Dermatologic Emergencies When to Act Fast!

ACOI Subspecialty Focused Review

May 12, 2022

Heather Layher, DO, MBA, FAAD

Objectives

- To recognize cutaneous manifestations of conditions that are considered dermatologic emergencies.
- To become familiar with the recommended work-up for various dermatologic emergencies.
- To be prepared to quickly manage dermatologic emergencies to provide patients with the best outcome.

Dermatologic Emergencies in Primary Care

- Adverse Drug Reactions
  - EM Major
  - SJS/TEN
  - DRESS
  - AGEP
- Infection Related Dermatoses
  - Eczema herpeticum
  - Staph scalded skin syndrome
  - Rocky Mountain spotted fever
  - Necrotizing fasciitis
- Immunobullous Exacerbations
  - Bullous pemphigoid
  - Pemphigus vulgaris

Adverse Drug Reactions

EM Major

SJS/TEN

DRESS

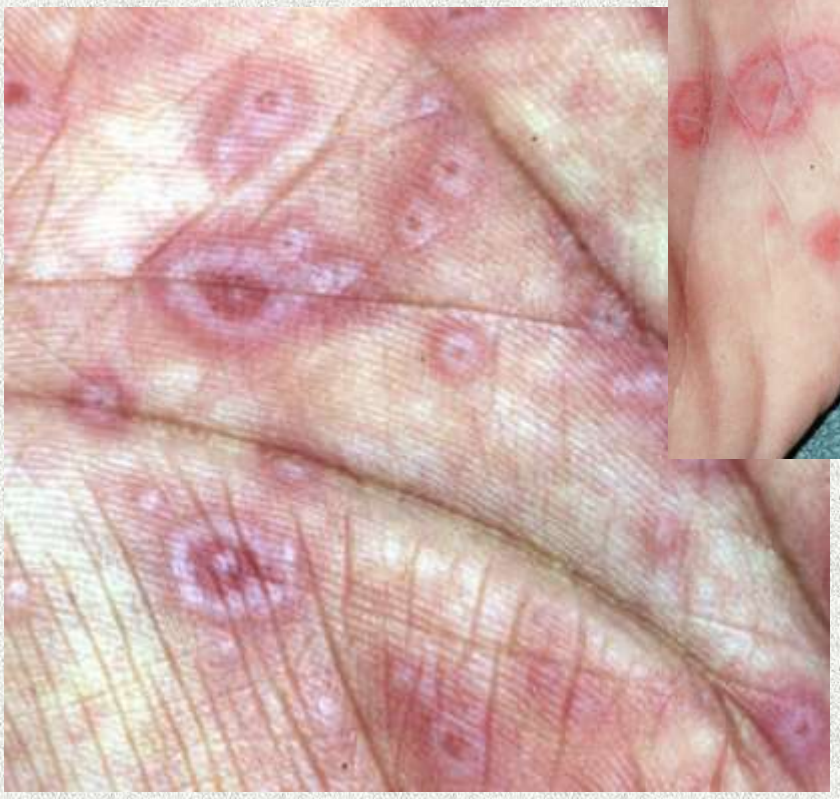
AGEP

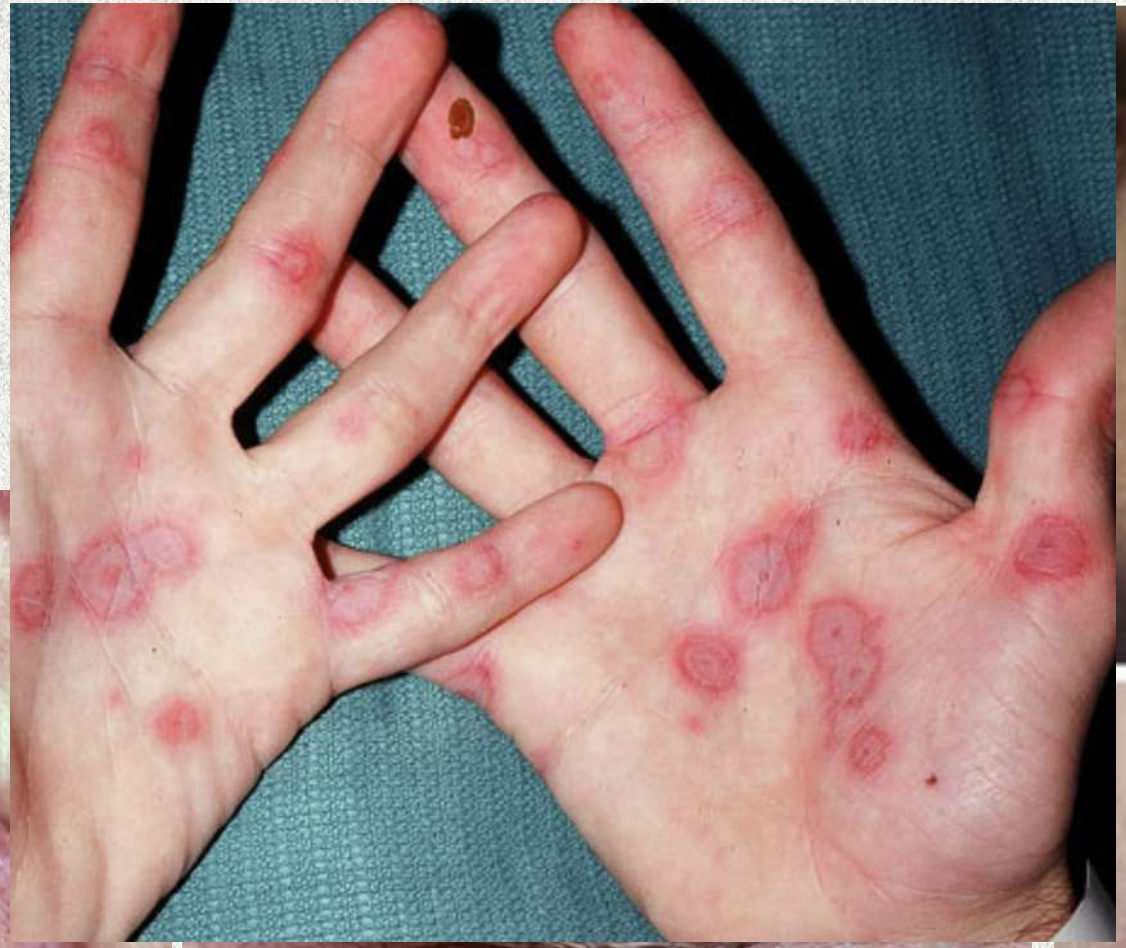
Erythema Multiforme (EM) Major

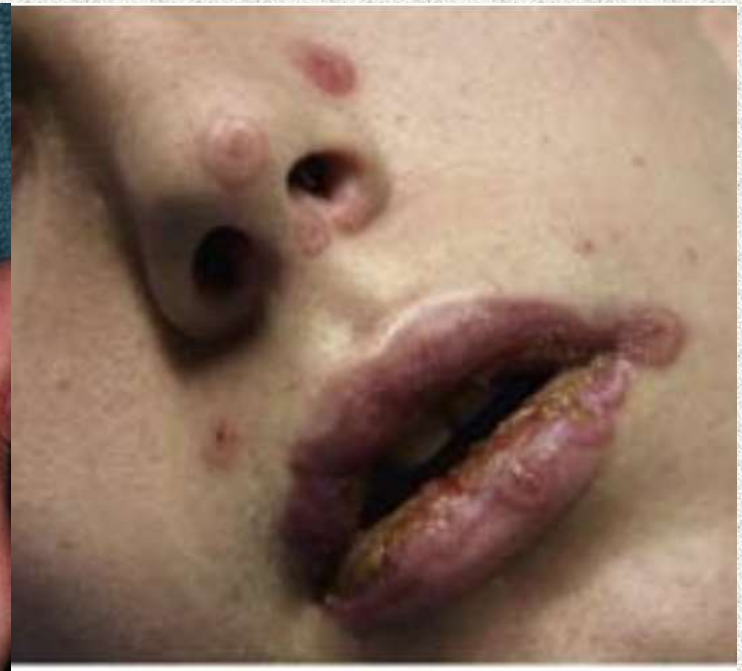
- Immune mediated mucocutaneous reaction most commonly to infection
  - Cutaneous eruption in both EM minor and EM major
  - Severe mucosal eruption in EM major only
- Population – young adults
- Causes – cutaneous reaction to HSV infection (most common), mycoplasma pneumoniae (associated with severe mucosal disease), systemic medications (NSAIDS, sulfadrugs, antiepileptics, allopurinol), other infections, radiation, malignancy, autoimmune disease
- Diagnosis – clinical, histopathological via biopsy and direct immunofluorescence
- Self resolving over 4-6 weeks, recurrence possible
  - Important note – EM is not in a spectrum with SJS/TEN and therefore does not progress

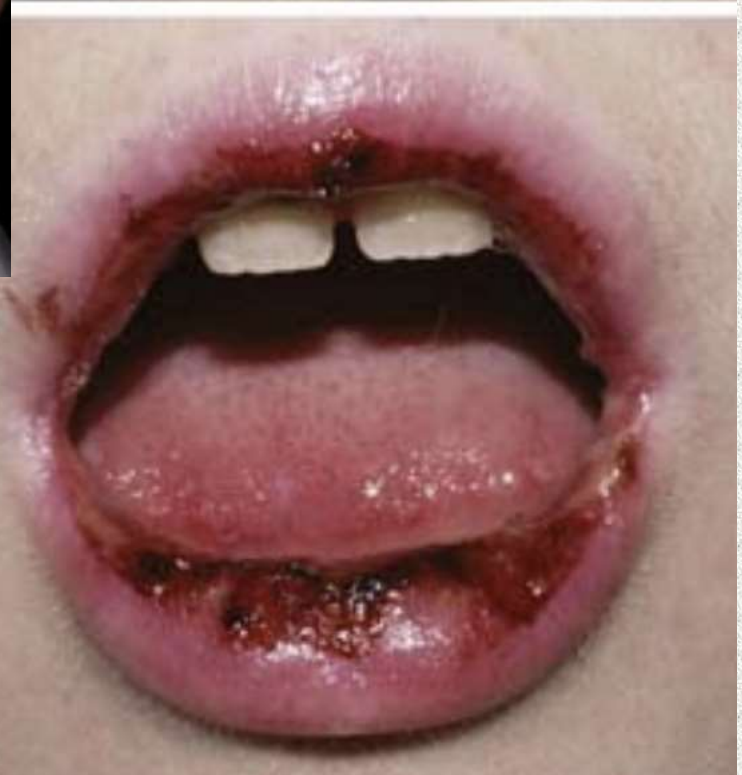
Erythema Multiforme (EM) Major – Presentation

- Prodrome – fever, fatigue, malaise, myalgia
- Classic cutaneous targetoid lesions appearing within 24 hours
  - 3 rings – central dusky erythematous papule surrounded by white ring surrounded by erythematous ring
  - Develop symmetrically on acral and facial surfaces and spread centrally to trunk
  - Painful, pruritis
- Mucosal involvement
  - Oral most common – blisters become erosions with whitish pseudo-membrane
  - Ocular – keratitis, uveitis, conjunctival scarring
  - Urogenital – blisters become erosions









Erythema Multiforme (EM) Major – Management

- Mucosal involvement is what makes EM major a dermatologic emergency
  - Decreased PO intake
  - Vision loss
  - Difficulty breathing due to erosions and sloughing of mucosa → although rare, may require intubation

Erythema Multiforme (EM) Major – Management

- Mild cutaneous disease
  - Topical steroids for skin (Triamcinolone, Clobetasol), swish-and-spit steroids for mouth (Betamethasone)
  - Antihistamines
  - Oral Lidocaine swish-and-spits
- Severe mucosal disease
  - Admission – oral intake support, possibly airway support
  - Prednisone
- Treatment of cause
  - Suppressive Acyclovir/Valacyclovir (questionable benefit)
  - Remove triggering medications if medication-induced

Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)

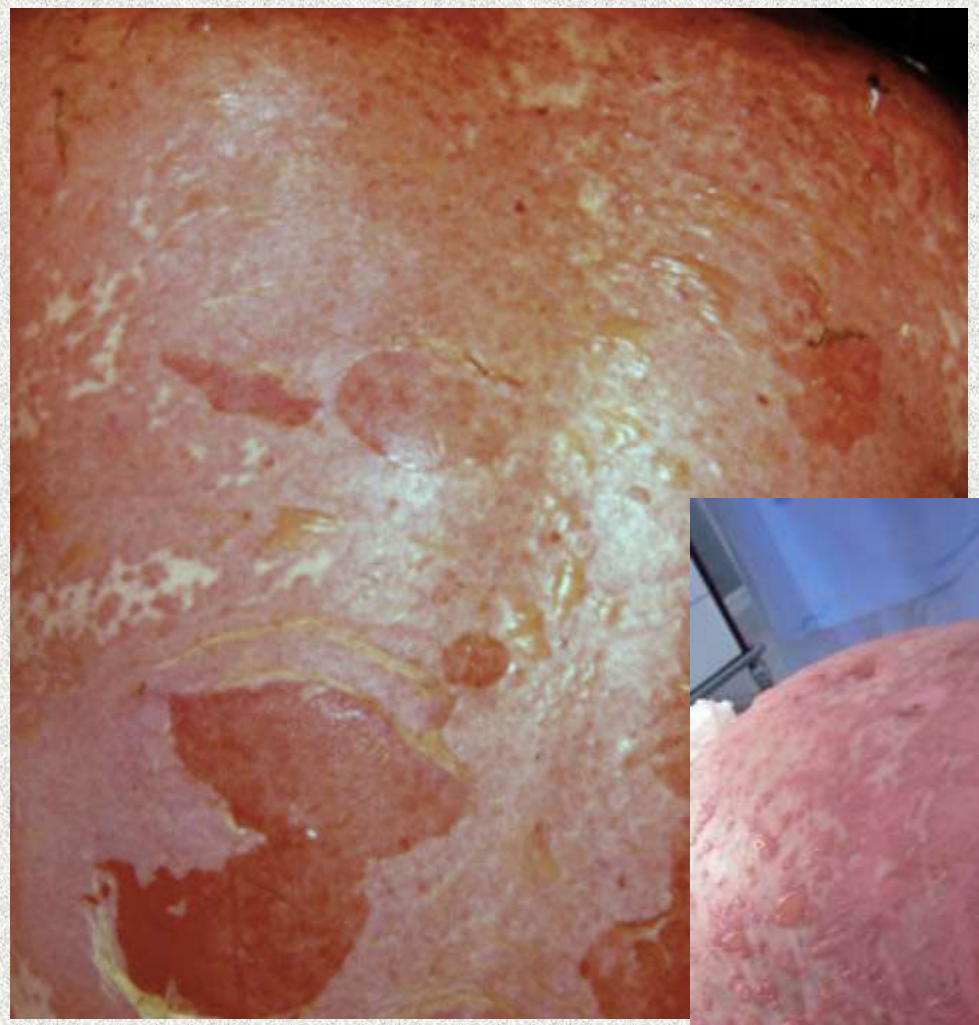
- Acute, severe cutaneous adverse reaction most commonly to medications
- Population – any age, gender, race
  - Higher risk in HIV
- Causes –
  - Medications (most common) –
    - Antibiotics (40%) – sulfonamides, penicillins, cephalosporins
    - Other common drugs – anticonvulsants and allopurinol
    - Less common drugs – acetaminophen, NSAIDs, nevirapine
  - Infections (very rare) – CMV

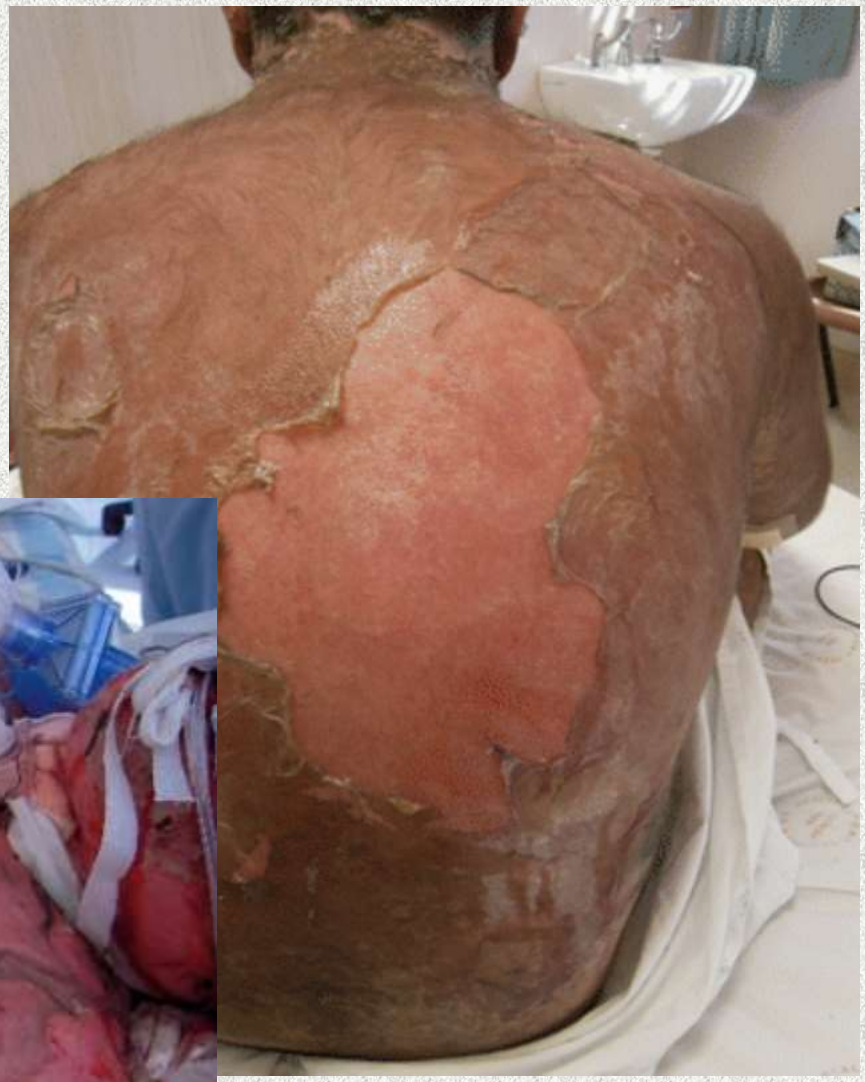
SJS/TEN – Presentation

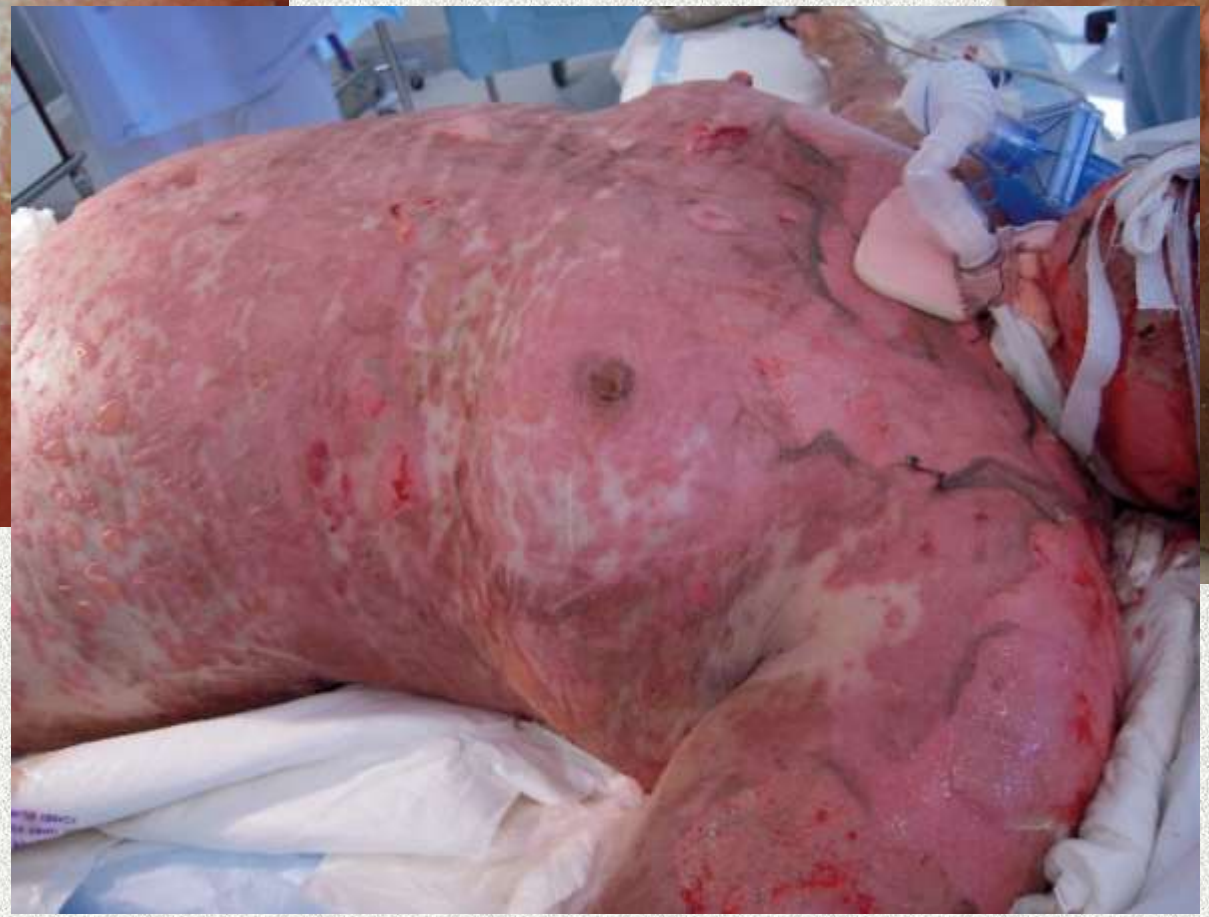
- Onset variable – within 1 week with antibiotics, few days to 3 weeks with most other drugs, up to 2 months with anticonvulsants
- Spectrum of diseases determined by % of skin involvement
  - SJS <10% TBSA >> SJS/TEN overlap 10-30% TBSA >> TEN >30% TBSA
- Prodrome – flu-like symptoms (fever, sore throat, runny nose, cough, conjunctivitis, red sore eyes, malaise and myalgias) + painful skin

SJS/TEN – Skin Presentation

- Abrupt onset of tender skin lesions starting on trunk and rapidly spreading to face and extremities over few days
  - Scalp, palms/soles – not involved
- Morphology
  - Erythematous, dusky or purpuric macules
  - Diffuse erythema
  - Targetoid or bullous (flacid)
- Skin lesions coalesce → skin sloughs in sheets → oozing red raw dermis
- Nikolsky sign – rubbing of finger on skin causes shearing of epidermis

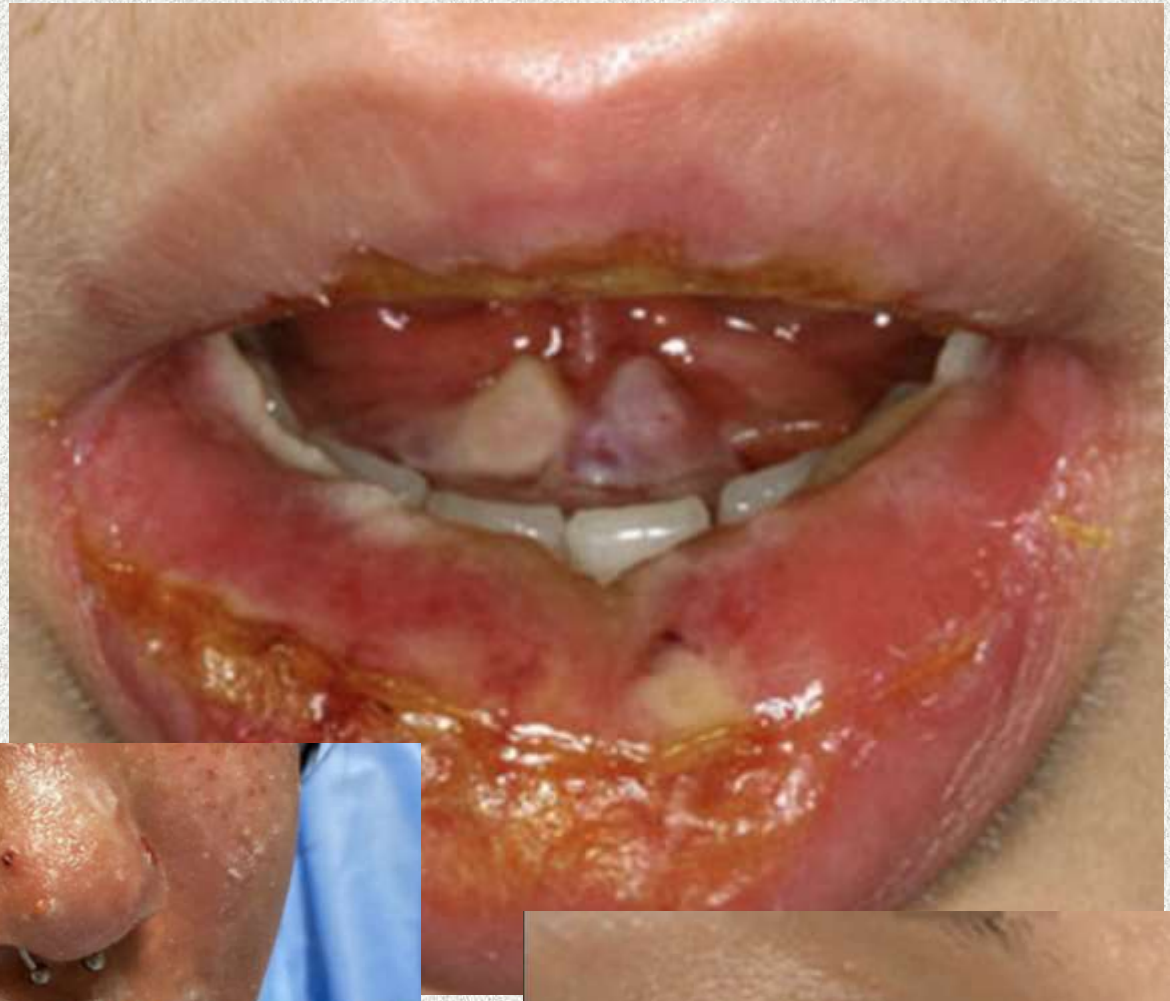


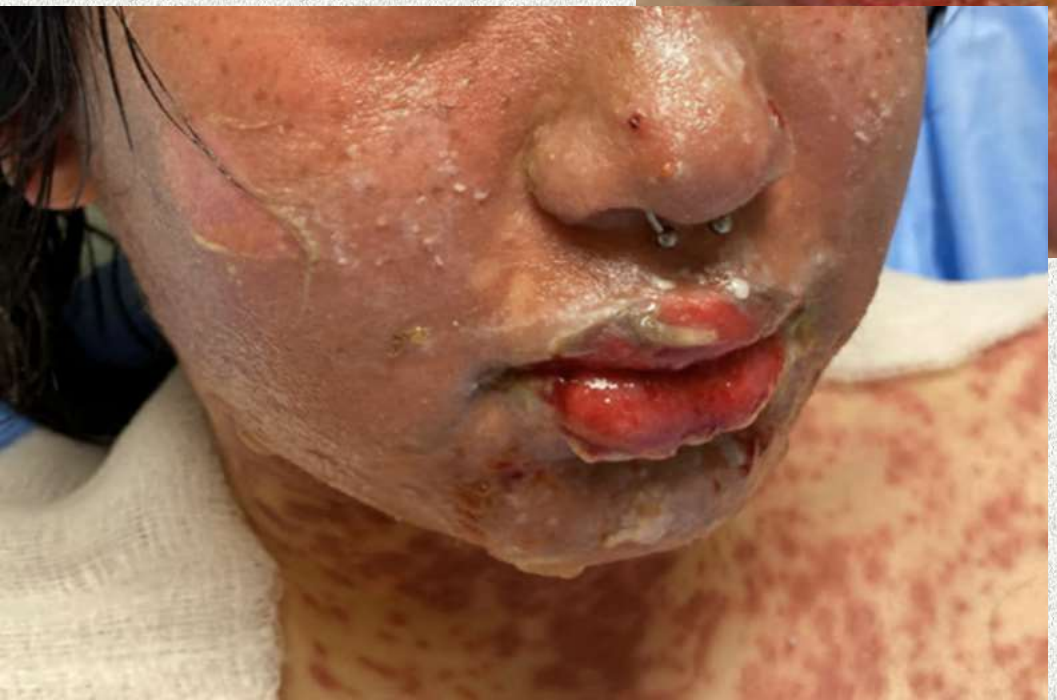




SJS/TEN – Mucosal Presentation

- Severe mucosal involvement classic with SJS/TEN
- Oral – chelitis, stomatitis → red crusted painful lips and mouth ulcers
- Ocular – conjunctivitis, ulceration, uveitis, photosensitivity → red sore eyes
- Genital – erosions/ulcers → urinary retention, scarring
- Respiratory – sloughing of trachea/bronchus → coughing, respiratory distress requiring intubation





SJS/TEN – Complications (Early)

- Mortality – 1-5% in SJS, 25-35% in TEN
- Dehydration
- Malnutrition
- Infection – cutaneous and hematologic
- Respiratory distress
- Gastrointestinal ulceration and perforation
- Shock, multiorgan failure

*Very low threshold for admission in SJS, absolute admission in TEN

SJS/TEN – Complications (Long-Term)

- Widespread pigment alteration
- Widespread scarring (may appear similar to burn scarring)
- Xerophthalmia, epiphora, conjunctivitis, corneal scarring, ectropion/entropion, trichiasis
- Scarring permanent loss of nails
- Phimosis (foreskin scarring), vaginal introitus scarring
- Joint contractures
- Chronic bronchitis, obstructive lung disease

SJS/TEN – Workup

- Skin biopsy can confirm
- Monitor labs – pancytopenia, transaminitis (hepatitis possible), proteinuria (renal failure possible)
- SCORTEN

1 point per criteria

- >40yo
- Malignancy
- HR >120
- >10% initial TBSA
- Urea >10mmol/L
- Glucose >14mmol/L
- Bicarbonate <20mmol/L

SCORETEN scores estimates mortality

- 0-1 – 3.2%
- 2 = 12.1%
- 3 = 35.3%
- 4 = 58.3%
- 5+ = 90%

SJS/TEN – Management

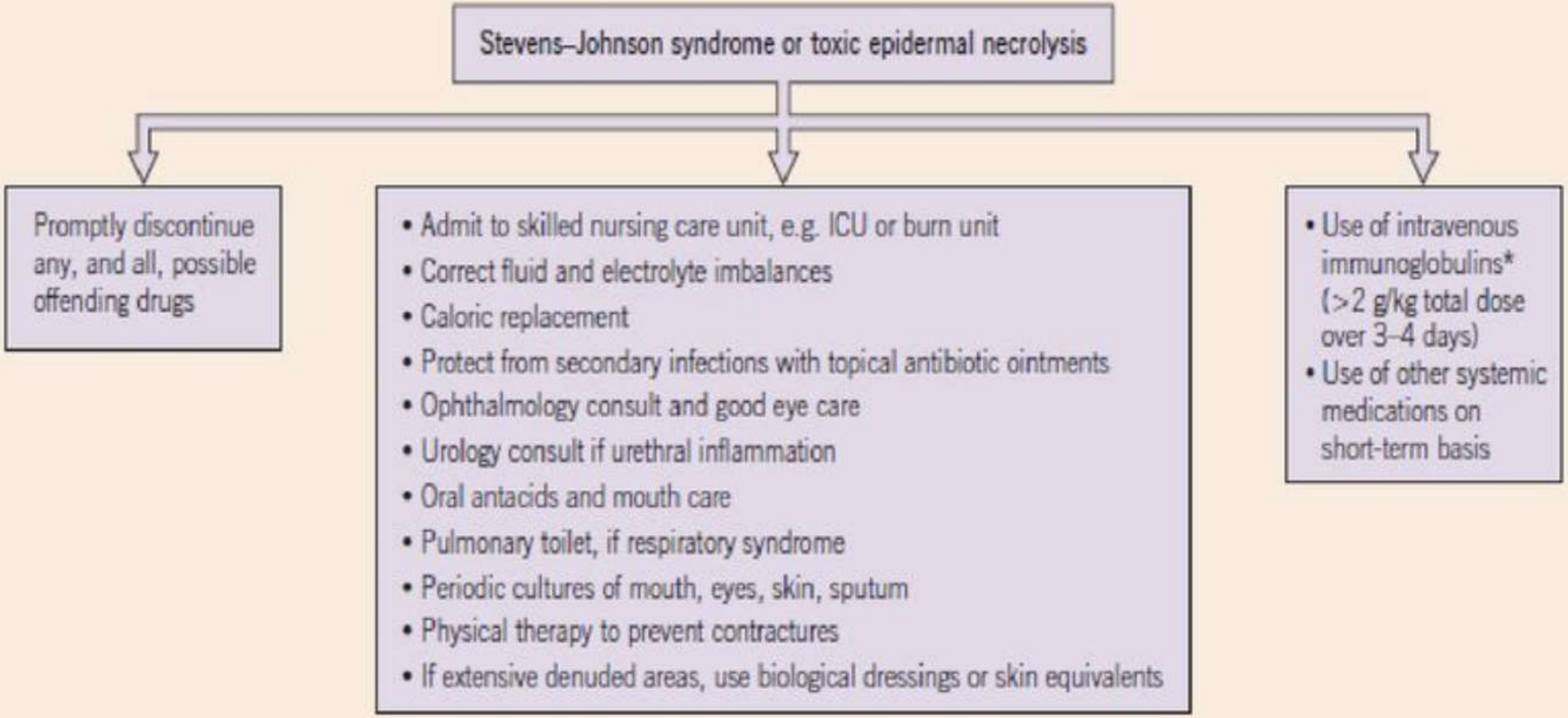
- Stop causative drug
- Admission – ICU or burn unit
  - Nutrition replacement
  - Fluid replacement (important to place Foley early)
  - Thermoregulation
  - Pain relief
  - Airway management (intubation)
- Skin – gentle skin care and cleaning (chlorhexidine, silver nitrate), Vaseline wraps, avoid adhesives
- Ocular – Ophtho consult, eyedrops (lubricating, antibacterial, and steroid) to prevent ocular scarring and vision loss
- Oral – steroid swish-and-spit, anesthetic swish-and-spit
- Vaginal – intravaginal topical steroids to prevent vaginal scarring

*Always monitor for cutaneous and systemic infection

SJS/TEN – Medication Management

- High dose systemic steroids during first 5 days (benefit still questionable)
- Ciclosporin may significantly reduce mortality
- Less common treatments
  - TNFa-inhibitors
  - Cyclophosphamide
  - IVIG
  - Plasmapheresis
  - GCSF

APPROACH TO THE PATIENT WITH STEVENS–JOHNSON SYNDROME OR TOXIC EPIDERMAL NECROLYSIS



Question 1

Which of the following is false regarding toxic epidermal necrolysis (TEN)?

A. >30% of total body surface area is involved in TEN
B. Sulfa drugs and antiepileptics are two of the most common causative agents
C. Mortality is low at less than 5%
D. General onset is within 3 weeks after starting causative agent

Question 2

T/F – TEN requires admission for airway support, thermal regulation, fluid monitoring and replacement, nutritional support and wound care. This is best accomplished in a burn unit or a unit familiar with managing such requirements.

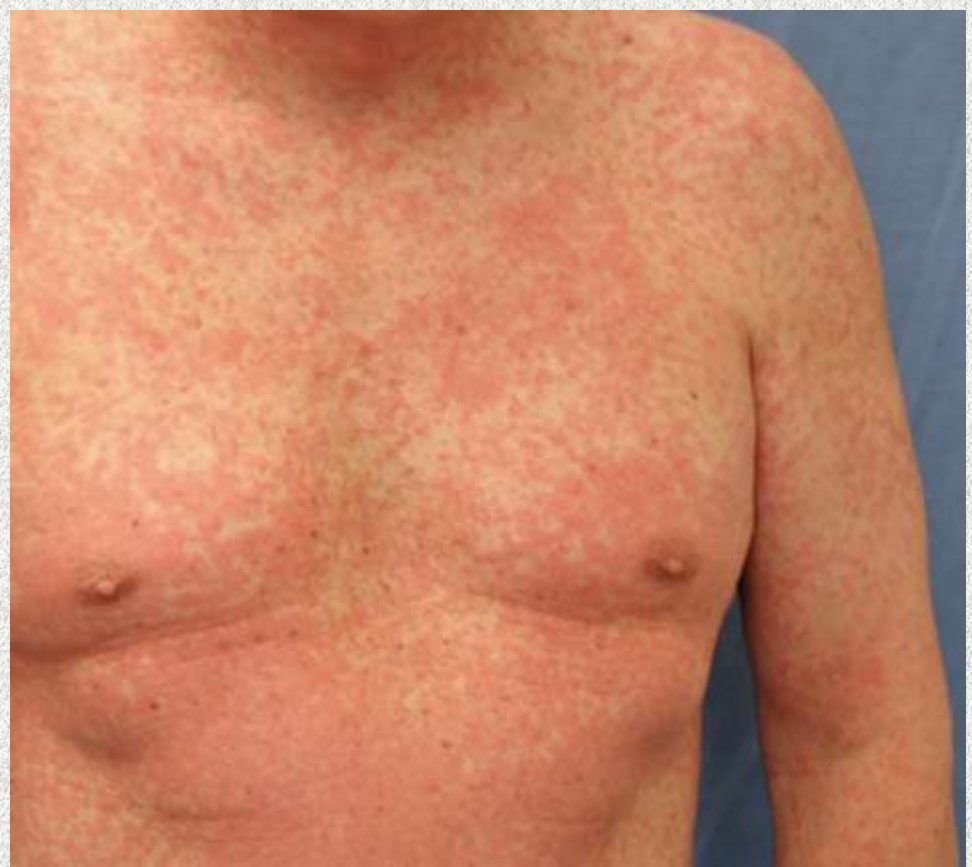
Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

- Acute, severe systemic adverse drug reaction
- Synonyms – drug hypersensitivity syndrome (DHS), drug-induced hypersensitivity syndrome (DIHS)
- Population – adults, M=F
- Causes – anticonvulsants (carbamazepine, phenobarbital, phenytoin), allopurinol, olanzapine, sulphonamide antibiotics
  - Onset – within 2 weeks with antibiotics, greater than 2 weeks with anticonvulsants and allopurinol
  - Anticonvulsants – estimated 1:10,000 patients
  - Allopurinol – risk increases in CKD and concomitant thiazide diuretics

DRESS – Skin Presentation

- Symptoms develop over several days
- Fever of 38-40C followed by widespread rash
  - Morbilliform eruption
  - Facial edema
  - Mucosal involvement less common

*Severity of cutaneous eruption does not correlate with severity of systemic involvement



DRESS – Systemic Presentation

- Systemic symptoms may continue to worsen and persist for several weeks even after drug discontinuation
  - Generalized lymphadenopathy*
  - Atypical lymphocytes*, eosinophilia*, leukocytosis, thrombocytopenia, anemia
  - Transaminitis*, hepatitis, liver failure
  - Myocarditis*, pericarditis
  - Thyroiditis* (autoimmune)
  - Interstitial nephritis (mild and rare)
  - Interstitial pneumonitis, pleuritis, pneumonia, ARDS
  - Meningitis, encephalitis, polyneuritis
  - Gastroenteritis, pancreatitis, GI bleeding, actue colitis
  - Myositis
  - Uveitis

DRESS – Diagnosis

- Diagnosis determined using regiSCAR scoring system
- Final score –
  - <2 – not DRESS
  - 2-3 – possible DRESS
  - 4-5 – probable DRESS
  - >5 – definite DRESS

RegiSCAR SCORING SYSTEM FOR DRESS

Criteria	No	Yes	Unknown/unclassifiable
Fever (≥38.5°C)	−1	0	−1
Lymphadenopathy (≥2 sites; >1 cm)	0	1	0
Circulating atypical lymphocytes	0	1	0
Peripheral hypereosinophilia	0		0
0.7–1.499 × 10^9/L - or - 10–19.9%*		1	
≥1.5 × 10^9/L - *or* - ≥20%*		2	
Skin involvement			
• Extent of cutaneous eruption > 50% BSA	0	1	0
• Cutaneous eruption suggestive of DRESS**	−1	1	0
• Biopsy suggests DRESS	−1	0	0
Internal organs involved†	0		0
One		1	
Two or more		2	
Resolution in ≥15 days	−1	0	−1
Laboratory results negative for at least three of the following (and none positive): (1) ANA; (2) blood cultures; (3) HAV/HBV/HCV serology; and (4) *Chlamydia* and *Mycoplasma* serology	0	1	0
Final score: < 2, no case; 2–3, possible case; 4–5, probable case; >5, definite case			

DRESS – Complications

- Delayed autoimmune thyroiditis
  - TSH/T4 during admission, at 6-12 weeks, as well as at 1 and 2 years post-DRESS
- Fulminant myocarditis
  - Echo during admission and at 3 weeks post-DRESS
- Hemophagocytic syndrome
- Hepatic failure
- Multiorgan failure

DRESS – Management

- Admission
- Withdrawal of causative drug
- Systemic workup

Basic laboratory screening during the acute phase with recommended repetitive tests *in italics*^
• *CBC with differential, platelet count,* peripheral smear for atypical lymphocytes • *BUN, creatinine, urinalysis,* spot urine for protein : creatinine ratio* • *LFTs, creatine kinase (CK),* lipase, CRP • *TSH, free T4* (repeat at 3 months, 1 year, and 2 years) • Fasting glucose (in anticipation of systemic corticosteroids)
Additional testing
• ECG, troponin T, baseline echocardiogram • Quantitative PCR for HHV-6, HHV-7, EBV, CMV • Wright stain of urine for eosinophilia (prior to instituting corticosteroids) • ANA, blood cultures (exclusion criteria in RegiSCAR scoring system) • If hemophagocytic lymphohistiocytosis suspected (see Ch. 91)**, ferritin, triglycerides, LDH, BM examination
Further testing based upon laboratory abnormalities or signs and symptoms**
• Liver – PT, PTT, albumin • Renal – albumin, renal ultrasound (if laboratory abnormalities) • Cardiac – ECG, troponin T, echocardiogram • Neurologic – brain MRI • Pulmonary – CXR, PFTs • Gastrointestinal – endoscopy

^Testing is more frequent during the acute phase (e.g. twice weekly) with frequency also a reflection of disease severity. Longitudinal evaluation is recommended for at least one year.

*Allows for immediate assessment for proteinuria.

**Including during longitudinal evaluation.

DRESS – Management

- Skin – wound care and emollients, topical steroids, oral antihistamines
- Systemic Prednisone in cases with severe systemic involvement
- Other systemic therapies – ciclosporin, IVIG, plasmapheresis, cyclophosphamide, mycophenolate, rituximab
- Fluid, electrolyte and calorie management in severe systemic cases

Question 3

Which of the following is not a potential finding in drug reaction with eosinophilia and systemic symptoms (DRESS)?

A. Centrofacial erythema and edema
B. Lymphadenopathy
C. Leukocytosis
D. Eosinophilia
E. Elevated LFTs
F. All of the above are potential findings in DRESS

Question 4

Which of the following is recommended in the management of drug reaction with eosinophilia and systemic symptoms (DRESS)?

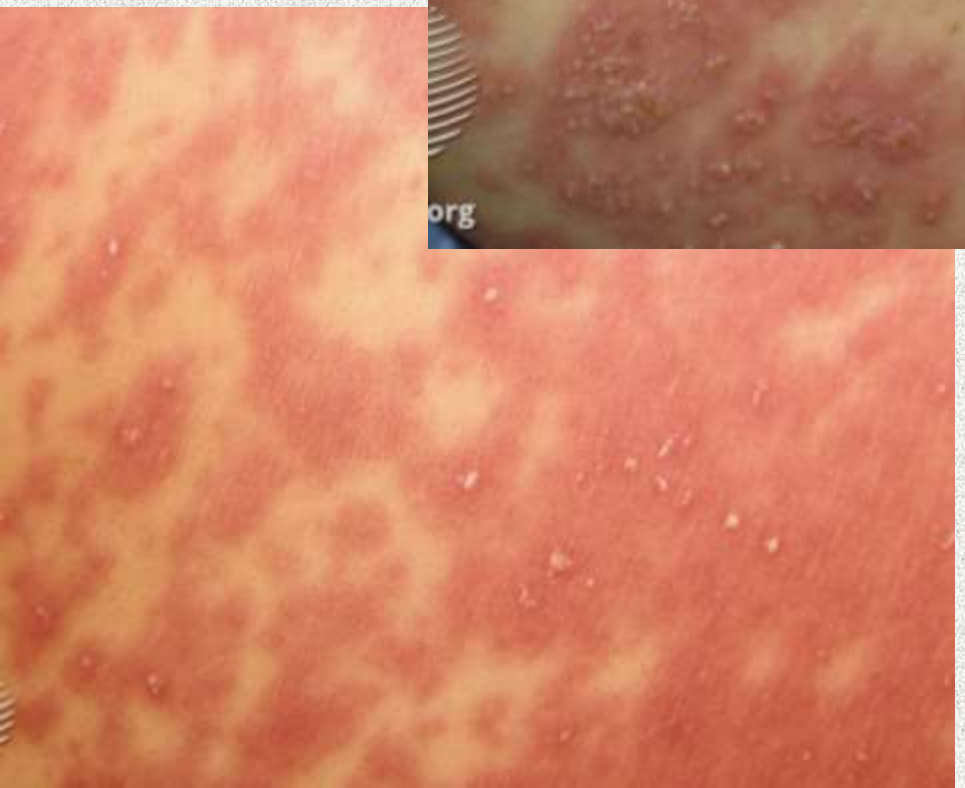
A. Admission to ICU or burn unit, withdrawal of causative agent, and in the setting of lab workup indicative of end-organ involvement, initiation of systemic steroids at at least 1mg/kg/day
B. LFTs, PTT/PT/INR and hepatitis panel due to risk of fulminant hepatitis
C. EKG and echocardiogram due to risk of myocarditis and heart failure during admission and within 3 months after recovery
D. TSH/T4 due to risk of autoimmune thyroiditis during admission and 6 weeks and 3 months after recovery
E. BUN/Cr, urinalysis, possible renal US due to risk of renal failure
F. All of the above are recommended

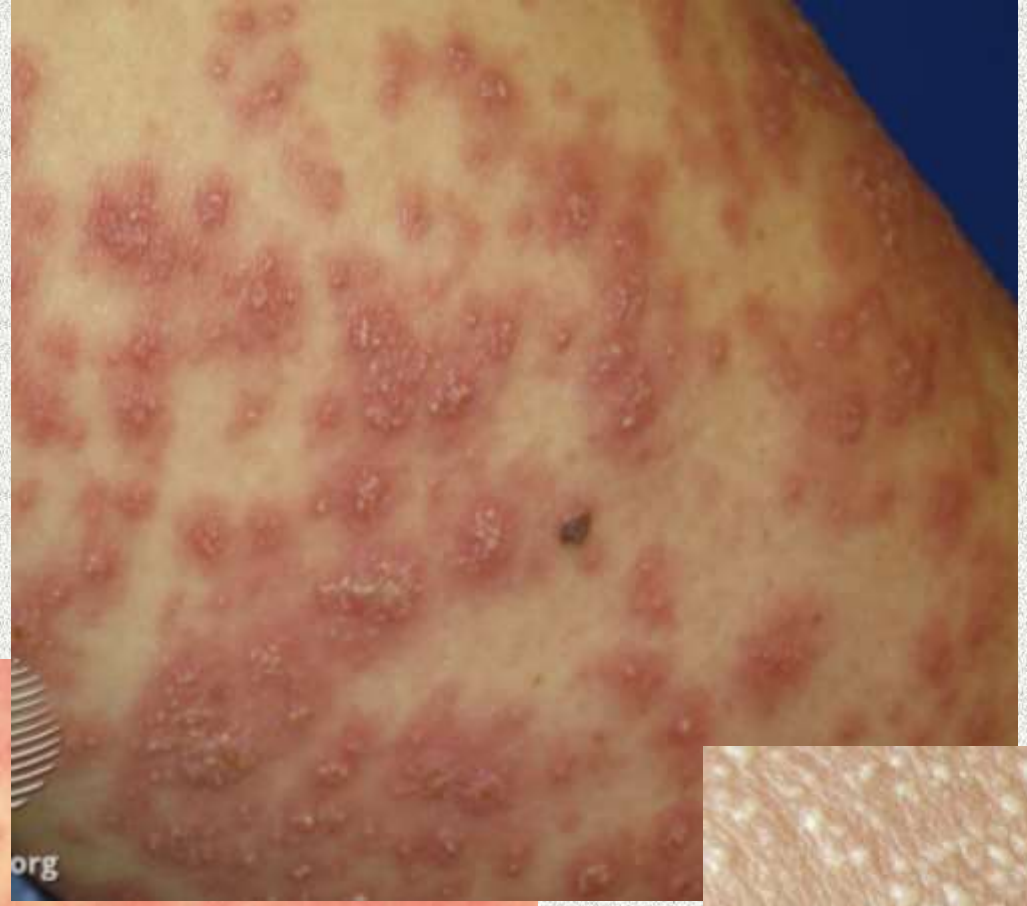
Acute Generalized Exanthematous Pustulosis (AGEP)

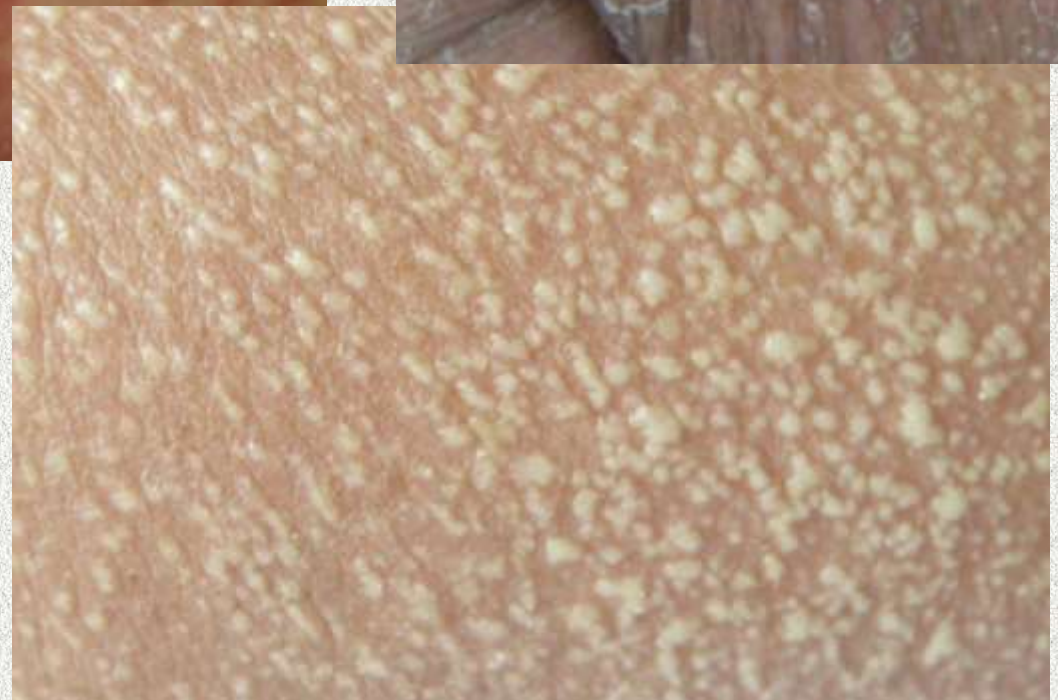
- Acute cutaneous eruption due to medication
- Population – all ages and genders
- Causes – beta-lactam antibiotics (penicillins, cephalosporins, quinolones), tetracyclines, sulfonamides, terbinafine, calcium channel blockers, hydroxychloroquine, carbamazepine, acetaminophen, viral infection (less common – EBV, HBV, CMV, enterovirus, adenovirus)

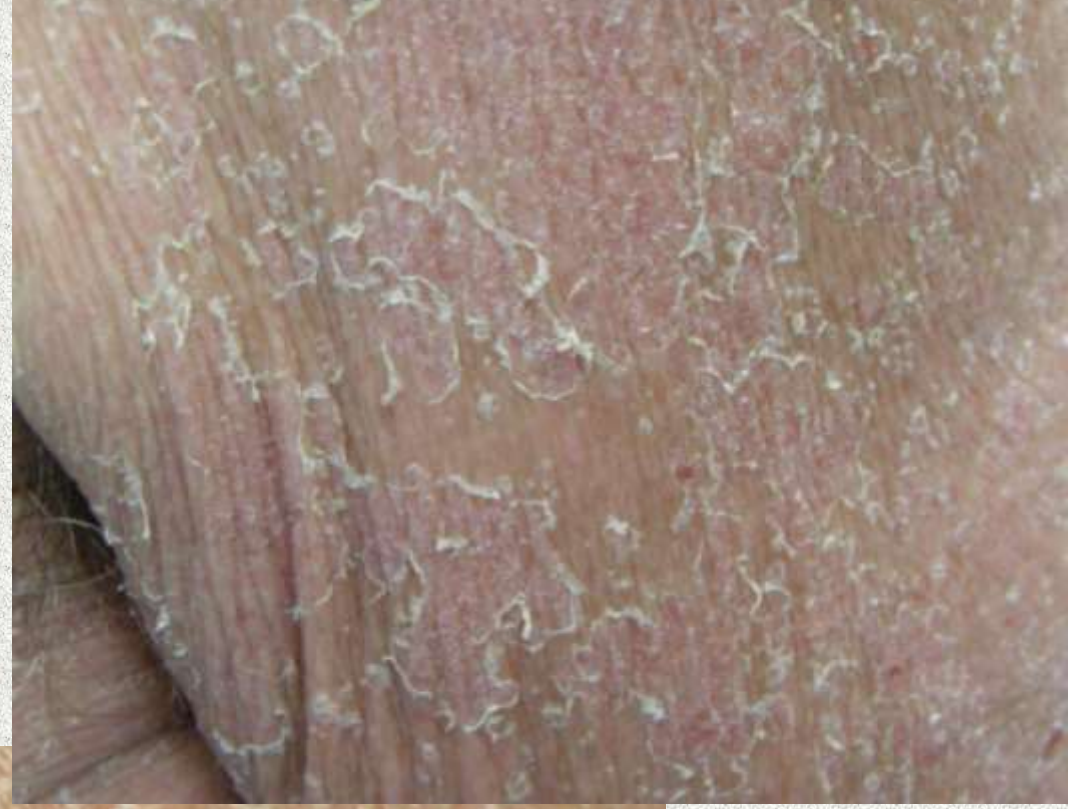
AGEP – Presentation

- Rapid onset
- Patchy erythema with tiny sterile pustules
  - Starts in armpits/groin then becomes more widespread, but remains more prominent in skin folds
- Facial swelling possible
- Oral lesions less common (~20%)
- Fever, malaise possible, but patient is generally not unwell
- Persists for 1-2 weeks followed by focal superficial skin desquamation
- Systemic involvement uncommon (~10%) – hepatic, renal, pulmonary, hematologic









AGEP – Management

- Typically admitted, although less severe cases can be managed outpatient
- Discontinue causative drug
- Topical steroids, oral antihistamines, wound care and emollients, topical analgesics
  - Systemic therapy rarely indicated

Infection Related Dermatoses

Eczema herpeticum

Staphylococcal scalded skin syndrome

Rocky Mountain spotted fever

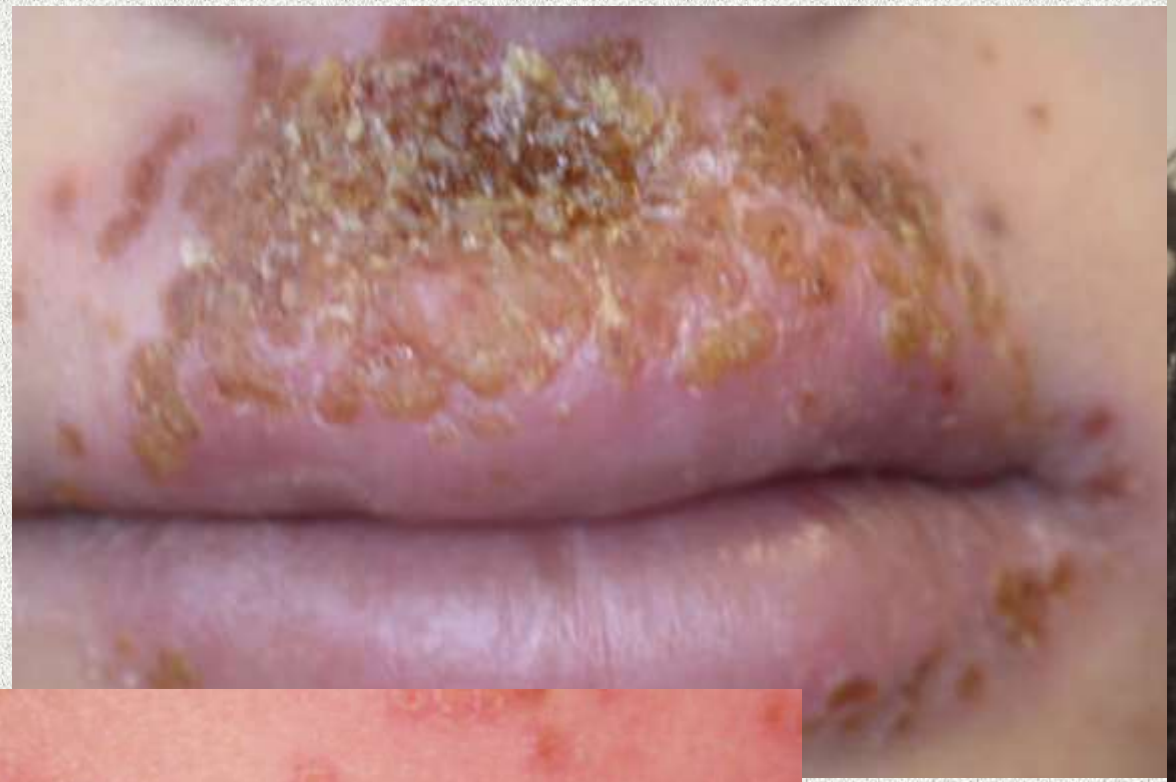
Necrotizing fasciitis

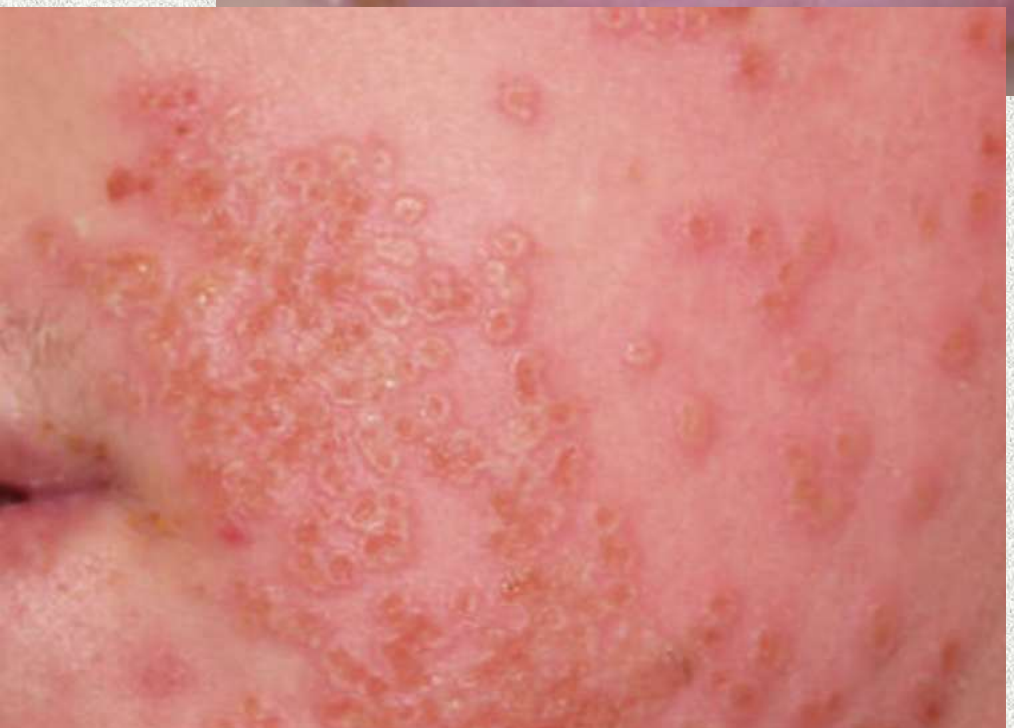
Eczema Herpeticum

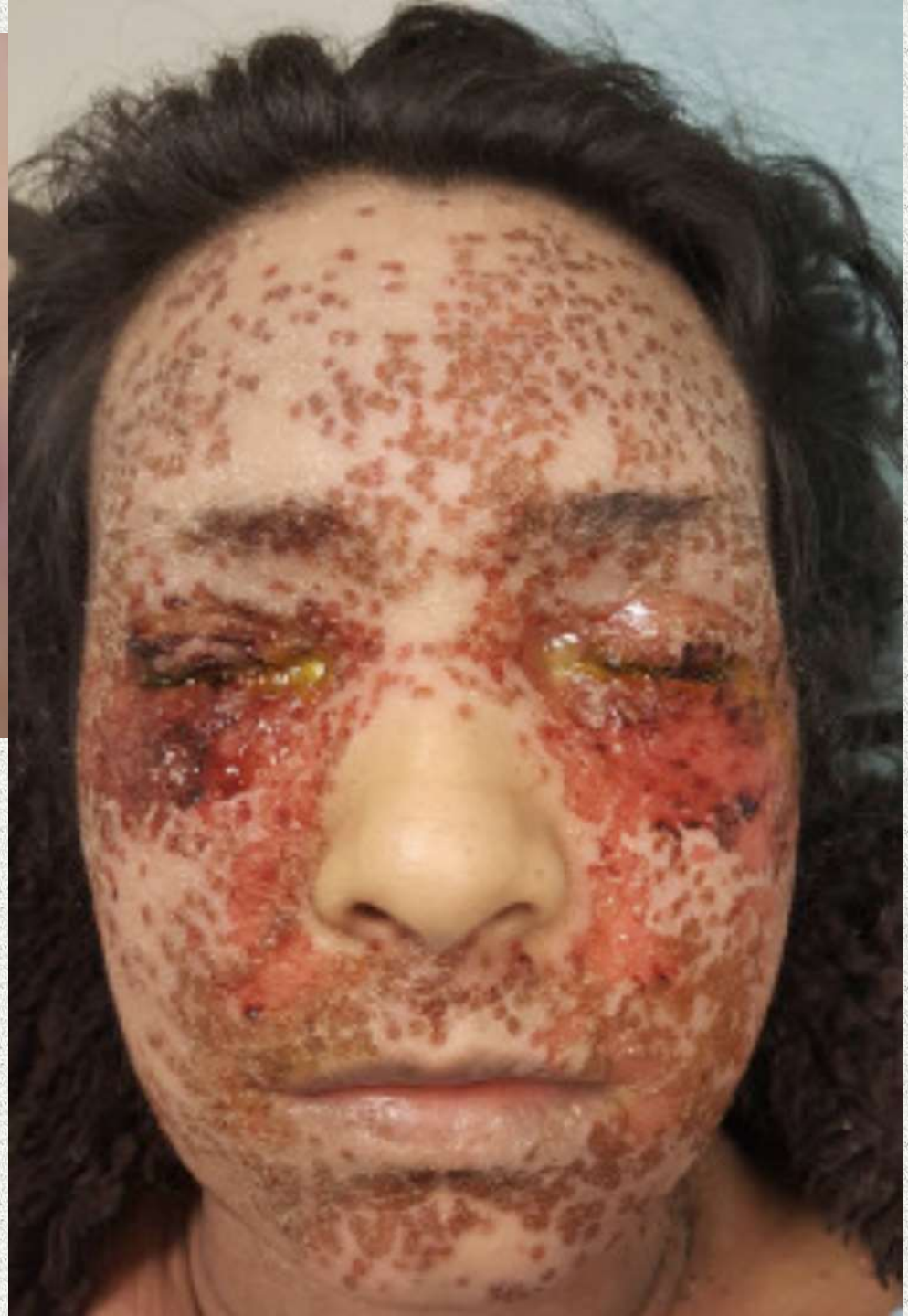
- Synonym – Kaposi varicelliform eruption
- Widespread HSV infection within atopic dermatitis
- Population – individuals with underlying atopic dermatitis (infants, children more common)
  - Can appear in other dermatoses and areas of skin breakdown
- Cause – HSV types 1 or 2
  - Typically occurs with first outbreak, recurrences are uncommon
  - Variants – eczema coxsackium (hand foot mouth disease), disseminated vaccinia (smallpox vaccine)

Eczema Herpeticum – Presentation

- Fever, malaise, LAD common
- Lesions may appear and spread over 7-10 days
- Clusters of monomorphic painful vesicles, some with umbilication, that progress to crusted erosions over several weeks
- Impetiginization common, especially around nose and mouth
- Ocular involvement possible when periorbital region involved and requires emergent management by Ophthalmology







Eczema Herpeticum – Management

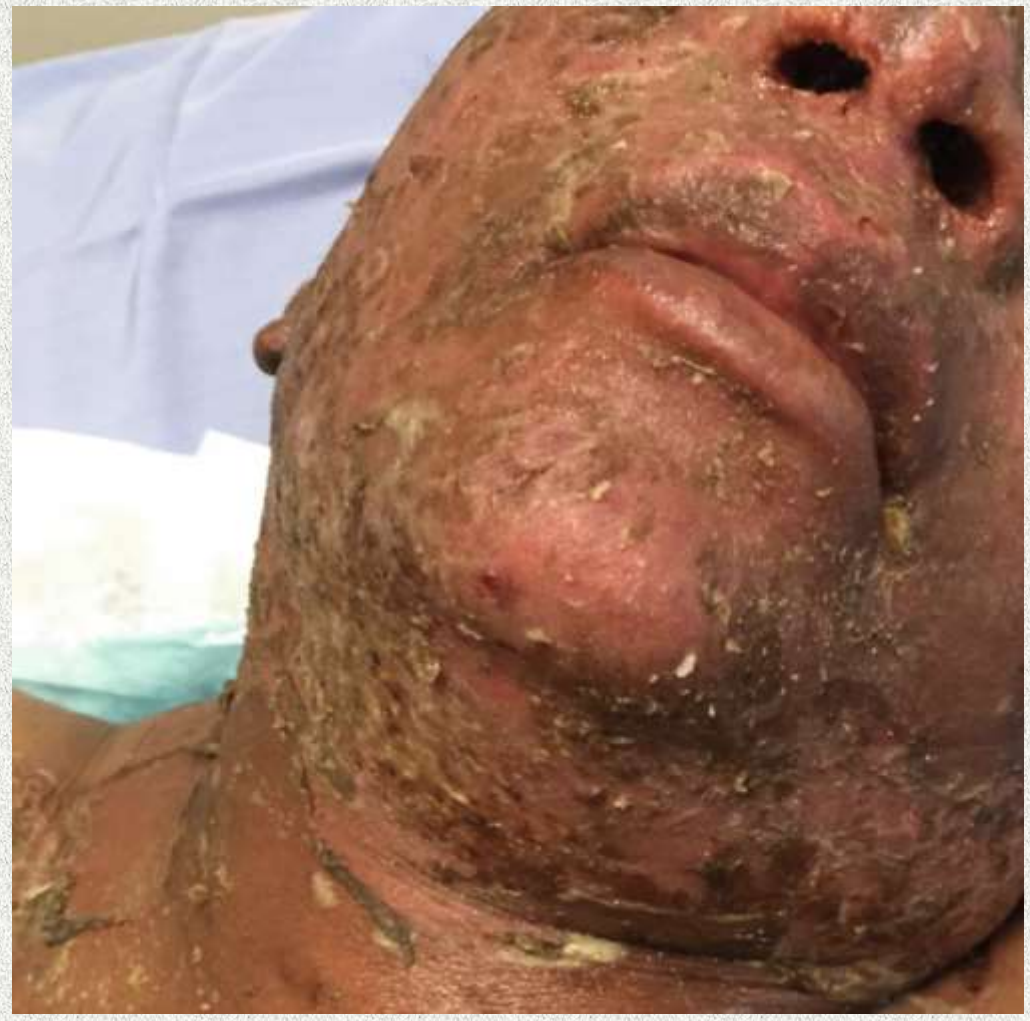
- Admission typically not required, but depends on symptoms and if underlying immunosuppression
- Urgent management with antivirals
  - Acyclovir 400-800mg 5 times daily x10-14 days
  - Valacyclovir 1g BID x10-14 days
  - IV Acyclovir 15mg/kg/d if admitted
- Management of impetiginization with antibiotics
- Topical steroids for symptoms control (only ok to use once antivirals are initiated)

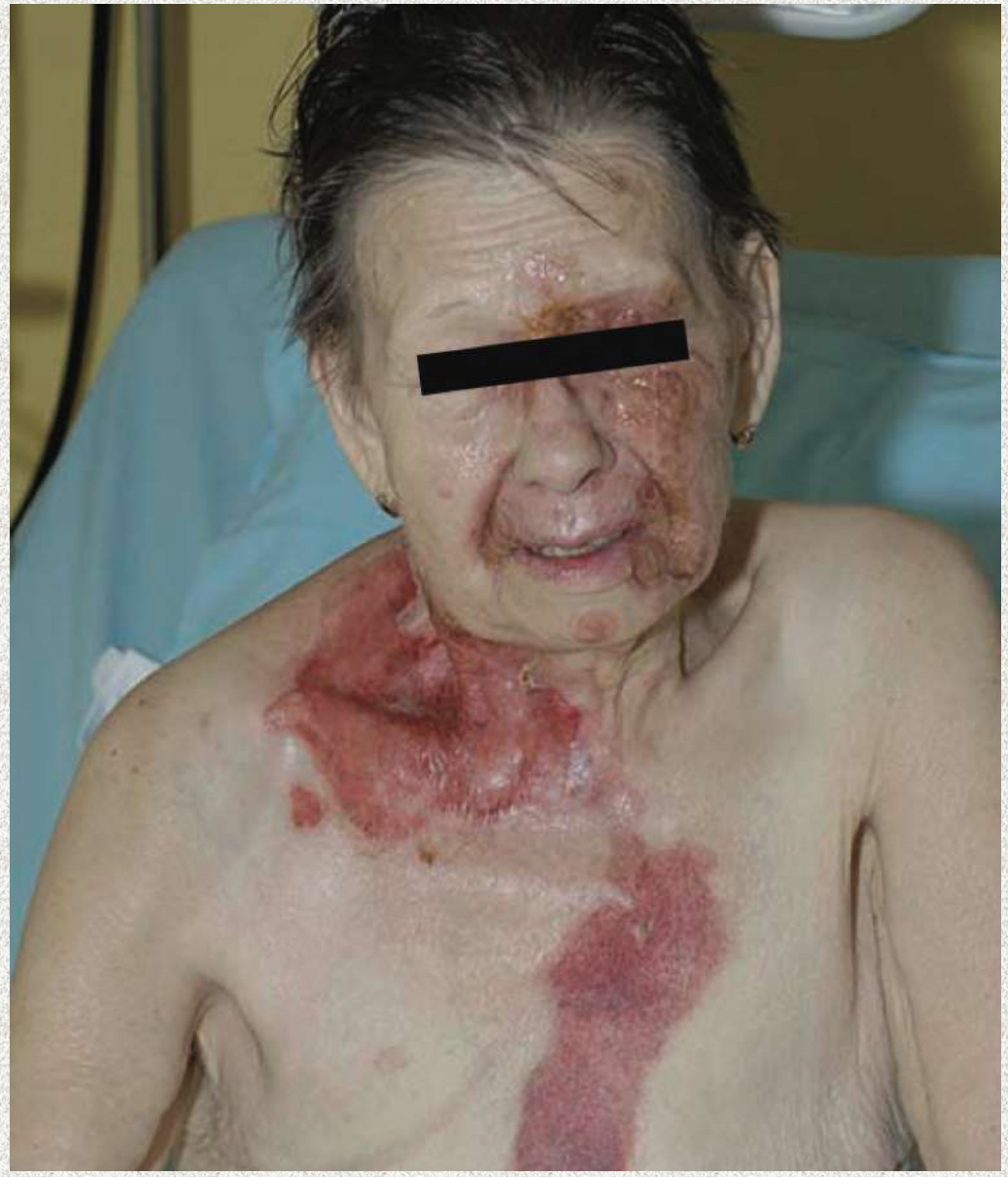
Staphylococcal Scalded Skin Syndrome (SSSS)

- Acute cutaneous reaction to S. aureus
- Population – infants and children (most common), may occur in adults with CKD and immunosuppression
  - Adults develop antibodies to exotoxins and therefore SSSS is rare unless immunocompromised or renal failure
- Cause – S. aureus infection of the skin/throat/ears/eyes releases two epidermolytic exotoxins A and B which target desmoglein 1 in desmosomes
  - Desmosomes form connections between keratinocytes in the epidermis → targeting of desmoglein causes breaks in the connections between keratinocytes resulting in desquamation of the epidermis
- Mortality - <5% in children, ~60% in adults

SSSS – Presentation

- Fever
- Erythema with tissue paper-like wrinkling of skin in armpits, groin, and around orifices → flaccid bulla and desquamation spreads to arms, legs, trunk leaving exposed moist red tender skin
- Nikolsky sign positive – sheering of epidermis from underlying dermis with rubbing of skin





SSSS – Management

- Hospital admission – IV antibiotics, fluid/electrolyte/thermal/nutrition management
  - IV antibiotics can be transitioned to oral antibiotics after few days depending on response
  - Topical antibiotics are not sufficient
- Penicillinase-resistant anti-staphylococcal antibiotics – flucloxacillin, nafcillin, oxacillin, cephalosporin, clindamycin, vancomycin
- Systemic steroids – contraindicated as they slow healing
- Adults – IVIg, plasma exchange
- Supportive – pain management, skin care with emollients and non-adherent dressing
- Data limited on dialysis as part of treatment in CKD, but should be considered
- Data limited on holding immunosuppressive agents, but should be considered

Question 5

Which of the following is false in staphylococcal scalded skin syndrome (SSSS)?

A. SSSS is more common in children compared to adults
B. SSSS is caused directly by staphylococcal bacterial infection in the skin
C. SSSS is caused by the exfoliative toxin produced by phage group II strains of S. aureus which targets desmosomes in keratinocytes
D. Treatment should include hospitalization for IV penicillin and wound care

Rocky Mountain Spotted Fever (RMSF)

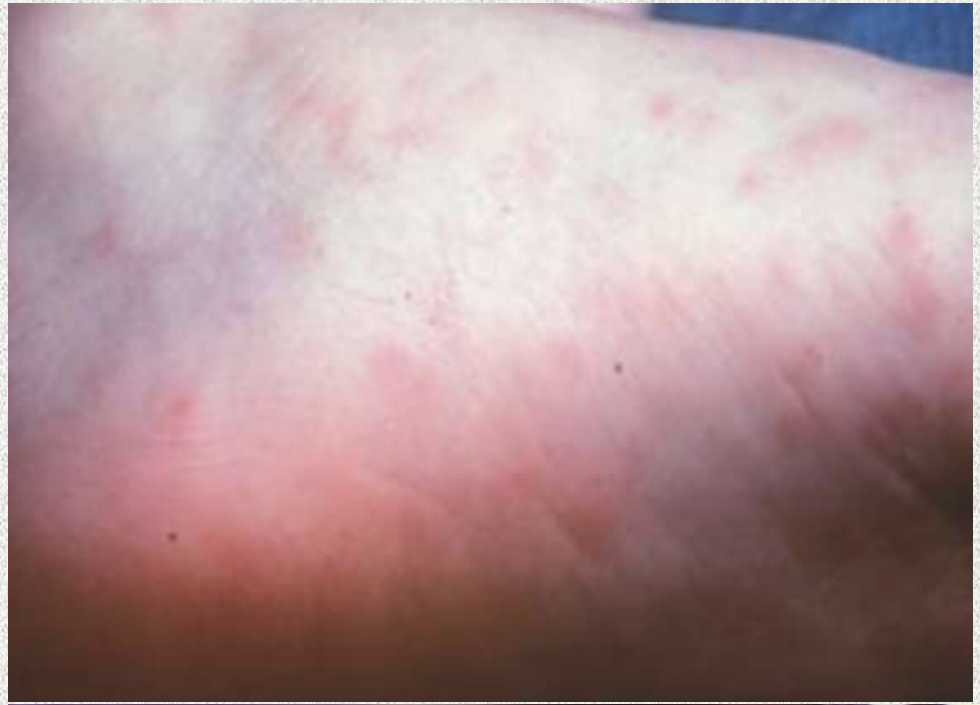
- Tick-borne bacterial infection resulting in blood vessel damage in multiple tissues and organs
- Population – any age or gender, more common in children
- Cause – Rickettsia rickettsia
- Vector – Dermacentor tick (must be attached >24 hours)
- Location – US, Canada, Mexico, South America
- Time – spring, summer
- Mortality – 1-4%, higher in <5yo and >70yo

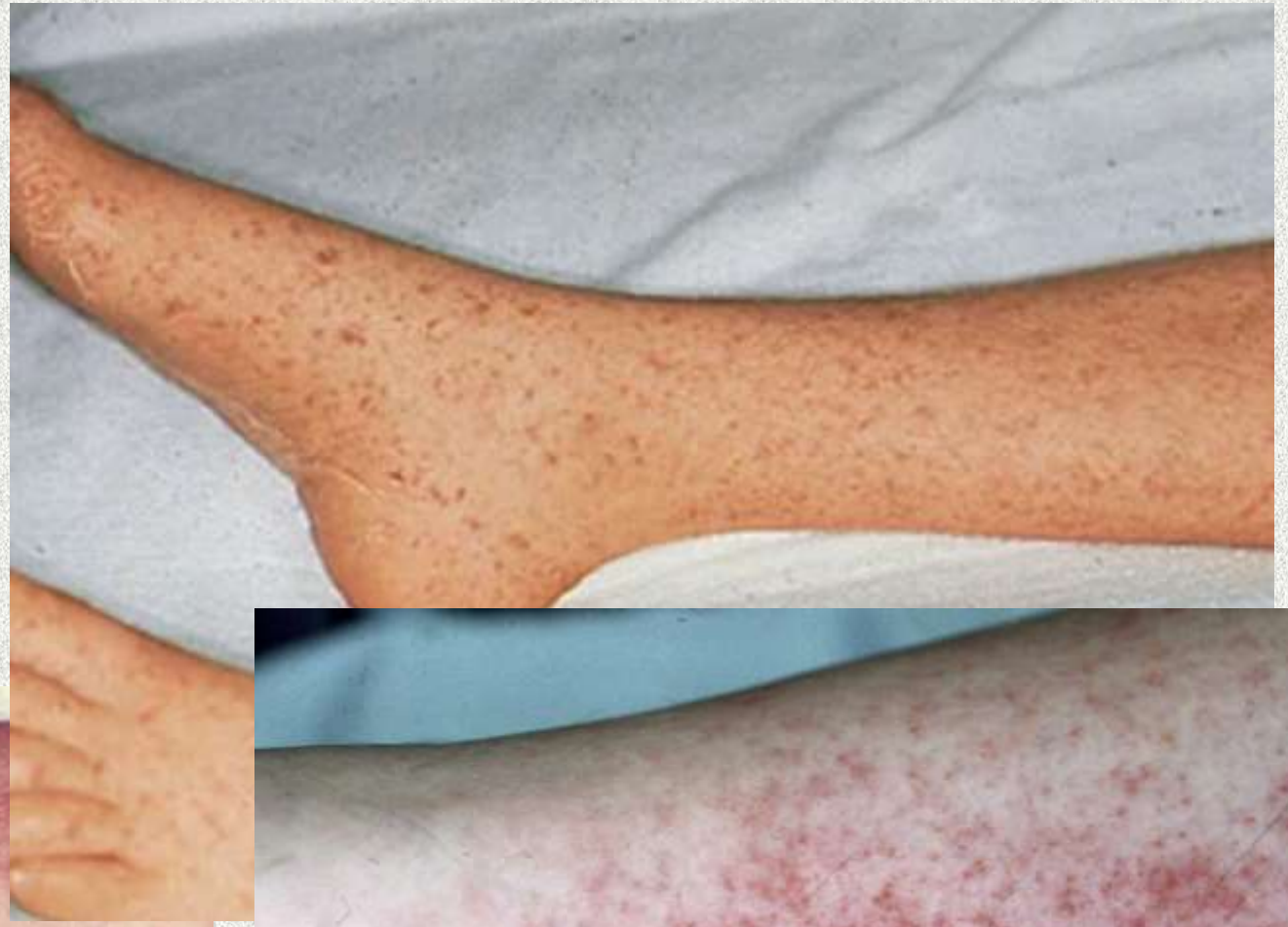
RMSF – Presentation

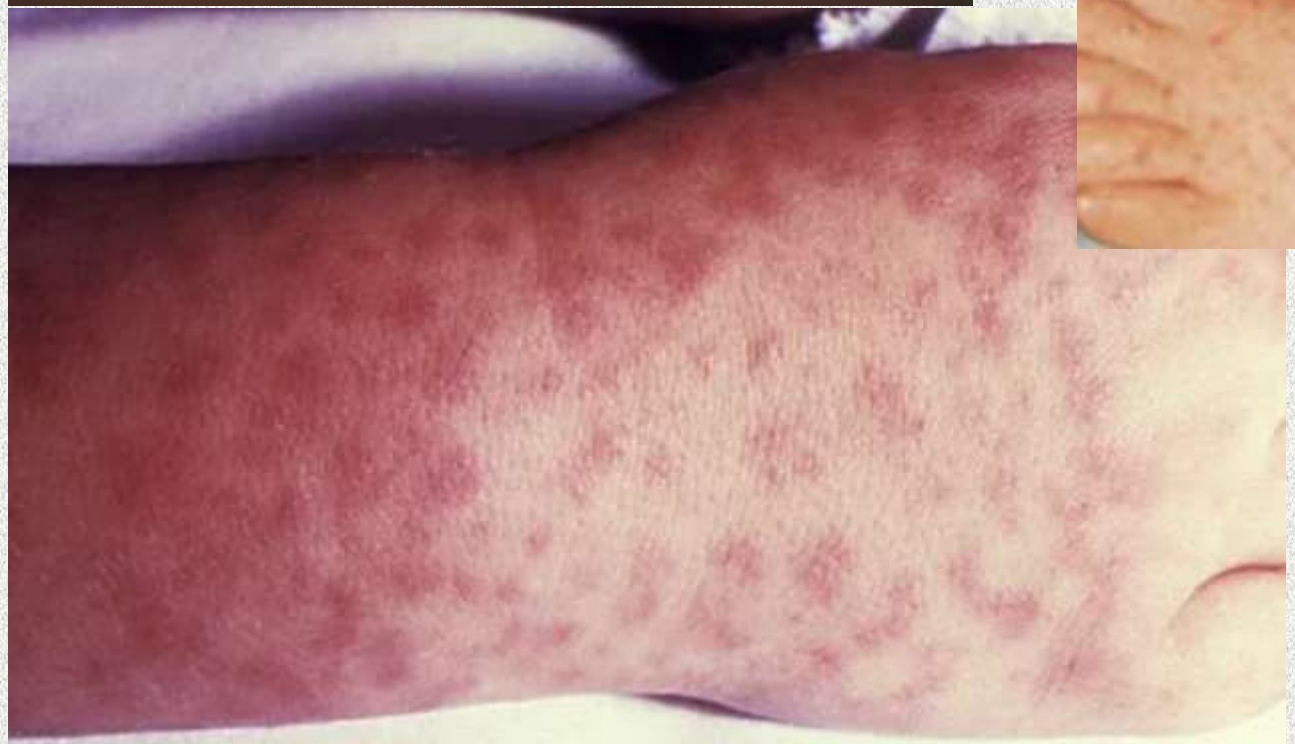
- Onset within 14 days of tick bite
- Fever and severe headache followed by rash 2-5 days later
- Myalgias
- Abdominal pain, nausea, vomiting
- Confusion, lethargy

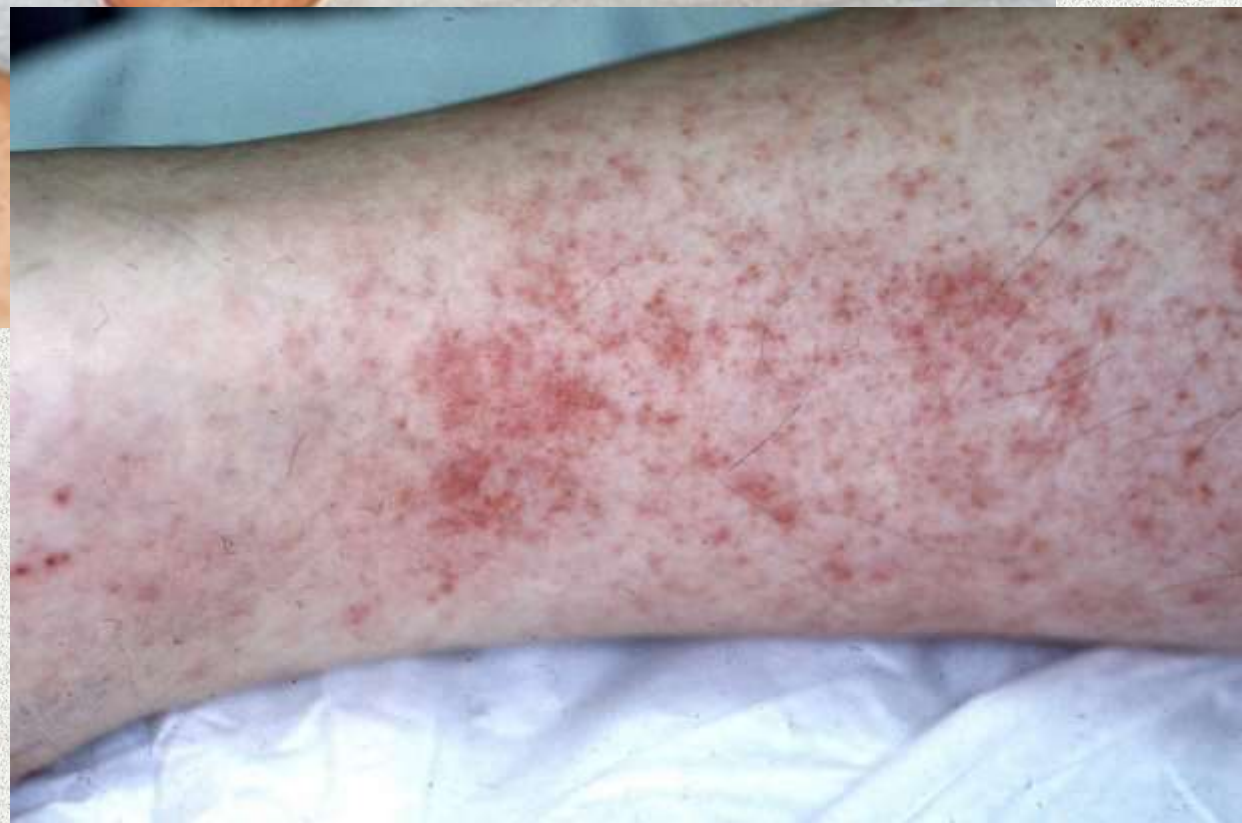
RMSF – Skin Presentation

- Appears around days 3-5
- Small (1-5mm) erythematous pruritic macules → progress to erythematous papules and petechiae → may become hemorrhagic and crusted or necrotic
- Begins on ankles and wrists then spreads to palms and soles then spreads centrally to the trunk, may spread to face but face usually spared
- With resolution, skin may desquamate or scar









RMSF – Complications

- Seizures
- Blindness, deafness
- Coma
- Damage to lungs, heart, kidneys, liver

RMSF – Management

- Serology – indirect fluorescent antibody test against rickettsial antigens is typically positive 10-14 days after infection
- Clinical – if suspicion is high, initiate treatment even if diagnosis is not yet confirmed
- Treatment – initiate Doxycycline 100mg BID and continue until absence of fever >2-3 days
  - Doxycycline is TOC even in children <8yo in RMSF
  - Pregnancy – Chloramphenicol

RMSF – Prevention in High Risk Areas

- Avoid forests and fields where ticks reside
- Wear long-sleeve shirts and pants that fit tightly around wrists, ankles and waist
- DEET insect repellents on skin, Permethrin on clothes
- If in exposed area, check skin twice daily
- Removal of tick – use gloves, grasp tick as close to skin as possible with tweezers and gently pull out

Necrotizing Fasciitis

- Severe rapidly spreading bacterial infection of soft tissue and fascia resulting in vascular occlusion and necrosis of tissue with possible rapid progression to septic shock, multiorgan failure and death
  - Infection starts in superficial fascia then spreads horizontally through fascial plane before spreading vertically to overlying skin and underlying muscle → diagnosis may be delayed due to initial horizontal spread
  - Mortality up to 25%
- Can involve any location
  - Leg most common site
  - Fournier gangrene – perineal, genital, perianal → 15-50% mortality rate
- Risk factors – advanced age, obesity, DM, chronic illness, malignancy, immunosuppression, ASA/NSAIDs, drug abuse

Necrotizing Fasciitis

Type I

- Polymicrobial – S. aureus, Haemophilus, vibrio, E.coli
- Older patients, diabetics, other comorbidities

Type II

- Hemolytic group A strep or staph (including MRSA)
- All ages
- Can involve healthy individuals

Type III

- Clostridium perfringens or septicum
- Injury, surgery, IV drug abuse
- Crepitus – gas within skin causes crackling

Fungal organisms

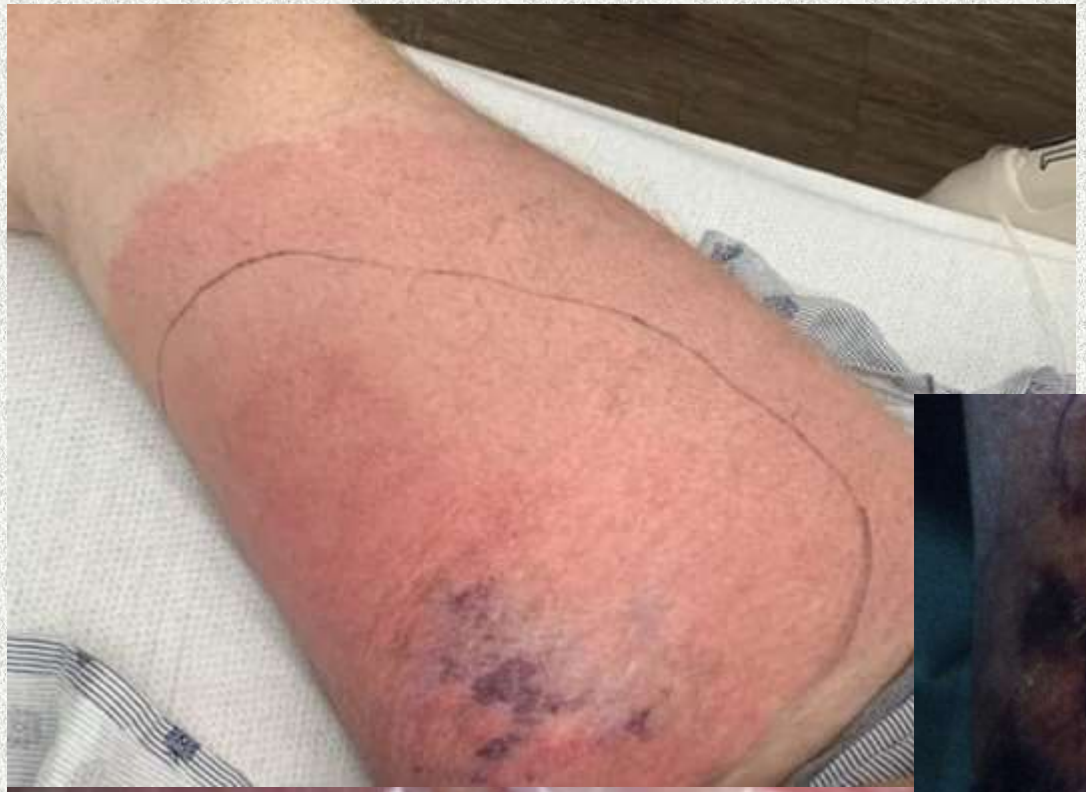
- Traumatic wounds
- Immunocompromised

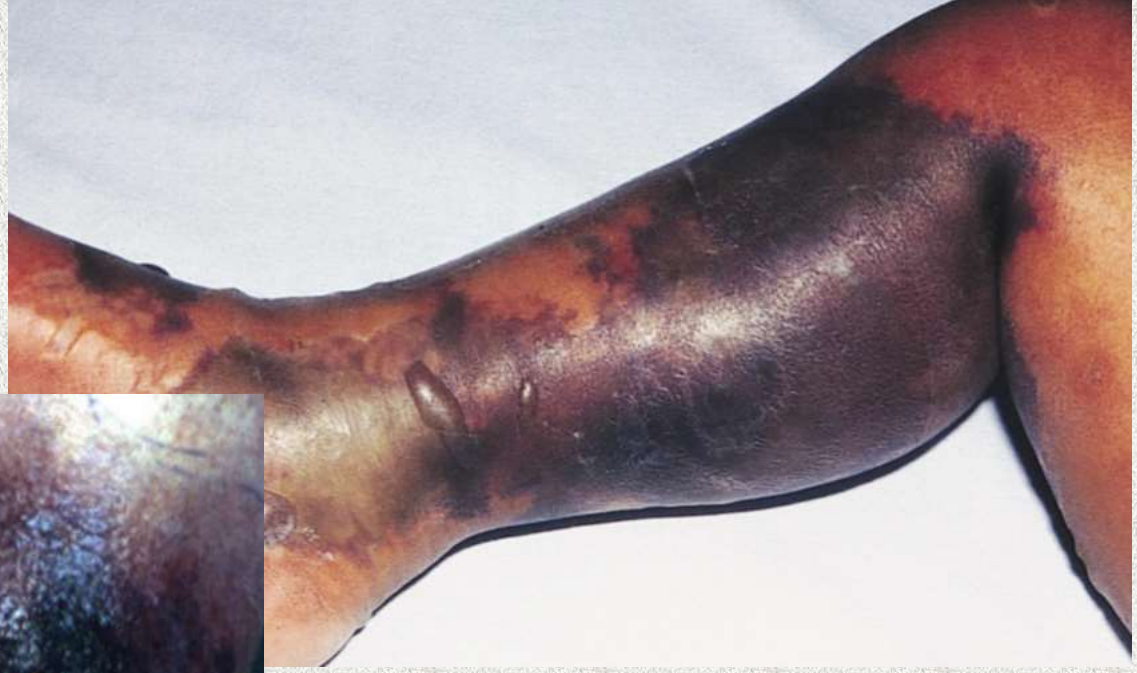
Marine organisms

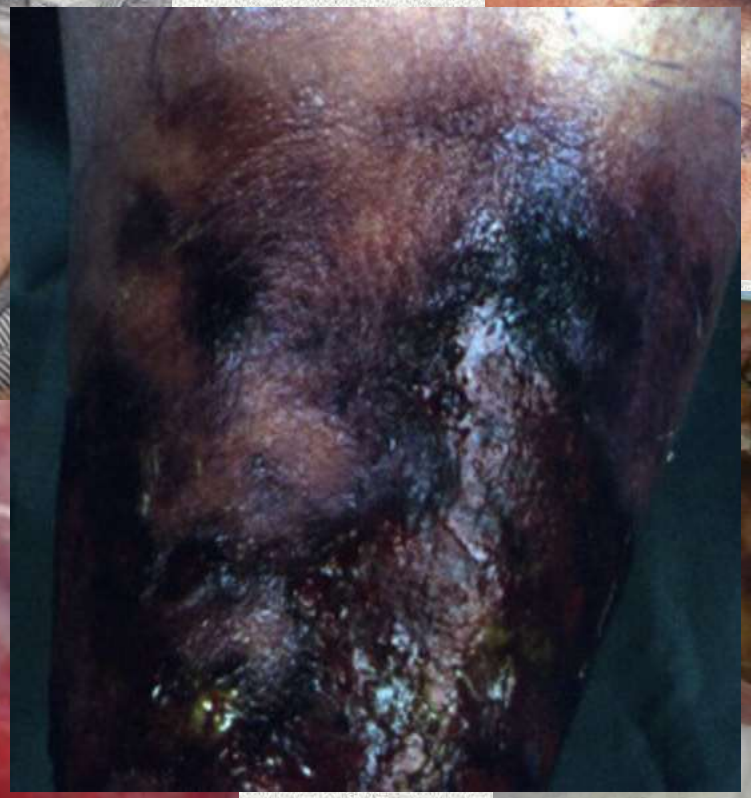
- Wounds by seawater, cuts by fins/stingers, consumption of raw seafood
- Liver disease
- Can be fatal within 48 hours

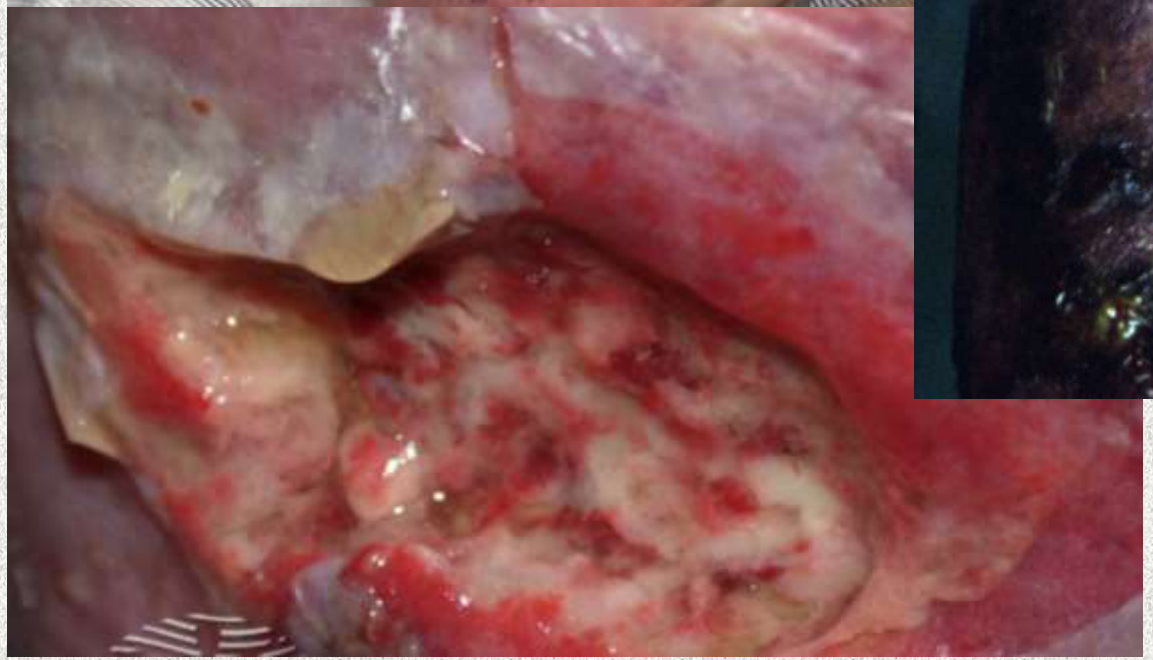
Necrotizing Fasciitis – Presentation

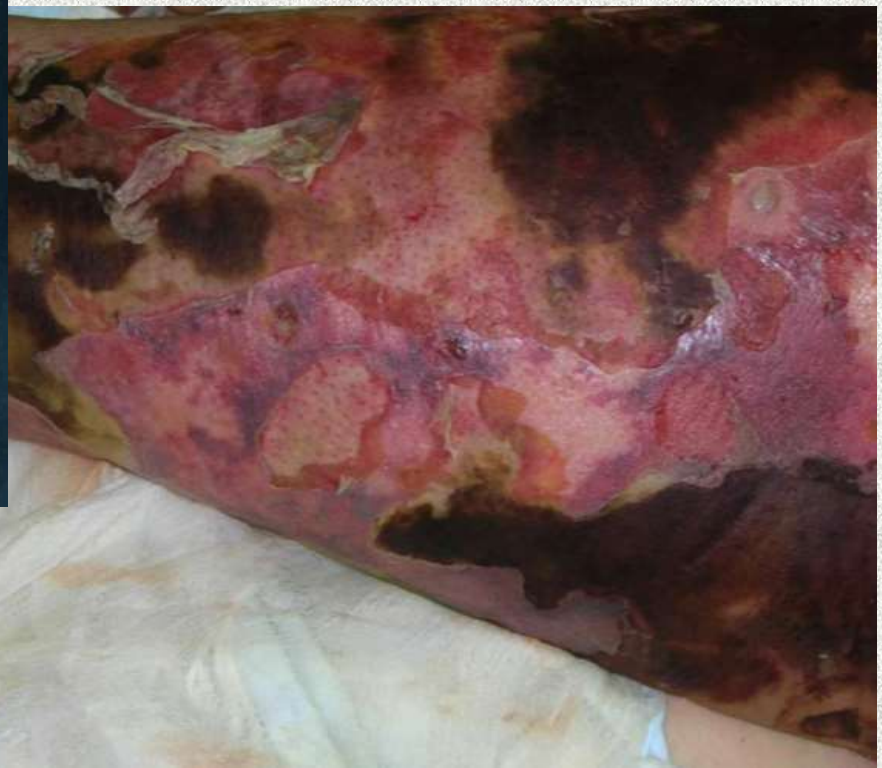
- Symptoms appear within 24 hours of injury with clinical features taking 3-4 days to appear
- Pain out of proportion to appearance that progressively worsens
- Flu-like symptoms
- Intense thirst common
- Site of infection – violaceous and edematous → duskiness with development of hemorrhagic and necrotic bulla → necrosis
  - Crepitus present due to gas within tissue
  - Severe pain followed by anesthesia due to necrosis involving sensory nerves











Necrotizing Fasciitis – Aggressive Progression

- Even with immediate antibiotic intervention, infection may not improve
- Within 4-5 days – high fevers, hypotension → septic shock and multiorgan failure
- Spread of abscesses to liver, lung, spleen, brain, pericardium, skin

Necrotizing Fasciitis – Management

- Diagnosis primarily clinical
  - Finger test – 2cm incision made in skin and index finger inserted → nec fasc confirmed if finger progresses with no resistance
- Labs – WBC >$15.4x10^9$/L, sodium <135mmol/L, CRP >16mg/dL, CK >600U/L, urea >18mg/dL
- Blood culture
- Deep tissue biopsy with gram stain and tissue culture to determine bacterial or fungal species
- Imaging – xray, CT, MRI → can identify gas in tissues

Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC)

- Can assist in distinguishing nec fasc from other infections
- Score of 6+ rule in nec fasc
- Score <6 does not completely rule out nec fasc

Variable	Unit	Score
C-reactive protein	mg/dL	
<15		0
≥15		4
WBC	per mm^3	
<15,000		0
15,000–25,000		1
>25,000		2
Hemoglobin	g/dL	
>13.5		0
11.0–13.5		1
<11.0		2
Na	mmol/L	
≥135		0
<135		2
Creatinine	mg/dl	
≤1.6		0
>1.6		2
Glucose	mg/dL	
≤180		0
>180		1

Necrotizing Fasciitis – Management

- ICU admission
- Supportive measures – oxygen, fluids, blood pressure management
- High dose IV antibiotics while awaiting tissue culture results
  - Penicillin, clindamycin, metronidazole, cephalosporins, carbapenems, vancomycin, linezolid
- Transition to high dose IV antibiotics specific to tissue culture results as soon as possible
- Urgent surgical debridement of all infected and necrotic tissue repeated frequently as disease progresses
  - Skin grafting usually required after infection completely cleared
- Hyperbaric oxygen therapy
- IVIg

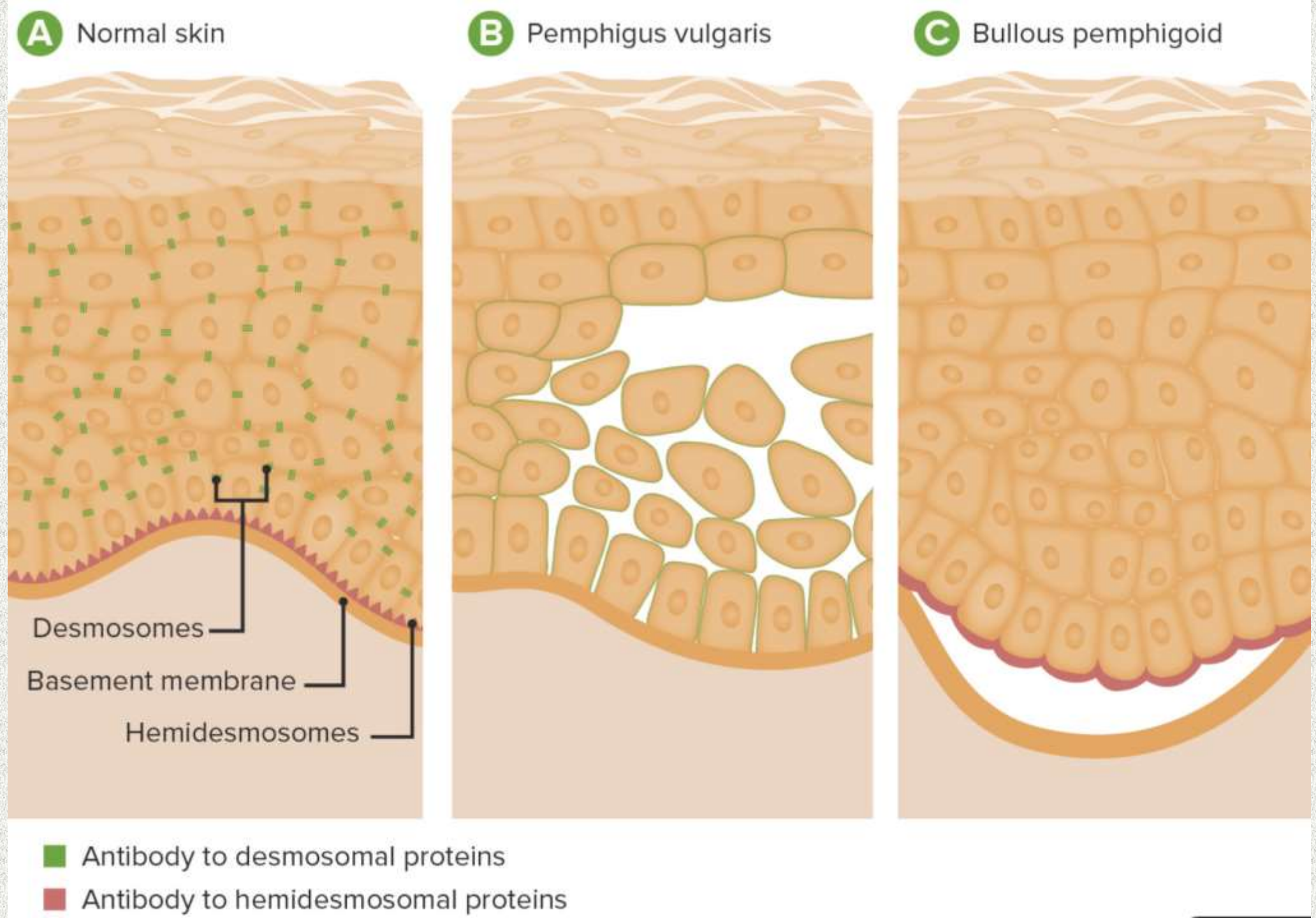
Immunobullous Exacerbations

Bullous pemphigoid

Pemphigus vulgaris

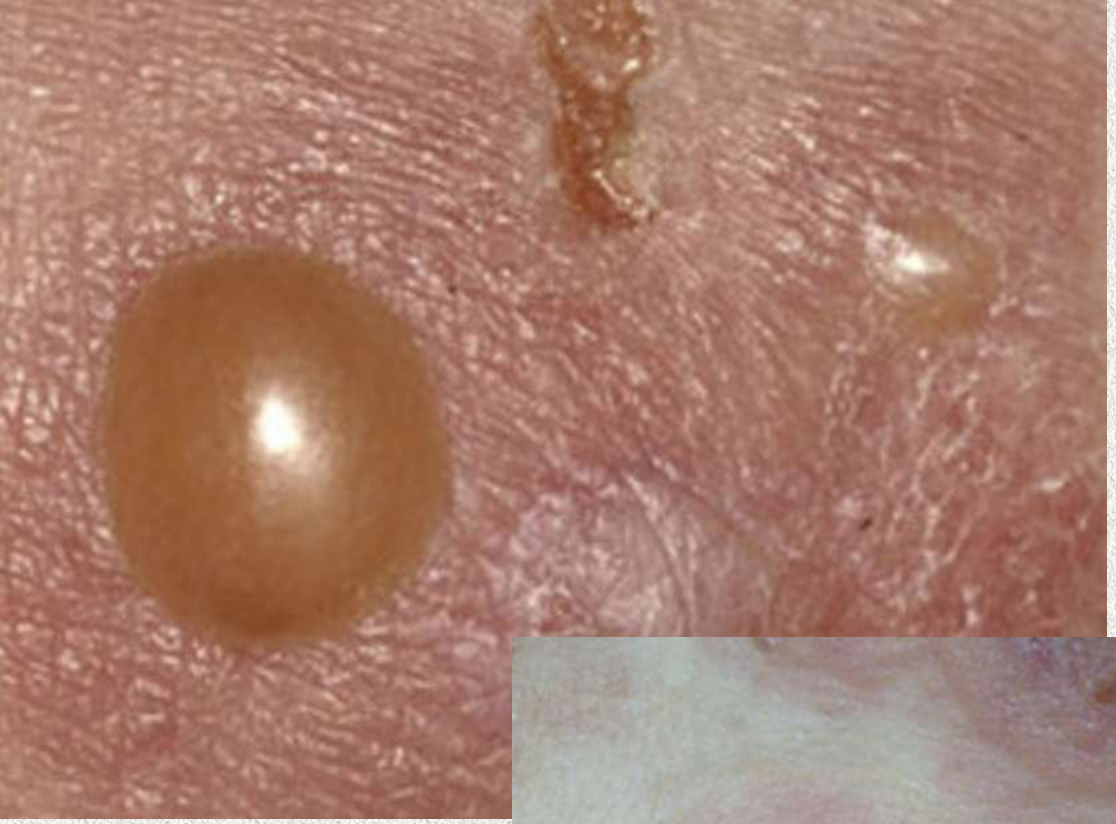
Bullous Pemphigoid

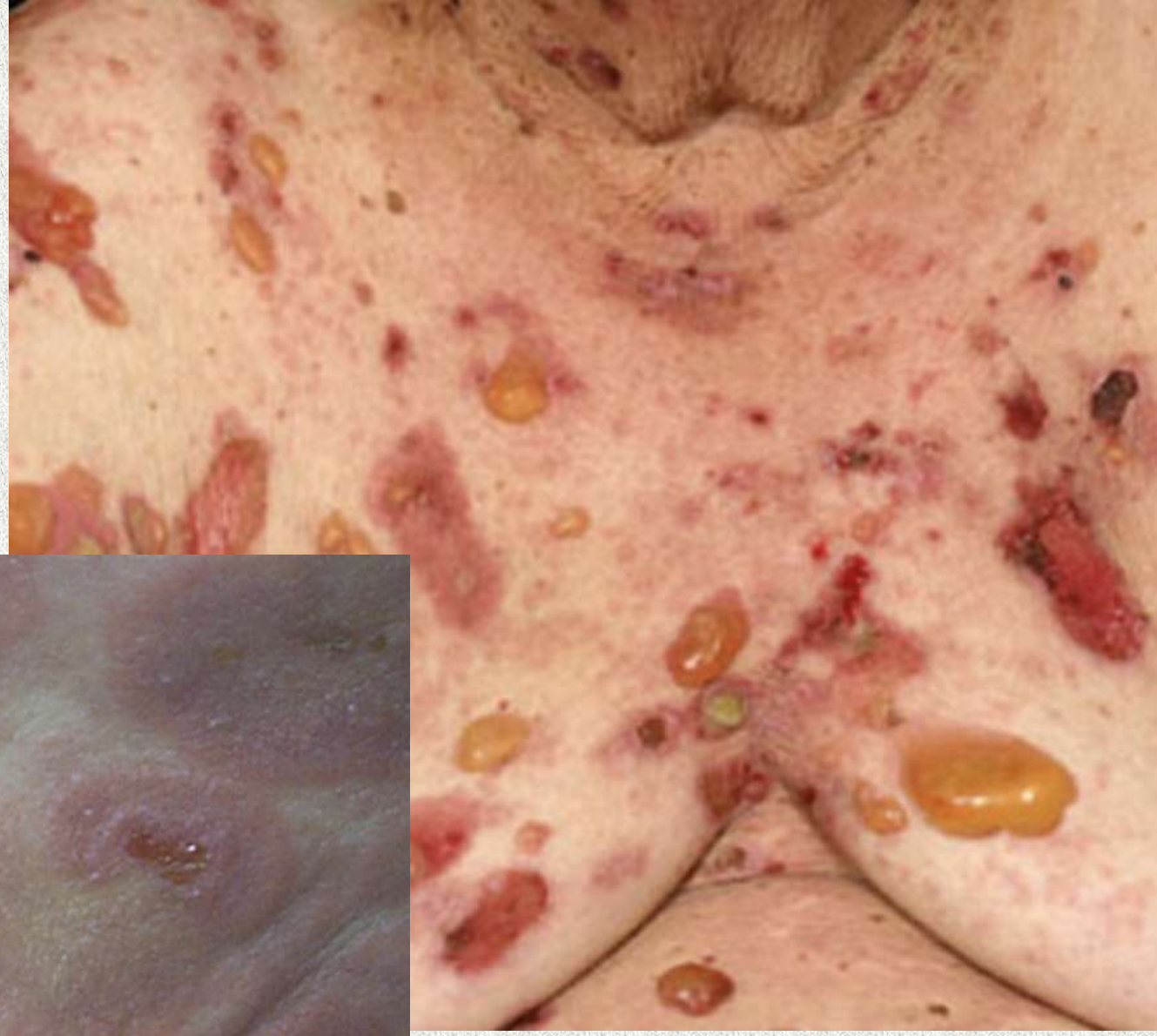
- Chronic autoimmune bullous disease
- Population – >50yo, classically in elderly
- Causes – drug, injury, infection, unknown
  - PD1-inhibitors (chemotherapeutic), dipeptidyl peptidase-4 inhibitors (gliptins for DM), antibiotics, penicillamine, potassium iodide, furosemide, captopril, gold, topical flurouracil
- Pathogenesis – antibodies against BP180 (type XVII collagen) in the hemidesmosomes of the cutaneous basement membrane zone
  - Destruction of hemidesmosomes causes separation of the epidermis from the dermis (subepidermal bulla) which are tense

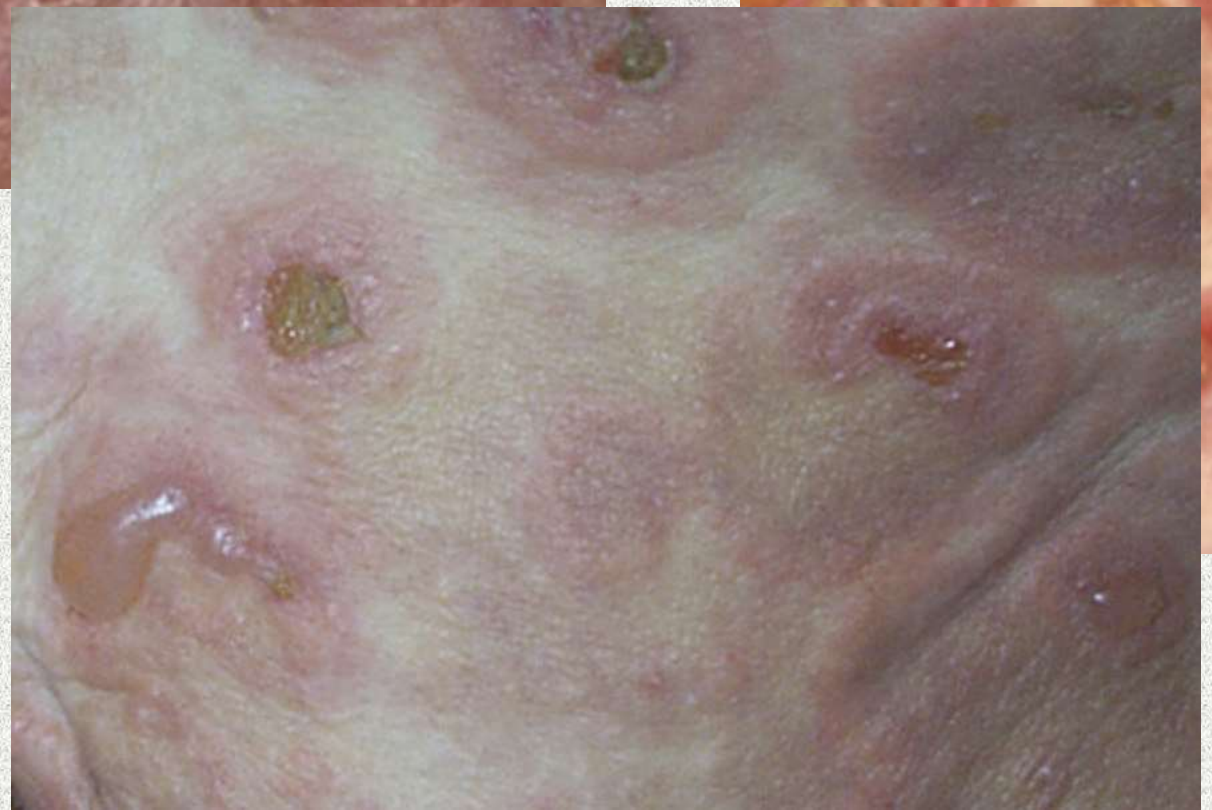

A Normal skin
B Pemphigus vulgaris
C Bullous pemphigoid
Desmosomes
Basement membrane
Hemidesmosomes
Antibody to desmosomal proteins
Antibody to hemidesmosomal proteins

BP – Presentation

- Erythematous pruritic plaques develop tense bulla that rupture with crusting, hyperpigmentation and areas of scarring
- Flexor surfaces and intertriginous regions common but can generalize
- Mucosal involvement uncommon





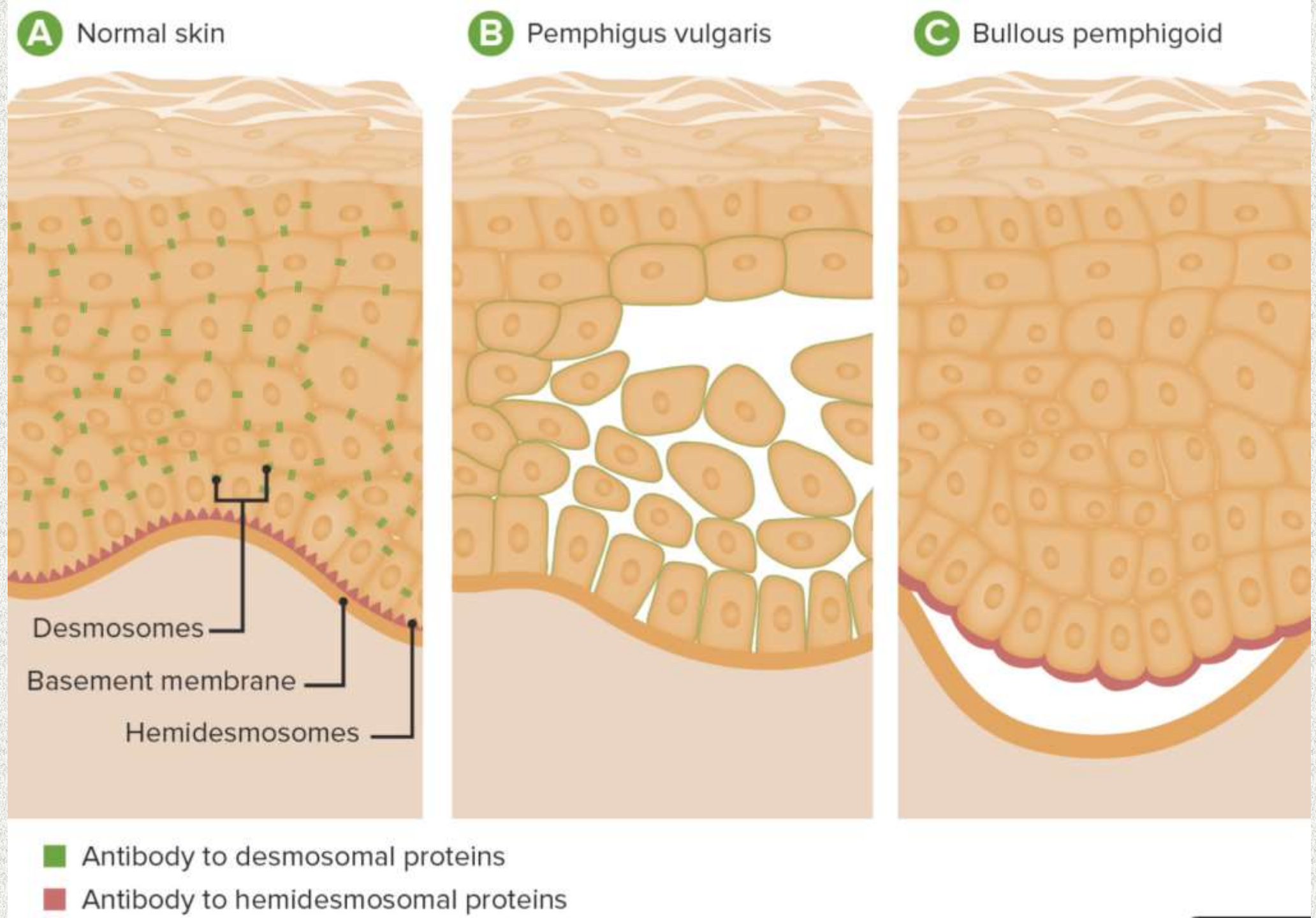


BP – Management

- Milder disease can be managed outpatient while more severe cases need admission to initiate management and monitor for complications such as secondary bacterial or viral skin infection
- Diagnosis – skin biopsy of early blister for H&E and DIF
- Treatment
  - Prednisone – 0.5-1mg/kg/d for several weeks (until no new blisters develop) then prolonged gradual taper over months
  - Ultrapotent topical steroids (Clobetasol)
  - Doxycycline 100mg BID
  - Initiation of steroid sparing agents while tapering prednisone – dapsone, methotrexate, nicotinamide, azathioprine, mycophenolate, IVIg, Rituximab
  - Analgesics
- Referral to Dermatology for continued management

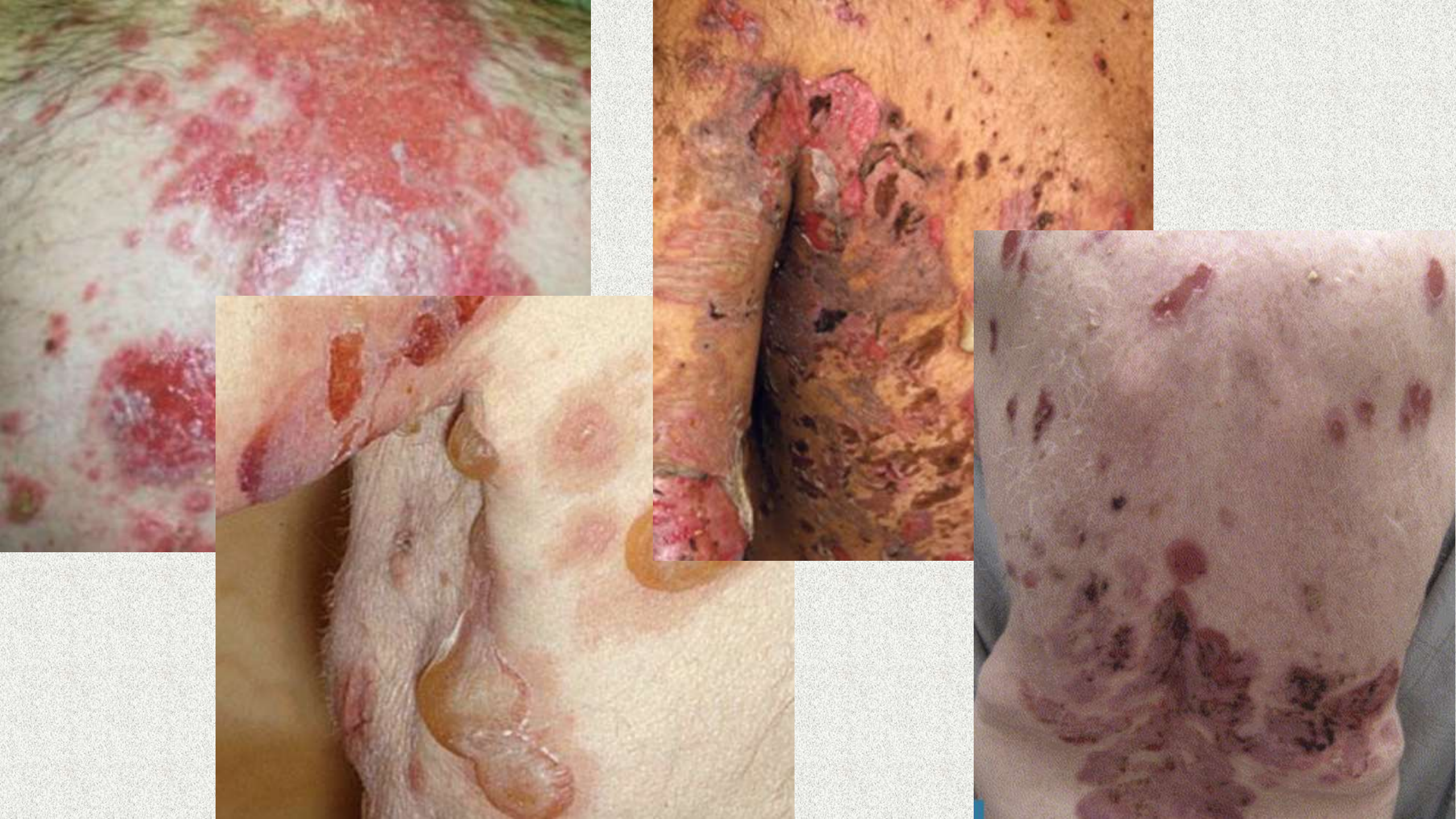
Pemphigus Vulgaris

- Chronic autoimmune bullous disease
- Population – most commonly 30-60yo
- Causes – unknown, malignancy, infection, trauma, drug
  - Drug-induced – penicillamine, ACE-inhibitors, ARBs, cephalosporins
- Pathogenesis – antibodies against desmoglein 3 in desmosomes between keratinocytes in the lower epidermis
  - Destruction of desmosomes causes separation between keratinocytes in the lower epidermis (intraepidermal bulla) which are flaccid
- Mortality – 5-15%


A Normal skin
B Pemphigus vulgaris
C Bullous pemphigoid
Desmosomes
Basement membrane
Hemidesmosomes
Antibody to desmosomal proteins
Antibody to hemidesmosomal proteins

PV – Presentation

- Mucosal involvement classically presents first followed by cutaneous involvement few weeks later
- Mucosa – oral erosions, pharyngeal/laryngeal erosions cause painful swallowing and hoarseness, nasal erosions cause congestion and bleeding, erosions of conjunctiva, esophagus, labia/vagina/cervix, penis, urethra, anus
- Cutaneous – flaccid thin-walled erythematous bulla that easily ruptured causing painful and pruritic erosions with scaling and crusting, most commonly on upper chest, back, scalp and face



PV – Management

- Milder disease can be managed outpatient while more severe cases need admission to initiate management and monitor for complications such as secondary bacterial/viral/fungal skin infection and malnutrition due to decreased PO intake
- Diagnosis – skin biopsy of early blister for H&E and DIF
- Treatment
  - Prednisone – 0.5-1mg/kg/d for several weeks (until no new blisters develop) then prolonged gradual taper over months
  - Ultrapotent topical steroids (Clobetasol)
  - Initiation of steroid sparing agents while tapering prednisone – azathioprine, mycophenolate, cyclophosphamide, rituximab, dapsone, methotrexate, doxycycline, IVIg, extracorporeal photopheresis, plasmapheresis
  - Gentle wound care, non-adherent bandages, emollients, antimicrobial washes, analgesics, oral swish-and-spit steroids and analgesics
- Referral to Dermatology and Ophthalmology for continued management

References

- Bolognia JL, Schaffer JV and Ceroni L. (2018). Dermatology, 4th Ed.
- Cribier B, Piemont Y and Grosshans E. (1994). Staphylococcal scalded skin syndrome in adults. *JAAD;*30(2):319-324.
- Husain Z, Reddy BY and Schwartz RA. (2013). DRESS Syndrome Parts I and II. *JAAD*;68(5):693.e1-e14 and 709.e1-e9.
- https://dermnetnz.org/topics/erythema-multiforme
- https://dermnetnz.org/topics/stevens-johnson-syndrome-toxic-epidermal-necrolysis
- https://dermnetnz.org/topics/drug-hypersensitivity-syndrome
- https://dermnetnz.org/topics/acute-generalised-exanthematous-pustulosis
- https://dermnetnz.org/topics/eczema-herpeticum
- https://dermnetnz.org/topics/staphylococcal-scalded-skin-syndrome
- https://dermnetnz.org/topics/rocky-mountain-spotted-fever
- https://dermnetnz.org/topics/necrotising-fasciitis
- https://dermnetnz.org/topics/bullous-pemphigoid
- https://dermnetnz.org/topics/pemphigus-vulgaris