

# Dermatology: Key Cases for the Internist

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- Assistant Professor, Part-time at HMS
- Director of the Lahey Skin Infection Program

# Disclosures

- None
- Will discuss off-label use of medications

# Objectives

- Use case vignettes to help the participants:
  - Optimize management of simple cellulitis
  - Recognize an easily overlooked, common, serious eruption
  - Distinguish between allergic contact dermatitis and infection (time-permitting)

# Case

- 54 yo F
- 5 days s/p excision of a BCC
- Progressive peri-incisional redness and pain
- Malaise
- Temp 100.5



# Cellulitis



# Which of the following characteristics is most SENSITIVE for cellulitis?

- A. Tenderness
- B. Fever
- C. Leukocytosis
- D. Pruritus
- E. Malaise

**Which of the following  
characteristics is most SENSITIVE  
for cellulitis?**

- A. **Tenderness**
- B. Fever
- C. Leukocytosis
- D. Pruritus
- E. Malaise

# 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

*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

### 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 SIMPLE Cellulitis

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

But which one???

# 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 acquired  
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,<sup>1,2</sup> William D. Binder,<sup>3</sup> Matthew B. Allen,<sup>1,4</sup> Molly Lederman,<sup>1,5</sup> Siddharth Parmar,<sup>1</sup> Michael R. Filbin,<sup>3</sup> David C. Hooper,<sup>6</sup> and Carlos A. Camargo Jr<sup>3</sup>**

<sup>1</sup>Department of Emergency Medicine, Brigham and Women's Hospital, <sup>2</sup>Division of Emergency Medicine, Boston Children's Hospital, and <sup>3</sup>Department of Emergency Medicine, Massachusetts General Hospital, Boston; <sup>4</sup>Perelman School of Medicine at the University of Pennsylvania, Philadelphia;

<sup>5</sup>Department of Pediatrics, and <sup>6</sup>Division of Infectious Diseases, Department of Medicine, Massachusetts General Hospital, Boston

# Pallin et al, CID 2013

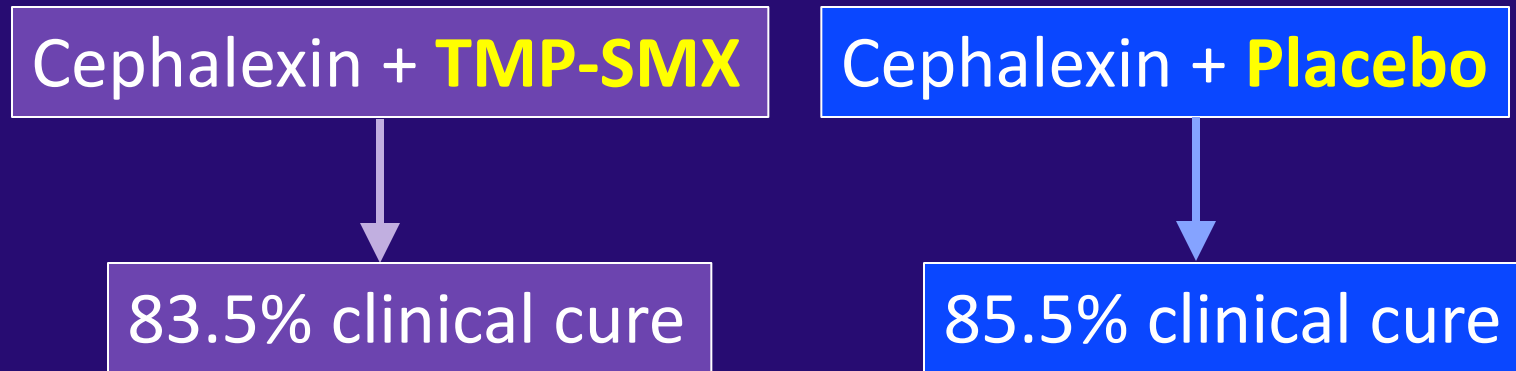
- 3 Boston Emergency Depts, 2007-11
- 153 Simple Cellulitis patients randomized



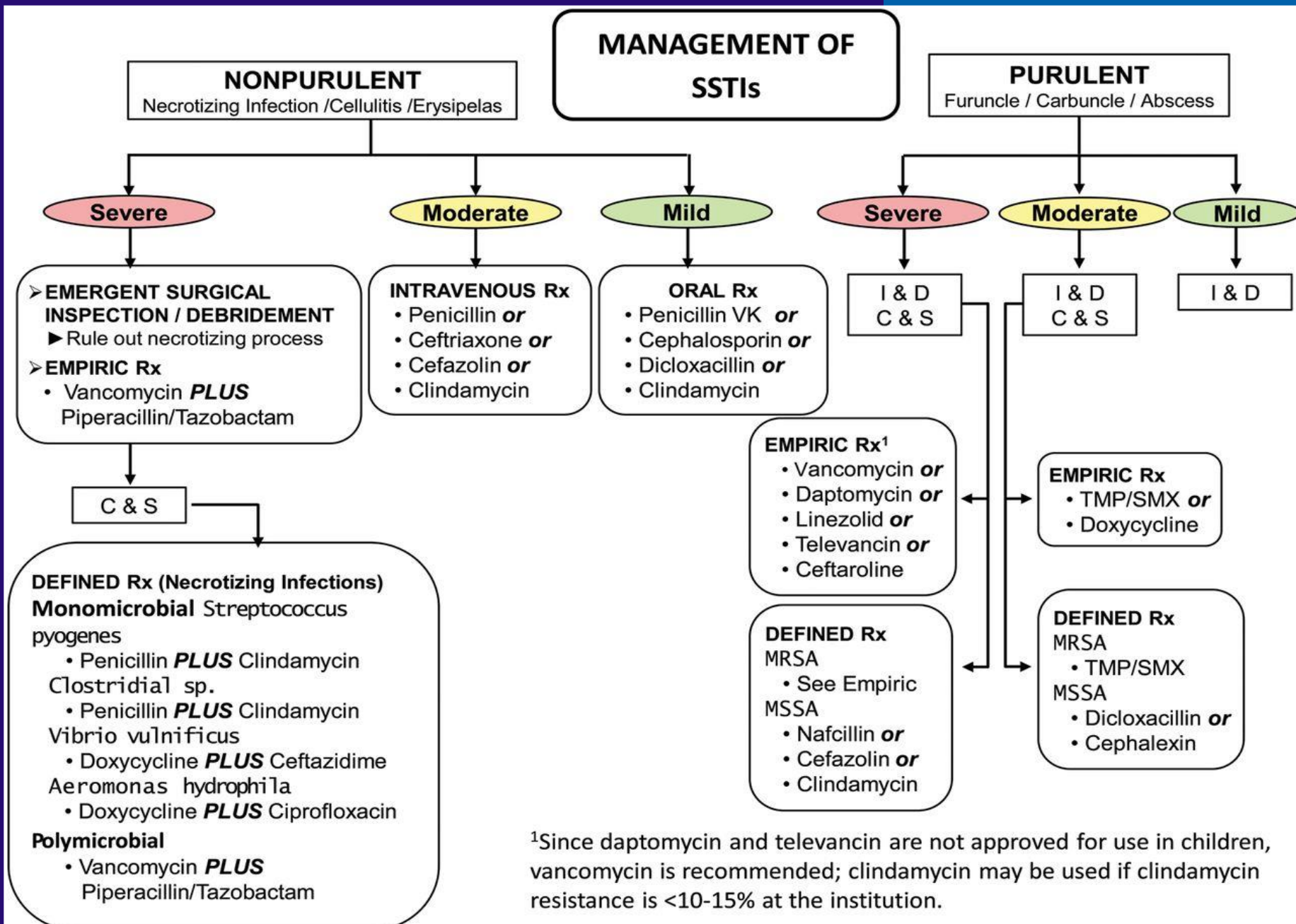
- Presence of nasal MRSA: no impact on outcome
- Conclusion: no benefit to adding sulfa

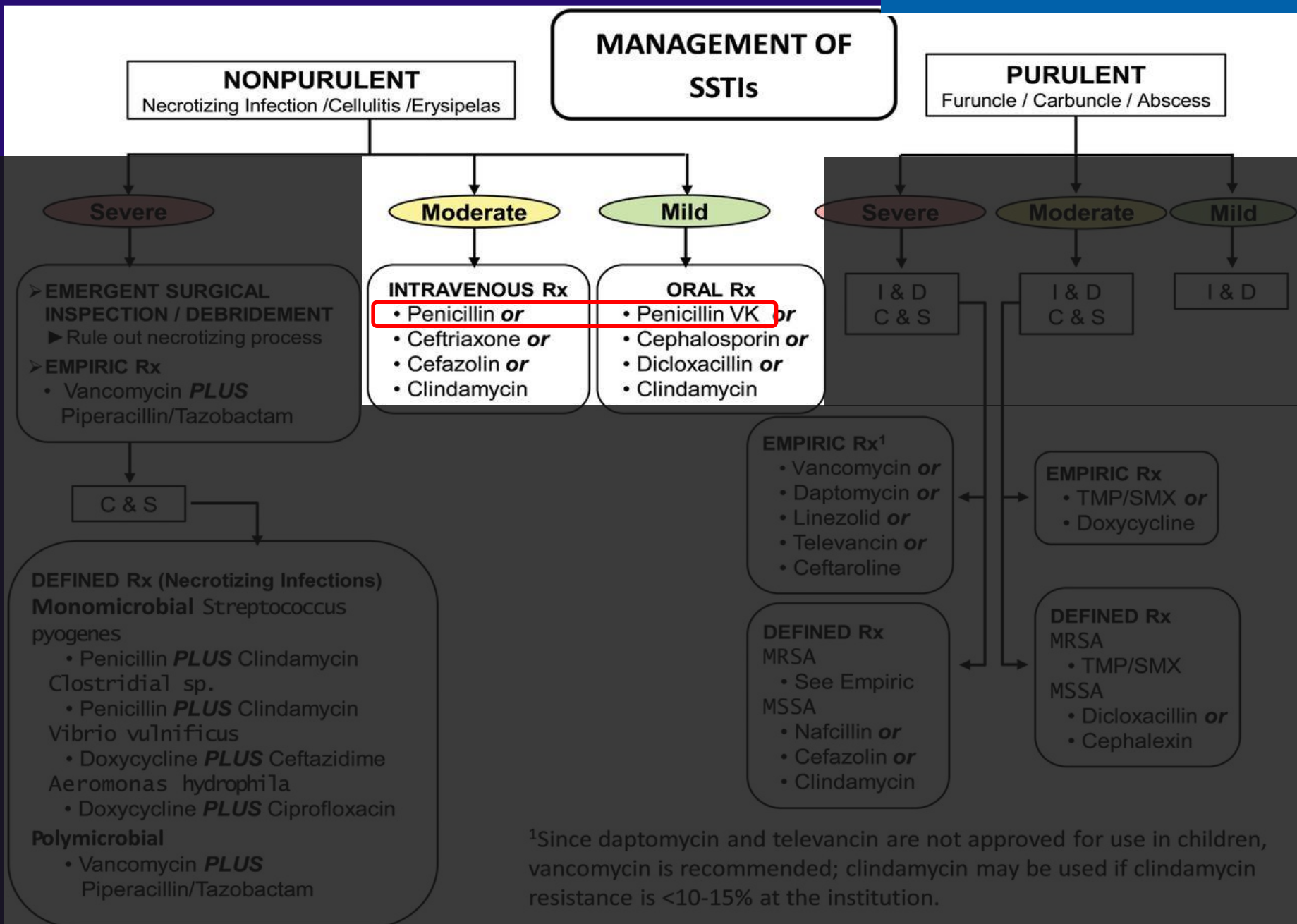
# Moran et al, JAMA 2017

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



- Conclusion: **no benefit to adding sulfa**





# 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 &  $\beta$ -lactam response** (Jeng et al)
  - Study Conclusions:
    - Serologies: “73% of non-culturable cellulitis caused by  **$\beta$ HS**”
    - $\beta$ -lactam response rate: 95.6%
  - **BUT!**
    - **31% lost without serologies. Intention-to-test analysis  $\rightarrow$  ~51%  $\beta$ HS+**
    - **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)

# Cellulitis empiric therapy:

## MOC REFLECTIVE STATEMENT

- 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  **$\beta$ -lactamase resistant agent**

# Brief Interlude

Time for a skin check

- Patient referred in by wife for rapidly changing mole



# Brief Interlude

## Time for a skin check

- Patient referred in by spouse for rapidly changing mole



### Two Questions to consider:

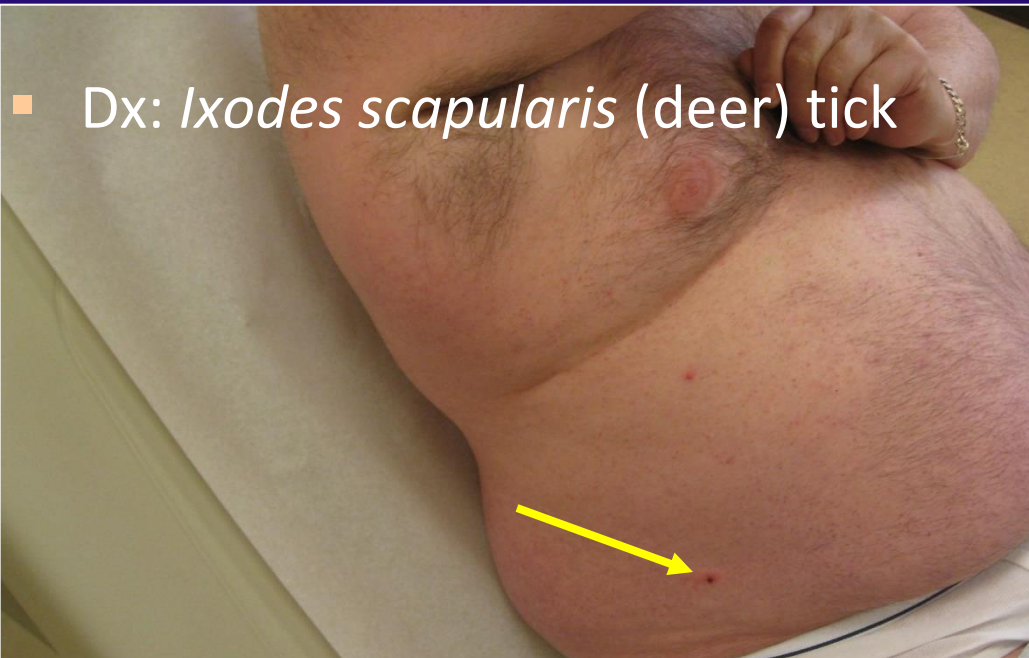
1. 'Doorway diagnosis' best guess?
2. Any desired procedures/referrals?

# Brief Interlude

## Time for a skin check

- Patient referred in by wife for rapidly changing mole

- Dx: *Ixodes scapularis* (deer) tick



### Two Questions to consider:

1. 'Doorway diagnosis' best guess?
2. Any desired procedures/referrals?

# Brief Interlude

## Time for a skin check

- Patient referred in by wife for rapidly changing mole
- Dx: *Ixodes scapularis* (deer) tick
- Procedure: Tick removal
- Treatment: doxy 200mg PO x 1, if:
  - *Ixodes* tick: BLACK LEGS
  - Present at least 36 hrs (engorged)
  - Within 72 hrs of removal
- Referral?



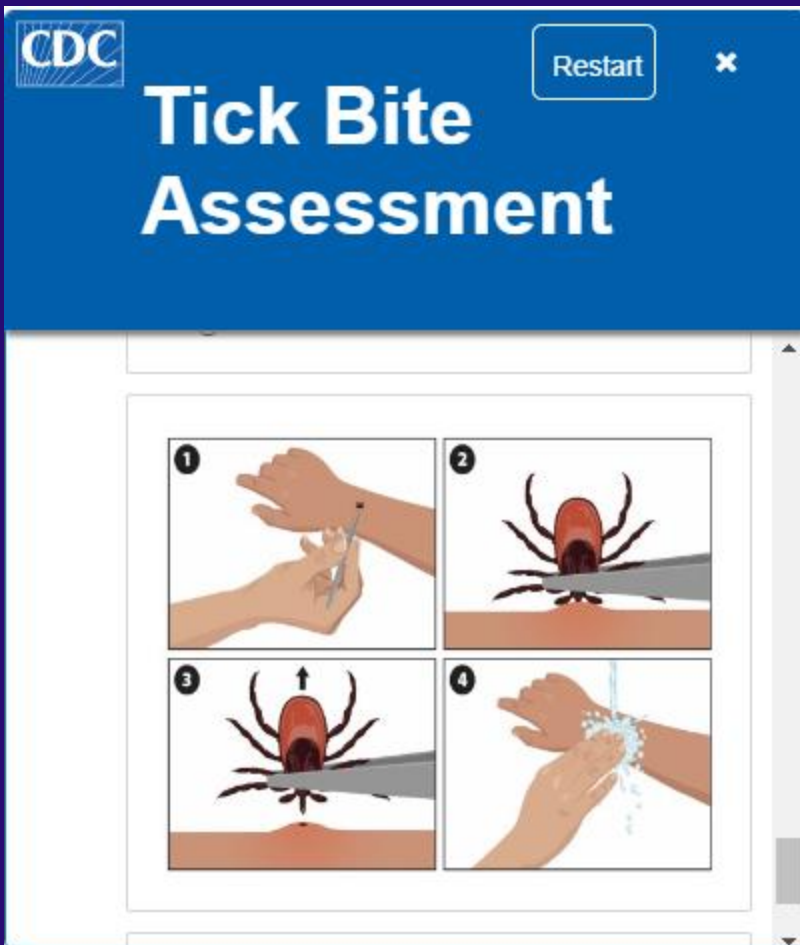
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  - Within 72 hrs of removal
- Referral: **Spouse, to ophtho**

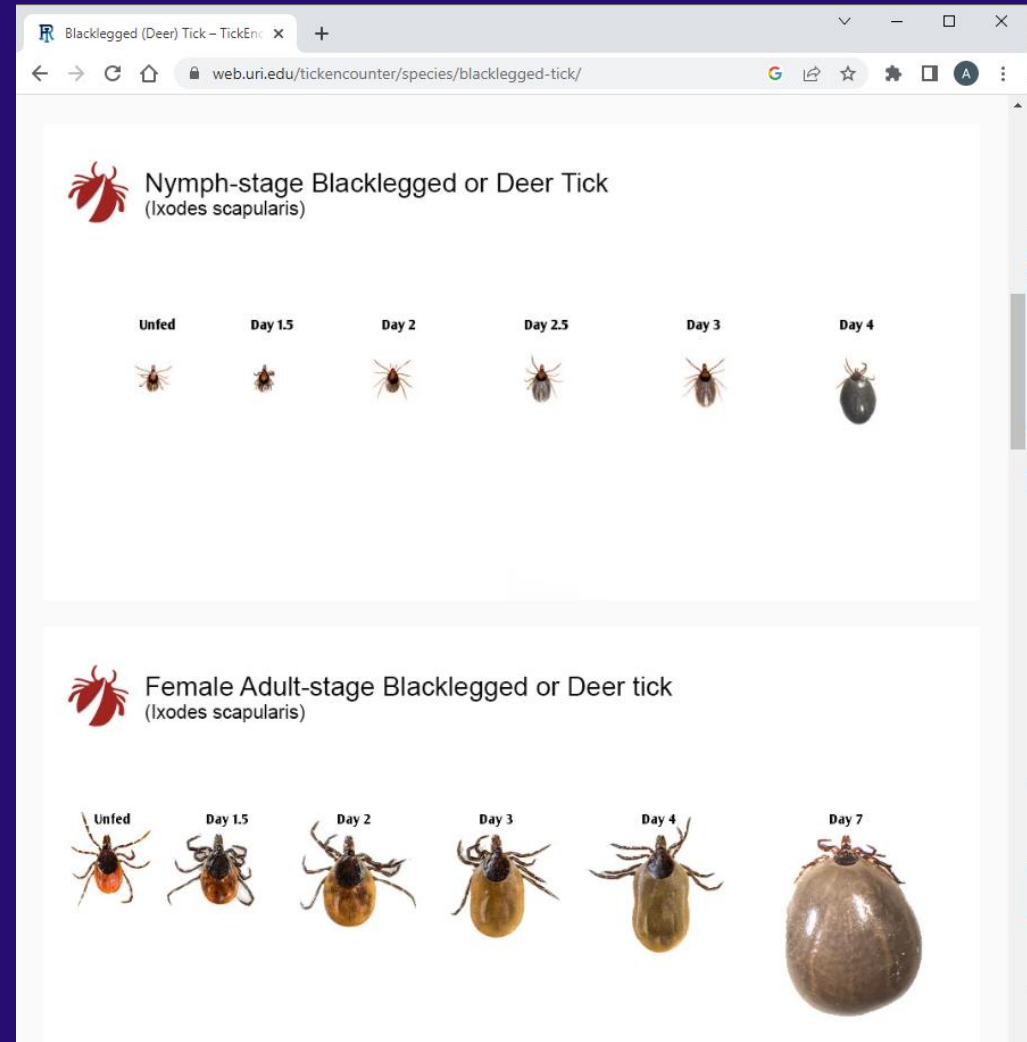


# Tick Bite Resources



CDC Tick Bite Bot

<https://tools.cdc.gov/medialibrary/index.aspx#/media/id/729305>



University of Rhode Island Tick Field Guide

<https://web.uri.edu/tickencounter/fieldguide/>

# Final Tick Bite Reminder

Many non-lyme tickborne illnesses

## Ixodes Ticks

- Anaplasmosis
- Babesiosis\*
- Lyme
- Powassan\*
- Tick-borne relapsing fever  
(*Borrelia miyamotoi*)

## Various Brown-legged ticks

- Anaplasmosis
- RMSF
- Tularemia\*\*
- Ehrlichiosis
- Acquired Red Meat Allergy\*  
(Alpha-gal syndrome)

\* Not Doxycycline sensitive

\*\* Doxycycline not first-line therapy

# Tick-Bite Mini Case

## MOC REFLECTIVE STATEMENT

- Tick Identification: Black Legs = likely able to carry Lyme

Resource to help with **tick identification**:

<https://web.uri.edu/tickencounter/fieldguide/>

- Prophylactic doxycycline for:

- Deer Tick (black legged)
- Present  $\geq 36$  hours / engorged
- Within 72H of removal

Resource to help with **decision to provide prophylaxis**:

<https://tools.cdc.gov/medialibrary/index.aspx#/media/id/729305>

# 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







**In what anatomic structure does the primary pathophysiology lie?**

**(ie: *Where is the 'lesion'?*)**



1. Epidermis
2. Dermal Interstitium
3. Fascia
4. Arterioles
5. Sweat Glands

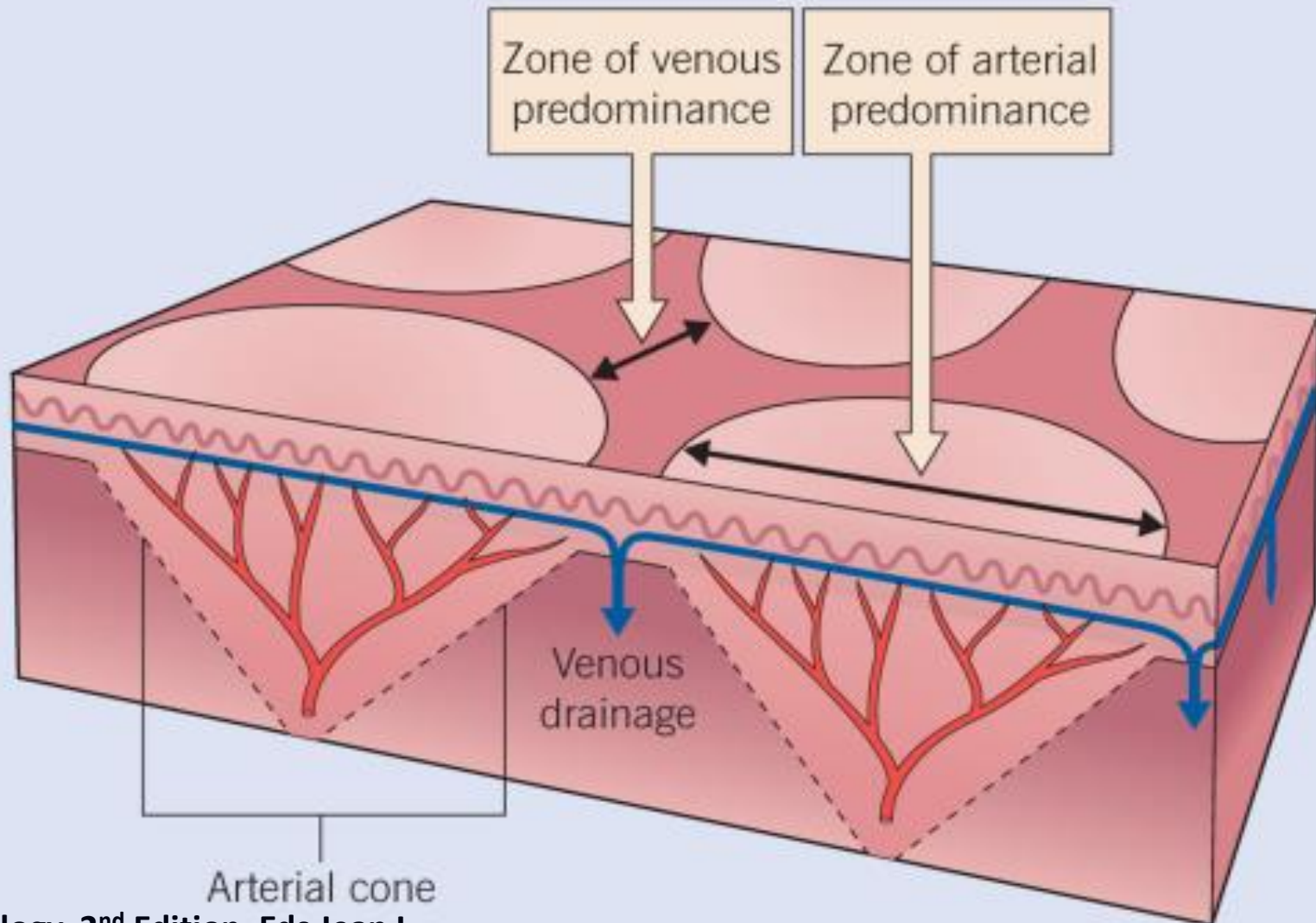
In what anatomic structure does the primary pathophysiology lie?

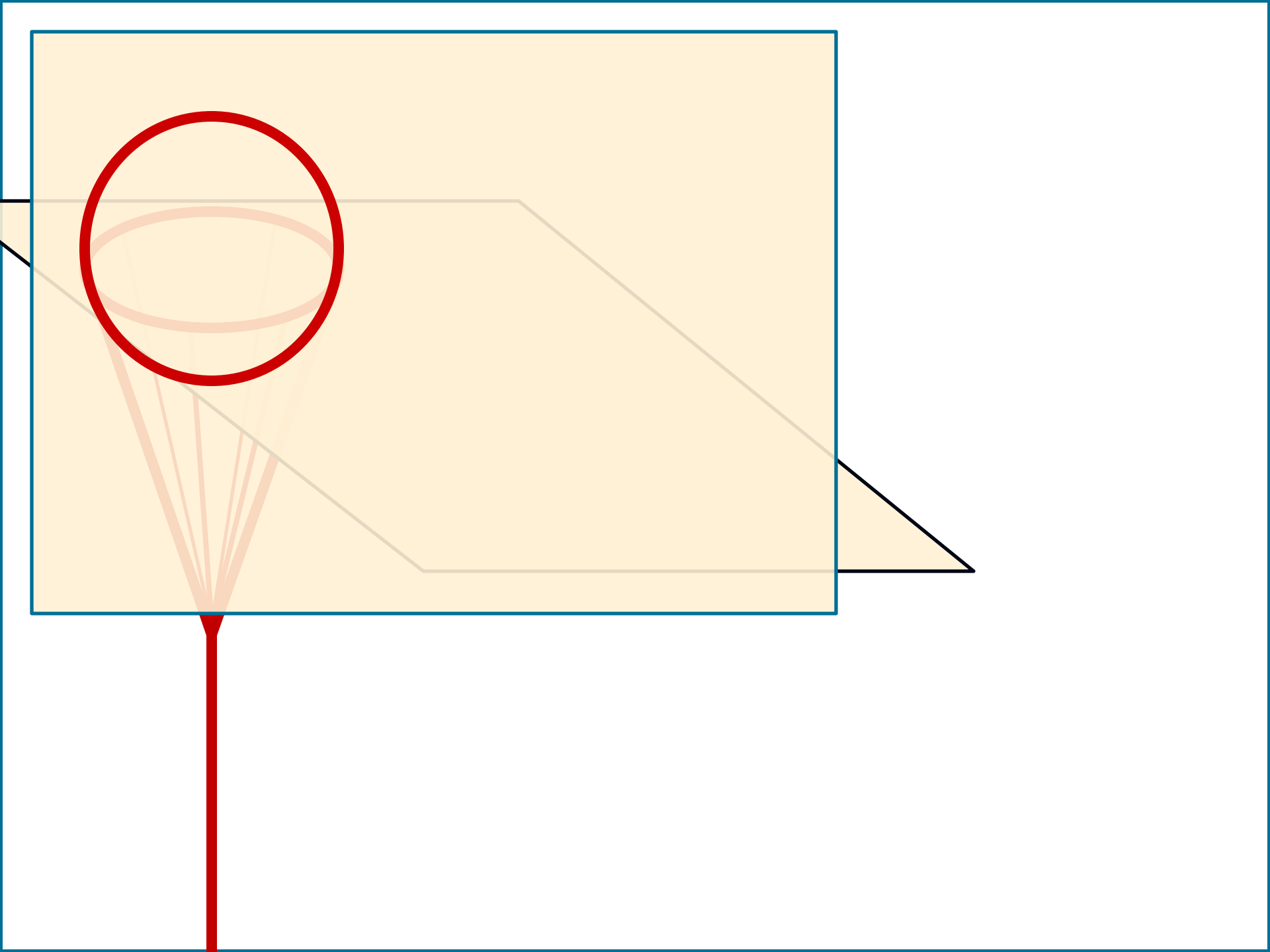
(ie: *Where is the 'lesion'?*)

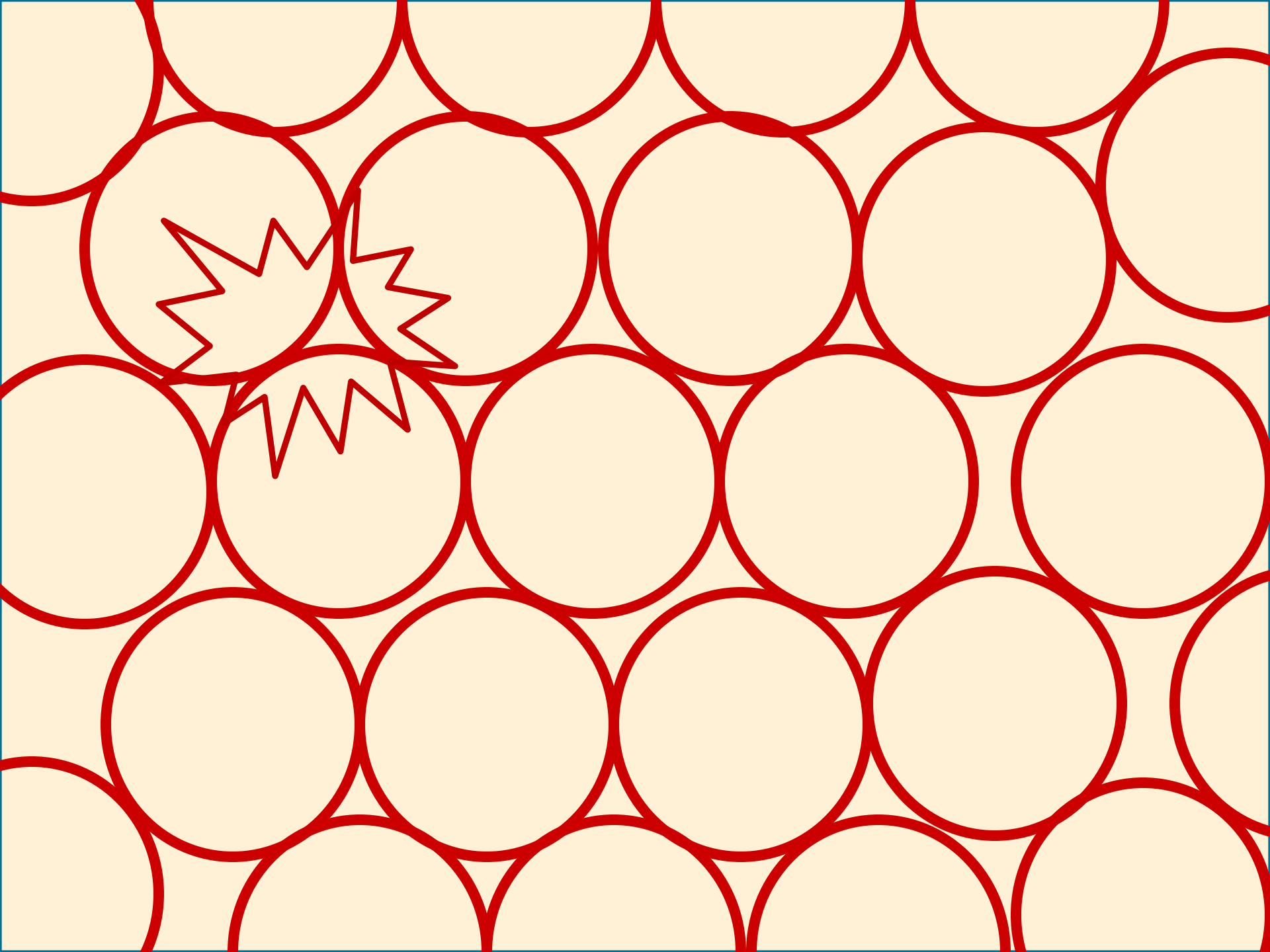


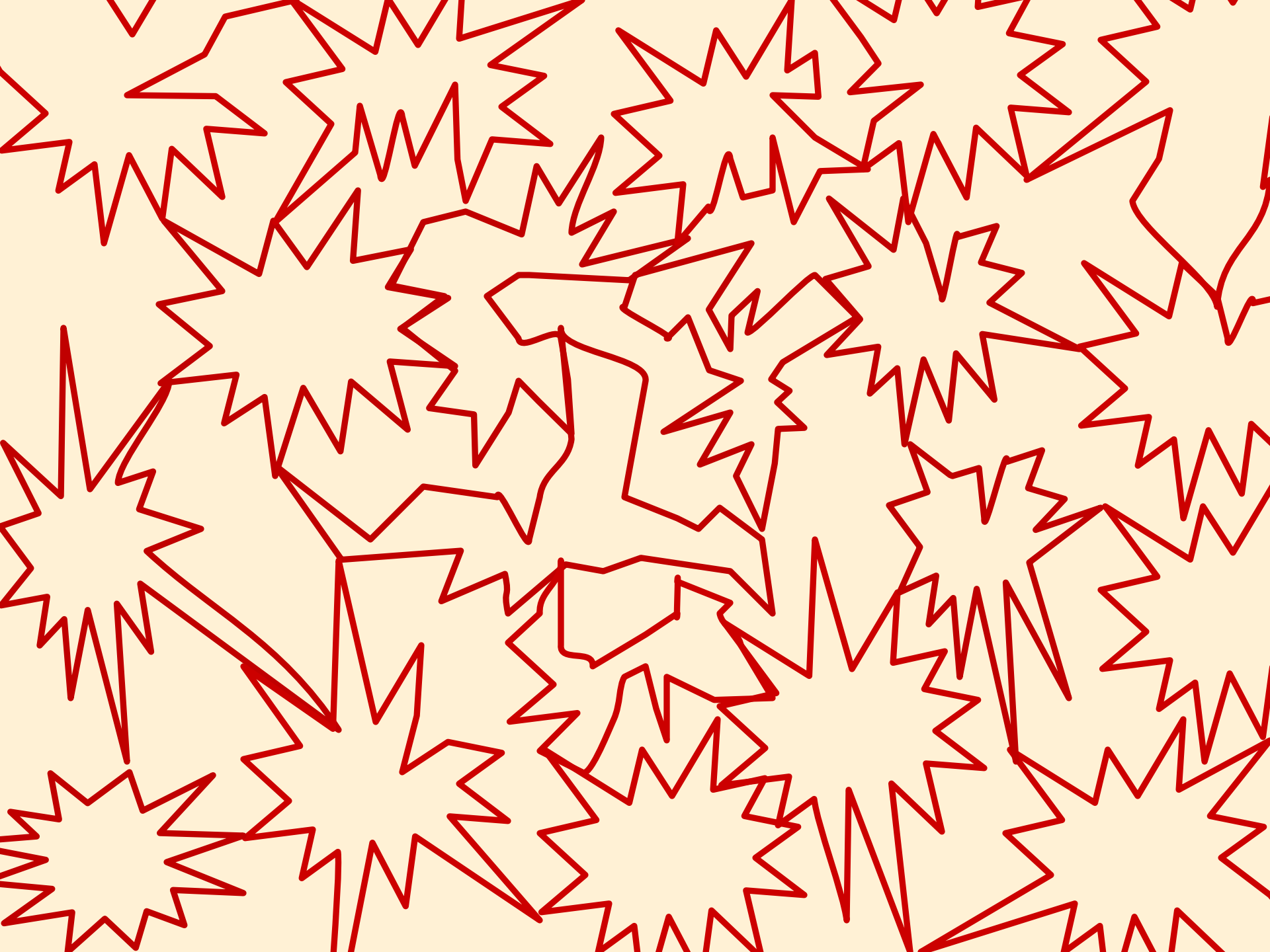
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- 4. Arterioles**
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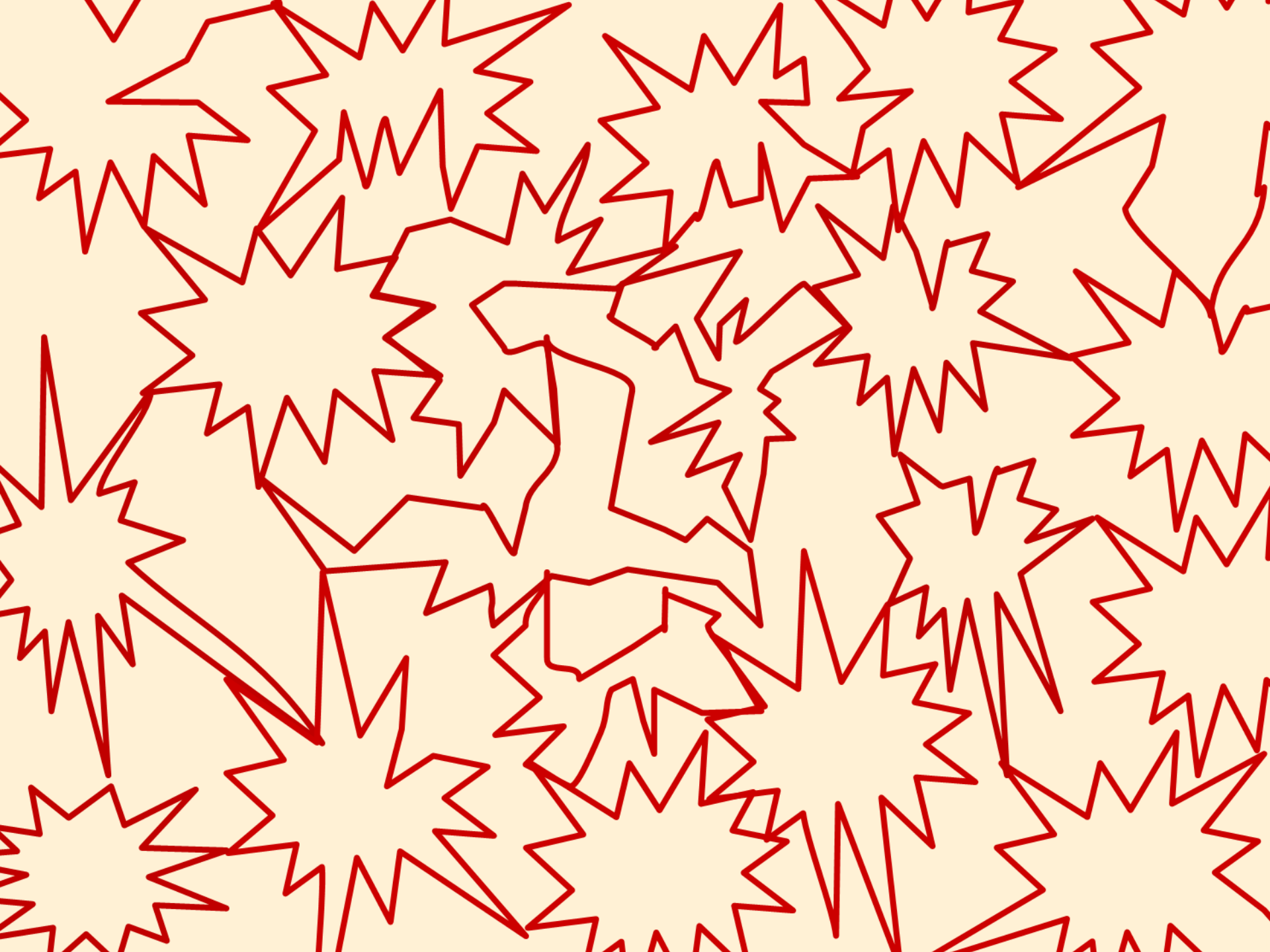
## ANATOMICAL BASIS FOR THE DEVELOPMENT OF LIVEDO RETICULARIS

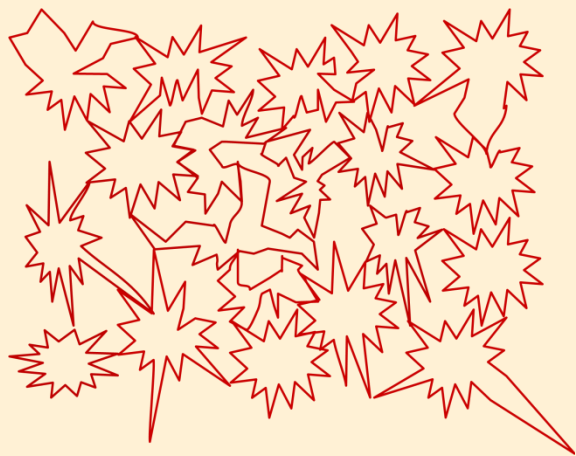
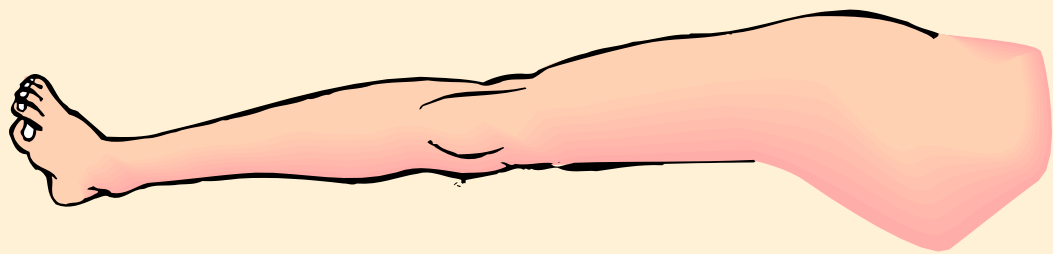


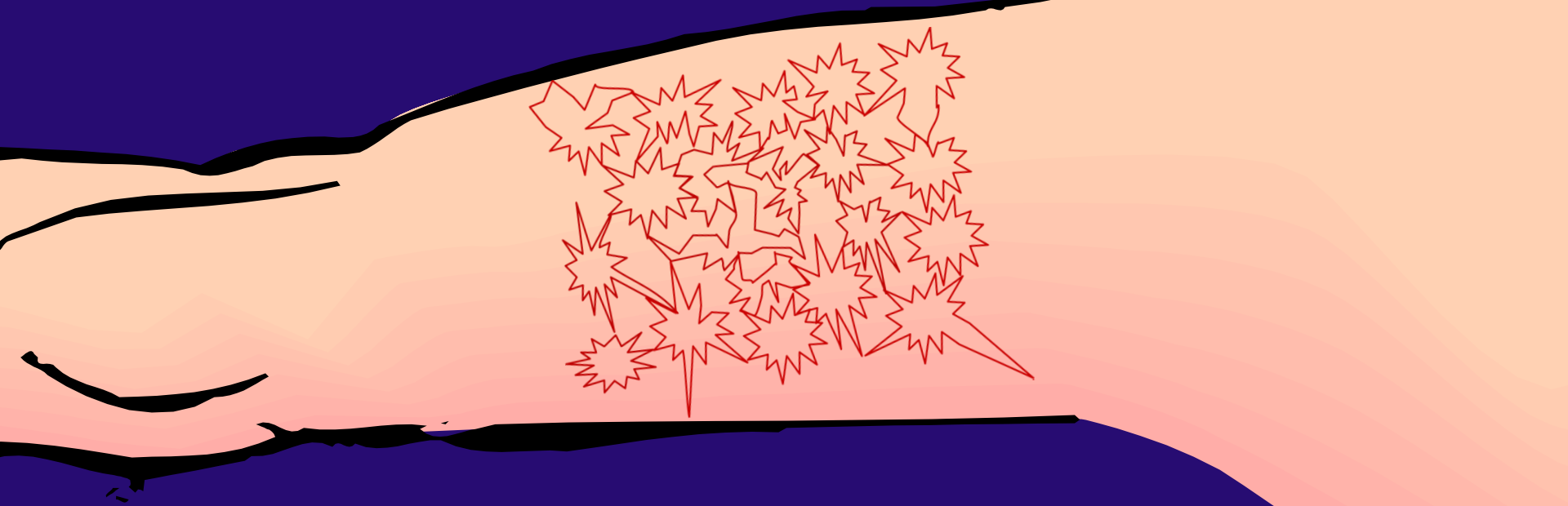










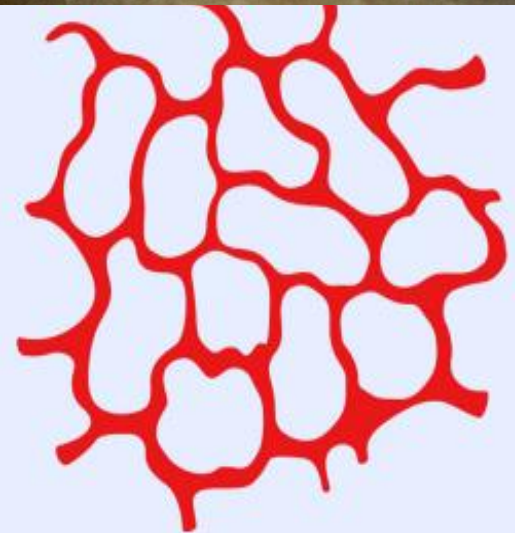
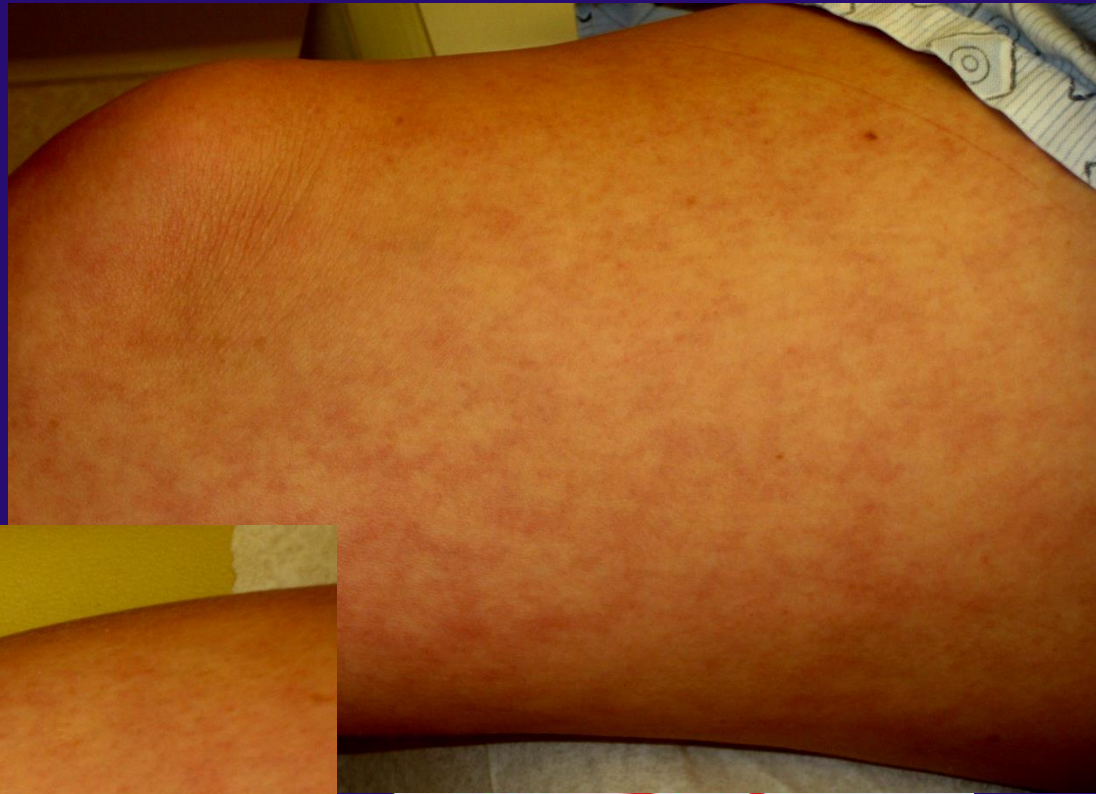


# 2 potential problems with this system

## 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

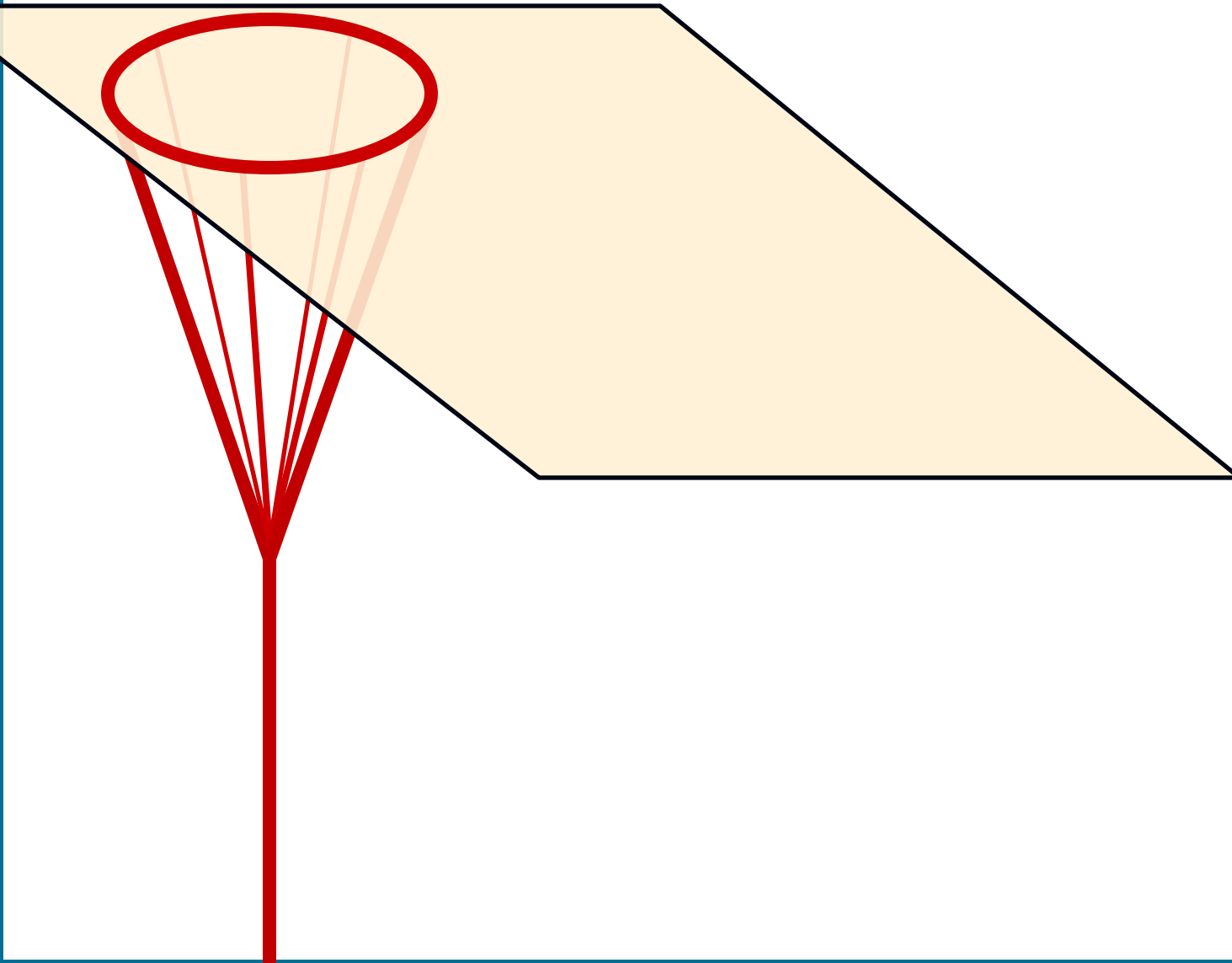


## Problem 2:

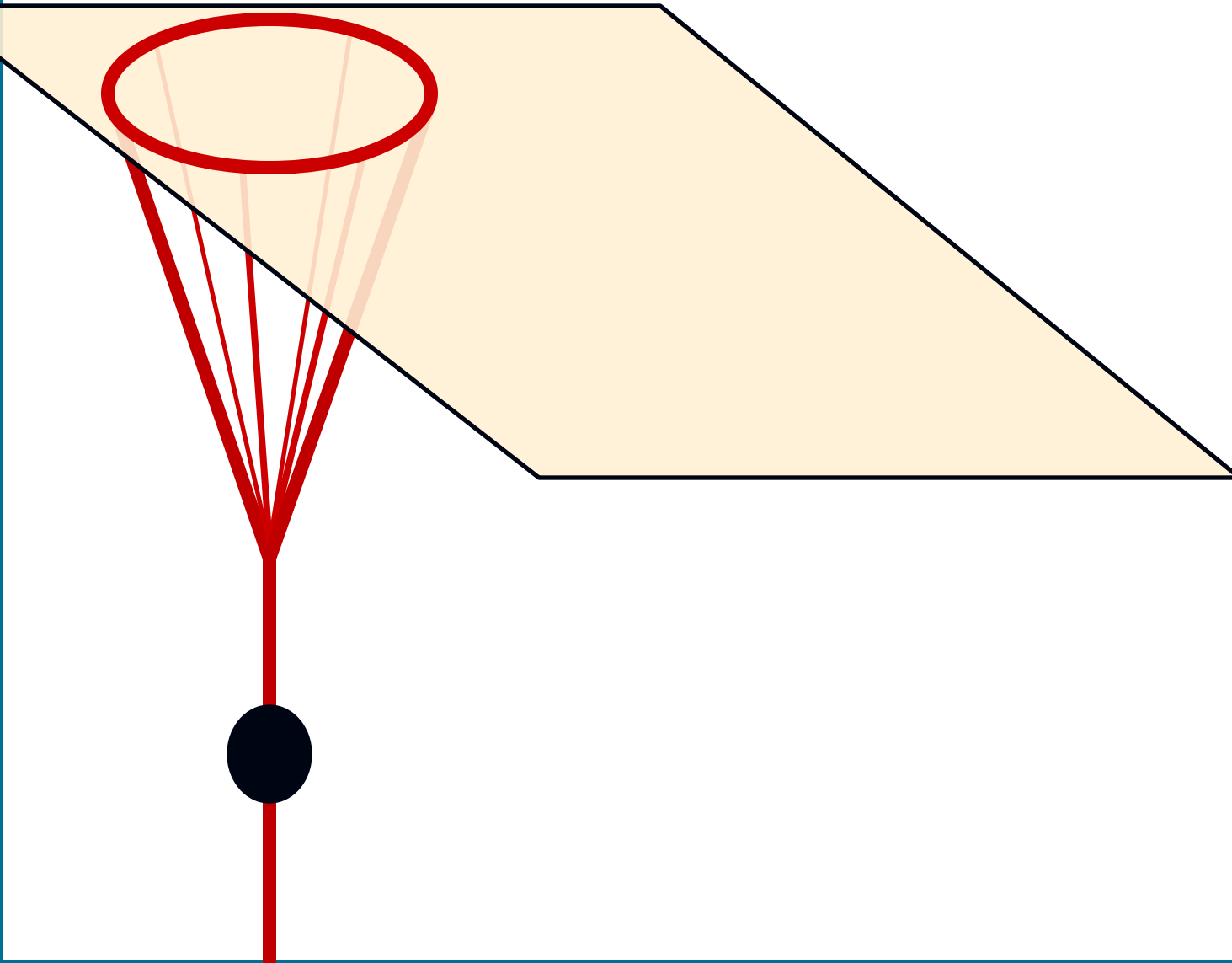
### Retiform Purpura

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

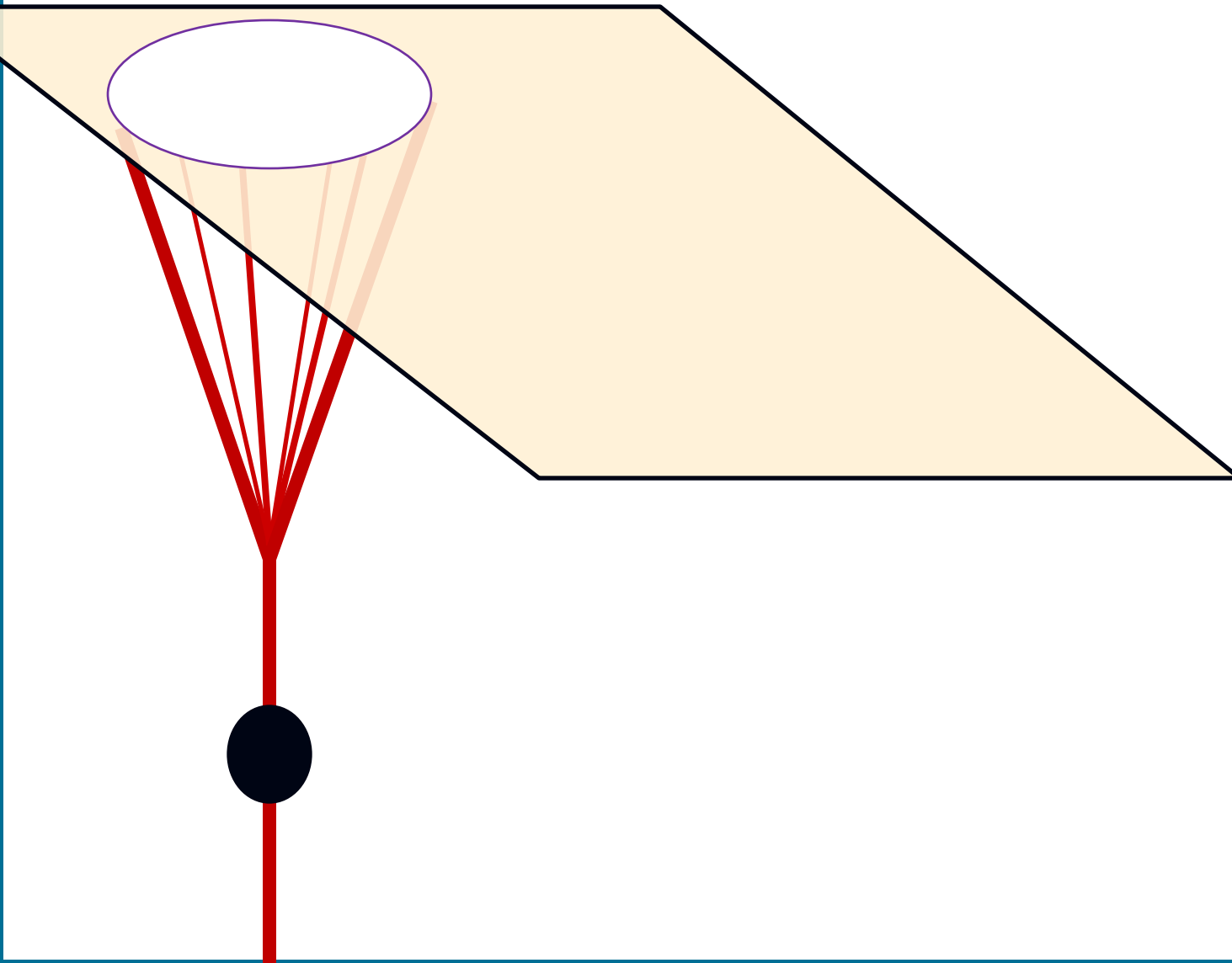
# Retiform Purpura



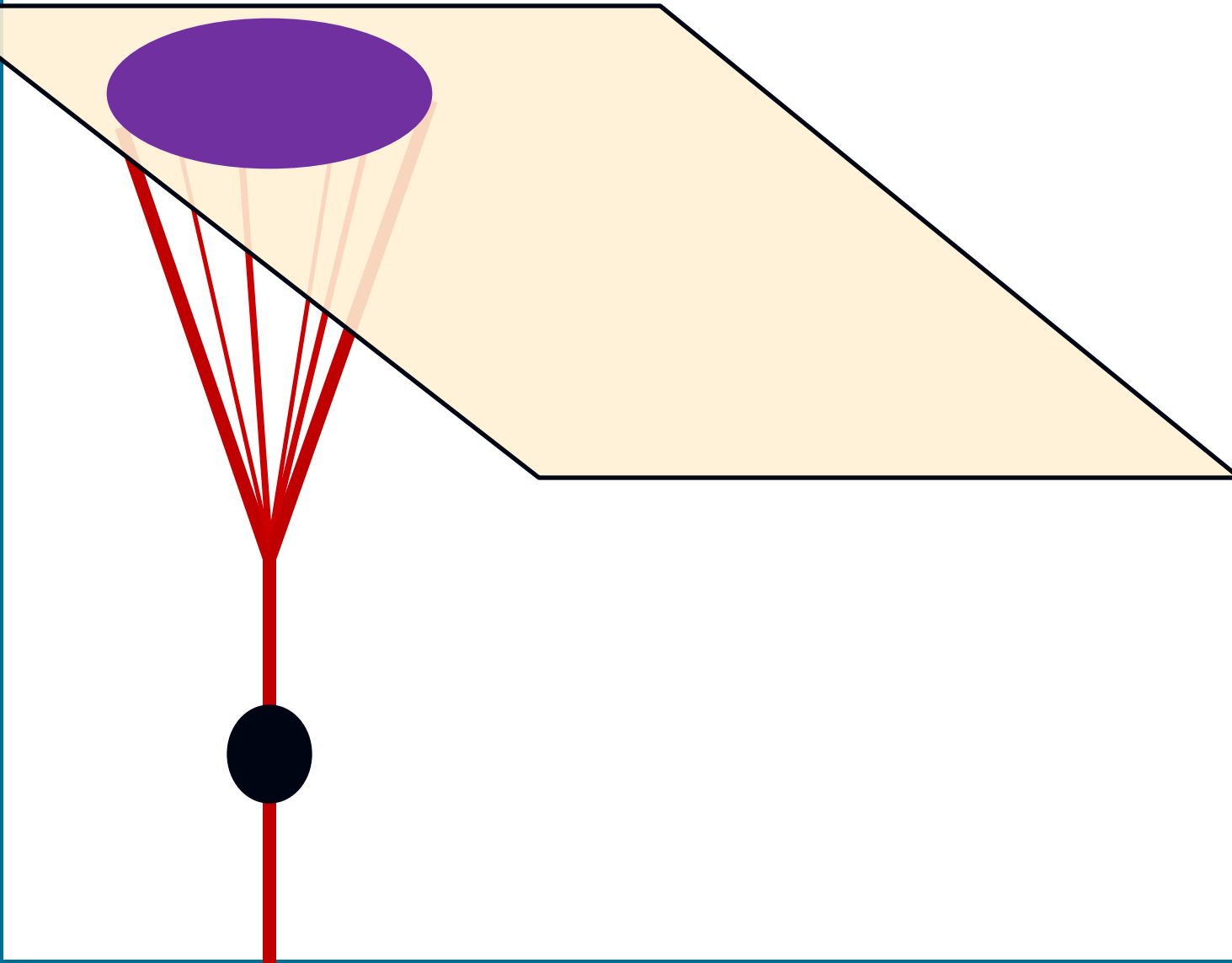
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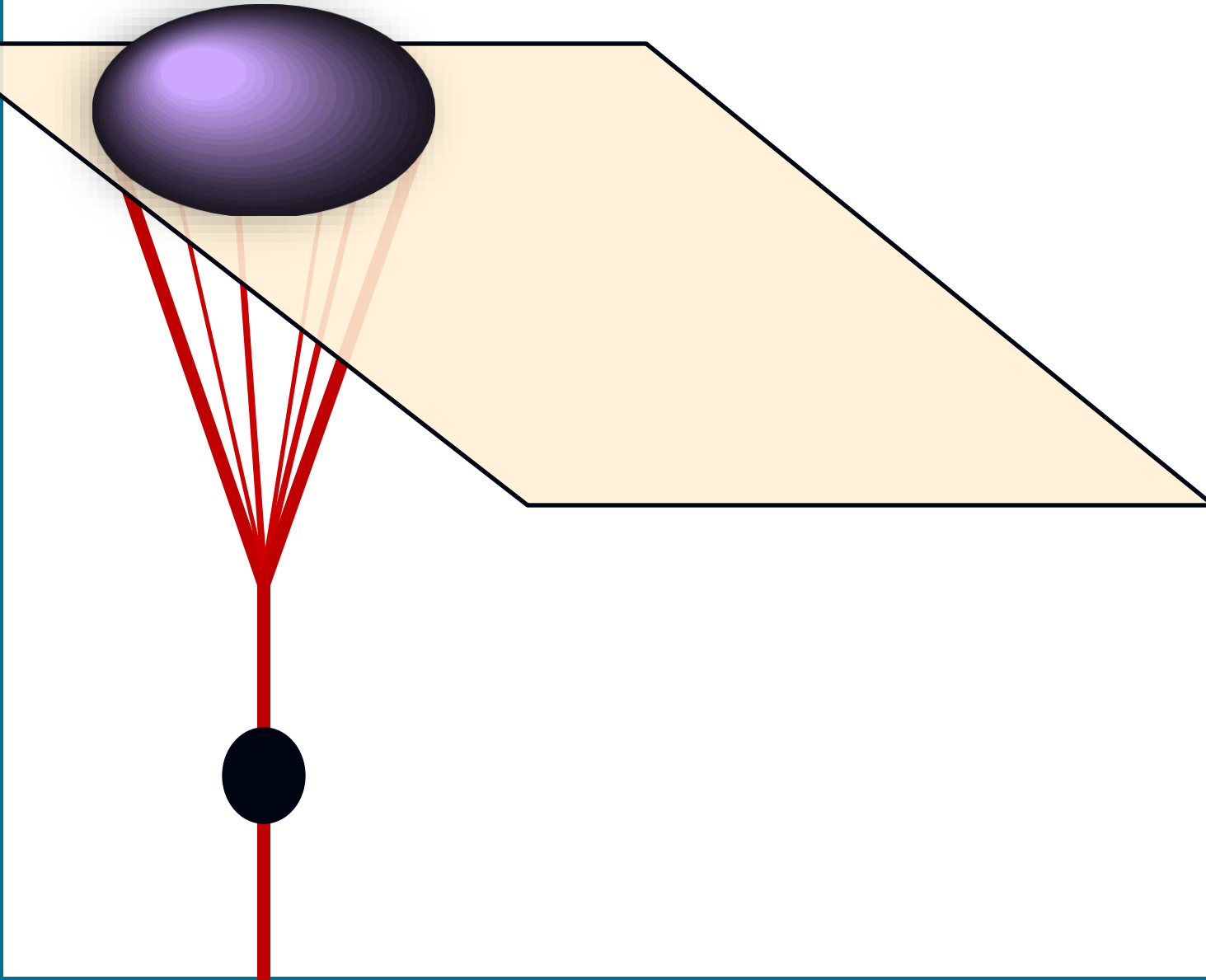
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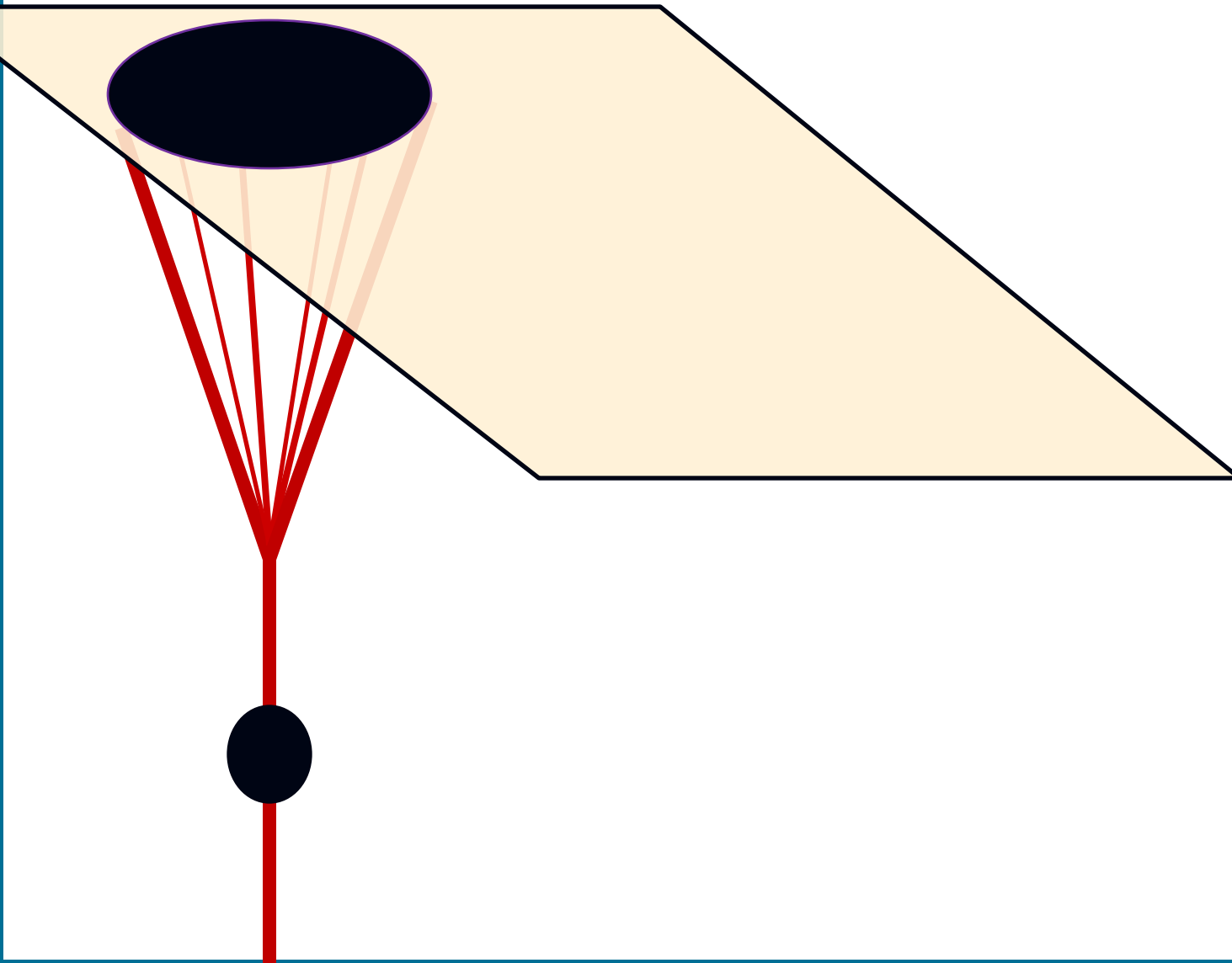
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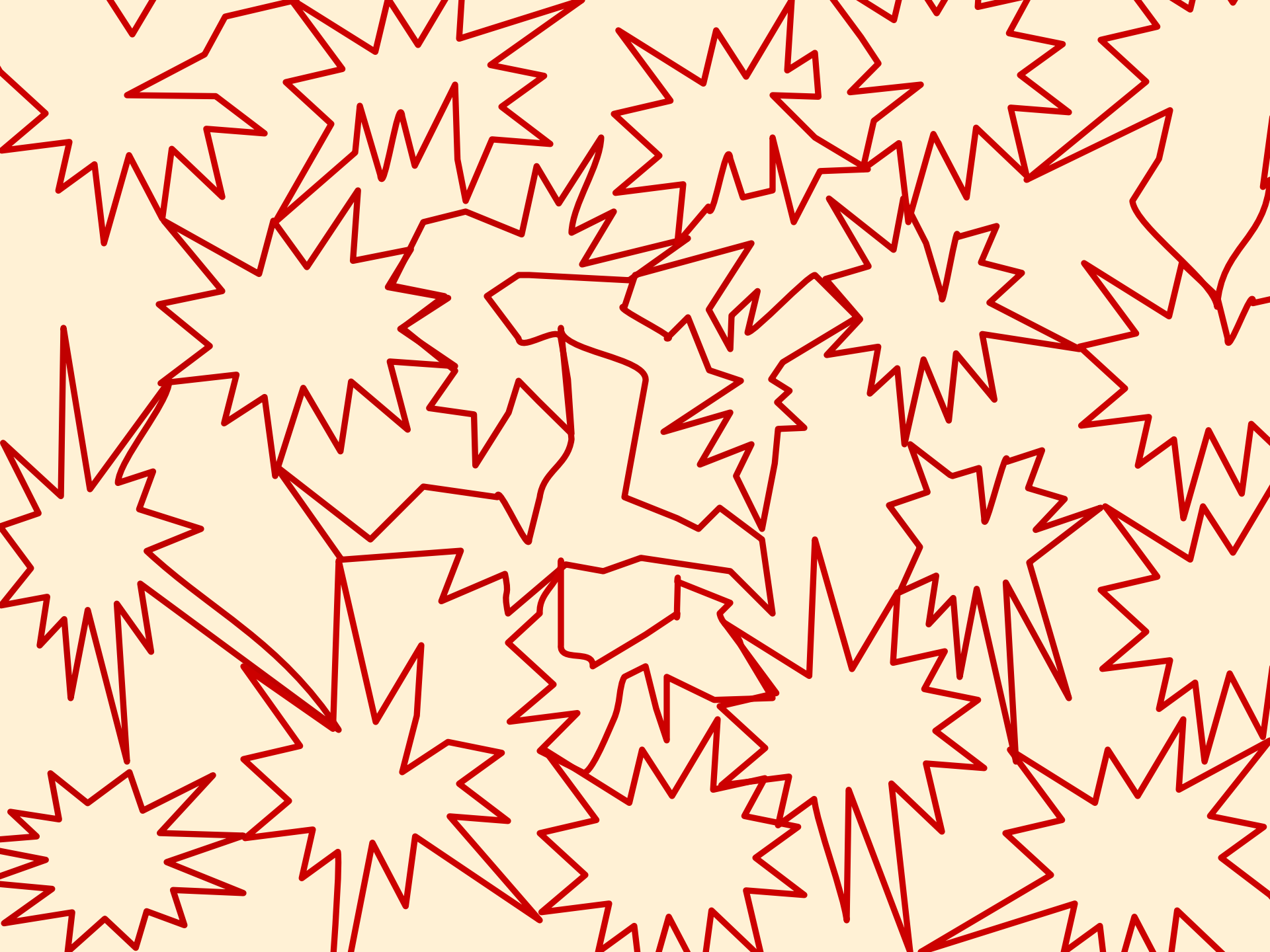


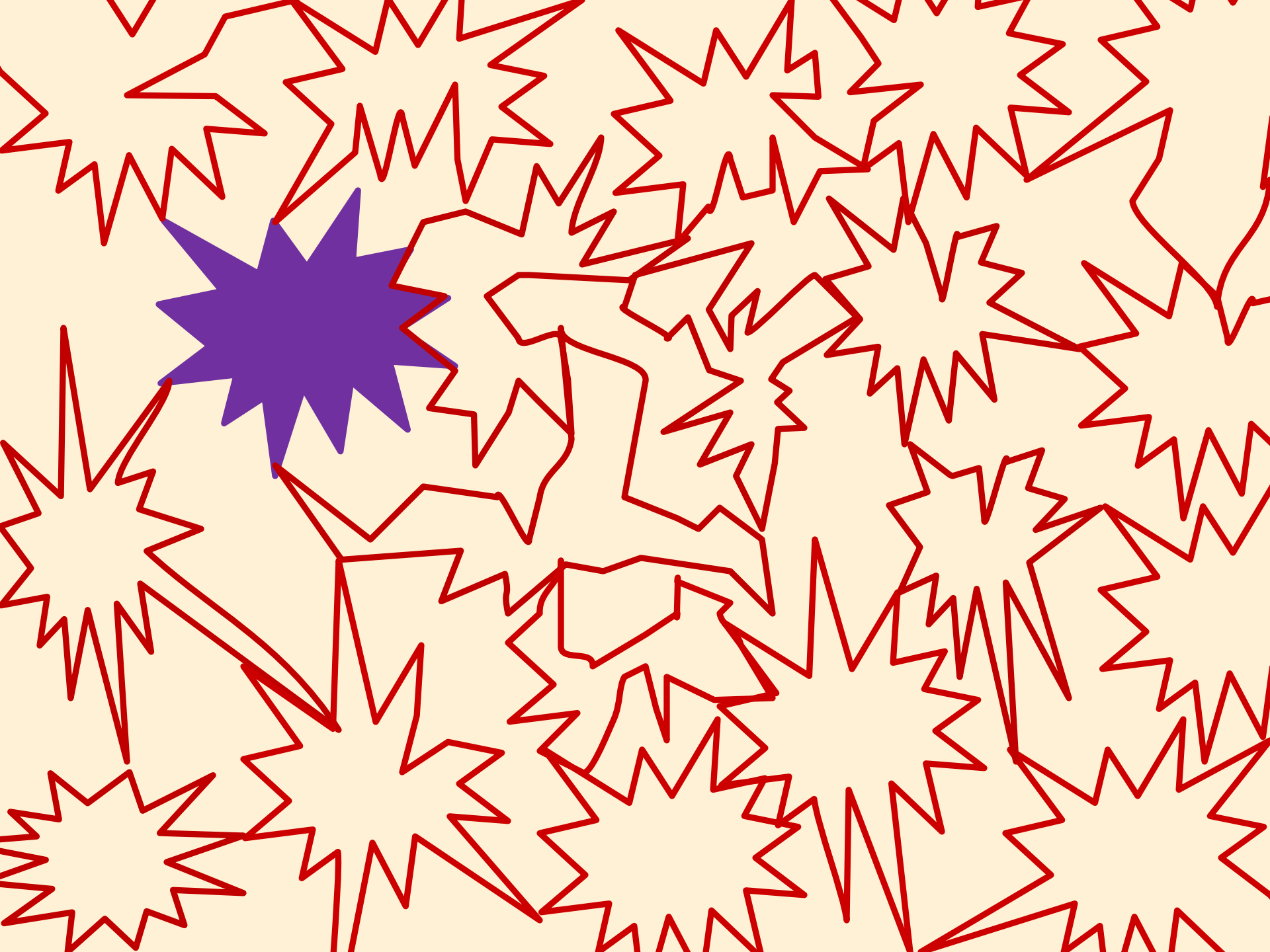
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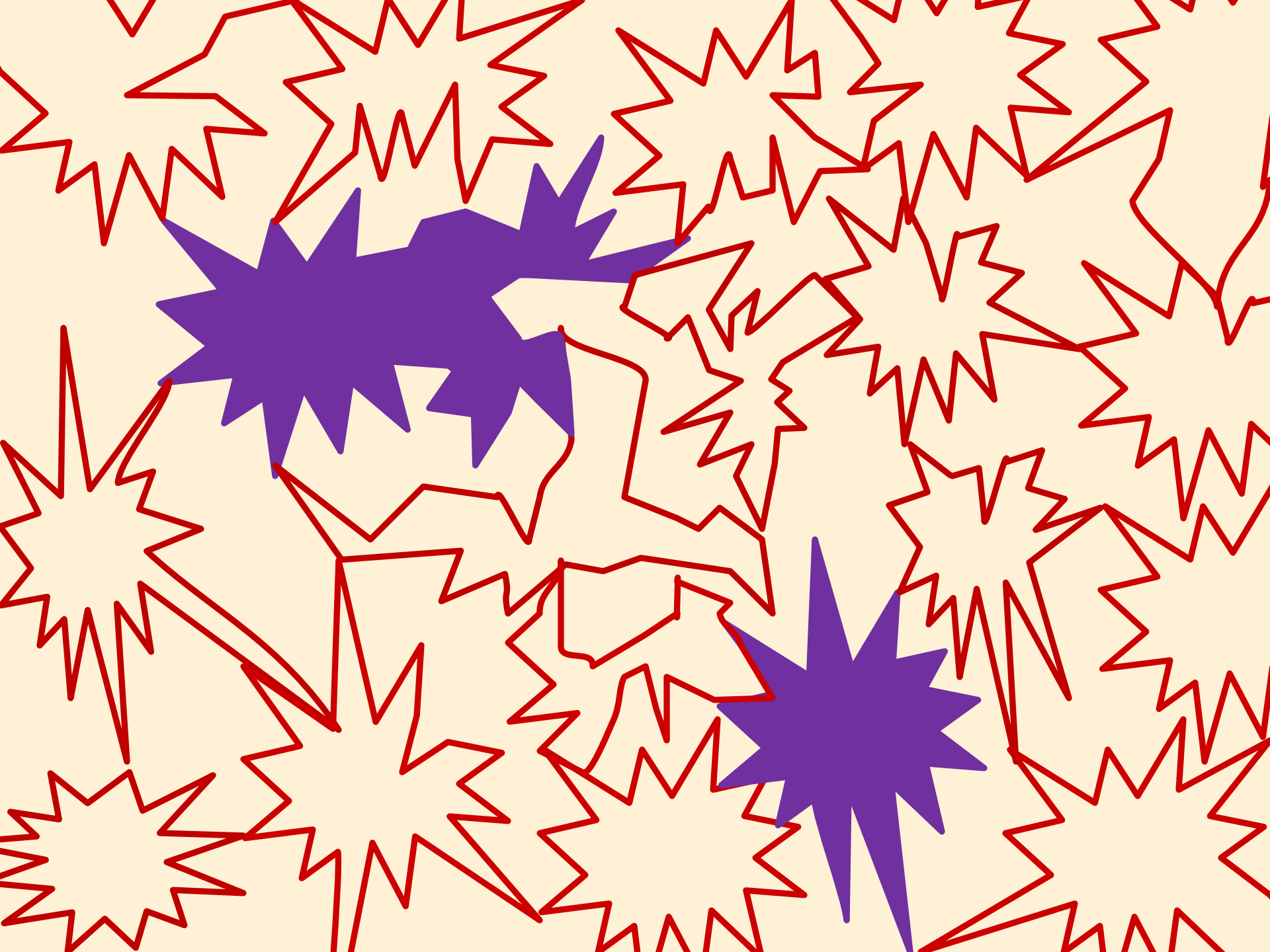


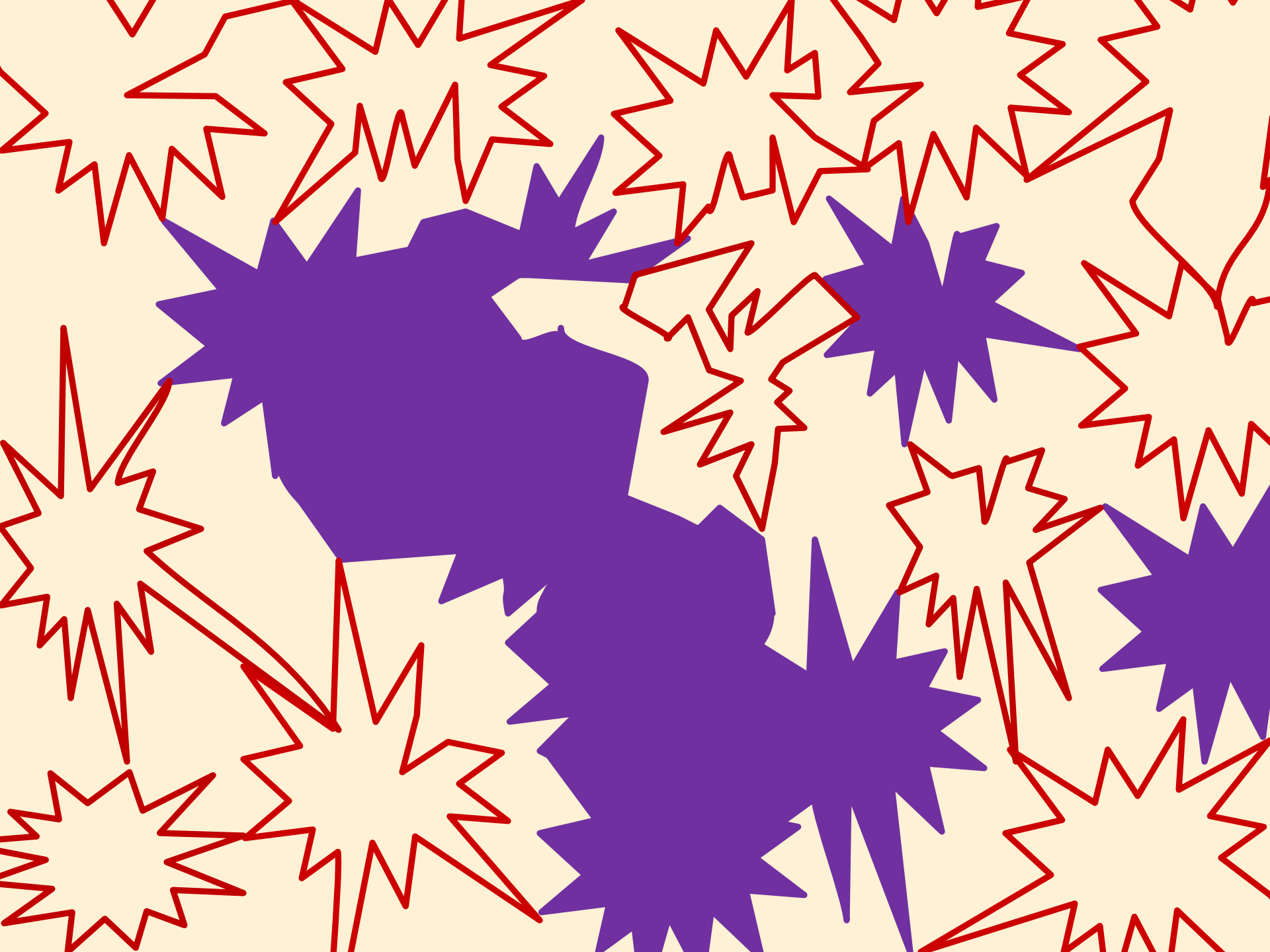
# Retiform Purpura











# Retiform Purpura

(with necrosis)







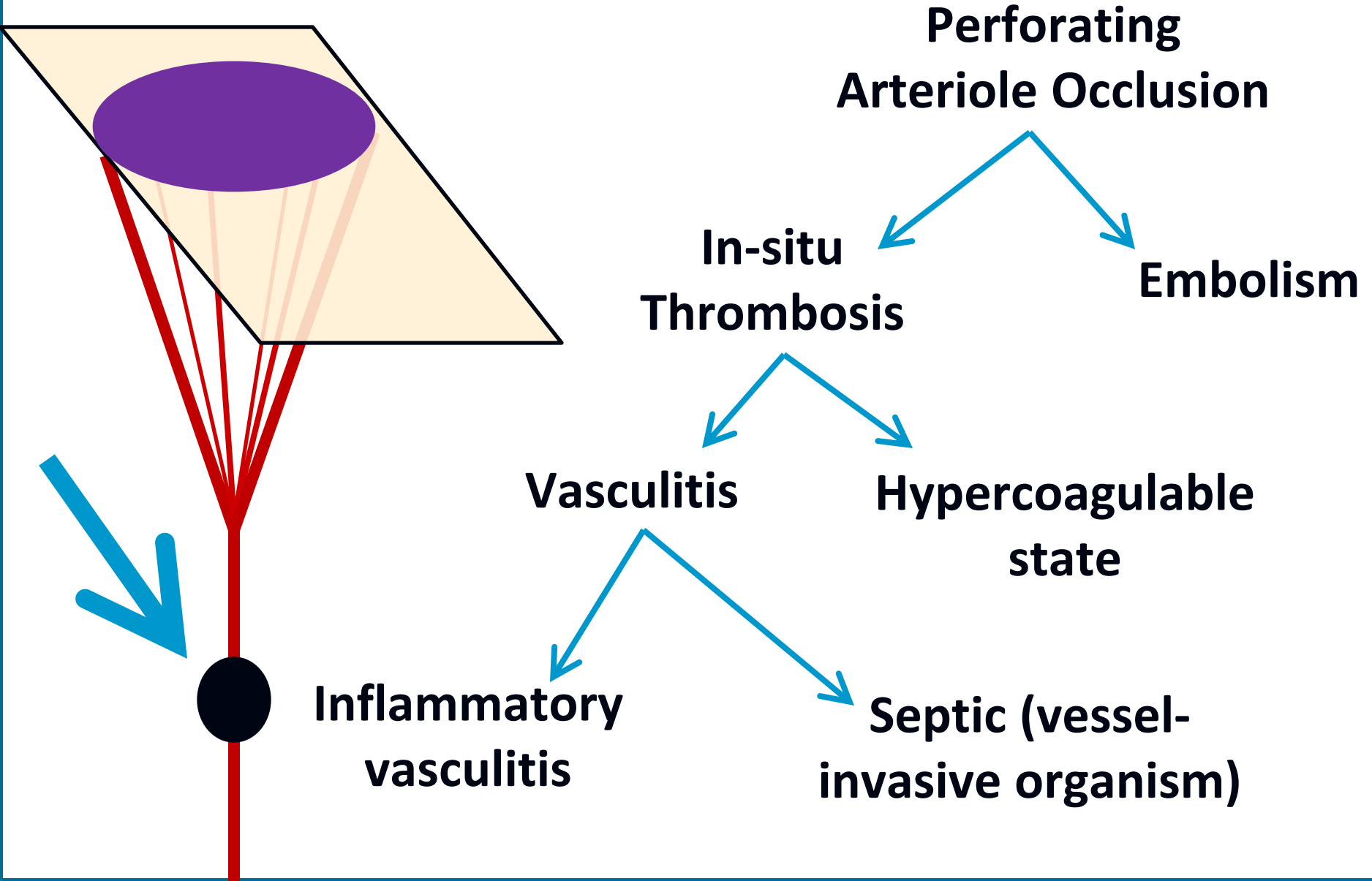


# Case Details

- PMH: Systemic lupus, lupus nephritis
- Meds: Mycophenolate mofetil, prednisone
- ED presentation:
  - Vitals: **T104.6**, **P140s**, **SBPs 80s**
  - Unresponsive, rash on right lower extremity
- 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)

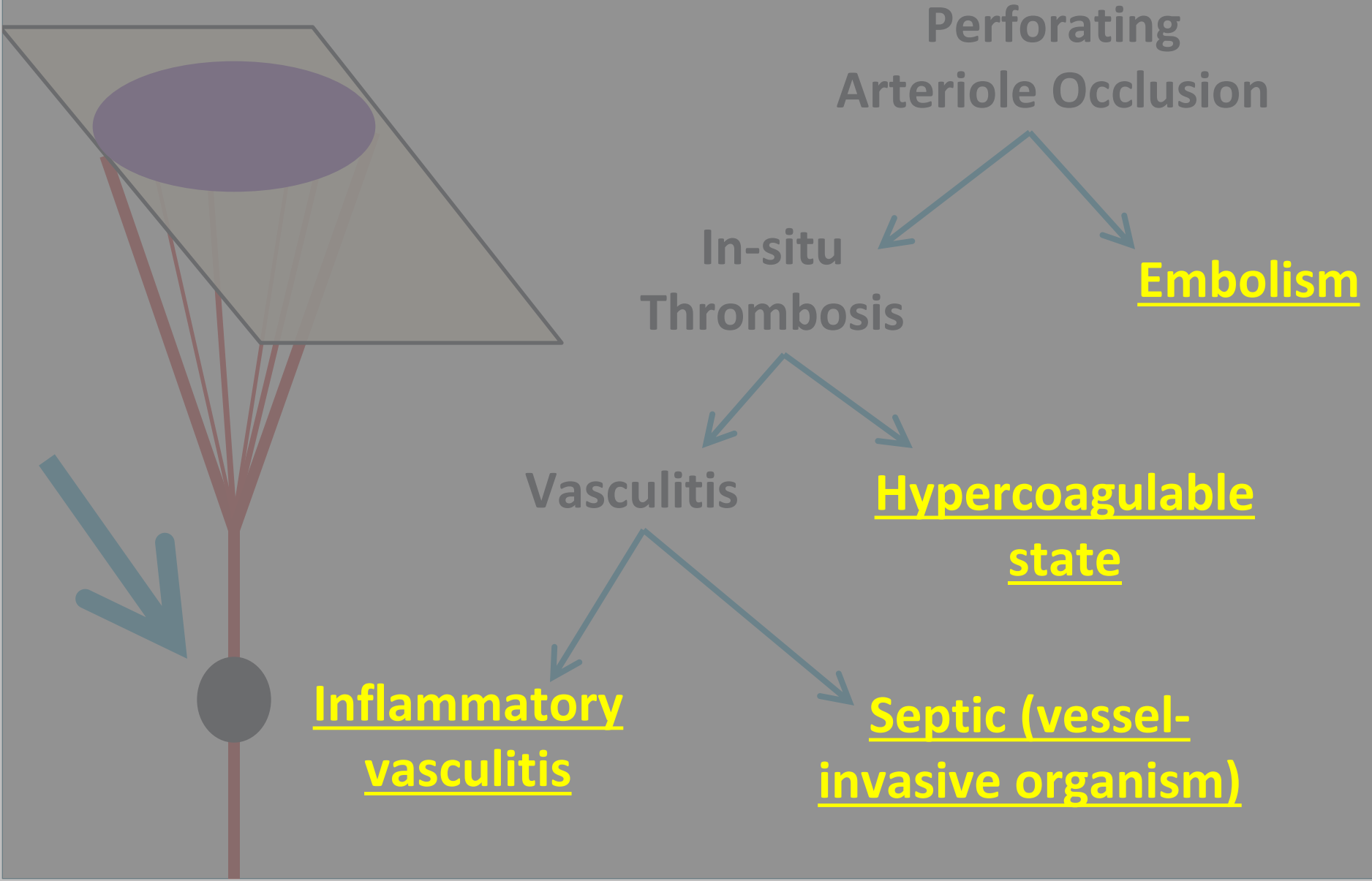
# Retiform Purpura:

## Differential Diagnosis



# Retiform Purpura:

## Differential Diagnosis



# Retiform Purpura: Select Differential Diagnosis

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

# **Please note:**

## **(regarding retiform purpura)**

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

# Retiform Purpura: Select Differential Diagnosis

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

**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

# More faces of Retiform Purpura

















10/1/14  
LAW



# **Retiform Purpura**

## **MOC REFLECTIVE STATEMENT**

- **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
- Other important physical exam features
  - Symptoms: Pruritic, non-tender
  - Lines/ geometric shapes









# Allergic Contact Dermatitis

## MOC REFLECTIVE STATEMENT

- Impetigo in an adult should prompt inquiry into underlying cause, such as contact dermatitis
- Allergic contact dermatitis is usually not tender
- Triple Antibiotic Ointment is a common cause of allergic contact dermatitis

# Take-Home Points

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

# Thank you

- Course organizers
- My patients who allowed me to photograph them to benefit others

# Key References

- 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.
- 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* (Advanced Access June 18, 2014)



# 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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# Case

18 yo female transferred from OSH for 2 complaints:



# Case

18 yo female transferred from OSH for 2 complaints:



**POLL: Diagnosis?**

# Scabies: Diagnostic Pearls

**Burrows**  
*and the*  
**“Delta Wing Sign”**

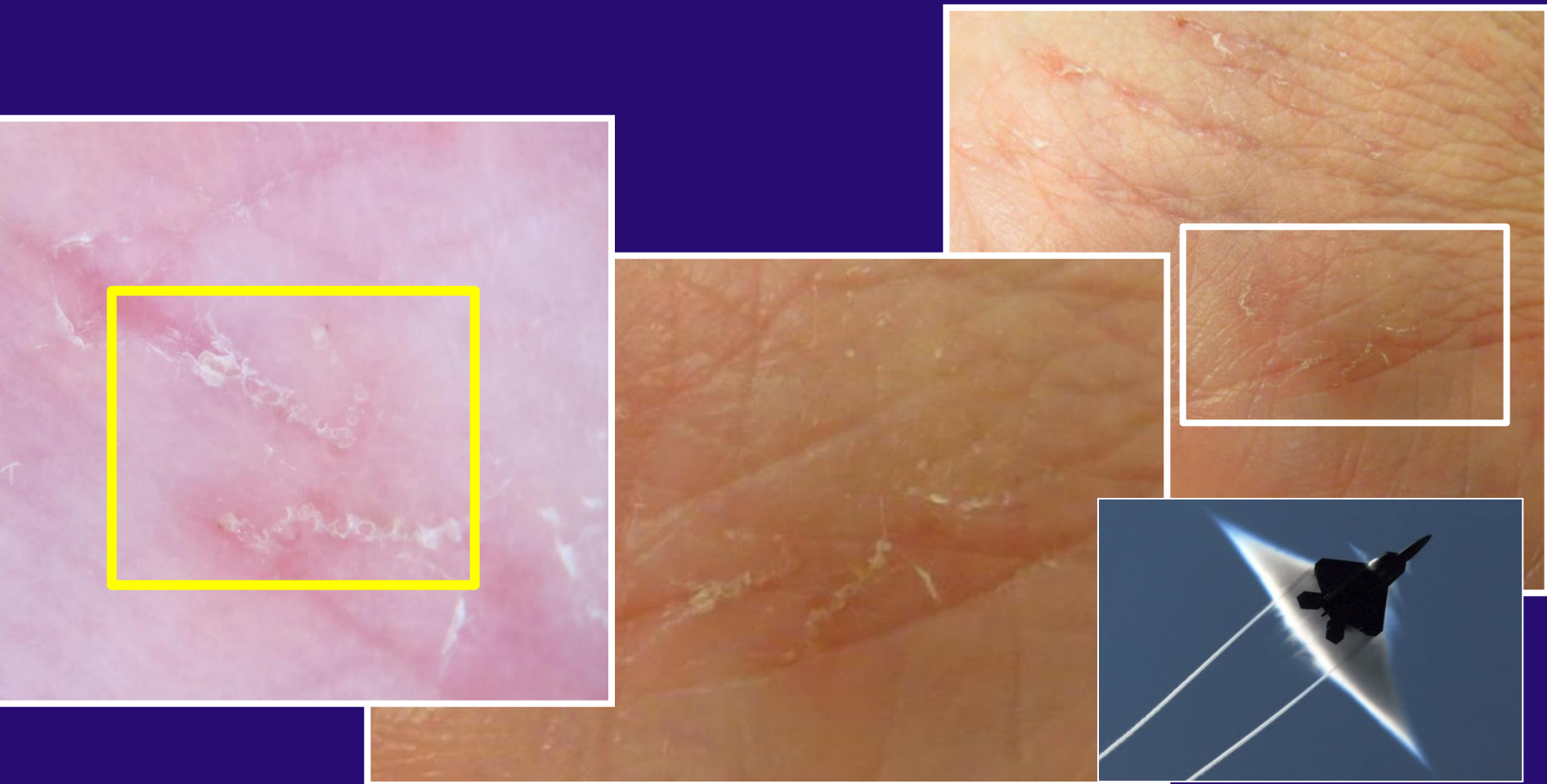


# Scabies: Diagnostic Pearls

**Burrows**  
*and the*  
**“Delta Wing Sign”**



# Scabies: Diagnostic Pearls

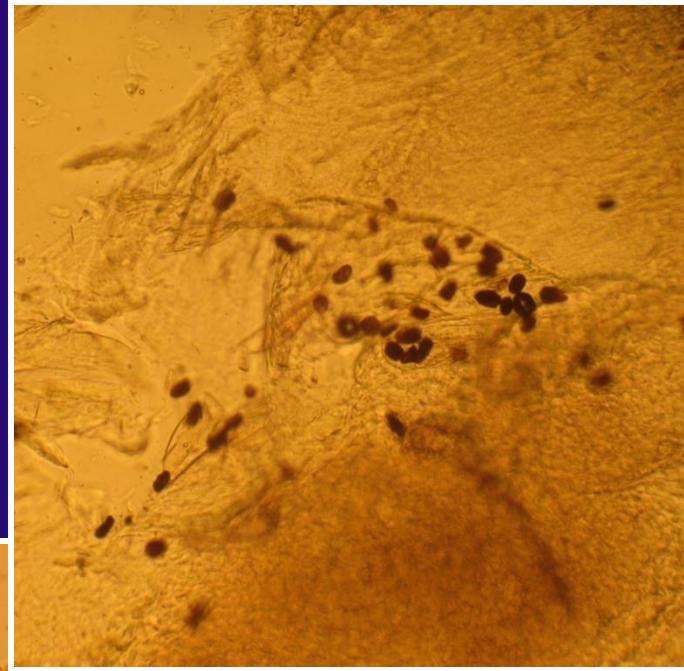
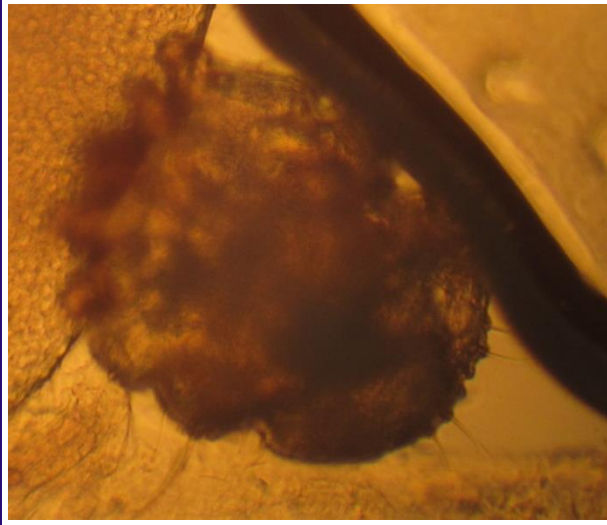


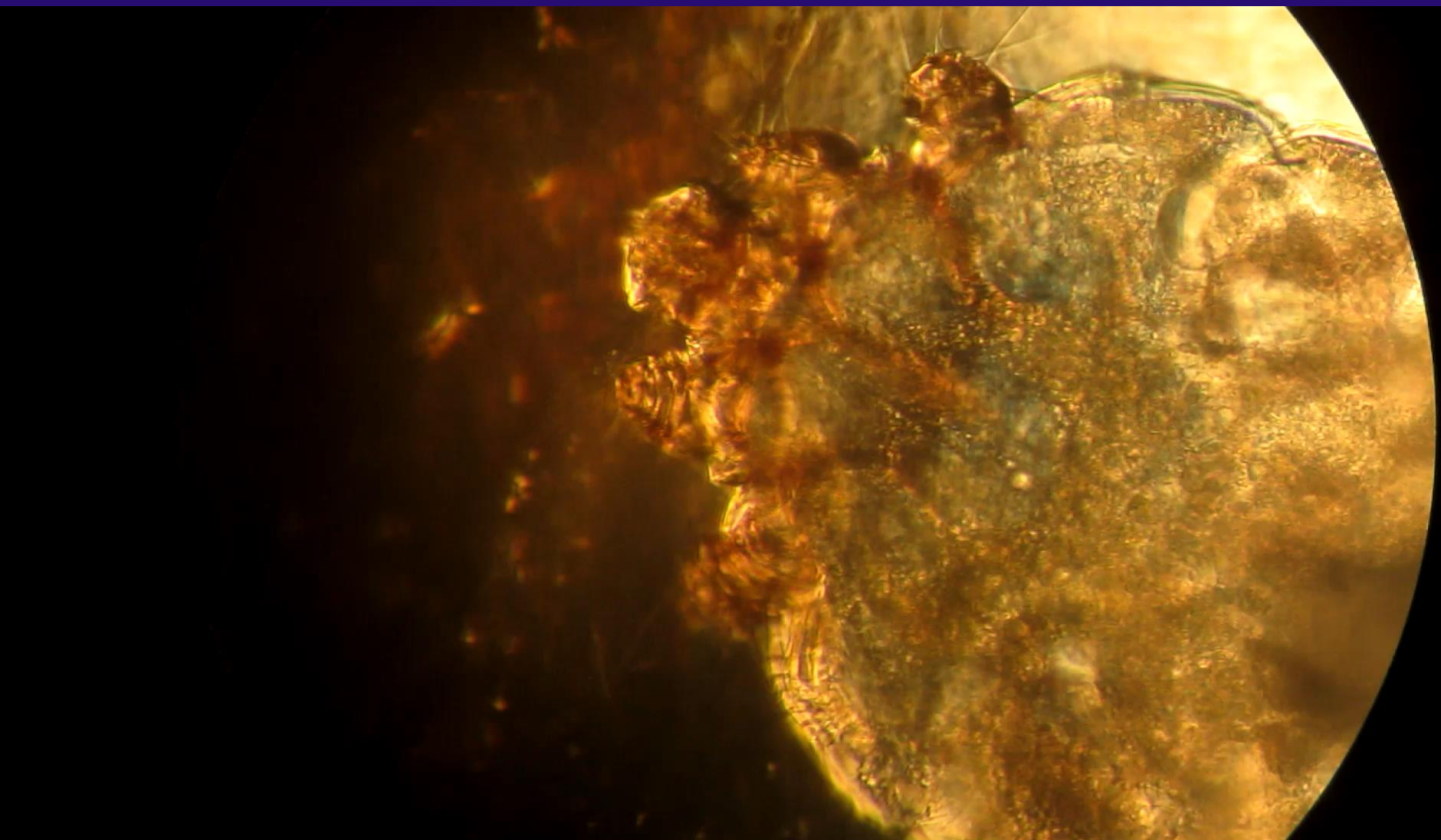
\*Argenziano G, Fabbrocini G, Delfino M. Epiluminescence Microscopy: A New Approach to In Vivo Detection of *Sarcoptes scabiei*. *Arch Dermatol.* 1997;133(6):751–753.

# Scabies: Diagnostic Pearls



# Scabies: Diagnostic Pearls





# 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

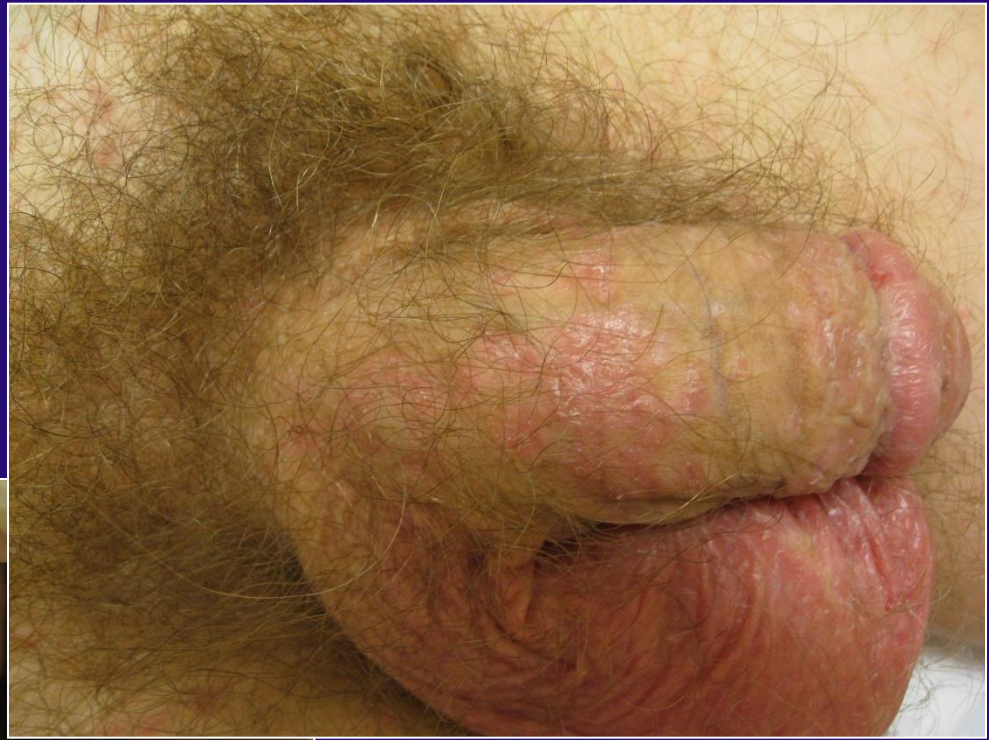


# Bonus Case (time permitting)

- 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



# Diagnosis?

- A. Syphilis
- B. Psoriasis
- C. Pityriasis rosea
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## INITIAL WORKUP

|                    |                                                                                                          |
|--------------------|----------------------------------------------------------------------------------------------------------|
| <b>RPR</b>         | <b>Negative</b>                                                                                          |
| <b>HIV ELISA</b>   | <b>Negative</b>                                                                                          |
| <b>Skin Biopsy</b> | <b>Lichenoid and superficial and deep lymphohistiocytic infiltrates with plasma cells and granulomas</b> |

Does this change anyone's mind?



# Diagnosis? (round 2)

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

| 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?

# Diagnosis? (round 2)

A. Syphilis!

B. Psoriasis

C. Pityriasis rosea

D. Measles

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

# Diagnosis? (round 2)

A. Syphilis!

B. Psoriasis

C. Pityriasis rosea

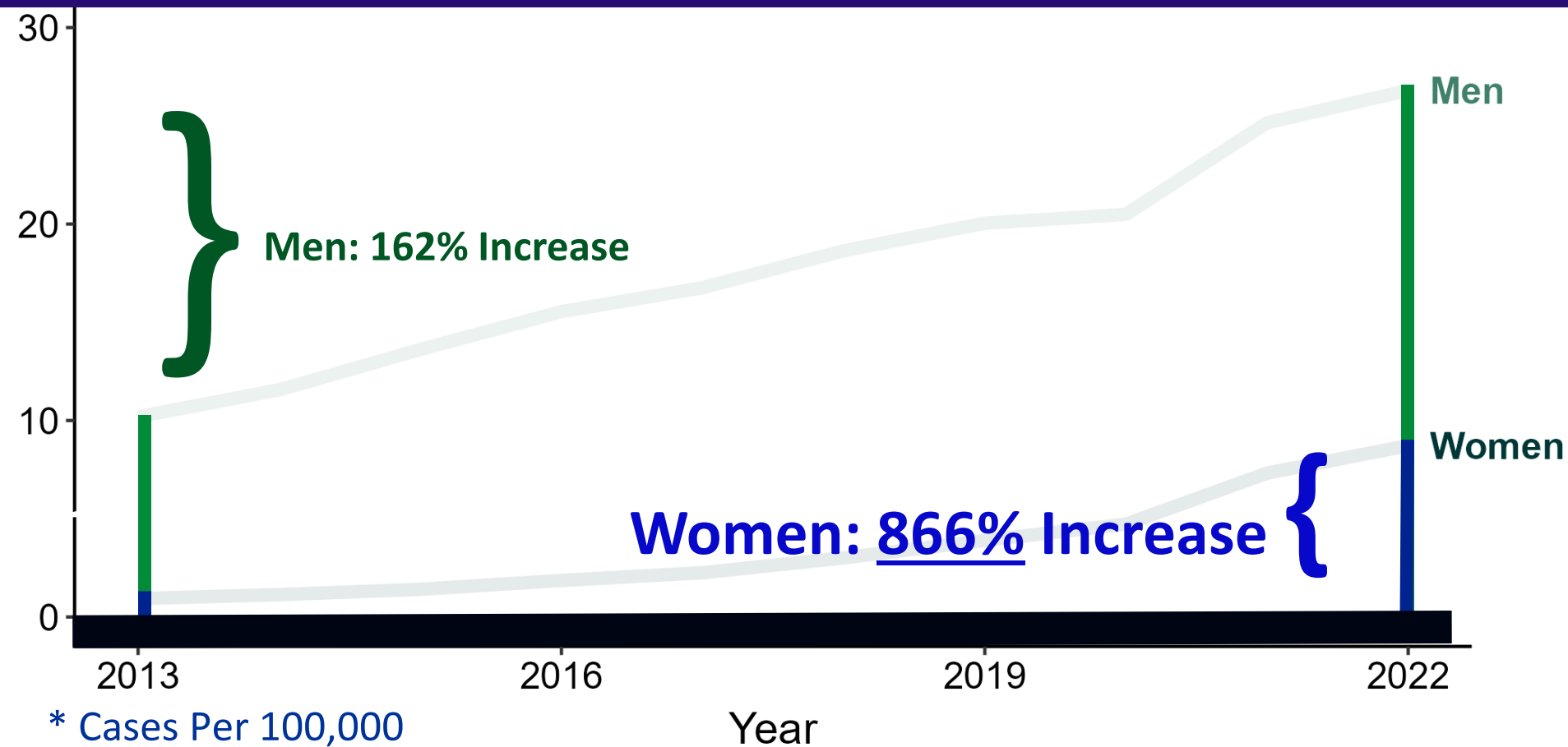
D. Measles

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

Why a false negative RPR?

But first, why revisit syphilis at all?

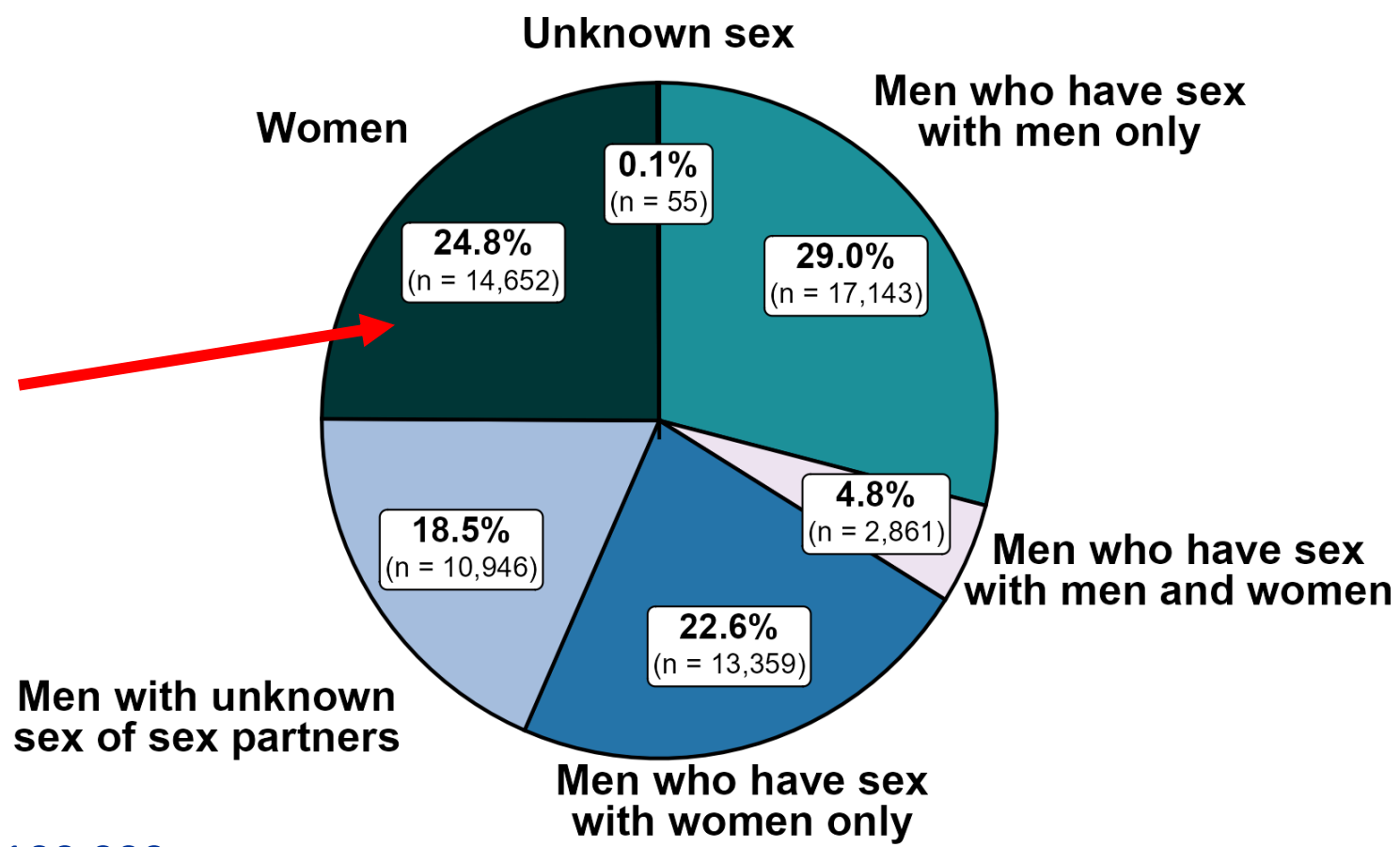
# Primary and Secondary Syphilis — Rates of Reported Cases by Sex, United States, 2013–2022



<https://wonder.cdc.gov/controller/datarequest/D128>

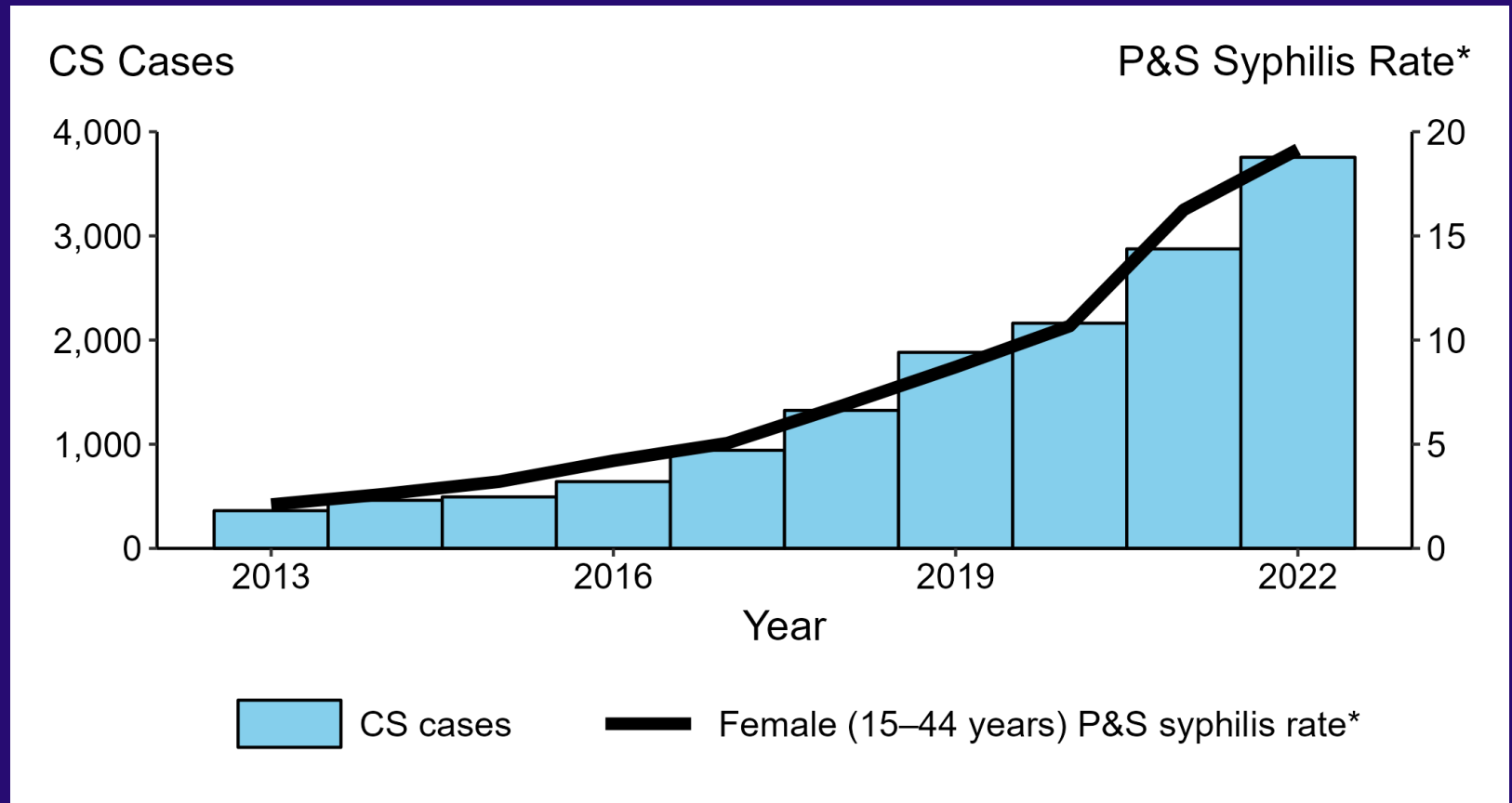
<https://www.cdc.gov/std/statistics/2022/default.htm>

# Primary and Secondary Syphilis — Rates of Reported Cases by Sex, United States, 2010–2022



\* Per 100,000

# Congenital Syphilis (by Year of Birth) and Syphilis Among Females Aged 15–44 Years, United States, 2010–2012



\* Per 100,000

[www.cdc.gov/std/statistics/2022/data.zip](http://www.cdc.gov/std/statistics/2022/data.zip)

**ACRONYMS:** CS = Congenital syphilis; P&S = Primary and secondary syphilis

# Syphilis

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



# Diagnosis?

- A. Syphilis
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- C. Pityriasis rosea
- D. Measles

| INITIAL WORKUP |                                                                                                   |
|----------------|---------------------------------------------------------------------------------------------------|
| RPR            | Negative                                                                                          |
| HIV ELISA      | Negative                                                                                          |
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**Why a false negative RPR?**

# Prozone Phenomenon

- Non-treponemal tests (RPR, VDRL)
  - Treponeme incorporates and modifies host cardiolipin
  - Host produces antibodies to cardiolipin

# Prozone Phenomenon

- 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**

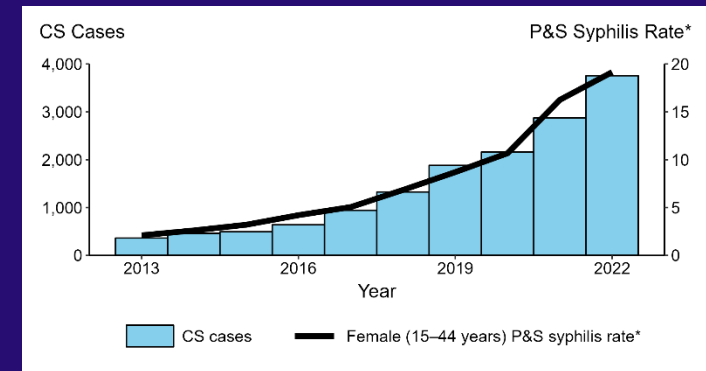
# Prozone Phenomenon

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)



**Congenital Syphilis (by Year of Birth) and Syphilis Among Females Aged 15–44 Years, U.S., 2010–2019**  
[www.cdc.gov/std/statistics/2022/data.zip](https://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

# Prozone Phenomenon

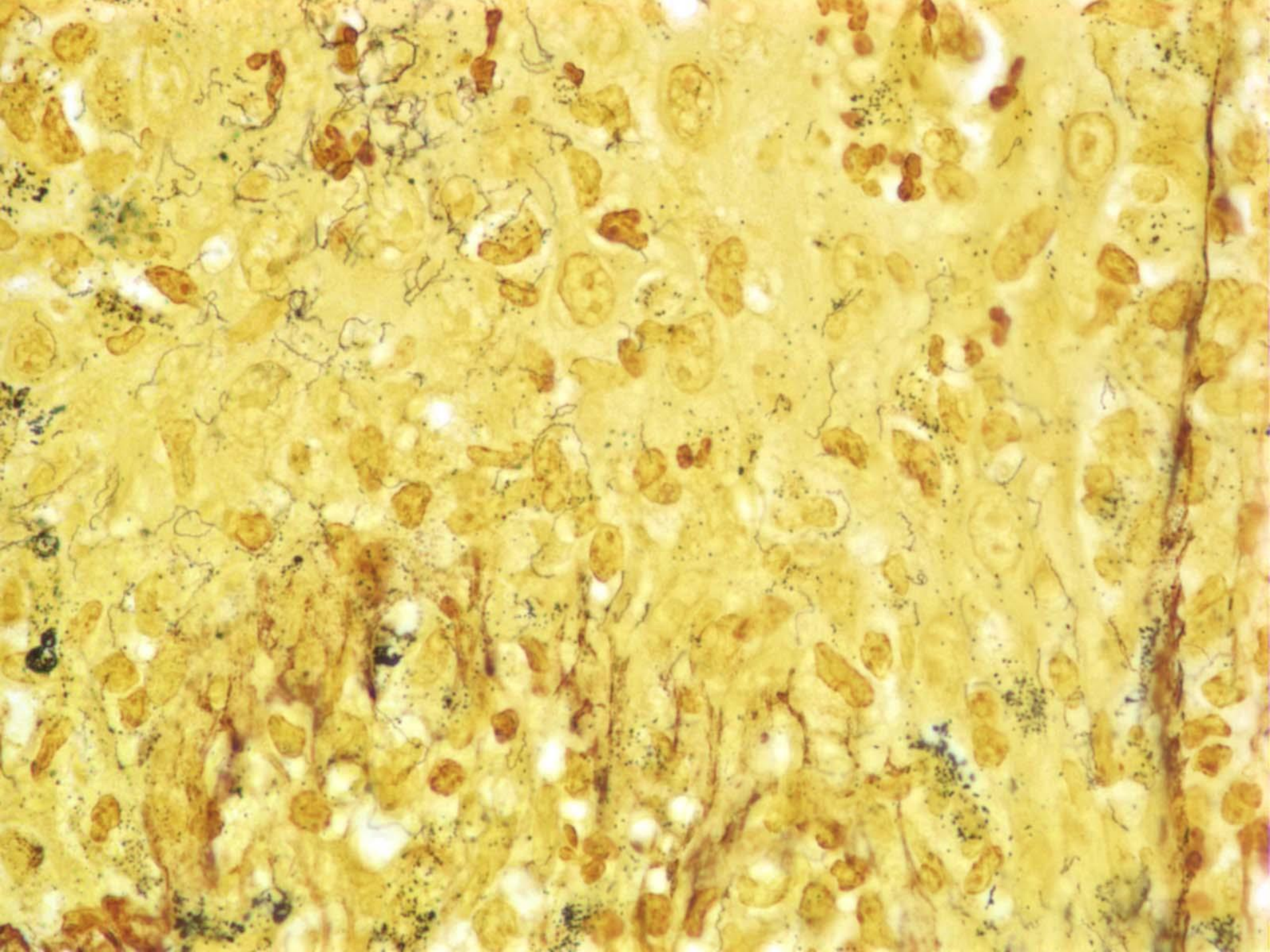
Prozone phenomenon: Notable antibody excess prevents agglutination

**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**

**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
  - Rupoid: “oyster shell”
  - Nodular
  - Lues maligna

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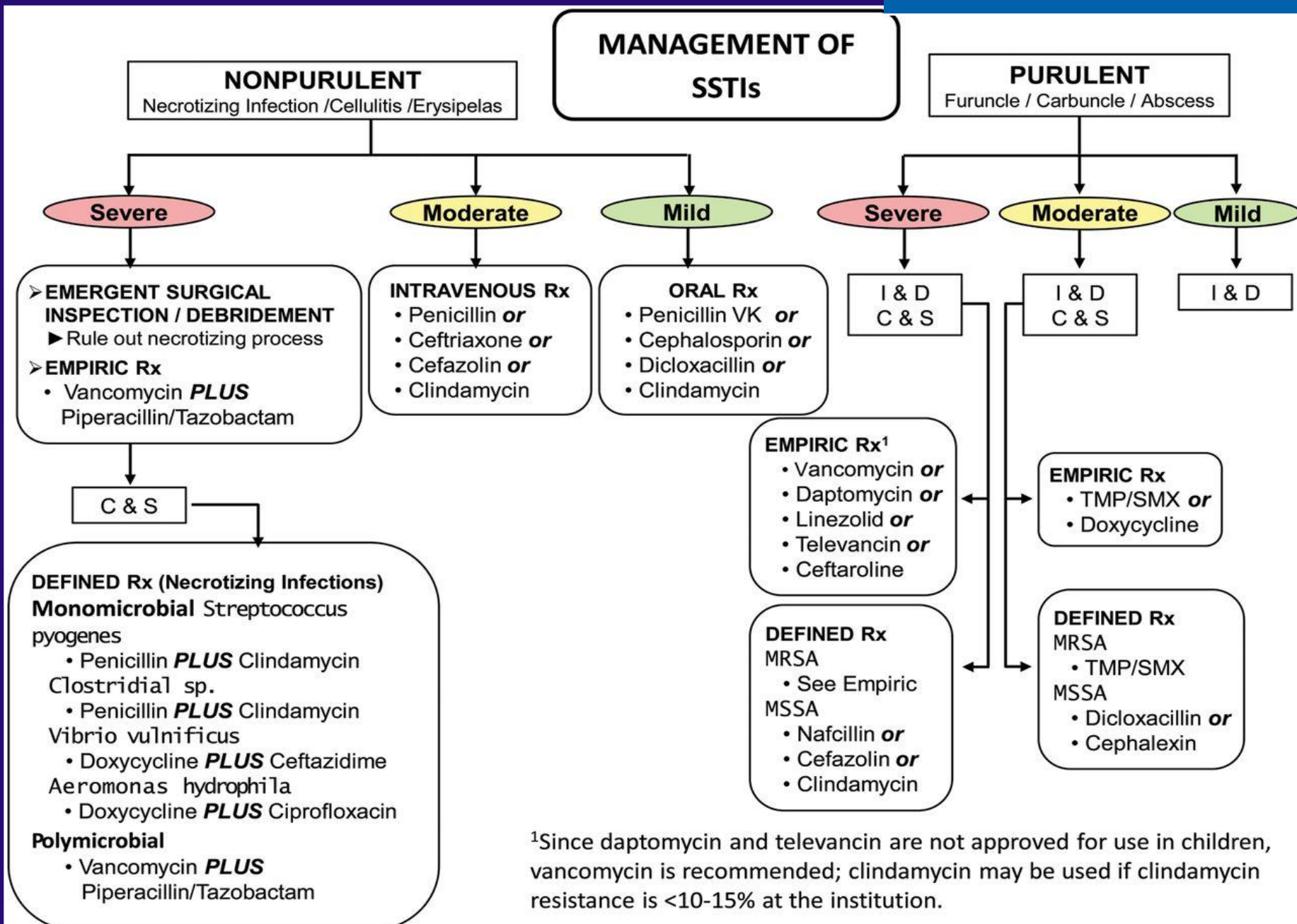
# Syphilis Key Points

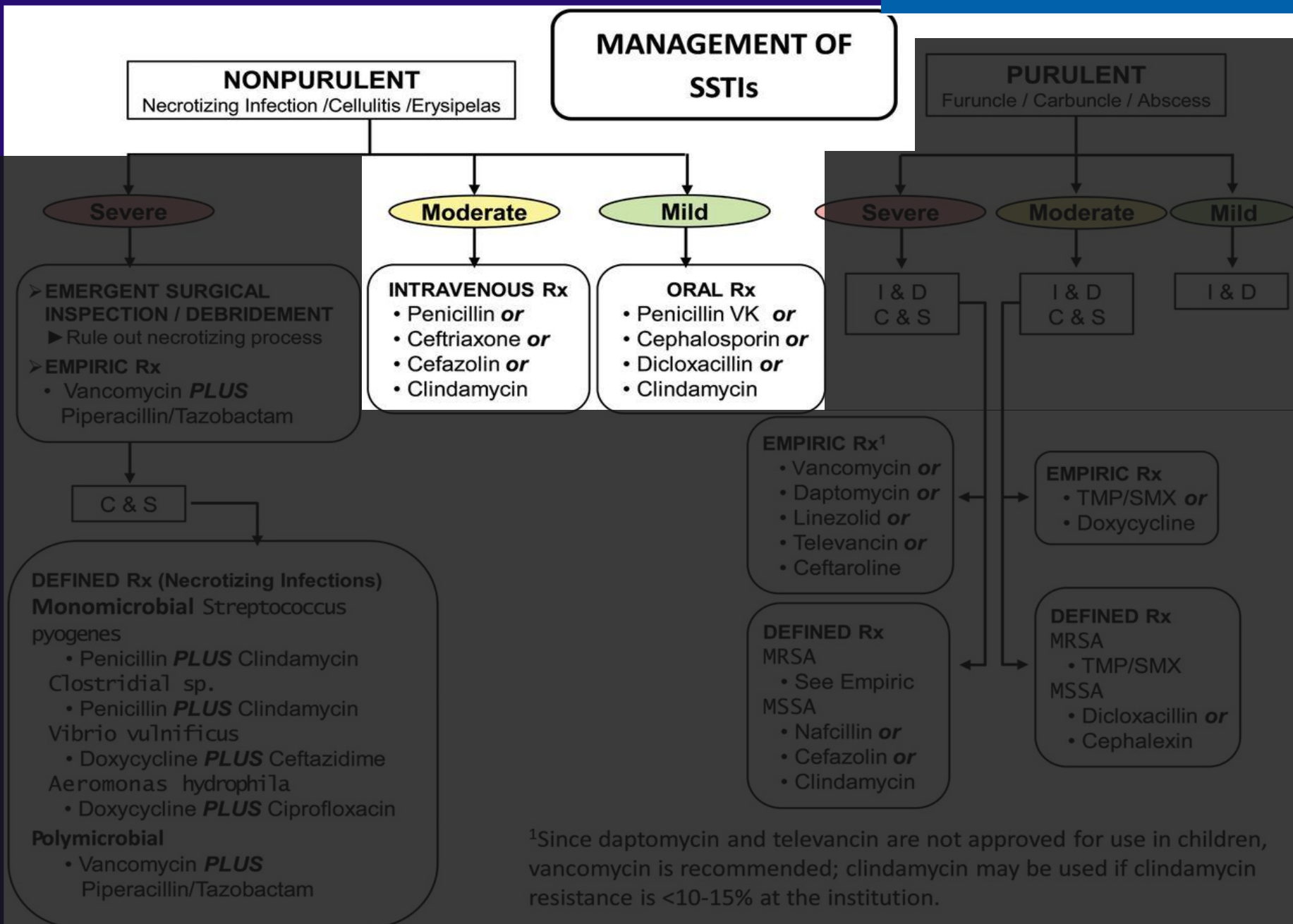
- Rates are rising, cases *are* being missed
- Presentations vary (of course)
- No test or testing algorithm is perfect
- Maintain a high index of suspicion & re-test if concerned



**IN CASE QUESTIONS ARISE:**

**Management of *Purulent* Skin  
Infections**





### MANAGEMENT OF SSTIs

#### NONPURULENT

Necrotizing Infection / Cellulitis / Erysipelas

#### Severe

- EMERGENT SURGICAL INSPECTION / DEBRIDEMENT
  - Rule out necrotizing process
- EMPIRIC Rx
  - Vancomycin *PLUS*

#### Moderate

##### INTRAVENOUS Rx

- Penicillin *or*
- Ceftriaxone *or*
- Cefazolin *or*
- Clindamycin

#### Mild

##### ORAL Rx

- Penicillin VK *or*
- Cephalosporin *or*
- Dicloxacillin *or*
- Clindamycin

#### PURULENT

Furuncle / Carbuncle / Abscess

#### Severe

I & D  
C & S

#### Moderate

I & D  
C & S

#### Mild

I & D

##### EMPIRIC Rx<sup>1</sup>

- Vancomycin *or*
- Daptomycin *or*
- Linezolid *or*
- Televancin *or*
- Ceftaroline

##### EMPIRIC Rx

- TMP/SMX *or*
- Doxycycline

##### DEFINED Rx

- MRSA
  - See Empiric
- MSSA
  - Nafcillin *or*
  - Cefazolin *or*
  - Clindamycin

##### DEFINED Rx

- MRSA
  - TMP/SMX
- MSSA
  - Dicloxacillin *or*
  - Cephalexin



and televancin are not approved for use in children, recommended; clindamycin may be used if clindamycin % at the institution.

Lin H-S, Lin P-T, Tsai Y-S, Wang S-H, Chi C-C.

Interventions for bacterial folliculitis and boils (furuncles and carbuncles).

*Cochrane Database of Systematic Reviews* 2021, Issue 2. Art. No.: CD013099.

## Authors Conclusions

**NONE** regarding efficacy and safety of:

- Topical antibiotics vs antiseptics
- Topical vs systemic antibiotics
- One systemic antibiotic vs another

**BUT, should we treat with antibiotics at all???**

**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 Med* 2010;54:401-407

Schmitt GR, Bruner J, 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 Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. *Clin Infect Dis* 2011;52:e18-e55

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
- All underwent I&D
- Then randomized to: 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                     |                  |
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| 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) |
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| 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) |
| <i>S. aureus</i> 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) |
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| 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) |
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| 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 <i>S. aureus</i> 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.

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| Children                           |                             |                    |              |                             |                   |              |                             |                  |
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| Adults                             |                             |                    |              |                             |                   |              |                             |                  |
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| Intention-to-treat population      | 57/68                       | 83.8 (74.3–93.3)   | <b>+0.7</b>  | 59/72                       | 81.9 (72.4–91.5)  | <b>-1.2</b>  | 69/83                       | 83.1 (74.5–91.8) |
| Population that could be evaluated | 57/63                       | 90.5 (82.4–98.5)   | <b>-0.3</b>  | 59/65                       | 90.8 (83.0–98.6)  | <b>0</b>     | 69/76                       | 90.8 (83.6–97.9) |

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| Adults                             |                             |                    |              |                             |                   |              |                             |                  |
| Intention-to-treat population      | 131/165                     | 79.4 (72.9–85.9)   | <b>+10.4</b> | 140/172                     | 81.4 (75.3–87.5)  | <b>+12.4</b> | 116/168                     | 69.0 (61.8–76.3) |
| Population that could be evaluated | 131/146                     | 89.7 (84.5–95.0)   | <b>+10.2</b> | 140/151                     | 92.7 (88.2–97.2)  | <b>+13.2</b> | 116/146                     | 79.5 (72.6–86.3) |
| <u>S. aureus isolated</u>          |                             |                    |              |                             |                   |              |                             |                  |
| Intention-to-treat population      | 157/188                     | 83.5 (77.9–89.1)   | <b>+19.7</b> | 149/179                     | 83.2 (77.5–89.0)  | <b>+19.4</b> | 102/160                     | 63.8 (56.0–71.5) |
| Population that could be evaluated | 157/167                     | 94.0 (90.1–97.9)   | <b>+17.9</b> | 149/160                     | 93.1 (88.9–97.4)  | <b>+17.0</b> | 102/134                     | 76.1 (68.5–83.7) |
| MRSA isolated                      |                             |                    |              |                             |                   |              |                             |                  |
| Intention-to-treat population      | 116/142                     | 81.7 (75.0–88.4)   | <b>+18.8</b> | 110/130                     | 84.6 (78.0–91.2)  | <b>+21.7</b> | 73/116                      | 62.9 (53.7–72.2) |
| Population that could be evaluated | 116/126                     | 92.1 (86.9–97.2)   | <b>+16.1</b> | 110/117                     | 94.0 (89.3–98.7)  | <b>+18.0</b> | 73/96                       | 76.0 (67.0–85.1) |
| MSSA isolated                      |                             |                    |              |                             |                   |              |                             |                  |
| Intention-to-treat population      | 41/46                       | 89.1 (79.0–99.2)   | <b>+23.2</b> | 39/49                       | 79.6 (67.3–91.9)  | <b>+13.7</b> | 29/44                       | 65.9 (50.8–81.1) |
| Population that could be evaluated | 41/41                       | 100.0 (98.8–100.0) | <b>+23.7</b> | 39/43                       | 90.7 (80.9–100.0) | <b>+14.4</b> | 29/38                       | 76.3 (61.5–91.1) |
| <u>No S. aureus isolated</u>       |                             |                    |              |                             |                   |              |                             |                  |
| Intention-to-treat population      | 57/68                       | 83.8 (74.3–93.3)   | <b>+0.7</b>  | 59/72                       | 81.9 (72.4–91.5)  | <b>-1.2</b>  | 69/83                       | 83.1 (74.5–91.8) |
| Population that could be evaluated | 57/63                       | 90.5 (82.4–98.5)   | <b>-0.3</b>  | 59/65                       | 90.8 (83.0–98.6)  | <b>0</b>     | 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}

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

| Group                              | Clindamycin                 |                   |       | TMP-SMX                     |                  |       | Placebo                     |                  |
|------------------------------------|-----------------------------|-------------------|-------|-----------------------------|------------------|-------|-----------------------------|------------------|
|                                    | No. with Cure/<br>Total No. | % (95% CI)        |       | No. with Cure/<br>Total No. | % (95% CI)       |       | No. with Cure/<br>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 | 90/99                       | 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) |
| 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 | 116/142                     | 86.9–97.2)        | +16.1 | 110/117                     | 94.0 (89.3–98.7) | +18.0 | 73/96                       | 76.0 (67.0–85.1) |
| <i>S. aureus</i> 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) |
| No <i>S. aureus</i> isolated       |                             |                   |       |                             |                  |       |                             |                  |
| Intention-to-treat population      | 57/68                       | 83.8 (74.3–93.3)  | +0.7  | 59/72                       | 81.5 (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) |

Likely more reflective of antibiotic impact on true abscesses

*S. aureus* isolated

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

\* 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.

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

|                                                                                                         | Clindamycin<br>n=266 | TMP-SMX<br>n=263    | Placebo<br>n=257    | Total<br>n=786 |
|---------------------------------------------------------------------------------------------------------|----------------------|---------------------|---------------------|----------------|
| Failures up to and including the OMFU visit                                                             | <del>57</del><br>44  | <del>71</del><br>45 | <del>96</del><br>50 | <del>224</del> |
| 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                                                                                           | <del>13</del>        | <del>26</del>       | <del>46</del>       | <del>85</del>  |
| 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 I&D + {Clinda vs TMP-SMX vs Placebo}

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

|                                                                                                         | Clindamycin<br>n=266 | TMP-SMX<br>n=263    | Placebo<br>n=257    | Total<br>n=786 |
|---------------------------------------------------------------------------------------------------------|----------------------|---------------------|---------------------|----------------|
| Failures up to and including the OMFU visit                                                             | <del>57</del><br>44  | <del>71</del><br>45 | <del>96</del><br>50 | <del>224</del> |
| 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                                                                                           | <del>13</del>        | <del>26</del>       | <del>46</del>       | <del>85</del>  |
| 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%               |                |

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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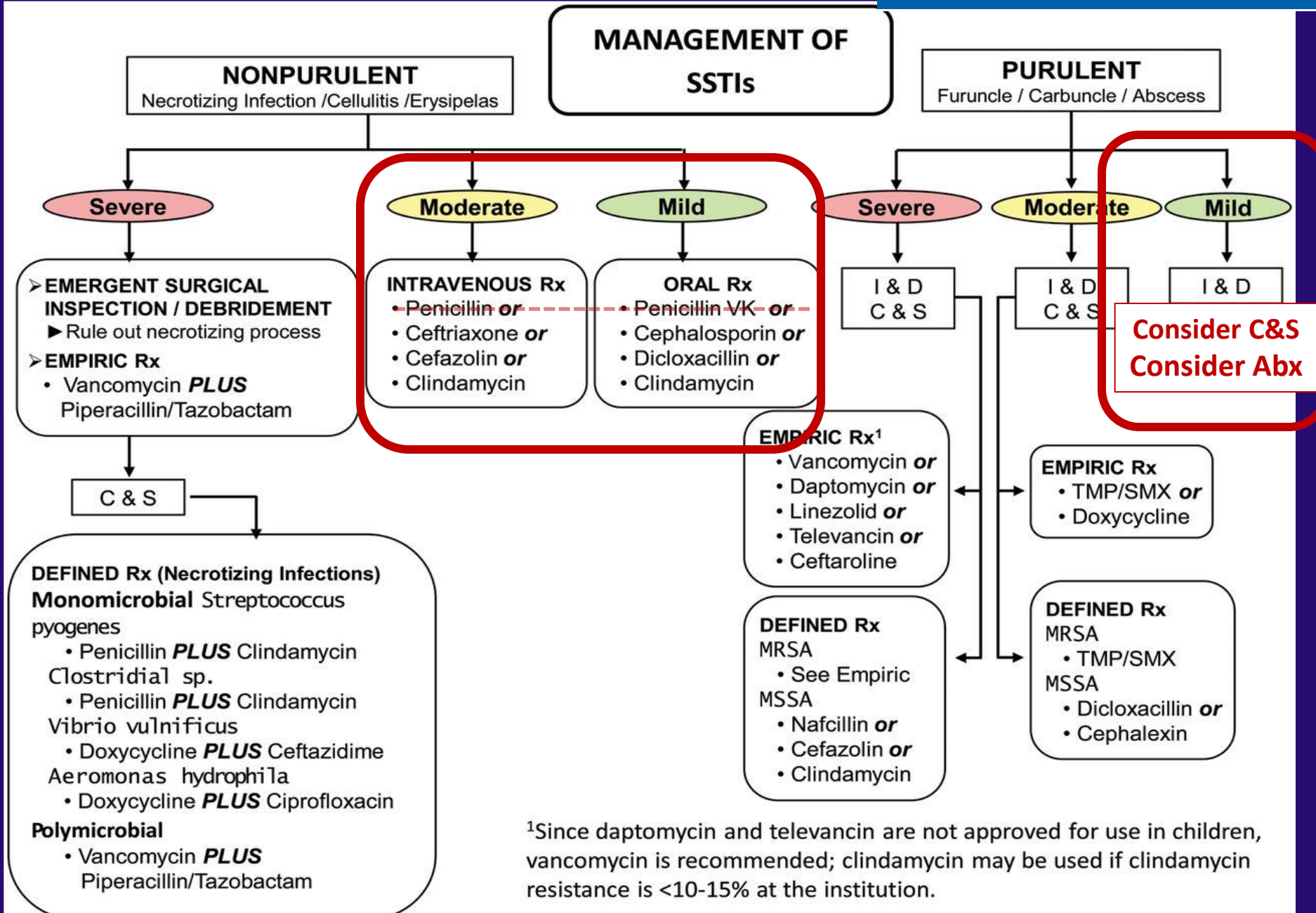


My Personal Approach:

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

# June 2014

## IDSA GUIDELINE



**Thank you again!**