HMS Update in Hospital Medicine Course

Common Consult Questions for Skin and Soft Tissue Infections

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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

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

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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

- 58 yo M
- CHF, Diabetes, CAD, morbid obesity
- 3 days worsening leg swelling, redness, warmth, pain
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- Chronic edema for years
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- + 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?**

A. Local warmth
B. Local tenderness
C. Leukocytosis
D. Fever
E. Positive surface culture

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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?

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D. PO Linezolid
E. **No antibiotics**

Management of Cellulitis

To cover MRSA or NOT to cover MRSA?

Management of Cellulitis

STEP 1: Cellulitis or NOT Cellulitis?

JAMA Dermatology | Original Investigation

Costs and Consequences Associated With Misdiagnosed Lower Extremity Cellulitis

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

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

Cellulitis misdiagnosis→

- 259 pts admitted from ED with cellulitis
  - 30% did not have cellulitis. 17% did not require admission
- Extrapolation to U.S.: 50,000-130,000 unnecessary admissions
- $195 million- $515 million avoidable healthcare $$s

Step 1: Cellulitis or NOT Cellulitis?

Tender? If not, consider alternative

If tender, then:

- Bilateral? Consider alternative
- Pruritic? Consider alternative
- Geometric? Consider alternative

Step 2: consider SEVERITY

- Assessment of severity
  - Ill-appearing patient
  - Severe co-morbidities
  - Evidence of deep infection
- Management of SEVERE cellulitis:
  - Admission/Observation, Debride if needed
  - Broad spectrum IV antibiotics: Cover GAS, MRSA, MSSA, et al.

Management of NON-SEVERE Cellulitis

- Supportive care: elevation, immobilization, wound care
- Antibiotics

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

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*
- Cultures are generally low yield

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

Data: Simple Cellulitis
Empiric Antibiotic Choice

Caution:
The data is messy and incomplete

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** → 83.5% clinical cure

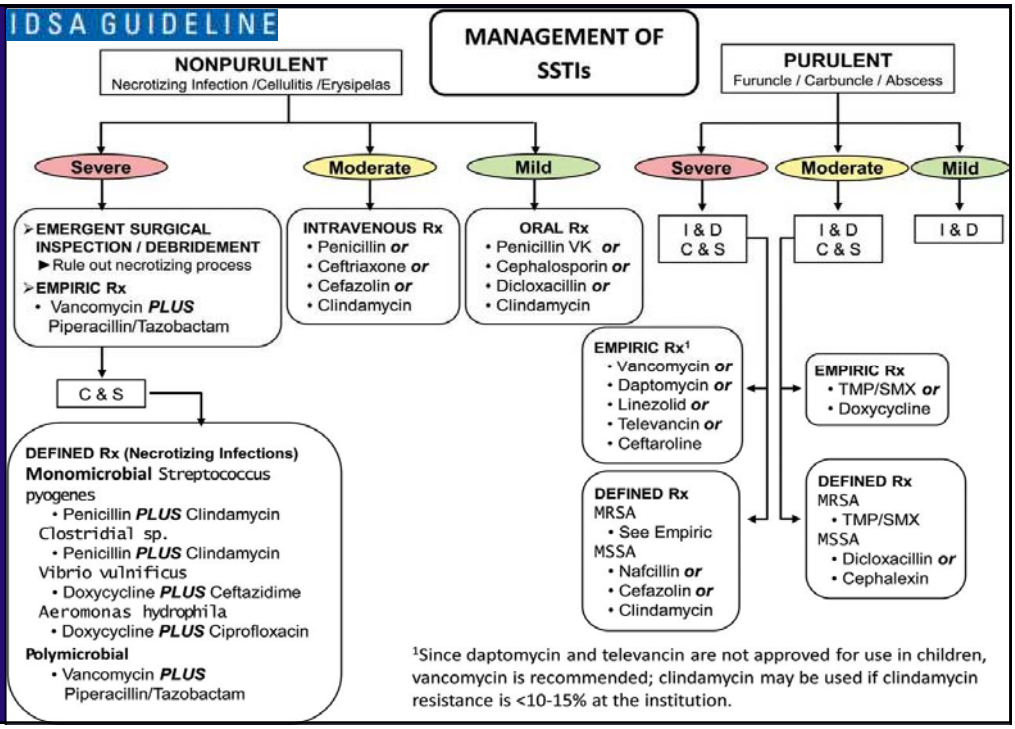
Cephalexin + **Placebo** → 85.5% clinical cure

- 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 Cellulitis: A Randomized Clinical Trial. *JAMA.* 2017;317(20):2088–2096.

June 2014

Clin Infect Dis, Volume 59, Issue 2
15 July 2014, Pages e10–e52



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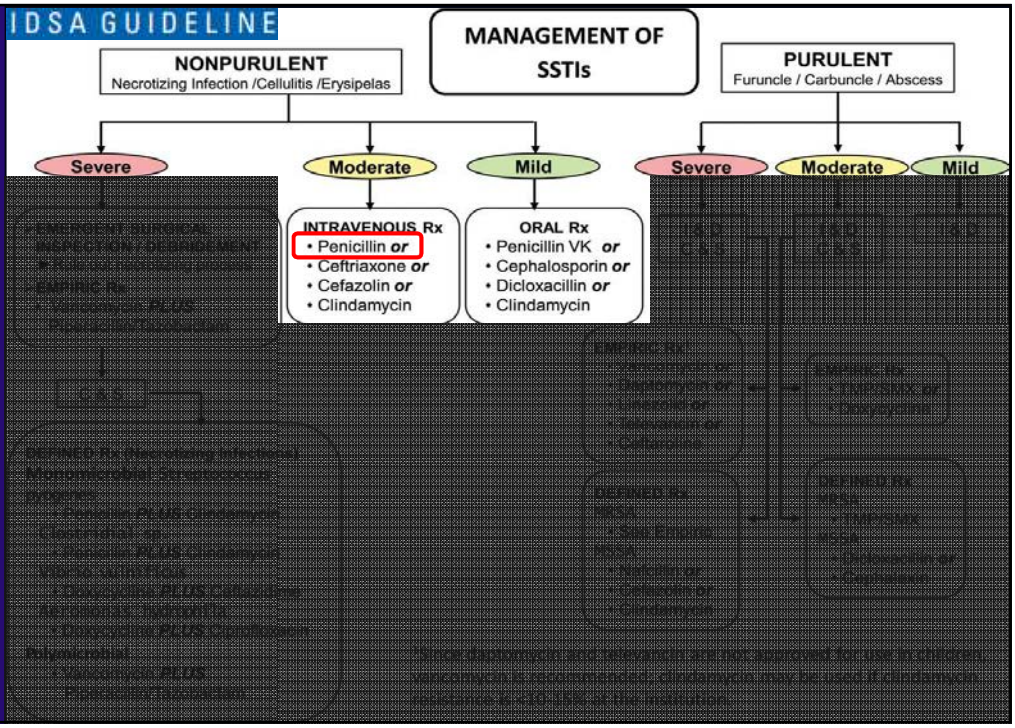


2014 Updated IDSA Guidelines
Caution Regarding Penicillin for Cellulitis

- Assumes Strep is dominant, minimal MSSA/MRSA
- 5 pre-1996 studies of *culture* data
- One 2010 study using **serologies** & **β-lactam response** (Jeng et al)
  - Study Conclusions: 1. Serologies: "73% of non-culturable cellulitis caused by **βHS**"
    2. β-lactam response rate: 95.6%
  - **BUT!**
    - **31% lost without serologies. Intention-to-test analysis → ~51% βHS+**
    - **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. ClinInfectious Diseases (Advanced Access June 18, 2014)

Cellulitis Empiric Therapy: Conclusions/Recommendations

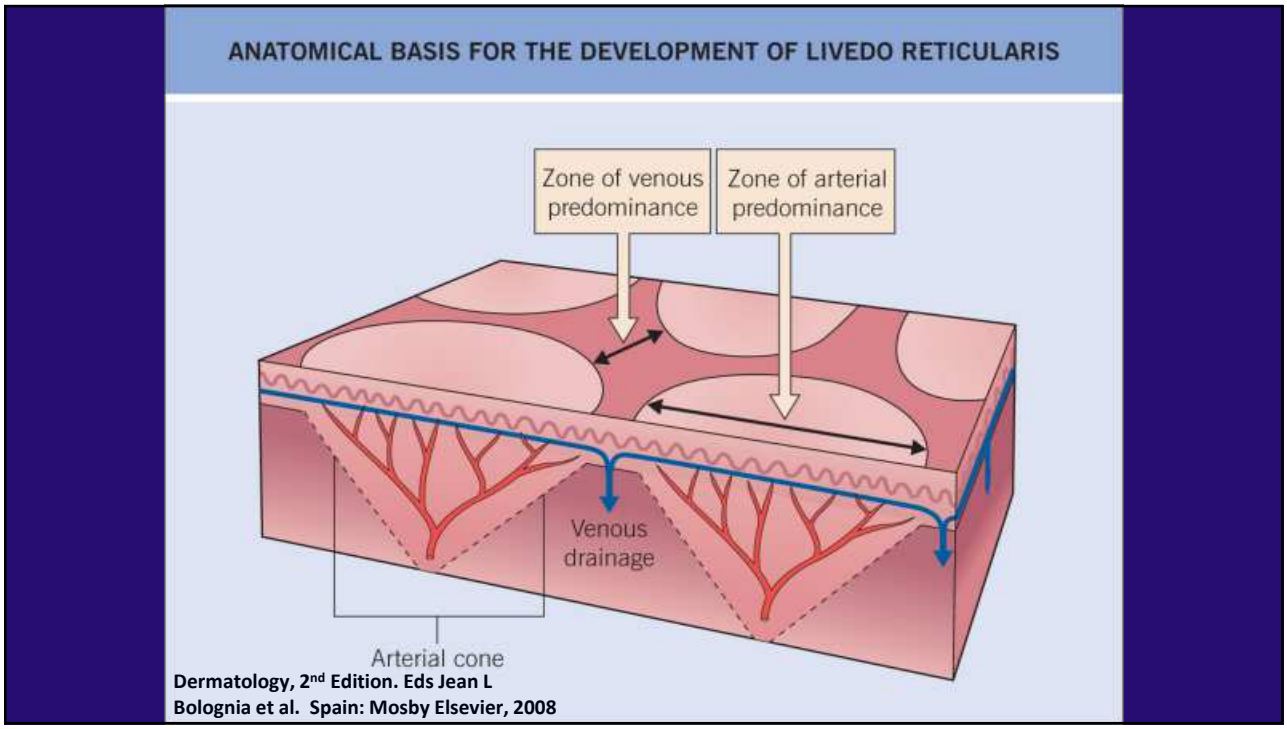
- Still a moving target, but data is improving
- Anything **severe**: Admit, monitor, broad IV abx, surgery
- Beta-lactam likely best for most simple, outpatient cases
  - Strongly consider a **β-lactamase resistant agent**

Case

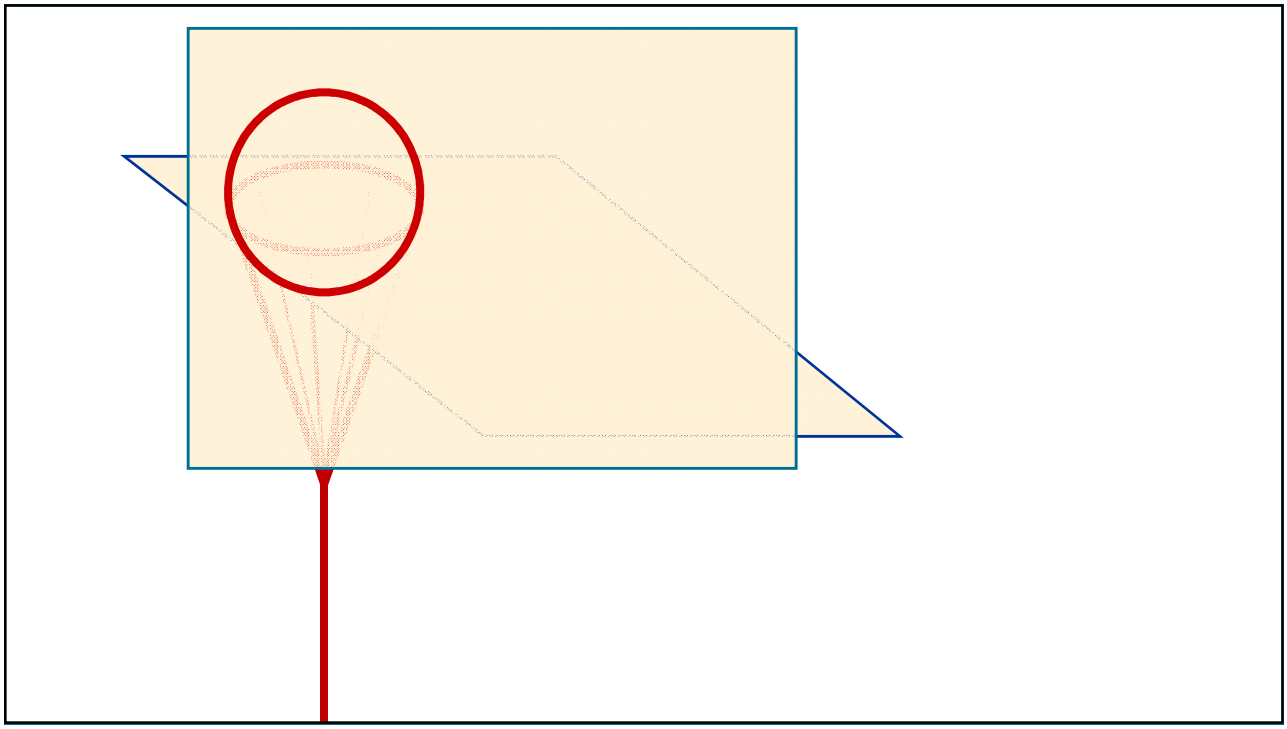
- 52 yo F with systemic lupus
- On mycophenolate mofetil and prednisone
- Presents unresponsive with rash on her right leg only
- Was well the night before
- Rapidly developed multi-organ failure in ED

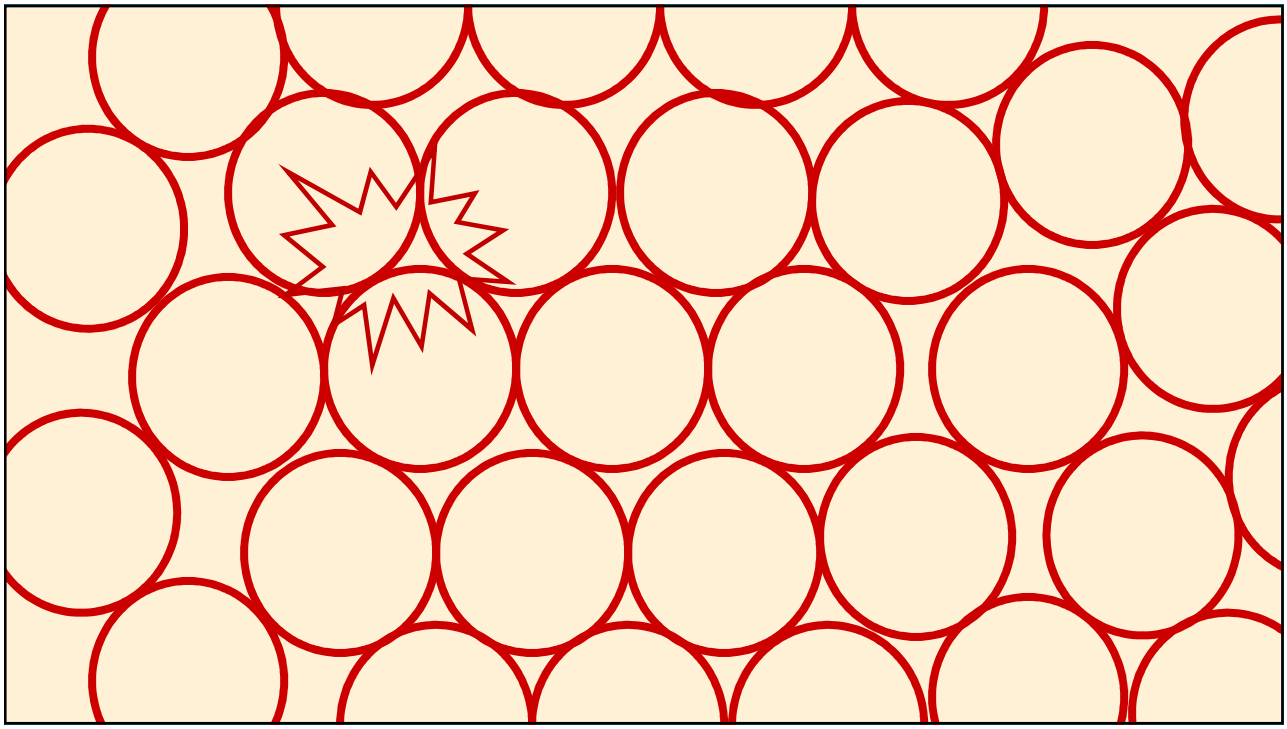
Hospital Day 1

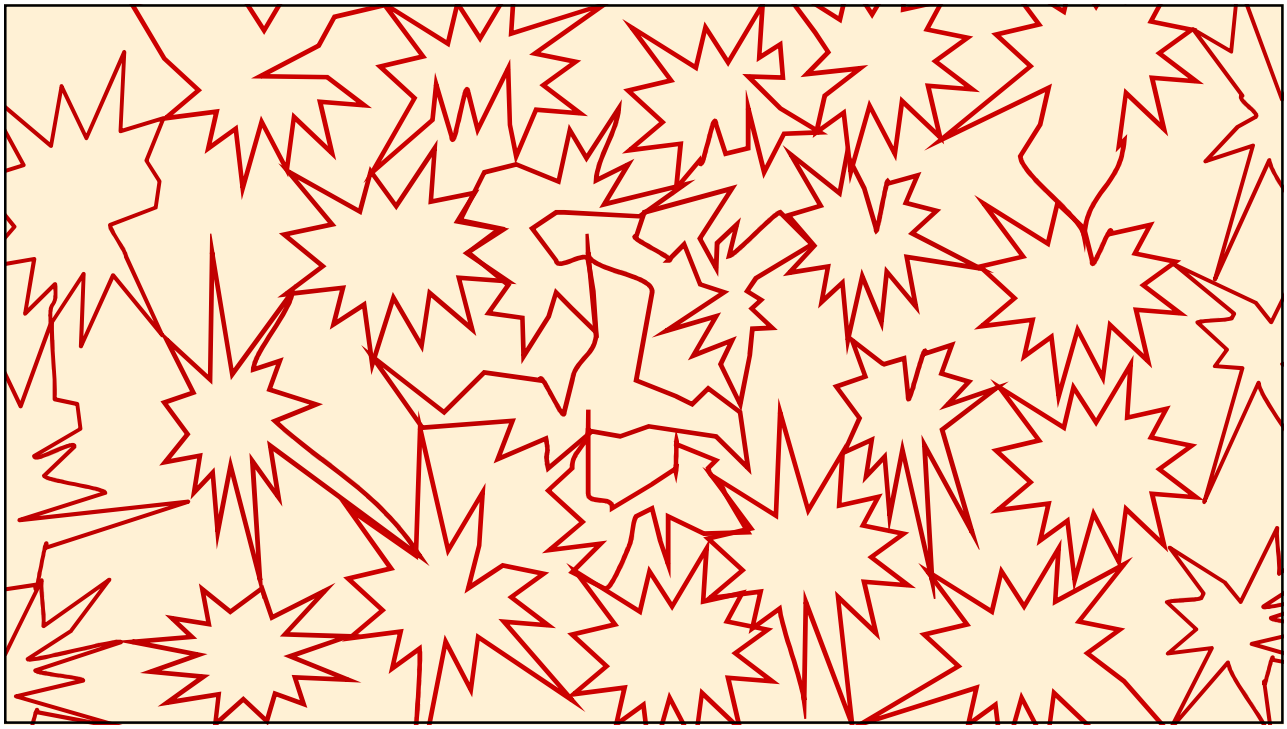
Hospital Day 3

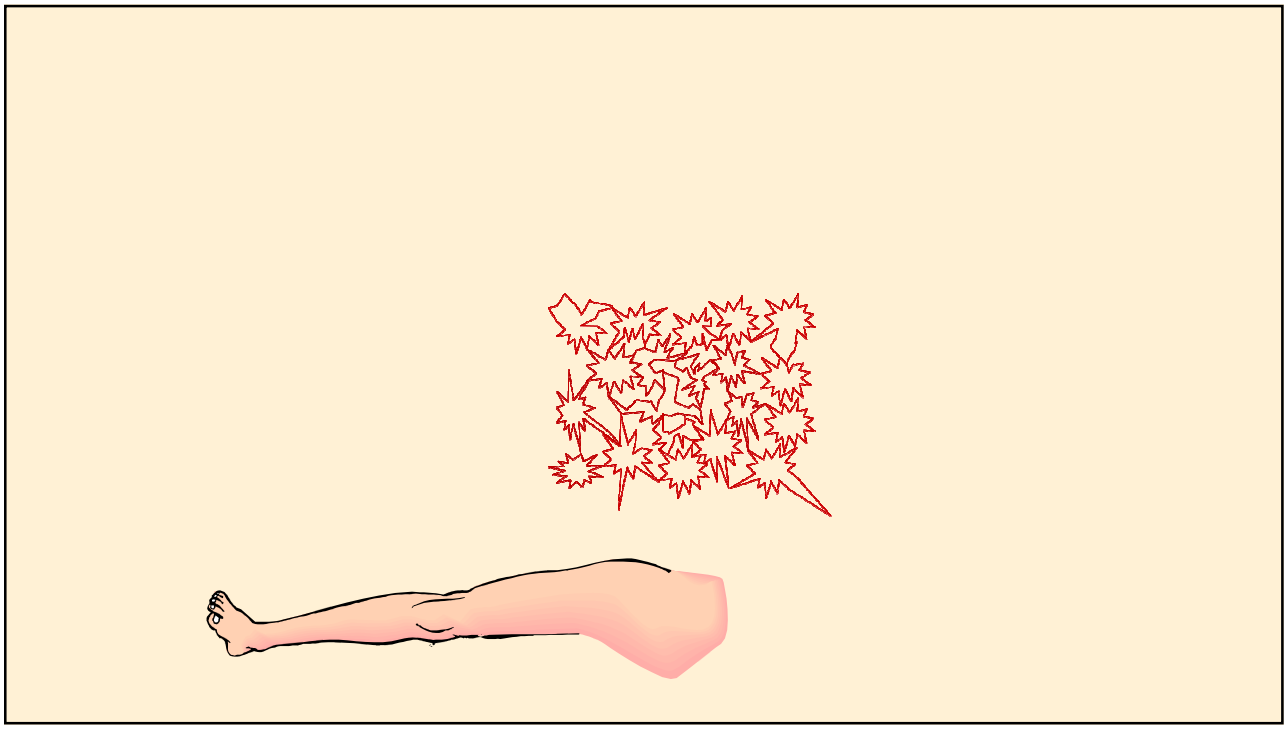


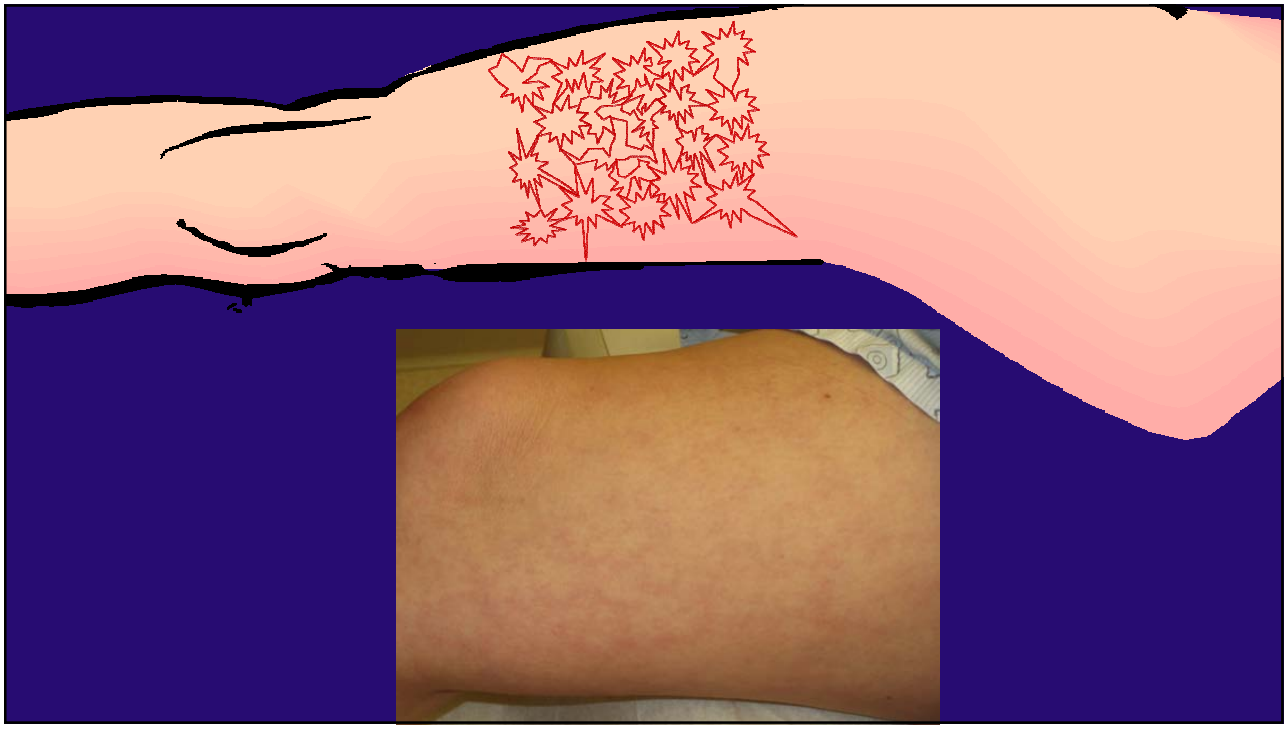
Dermatology, 2nd Edition. Eds Jean L Bolognia et al. Spain: Mosby Elsevier, 2008











2 potential problems with this system

Problem 1: Livedo Reticularis

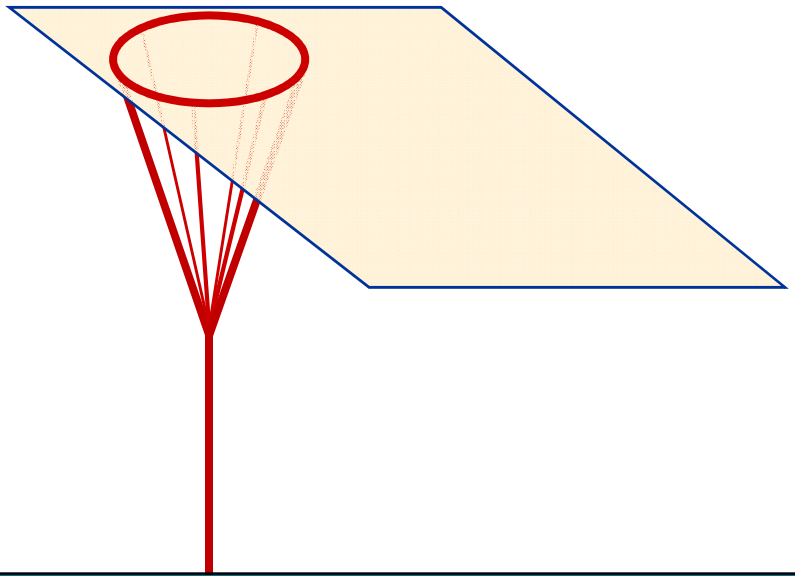
- Violaceous erythema
- Outlines 1-3cm stellate patches
- Surface of cones fed by individual perforating arterioles
- From enhanced visibility of zones of venous predominance
  - Increased deoxygenated blood in the venules
  - From engorged veins, constricted arterioles, local hypoxia…

Livedo Reticularis

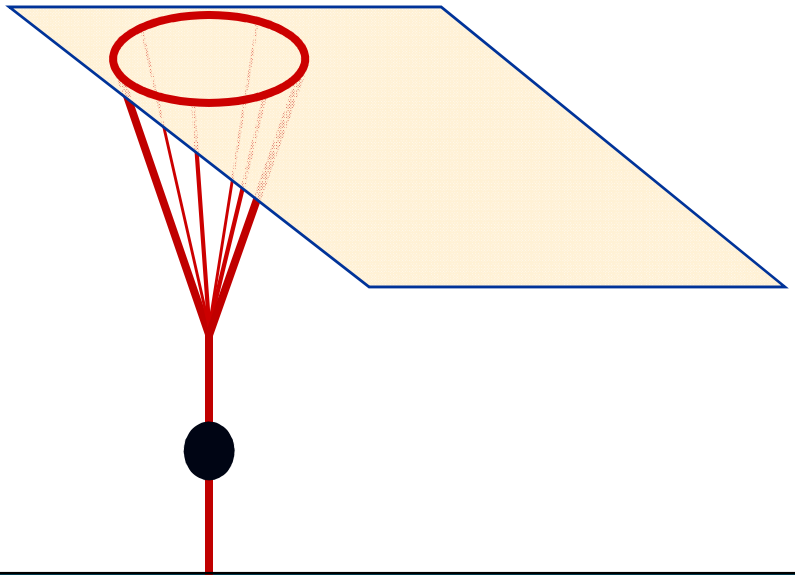
Problem 2:
Retiform Purpura

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

Retiform Purpura



Retiform Purpura



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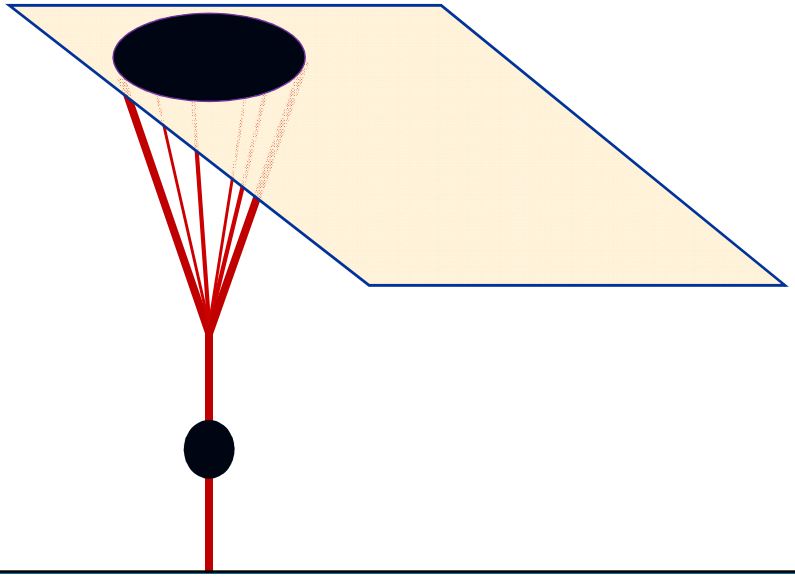

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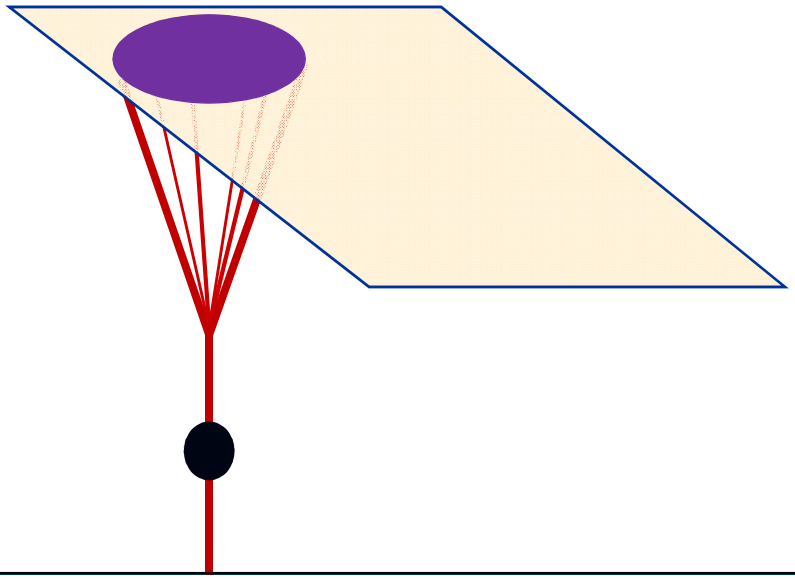

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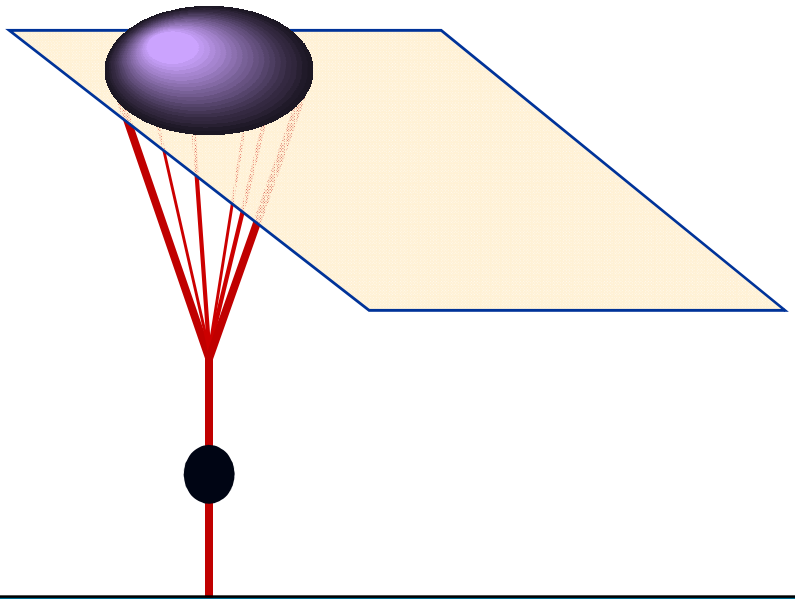
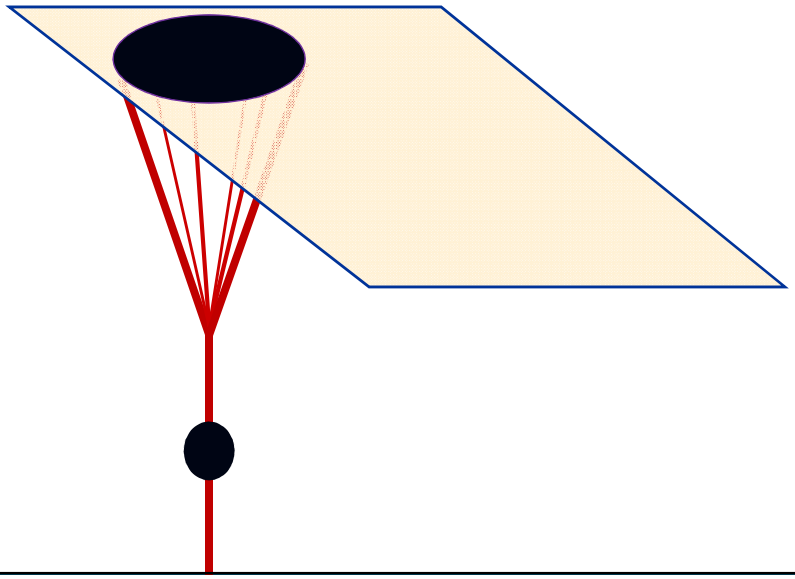
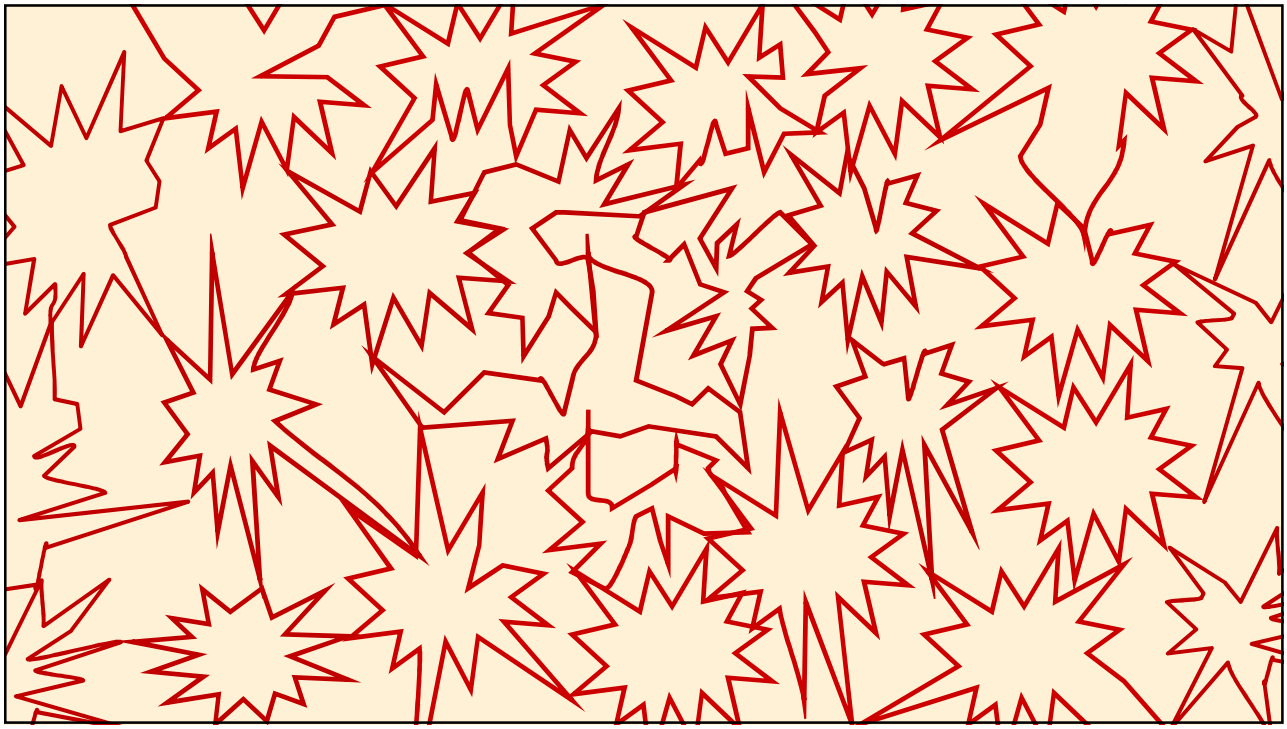
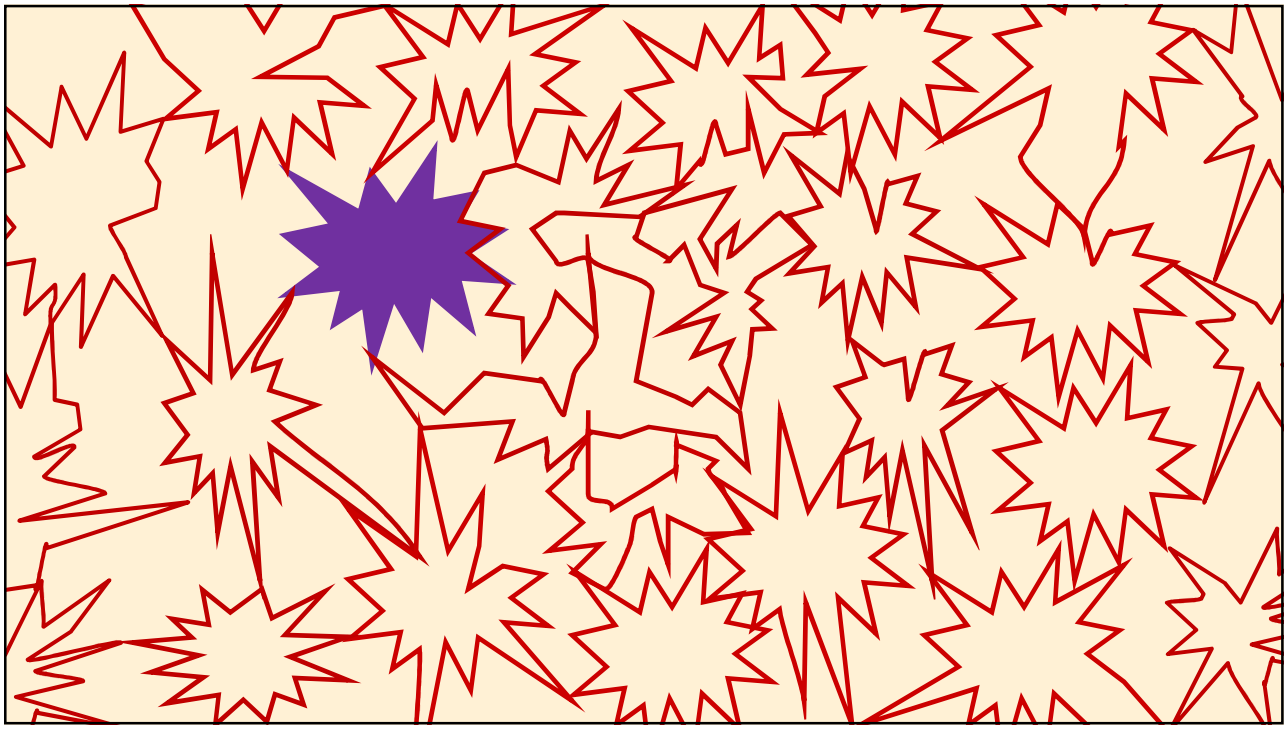
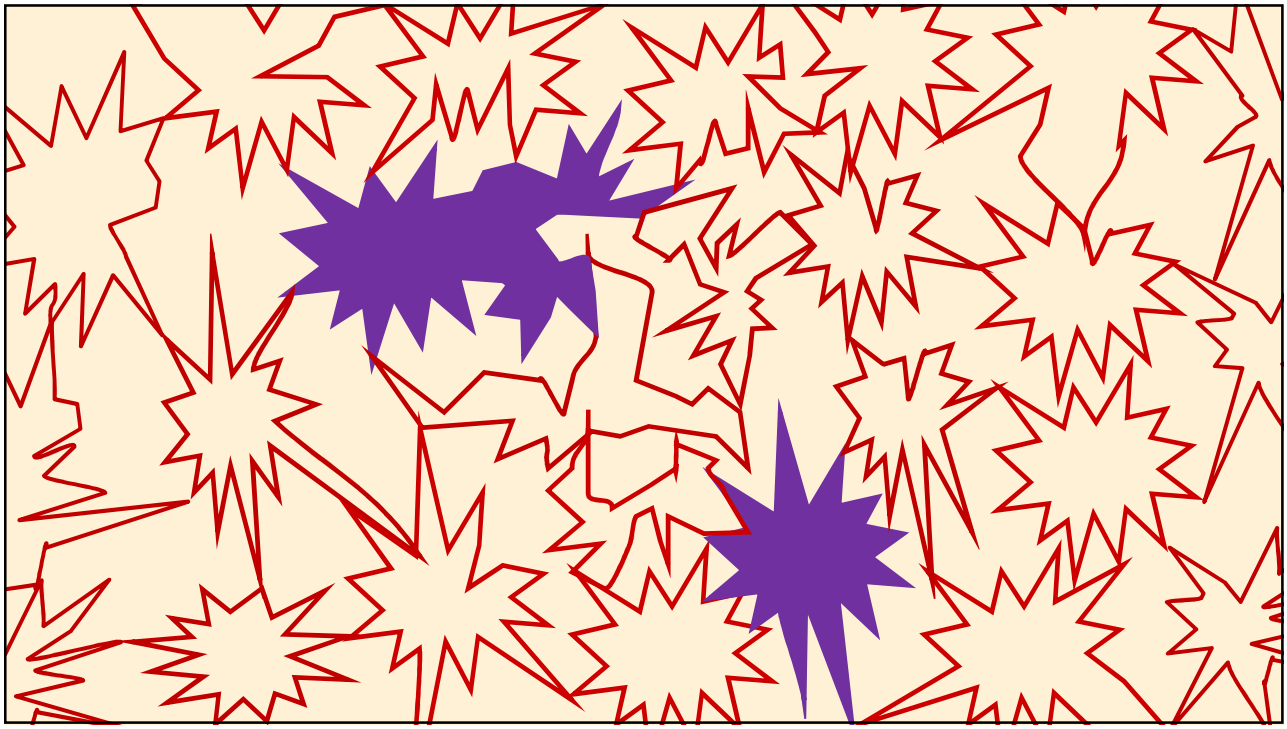


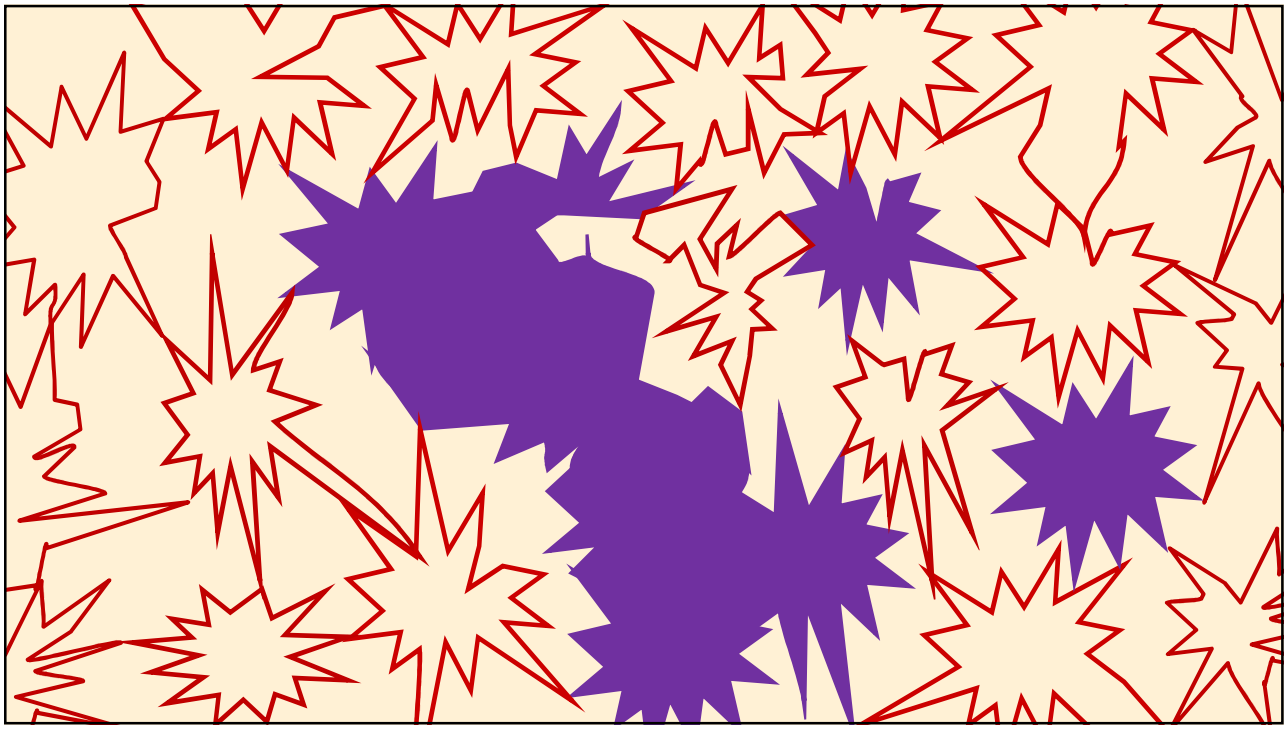
Retiform Purpura











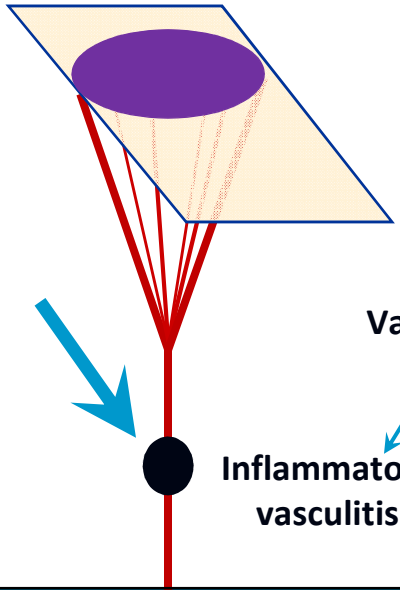
Retiform Purpura

(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

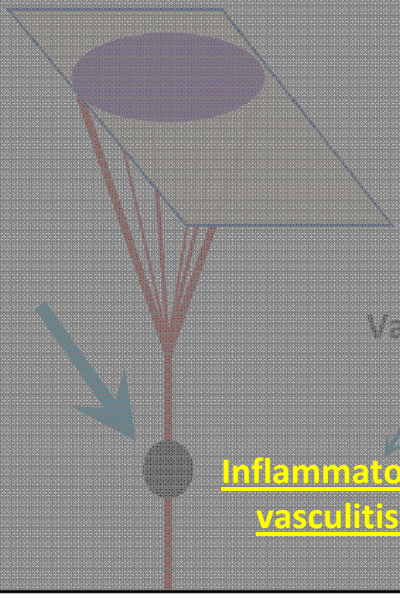
Vasculitis

Hypercoagulable state

Inflammatory vasculitis

Septic (vessel-invasive organism)

Retiform Purpura:
Differential Diagnosis



Perforating Arteriole Occlusion

In-situ Thrombosis

Embolism

Vasculitis

Hypercoagulable state

Inflammatory vasculitis

Septic (vessel-invasive organism)

Retiform Purpura: Select Differential Diagnosis	
Emboli	Amniotic Fluid, Atrial Myxoma, Cholesterol, Fat, Nitrogen, Septic, Ventilator Gas
Hypercoagulable States	Amyloidosis, AT III Deficiency, Atrophie Blanche / Livedoid Vasculopathy, APLAS, Calciphylaxis, COVID-19, Cryoglobulinemia, DIC, DVT, Hyperoxaluria, Protein C/S Deficiency, Sneddons Dz, TTP, Xylazine
Inflammatory Vasculitis	Microscopic Polyangiitis, PAN, Rheumatoid Vasculitis, Takayasu's, Wegeners
Septic vasculitis (Angioinvasive pathogens)	GPC: S. aureus GNRs: Aeromonas, E.coli, Klebsiella, Moraxella, Morganella, Pseudomonas, Serratia, Vibrio Fungi: Aspergillus, Candida, Fusarium, Mucor

Please Note:
(Regarding Retiform Purpura)

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

Retiform Purpura: Select Differential Diagnosis

Emboli	Amniotic Fluid, Atrial Myxoma, Cholesterol, Fat, Nitrogen, **Septic**, Ventilator Gas
Hypercoagulable States	Amyloidosis, AT III Deficiency, Atrophie Blanche / Livedoid Vasculopathy, **APLAS**, Calciphylaxis, COVID-19, Cryoglobulinemia, **DIC**, DVT, Hyperoxaluria, Protein C/S Deficiency, Sneddons Dz, **TTP**, Xylazine
Inflammatory Vasculitis	Microscopic Polyangiitis, PAN, Rheumatoid Vasculitis, Takayasu's, Wegeners
Septic vasculitis (Angioinvasive pathogens)	**GPC: S. aureus** **GNRs: Aeromonas, E.coli, Klebsiella, Moraxella, Morganella, Pseudomonas, Serratia, Vibrio** Fungi: Aspergillus, Candida, Fusarium, Mucor

DifferentiaL Dx:

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

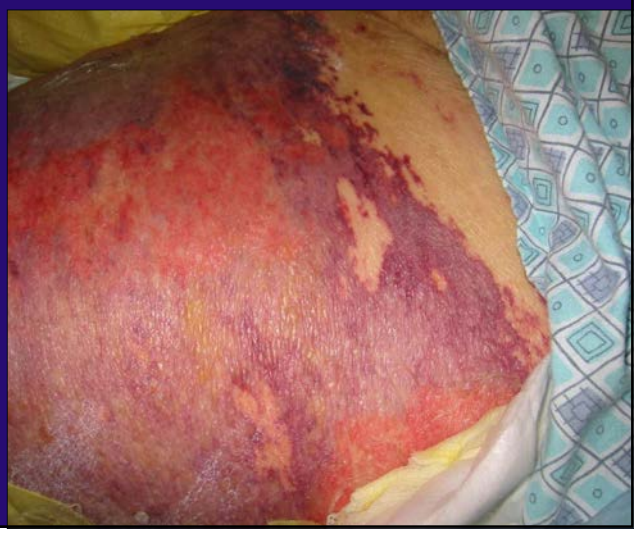
Serratia marcescens sepsis with necrotic retiform purpura of a seeded limb

More faces of Retiform Purpura

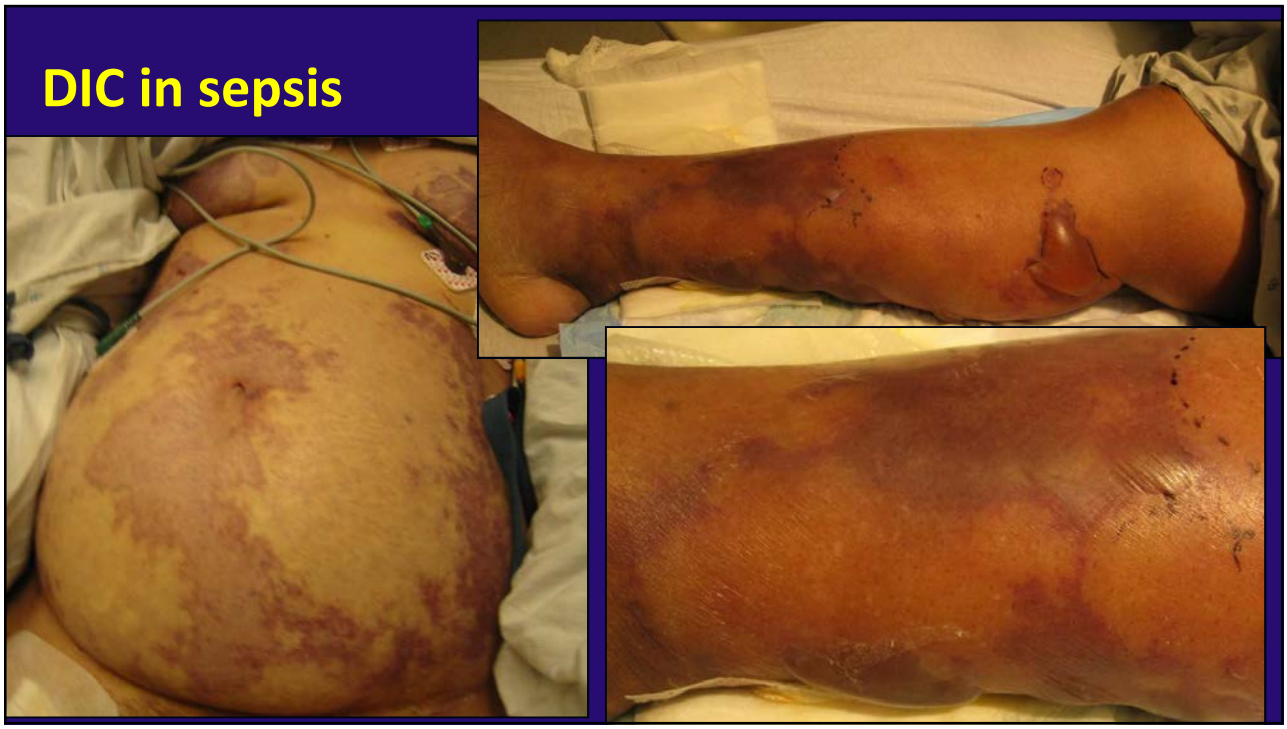
Cholesterol Emboli

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

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Bonus Case (time permitting)

18 yo female transferred from OSH for 2 complaints:

1. Abdominal pain x 4 years
2. Pruritic Rash x 6 months

Both undiagnosed despite extensive workup

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Scabies: Diagnostic Pearls

Burrows
and the
"Delta Wing Sign"

Scabies: Diagnostic Pearls

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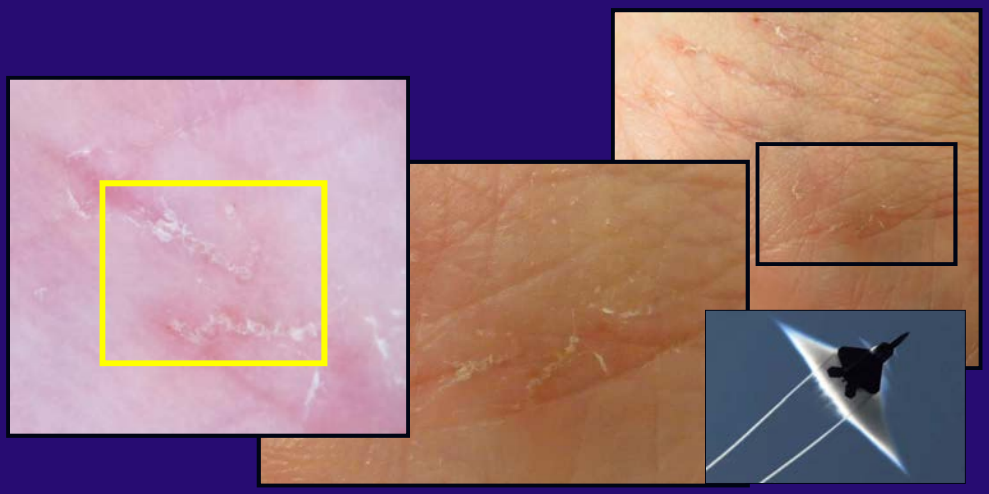
and the
"Delta Wing Sign"

Scabies: Diagnostic Pearls



*Argenziano G, Fabbrocini G, Delfino M. Epiluminescence Microscopy: A New Approach to In Vivo Detection of Sarcoptes scabiei. *Arch Dermatol.* 1997;133(6):751–753.

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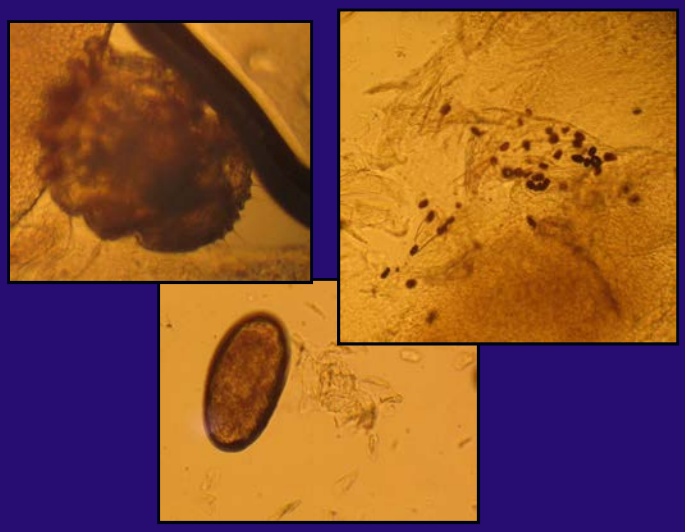

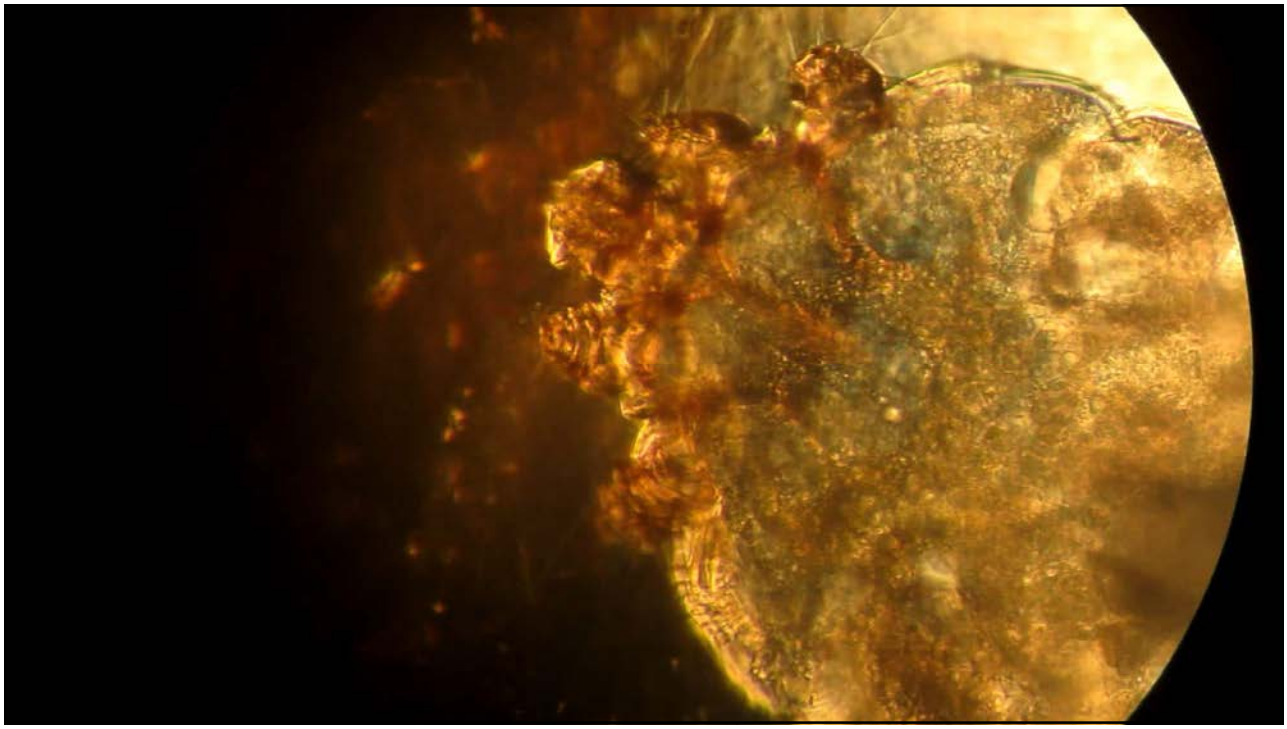

Scabies: Management

Topical Permethrin or PO Ivermectin
for patient and all household & sexual contacts

- Topical Permethrin:
  - Neck down, including all folds
  - 8-14 hours (overnight)
  - Wash & Dry all bedclothes and bedding high heat
  - Shower
  - Repeat 7-14 days later

- PO Ivermectin: 200mcg/kg x 1, repeat 7-14 days later
  - Wash & Dry all bedclothes and bedding high heat
  - Shower

Bonus Case 2 (time permitting)

- 49 yo M
- 5 weeks of pruritic rash
  - Whole cutaneous surface, *except* palms and soles
  - Tongue sores, eye discharge
  - Low grade fevers, myalgias, headaches, lethargy

- PMH: Bipolar disorder (stable off medication x several years)
- Meds: diphenhydramine, lorazepam, sildenafil

*Diagnosis?

A. Syphilis
B. Psoriasis
C. Pityriasis rosea
D. Measles

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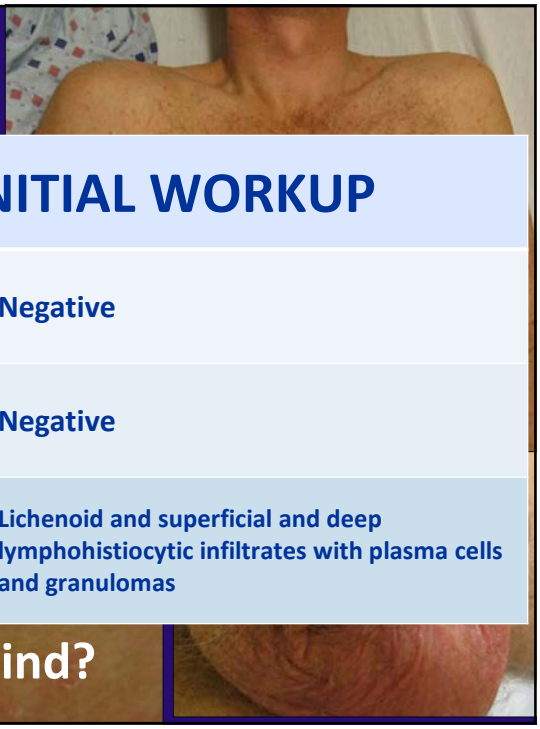

INITIAL WORKUP	
RPR	Negative
HIV ELISA	Negative
Skin Biopsy	Lichenoid and superficial and deep lymphohistiocytic infiltrates with plasma cells and granulomas

Does this change anyone's mind?

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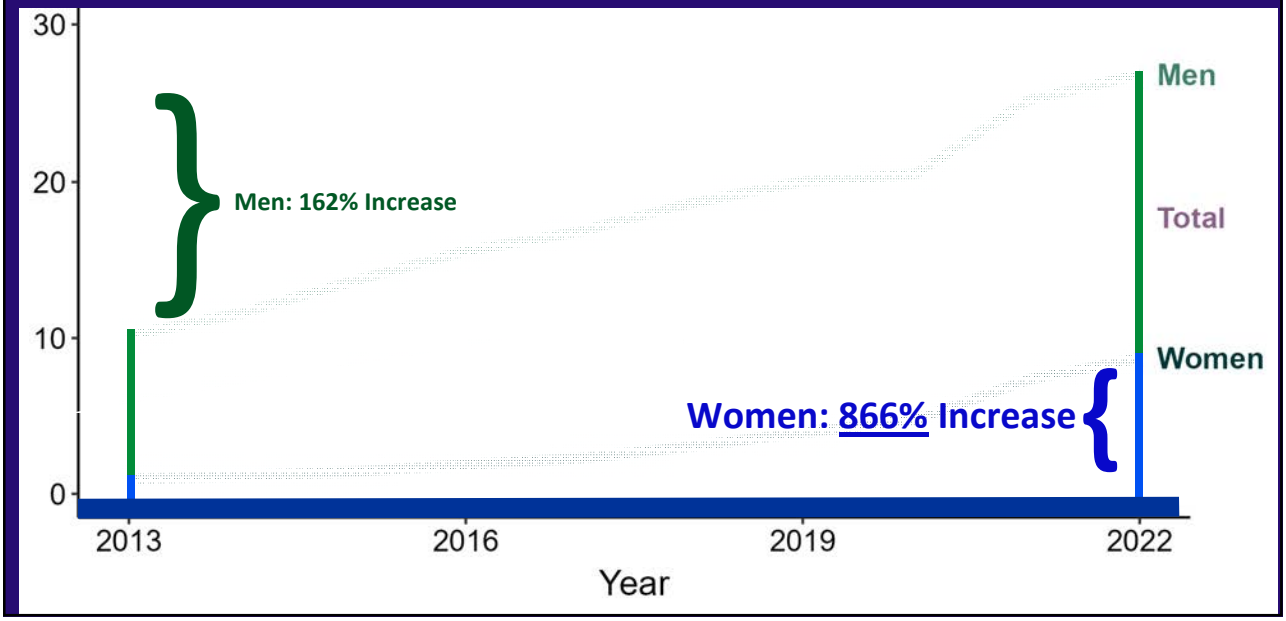
Why a false negative RPR?

But first, why revisit syphilis at all?

Primary and Secondary Syphilis — Rates of Reported Cases by Sex, United States, 2013–2022



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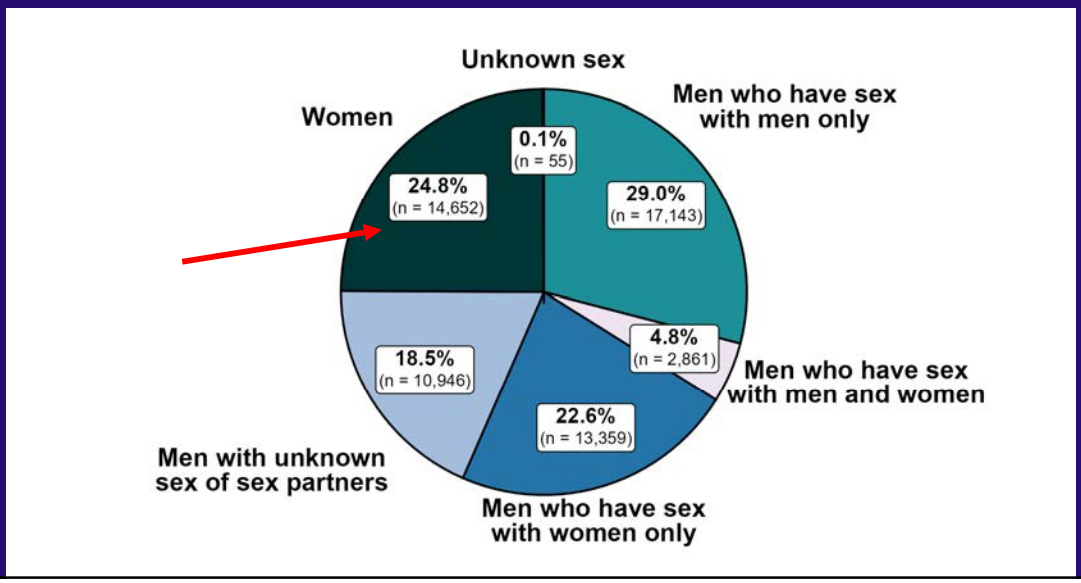
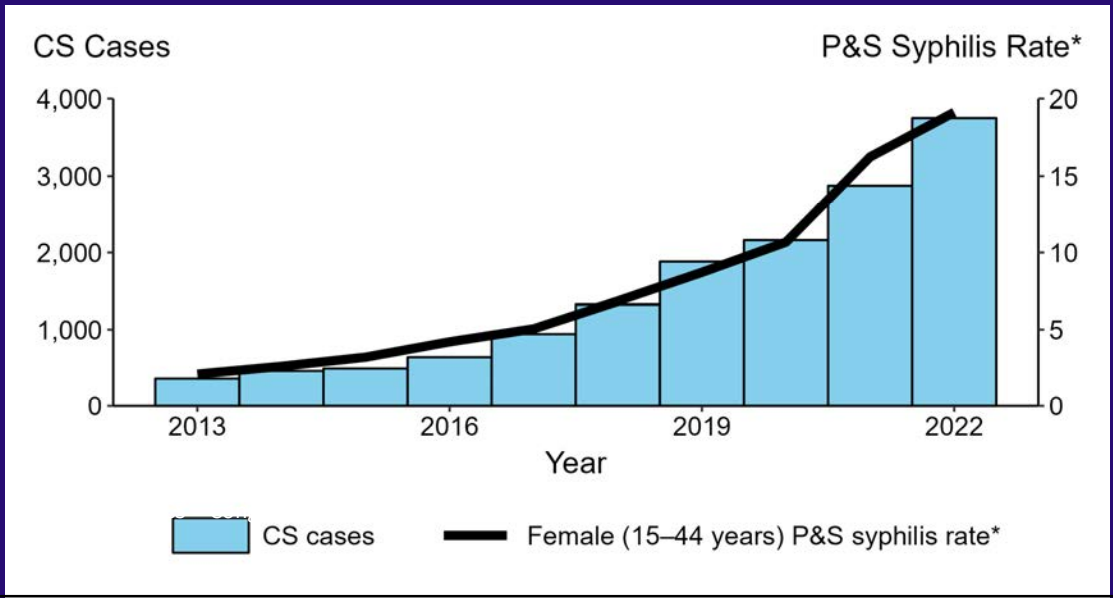


Congenital Syphilis (by Year of Birth) and Syphilis Among Females Aged 15–44 Years, United States, 2013-2022



Syphilis

- We have an epidemic
- Rising fastest in women
- Congenital syphilis rising in parallel
- Diagnosis *can* be tricky

Diagnosis? *(ROUND 2)*

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Prozone Phenomenon

- Non-treponemal tests (RPR, VDRL)
  - Treponeme incorporates and modifies host cardiolipin
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- Non-treponemal tests (RPR, VDRL)
  - Treponeme incorporates and modifies host cardiolipin
  - Host produces antibodies to cardiolipin
- Test mechanism
  - Patient serum + cardiolipin→ precipitation / flocculation
  - False positives from other sources of cardiolipin antibodies
  - False negatives:
    - Too early, too late, too immunosuppressed, or
    - **Prozone phenomenon: Notable antibody excess → *no* agglutination**

Prozone Phenomenon

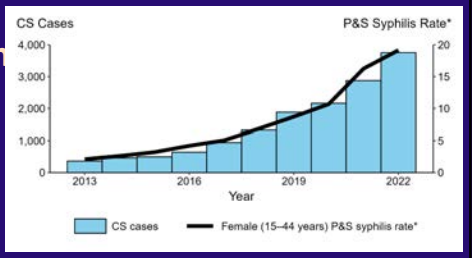
Prozone phenomenon: Notable antibody excess prevents agglutination

Fastest way to check if negative RPR is from Prozone Phenomenon?

- **Dilute the patient's serum and re-test RPR**
- **This patient: RPR Positive at a 1:16 dilution**

Risk factors for Prozone Phenomenon:

Neurosyphilis and **Pregnancy** **(CID 2014)**



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www.cdc.gov/std/statistics/2022/data.zip

Li-Li Liu, Li-Rong Lin, Man-Li Tong, Hui-Lin Zhang, Song-Jie Huang, Yu-Yan Chen, Xiao-Jing Guo, Ya Xi, Long Liu, Fu-Yi Chen, Ya-Feng Zhang, Qiao Zhang, Tian-Ci Yang, Incidence and Risk Factors for the Prozone Phenomenon in Serologic Testing for Syphilis in a Large Cohort, *Clinical Infectious Diseases*, Volume 59, Issue 3, 1 August 2014, Pages 384–389

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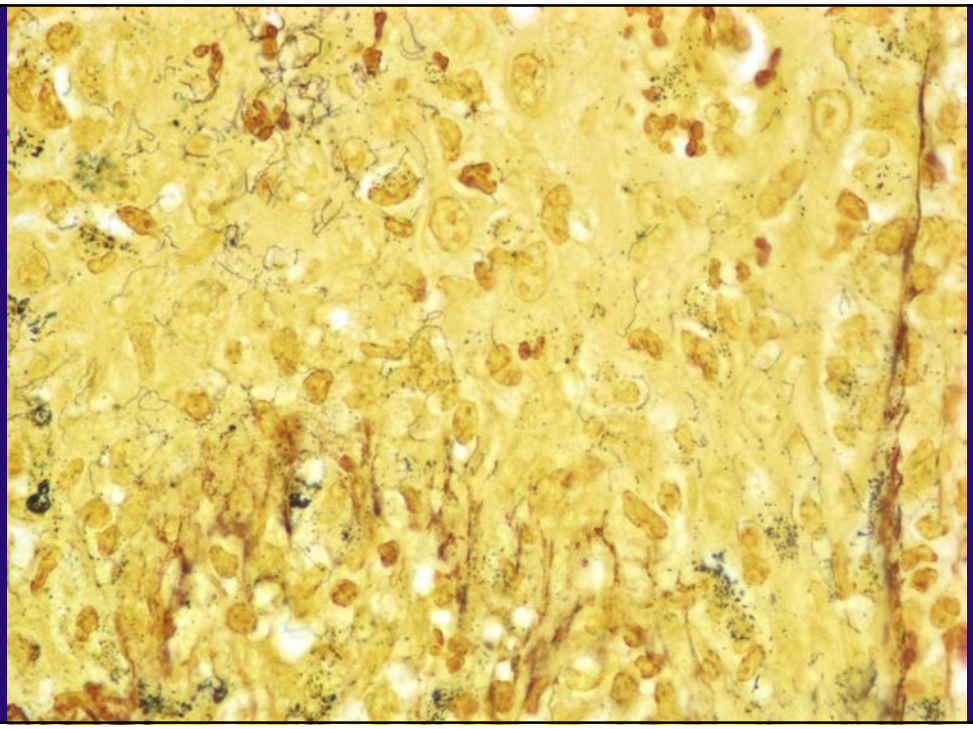
Alternative means to confirm a diagnosis of syphilis:

- Treponemal-specific antibodies: blood or tissue immunohistochemistry
- PCR from blood or tissue
- Darkfield microscopy: rare in United States
- Silver staining of tissue



Final syphilis pearl: Why did the papules *spare* the palms and soles?

- Classic Secondary Syphilis:
  - early macular phase: ham colored macules + adenopathy
  - late papular phase: pink papules with scale
  - +/- mucous patches, moth-eaten alopecia, condyloma lata, et al

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- Other Variants: Syphilids
  - Psoriasiform
  - Lichenoid
  - Follicular
  - Annular – “nickels & dimes”
  - Corymbose: central + satellites
  - Pustular
  - Ecthymatous: deep ulcers
  - Rupioid: “oyster shell”
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Syphilis Key Points

- Rates are rising, cases *are* being missed
- Presentations vary (of course)
- No test or testing algorithm is perfect
- Maintain a high index of suspicion & re-test if concerned