Dermatology: Key Cases for the Internist

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HARVARD MEDICAL SCHOOL | Postgraduate Medical Education

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- University of Pennsylvania School of Medicine
- Internship in Internal Medicine at MGH
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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

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 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 aquired
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

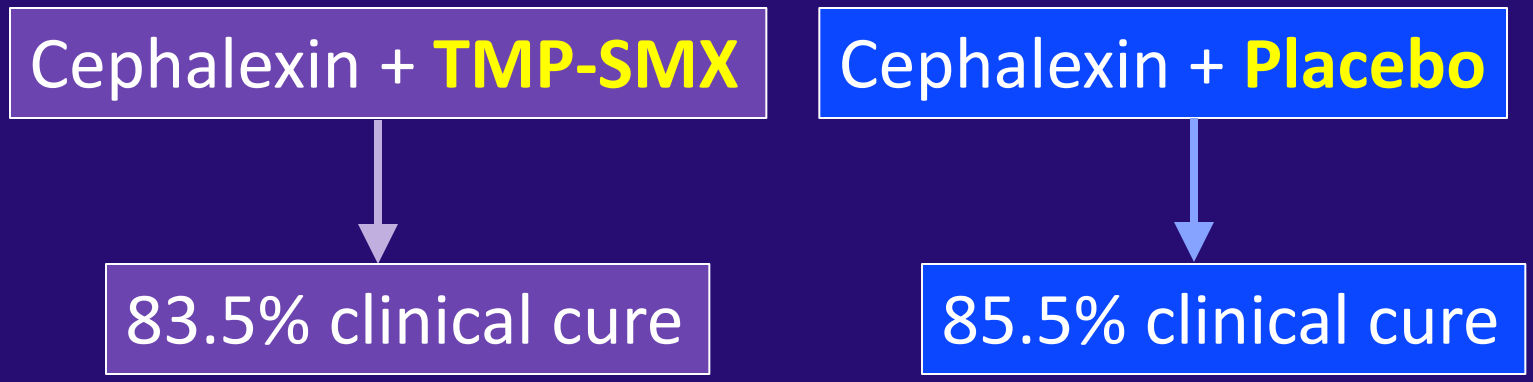
- 3 Boston Emergency Depts, 2007-11
- 153 Simple Cellulitis patients randomized

- 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



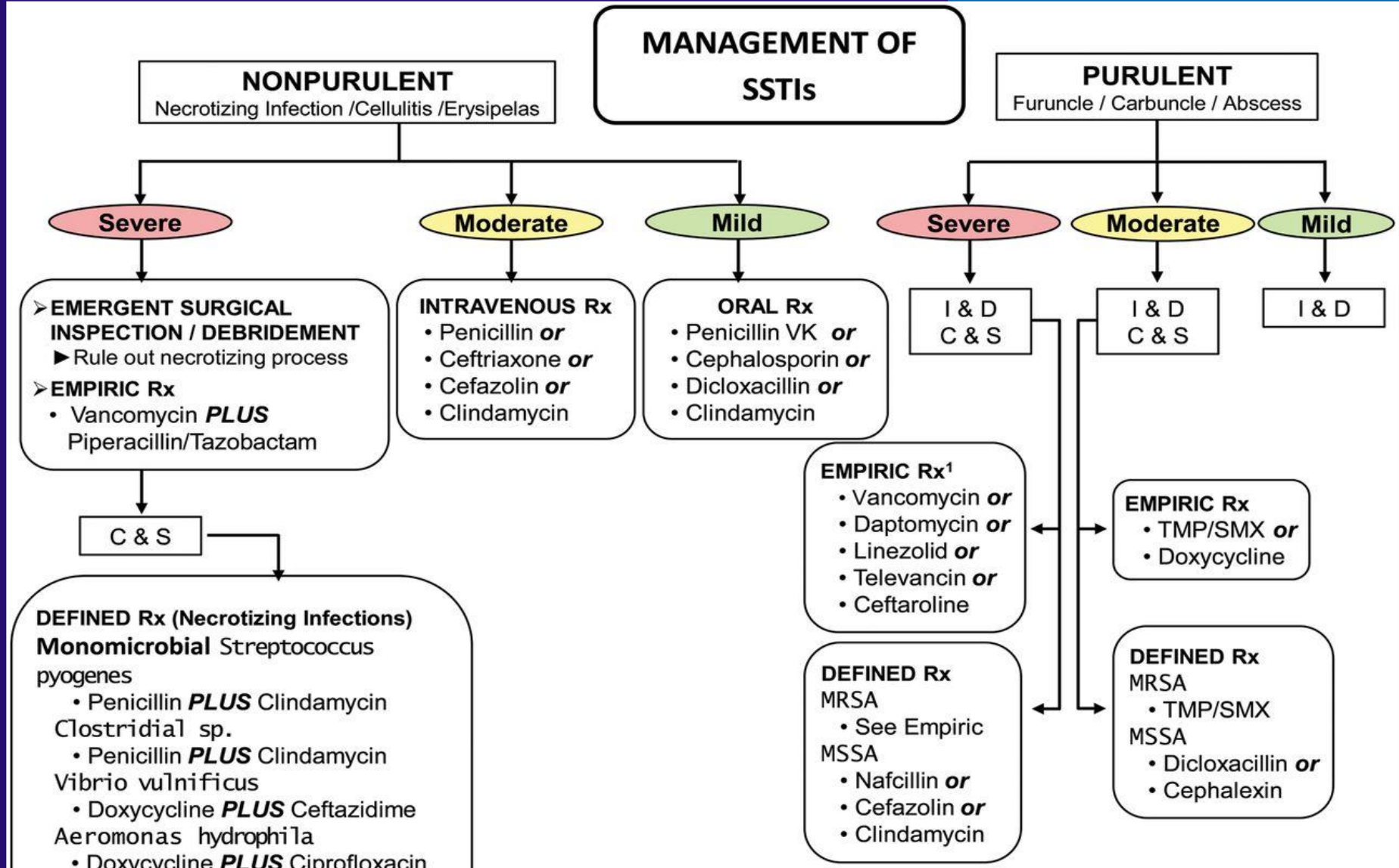
- Conclusion: **no benefit to adding sulfa**

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

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

IDSA GUIDELINE

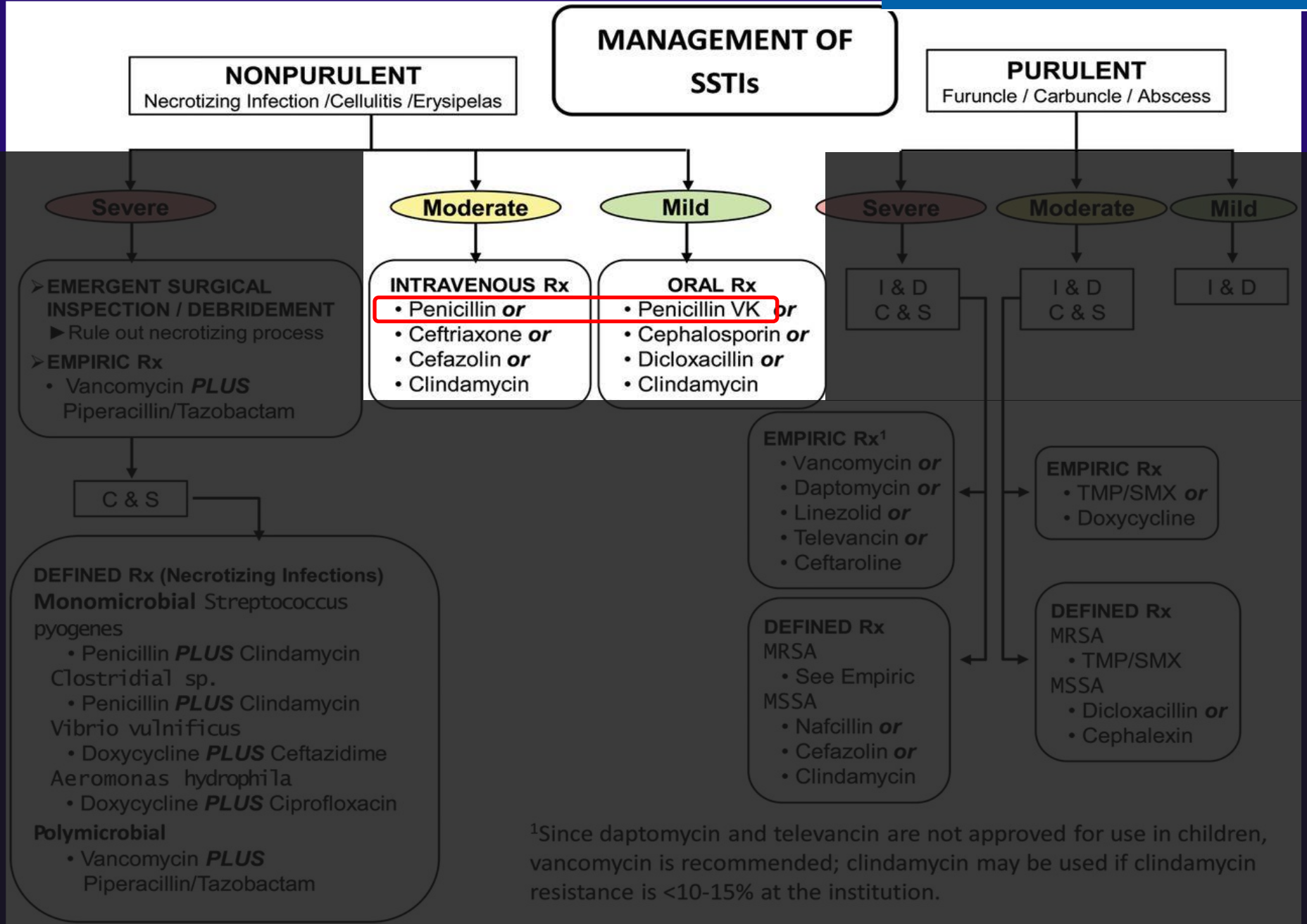


[1]Since daptomycin and televancin are not approved for use in children, vancomycin is recommended; clindamycin may be used if clindamycin resistance is <10-15% at the institution.

June 2014

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

IDSA GUIDELINE



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:
    - Serologies: "73% of non-culturable cellulitis caused by **βHS**"
    - 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. 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 **β-lactamase resistant agent**

Brief Interlude

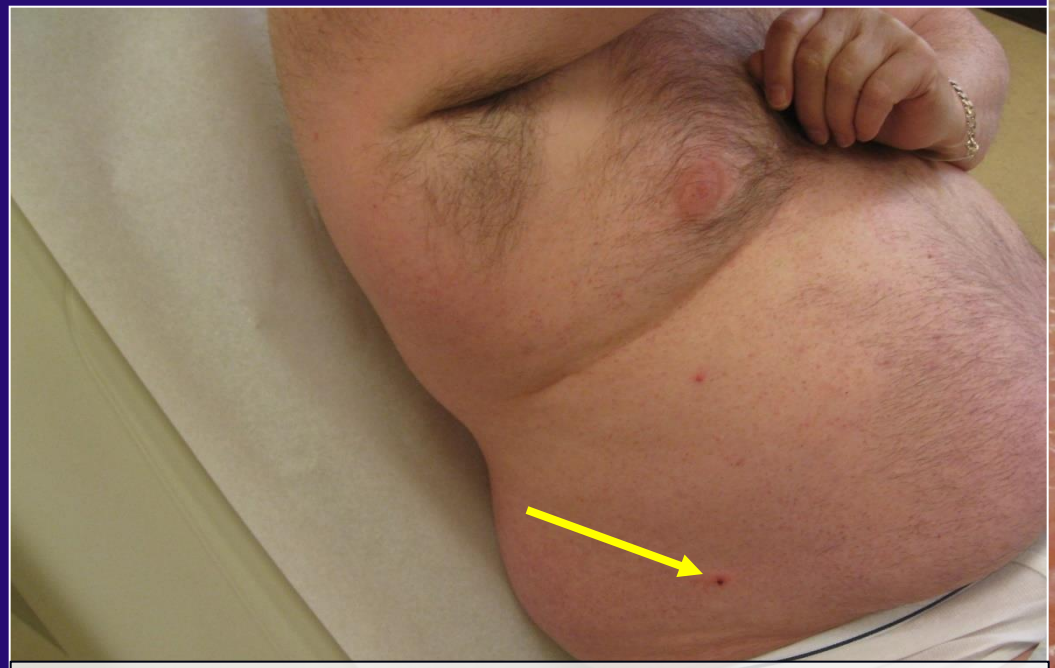
Time for a skin check

- 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



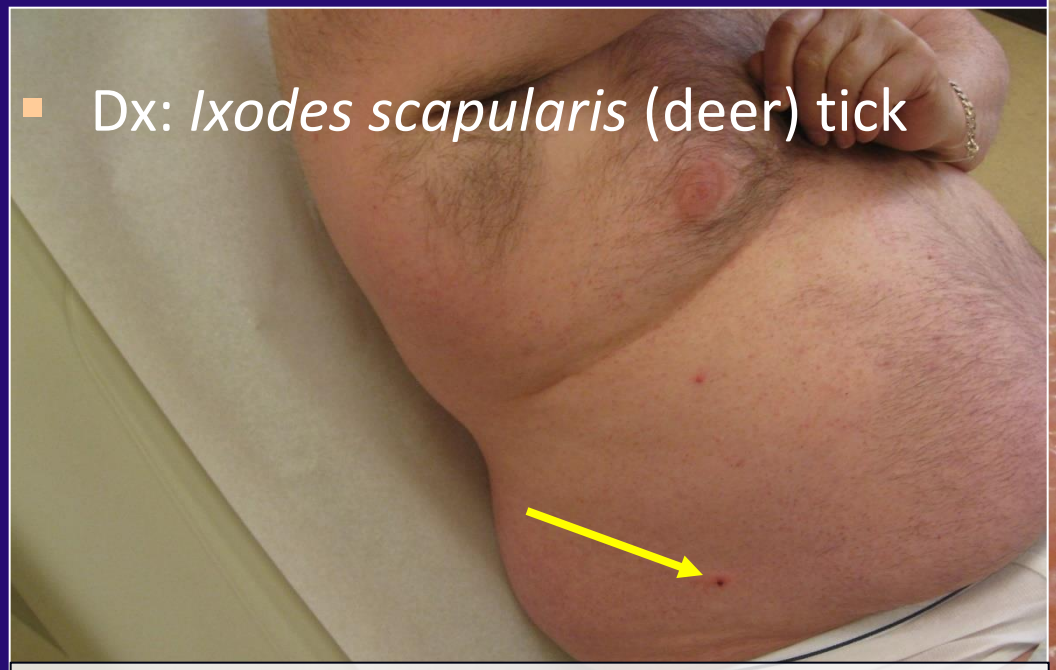
Two Questions to consider:

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

<u>Two Questions to consider:</u>

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?

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)
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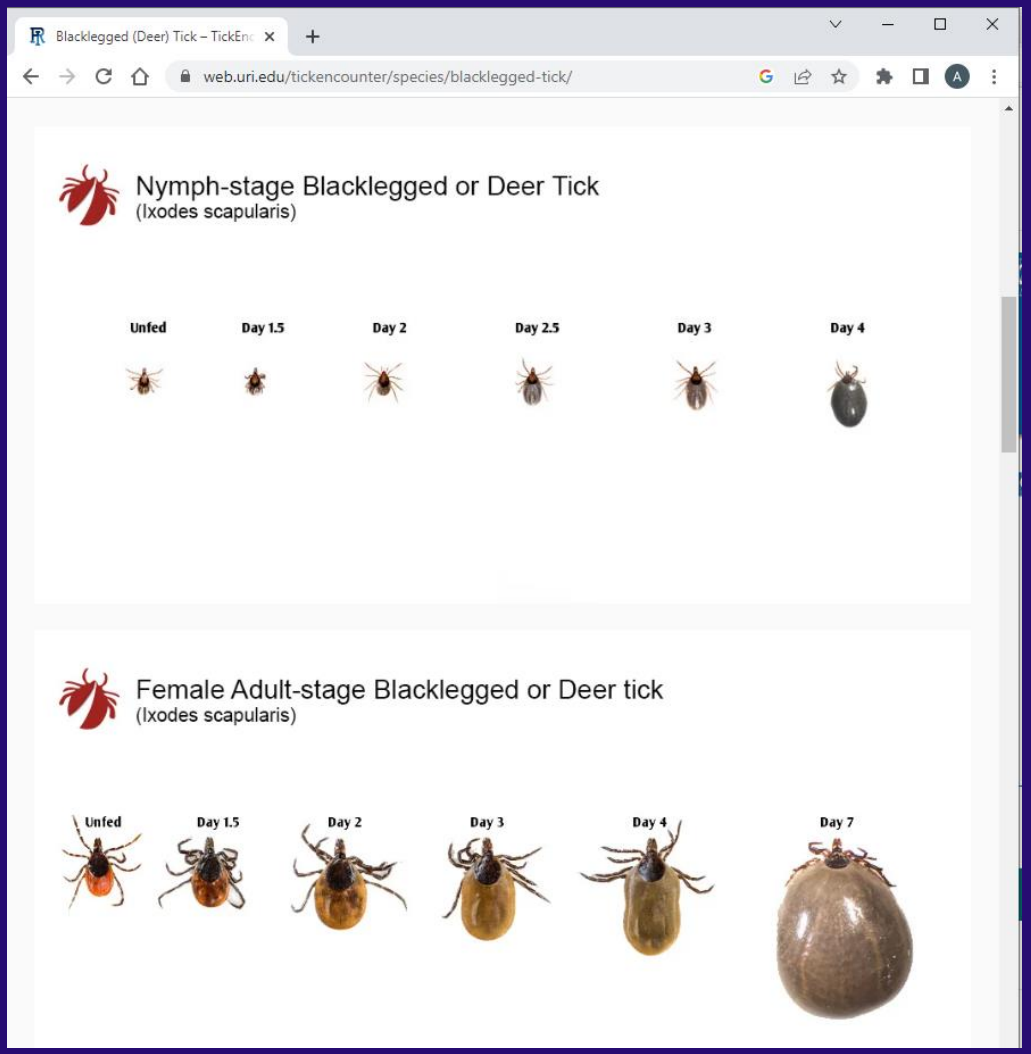
- Referral: **Spouse, to ophtho**

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**
- Ehrilichiosis
- 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 >=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

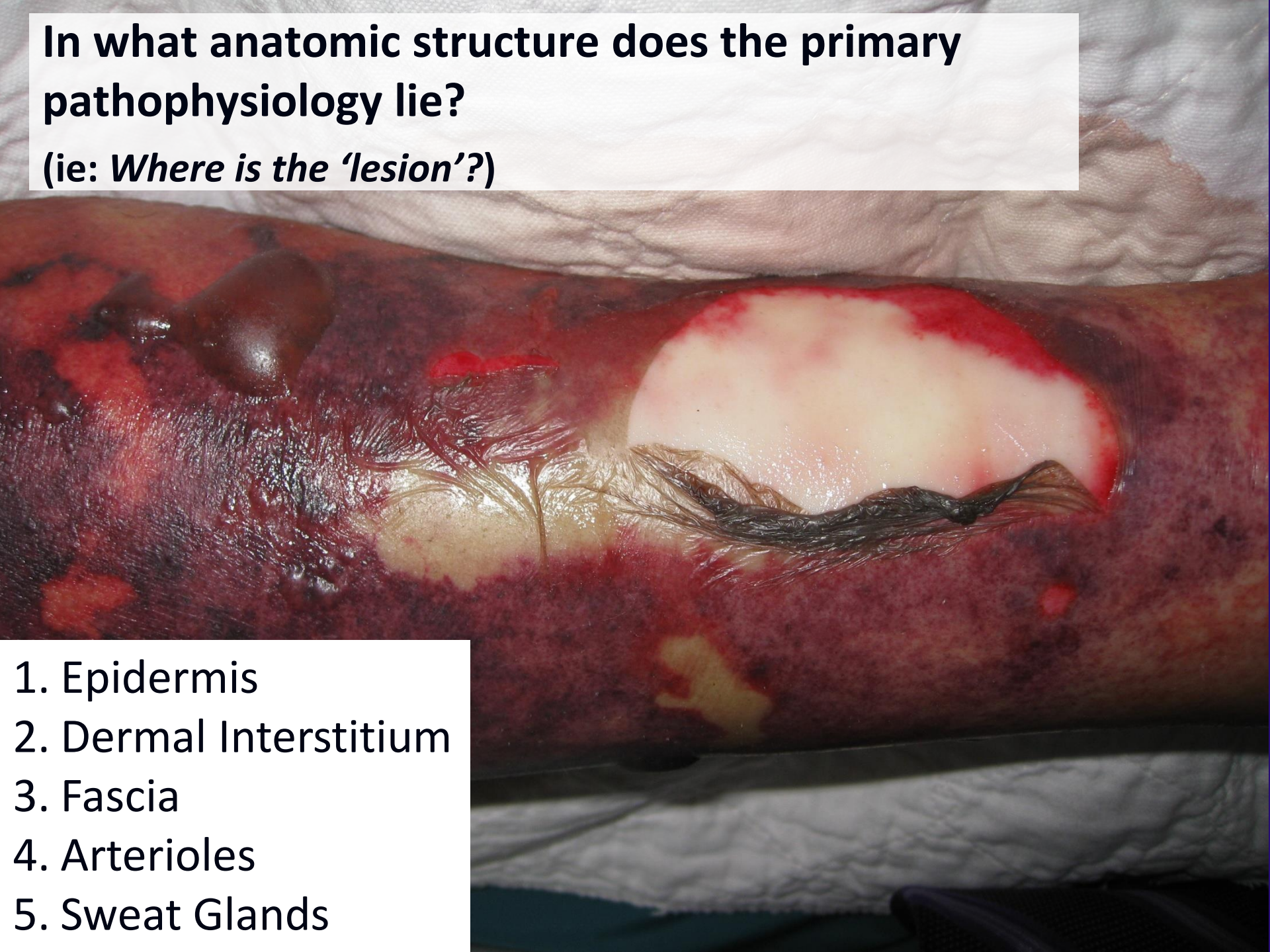
Hospital Day 1


MEDCOR

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

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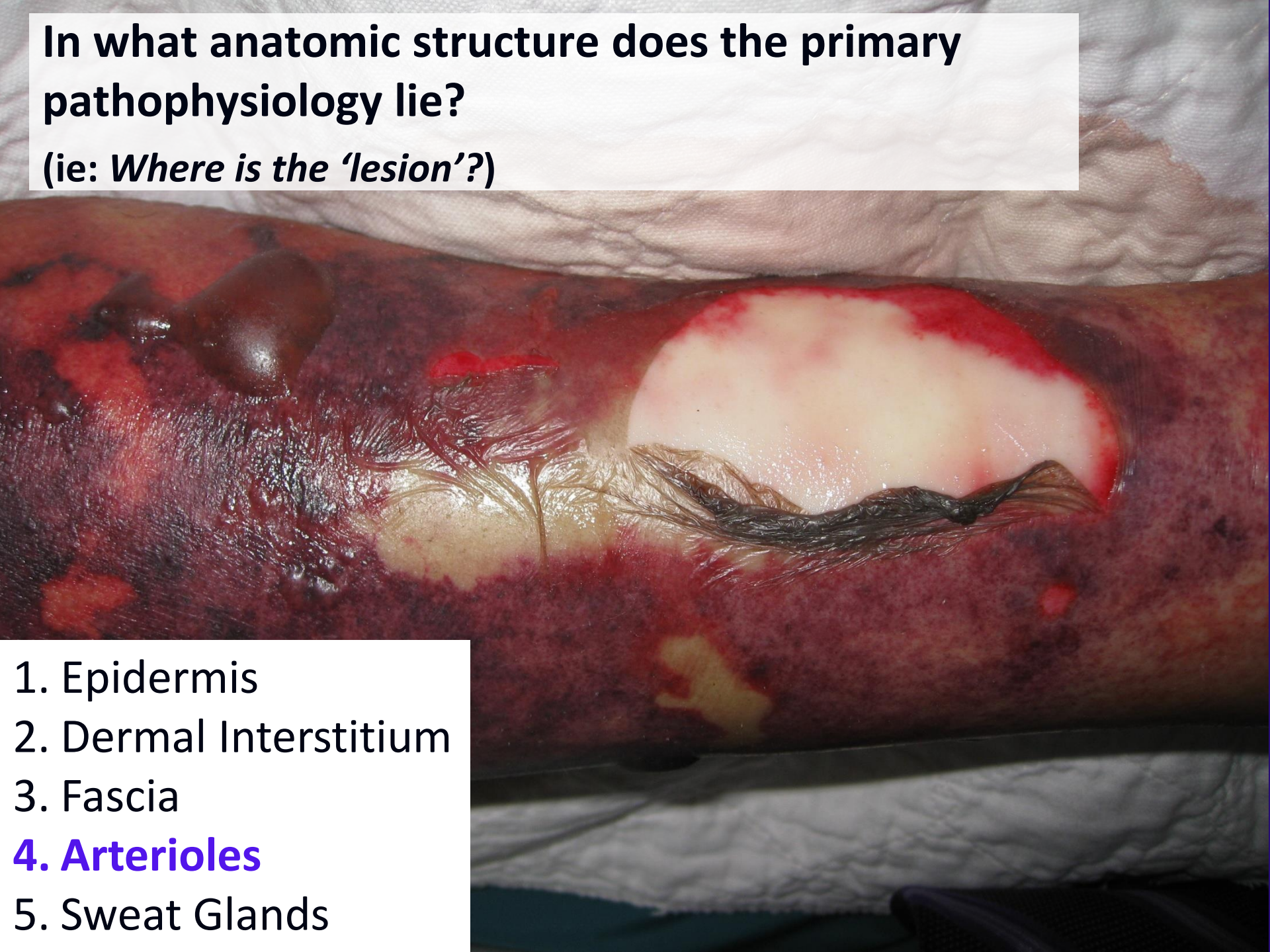
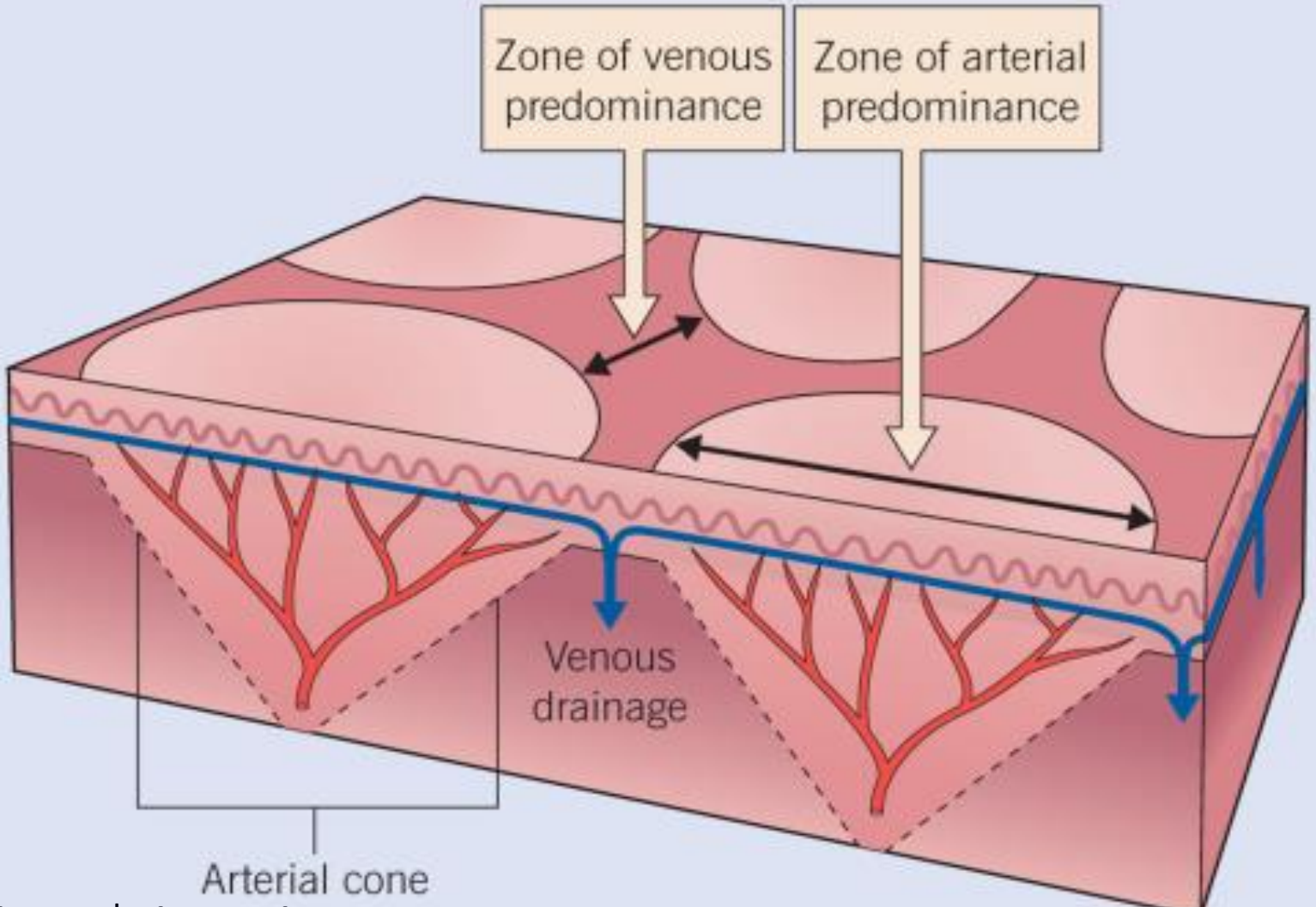
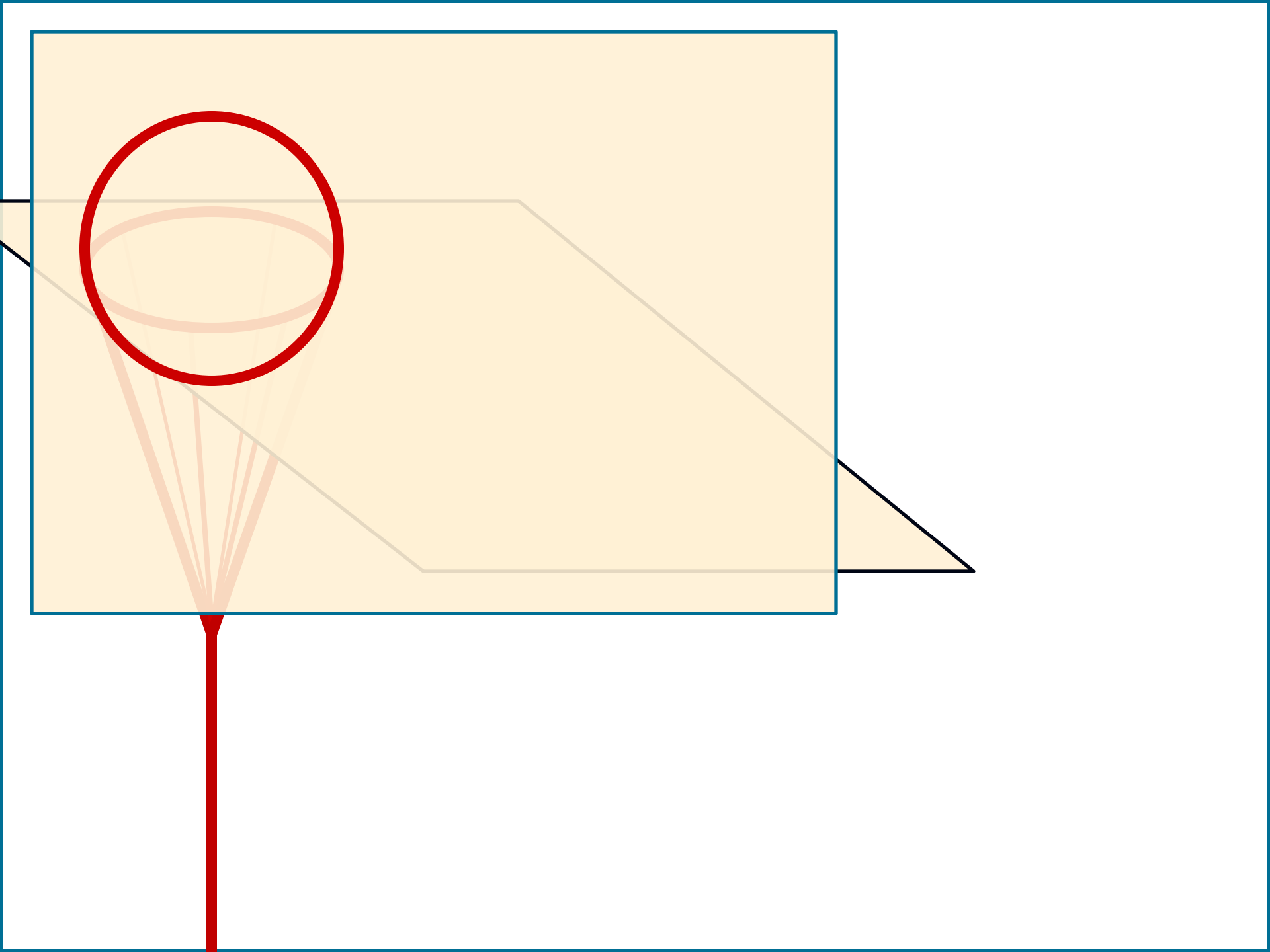


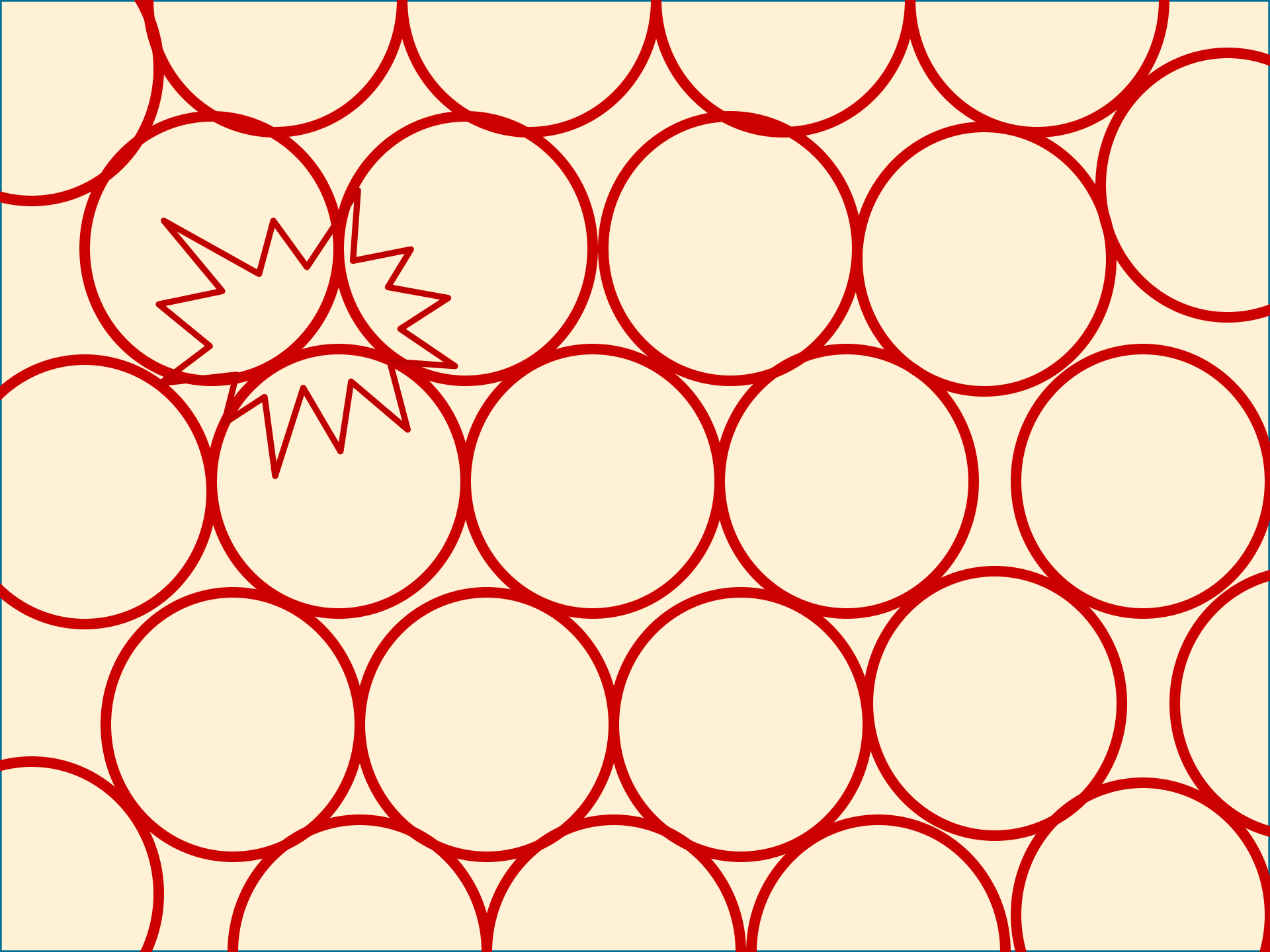
1. Epidermis
2. Dermal Interstitium
3. Fascia
4. **Arterioles**
5. Sweat Glands

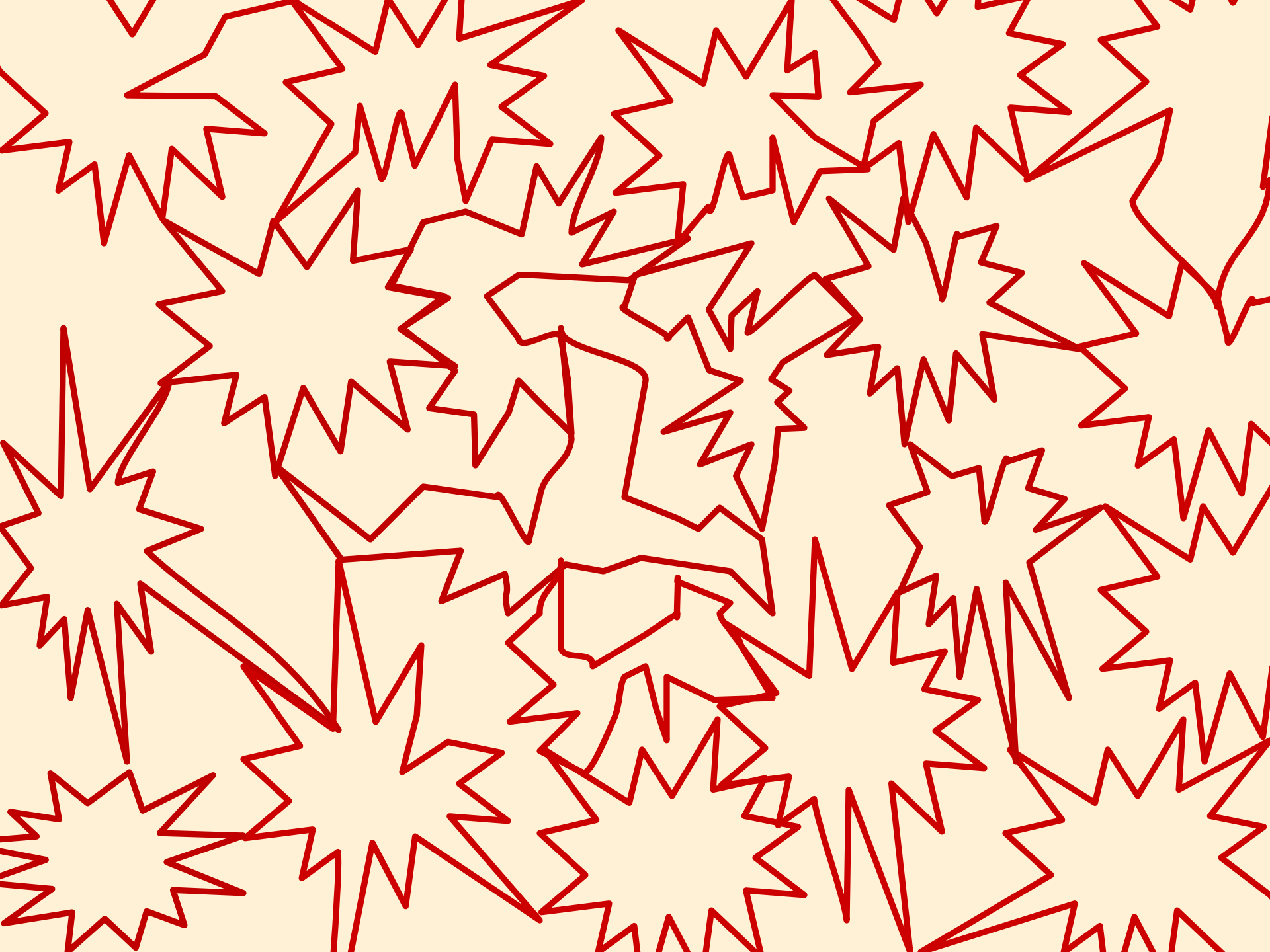
ANATOMICAL BASIS FOR THE DEVELOPMENT OF LIVEDO RETICULARIS

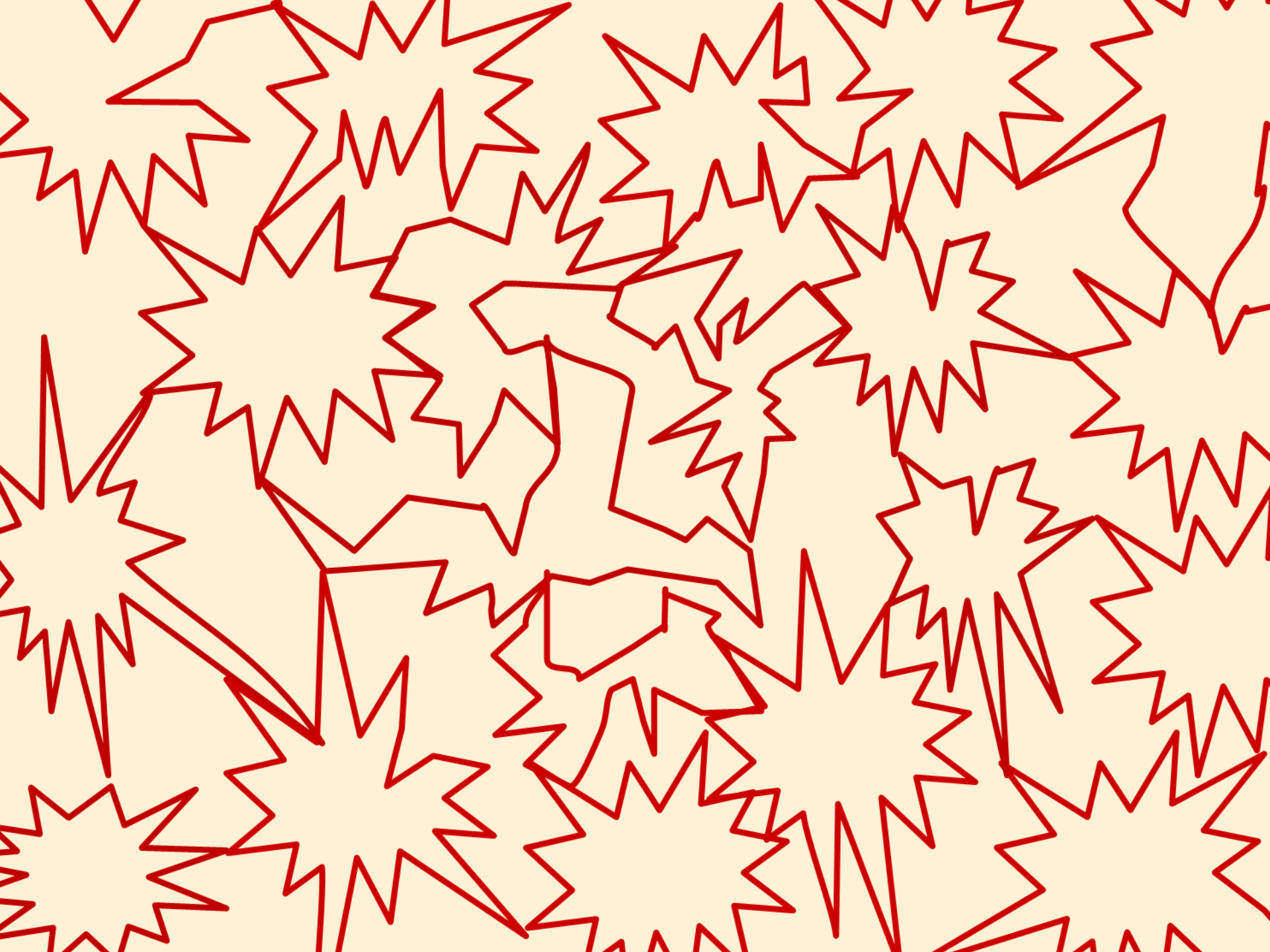


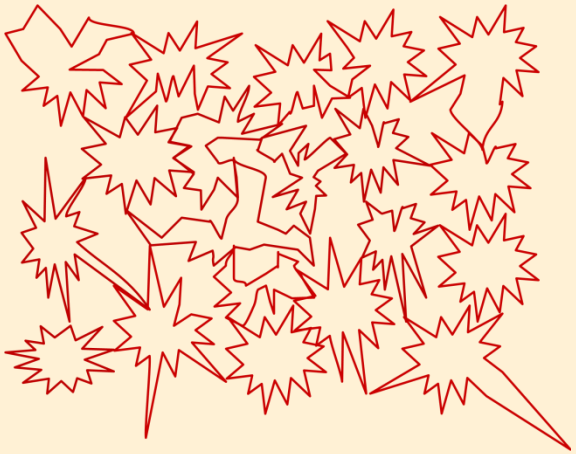
Dermatology, 2nd Edition. Eds Jean L Bolognia et al. Spain: Mosby Elsevier, 2008

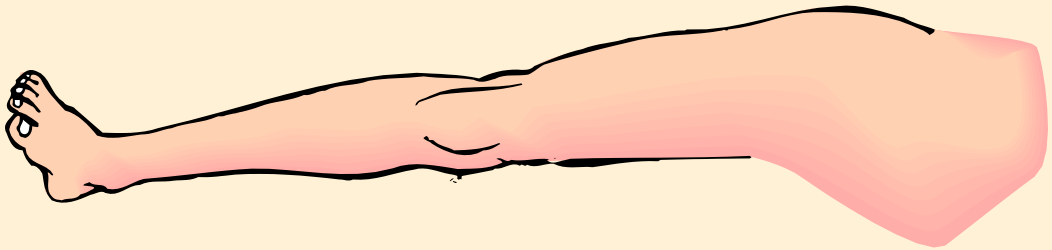










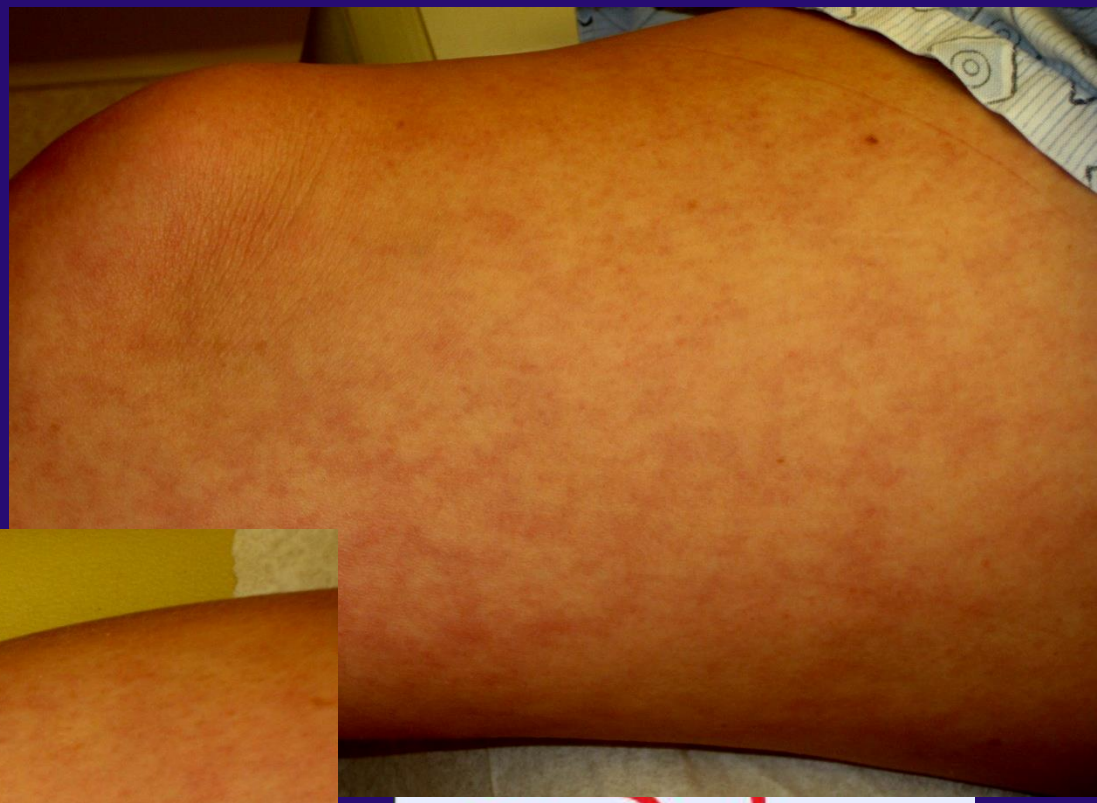


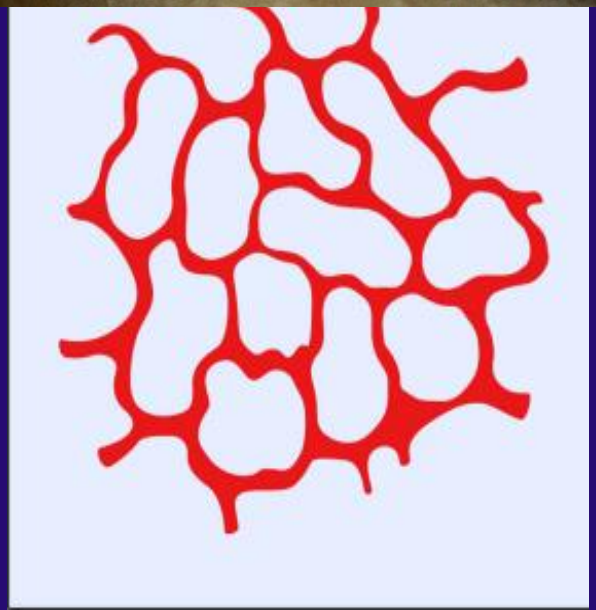
2 potential problems with this system

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



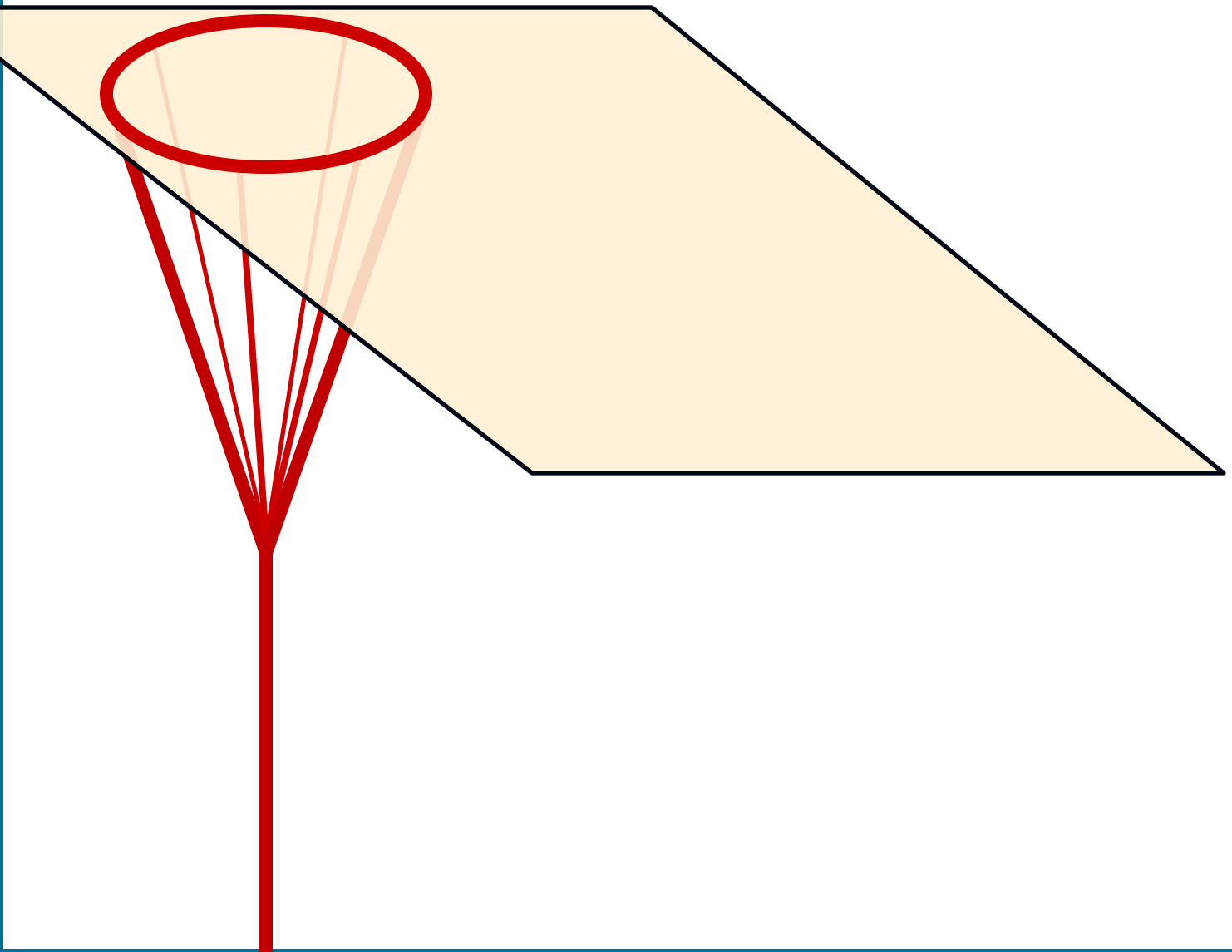


Problem 2:

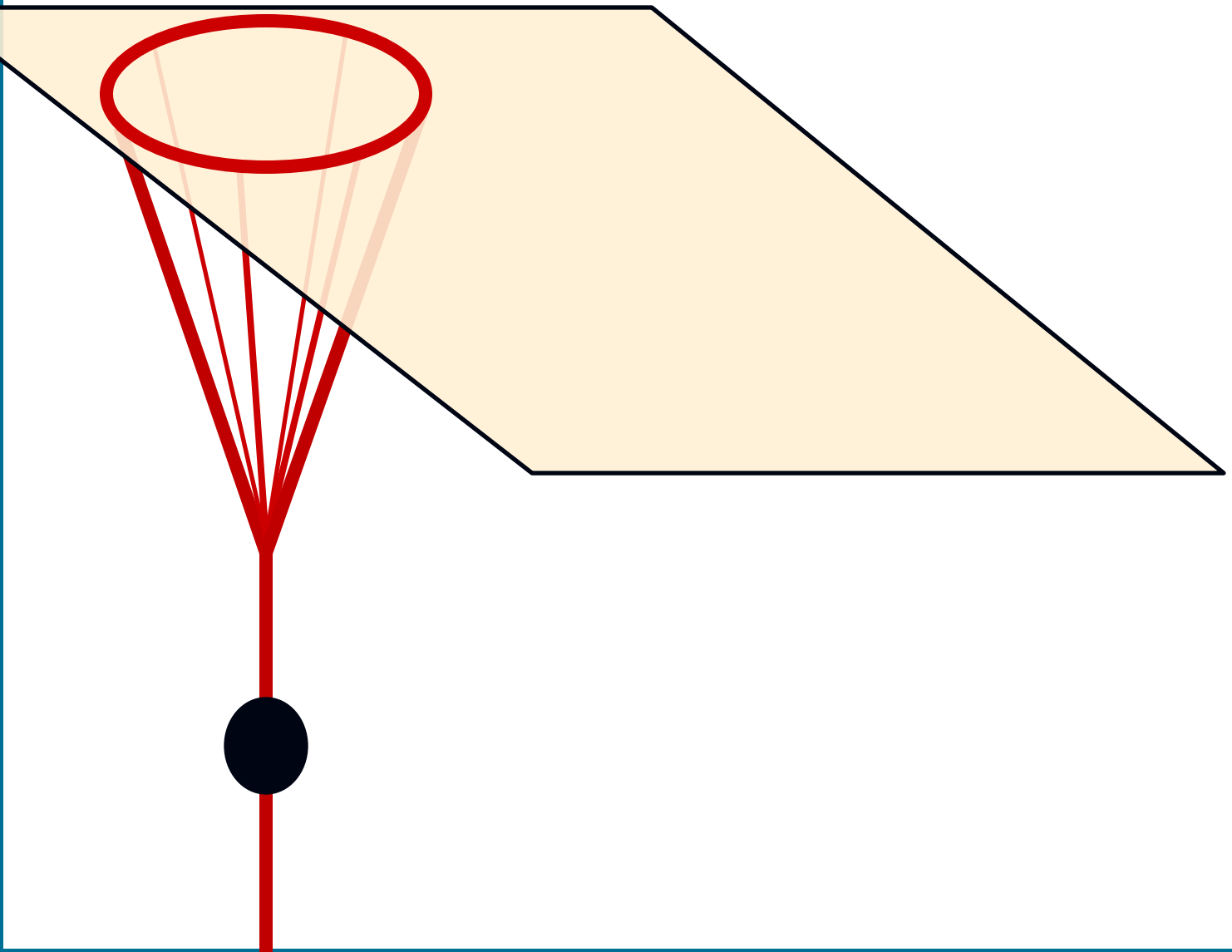
Retiform Purpura

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

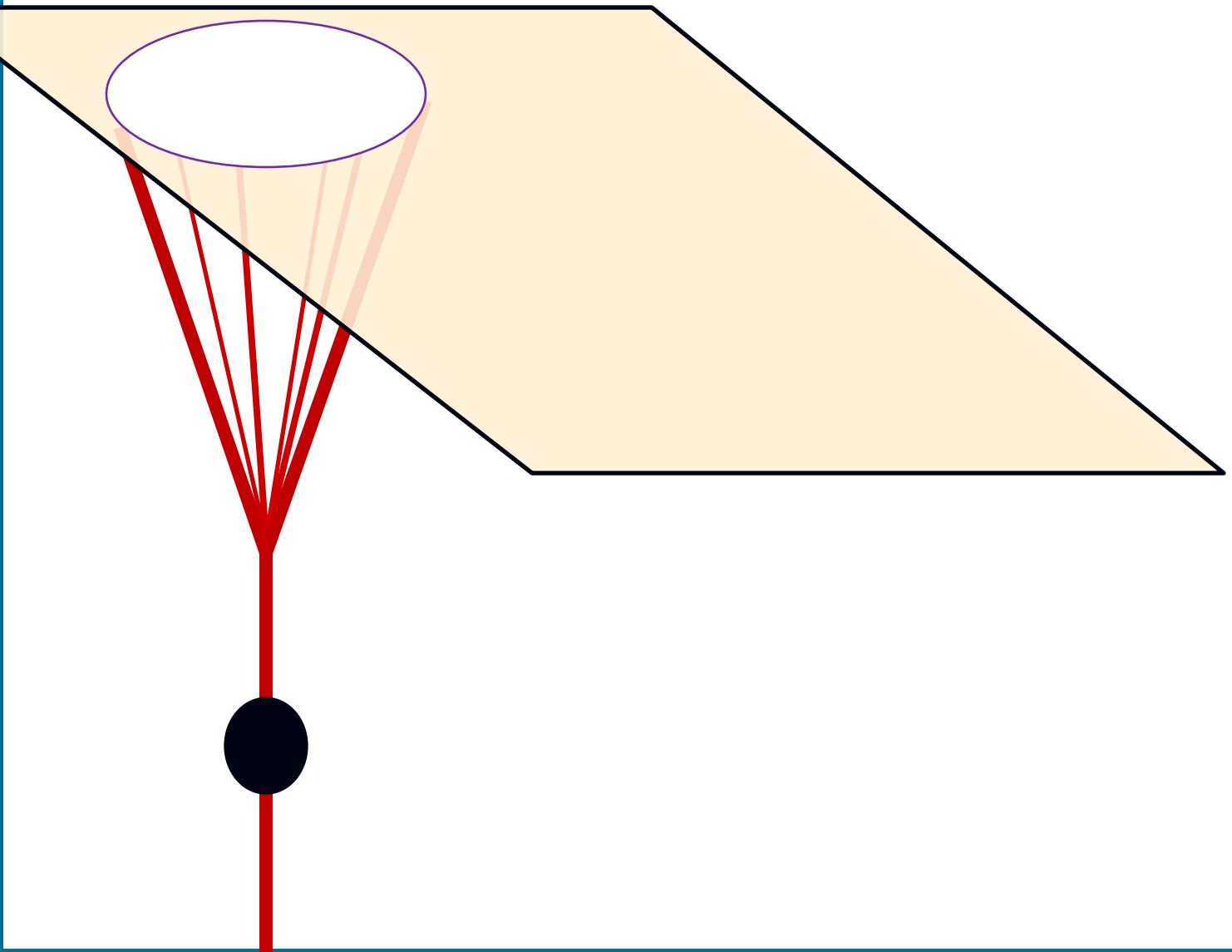
Retiform Purpura



Retiform Purpura



Retiform Purpura



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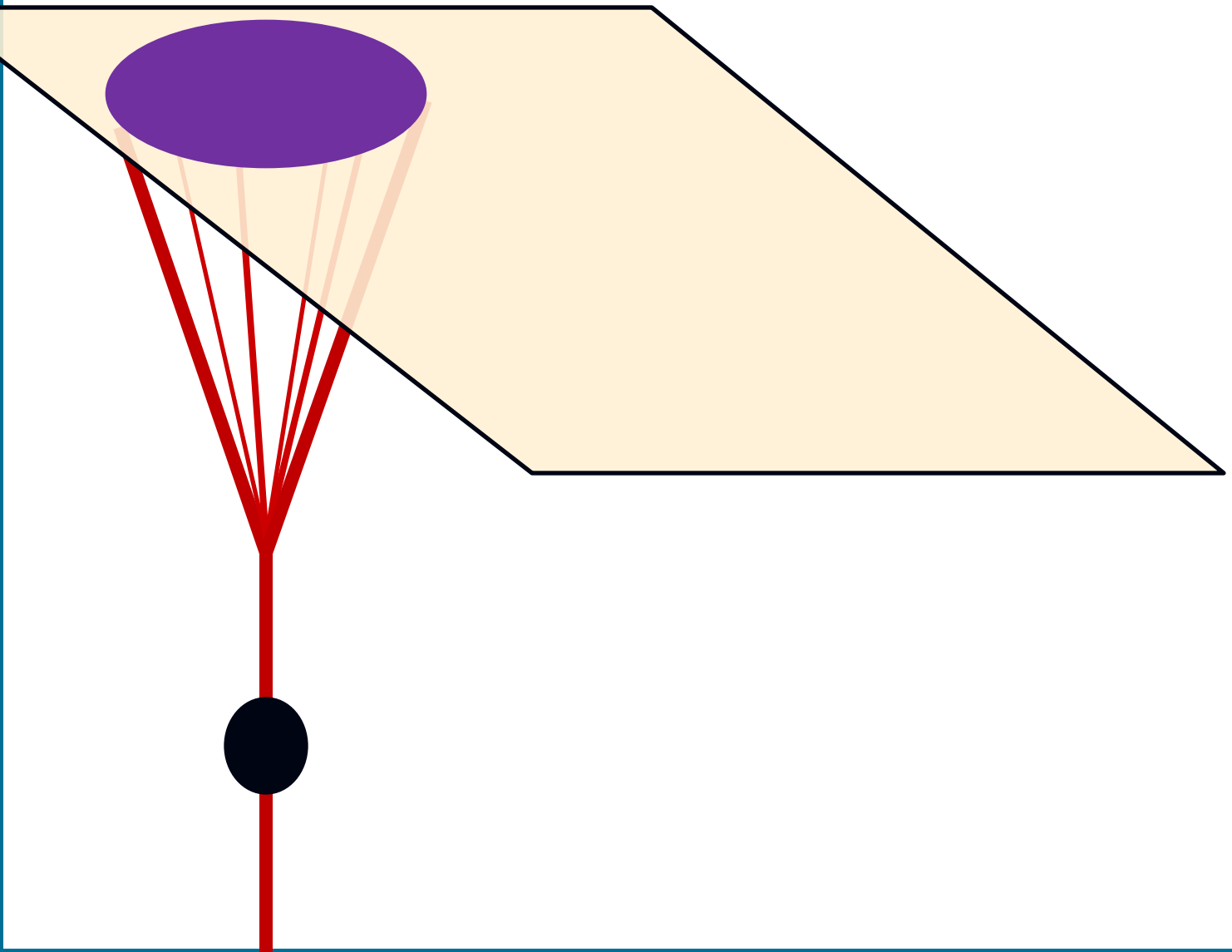

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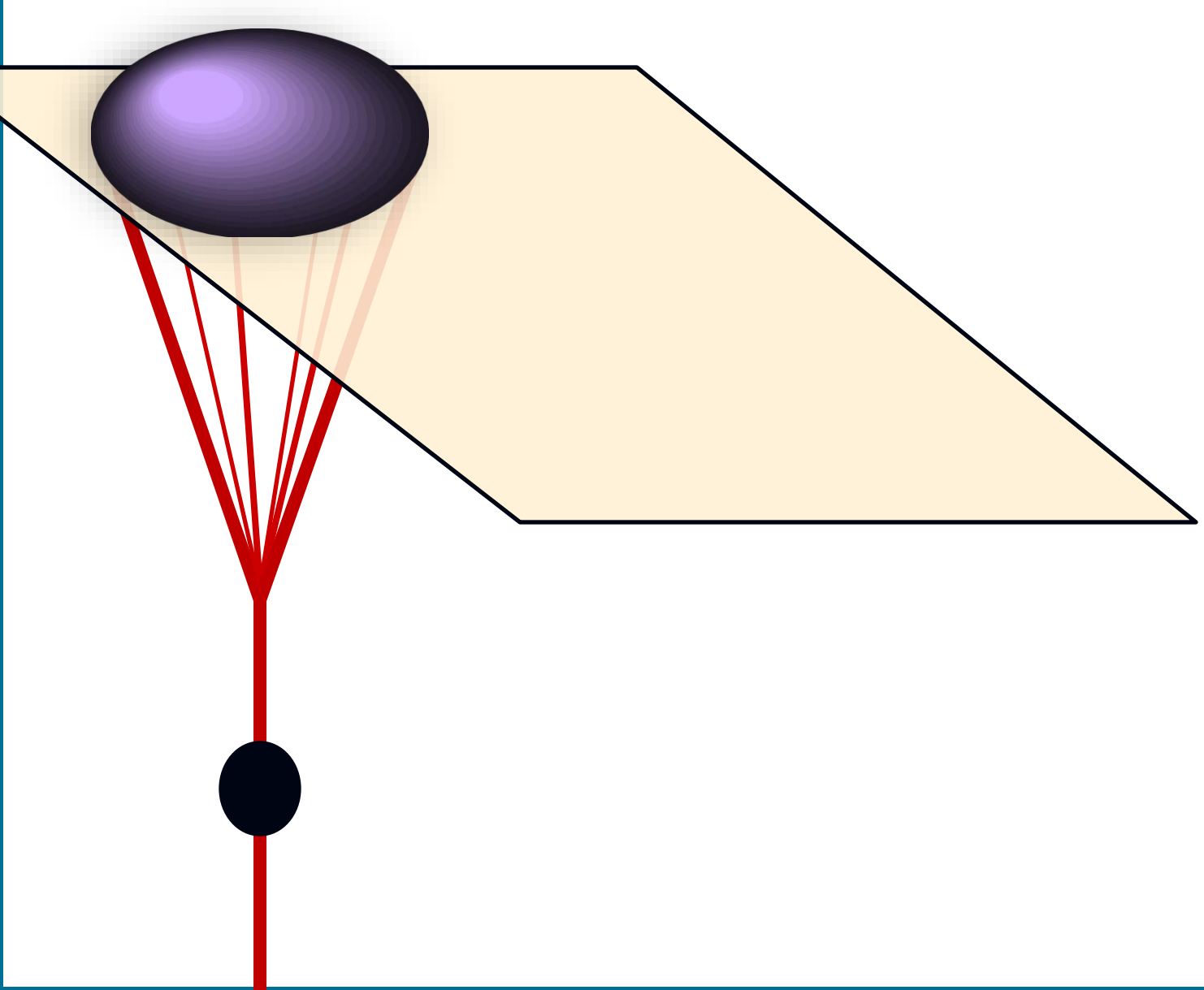

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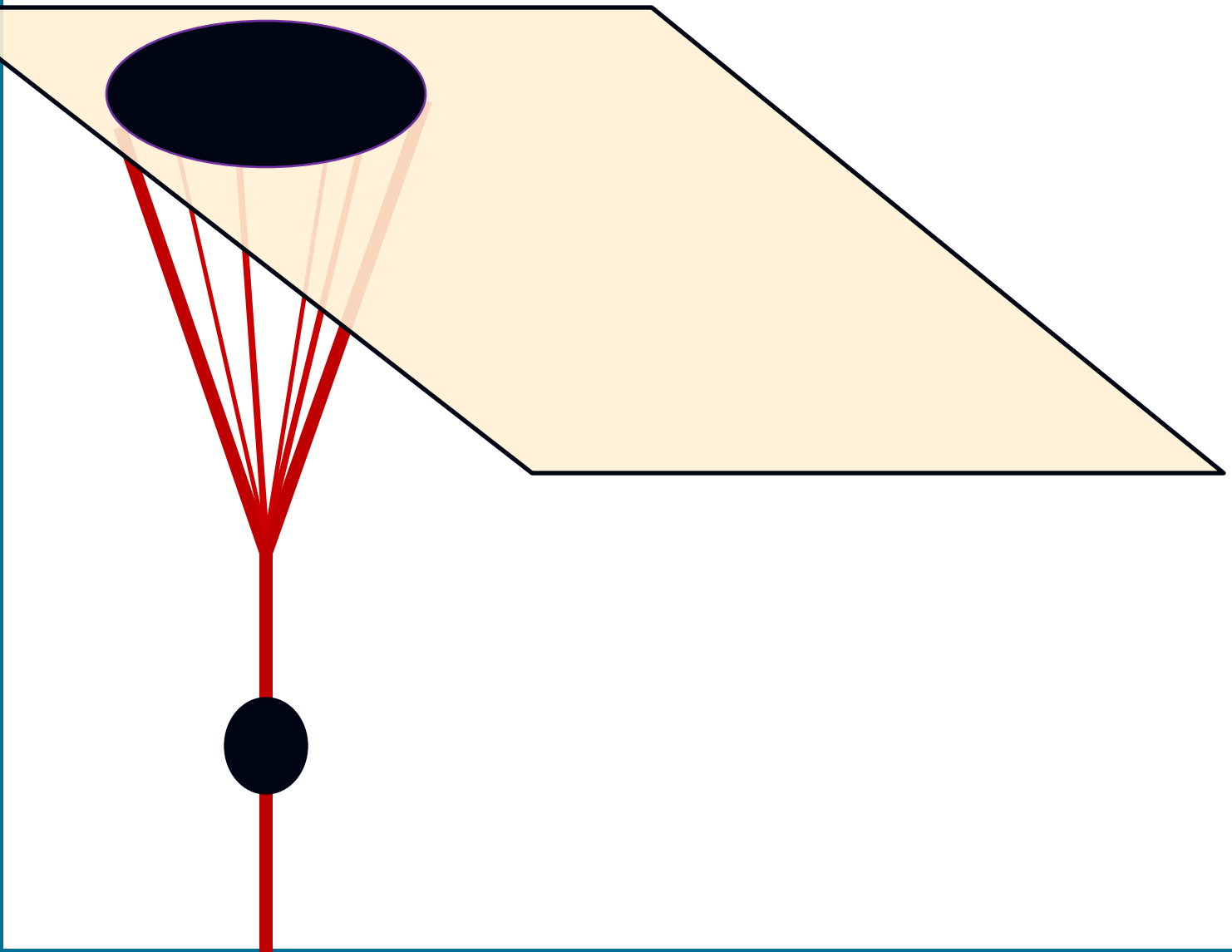
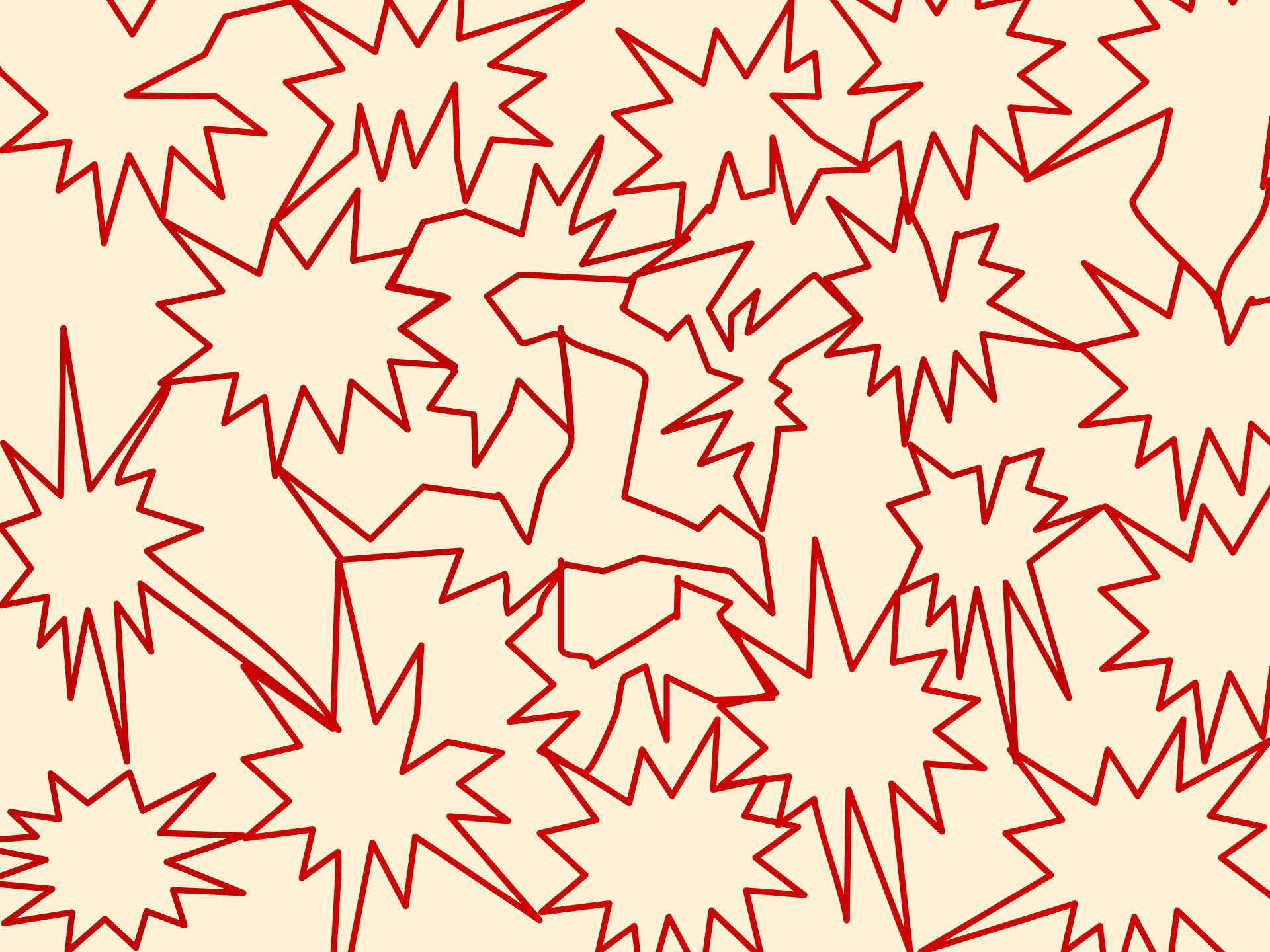
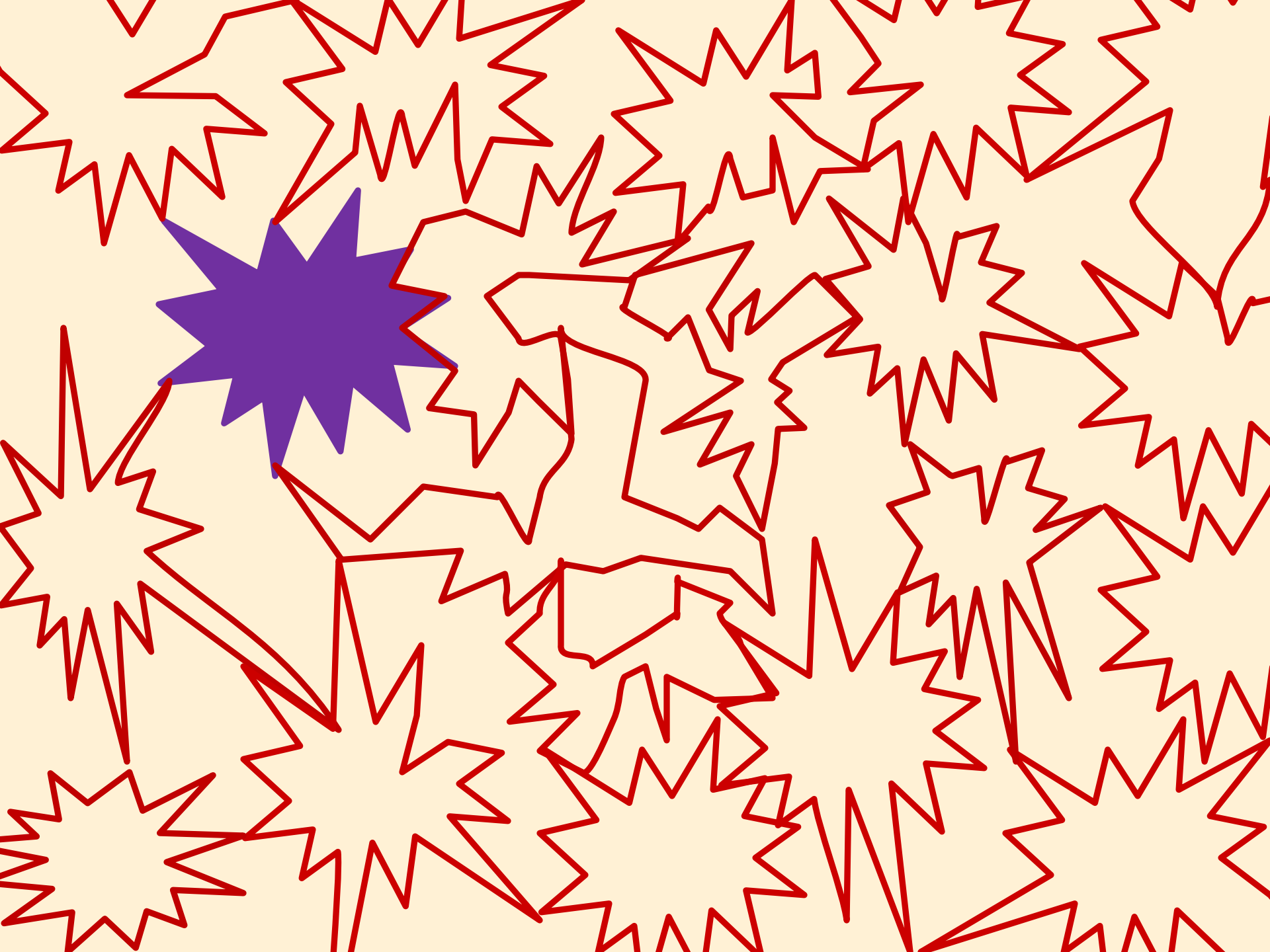
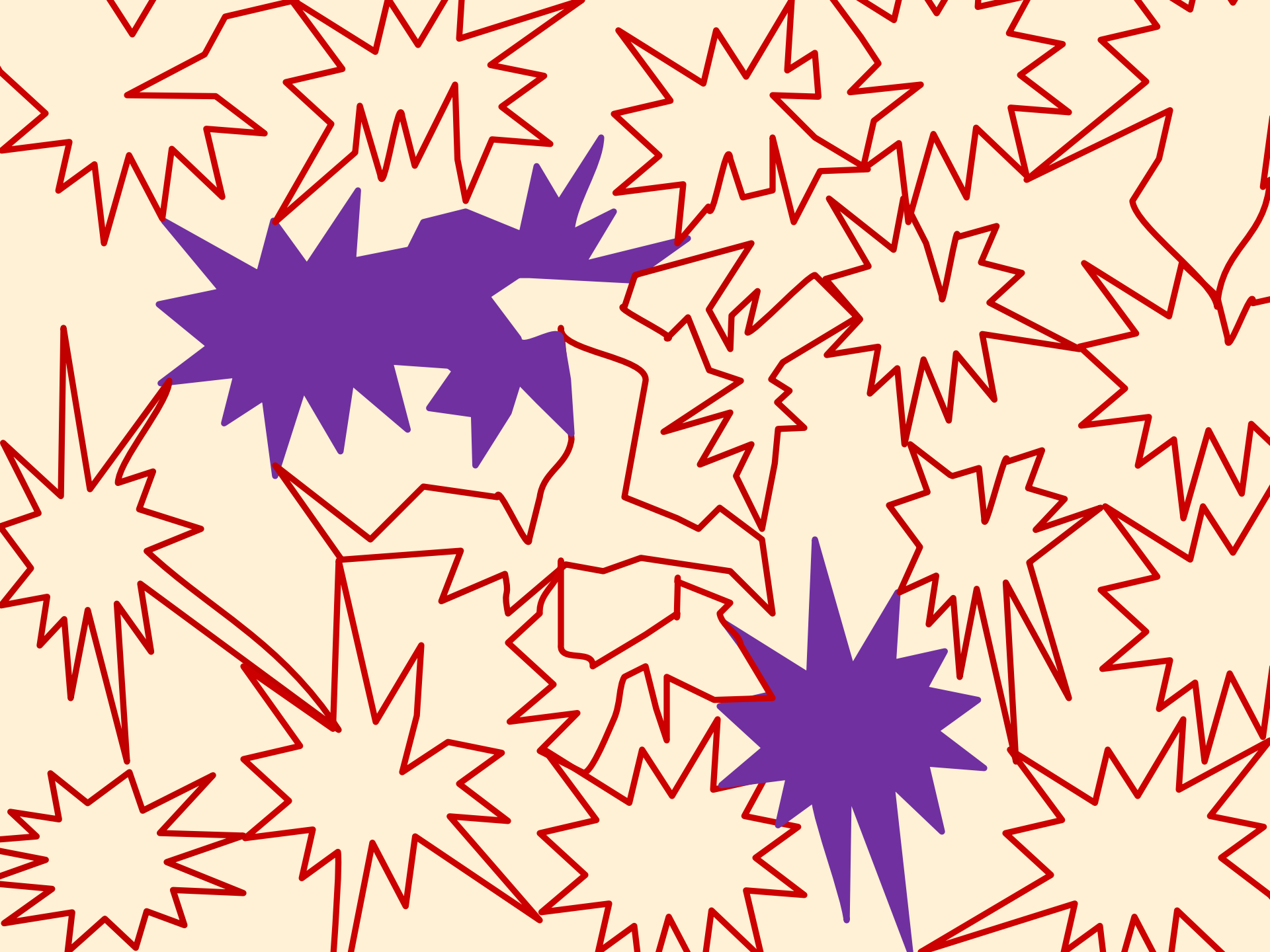
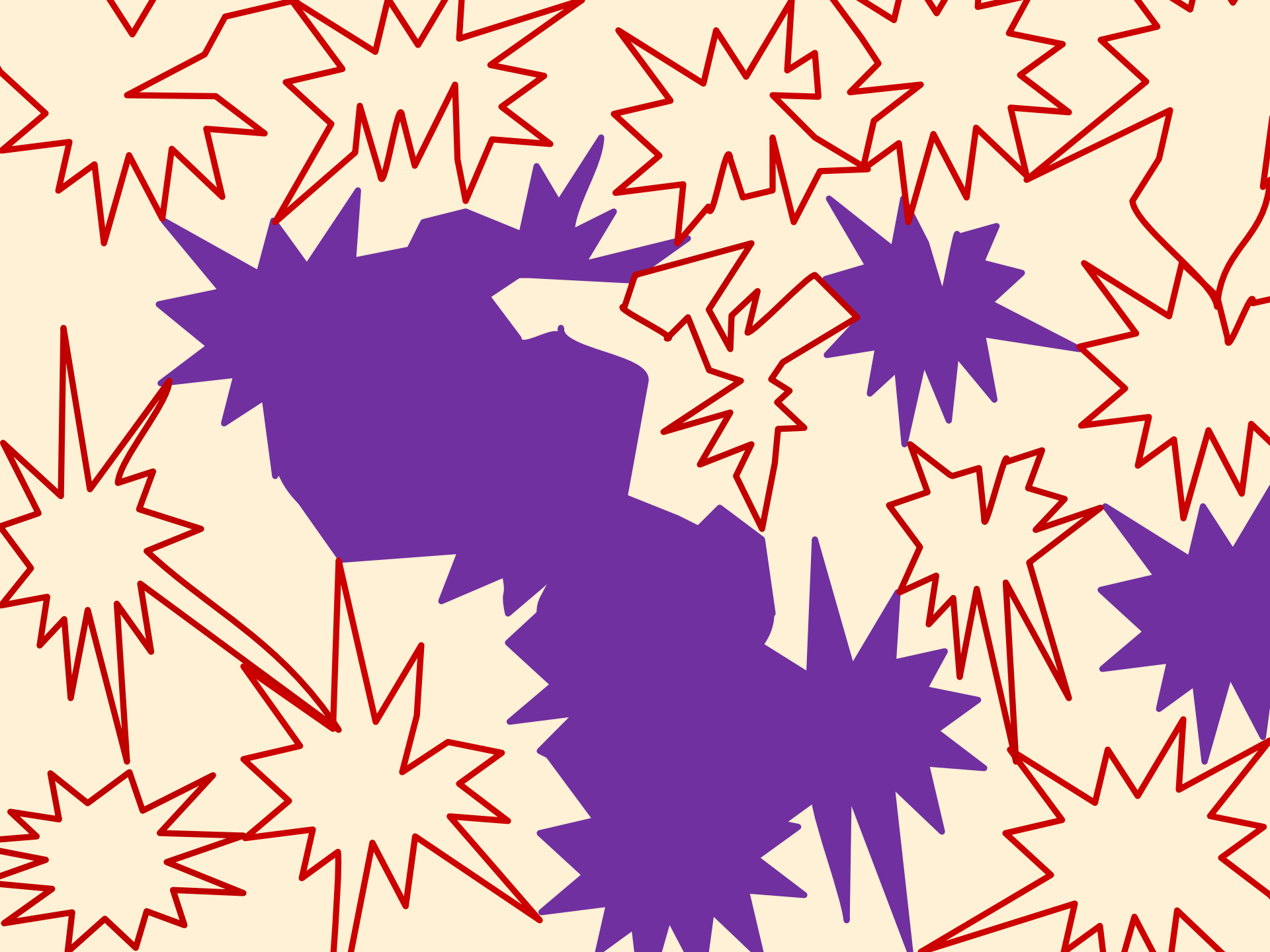










Retiform Purpura

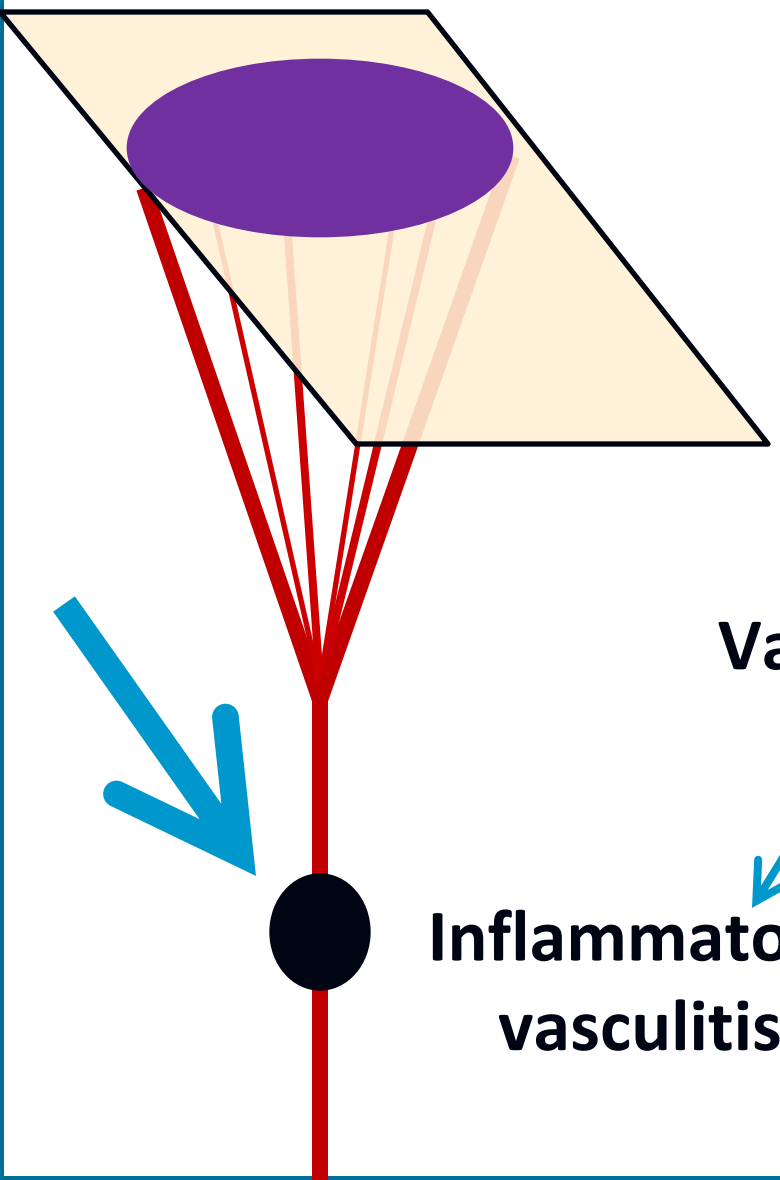
(with necrosis)

Case Details

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



Perforating Arteriole Occlusion

In-situ Thrombosis

Embolism

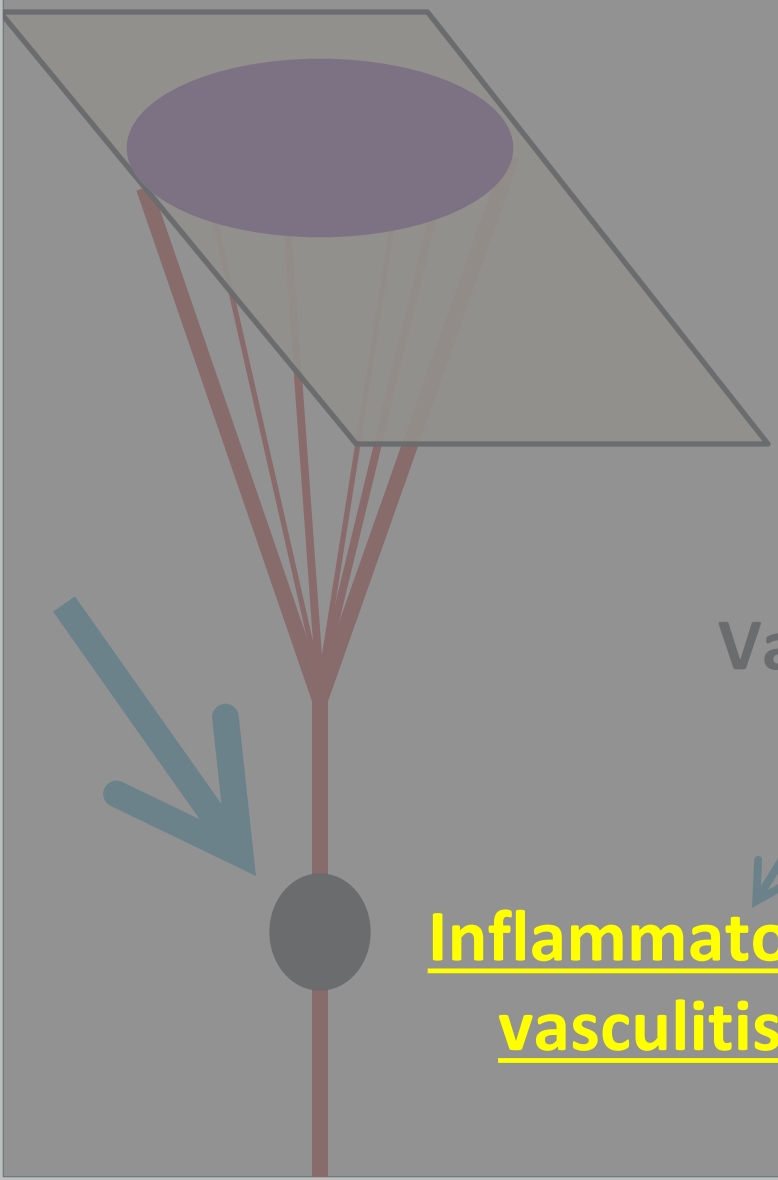
Vasculitis

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:	**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

NURSE
SEL

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

- Impeitigo 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

Case

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Case

18 yo female transferred from OSH for 2 complaints:

POLL: Diagnosis?

Scabies: Diagnostic Pearls

Burrows

and the

“Delta Wing Sign”

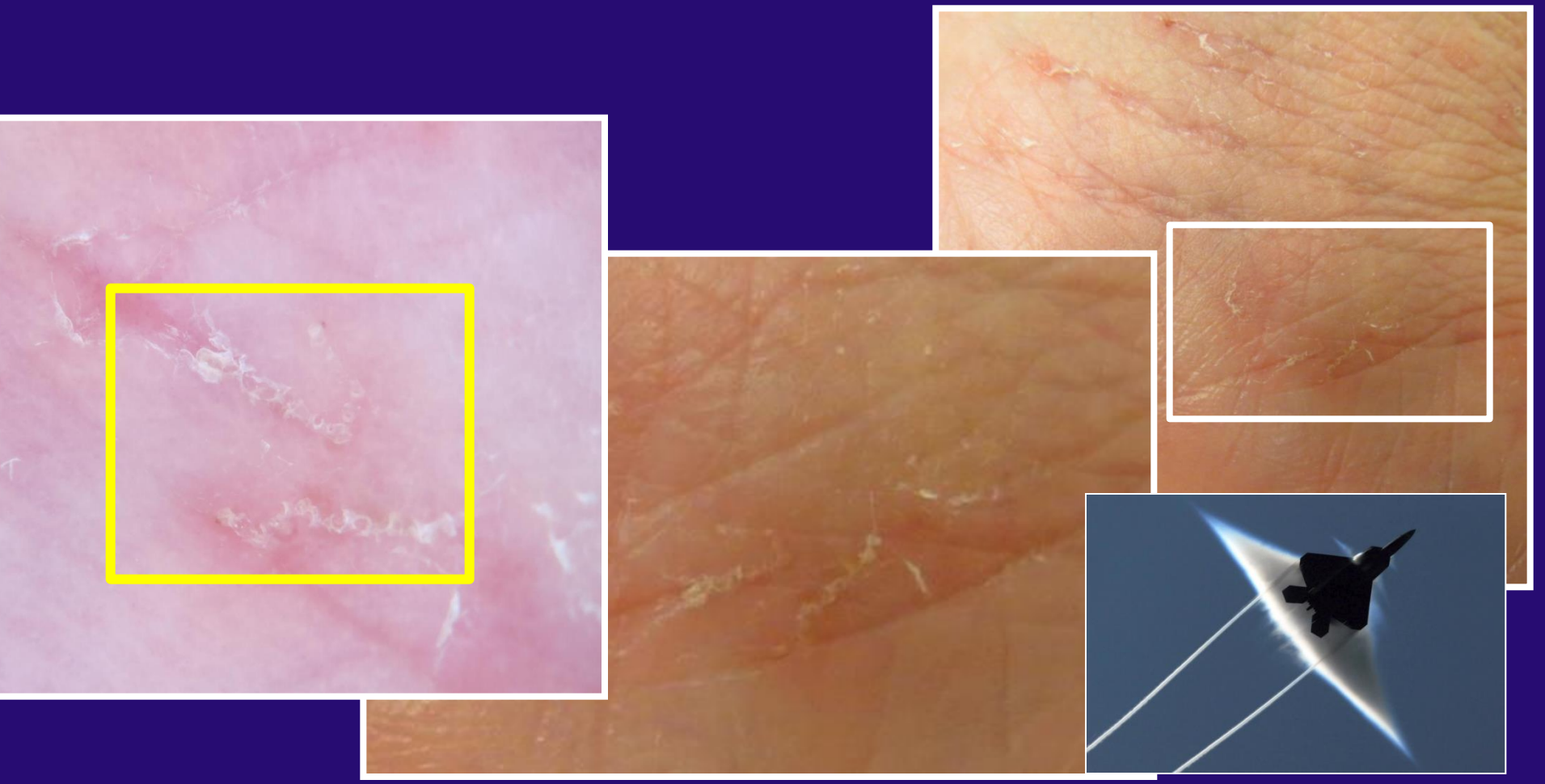
Scabies: Diagnostic Pearls

Burrows

and the

"Delta Wing Sign"

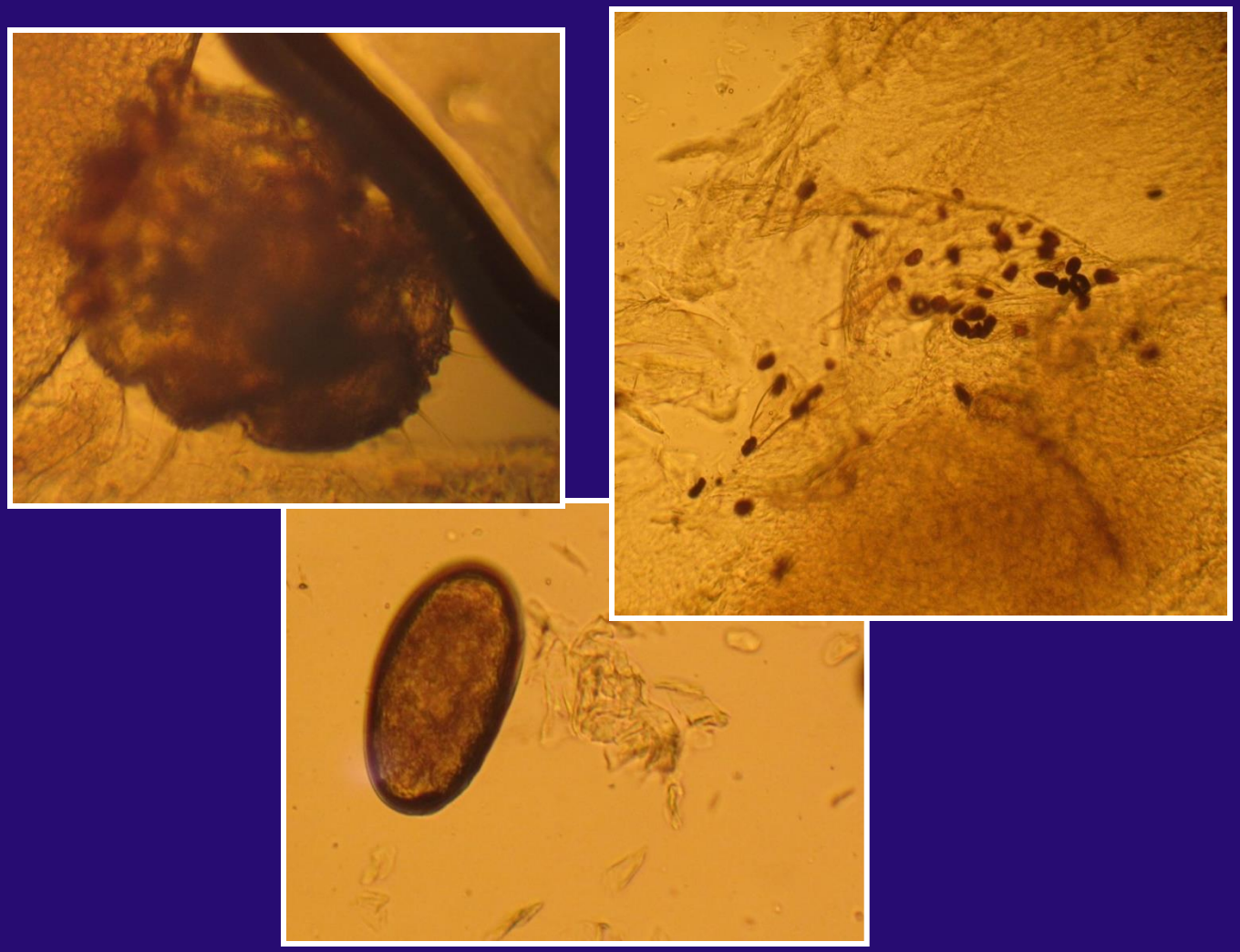
Scabies: Diagnostic Pearls

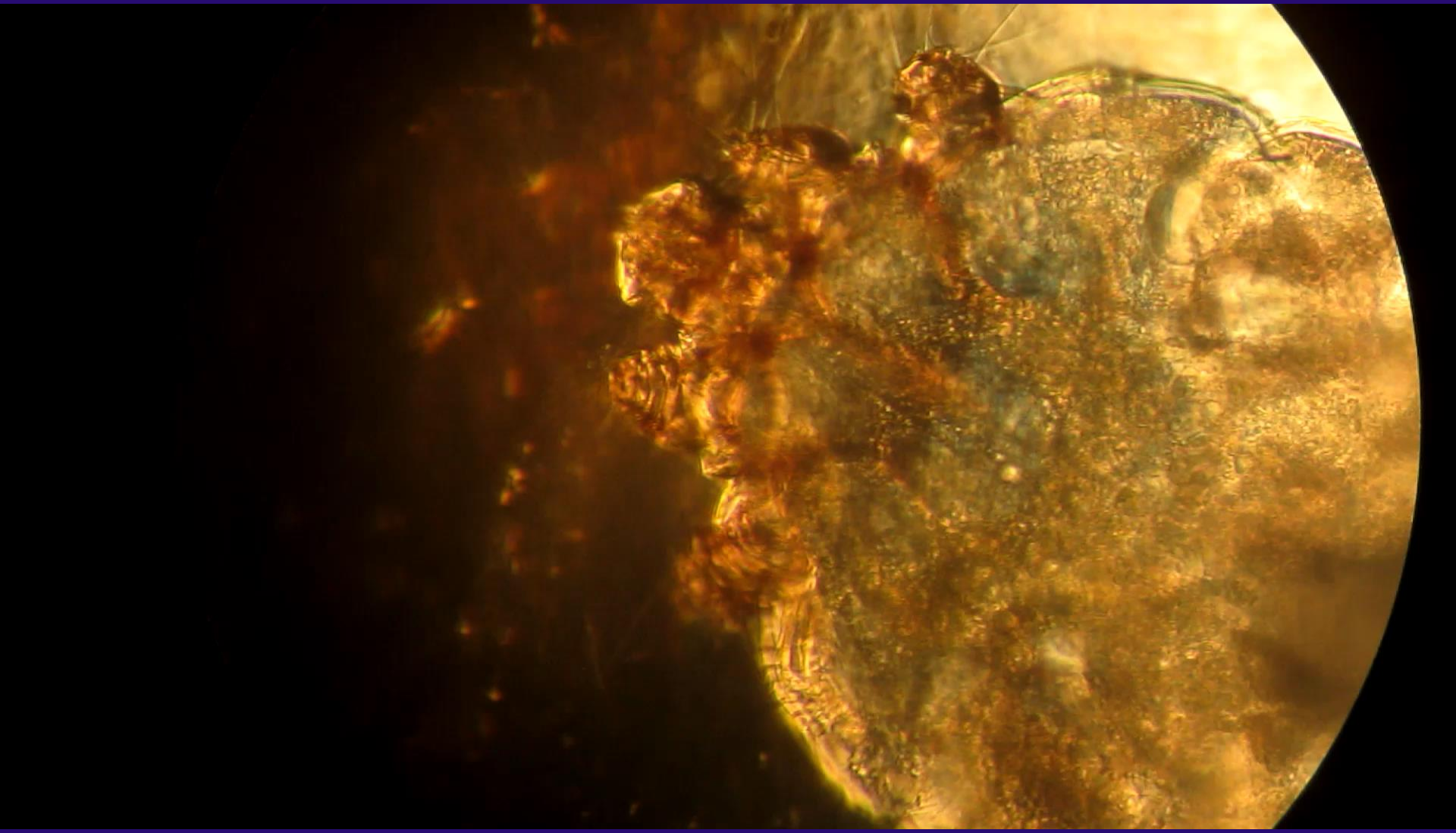


*Argenziano G, Fabbrocini G, Delfino M. Epiluminescence Microscopy: A New Approach to In Vivo Detection of Sarcoptes scabiei. *Arch Dermatol.* 1997;133(6):751–753.

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

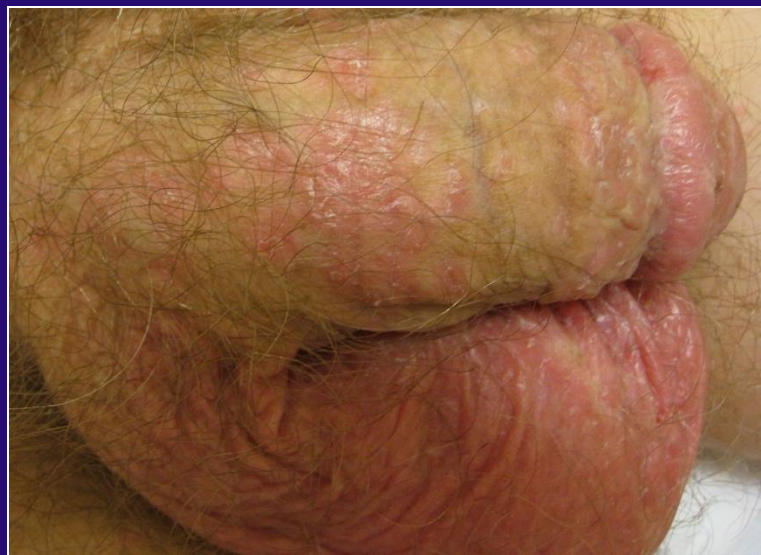
Bonus Case (time permitting)

- 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
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**

Does this change anyone's mind?

Diagnosis? (round 2)

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

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RPR	**Negative**
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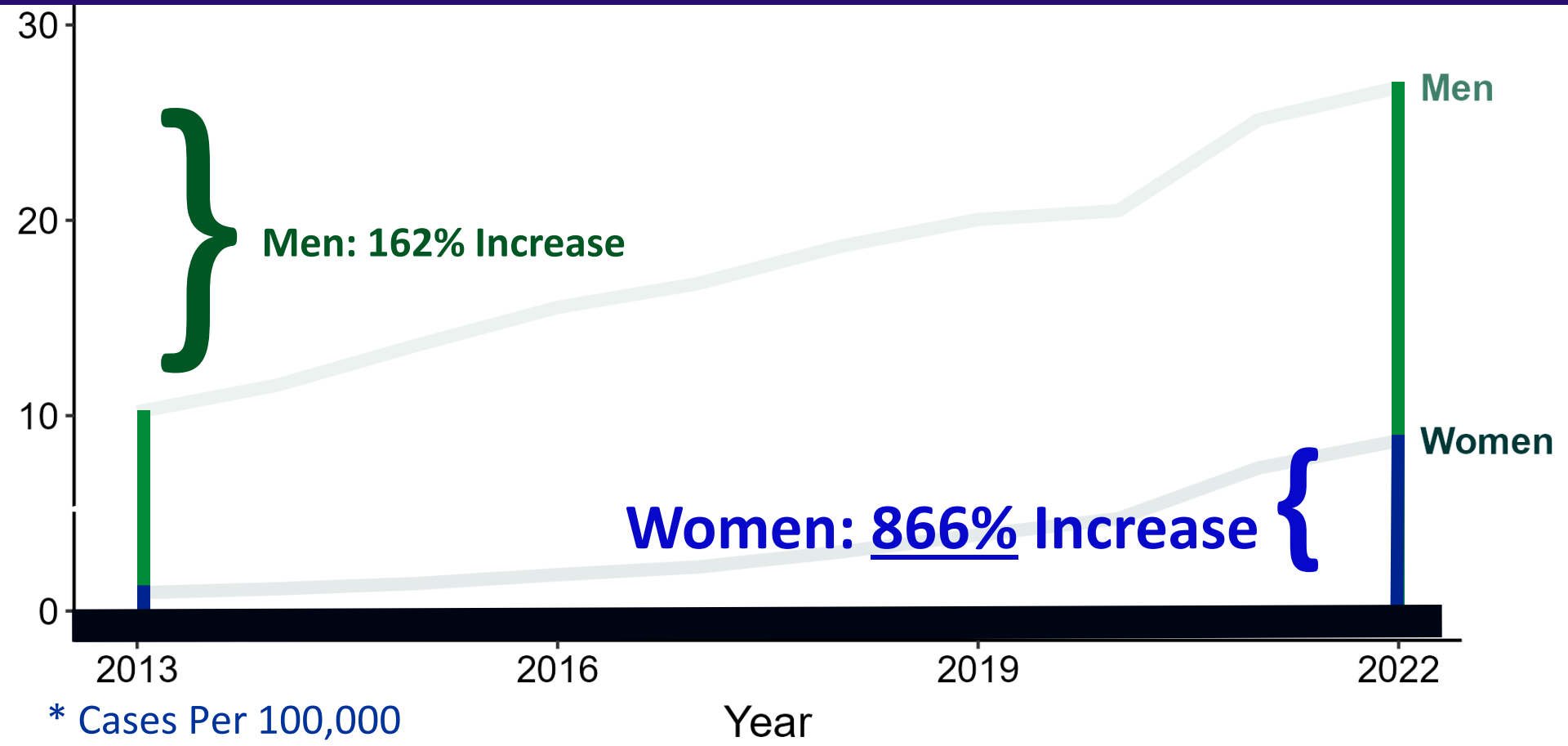
Skin Biopsy	**Lichenoid and superficial and deep lymphohistiocytic infiltrates with plasma cells and granulomas**

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

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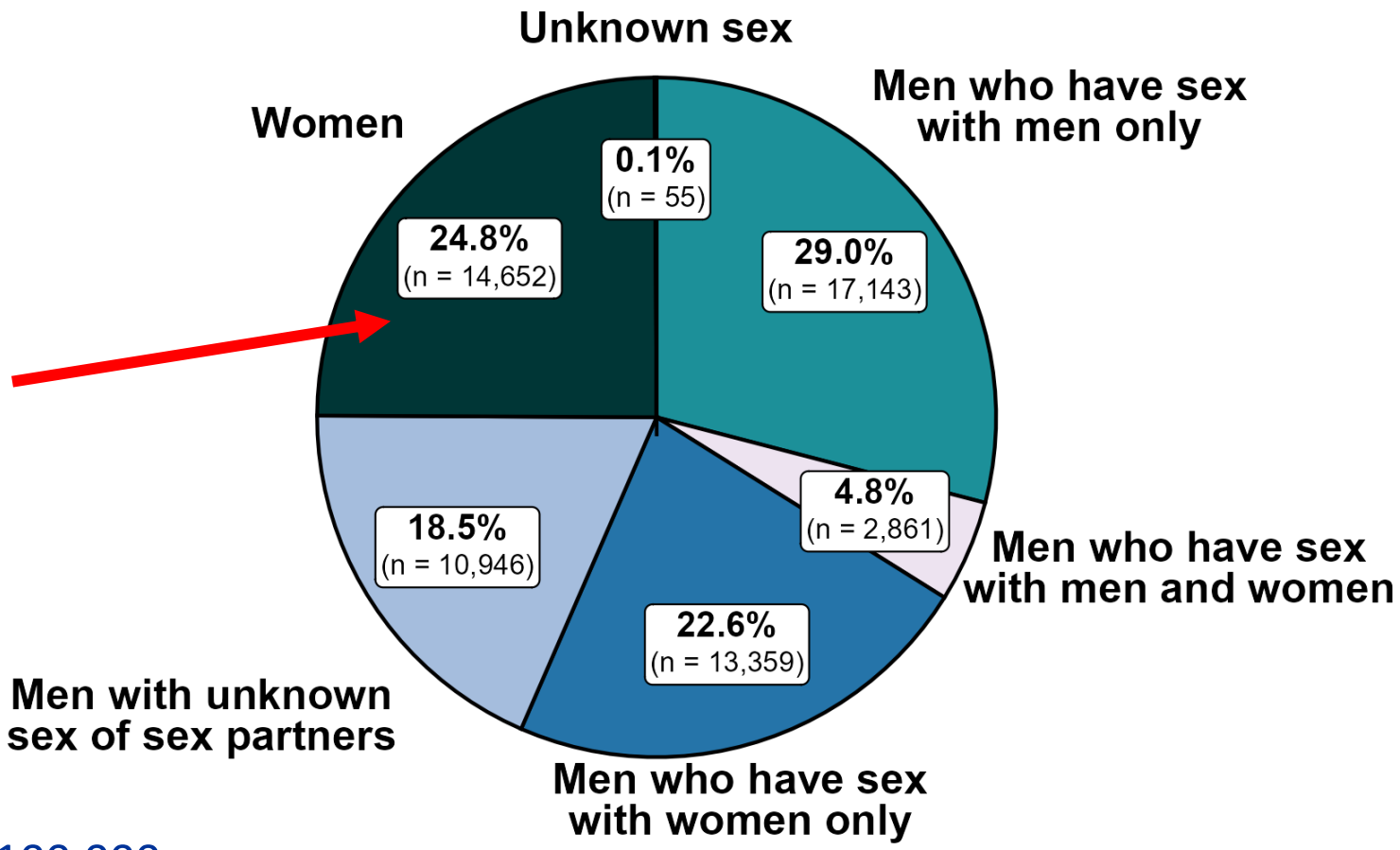
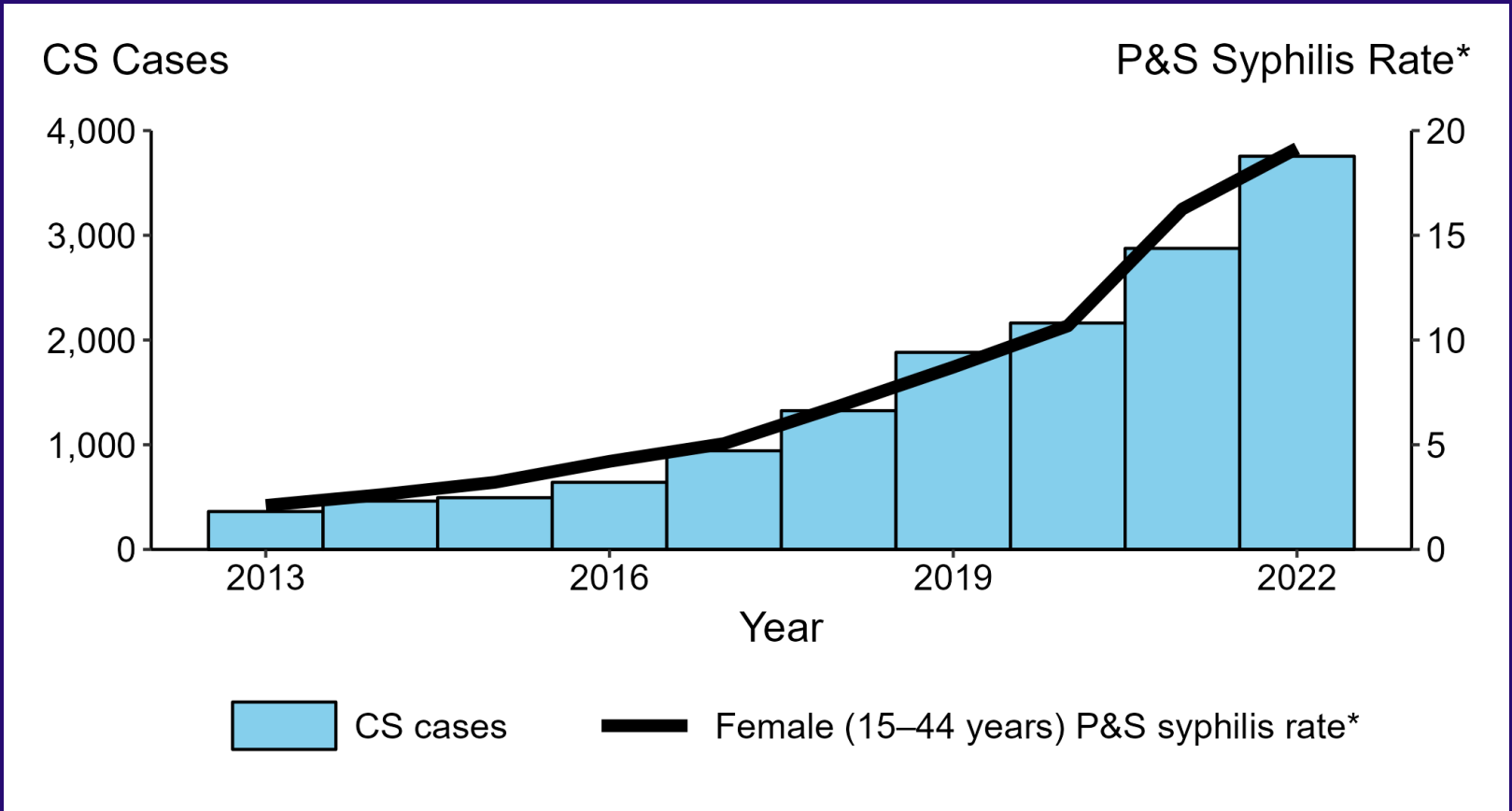


* Per 100,000

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

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

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**
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?

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

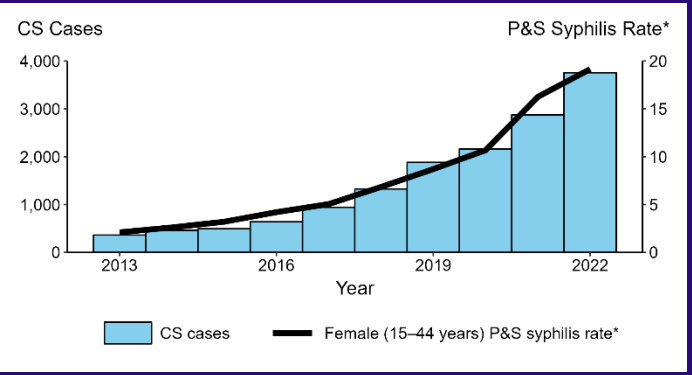
Prozone phenomenon: Notable antibody excess prevents agglutination

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)**



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

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

Prozone Phenomenon

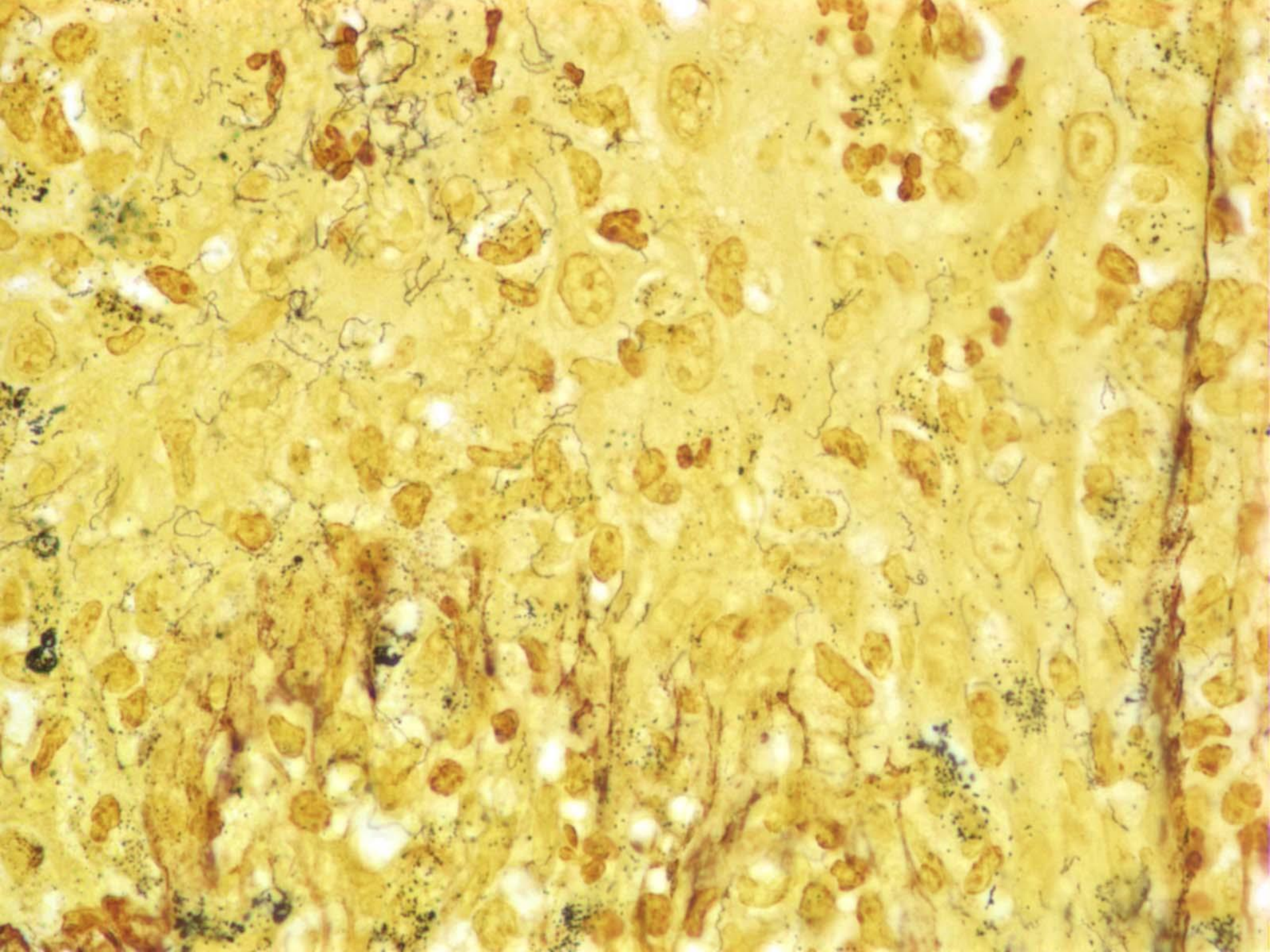
Prozone phenomenon: Notable antibody excess prevents agglutination

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
  - Rupioid: “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

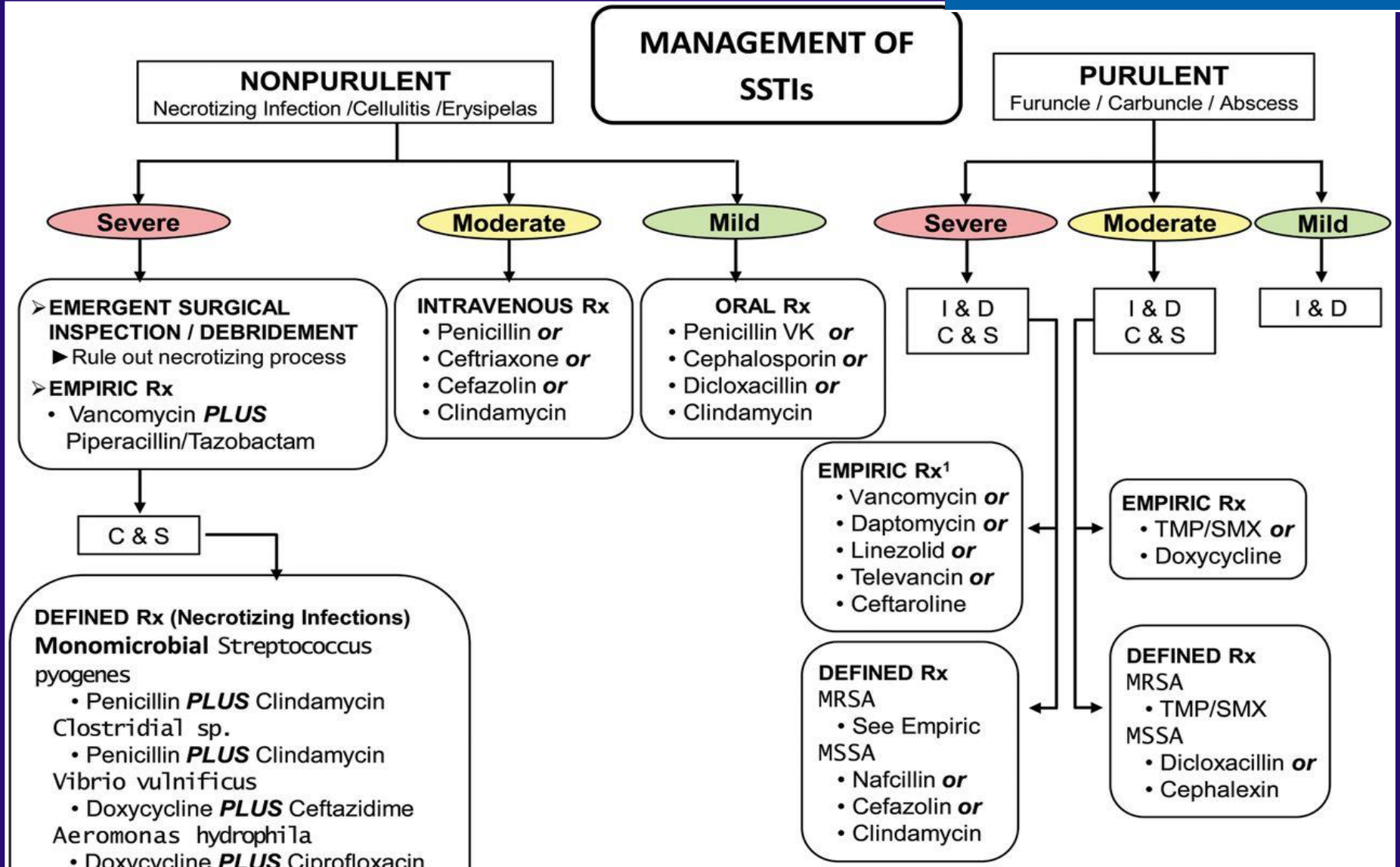
IN CASE QUESTIONS ARISE:

Management of *Purulent* Skin Infections

June 2014

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

IDSA GUIDELINE

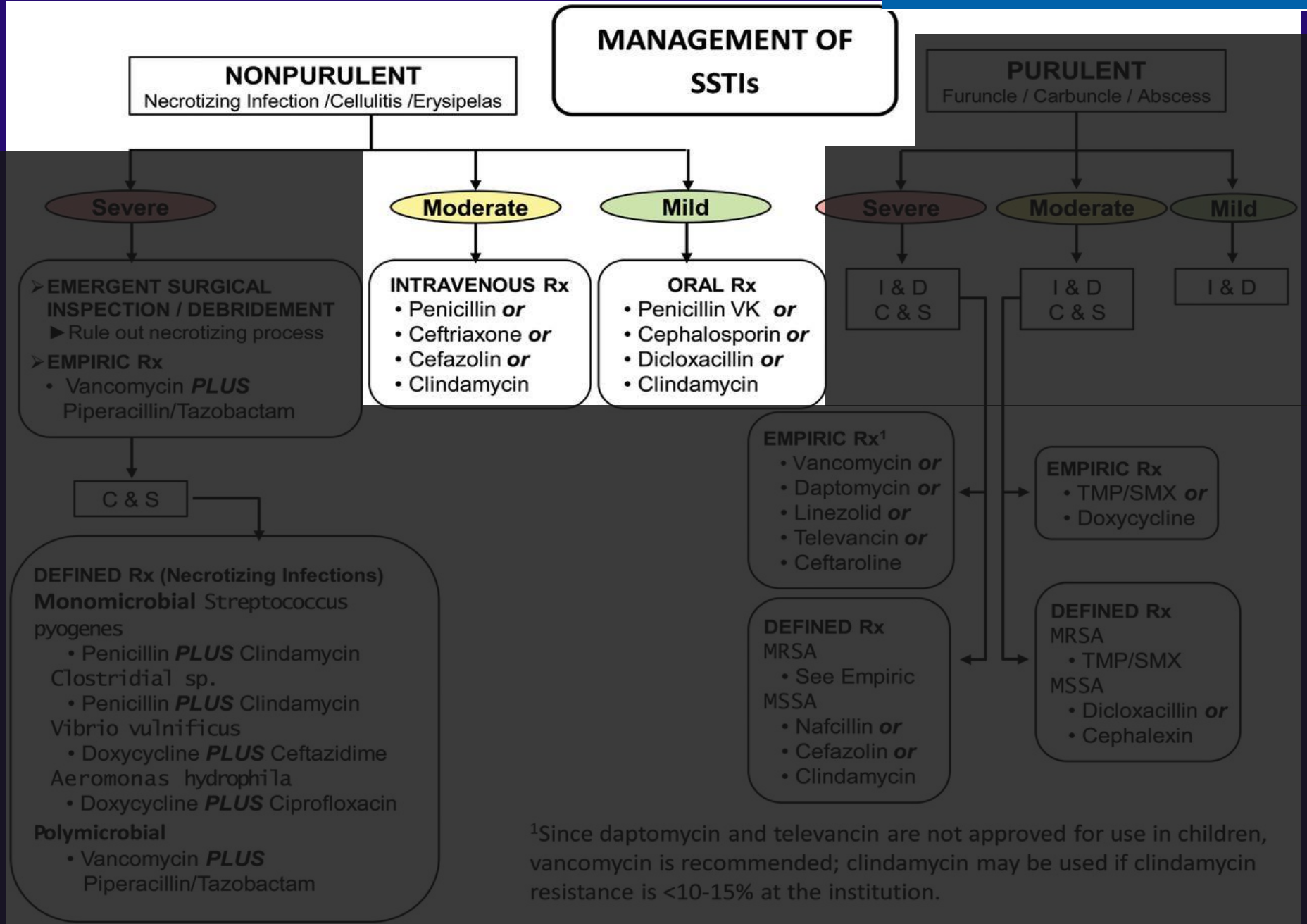


[1]Since daptomycin and televancin are not approved for use in children, vancomycin is recommended; clindamycin may be used if clindamycin resistance is <10-15% at the institution.

June 2014

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

IDSA GUIDELINE



June 2014

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

IDSA GUIDELINE

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
  - **EMPIRIC Rx[1]**
    - Vancomycin *or*
    - Daptomycin *or*
    - Linezolid *or*
    - Televancin *or*
    - Ceftaroline
  - **DEFINED Rx**
    - MRSA
      - See Empiric
    - MSSA
      - Nafcillin *or*
      - Cefazolin *or*
      - Clindamycin
- Moderate
  - I & D
  - C & S
  - **EMPIRIC Rx**
    - TMP/SMX *or*
    - Doxycycline
  - **DEFINED Rx**
    - MRSA
      - TMP/SMX
    - MSSA
      - Dicloxacillin *or*
      - Cephalexin
- Mild
  - I & D

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

Cochrane Library

Cochrane Database of Systematic Reviews

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 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
- 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	
	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}

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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)
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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.

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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)
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)
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		(86.9–97.2)	+16.1	110/117	94.0 (89.3–98.7)	+18.0	73/96	76.0 (67.0–85.1)
		(89.2)	+23.2	39/49	79.6 (67.3–91.9)	+13.7	29/44	65.9 (50.8–81.1)
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Likely more reflective of antibiotic impact on true abscesses

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

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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%**	

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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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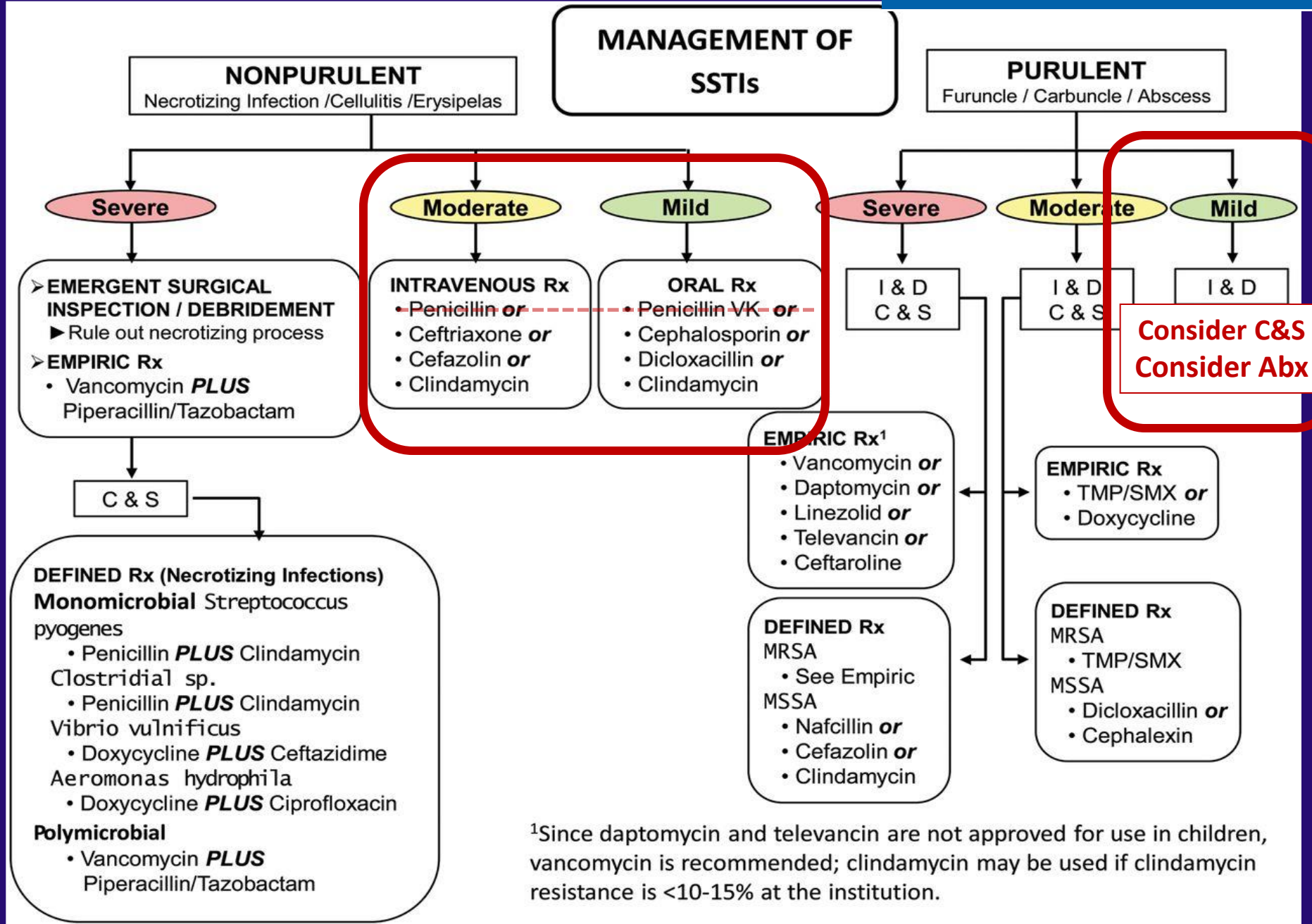
My Personal Approach:

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



[1]Since daptomycin and televancin are not approved for use in children, vancomycin is recommended; clindamycin may be used if clindamycin resistance is <10-15% at the institution.

Thank you again!