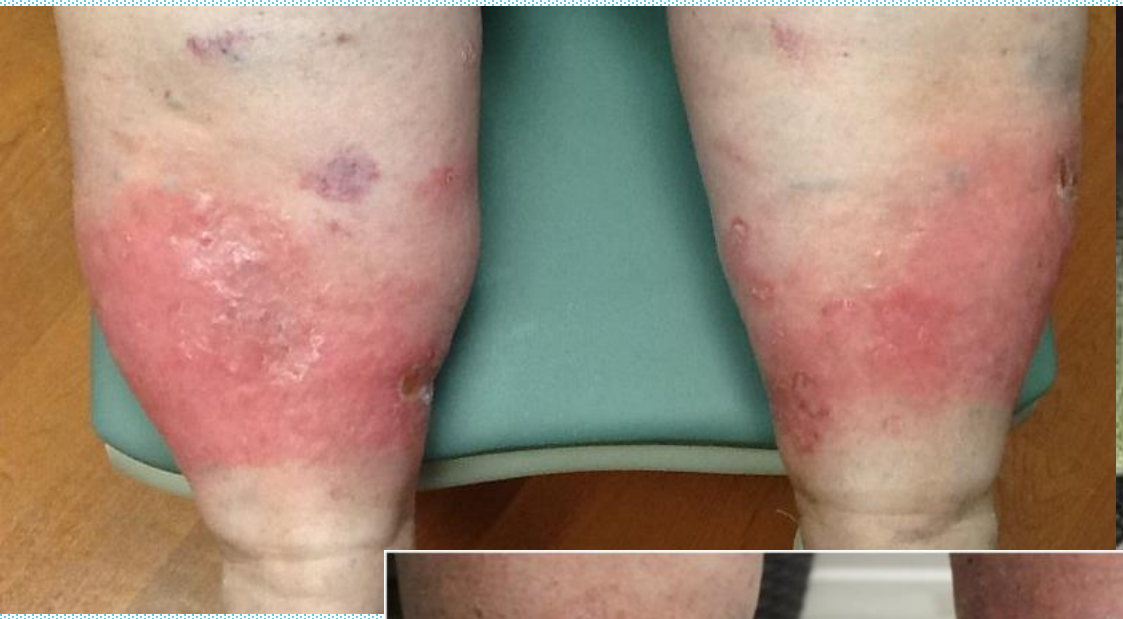
Cellulitis

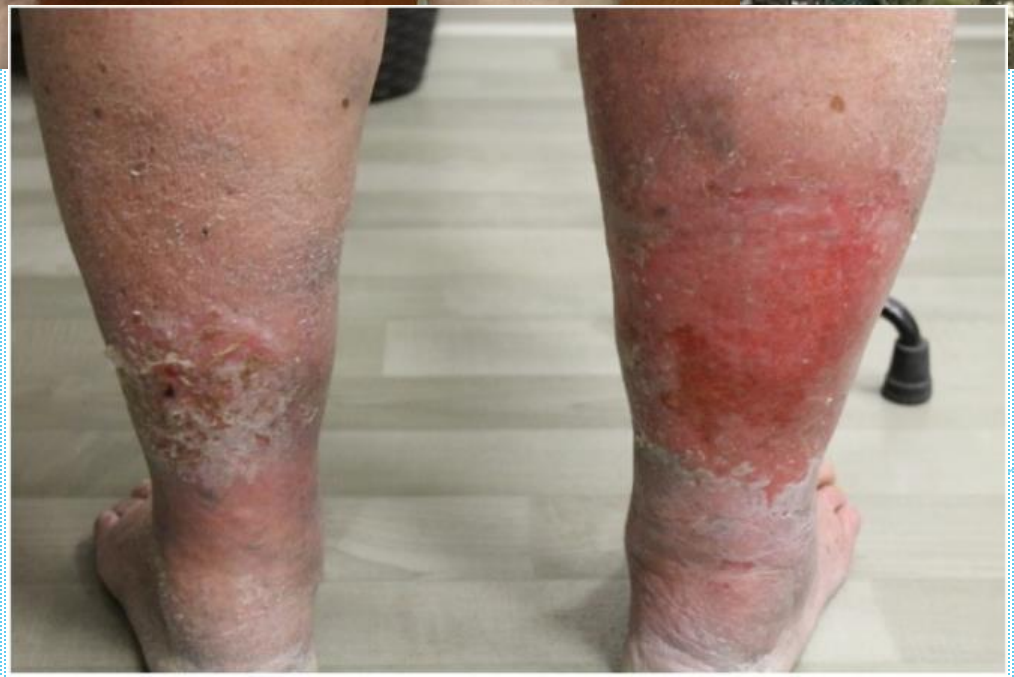
- **Cellulitis is almost always unilateral, if bilateral, think stasis dermatitis**
- Complications (rare in immunocompetent hosts)
  - Gangrene
  - Metastatic abscesses
  - Septicemia
- Initial therapy **cover *staph* and *strep*:**
  - **1st gen ceph or pcn' ase resistant pcn**
  - Suspect MRSA if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





Don’t be Fooled



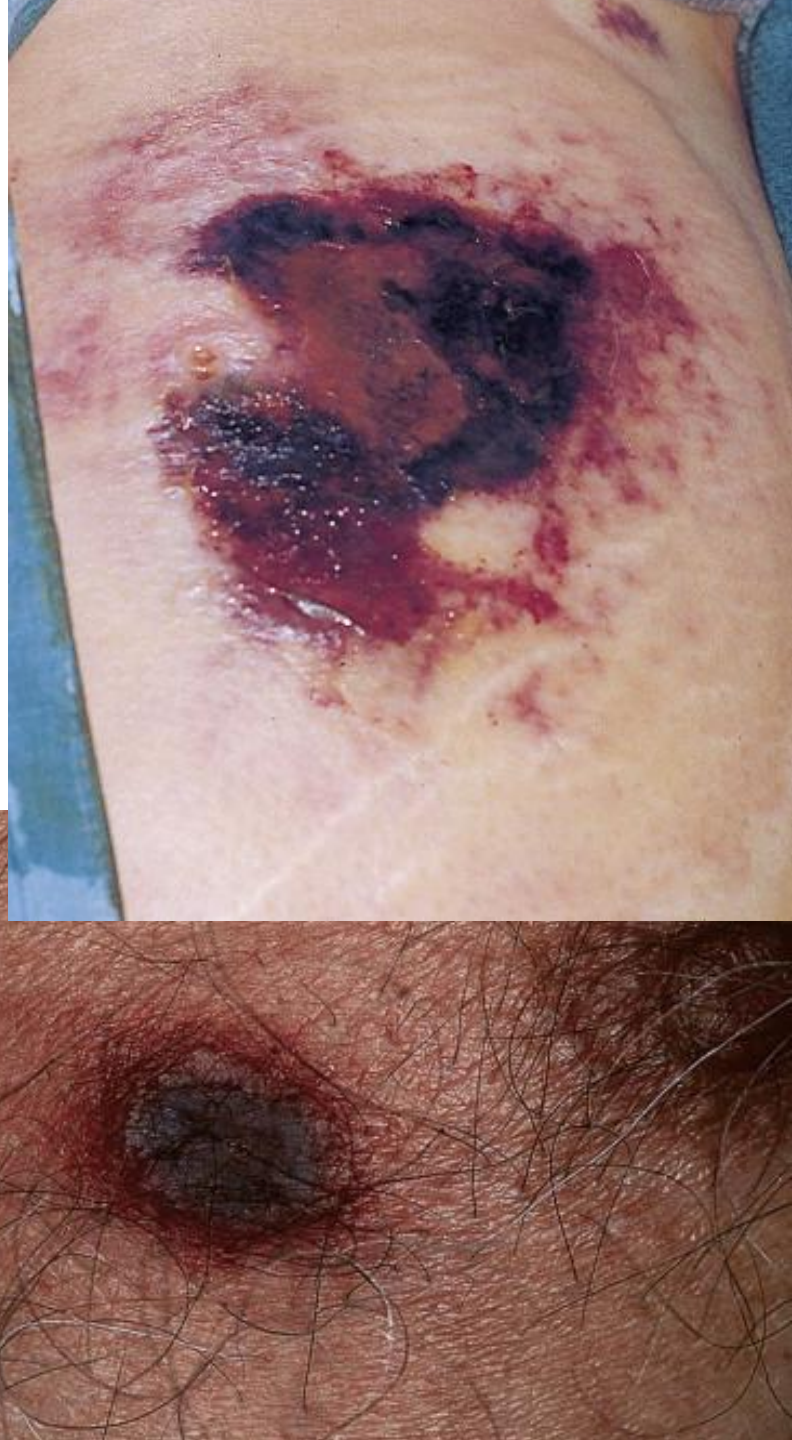


Pseudomonas aeruginosa

- 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

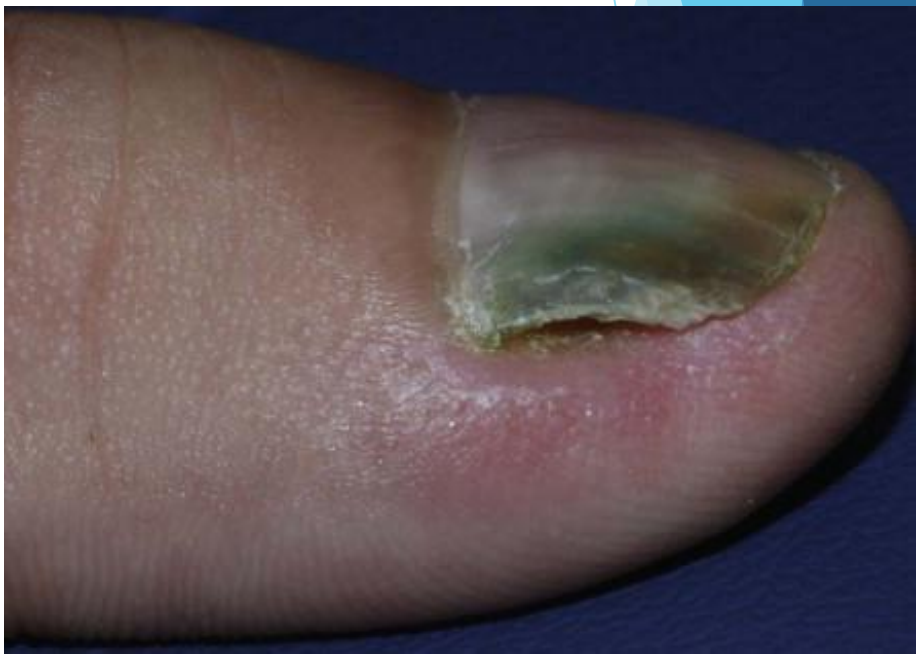
Pseudomonas aeruginosa

- **Ecthyma 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
    - Amioglycosiede + piperacillin
    - +/- GM-CSF

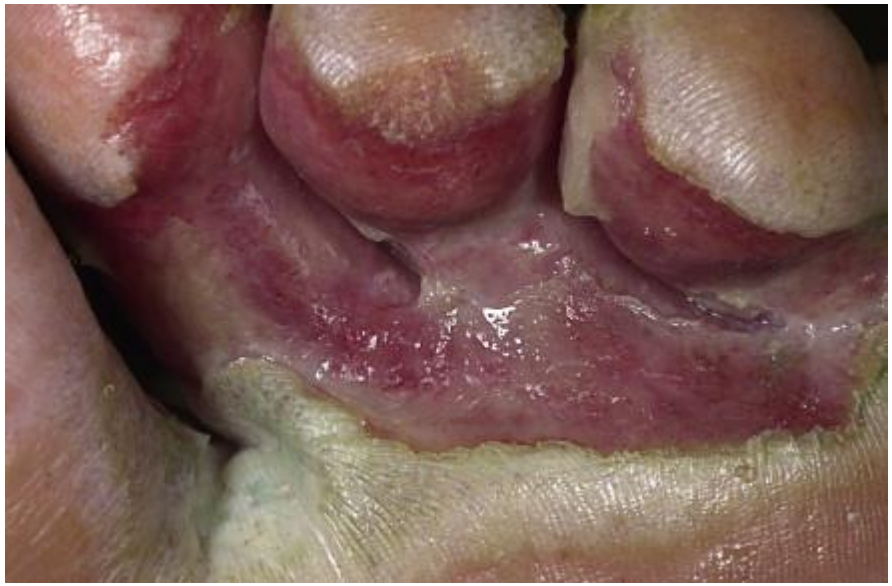


Pseudomonas aeruginosa

- 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, Aspirgillus infection
  - Benzoyl peroxide; 1% acetic acid soaks, debridement



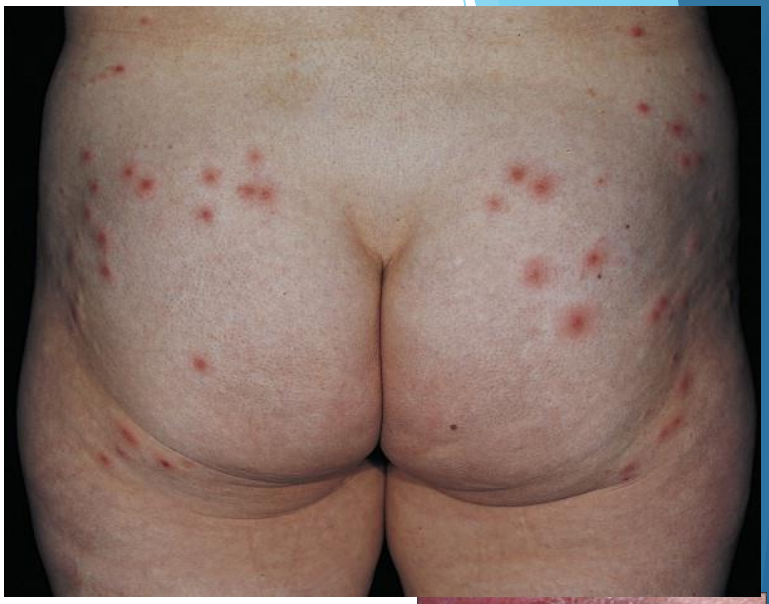
Gram-negative toe web infection



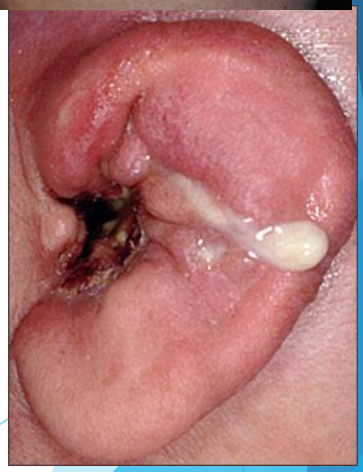
- Toe-web infection
  - **Pseudomonas**
  - Occurs in chronically moist areas i.e. wet feet
  - Tx - dry area, vinegar soaks, ciprofloxacin

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 otits (facial nerve palsy in 30%)**
  - Folliculitis self-limiting (7-14 days)
  - Cipro for systemic symptoms



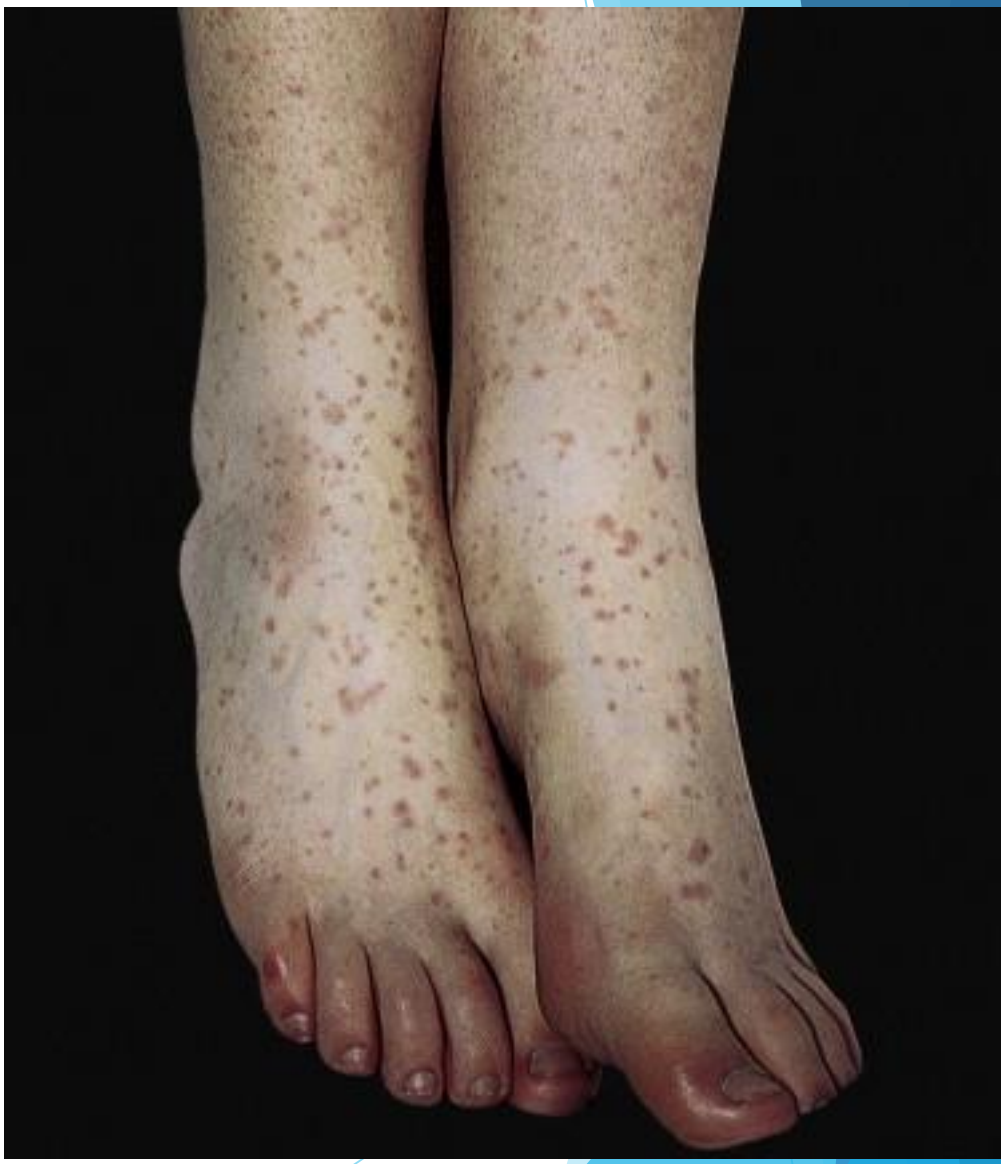
Hot tub folliculitis



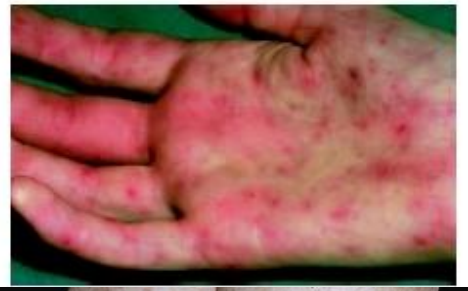
Otitis externa

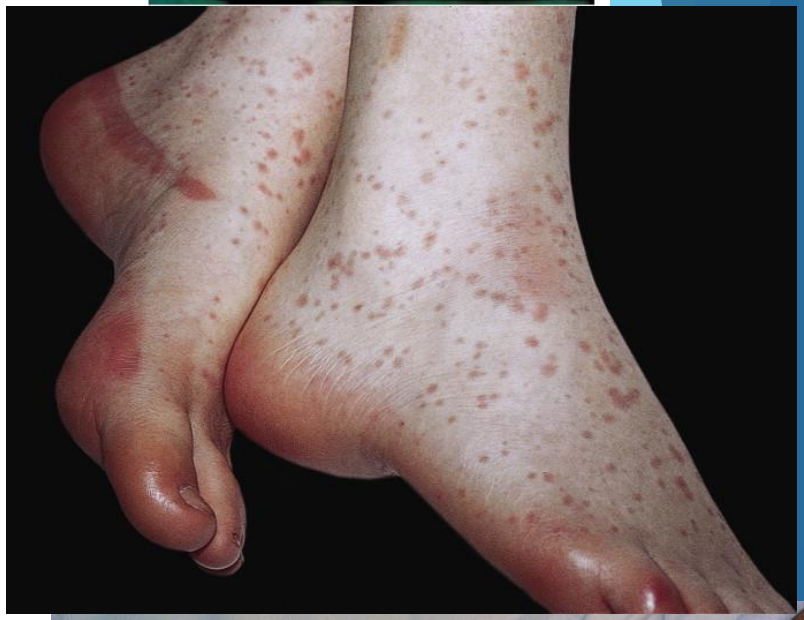
Meningococcemia

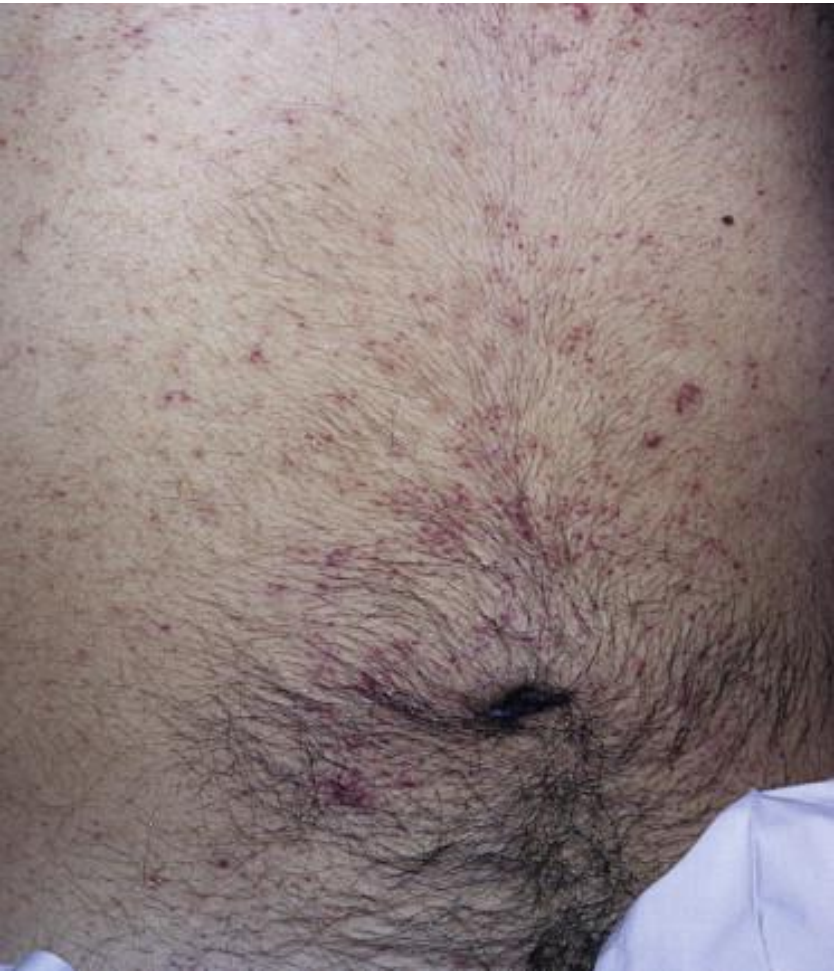
- *N. meningitidis*
  - gram-negative diplococcus
- Virulence related to polysaccharide capsule (gonorrhea does not have)
- Endotoxin → inflammation
- Serogroups A, B, C, W135, X, Y and Z
  - Vaccines cover A, C, Y, W-135
- Transmitted from person to person via **respiratory** secretions
- **Complement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

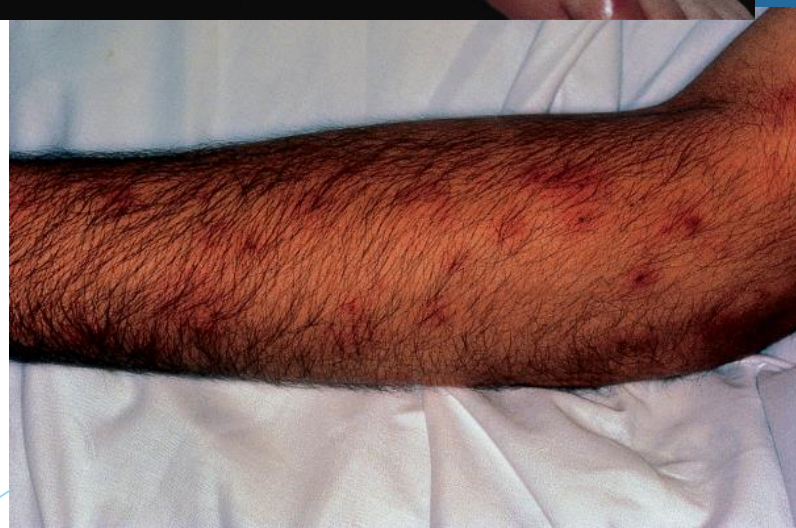


Meningococcemia





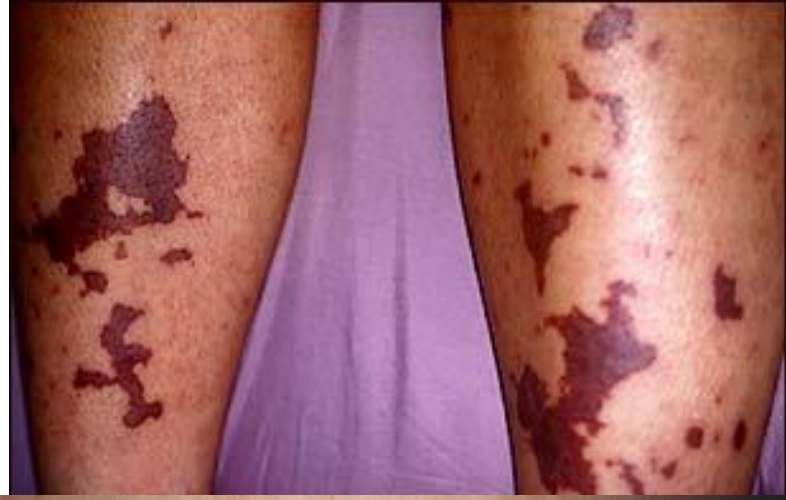


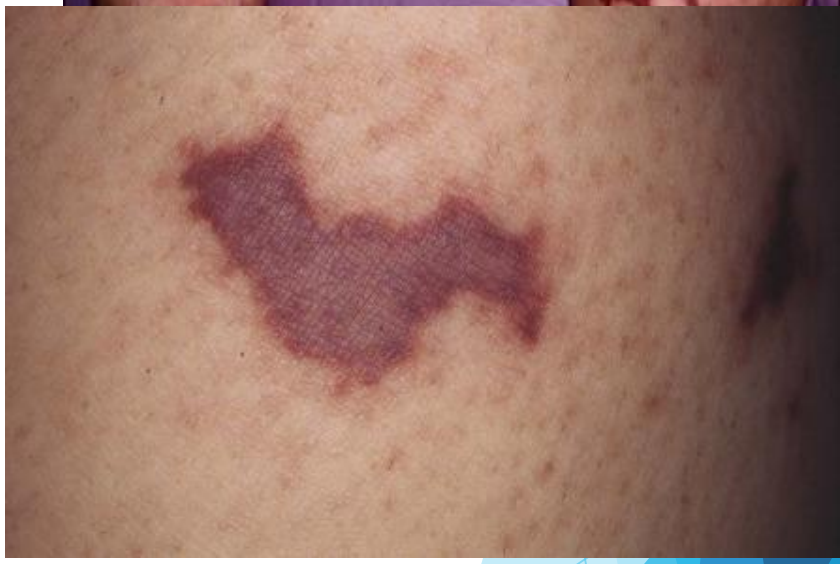


Meningococcemia

- 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**

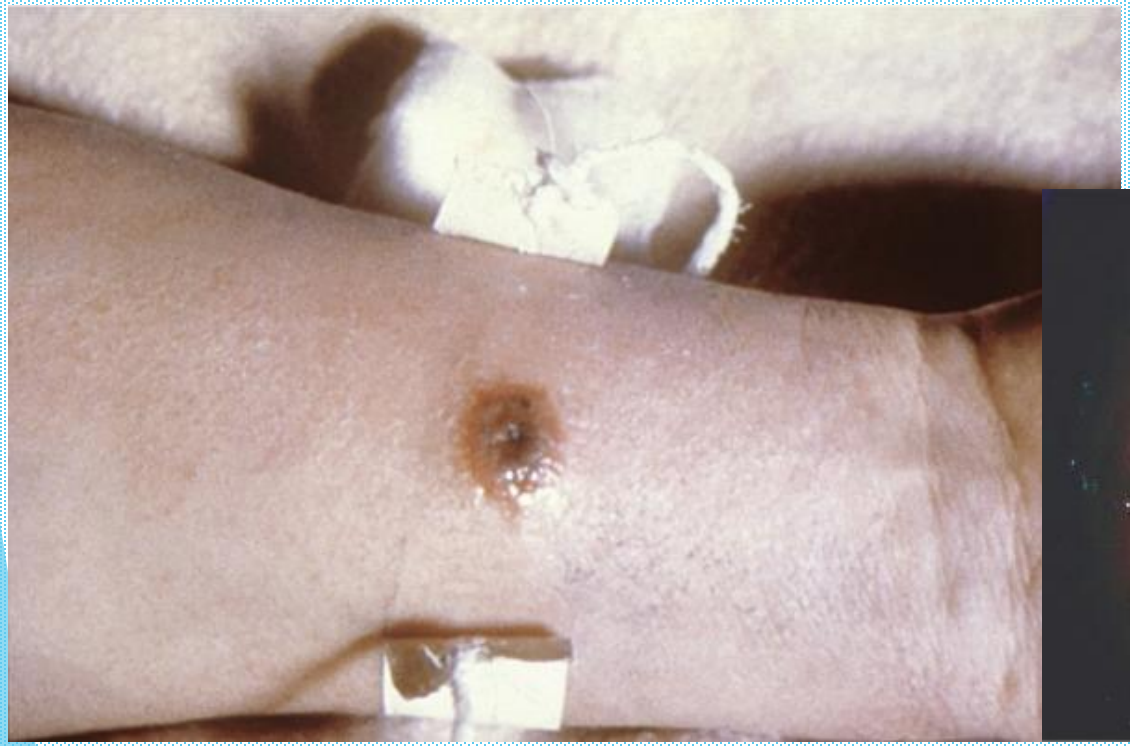
- ***Waterhouse-Friderichsen Syndrome"** (adrenal hemorrhage/ infarct) may occur 2* hypotension
  - Nasal carriage in 5-10%
  - Chronic form, very rare

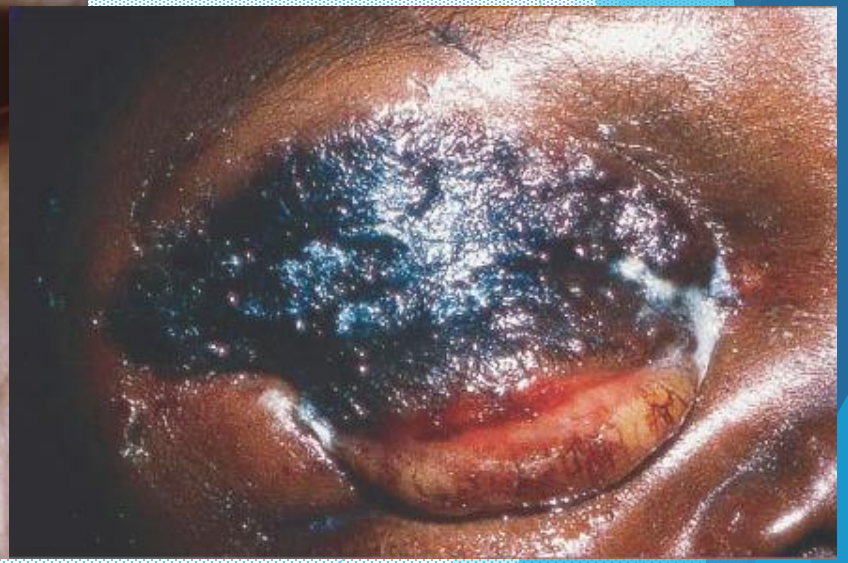




DDX: Acute-- septic vasculitis due to acute bacteremias and endocarditis, acute hypersensitivity vasculitides, enteroviral infections, RMSF, TSS, purpura fulminans and leptospirosis. Chronic-- subacute bacterial endocarditis, Sweet's syndrome, Henoch–Schönlein purpura, rat-bite fever, erythema multiforme 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 innoculation**
  - 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

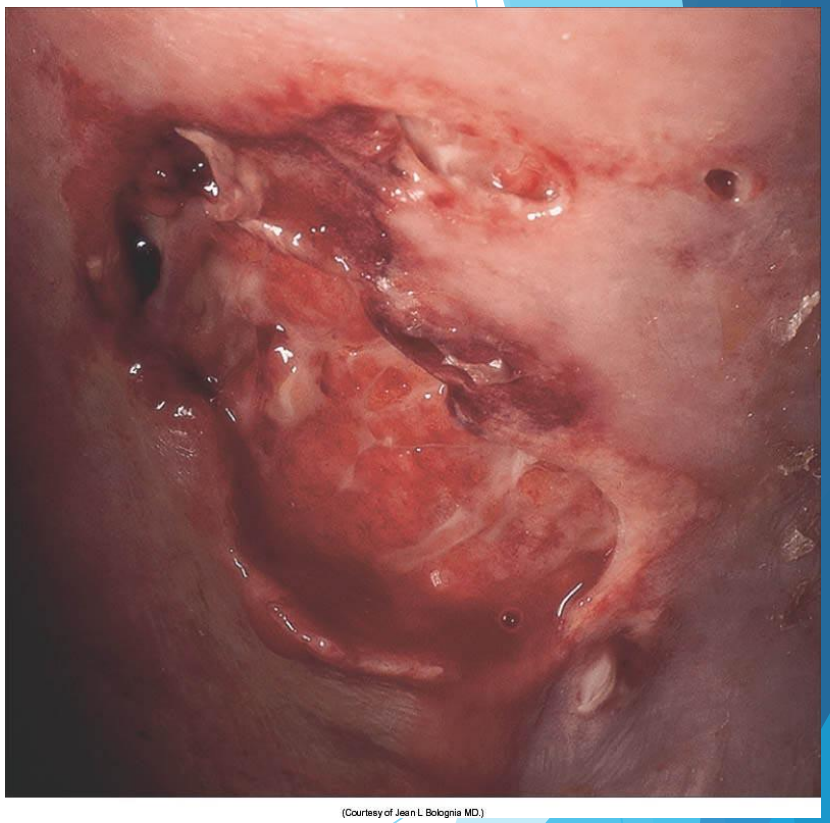
Anthrax

- 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, +/- serosanguinous blisters
- **Anesthesia** of involved skin
  - Suggests deep involvement & nerve destruction

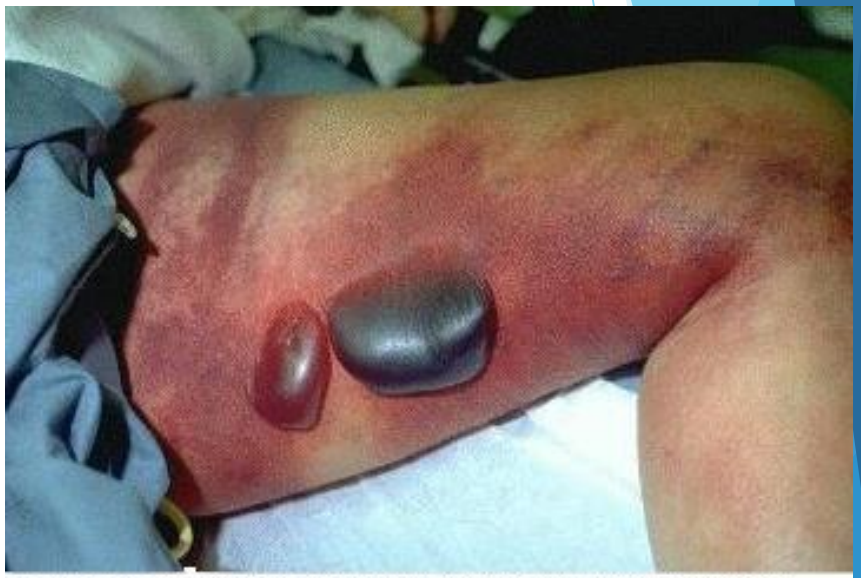


(Courtesy of Jean L. Bolognia MD.)

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

Necrotizing Fasciitis

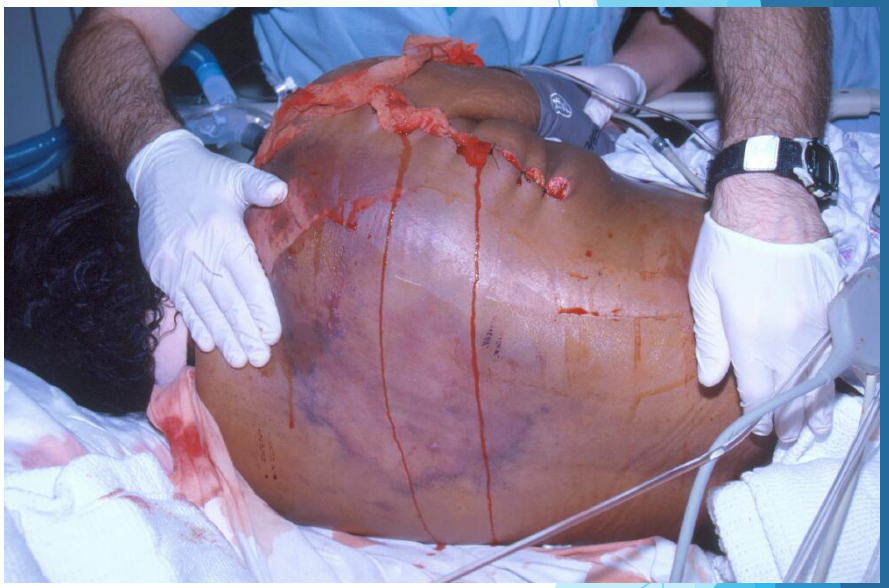
- Probe test: 2cm incision, probe with finger… lack of bleeding, murky discharge and lack of resistance = ominous signs
- Early surgical debridement is essential for successful therapy and IV Abx (broad spectrum & then more focused)
- Poor prognostic factors: age > 50, Diabetes, atherosclerosis, delay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



These large, dark, boil-like blisters are a diagnostic symptom of necrotizing fasciitis (also known as flesh-eating disease).
(Source: EMBBS, 1996 http://mdchoice.com/)

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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