HMS Update in Hospital Medicine Course

# Common Consult Questions for Skin and Soft Tissue Infections

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HARVARD MEDICAL SCHOOL | Postgraduate Medical Education

HMS Update in Hospital Medicine Course

Common Consult Questions for Skin and Soft Tissue Infections

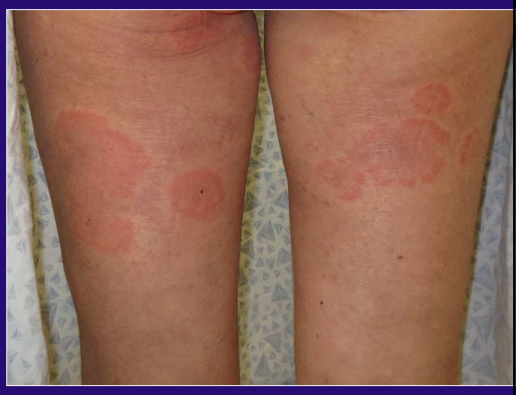
- No disclosures

# Plan

- Management controversies for common skin infections
- Overlooked or underappreciated diagnoses
- Diagnostic pearls you can't easily Google

# True/False

A patient is admitted with cough and hypoxia, after testing positive for COVID-19. During the intake exam, he is noted to have this widespread urticarial eruption, which was not present hours earlier.



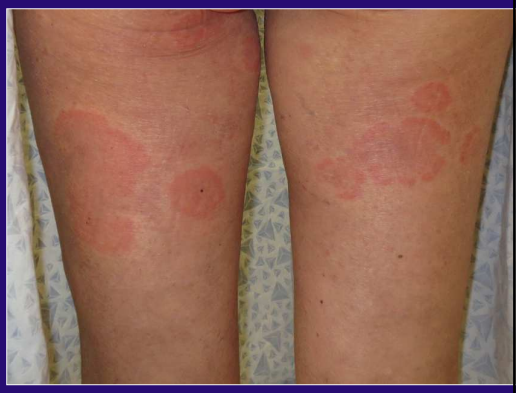
True/false: The rash is an excellent prognostic sign.

A. True

B. False

# True/False

A patient is admitted with cough and hypoxia, after testing positive for COVID-19. During the intake exam, he is noted to have this widespread urticarial eruption, which was not present hours earlier.



True/false: The rash is an excellent prognostic sign.

A. True

**B. False**

Urticaria not an independent predictor of mortality/survival

Tan SW, Tam YC, Oh CC. Skin manifestations of COVID-19: A worldwide review. JAAD Int. 2021 Mar;2:119-133. Epub 2020 Dec 16.

# COVID-19 Acute Eruptions For the Hospitalist

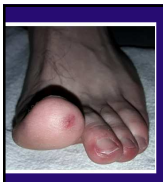
| Eruptions COVID patients may be admitted ***WITH*** | Eruptions COVID patients may be admitted ***FOR*** |
|---|---|

## COVID-19 Acute Eruptions For the Hospitalist

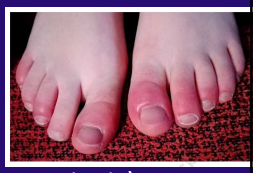
| Eruptions COVID patients may be admitted ***WITH*** | Eruptions COVID patients may be admitted ***FOR*** |
|---|---|
| COVID Toes<br>Maculopapular<br>Urticarial<br>Vesicular | |

## COVID-19 Acute Eruptions For the Hospitalist

| Eruptions COVID patients may be admitted ***WITH*** | Eruptions COVID patients may be admitted ***FOR*** |
|---|---|
| COVID Toes<br>Maculopapular<br>Urticarial<br>Vesicular | Vaso-occlusive disease |

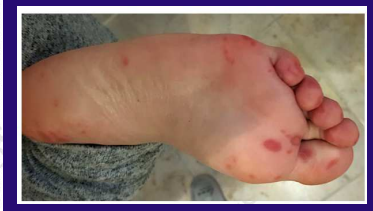


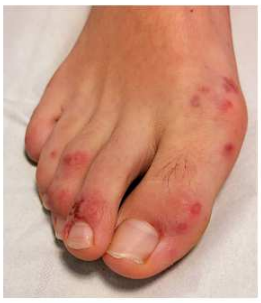
# COVID-19 Acute Eruptions For the Hospitalist



Eruptions COVID patients may be admitted ***WITH***

COVID Toes (AKA chilblains, pseudo-chilblains, perniosis)





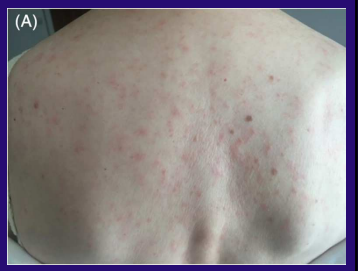
Fernandez-Nieto D, Jimenez-Cauhe J, Suarez-Valle A, Moreno-Arrones OM, Saceda-Corralo D, Arana-Raja A, Ortega-Quijano D. Characterization of acute acral skin lesions in nonhospitalized patients: A case series of 132 patients during the COVID-19 outbreak. J Am Acad Dermatol. 2020 Jul;83(1):e61-e63. Epub 2020 Apr 24.

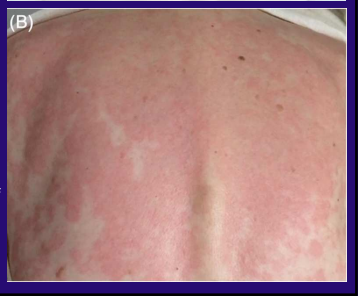
# COVID-19 Acute Eruptions For the Hospitalist

Eruptions COVID patients may be admitted ***WITH***

COVID Toes

Maculopapular AKA Morbilliform




Maculopapular eruptions associated to COVID-19: A subanalysis of the COVID-Piel study. Dermatologic Therapy, Volume: 33, Issue: 6, First published: 10 August 2020, DOI: (10.1111/dth.14170)

# COVID-19 Acute Eruptions For the Hospitalist

Eruptions COVID patients may be admitted ***WITH***

COVID Toes

Maculopapular

Urticarial AKA Hives


Skin manifestations of COVID-19. Sarah Young, Anthony P. Fernandez Cleveland Clinic Journal of Medicine May2020

# COVID-19 Acute Eruptions For the Hospitalist

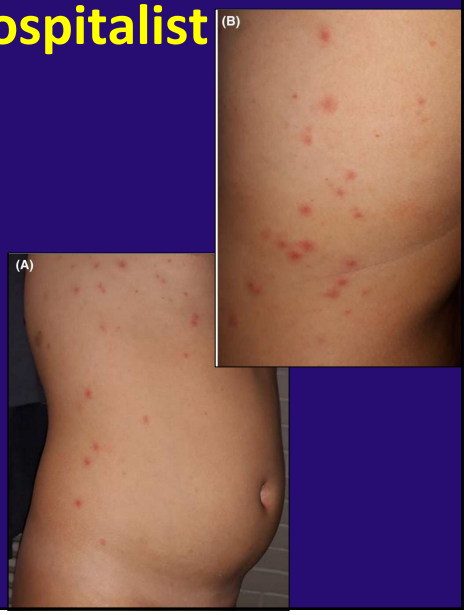
Eruptions COVID patients may be admitted ***WITH***

COVID Toes

Maculopapular

Urticarial

Vesicular AKA Varicella-like




Varicella-like exanthem associated with COVID-19 in an 8-year-old girl: A diagnostic clue? Pediatric Dermatology, Volume: 37, Issue: 3, Pages: 435-436, First published: 21 April 2020

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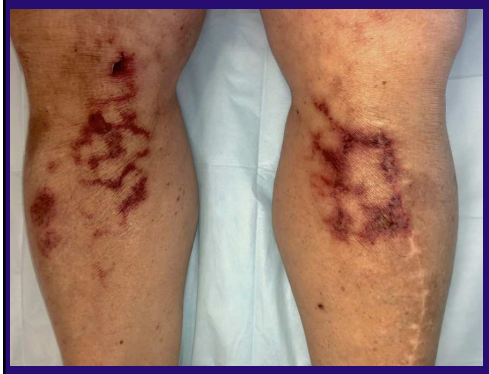
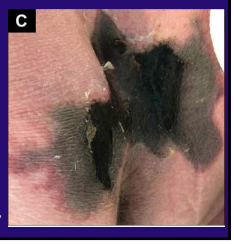


Retiform purpura as a dermatological sign of coronavirus disease 2019 (COVID-19) coagulopathy Journal of the European Academy of Dermatology and Venereology, Volume: 34, Issue: 10, Pages: e548-e549, First published: 03 June 2020

Eruptions COVID patients may be admitted ***FOR***

Vaso-occlusive disease

i.e. Retiform purpura, livedo racemose, livedo reticularis




Skin manifestations of COVID-19. Sarah Young, Anthony P. Fernandez Cleveland Clinic Journal of Medicine May 2020,

# COVID-19 Acute Eruptions For the Hospitalist

Eruptions COVID patients may be admitted ***WITH***

COVID Toes

Maculopapular

Urticarial

Vesicular

Eruptions COVID patients may be admitted ***FOR***

Vaso-occlusive disease

Tan SW, Tam YC, Oh CC. Skin manifestations of COVID-19: A worldwide review. JAAD Int. 2021 Mar;2:119-133. doi: 10.1016/j.jdin.2020.12.003. Epub 2020 Dec 16. PMID: 33479703; PMCID: PMC7754879.

# COVID-19 Acute Eruptions For the Hospitalist

| Skin Manifestation | Eruptions COVID patients may be admitted ***WITH*** | Eruptions COVID patients may be admitted ***FOR*** |
|---|---|---|
| COVID Toes | | Vaso-occlusive disease |
| Maculopapular | | |
| Urticarial | | |
| Vesicular | | |
| Vaso-occlusive | | |

Tan SW, Tam YC, Oh CC. Skin manifestations of COVID-19: A worldwide review. JAAD Int. 2021 Mar;2:119-133. doi: 10.1016/j.jdin.2020.12.003. Epub 2020 Dec 16. PMID: 33479703; PMCID: PMC7754879.

# COVID-19 Acute Eruptions For the Hospitalist

| Skin Manifestation | % of rashes |
|---|---|
| COVID Toes | 41% |
| Maculopapular | 28% |
| Urticarial | 12.5% |
| Vesicular | 10.5% |
| Vaso-occlusive | 4.5% |
| Other | 3% |

Tan SW, Tam YC, Oh CC. Skin manifestations of COVID-19: A worldwide review. JAAD Int. 2021 Mar;2:119-133. doi: 10.1016/j.jdin.2020.12.003. Epub 2020 Dec 16. PMID: 33479703; PMCID: PMC7754879.

# COVID-19 Acute Eruptions For the Hospitalist

| Skin Manifestation | % of rashes | Rash Onset timing | |
|---|---|---|---|
| | | With Other sxs | Late / Only |
| COVID Toes | 41% | | **70%** (36 / 34) |
| Maculopapular | 28% | 56% | 32% |
| Urticarial | 12.5% | 52% | 33% |
| Vesicular | 10.5% | 38% | 48% |
| Vaso-occlusive | 4.5% | **68%** | |
| Other | 3% | | |

Tan SW, Tam YC, Oh CC. Skin manifestations of COVID-19: A worldwide review. JAAD Int. 2021 Mar;2:119-133. doi: 10.1016/j.jdin.2020.12.003. Epub 2020 Dec 16. PMID: 33479703; PMCID: PMC7754879.

# COVID-19 Acute Eruptions For the Hospitalist

| Skin Manifestation | % of rashes | Rash Onset timing | | Prognosis? |
|---|---|---|---|---|
| | | With Other sxs | Late / Only | |
| COVID Toes | 41% | | **70%** (36 / 34) | **Good** |
| Maculopapular | 28% | 56% | 32% | **N/A** |
| Urticarial | 12.5% | 52% | 33% | **N/A** |
| Vesicular | 10.5% | 38% | 48% | **N/A** |
| Vaso-occlusive | 4.5% | **68%** | | **Poor** |
| Other | 3% | | | |

Tan SW, Tam YC, Oh CC. Skin manifestations of COVID-19: A worldwide review. JAAD Int. 2021 Mar;2:119-133. doi: 10.1016/j.jdin.2020.12.003. Epub 2020 Dec 16. PMID: 33479703; PMCID: PMC7754879.

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| Skin Manifestation | % of rashes | Rash Onset timing | | Prognosis? |
|---|---|---|---|---|
| | | With Other sxs | Late / Only | |
| COVID Toes | 41% | | **70%** (36 / 34) | **Good** |
| Maculopapular | 28% | **Not informative** | | **N/A** |
| Urticarial | 12.5% | **Not informative** | | **N/A** |
| Vesicular | 10.5% | **Not informative** | | **N/A** |
| Vaso-occlusive | 4.5% | **68%** | | **Poor** |
| Other | 3% | | | |

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# COVID-19 Acute Eruptions For the Hospitalist

**Skin Manifestation**

**VASCULOPATHY**

COVID Toes

Common among COVID eruptions (Late sign)
**Good Prognosis**

Uncommon among COVID eruptions
**Poor Prognosis**

Vaso-occlusive

ie retiform purpura

Tan SW, Tam YC, Oh CC. Skin manifestations of COVID-19: A worldwide review. JAAD Int. 2021 Mar;2:119-133. doi: 10.1016/j.jdin.2020.12.003. Epub 2020 Dec 16. PMID: 33479703; PMCID: PMC7754879.

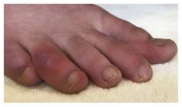
# COVID-19 Acute Eruptions For the Hospitalist

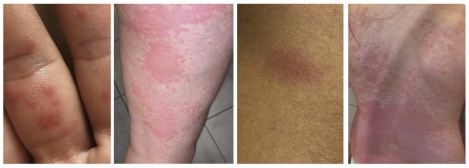
| Skin Manifestation | % of rashes | Mechanism | Onset / Severity |
|---|---|---|---|
| COVID Toes | 41% | Vasculopathy | **Late** sign, **Mild** disease |
| Maculopapular | 28% | **Other** | Contemporaneous with other symptoms; |
| Urticarial | 12.5% | | |
| Vesicular | 10.5% | | **Any** severity disease |
| Vaso-occlusive ie retiform purpura | 4.5% | Vasculopathy | **Contemporaneous** with other symptoms; **SEVERE** disease |

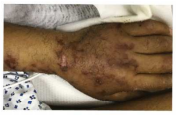
Tan SW, Tam YC, Oh CC. Skin manifestations of COVID-19: A worldwide review. JAAD Int. 2021 Mar;2:119-133. doi: 10.1016/j.jdin.2020.12.003. Epub 2020 Dec 16. PMID: 33479703; PMCID: PMC7754879.

# COVID-19 Acute Eruptions For the Hospitalist

**Severity of COVID-19***







**Pernio**

- Feet (84%) and hands (32%)
- Pain/burning (71%) and pruritus (36%)
- After other COVID-19 symptoms (49%)
- Fever (35%), cough (35%);19% asymptomatic
- 16% hospitalized

**Vesicular/ Urticarial/ Macular Erythema/ Morbilliform**

- Trunk and extremities
- Pruritus in 61-74%
- Typically after other COVID-19 symptoms (19%)
- Fever (65-74%), cough (52-66%), sore throat (39-50%), shortness of breath (28-45%)
- 22-45% hospitalized across groups

**Retiform purpura**

- Extremities and buttocks
- Often asymptomatic (73%)
- After other COVID -19 symptoms (91%)
- Fever (64%), cough (73%), and shortness of breath (73%)
- 100% hospitalized
- 82% with ARDS

*Severity calculated based on percentage of patients hospitalized for COVID-19

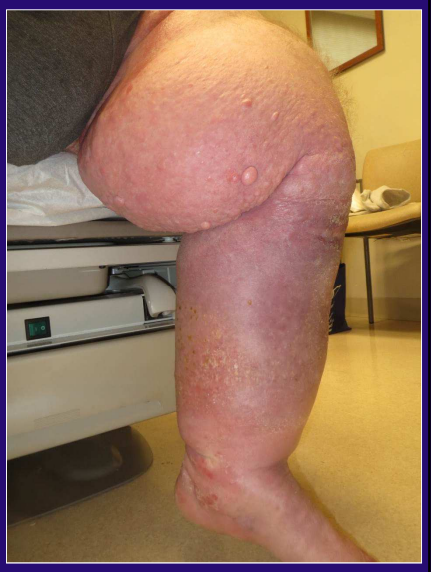
The spectrum of COVID-19–associated dermatologic manifestations: An international registry of 716 patients from 31 countries. Esther E. Freeman, MD, PhD, Devon E. McMahon, BA, Jules B. Lipoff, MD, Misha Rosenbach, MD, Carrie Kovarik, MD, Seemal R. Desai, MD, Joanna Harp, MD, Junko Takeshita, MD, PhD, MSCE, Lars E. French, MD, Henry W. Lim, MD, Bruce H. Thiers, MD, George J. Hruza, MD, MBA, Lindy P. Fox, MD. Journal of the American Academy of Dermatology. Volume 83 Issue 4 Pages 1118-1129 (October 2020)

# Key COVID-19 Points

- COVID Toes suggests mild disease
- Retiform purpura suggests severe disease

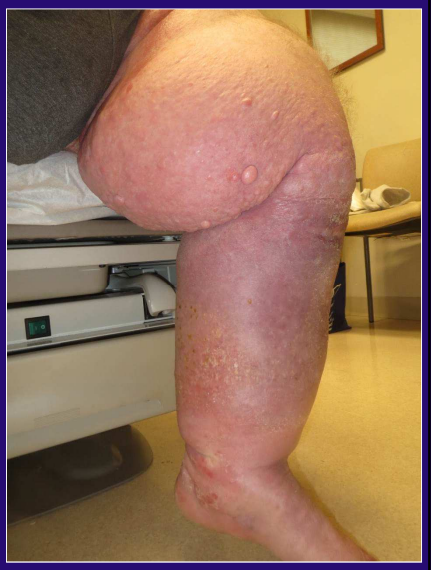
# Case

- 58 yo M
- CHF, Diabetes, CAD, morbid obesity
- 3 days worsening leg swelling, redness, warmth
- Admitted for IV antibiotics



# How should you manage?

A. IV Vancomycin
B. IV Cefazolin
C. IV Cefazolin + PO sulfa agent
D. PO Linezolid
E. No antibiotics



# How should you manage?

A. IV Vancomycin
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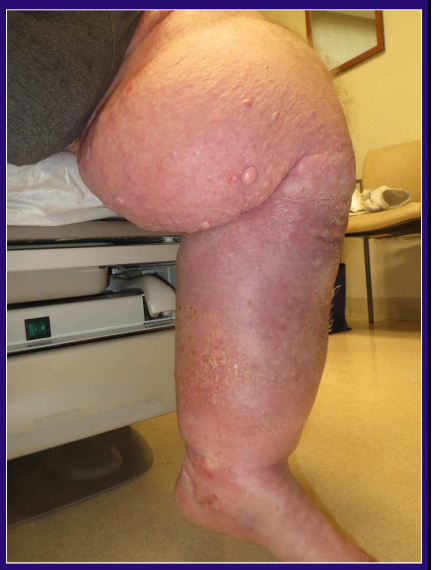
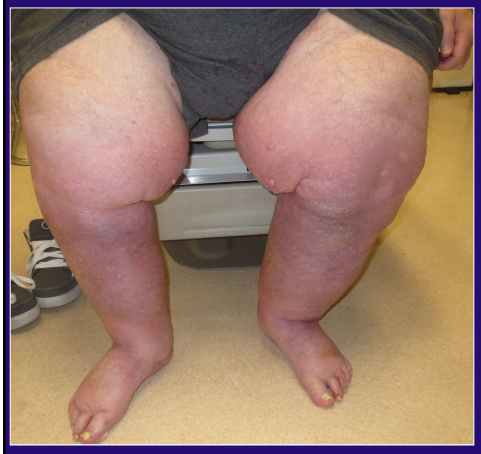
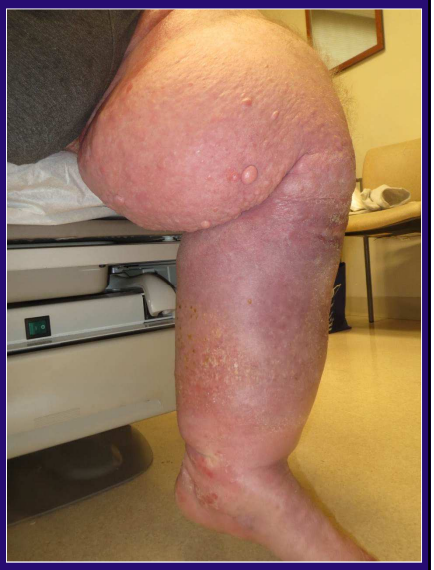
**UNFAIR QUESTION!**

**Not enough data**

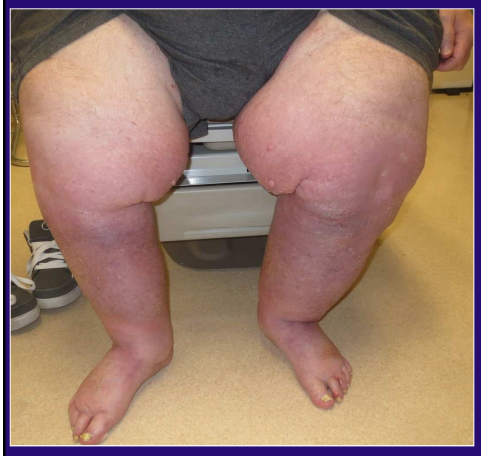


# You walk in the room and see this:





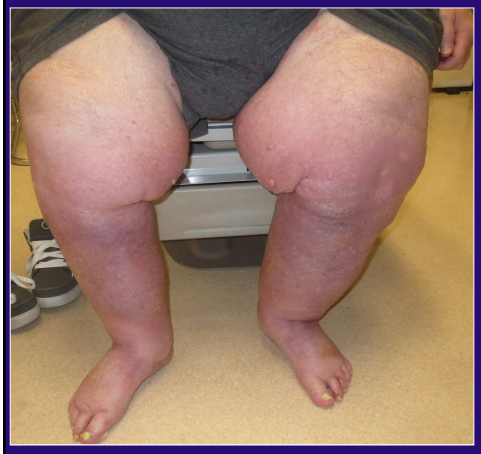
# You take some additional history:



- 58 yo M
- CHF, Diabetes, CAD, morbid obesity
- 3 days worsening leg swelling, redness, warmth, pain
- Admitted for IV antibiotics

- Chronic edema for years
- Worse in past 3 days
- Symmetric progression
- No subjective fevers
- + Pruritus
- + Pain, mild to moderate

## You become skeptical of the cellulitis diagnosis



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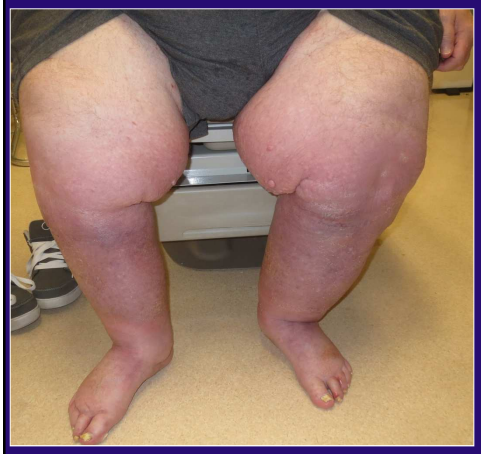
- Chronic edema for years
- Worse in past 3 days
- Symmetric progression
- No subjective fevers
- + Pruritus
- + Pain, mild to moderate

## You get paged out of the room, and have time for only 1 more quick action on the way out. To best *rule OUT* cellulitis, you should:



A. Feel the legs for warmth
B. Press the legs to check for tenderness
C. Order a CBC
D. Check systemic temperature
E. Swab the skin surface for culture

*** Alternative question phrasing:**
**Which of the following characteristics is most *SENSITIVE* for cellulitis?**

1. Local warmth
2. Local tenderness
3. Leukocytosis
4. Fever
5. Positive surface culture

*** Alternative question phrasing:**
**Which of the following characteristics is most *SENSITIVE* for cellulitis?**

1. Local warmth
2. **Local tenderness**
3. Leukocytosis
4. Fever
5. Positive surface culture

# Cellulitis

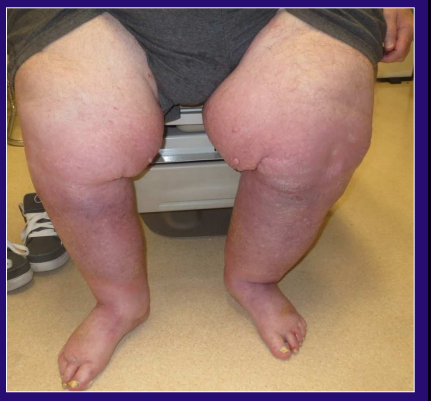
- Infection of deep dermis and subcutaneous fat
- Red, warm, **tender**, edematous (rubor, calor, dolor, tumor)
- *S. aureus*, *S. pyogenes* (but cultures low yield)
- Common: fever, leukocytosis

- Risks
  - Immunosuppression: e.g. diabetes (**consider GNRs**)
  - Anatomic anomaly: e.g. lymphedema, obesity
  - Loss of skin integrity: e.g. tinea pedis, ulcer, incision

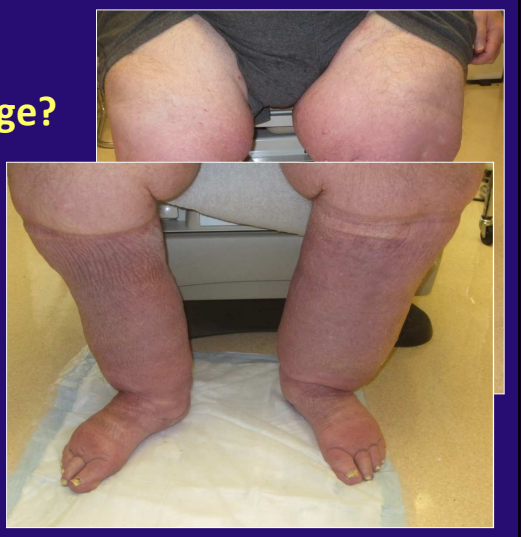
**You quickly palpate his legs: they are *minimally* tender bilaterally and circumferentially. No specific points of greater tenderness anywhere.**

**How should you manage?**

A. IV Vancomycin
B. IV Cefazolin
C. IV Cefazolin + PO sulfa agent
D. PO Linezolid
E. No antibiotics



**You quickly palpate his legs: they are *minimally* tender bilaterally and circumferentially. No specific points of greater tenderness anywhere.**



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A. IV Vancomycin
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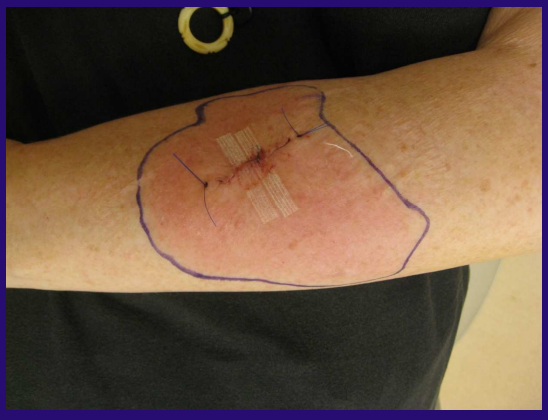
D. PO Linezolid
**E. No antibiotics**

# Management of Cellulitis

STEP 1: Cellulitis or NOT Cellulitis?



## Step 1: Cellulitis or NOT Cellulitis?

JAMA Dermatology | Original Investigation

### Costs and Consequences Associated With Misdiagnosed Lower Extremity Cellulitis

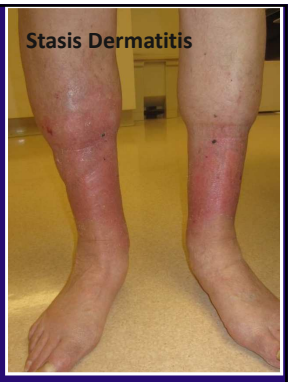
*JAMA Dermatol*. doi:10.1001/jamadermatol.2016.3816
Published online November 2, 2016.

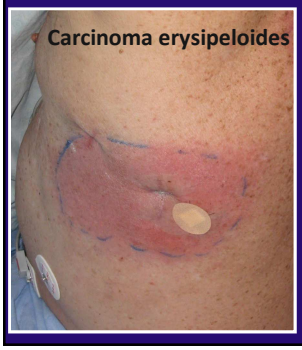
Qing Yu Weng, MD; Adam B. Raff, MD, PhD; Jeffrey M. Cohen, MD; Nicole Gunasekera, BS; Jean-Phillip Okhovat, BS; Priyanka Vedak, MD; Cara Joyce, PhD; Daniela Kroshinsky, MD, MPH; Arash Mostaghimi, MD, MPA, MPH

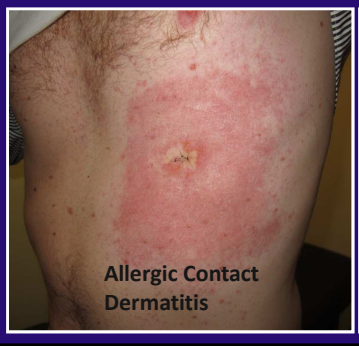
- 259 pts admitted from ED with "cellulitis"
- 79 (30.5%) did not have cellulitis
- 52 admitted specifically for "cellulitis"
  - 44 (84%) did not require hospitalization
  - 48 (92%) received unnecessary antibiotics
- **Cellulitis misdiagnosis→**
  - 50,000-130,000 unnecessary admissions (annual)
  - $195 million- $515 million avoidable healthcare $$s (annual)

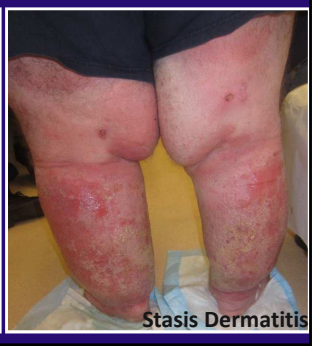
## Step 1: Cellulitis or NOT Cellulitis?

- **Tender?** If not, consider alternative
- Bilateral? Consider alternative
- Pruritic? Consider alternative
- Geometric? Consider alternative



# Management of Cellulitis

STEP 1: Cellulitis or NOT Cellulitis?

STEP 2: Severe or NOT Severe?

# Step 2: consider SEVERITY

- Assessment of severity
  - Ill appearing patient
  - Severe co-morbidities
  - Evidence of deep infection
    - Pyomyositis, gangrenous cellulitis, necrotizing fasciitis
    - NSAIDs perhaps masking signs of deep infection?
- Management of SEVERE cellulitis:
  - Admission/Observation
  - Debride if needed
  - Broad spectrum IV antibiotics: Cover GAS, MRSA, MSSA
  - Consider GNR & anaerobe coverage in select situations

# Management of SIMPLE Cellulitis

- Supportive care: elevation, immobilization, wound care
- Oral antibiotics

  But which one?
  - β-lactam?
  - Clindamycin? Sulfa? Minocycline? Fluoroquinolone?
  - 2 oral antibiotics together?
  - IV vancomycin? PO linezolid? Other?

NOTE: Same clinical question when transitioning from IV therapy to oral antibiotics for cellulitis

# Cellulitis empiric therapy: Key principles

- Common pathogens: GAS, MSSA, CA-MRSA
- Susceptibility
  - MSSA and GAS susceptible to beta-lactams
  - MSSA and CA-MRSA *generally* susceptible to TMP-SMX
  - GAS is *unreliably* susceptible to TMP-SMX
  - Susceptibility to clinda, fluoroquinolones, tetracyclines, macrolides, etc. *varies*
- Rates of MRSA: vary by region– often >50%
- Some infections will worsen despite "correct" empiric abx
- MANY infections will resolve despite "incorrect" empiric abx
- Cultures are generally low yield

Legend: GAS = Group A Streptococcus
MSSA = methicillin sensitive S. aureus
MRSA = methicillin resistant S. aureus
CA = community aquired
TMP-SMX = Trimethoprim/Sulfamethoxazole

# Data: Simple Cellulitis Empiric Antibiotic Choice

## Caution:
## The data is messy and incomplete

# SSTI empiric therapy 2007-2010

| Pro-B-lactam | Description | Result |
|---|---|---|
| Phillips et al 2007 | • Cost effectiveness analysis<br>• *Simple* SSTIs<br>• Cephalexin vs Clindamycin vs TMP-SMX | • Cephalexin dominates nearly all situations<br>• Unless chance of *S. aureus* (vs Group A Strep) is very high<br>• Or, MRSA prevalence rises well above current levels |
| Madaras-Kelly 2008 | • Retrospective case control<br>• Multicenter, adult practices, Idaho | • Adverse effects: More with anti-MRSA therapy<br>• Effectiveness: No differences β-lactams vs anti-MRSA therapy |
| Elliot et al 2009 | • Retrospective case control<br>• Multicenter, Pediatric practices | • Host factors predict failure more than antibiotic choice<br>• TMP-SMX failed more than clinda or cephalexin |

| Anti-B-lactam | Description | Result |
|---|---|---|
| Khawcharoenpom and Tice, 2010 | • Retrospective analysis,<br>• Hawaii clinics<br>• 405 cases | • TMP-SMX success rate > cephalexin (94% vs 71%)<br>• MRSA rate in culture positive cases = 62% (of 117 cultured) |
| Pokharna et al, 2010 ABSTRACT ONLY | • Retrospective analysis, Detroit<br>• Tertiary care **hospital (inpatients)**<br>• **Culture positive cellulitis only** | • Success rates: vancomycin > beta-lactam (90% vs 45%, OR 11 ) |


Phillips A, MacDougall C, Holdford DA. Analysis of Empiric Antimicrobial Strategies for Cellulitis in the Era of MRSA. *Annals of Pharmacotherapy*: 2007; Vol. 41, No. 1, pp. 13-20
Elliott DJ, Zaoutis TE, Troxel AB, et al: Empiric antimicrobial therapy for pediatric skin and soft-tissue infections in the era of methicillin-resistant Staph aureus. Pediatrics 123:e959-66, 2009
Madaras-Kelly KJ, Remington RE, Oliphant CM, et al: Efficacy of oral beta-lactam versus non-beta-lactam treatment of uncomplicated cellulitis. Am J Med 121:419-25, 2008
Khawcharoenpom T, Tice A. Empiric outpatient therapy with trimethoprim-sulfamethoxazole, cephalexin, or clindamycin for cellulitis. Am J Med.123 (10): 942-50, 2010
Pokharna H, Haque N, Zervos M. Vancomycin Vs B-Lactam – Drug of Choice for Empiric Treatment of Cellulitis Requiring Hospitalization. Abstract 1238 in Infectious Diseases Society of America 48th Annual Meeting: Oct 23, 2010.

# SSTI empiric therapy 2007-2010

## General conclusions

1. **Weak: Most studies slightly favor B-lactams**
2. **Consistent: Patient/disease characteristics predict failure better than abx choice**


Phillips A, MacDougall C, Holdford DA. Analysis of Empiric Antimicrobial Strategies for Cellulitis in the Era of MRSA. *Annals of Pharmacotherapy*: 2007; Vol. 41, No. 1, pp. 13-20
Elliott DJ, Zaoutis TE, Troxel AB, et al: Empiric antimicrobial therapy for pediatric skin and soft-tissue infections in the era of methicillin-resistant Staph aureus. Pediatrics 123:e959-66, 2009
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Pokharna H, Haque N, Zervos M. Vancomycin Vs B-Lactam – Drug of Choice for Empiric Treatment of Cellulitis Requiring Hospitalization. Abstract 1238 in Infectious Diseases Society of America 48th Annual Meeting: Oct 23, 2010.


# Cochrane Review 2010

**Authors' conclusions:**

We cannot define the best treatment for cellulitis and most recommendations are made on single trials. There is a need for trials to evaluate the efficacy of oral antibiotics against intravenous antibiotics in the community setting as there are service implications for cost and comfort.

Read the full abstract...


Kilburn SA, Featherstone P, Higgins B, Brindle R. Interventions for cellulitis and erysipelas. Cochrane Database of Systematic Reviews 2010, Issue 6. Art. No.: CD004299.

# June 2013

OXFORD JOURNALS
Clinical Infectious Diseases

## Clinical Trial: Comparative Effectiveness of Cephalexin Plus Trimethoprim-Sulfamethoxazole Versus Cephalexin Alone for Treatment of Uncomplicated Cellulitis: A Randomized Controlled Trial

**Daniel J. Pallin,[1,2] William D. Binder,[3] Matthew B. Allen,[1,4] Molly Lederman,[1,5] Siddharth Parmar,[1] Michael R. Filbin,[3] David C. Hooper,[6] and Carlos A. Camargo Jr[3]**

[1]Department of Emergency Medicine, Brigham and Women's Hospital, [2]Division of Emergency Medicine, Boston Children's Hospital, and [3]Department of Emergency Medicine, Massachusetts General Hospital, Boston; [4]Perelman School of Medicine at the University of Pennsylvania, Philadelphia; [5]Department of Pediatrics, and [6]Division of Infectious Diseases, Department of Medicine, Massachusetts General Hospital, Boston

**CID 2013:56 (15 June)**

# Pallin et al, CID 2013

- 3 Boston Emergency Depts, 2007-11
- 153 Simple Cellulitis patients randomized

| Cephalexin + **TMP-SMX** | Cephalexin + **Placebo** |
|---|---|
| 85% clinical cure | 82% clinical cure |

- Presence of nasal MRSA: no impact on outcome
- Conclusion: **no benefit to adding sulfa**

Pallin DJ, et al. "Clinical Trial: Comparative Effectiveness of Cephalexin Plus Trimethoprim-Sulfamethoxazole Versus Cephalexin Alone for Treatment of Uncomplicated Cellulitis: A Randomized Controlled Trial." Clin Infect Dis, 56: 2013 1754-62

# Moran et al, JAMA 2017

- 5 U.S. Emergency Depts, 2009-12
- 500 Simple Cellulitis patients randomized

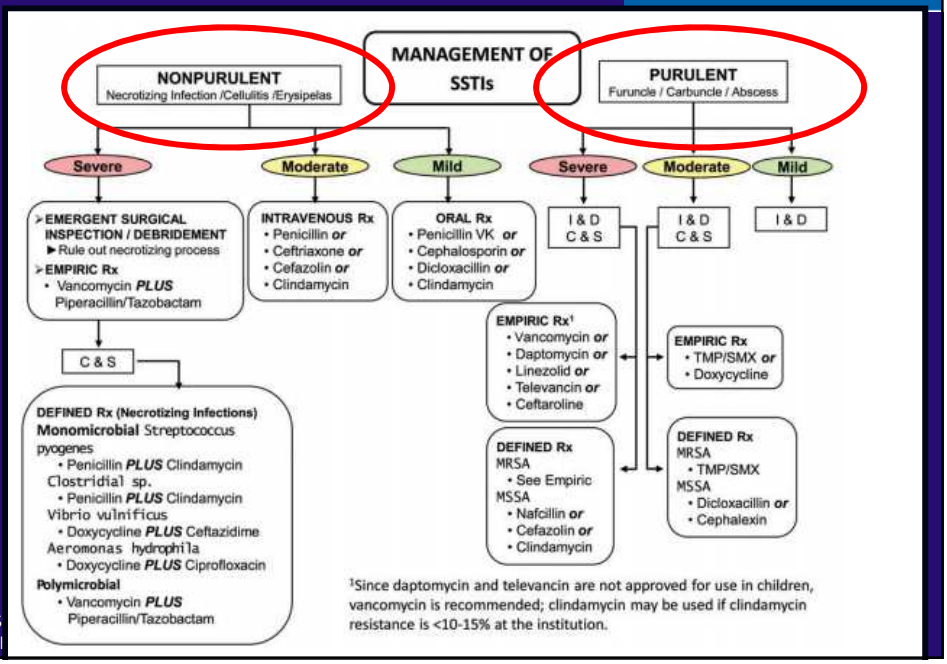
| Cephalexin + **TMP-SMX** | Cephalexin + **Placebo** |
|---|---|
| ↓ | ↓ |
| 83.5% clinical cure | 85.5% clinical cure |

- Conclusion: **no benefit to adding sulfa**
- Modified Intention-to-treat analysis trended toward combo therapy (7.3%, 95%CI -1.0 to 15.5%, p = 0.07)

Moran GJ, Krishnadasan A, Mower WR, Abrahamian FM, LoVecchio F, Steele MT, Rothman RE, Karras DJ, Hoagland R, Pettibone S, Talan DA. Effect of Cephalexin Plus Trimethoprim-Sulfamethoxazole vs Cephalexin Alone on Clinical Cure of Uncomplicated CellulitisA Randomized Clinical Trial. *JAMA*. 2017;317(20):2088–2096.

# June 2014

IDSA GUIDELINE



# 2014 Updated IDSA Guidelines

- Purulent Infections (eg abscesses)
  - Always I&D
  - If moderate or severe: anti-MRSA abx empirically

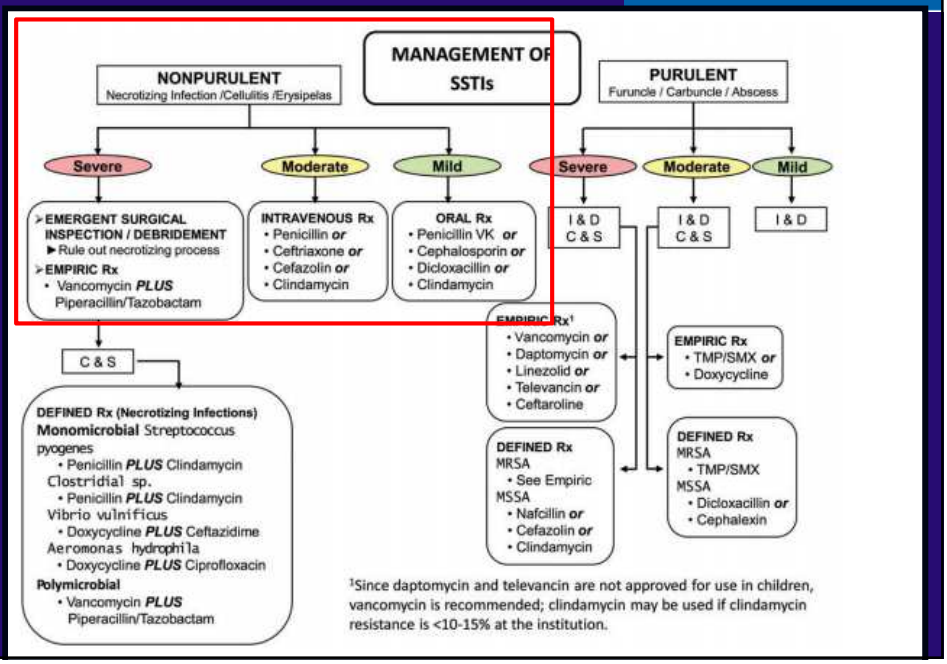
  (Daum et al, NEJM 2017: also suggests PO Abx for small abscesses)

- Non-purulent infections (eg cellulitis)
  - If severe: debride, support, broad spectrum IV Abx
  - If not severe: systemic abx with Strep coverage

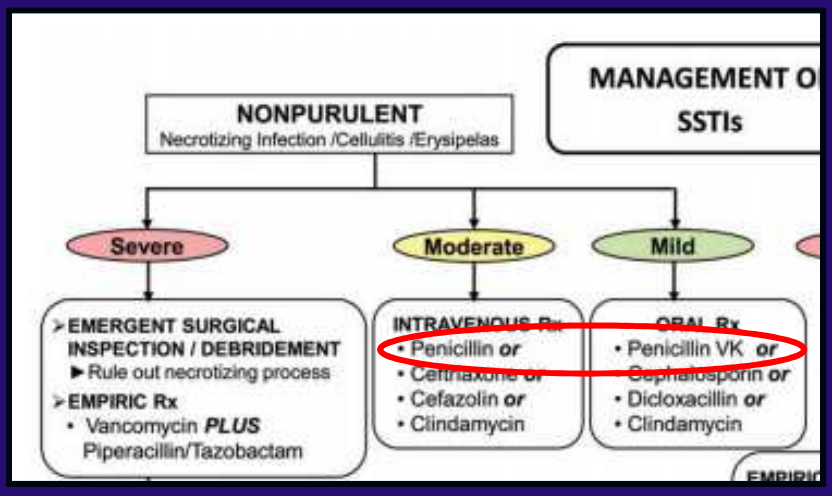
Stevens DL, et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America. Clinical Infectious Diseases (Advanced Access June 18, 2014)

# June 2014

IDSA GUIDELINE



# 2014 Updated IDSA Guidelines
## Caution regarding non-purulent infections




Stevens DL, et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America. Clinical Infectious Diseases (Advanced Access June 18, 2014)

# 2014 Updated IDSA Guidelines
## Caution regarding non-purulent infections

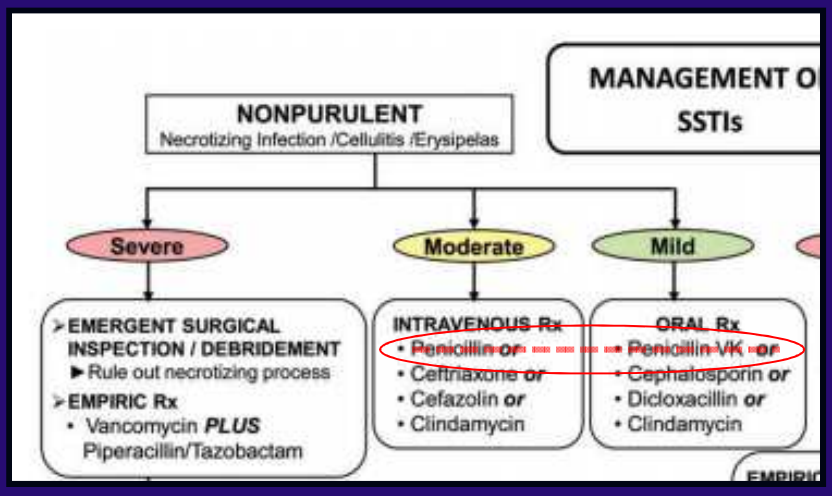
- Assumes Strep is dominant, minimal MSSA/MRSA
- Cites 6 studies: mostly old culture data (5 are pre-1996)
- Exception: Jeng et al, 2010– serologies & β-lactam response
  - Claim: "73% of non-culturable cellulitis caused by BHS"
    - **BUT: Not "intention to test"– 31% lost without serologies**
  - Claim: β-lactam response rate 95.6%
    - **BUT: They recommended cefazolin or oxacillin, which cover MSSA**
  - **Only included patients admitted to hospital**

Jeng A, Beheshti M, Li J, Nathan R. The role of beta-hemolytic streptococci in causing diffuse, non-culturable cellulitis: a prospective investigation. Medicine (Baltimore) 2010; 89: 217-26

Stevens DL, et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the IDSA. Clinical Infectious Diseases (Advanced Access June 18, 2014)

# 2014 Updated IDSA Guidelines

## Caution regarding non-purulent infections




Stevens DL, et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America. Clinical Infectious Diseases (Advanced Access June 18, 2014)

# Newer data

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 19, 2015 VOL. 372 NO. 12

Clindamycin versus Trimethoprim–Sulfamethoxazole for Uncomplicated Skin Infections

Loren G. Miller, M.D., M.P.H., Robert S. Daum, M.D., C.M., C. Buddy Creech, M.D., M.P.H., David Young, M.D., Michele D. Downing, R.N., M.S.N., Samantha J. Eells, M.P.H., Stephanie Pettibone, B.S., Rebecca J. Hoagland, M.S., and Henry F. Chambers, M.D., for the DMID 07-0051 Team*

van Bijnen et al. BMC Family Practice 2014, 15:175
http://www.biomedcentral.com/1471-2296/15/175

BMC Family Practice

RESEARCH ARTICLE Open Access

Primary care treatment guidelines for skin infections in Europe: congruence with antimicrobial resistance found in commensal *Staphylococcus aureus* in the community

Evelien ME van Bijnen[1*], W John Paget[1], Casper DJ den Heijer[2], Ellen E Stobberingh[2], Cathrien A Bruggeman[2], François G Schellevis[1,3] and in collaboration with the APRES Study Team

Academic Emergency Medicine
Official Journal of the Society for Academic Emergency Medicine

ORIGINAL CONTRIBUTION

Predictors of Failure of Empiric Outpatient Antibiotic Therapy in Emergency Department Patients With Uncomplicated Cellulitis

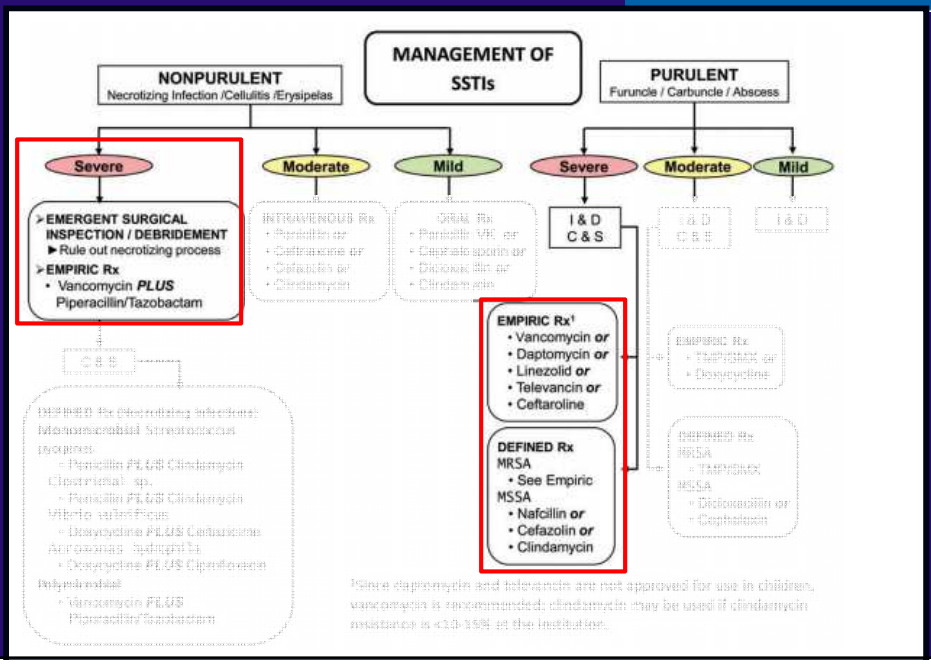
Daniel Peterson, MD, FRCP(C), PhD, Shelley McLeod, MSc, Karen Woolfrey, MD, FRCP(C), and Andrew McRae, MD, FRCP(C), PhD

# Cellulitis empiric therapy: Conclusions/Recommendations

- Still a moving target, but data is improving
- Anything severe: Admit, monitor, broad IV abx, surgery
- Beta-lactam likely best for most simple, outpatient cases
- Despite IDSA guidelines:
  - Strongly consider a β-lactamase resistant agent

# June 2014

IDSA GUIDELINE

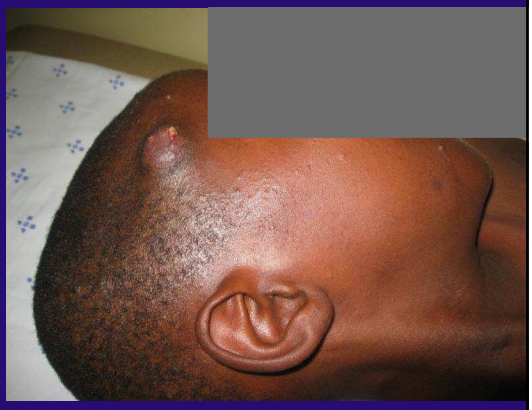


# Newly Approved Antibiotics for SSTI

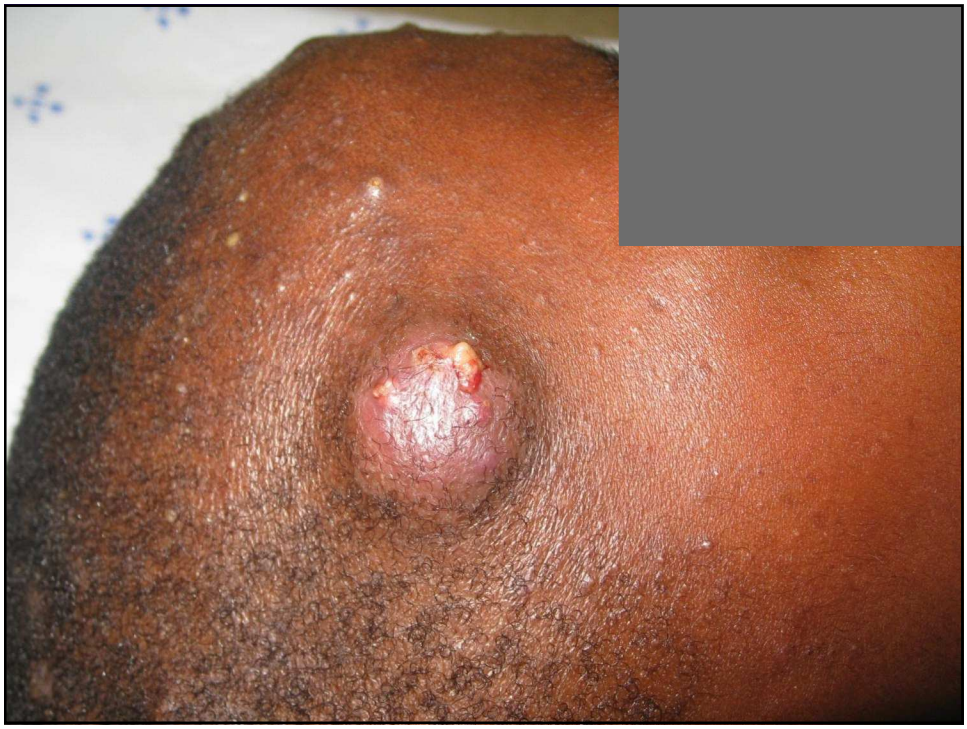
| Antibiotic | Year | Route | Class | SSTI spectrum |
|---|---|---|---|---|
| **Omadacycline** | 2018 | IV, PO | Modernized Tetracycline | Staph spp (incl MRSA), Strep spp, VRE/VSE, *E. cloacae, K. pneumoniae,* |
| **Delafloxacin** | 2017 | IV, PO | Fluoroquinolone | Staph spp (incl MRSA), Strep spp, VRE/VSE, *E. coli, E. cloacae, K. pneumoniae, P. aeruginosa* |
| **Ozenaxacin** | 2017 | Topical | Quinolone | Impetigo (including MRSA) |
| **Dalbavancin** | 2014 | IV (Qwk) | Lipoglycopeptide | Staph spp (incl MRSA), Strep spp, VSE |
| **Oritavancin** | 2014 | IV x 1 | Lipoglycopeptide | Staph spp (incl MRSA), Strep spp, VSE |
| **Tedizolid** | 2014 | IV, PO | Oxazolidinone | Staph spp (incl MRSA), Strep spp, VRE/VSE |
| **Ceftaroline** | 2010 | IV | Cephalosporine | Staph spp (incl MRSA), Strep spp (incl MDR *S. pneumoniae*), VRE/VSE (limited), *H. influenzae, E. cloacae, E. coli, K. pneumoniae,* Shigella spp. |
| **Televancin** | 2009 | IV | Lipoglycopeptide | Staph spp (incl MRSA), Strep spp, VSE |

# Case

- 12 year-old female
- Fluctuant nodule R temple
- Increasing pain x 1 week
- HIV+ (congenital)
- CD4+ > 200
- on ARVs



- Many similar lesions over past year



## What is the most appropriate next step in management of the furuncle/abscess?

1. Daily chlorhexidine washes
2. Oral cephalexin
3. Oral cephalexin plus oral TMP-SMX
4. IV vancomycin
5. Incision and Drainage

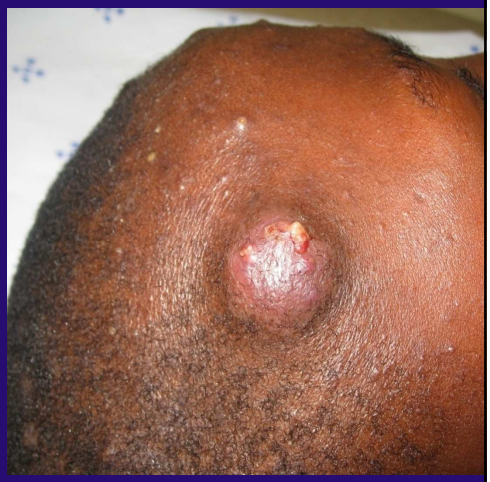
# What is the most appropriate next step in management of the furuncle/abscess?

1. Daily chlorhexidine washes
2. Oral cephalexin
3. Oral cephalexin plus oral TMP-SMX
4. IV vancomycin
5. Incision and Drainage

**No longer a fair question because of data on the following slides**

# Furunculosis

- *Staph aureus* most common
- Treatment:
  - Warm compresses
  - Incision & Drainage if >1cm



**I&D alone - I&D + PO antibiotics**

??????????


Duong M, Markwell S, Peter J, Barenkamp S. Randomized, controlled trial of antibiotics in the management of community-acquired skin abscesses in the pediatric patient. Ann Emerg Med2010;55:401-407

Schmitz GR, Bruner D, Pitotti R, et al. Randomized controlled trial of trimethoprim-sulfamethoxazole for uncomplicated skin abscesses in patients at risk for community-associated methicillin-resistant Staphylococcus aureus infection. Ann Emerg Med 2010;56:283-287[Erratum, Ann Emerg Med 2010;56:588

Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Disease Society of America for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. Clin Infect Dis 2011;52:e18-e55


??????????

N ENGL J MED 376;26 NEJM.ORG JUNE 29, 2017

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# A Placebo-Controlled Trial of Antibiotics for Smaller Skin Abscesses

Robert S. Daum, M.D., C.M., Loren G. Miller, M.D., M.P.H., Lilly Immergluck, M.D., Stephanie Fritz, M.D., M.S.C.I., C. Buddy Creech, M.D., M.P.H., David Young, M.D., Neha Kumar, M.D., Michele Downing, R.N., M.S.N., Stephanie Pettibone, B.S., Rebecca Hoagland, M.S., Samantha J. Eells, M.P.H., Mary G. Boyle, R.N., M.S.N., Trisha Chan Parker, M.P.H., and Henry F. Chambers, M.D., for the DMID 07-0051 Team*

- 6 centers: U. Chicago, SF General, Harbor UCLA, Vanderbilt, Wash U., Morehouse
- Double Blinded, Randomized, Placebo Controlled; Appropriate exclusions/inclusion
- Single abscess, <5cm, uncomplicated, adults & children
- Clinda 300mg TID vs Bactrim DS BID vs Placebo
- 786 Enrolled

# NEJM 2017: Simple Abscess Treatment
# I&D + {Clinda vs TMP-SMX vs Placebo}

**Table 3. Cure Rate at Test-of-Cure Visit in the Overall Population and Relevant Subgroups.***

| Group | Clindamycin | | TMP-SMX | | Placebo | |
|---|---|---|---|---|---|---|
| | No. with Cure/ Total No. | % (95% CI) | No. with Cure/ Total No. | % (95% CI) | No. with Cure/ Total No. | % (95% CI) |
| All participants | | | | | | |
| Intention-to-treat population | 221/266 | 83.1 (78.3–87.9) | 215/263 | 81.7 (76.8–86.7) | 177/257 | 68.9 (62.9–74.9) |
| Population that could be evaluated | 221/238 | 92.9 (89.3–96.4) | 215/232 | 92.7 (89.0–96.3) | 177/220 | 80.5 (74.8–86.1) |
| Children | | | | | | |
| Intention-to-treat population | 90/101 | 89.1 (82.5–95.7) | 75/91 | 82.4 (74.0–90.8) | 61/89 | 68.5 (58.3–78.7) |
| Population that could be evaluated | 90/92 | 97.8 (94.3–100.0) | 75/81 | 92.6 (86.3–98.9) | 61/74 | 82.4 (73.1–91.8) |
| Adults | | | | | | |
| Intention-to-treat population | 131/165 | 79.4 (72.9–85.9) | 140/172 | 81.4 (75.3–87.5) | 116/168 | 69.0 (61.8–76.3) |
| Population that could be evaluated | 131/146 | 89.7 (84.5–95.0) | 140/151 | 92.7 (88.2–97.2) | 116/146 | 79.5 (72.6–86.3) |
| *S. aureus* isolated | | | | | | |
| Intention-to-treat population | 157/188 | 83.5 (77.9–89.1) | 149/179 | 83.2 (77.5–89.0) | 102/160 | 63.8 (56.0–71.5) |
| Population that could be evaluated | 157/167 | 94.0 (90.1–97.9) | 149/160 | 93.1 (88.9–97.4) | 102/134 | 76.1 (68.5–83.7) |
| MRSA isolated | | | | | | |
| Intention-to-treat population | 116/142 | 81.7 (75.0–88.4) | 110/130 | 84.6 (78.0–91.2) | 73/116 | 62.9 (53.7–72.2) |
| Population that could be evaluated | 116/126 | 92.1 (86.9–97.2) | 110/117 | 94.0 (89.3–98.7) | 73/96 | 76.0 (67.0–85.1) |
| MSSA isolated | | | | | | |
| Intention-to-treat population | 41/46 | 89.1 (79.0–99.2) | 39/49 | 79.6 (67.3–91.9) | 29/44 | 65.9 (50.8–81.1) |
| Population that could be evaluated | 41/41 | 100.0 (98.8–100.0) | 39/43 | 90.7 (80.9–100.0) | 29/38 | 76.3 (61.5–91.1) |
| No *S. aureus* isolated | | | | | | |
| Intention-to-treat population | 57/68 | 83.8 (74.3–93.3) | 59/72 | 81.9 (72.4–91.5) | 69/83 | 83.1 (74.5–91.8) |
| Population that could be evaluated | 57/63 | 90.5 (82.4–98.5) | 59/65 | 90.8 (83.0–98.6) | 69/76 | 90.8 (83.6–97.9) |

* The actual confidence interval was 95.6% after adjustment for the interim analysis. The intention-to-treat population includes all participants who underwent randomization, and the population that could be evaluated includes participants who received treatment or placebo and completed the required study visits.

N ENGL J MED 376;26 NEJM.ORG JUNE 29, 2017

# NEJM 2017: Simple Abscess Treatment
# I&D + {Clinda vs TMP-SMX vs Placebo}

N ENGL J MED 376;26 NEJM.ORG JUNE 29, 2017

**Table 3.** Cure Rate at Test-of-Cure Visit in the Overall Population and Relevant Subgroups.*

| Group | Clindamycin | | | TMP-SMX | | | Placebo | |
|---|---|---|---|---|---|---|---|---|
| | No. with Cure/ Total No. | % (95% CI) | | No. with Cure/ Total No. | % (95% CI) | | No. with Cure/ Total No. | % (95% CI) |
| All participants | | | | | | | | |
| Intention-to-treat population | 221/266 | 83.1 (78.3–87.9) | +14.2 | 215/263 | 81.7 (76.8–86.7) | +12.8 | 177/257 | 68.9 (62.9–74.9) |
| Population that could be evaluated | 221/238 | 92.9 (89.3–96.4) | +12.4 | 215/232 | 92.7 (89.0–96.3) | +12.2 | 177/220 | 80.5 (74.8–86.1) |
| Children | | | | | | | | |
| Intention-to-treat population | 90/101 | 89.1 (82.5–95.7) | +20.6 | 75/91 | 82.4 (74.0–90.8) | +13.9 | 61/89 | 68.5 (58.3–78.7) |
| Population that could be evaluated | 90/92 | 97.8 (94.3–100.0) | +15.4 | 75/81 | 92.6 (86.3–98.9) | +10.2 | 61/74 | 82.4 (73.1–91.8) |
| Adults | | | | | | | | |
| Intention-to-treat population | 131/165 | 79.4 (72.9–85.9) | +10.4 | 140/172 | 81.4 (75.3–87.5) | +12.4 | 116/168 | 69.0 (61.8–76.3) |
| Population that could be evaluated | 131/146 | 89.7 (84.5–95.0) | +10.2 | 140/151 | 92.7 (88.2–97.2) | +13.2 | 116/146 | 79.5 (72.6–86.3) |
| *S. aureus* isolated | | | | | | | | |
| Intention-to-treat population | 157/188 | 83.5 (77.9–89.1) | +19.7 | 149/179 | 83.2 (77.5–89.0) | +19.4 | 102/160 | 63.8 (56.0–71.5) |
| Population that could be evaluated | 157/167 | 94.0 (90.1–97.9) | +17.9 | 149/160 | 93.1 (88.9–97.4) | +17.0 | 102/134 | 76.1 (68.5–83.7) |
| MRSA isolated | | | | | | | | |
| Intention-to-treat population | 116/142 | 81.7 (75.0–88.4) | +18.8 | 110/130 | 84.6 (78.0–91.2) | +21.7 | 73/116 | 62.9 (53.7–72.2) |
| Population that could be evaluated | 116/126 | 92.1 (86.9–97.2) | +16.1 | 110/117 | 94.0 (89.3–98.7) | +18.0 | 73/96 | 76.0 (67.0–85.1) |
| MSSA isolated | | | | | | | | |
| Intention-to-treat population | 41/46 | 89.1 (79.0–99.2) | +23.2 | 39/49 | 79.6 (67.3–91.9) | +13.7 | 29/44 | 65.9 (50.8–81.1) |
| Population that could be evaluated | 41/41 | 100.0 (98.8–100.0) | +23.7 | 39/43 | 90.7 (80.9–100.0) | +14.4 | 29/38 | 76.3 (61.5–91.1) |
| No *S. aureus* isolated | | | | | | | | |
| Intention-to-treat population | 57/68 | 83.8 (74.3–93.3) | +0.7 | 59/72 | 81.9 (72.4–91.5) | -1.2 | 69/83 | 83.1 (74.5–91.8) |
| Population that could be evaluated | 57/63 | 90.5 (82.4–98.5) | -0.3 | 59/65 | 90.8 (83.0–98.6) | 0 | 69/76 | 90.8 (83.6–97.9) |

* The actual confidence interval was 95.6% after adjustment for the interim analysis. The intention-to-treat population includes all participants who underwent randomization, and the population that could be evaluated includes participants who received treatment or placebo and completed the required study visits.


# NEJM 2017: Simple Abscess Treatment
# I&D + {Clinda vs TMP-SMX vs Placebo}

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**Table 3.** Cure Rate at Test-of-Cure Visit in the Overall Population and Relevant Subgroups.*

| Group | Clindamycin | | | TMP-SMX | | | Placebo | |
|---|---|---|---|---|---|---|---|---|
| | No. with Cure/ Total No. | % (95% CI) | | No. with Cure/ Total No. | % (95% CI) | | No. with Cure/ Total No. | % (95% CI) |
| All participants | | | | | | | | |
| Intention-to-treat population | 221/266 | 83.1 (78.3–87.9) | +14.2 | 215/263 | 81.7 (76.8–86.7) | +12.8 | 177/257 | 68.9 (62.9–74.9) |
| Population that could be evaluated | 221/238 | 92.9 (89.3–96.4) | +12.4 | 215/232 | 92.7 (89.0–96.3) | +12.2 | 177/220 | 80.5 (74.8–86.1) |
| Children | | | | | | | | |
| Intention-to-treat population | 90/101 | 89.1 (82.5–95.7) | +20.6 | 75/91 | 82.4 (74.0–90.8) | +13.9 | 61/89 | 68.5 (58.3–78.7) |
| Population that could be evaluated | 90/92 | 97.8 (94.3–100.0) | +15.4 | 75/81 | 92.6 (86.3–98.9) | +10.2 | 61/74 | 82.4 (73.1–91.8) |
| Adults | | | | | | | | |
| Intention-to-treat population | 131/165 | 79.4 (72.9–85.9) | +10.4 | 140/172 | 81.4 (75.3–87.5) | +12.4 | 116/168 | 69.0 (61.8–76.3) |
| Population that could be evaluated | 131/146 | 89.7 (84.5–95.0) | +10.2 | 140/151 | 92.7 (88.2–97.2) | +13.2 | 116/146 | 79.5 (72.6–86.3) |
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# NEJM 2017: Simple Abscess Treatment
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**Table 3. Cure Rate at Test-of-Cure Visit in the Overall Population and Relevant Subgroups.***

| Group | Clindamycin | | | TMP-SMX | | | Placebo | |
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| *S. aureus* isolated | | | | | | | | |
| Intention-to-treat population | 157/188 | 83.5 (77.9–89.1) | +19.7 | 149/179 | 83.2 (77.5–89.0) | +19.4 | 102/160 | 63.8 (56.0–71.5) |
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**Likely more reflective of antibiotic impact on true abscesses**

**Likely includes a number of non-infectious, inflamed epidermal inclusion cysts**

# NEJM 2017: Simple Abscess Treatment
# I&D + {Clinda vs TMP-SMX vs Placebo}

Table S8: Reasons for failure at the TOC in the ITT population and OMFU visit

| | Clindamycin n=266 | TMP-SMX n=263 | Placebo n=257 | Total n=786 |
|---|---|---|---|---|
| Failures up to and including the OMFU visit | ~~57~~ **44** | ~~71~~ **45** | ~~96~~ **50** | ~~224~~ |
| Excluded from the secondary efficacy analysis due to lost to follow up and other administrative reasons | 32 | 37 | 39 | 108 |
| Worsening original lesion | 1 | 0 | 1 | 2 |
| New infection | ~~13~~ | ~~26~~ | ~~46~~ | ~~85~~ |
| Used Rescue Meds | 12 | 15 | 33 | 60 |
| Treatment stopped within 48 hours | 4 | 1 | 1 | 6 |
| Unplanned surgery | 3 | 3 | 3 | 9 |
| Used non-study antibiotics for other lesion | 5 | 4 | 3 | 12 |
| **Cure at 1 month** | **83.5%** | **82.9%** | **80.5%** | |

# NEJM 2017: Simple Abscess Treatment
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| Used non-study antibiotics for other lesion | 5 | 4 | 3 | 12 |
| **Cure at 1 month** | **83.5%** | **82.9%** | **80.5%** | |

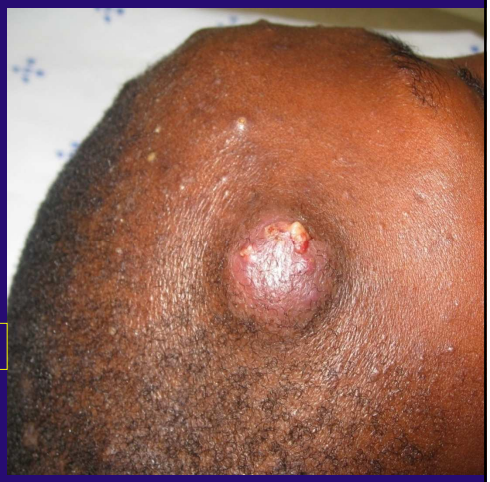
**What are we treating here?**

# Furunculosis

- *Staph aureus* most common
- Treatment:
  - Warm compresses
  - Incision & Drainage if >1cm

~~I&D alone = I&D + PO antibiotics~~

**Consider anti-staph (MRSA) Abx**



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My Personal Approach:

1. I&D, with culture
2. If not resolved by time of culture result, start PO abx based on culture result

## *S. aureus* Decolonization

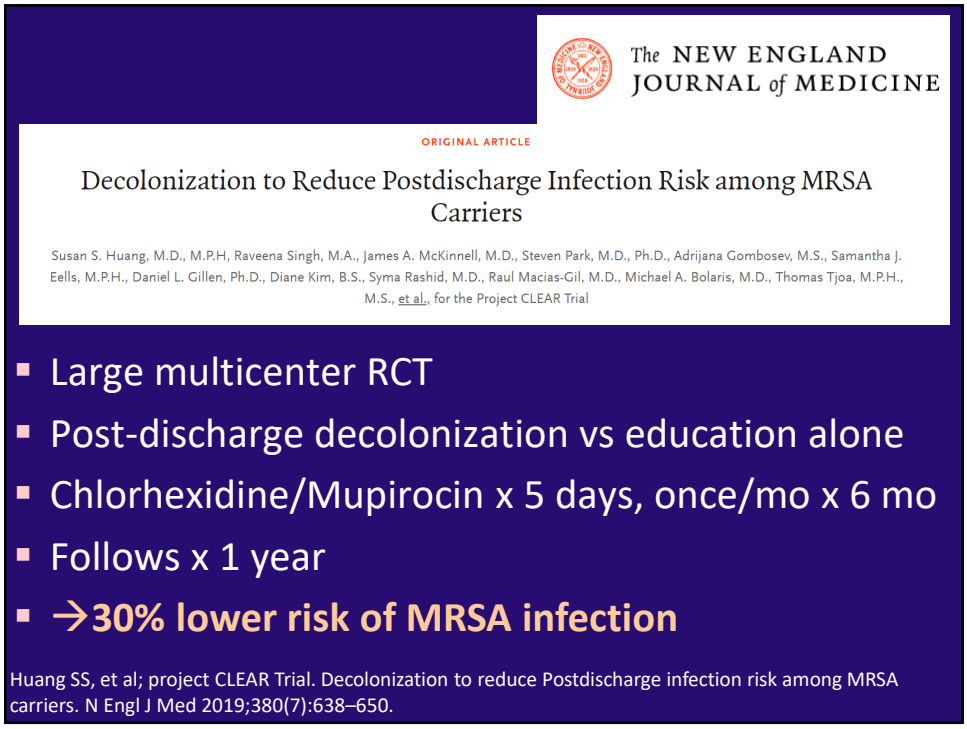
- Data is poor quality
- Data is highly **fragmented**
  - By setting: ambulatory, hospital, ICU, nursing home…
  - By indication: pre-op, carrier-status, recurrent infection…
  - By intervention: mupirocin, chlorhexidine, PO abx, et al...
  - By outcome: decolonization vs lower infection rate
  - By endpoint: 1 mo, 3 mo, 6 mo, 1 year, 5 year….

## *S. aureus* Decolonization

- Cochrane review concludes:

"In people who are nasal carriers of *S. aureus*, the use of mupirocin ointment results in a statistically significant reduction in *S. aureus* infections."

van Rijen M, Bonten M, Wenzel R, Kluytmans J. Mupirocin ointment for preventing Staphylococcus aureus infections in nasal carriers. Cochrane Database of Systematic Reviews 2008, Issue 4.




# *S. aureus* Decolonization

- Nasal *S. aureus* carriers:
  - Mupirocin → lower *S. aureus* infection rate
  - But, *possibly* higher rates of other nosocomial infections
- Other groups/settings:
  - Many studies demonstrate transient decolonization
    - Simple cases: mupirocin to nares, chlorhexidine wash
    - Complex cases: add 2 PO antibiotics
    - Remember benzoyl peroxide, bleach baths, hexachlorophene, et al
  - A few demonstrate lasting effect or decreased infection


Finnell SM, et al. Decolonization of children after incision and drainage for MRSA abscess: a retrospective cohort study. Clin Pediatr (Phila). 2015 May;54(5):445-50
Huang SS, et al. Targeted versus universal decolonization to prevent ICU infection. N Engl J Med. 2013 Jun 13;368(24):2255-65.
Miller LG, et al. Prospective investigation of nasal mupirocin, hexachlorophene body wash, and systemic antibiotics for prevention of recurrent community-associated methicillin-resistant Staphylococcus aureus infections. Antimicrob Agents Chemother 2012;56:1084-108
Ammerlaan HS et al. Eradication of carriage with methicillin-resistant Staphylococcus aureus effectiveness of a national guideline. J Antimicrobial Chemother. 2011: 66(10):2409-17
Hughes C, Smith M, Tunney M. Infection control strategies for preventing the transmission of meticillin-resistant *Staphylococcus aureus* (MRSA) in nursing homes for older people. Cochrane Collaboration, 20 Jan 2010.
Loeb MB, Main C, Eady A, Walker-Dilks C. Antimicrobial drugs for treating methicillin-resistant Staphylococcus aureus colonization. Cochrane Collaboration, 8 Oct 2008.
Weintrob A, et al. Randomized, Double-Blind, Placebo-Controlled Study on Decolonization Procedures for Methicillin-Resistant Staphylococcus aureus (MRSA) among HIV-Infected Adults. PLoS One. 2015 May 27;10(5)

# *S. aureus* Decolonization

- We can return to this at the end
- Bottom line:
  - Jury is still very much out
  - I do use decolonization regimens in select, usually ambulatory, patients


Finnell SM, et al. Decolonization of children after incision and drainage for MRSA abscess: a retrospective cohort study. Clin Pediatr (Phila). 2015 May;54(5):445-50

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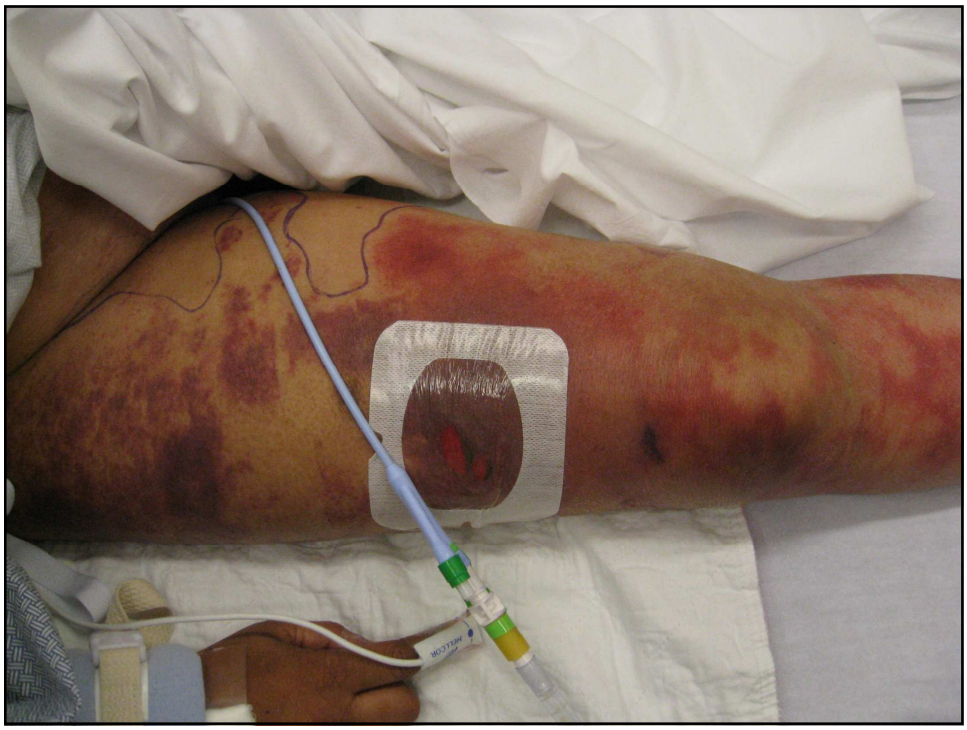
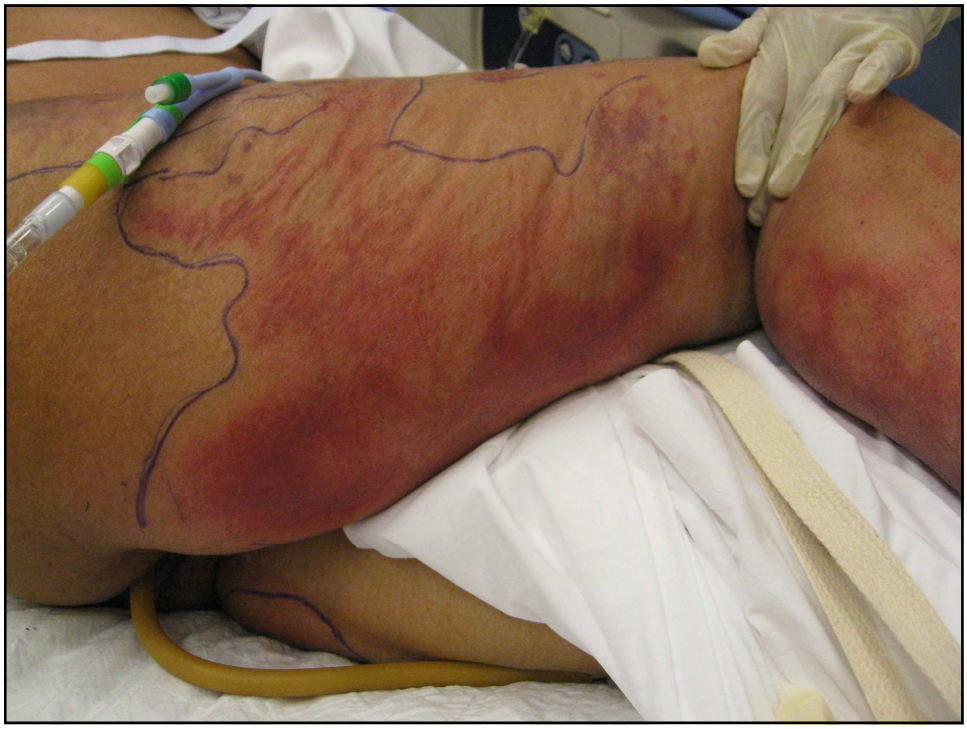
# Case

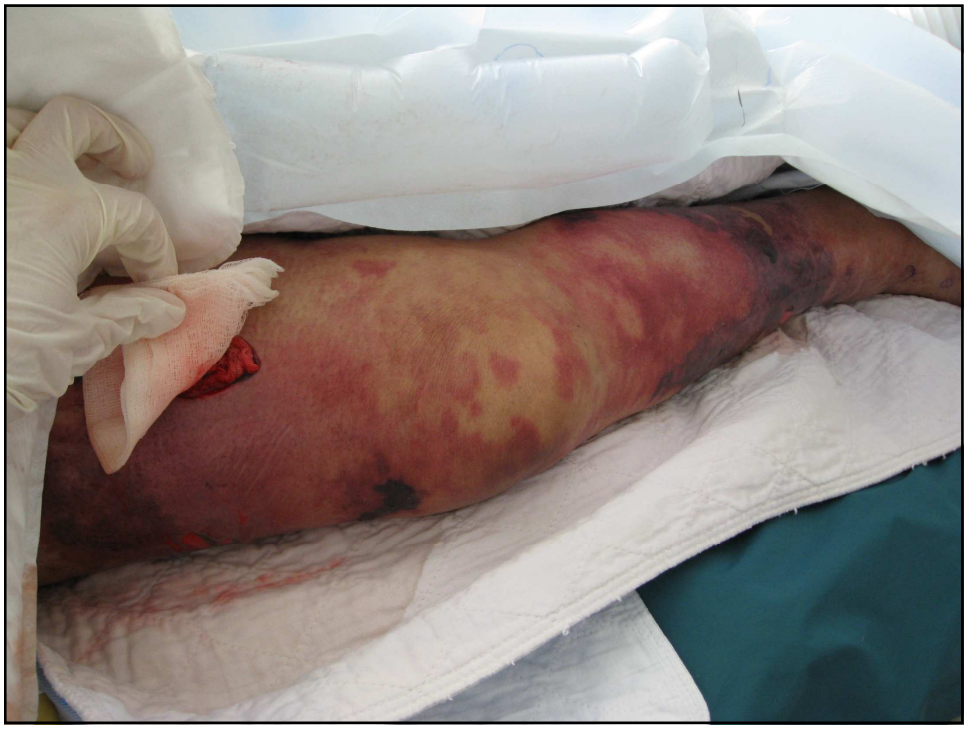
- **52 yo F with systemic lupus**
- **On mycophenolate mofetil and prednisone**
- **Presents unresponsive with rash on her right leg only**
- **Was well the night before**
- **Rapidly developed multi-organ failure in ED**

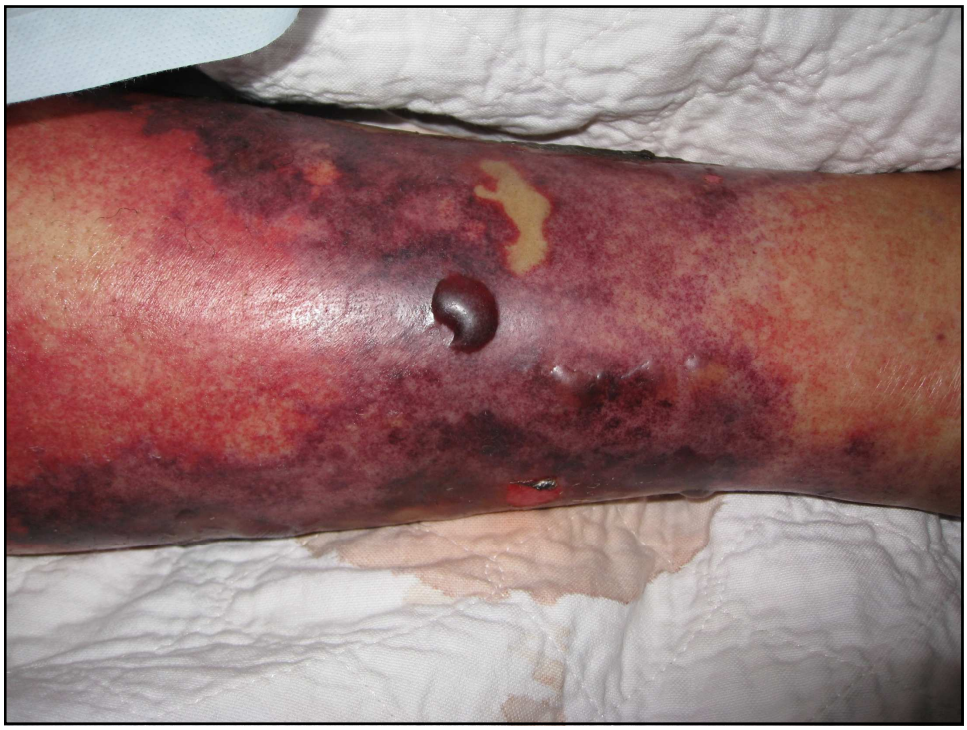
# Hospital Day 1

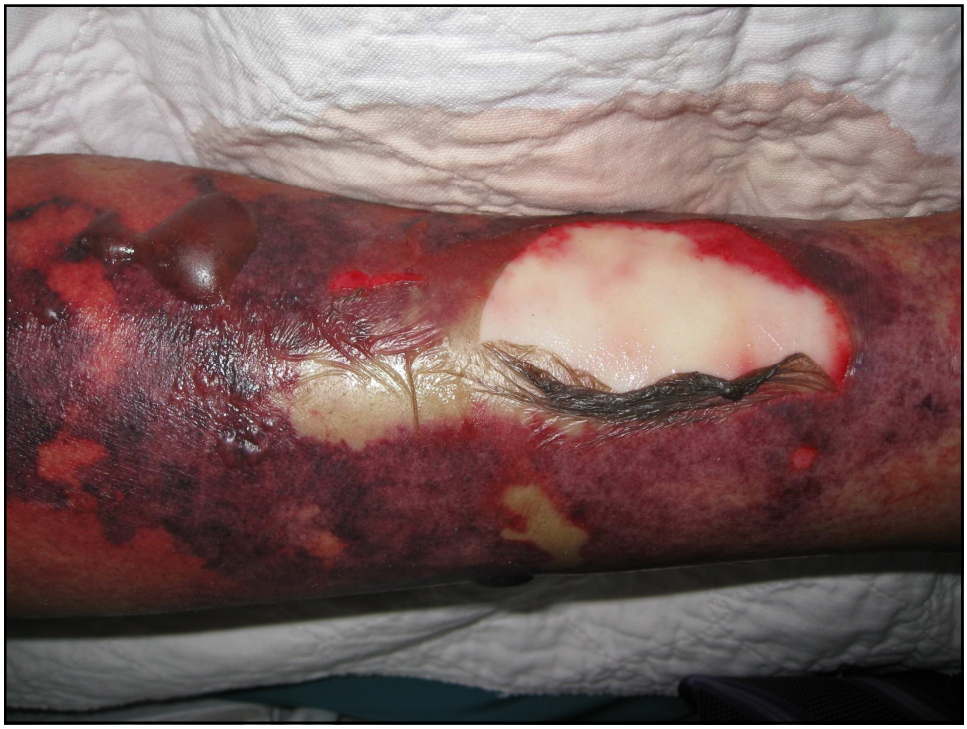




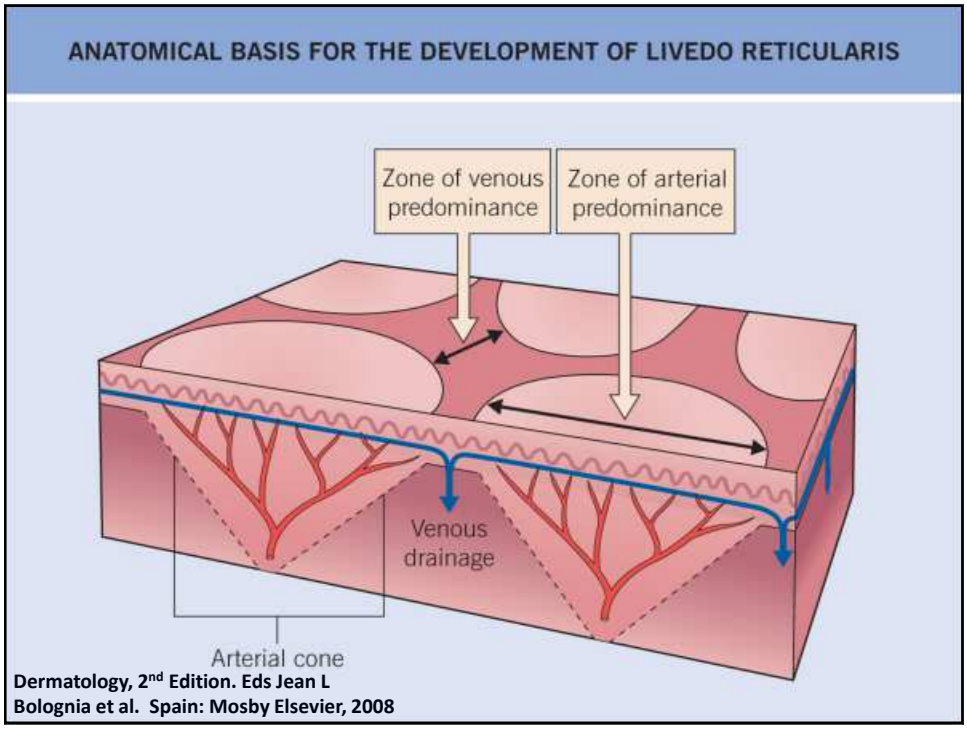
# Hospital Day 3



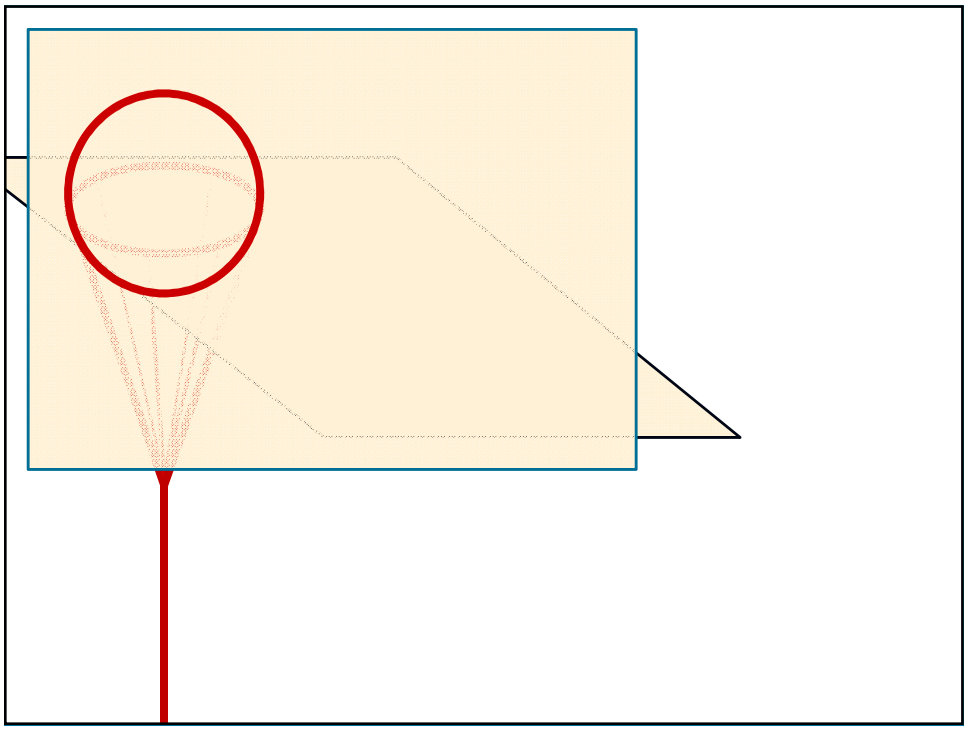


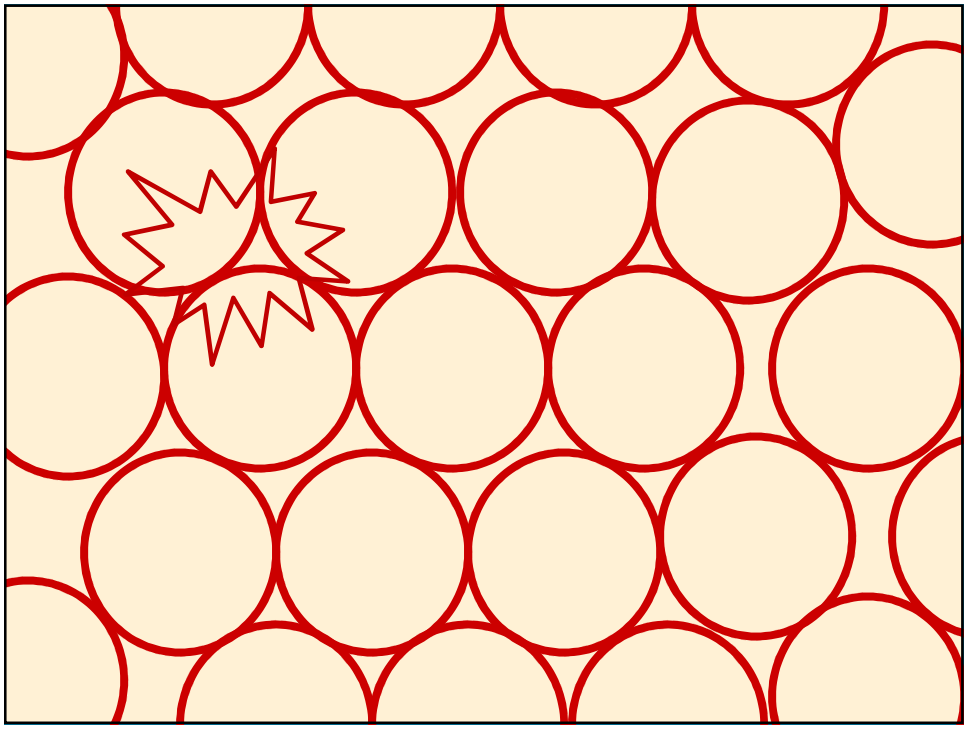


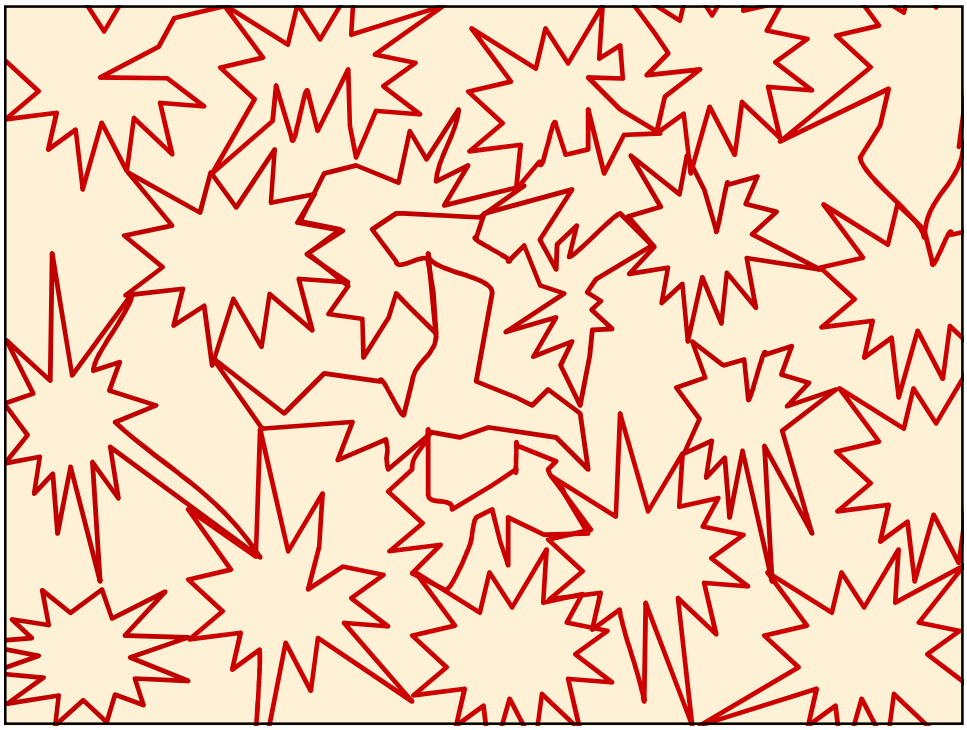
What can morphology tell us about pathophysiology?

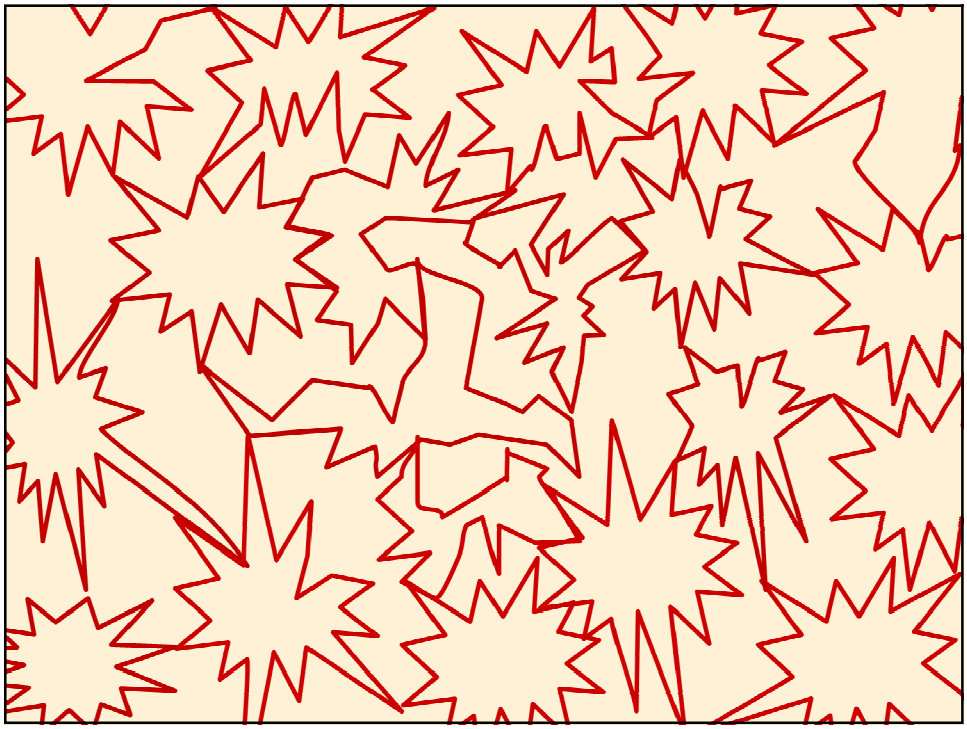


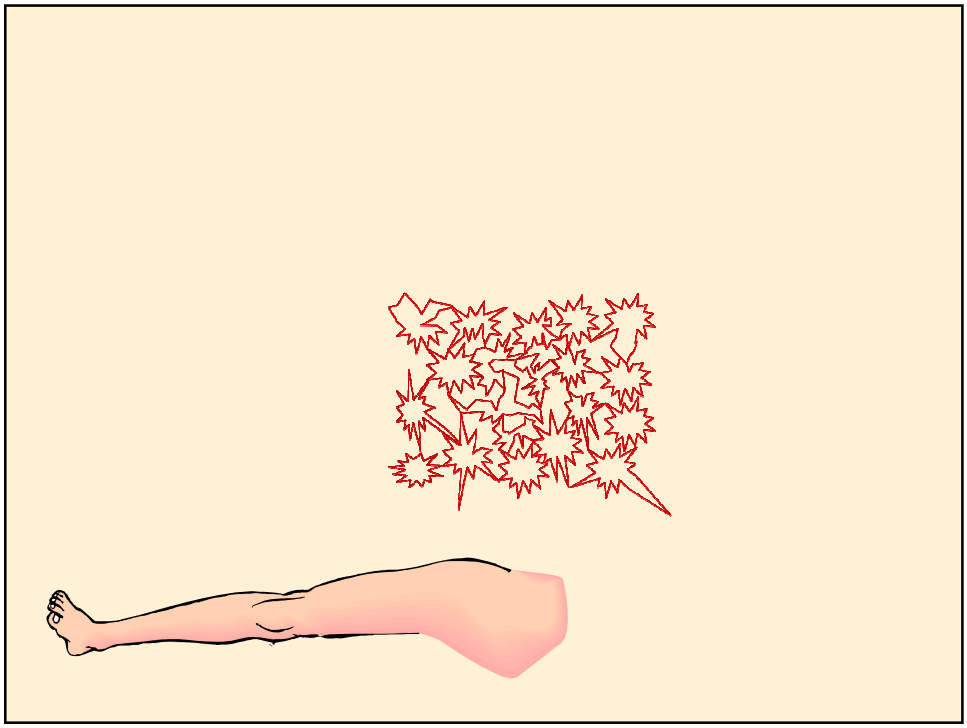

**Dermatology, 2nd Edition. Eds Jean L Bolognia et al. Spain: Mosby Elsevier, 2008**

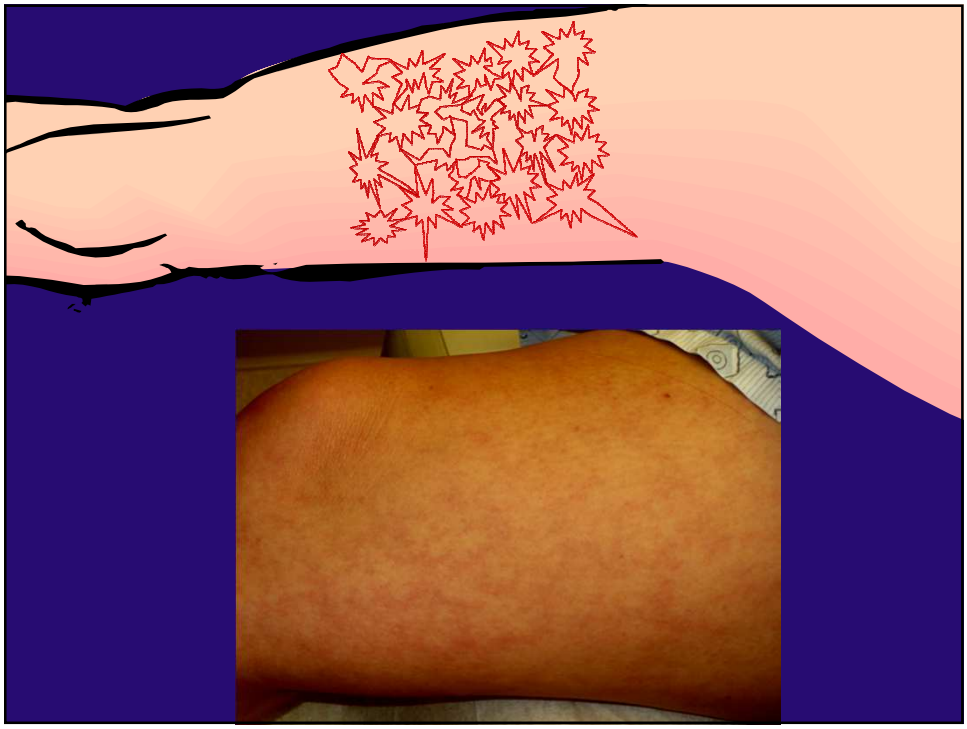










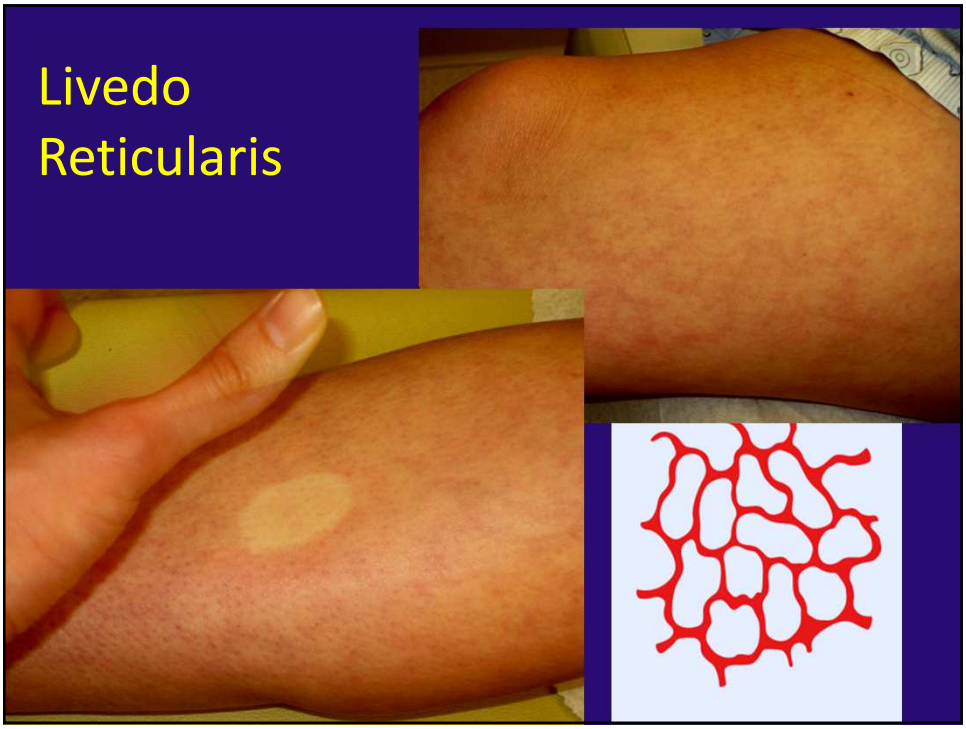


## 2 potential problems with this system

## Problem 1: Livedo Reticularis

- Violaceous erythema
- Outlines 1-3cm stellate patches
- Surface of cones fed by individual perforating arterioles
- From enhanced visibility of zones of venous predominance
  - Increased deoxygenated blood in the venules
  - From engorged veins, constricted arterioles, local hypoxia…

Livedo Reticularis

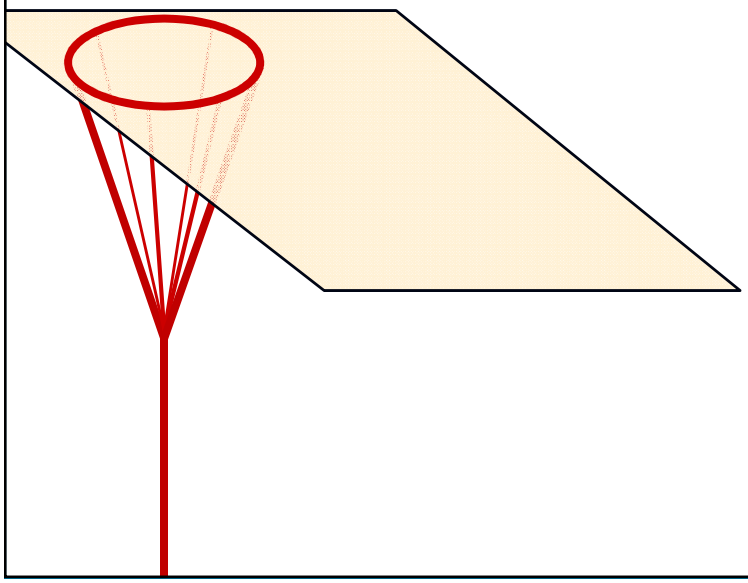


## Problem 2:

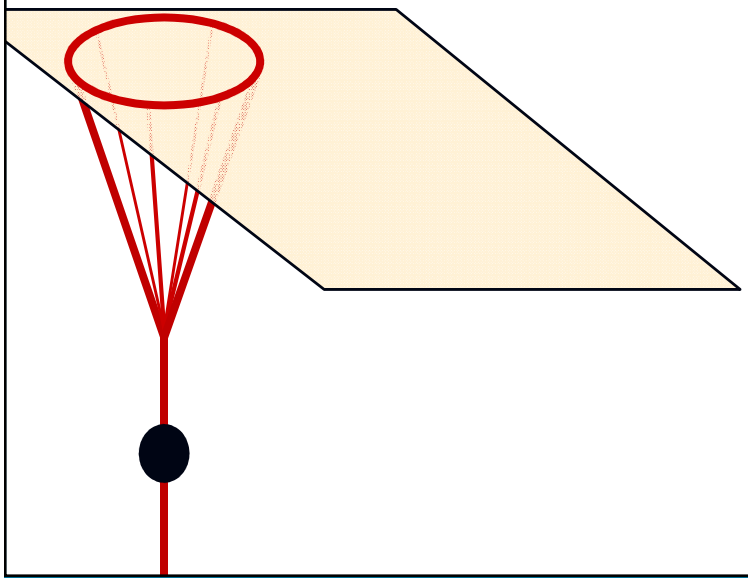
## Retiform Purpura

- Purpura of these same stellate patches/plaques
- From ***occlusion*** of the perforating arterioles.

## Retiform Purpura



## Retiform Purpura



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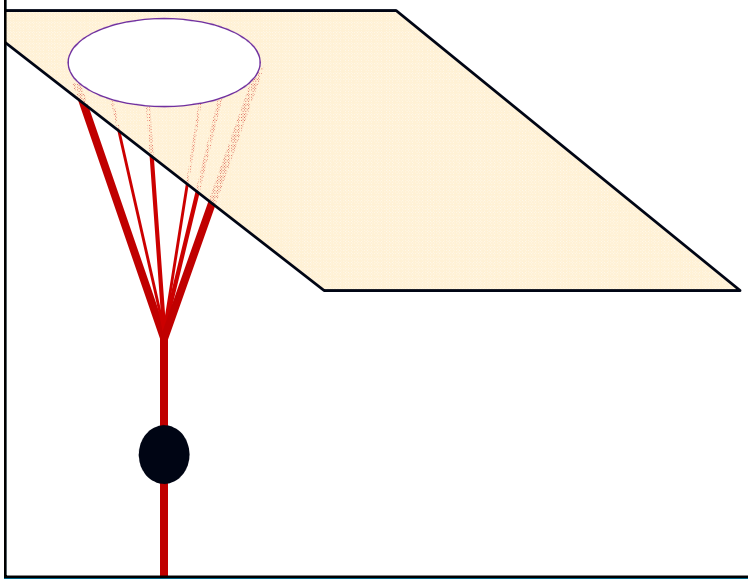

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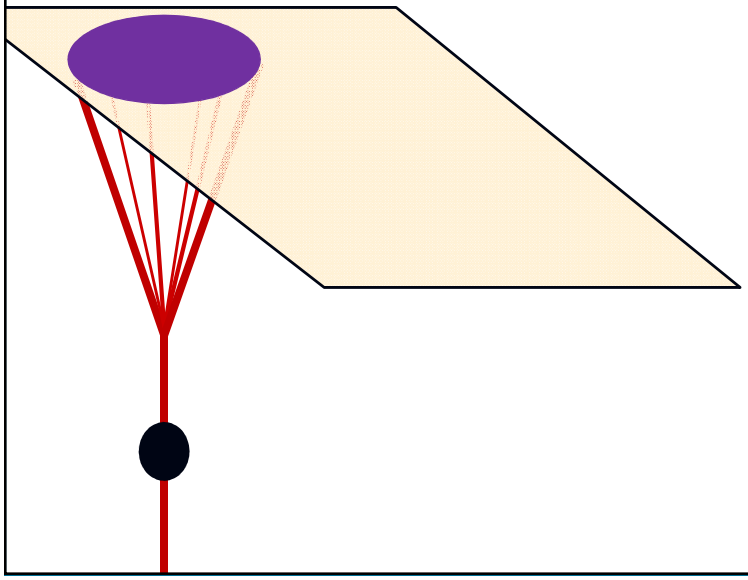

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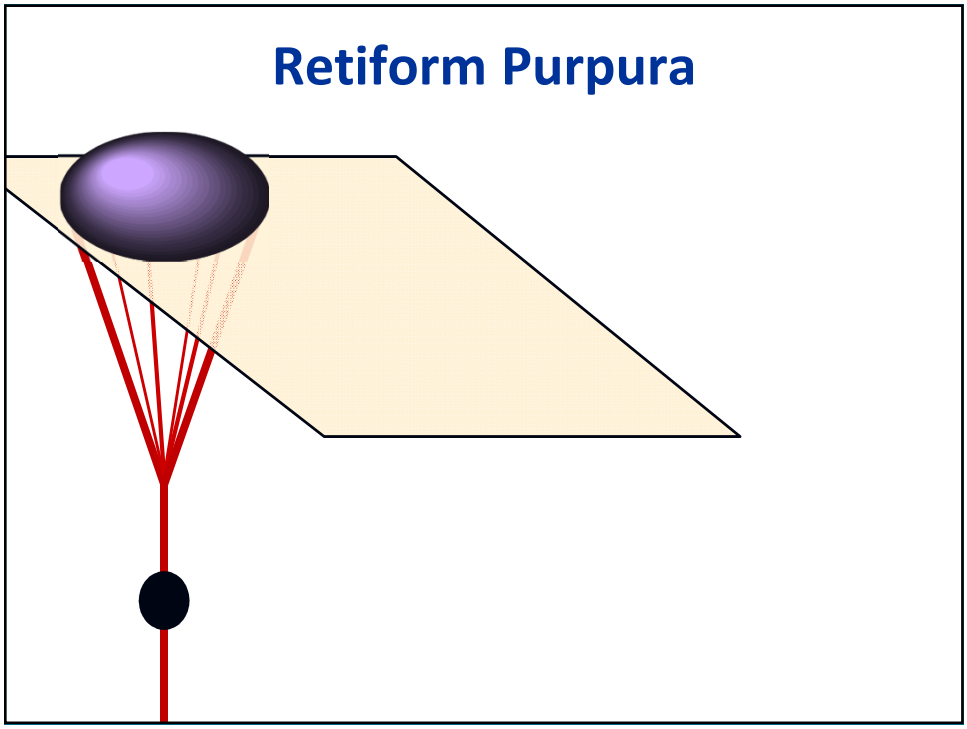

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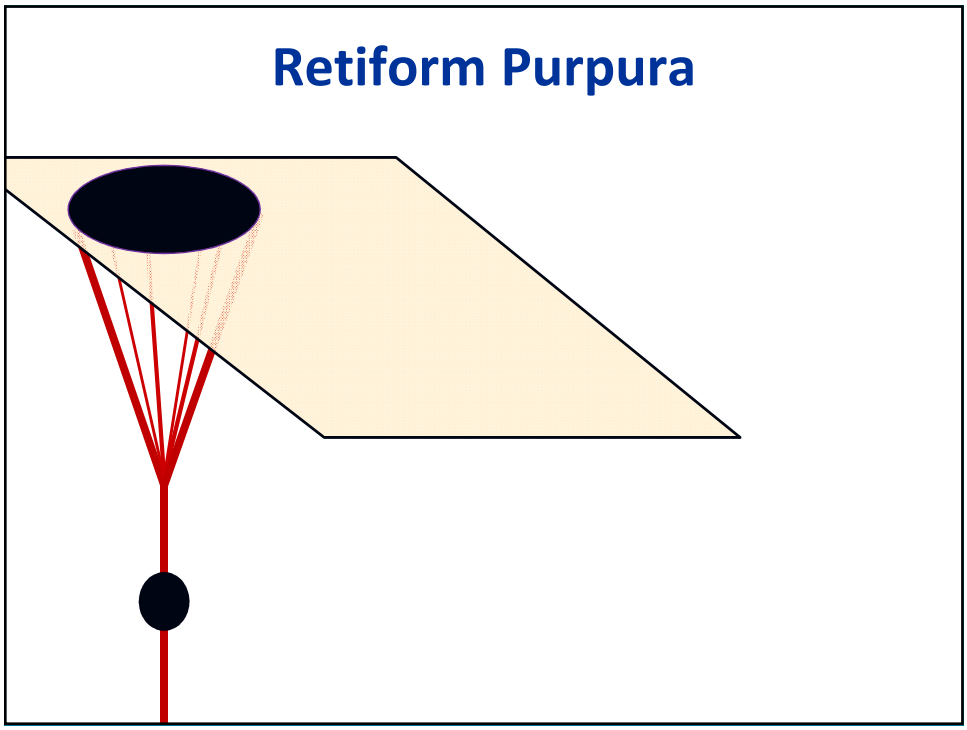
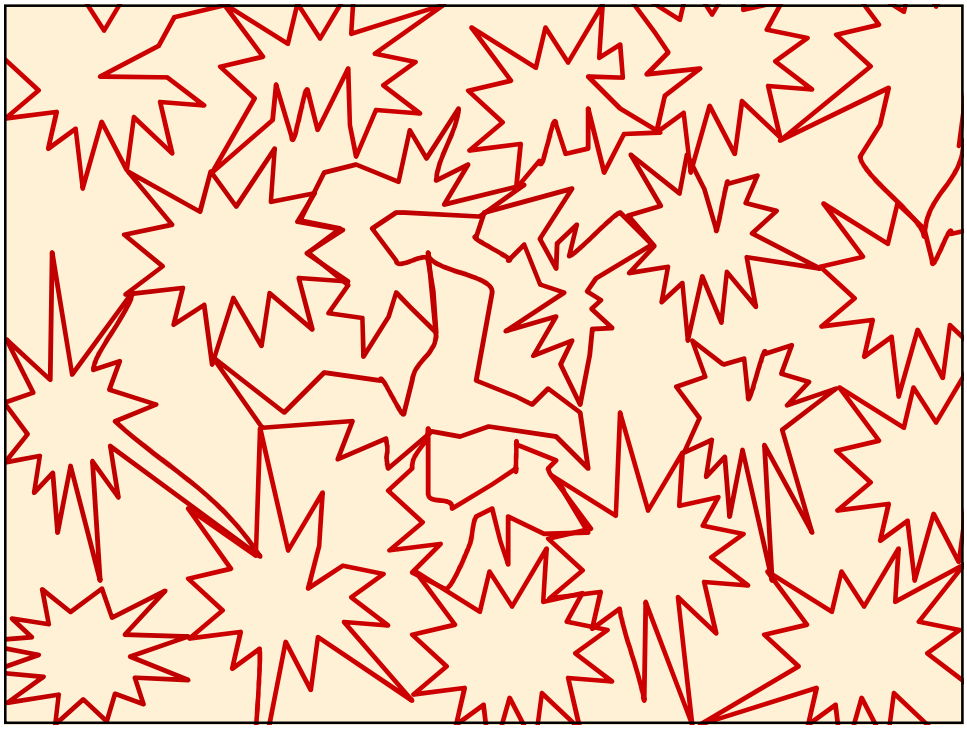
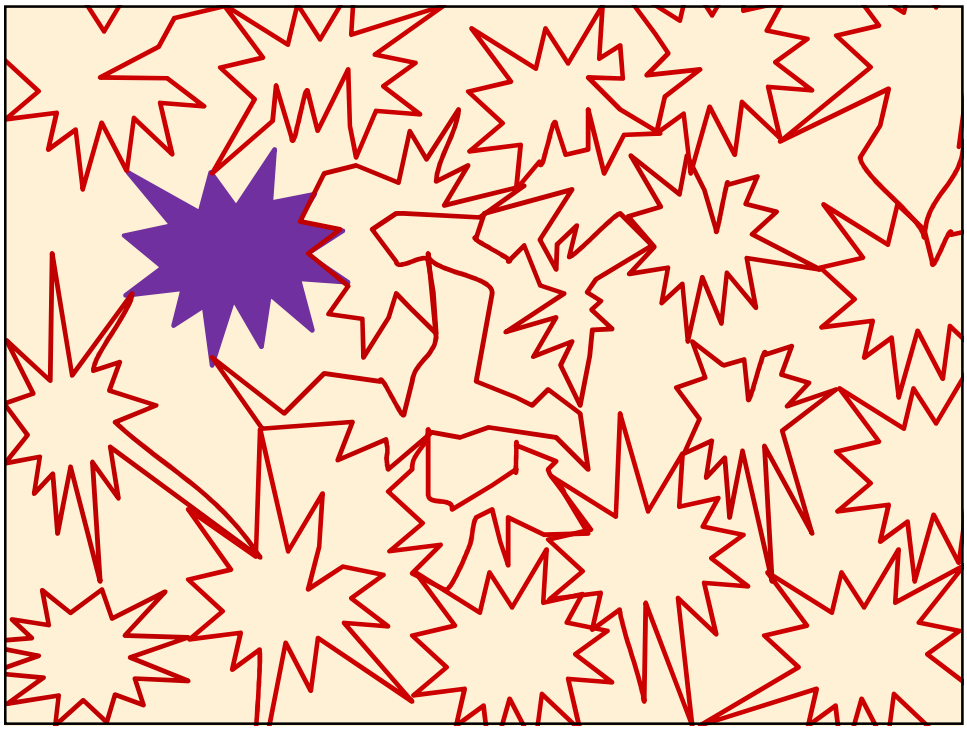
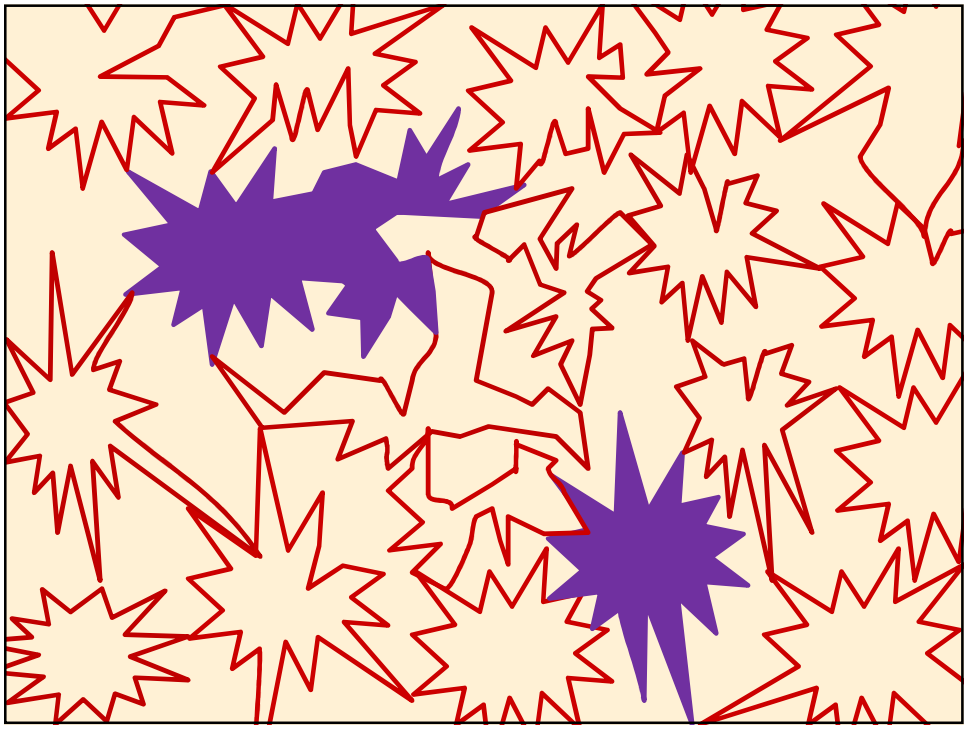
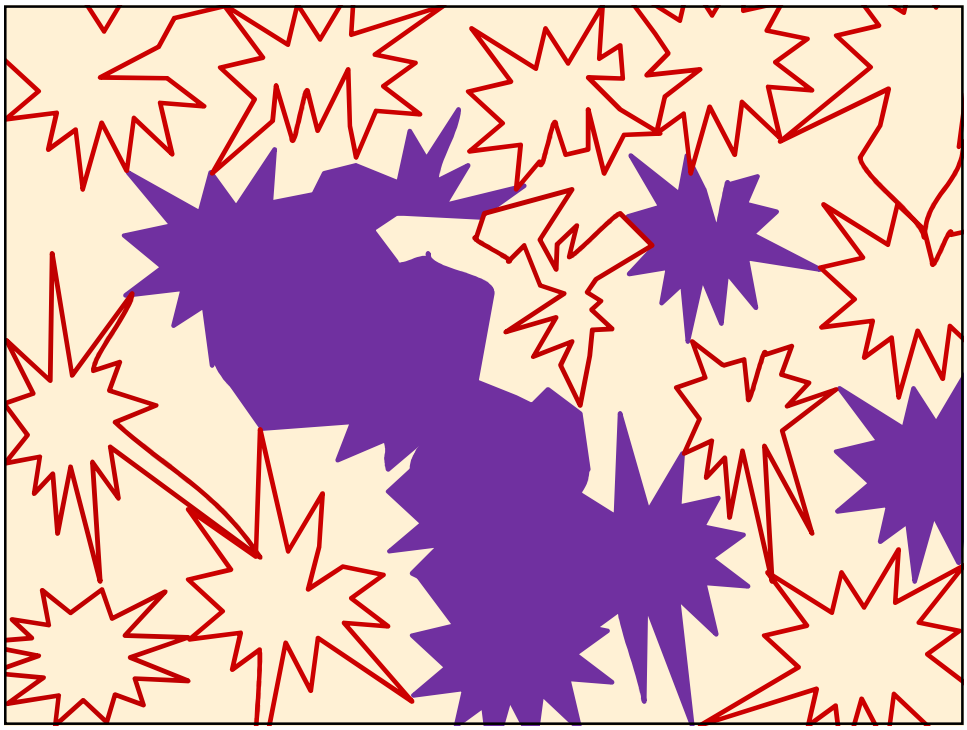




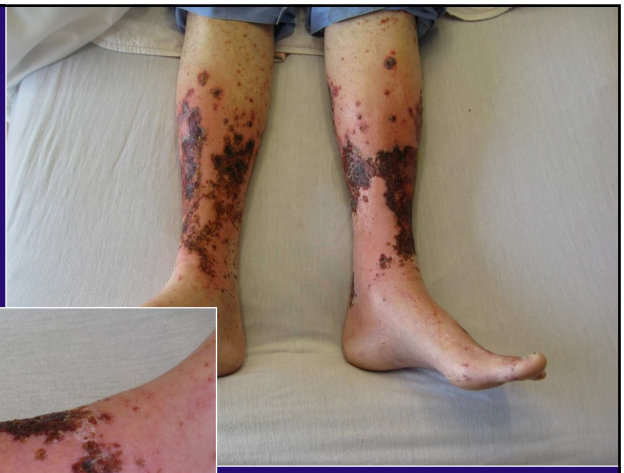


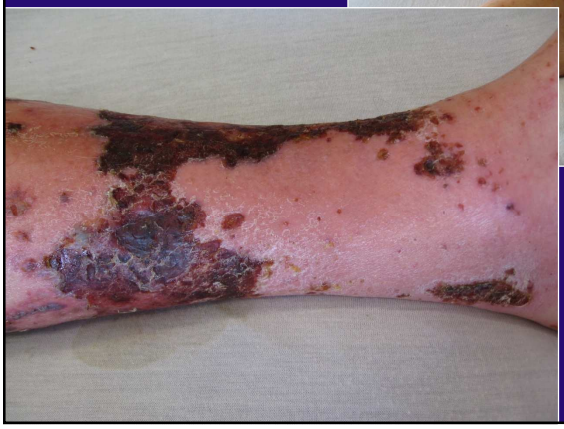


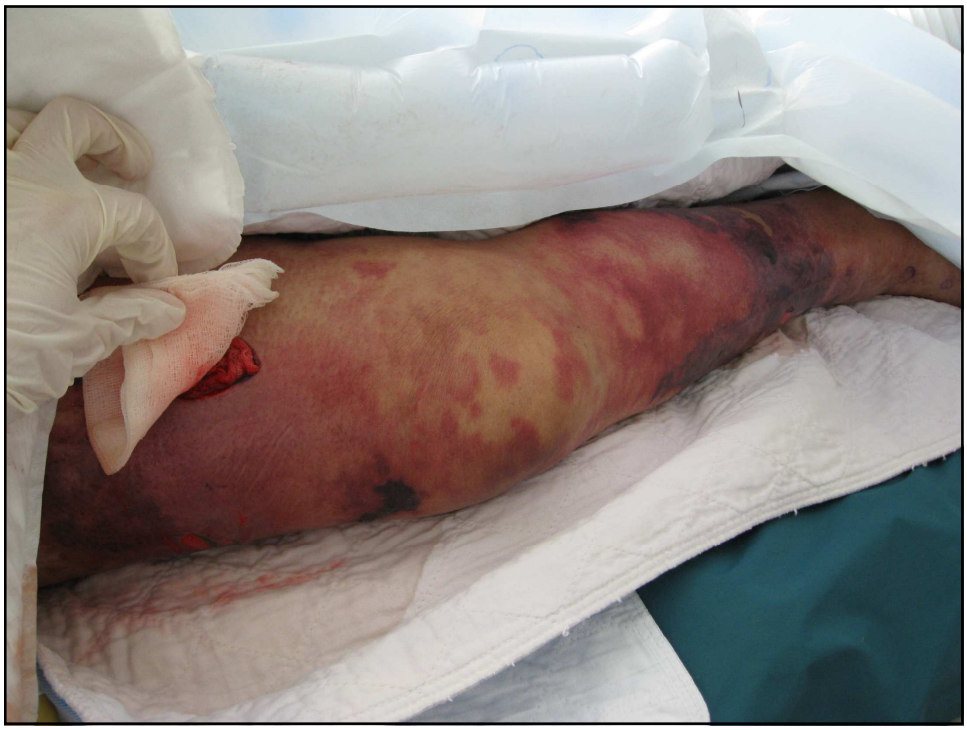


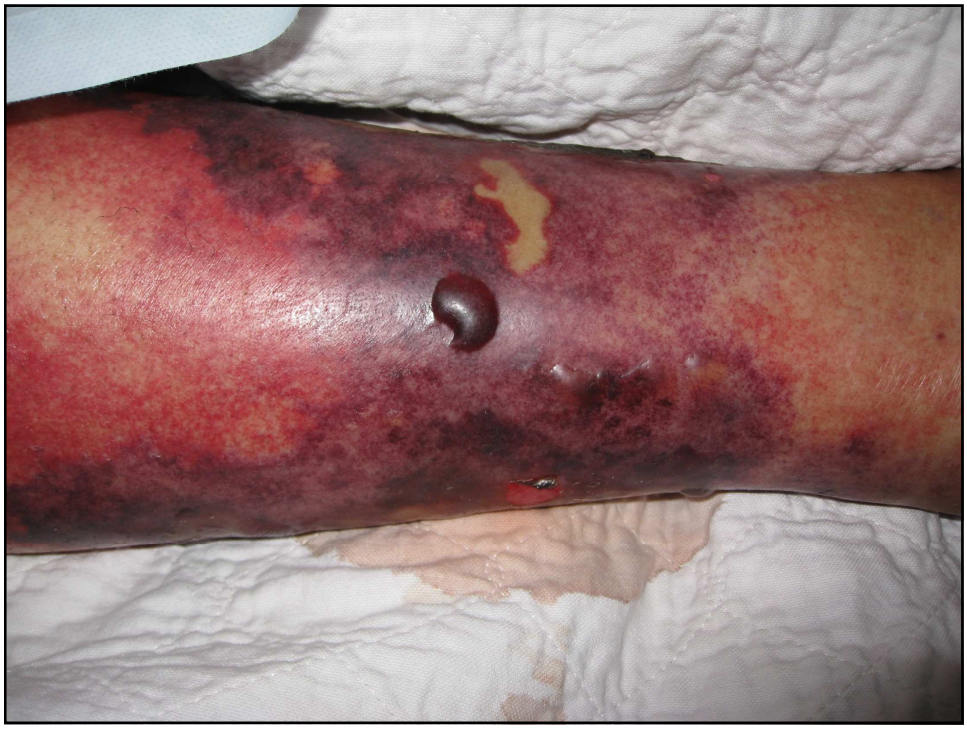
# Retiform Purpura

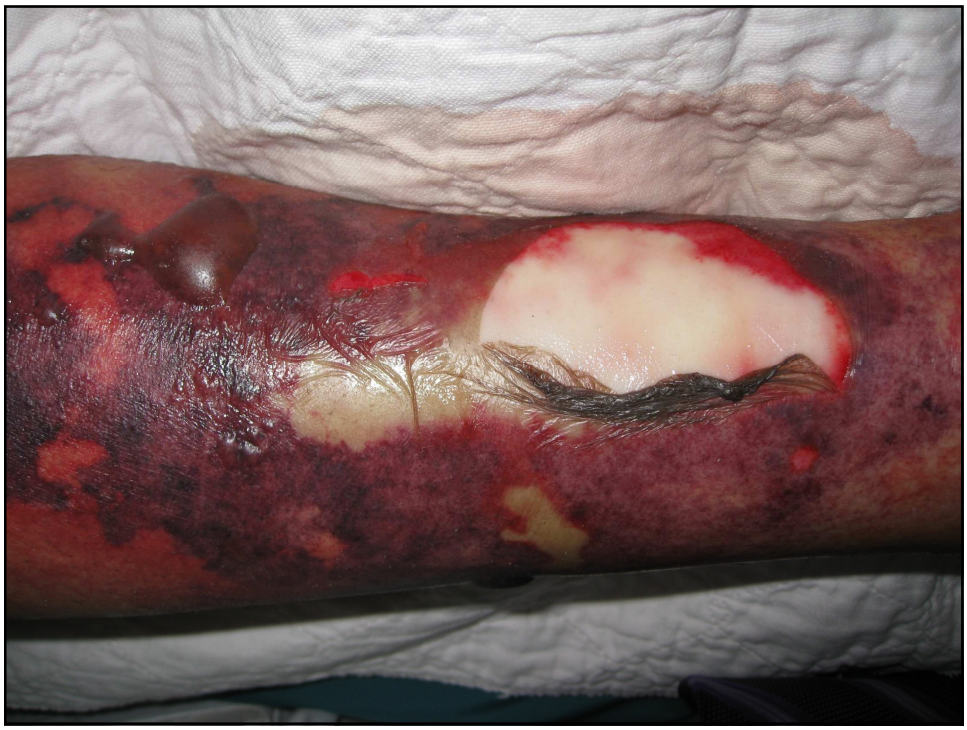
(with necrosis)









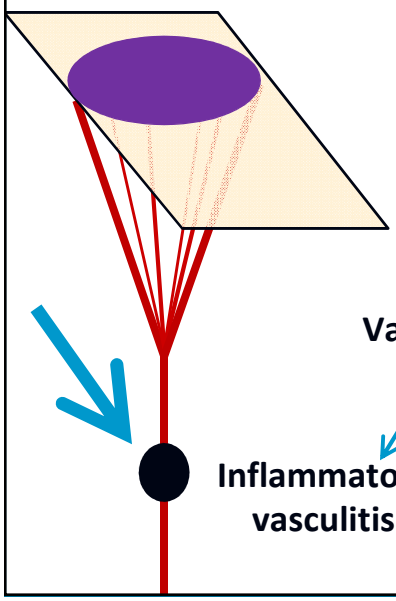


# Case Details

- PMH: Systemic lupus, lupus nephritis
- Meds: Mycophenolate mofetil, prednisone
- ED presentation:
  - Vitals: **T104.6, P140s, SBPs 80s**
  - Unresponsive, rash on right leg
- Labs: BASELINES in parentheses after figures
  - **WBC 1.8** (4-9), **HCT 22.7** (24-37), **Plt 76** (150-350)
  - Na 142, K 4.3, Cl 112, HCO3 20, **BUN 79, Creatinine 2.7** (1.2)

# Retiform Purpura:

## Differential Diagnosis



**Perforating Arteriole Occlusion**

**In-situ Thrombosis**

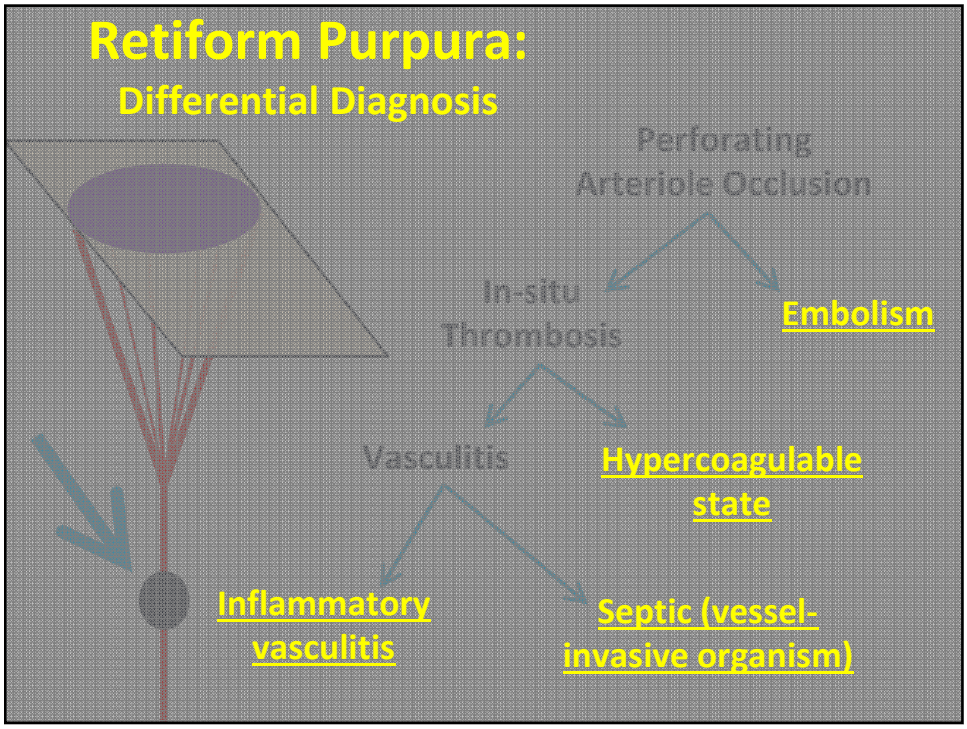
**Embolism**

**Vasculitis**

**Hypercoagulable state**

**Inflammatory vasculitis**

**Septic (vessel-invasive organism)**




## Retiform Purpura: Select Differential Diagnosis

| | |
|---|---|
| **Emboli** | Cholesterol, Fat, Septic, Calciphylaxis, Amyloidosis, Nitrogen, Atrial myxoma, Ventilator Gas, Hyperoxaluria |
| **Hypercoagulable states** | APLAS, Sneddons, Cryos, AT III deficiency, Protein C/S def (especially with meningococcemia or coumadin), DVT, DIC, TTP |
| **Inflammatory Vasculitis** | PAN, Wegeners, Takayasu's, microscopic polyangitis, Rheumatoid vasculitis, livedoid vasculitis |
| **Septic vasculitis** (Angioinvasive pathogens) | Pseudomonas, Serratia, Aeromonas, Klebsiella, Vibrio, Moraxella, Morganella, E.coli, Staph aureus, Candida, Mucor, Aspergillus, Fusarium |

Adapted from:
Gibbs MB, English, JC, Zirwas MJ. Livedo Reticularis: An Update. J Am Acad Dermatol 2005; 52: 1009-19

# Please note:
## (regarding retiform purpura)

- **Nothing on the differential is primary cutaneous**
- **Everything on the differential is bad**

## Retiform Purpura: Select Differential Diagnosis

| | |
|---|---|
| Emboli | Cholesterol, Fat, **Septic**, Calciphylaxis, Amyloidosis, Nitrogen, Atrial myxoma, Ventilator Gas, Hyperoxaluria |
| Hypercoagulable states | **APLAS**, Sneddons, Cryos, AT III deficiency, Protein C/S def (especially with meningococcemia or coumadin), DVT, **DIC, TTP** |
| Inflammatory Vasculitis | PAN, Wegeners, Takayasu's, microscopic polyangitis, Rheumatoid vasculitis, livedoid vasculitis |
| Septic vasculitis (Angioinvasive pathogens) | **Pseudomonas, Serratia, Aeromonas, Klebsiella, Vibrio, Moraxella, Morganella, E.coli, Staph aureus, Candida, Mucor, Aspergillus, Fusarium** |

**Differential:**
**Catastrophic APLAS ("thrombotic storm")**
**Thrombotic thrombocytopenic purpura**
**Systemic infection (Sepsis/DIC, emboli, vascular invasion)**

## Dermatologic Workup and Results

- Day 0:
  - Biopsies by derm and surgery
  - Later that night: Blood cultures stain for **GNR in 4/4 bottles**
- Day 1 post admission: Pathology preliminary results—
  - Neutrophilic inflammation in dermis and adipose with hemorrhage.
  - Deep biopsy has sparse GNR on Gram stain
- Day 2: blood and deep biopsy tissue—
  - ***Serratia marcescens***
- Day 3: Abd CT with contrast shows pan-enterocolitis

# Diagnosis

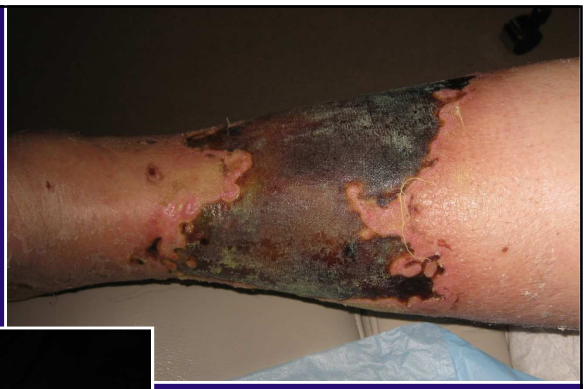
*Serratia marcescens* sepsis with necrotic retiform purpura of a seeded limb

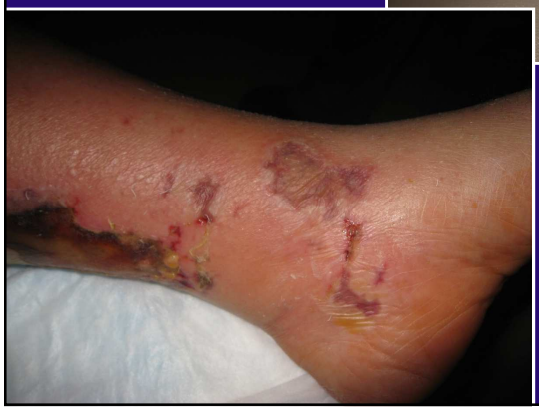
## Retiform Purpura: Select Differential Diagnosis

| | |
|---|---|
| **Emboli** | Cholesterol, Fat, Septic, Calciphylaxis, Amyloidosis, Nitrogen, Atrial myxoma, Ventilator Gas, Hyperoxaluria |
| **Hypercoagulable states** | APLAS, Sneddons, Cryos, AT III deficiency, Protein C/S def (especially with meningococcemia or coumadin), DVT, DIC, TTP, **COVID-19** |
| **Inflammatory Vasculitis** | PAN, Wegeners, Takayasu's, microscopic polyangitis, Rheumatoid vasculitis, livedoid vasculitis |
| **Septic vasculitis** (Angioinvasive pathogens) | Pseudomonas, Serratia, Aeromonas, Klebsiella, Vibrio, Moraxella, Morganella, E.coli, Staph aureus, Candida, Mucor, Aspergillus, Fusarium |

Adapted from:
Gibbs MB, English, JC, Zirwas MJ. Livedo Reticularis: An Update. J Am Acad Dermatol 2005; 52: 1009-19

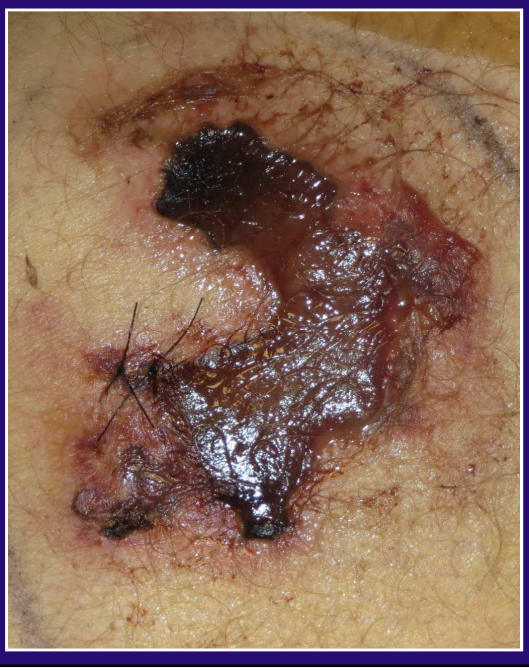
## More faces of Retiform Purpura

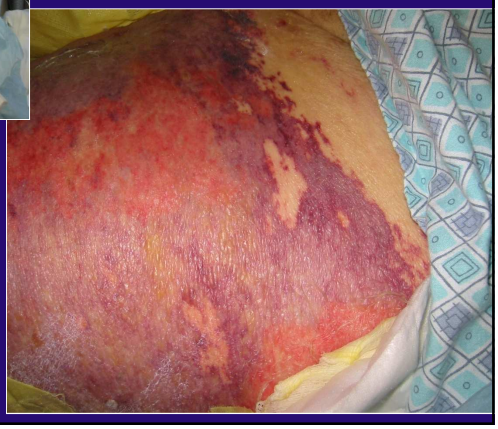




**Cholesterol Emboli**

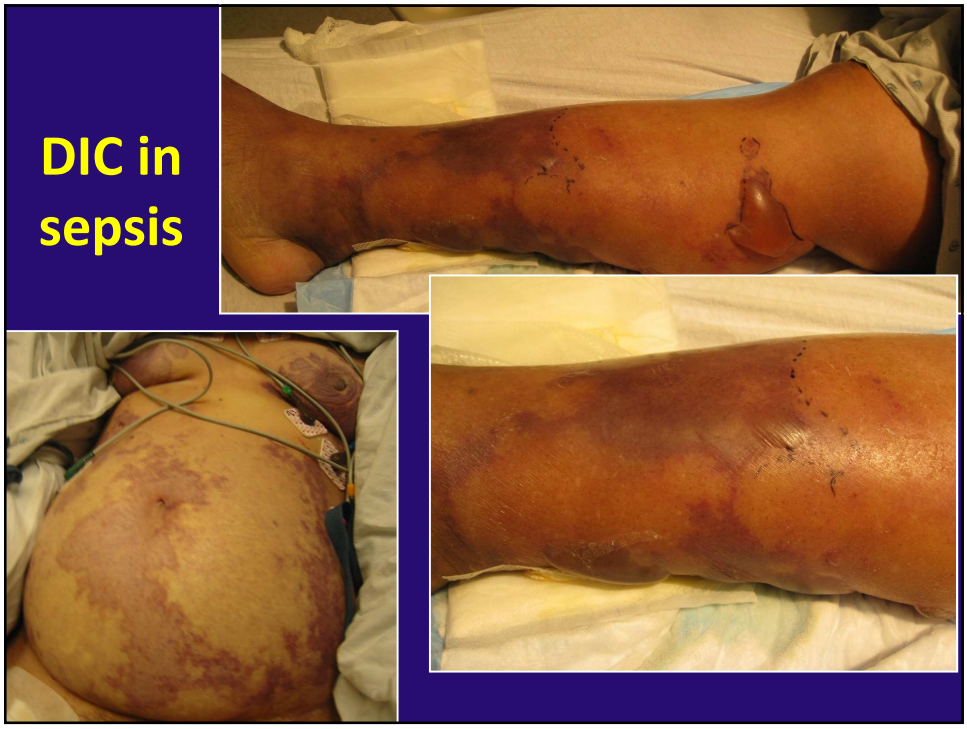
## Ecthyma Gangrenosum

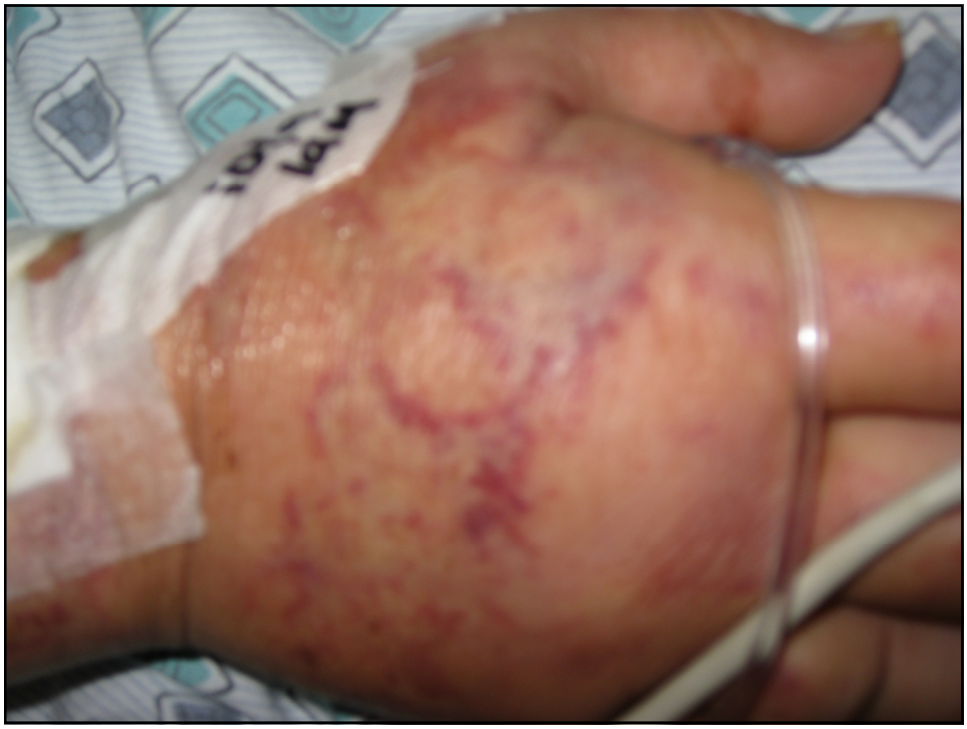




## DIC in sepsis

# DIC in sepsis



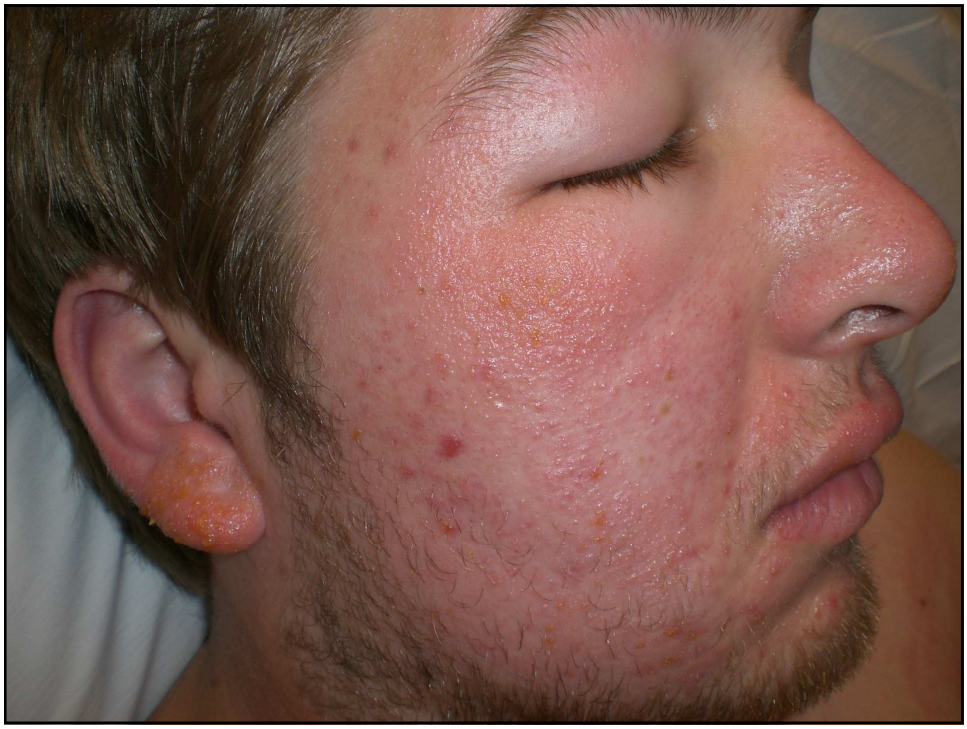


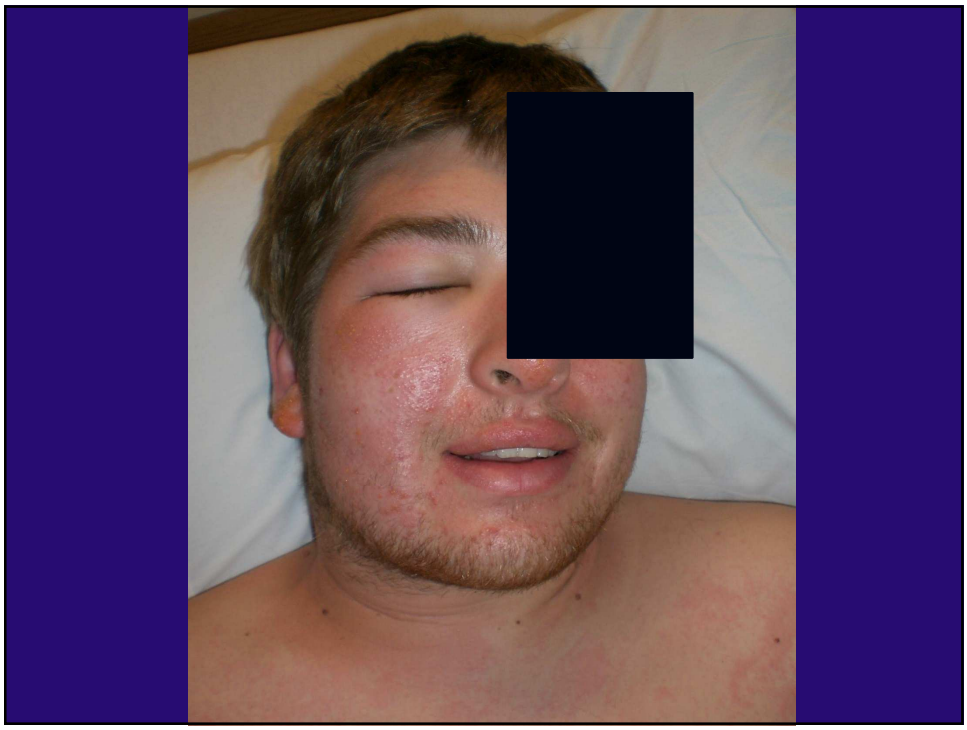
## CASE KEY POINTS

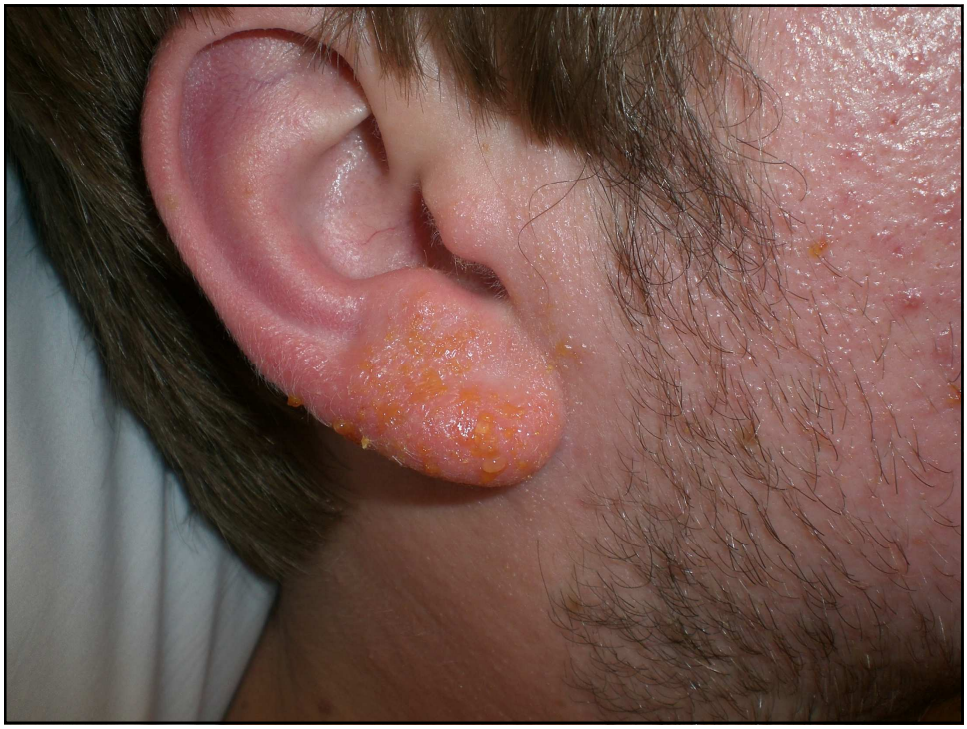
- **Recognize Retiform Purpura:**
  - **Well demarcated purpuric patches with jagged edges**
  - **Violaceous, dusky, white, black**
  - **Evidence of necrosis (bullae, ulcers, eschars)**
- **Early indicator of a systemic, generally malignant process**

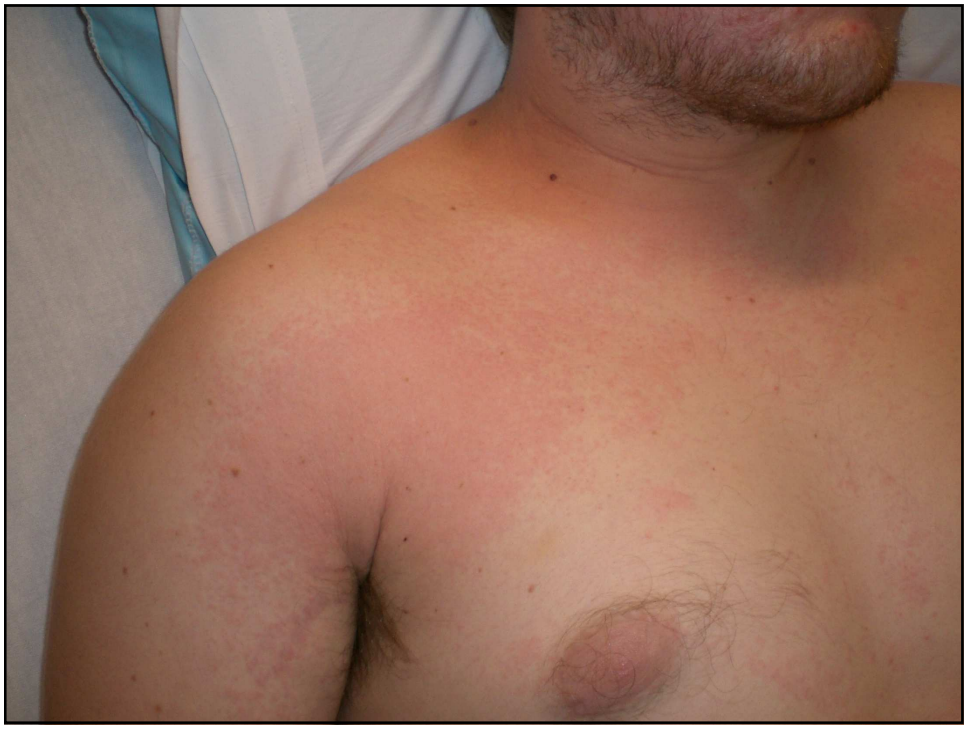
## Case

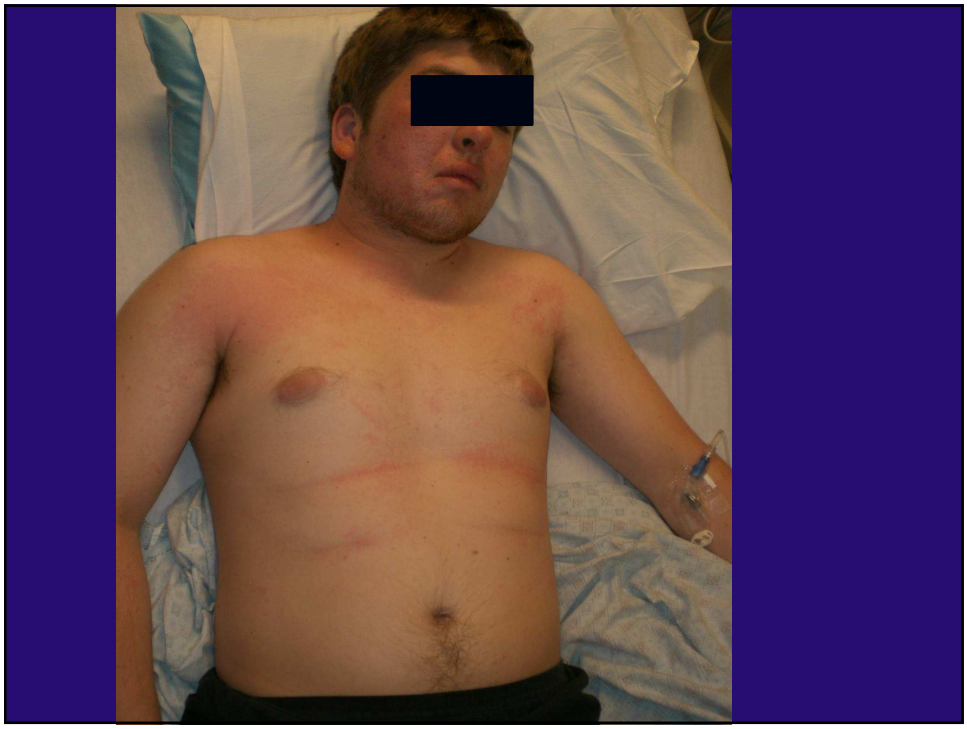
- Healthy 18 year-old male
- 1 day of worsening pruritic rash on face
- ED Diagnosis: impetigo
- Admitted to ED-Observation IV antibiotics
- Next AM: rash extended toward lip and eye
- Derm Consulted

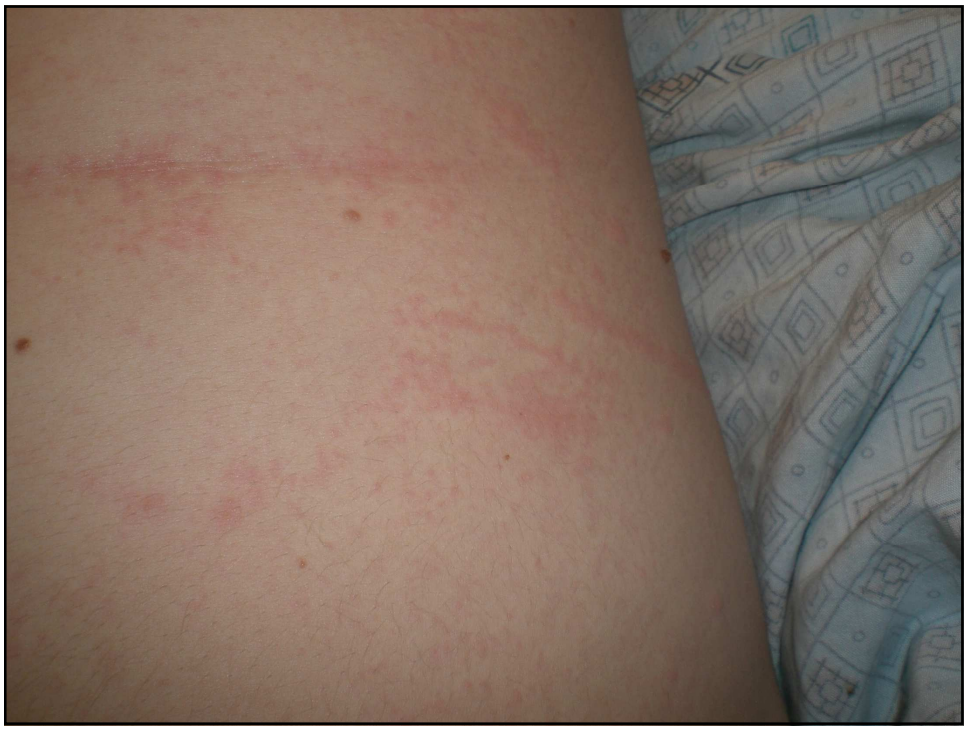


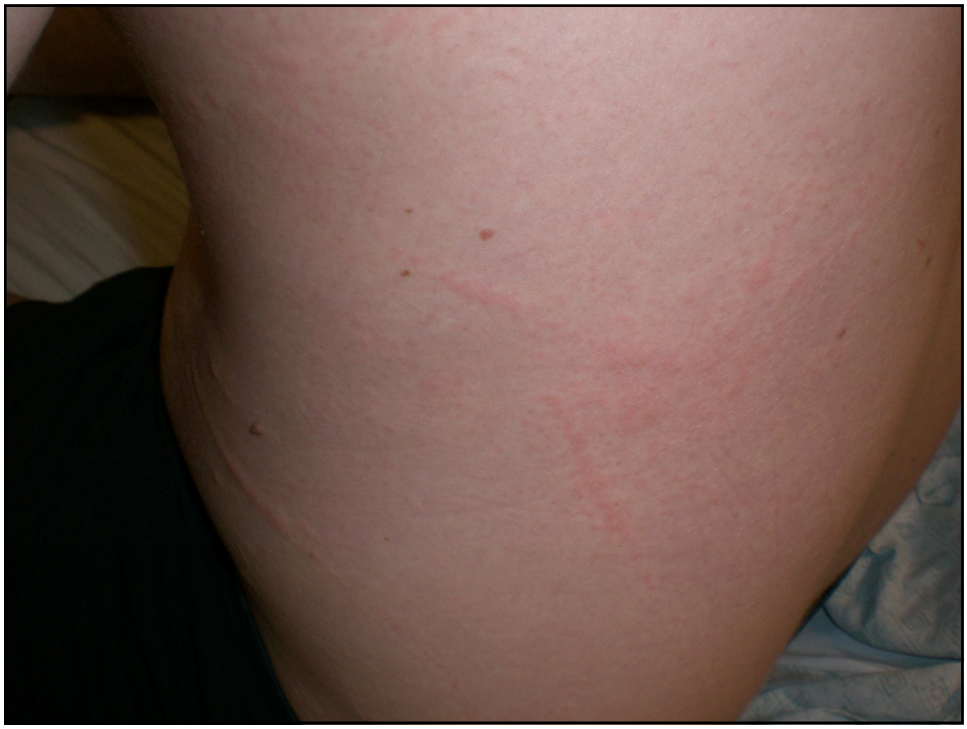




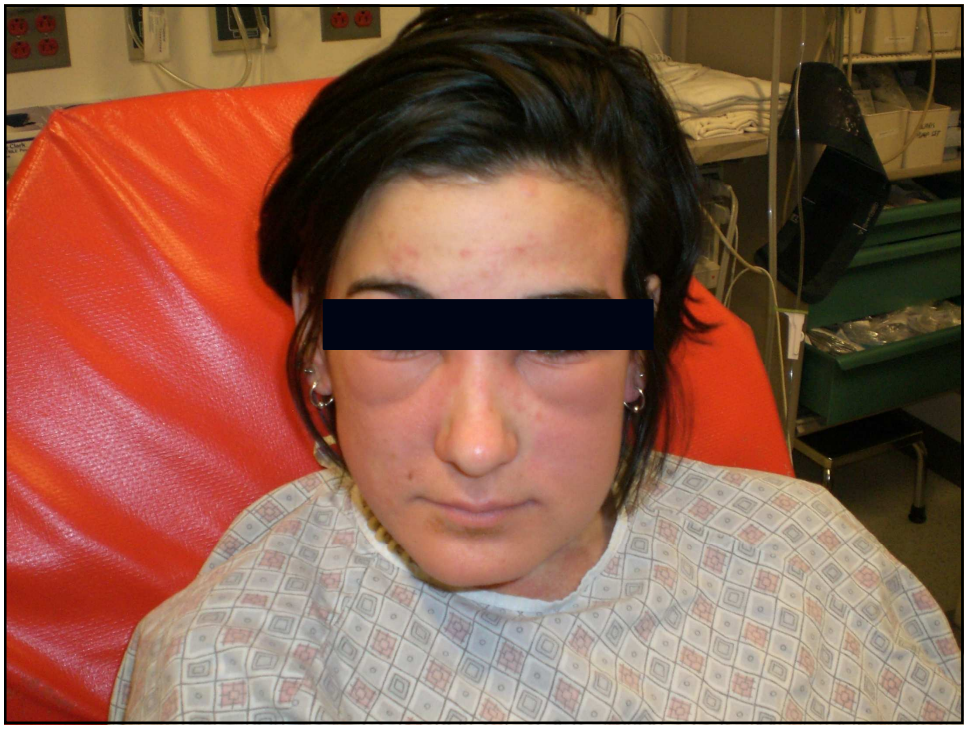


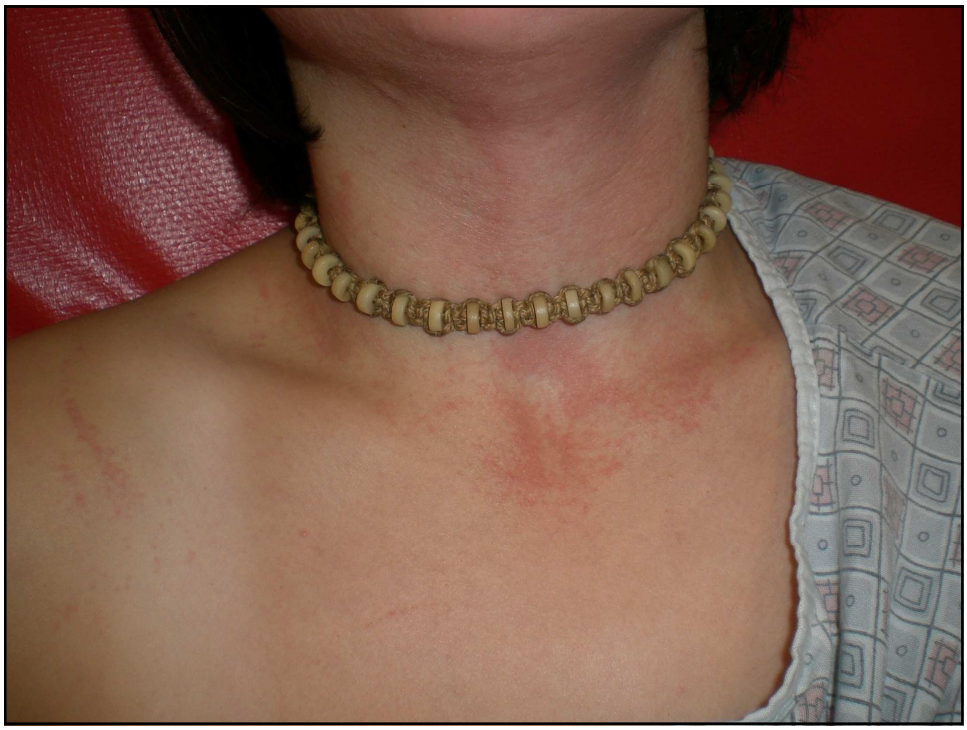






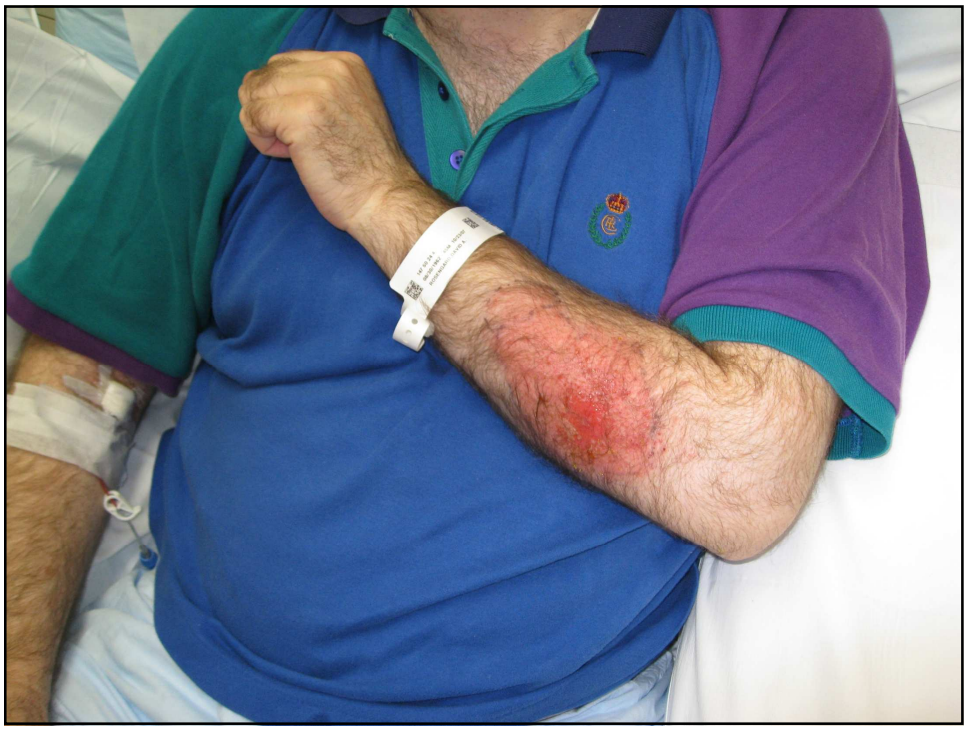
**Meanwhile, 40 feet away…**

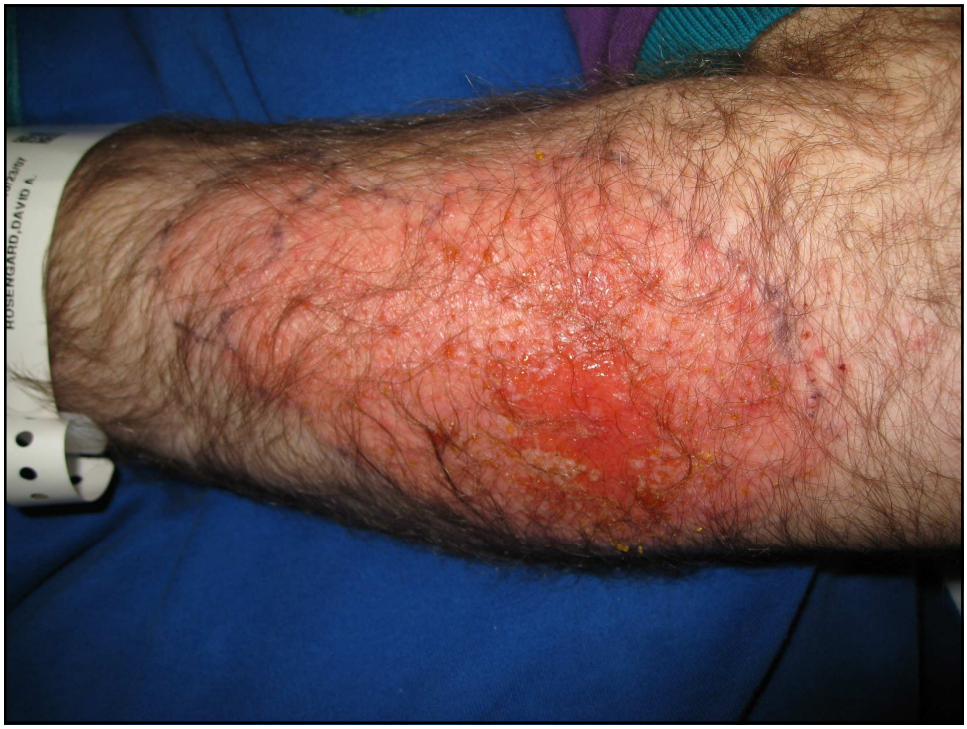


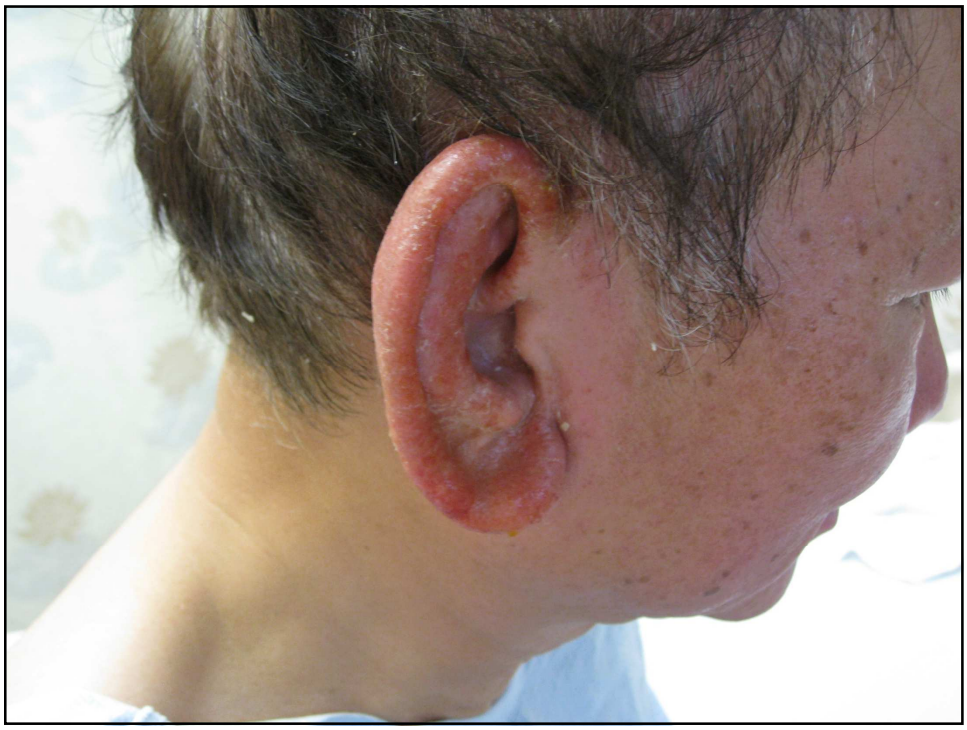


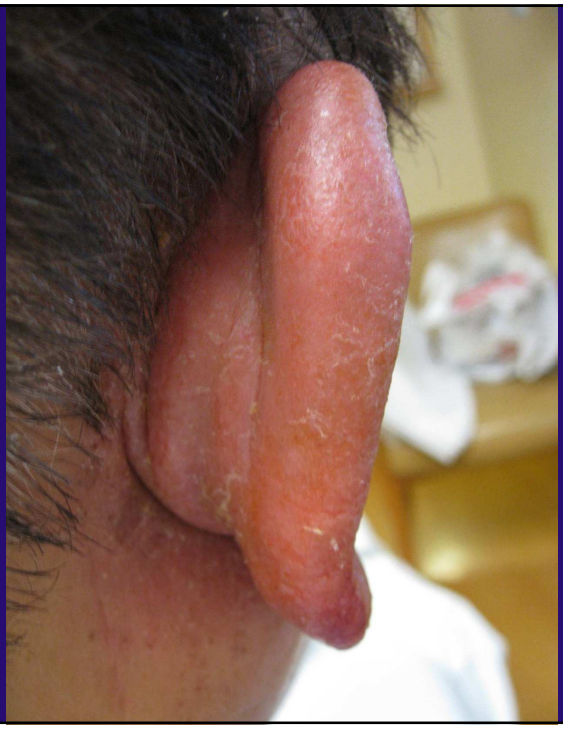
# Allergic Contact Dermatitis (to poison ivy: toxin = urushiol)

- Type IV, T-cell mediated hypersensitivity
- Eczematous reaction pattern
  - Acute: vesicles, erythema, serous fluid
  - Subacute: erosions, erythema, serous fluid
  - Chronic: scaling, lichenification, dyspigmentation, prurigo nodules
- Other important physical exam features
  - Symptoms: Pruritic, non-tender
  - Lines/ geometric shapes









## Take-Home Points

- Cellulitis is tender
- Recognize retiform purpura
- Triple antibiotic oint causes contact dermatitis

# Thank you

- Richard Johnson
- Arturo Saavedra
- Anisa Mosam
- Ncoza Dlova
- My patients who allowed me to photograph them to benefit others

# Key References


- Daum RS et al, A Placebo-Controlled Trial of Antibiotics for Smaller Skin Abscesses. N Engl J Med 2017; 376: 2545-2555
- Moran GJ, Krishnadasan A, Mower WR, Abrahamian FM, LoVecchio F, Steele MT, Rothman RE, Karras DJ, Hoagland R, Pettibone S, Talan DA. Effect of Cephalexin Plus Trimethoprim-Sulfamethoxazole vs Cephalexin Alone on Clinical Cure of Uncomplicated CellulitisA Randomized Clinical Trial. *JAMA*. 2017;317(20):2088–2096.
- Pallin DJ, et al. "Clinical Trial: Comparative Effectiveness of Cephalexin Plus Trimethoprim-Sulfamethoxazole Versus Cephalexin Alone for Treatment of Uncomplicated Cellulitis: A Randomized Controlled Trial." Clin Infect Dis, 56: 2013 1754-62
- Stevens DL, et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America. Clinical Infectious Diseases
- The spectrum of COVID-19–associated dermatologic manifestations: An international registry of 716 patients from 31 countries. Esther E. Freeman, MD, PhD, Devon E. McMahon, BA, Jules B. Lipoff, MD, Misha Rosenbach, MD, Carrie Kovarik, MD, Seemal R. Desai, MD, Joanna Harp, MD, Junko Takeshita, MD, PhD, MSCE, Lars E. French, MD, Henry W. Lim, MD, Bruce H. Thiers, MD, George J. Hruza, MD, MBA, Lindy P. Fox, MD. Journal of the American Academy of Dermatology. Volume 83 Issue 4 Pages 1118-1129 (October 2020)