Skin and Soft Tissue Infections:

A 2022 update

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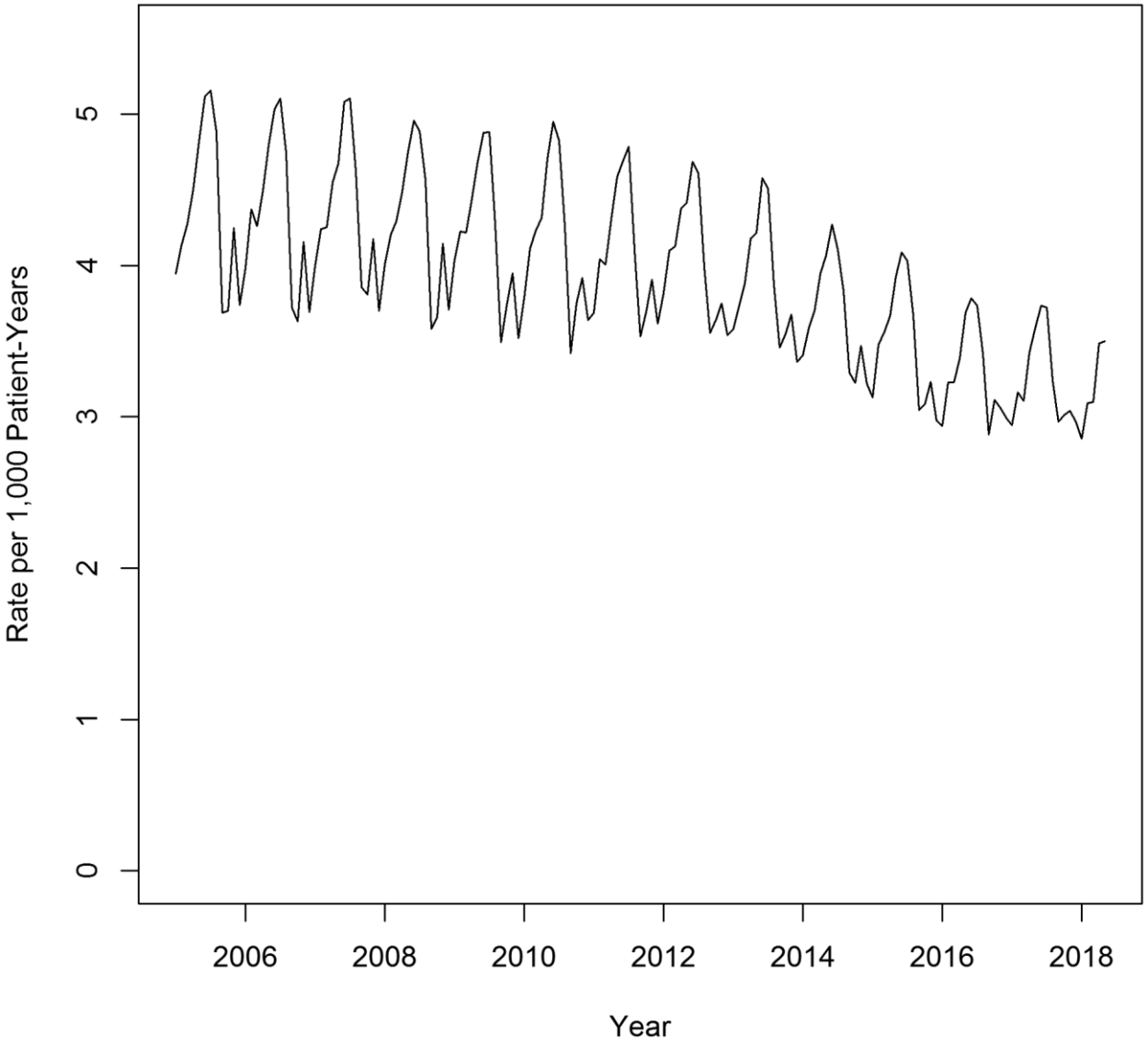
No Disclosures

Learning Objectives

- A brief word on epidemiology
- Review the optimal management of purulent and non-purulent cellulitis
- Understand the differential diagnosis of cellulitis
- Learn the clinical findings suggestive of necrotizing skin and soft tissue infections
- Understand how to approach skin infections in persons who inject drugs
- Review preventive strategies

Declining Incidence of SSTIs, 2005-2018



Rhoads *et al*. Clin Infect Dis 2021;72:675

Declining Incidence of CA-MRSA

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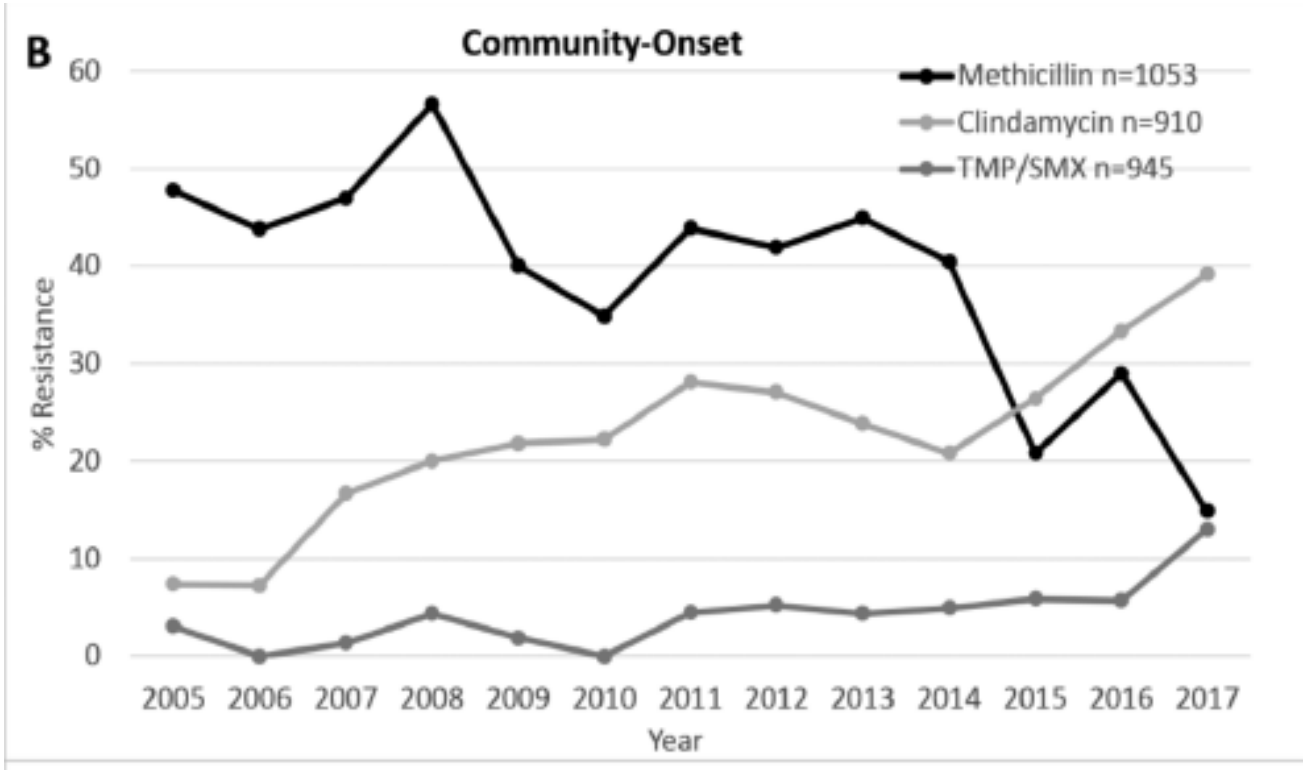
Percent *Staph aureus* isolates resistant to methicillin



Khamash *et al*. JPIDS 2019;8:351

Declining Incidence of SSTIs

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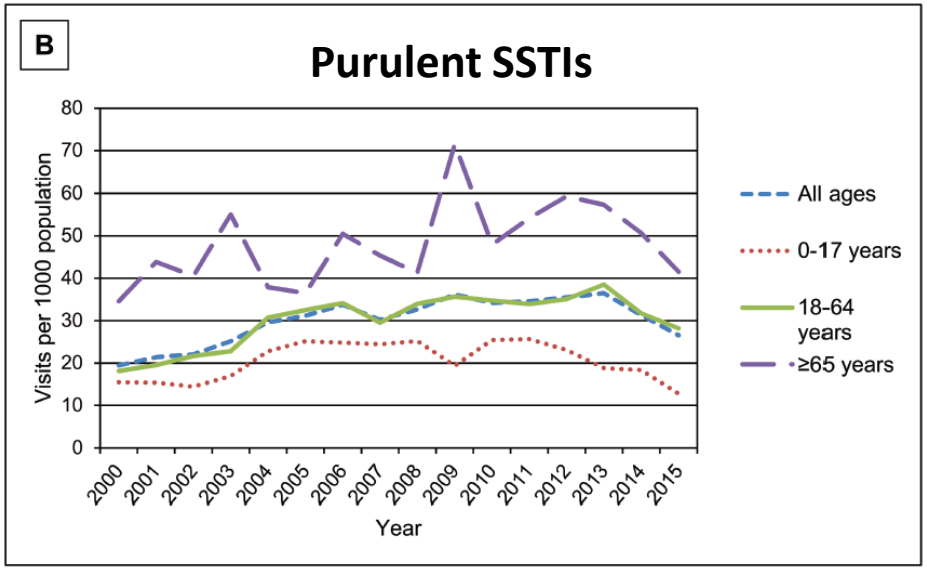
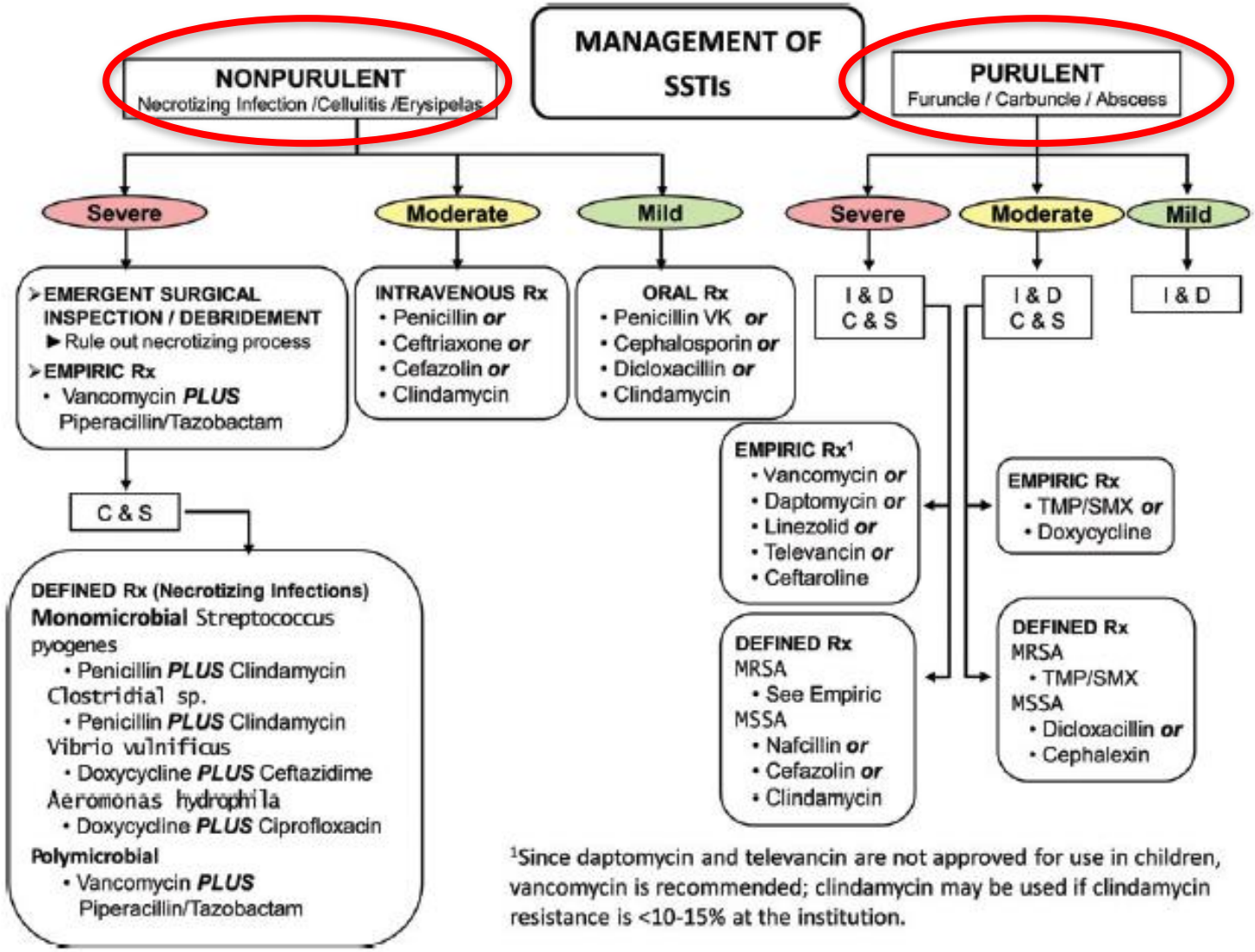
- Both purulent and non-purulent infections
  - Natural evolution of the USA300 epidemic
  - Immune adaptations
  - Increasingly appropriate antimicrobial treatment
  - Unattended SSTIs

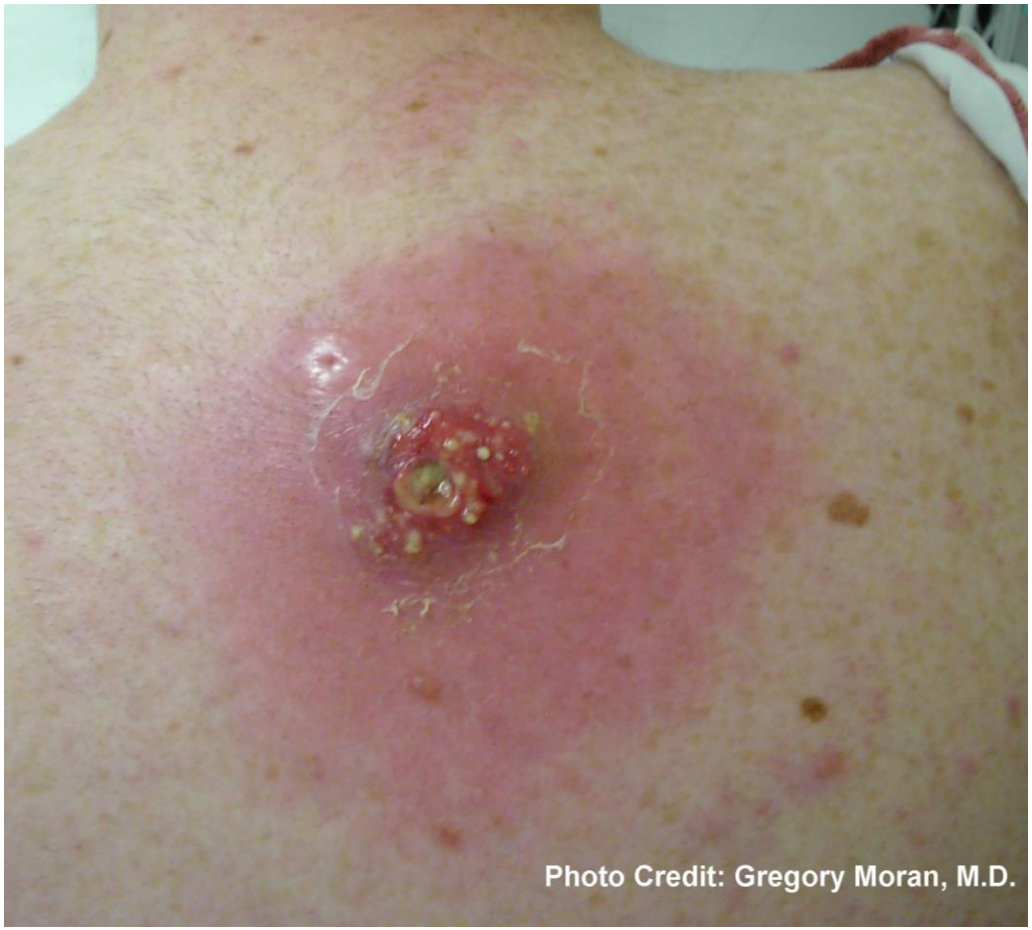


Fritz *et al*. Clin Infect Dis 2020;70:2715
Rhoads *et al*. Clin Infect Dis 2021;72:675



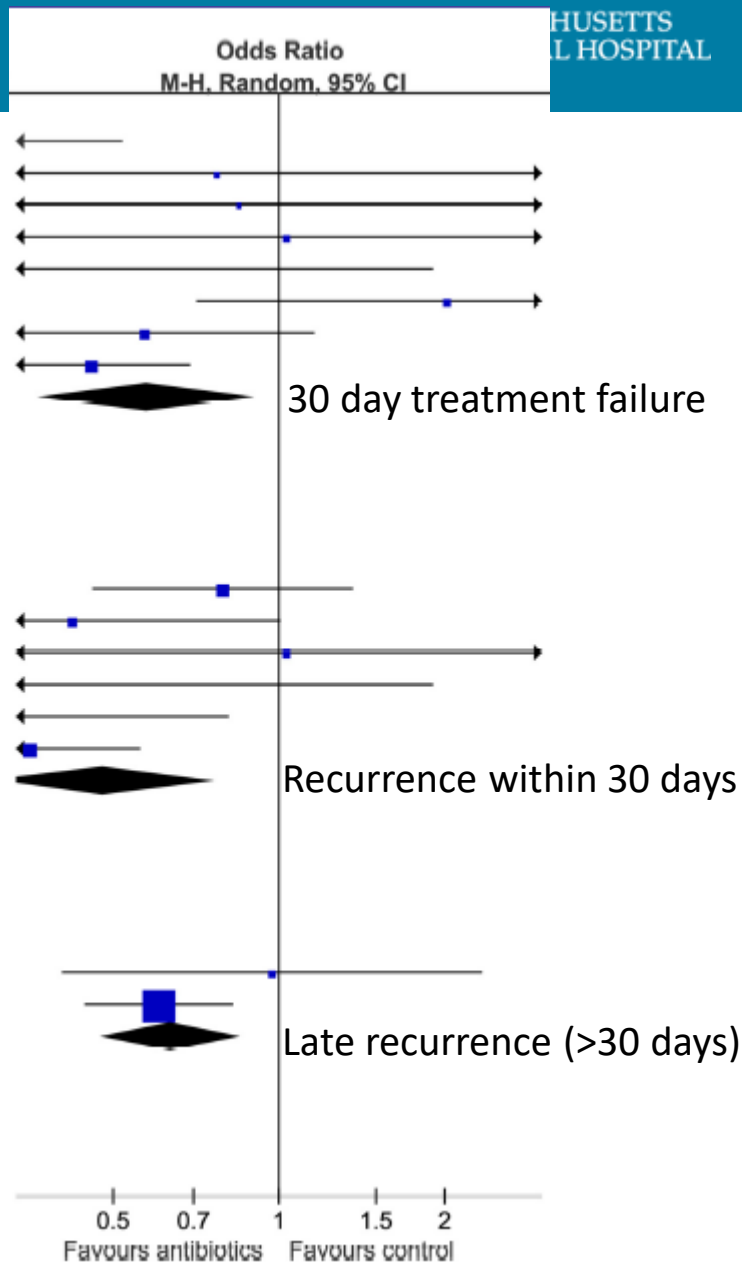
Stevens *et al*. Clin Infect Dis 2014; 59 (2): e10

Purulent SSTIs: Cutaneous abscesses



Cutaneous Abscess: Treatment

- Mainstay: Incision and drainage (I&D)
- Multiple randomized controlled trials
  - Inpatient and Outpatient studies
- Antibiotic therapy:
  - Less treatment failure
  - Less recurrence
  - Reduction in hospitalization & surgery
  - Reduction in household spread
- Only MRSA-active antibiotics show benefit
- More adverse effects with antibiotics



Wang *et al*. BMJ Open 2018;8e020991

Antibiotics for purulent SSTIs: a deeper dive

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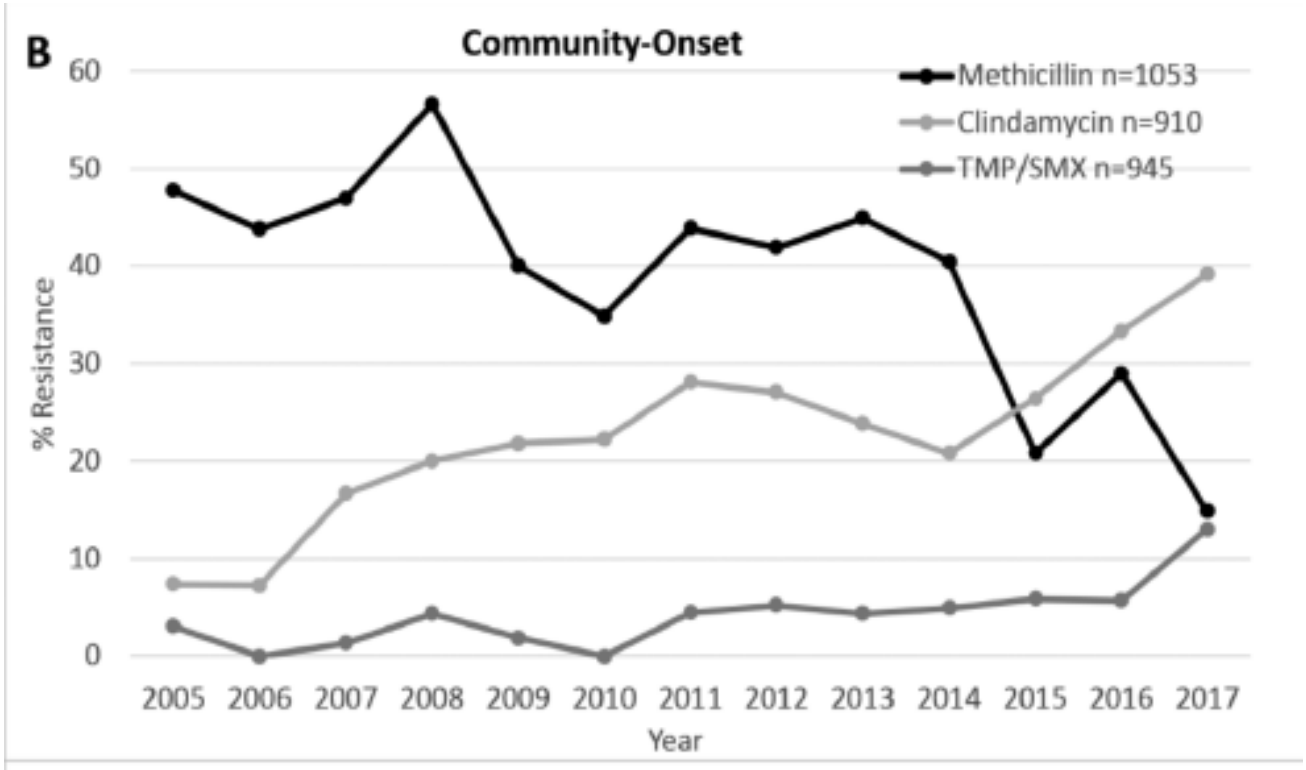
- Literature supports antibiotics for purulent SSTIs > 2 cm
- Antibiotic duration >7 days associated with greater likelihood of cure and lower likelihood of recurrence
- No difference for abscesses not due to *Staph aureus*
- Clindamycin more effective than TMP/SMX at preventing recurrence
  - Greater impact on colonized state
  - Geographic differences in clindamycin resistance (10-50%)
  - Clindamycin resistance in *Staph aureus* increasing over time
  - Clindamycin may be less well tolerated

Talan *et al*. Ann Emerg Med 2018;71:21
Lake *et al.* Clin Infect Dis 2020;71:661
Hogan *et al*. Clin Infect Dis 2018;66:191
Sutter *et al*. Pediatrics 2016;137:e20153099

Increasing clindamycin and TMP/SMX resistance

Percent *Staph aureus* isolates resistant to antibiotics



Khamash *et al*. J Pediatric Infect Dis Soc 2019;8:351

CA-MRSA: Recurrence

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- 16-19% of patients with *Staph aureus* SSTI have recurrence
  - Most individuals have only one recurrence; half within 3 months
- Decolonization studies have been disappointing in preventing SSTI
  - Recent RCT: no added benefit of decolonizing the household
- Methods and schedules for decolonization vary
  - Nasal mupirocin (alternative: nasal povidone iodine)
  - 4% chlorhexidine versus dilute bleach (1/4 cup in 1/4 tub)
  - Resistance to mupirocin and chlorhexidine occurs
- Small studies suggest role of oral antibiotics in decolonization
- Role of environmental decontamination unknown
  - Household colonization a predictor of recurrence

Cluzet *et al*. Clin Infect Dis 2015;60:1489
Jorgensen *et al*. Infect Dis 2018;50:687
Lindgren *et al*. Int J Antimicrob Agents 2018;51:642
Vella *et al*. Clin Infect Dis 2021;73:e1045

Nonpurulent SSTIs

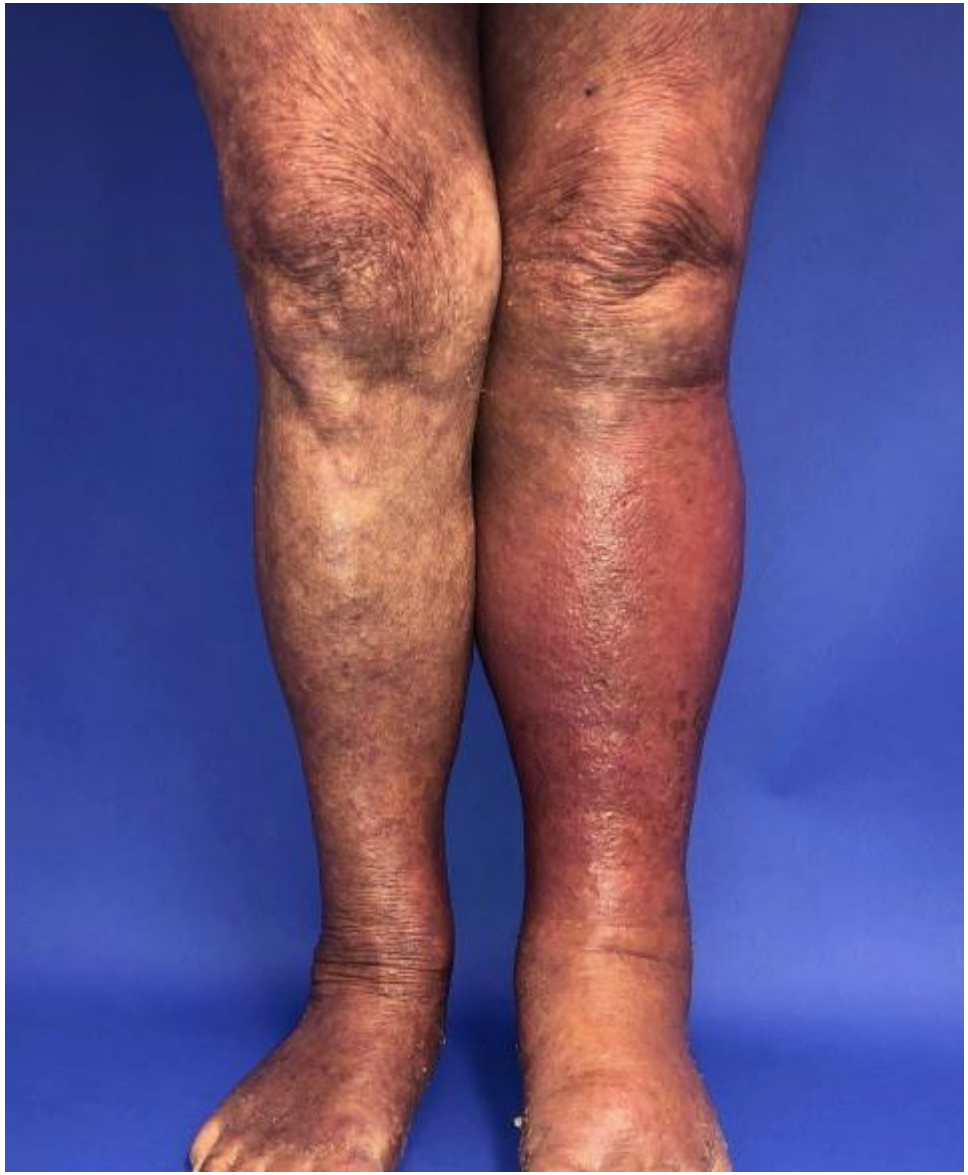
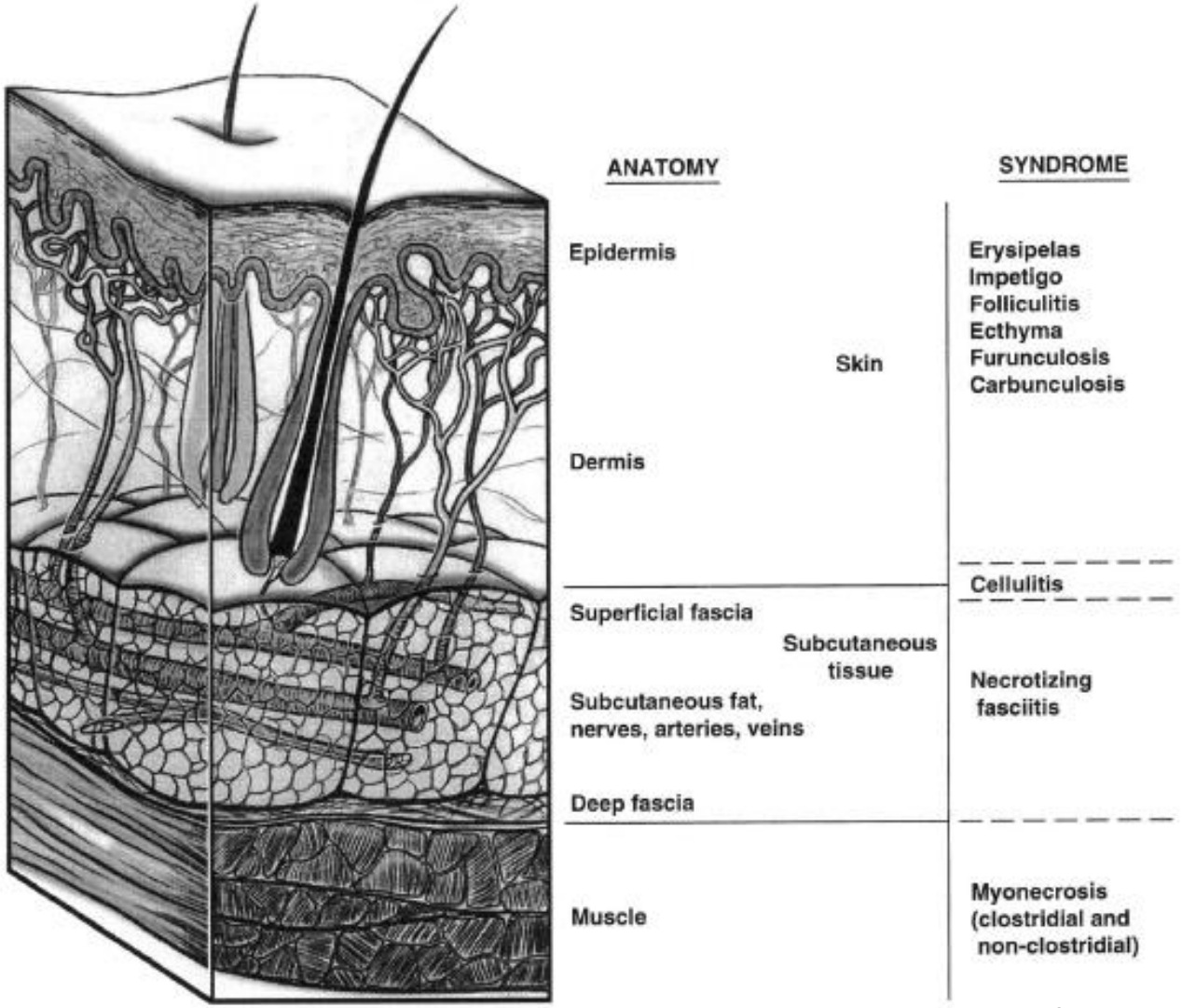


Photo: DermNetNZ.org

Nonpurulent SSTIs

Erysipelas: Infection of the papillary dermis

Cellulitis: Infection of the reticular dermis and subcutaneous fat



Green RJ Chest 1996: 219-29

Nonpurulent cellulitis in era of MRSA

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- Treatment of nonpurulent cellulitis is empiric
  - Blood cultures rarely positive (2-7%)
- Most nonculturable cellulitis due to pyogenic streptococci (70-75%)
  - Even when wounds culture *Staph aureus*
- β-lactam therapy remains optimal with high cure rates
  - Inpatient and outpatient clinical studies
  - No benefit seen with addition of TMP/SMX to cephalexin in small RCT
- MRSA should be considered if:
  - Penetrating trauma, illicit drug use, prior MRSA, inability to exclude associated abscess, and in severe infection

Bruun *et al*. Open Forum Infect Dis 2015 Nov 25; 3(1)
Torres *et al*. Am J Emerg Med 2017;35:1159
Moran *et al*. JAMA 2017; 317: 2088

Gram-Negative Cellulitis

- Host Risk Factors:
  - Age, diabetes, peripheral vascular disease, chronic liver disease, immunocompromise
- Relevant Exposures:
  - Saltwater or freshwater exposure, animal bites
- Organisms:
  - *E. coli, Klebsiella, Campylobacter/Helicobacter, Vibrio, Aeromonas, Shewanella, Pseudomonas, Pasteurella*
- Consider empiric coverage for Gram-negative organisms:
  - Severe cellulitis including septic physiology
  - Appropriate epidemiologic risk factors

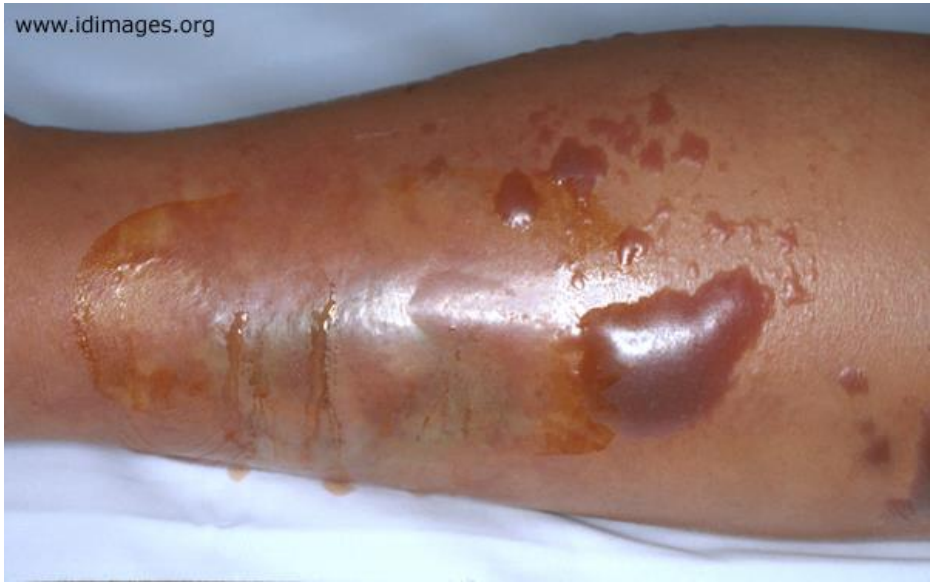
Vibrio infections

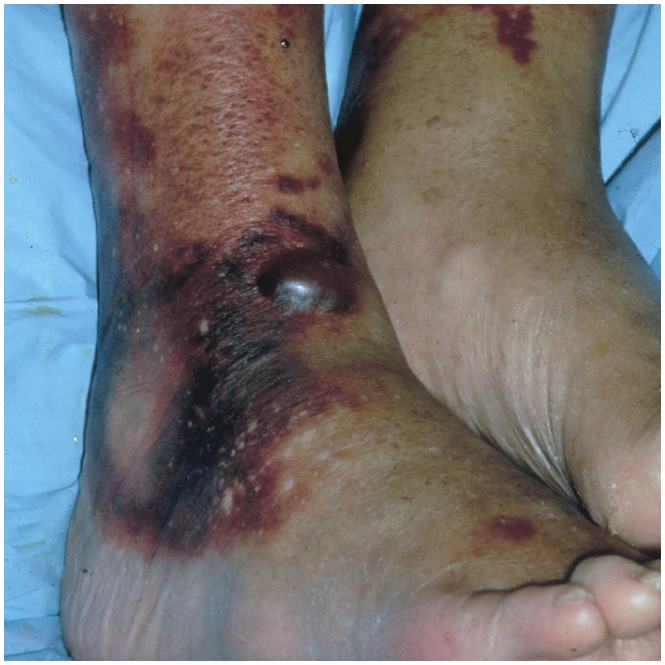
- Gram negative organisms accumulated by filter-feeding fish
- Seasonal, May-October (water temperatures > 22º Celsius)
- Seen now at higher latitudes
- Seen with saltwater exposure
  - Handling seafood or fishing equipment
  - Swimming, walking on beach
- Ingestion of raw oysters (*vulnificus*)
  - Primary septicemia
- Comorbidities common
  - Liver disease, alcohol use
- Treatment:
  - Doxycycline plus 3rd gen cephalosporin

King *et al*. Ann Intern Med 2019;171:520

Vibrio vulnificus

- A "can't miss" diagnosis
- Clinical infection is usually severe and progressive
  - Cellulitis with hemorrhagic bullae, rapid necrosis and ulceration
- Underlying liver disease (80%)
- Fatality rate 53% in primary septicemic form





Haq. Am J Gastroenterol 2005;100:1195

Anti-inflammatories for cellulitis?

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- Three small randomized controlled trials have shown trend towards benefit for addition of anti-inflammatories
  - All uncomplicated cellulitis or erysipelas
  - Outcome measured time to regression of inflammation
  - Studies underpowered, results not significant
    - Benefit approximately equivalent to one day difference
- Regimens studied:
  - 8-day prednisolone taper; 5 days Ibuprofen 400 mg TID-QID
- Cautions:
  - avoid if concern for complicated, deep or necrotizing SSTI
  - not studied in diabetics, renal disease

Bergkvist and Sjobeck. Scand J Infect Dis 1997;29:377
Dall *et al*. Cutis 2005;75:177
Davis *et al*. Clin Microbiol Infect 2017;23:242

Prevention of Cellulitis

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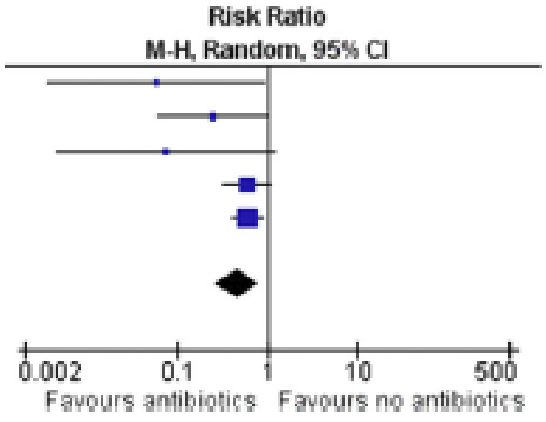
- Risk of recurrence 16-30%
  - Cellulitis leads to impaired lymphatic function
  - Impaired lymphatic function predisposes to cellulitis
- Address Modifiable Risk Factors
  - Stasis / lymphedema
  - Underlying skin disease (e.g. intertrigo, tinea, xerosis)
  - Optimize diabetes control
  - Assess vasculature
  - Wound care
- Antibiotic prophylaxis lowers risk of recurrence by 50%
  - Consider if 3-4 episodes per year
  - Oral or intramuscular penicillin best studied
  - Benefit only accrues while on antibiotic prophylaxis



Oh *et al*. J Infect 2014;69:26
Cannon *et al*. Clin Microbiol Infect 2018;24:1084

Compression to prevent cellulitis

- 84 patients with chronic edema and recurrent cellulitis
  - Randomized: compression or no compression
    - Fit by wound specialist
    - Most knee high
    - 23 – 32 mm Hg
- Stopped early at interim analysis
  - HR for recurrence: 0.23 (0.09 – 0.59); NNT 4
  - Also: improved quality of life
- Cautions:
  - Avoid in arterial disease, acute infection, open wounds

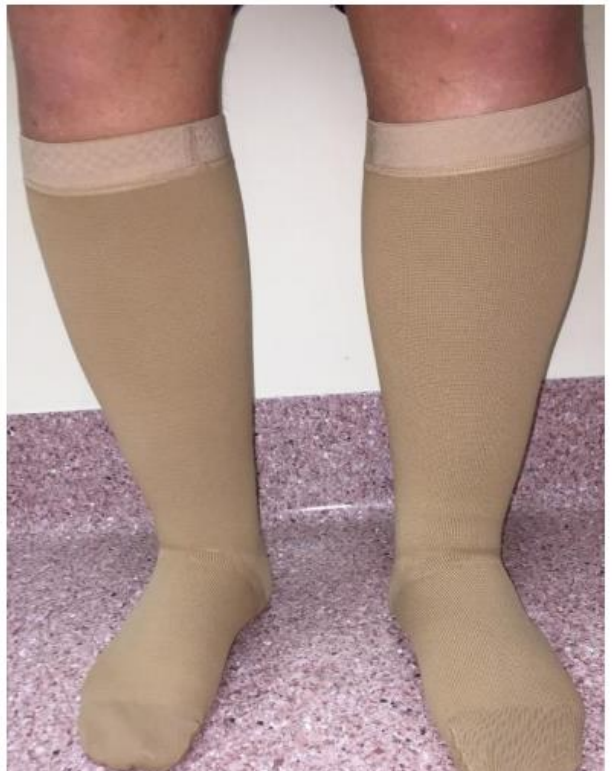
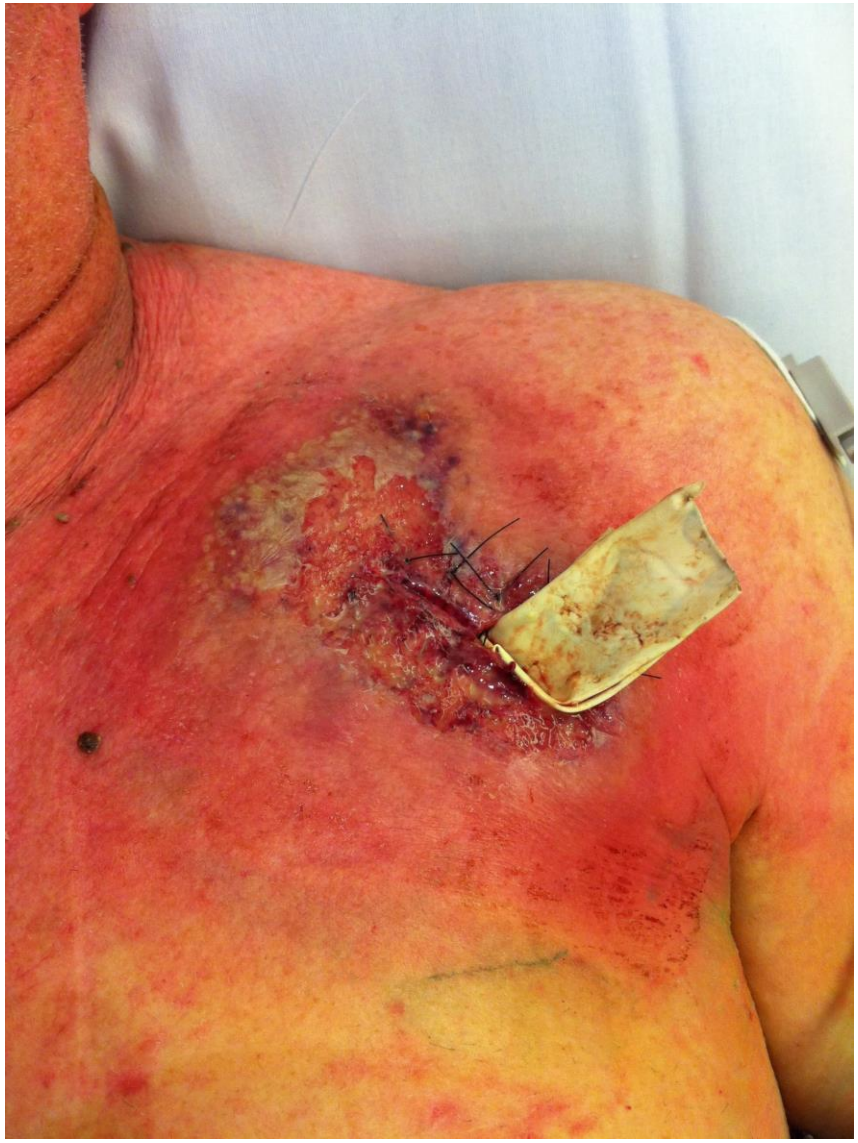


Figure 2. Freedom from Recurrence of Cellulitis over Time.
Shown are the Kaplan–Meier estimates of the freedom from recurrence of cellulitis in the compression group and the control group. The shaded areas indicate 95% confidence intervals. The median follow-up was 186 days.

Webb *et al*. NEJM 2020;383:630

Cellulitis that doesn't improve…



78-year-old male underwent pacemaker placement for sick sinus syndrome

- 6 days later developed cellulitis overlying incision
- Fevers and purulent drainage
- Started on vancomycin and ceftriaxone
- Device explanted, cultures negative at 48 hours
- Persistent fevers to 103°; WBC to 30K, spreading erythema and necrosis

Common causes of Pseudocellulitis:

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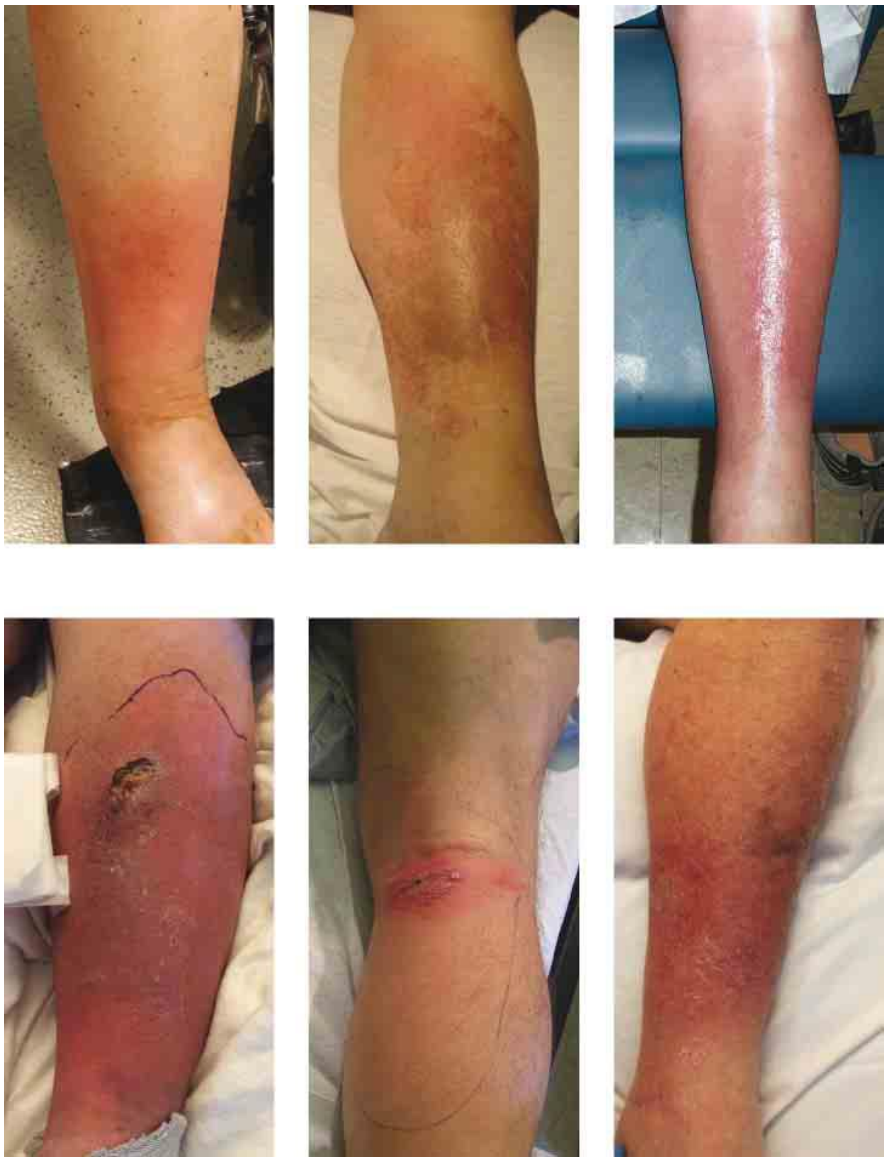
- Stasis dermatitis (most common misdiagnosis)
- Inflammatory
  - panniculitis, connective tissue disorders
- Malignancy
  - carcinoma erysipeloides, leukemia cutis, Paget's of breast
- Neutrophilic dermatoses (e.g. Sweet syndrome)
- Contact dermatitis
- Radiation dermatitis
- Metabolic (e.g. gout)
- Drug reactions
- Insect bites

Raff and Kroshinsky. JAMA 2016;316:325

Which of these in cellulitis?



- Deep vein thrombosis
- Calciphylaxis
- Stasis Dermatitis
- Cellulitis
- Erythema migrans
- Hematoma

Raff and Kroshinsky. JAMA 2016;316:325

Cellulitis versus Pseudocellulitis

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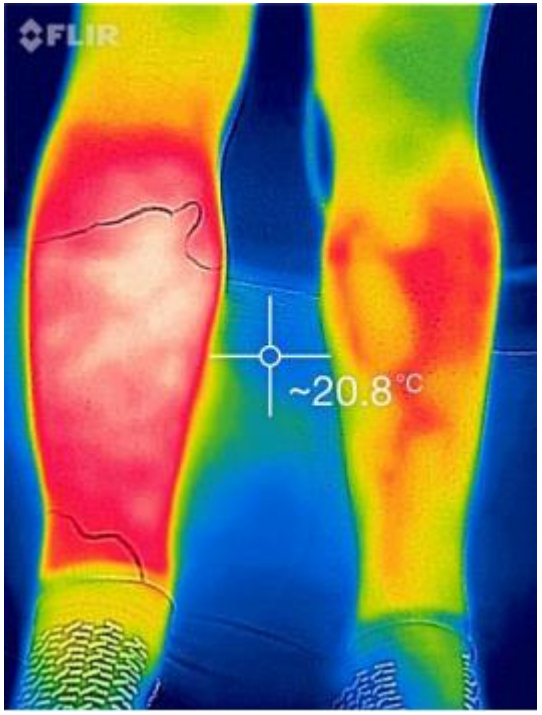
- 30% of inpatient cellulitis misdiagnosed
  - Adds to cost and toxicity
- Favors Pseudocellulitis:
  - Gradual onset of symptoms
  - Bilateral lower extremity involvement
  - Frequent recurrences after discharge
  - Failure to resolve with beta-lactam therapy
- Favors Cellulitis:
  - Temperature difference between extremities (thermal imaging)
  - Unilateral extremity involvement
  - Fever, leukocytosis, tachycardia
- Scoring systems being developed
  - "Diagnostic" trial off antibiotics

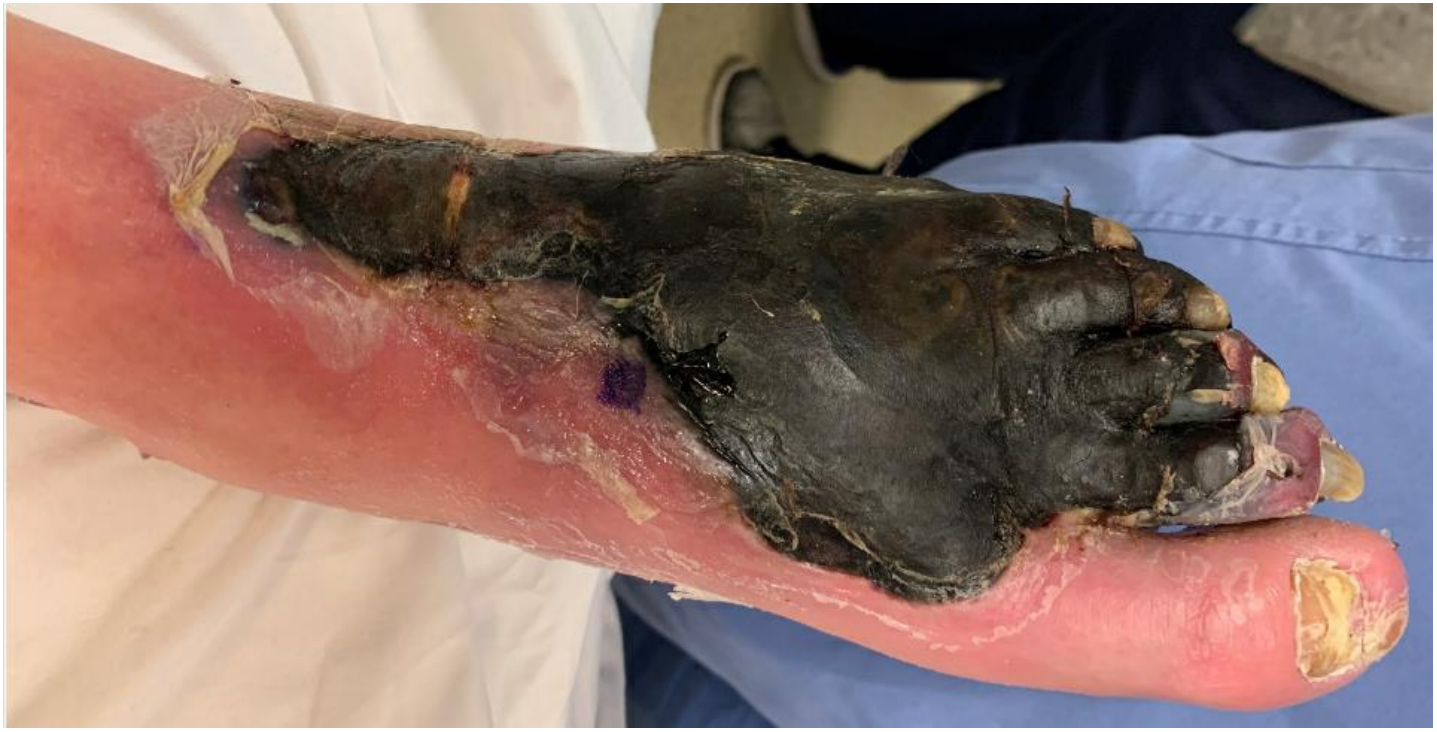


Brindle et al. Abstract 1159
IDWeek 2016

Raff *et al*. J Am Acad Dermatol 2017;76:618
Ezaldein *et al*. Cutis 2018;102:e8
Li *et al*. J Amer Acad Dermatol 2018;79:1076
Brett *et al*. Dermatol Online J 2019;25:14
Ko et al. J Invest Dermatol 2018;138:520

Necrotizing Fasciitis

- Necrosis of deep and/or superficial fascia, along with deeper dermis, subcutaneous tissues and muscle
  - Microvascular thrombosis leads to ischemia
- Characterized by clinical urgency and high mortality



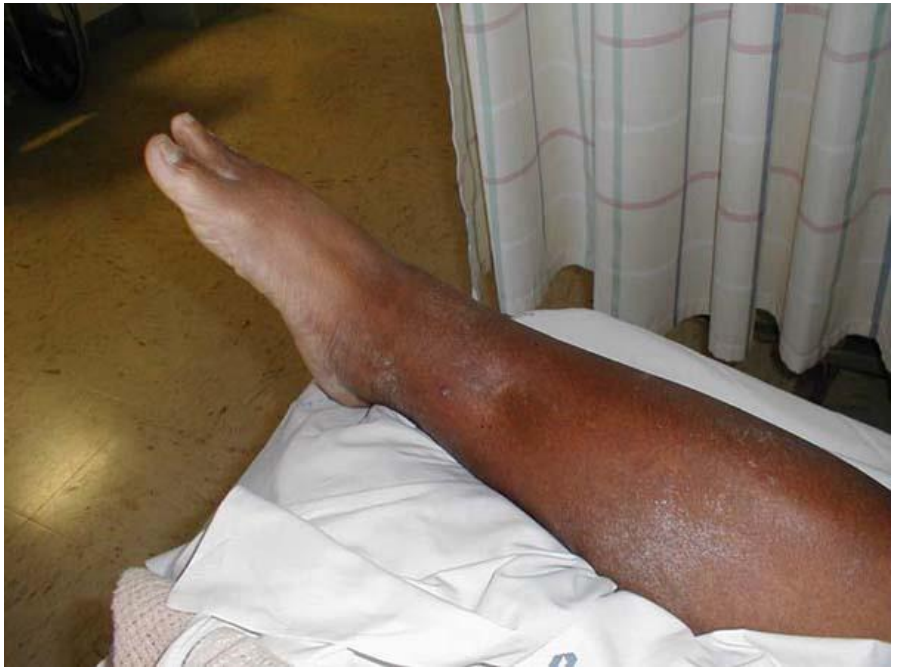
Necrotizing Fasciitis

- Necrotizing Fasciitis Type 1 (2/3 of cases)
  - Polymicrobial: gram positives, gram negatives, anaerobes
  - Perineal infections, penetrating abdominal injury or bowel surgeries, decubitus ulcers
  - Underlying risk factors (diabetes, illicit drug use, vascular disease) common
  - Recently reported association with SGLT2 inhibitors (Fournier's)

- Necrotizing Fasciitis Type 2 (1/3 of cases)
  - Monomicrobial: GAS; also Groups B/C/G streptococcus, *Staph aureus*; Vibrio and Aeromonas species
  - Often a normal host
  - Minor trauma may predispose
  - Limbs predominate

Necrotizing Fasciitis: Clinical Clues

- Woody induration
- Tenderness beyond area of skin involvement
- Rapid extension of skin changes despite antibiotic therapy:
  - discoloration, ecchymoses and bullae, gangrene



- Pain and toxicity out of proportion to local findings
- Cutaneous anesthesia
- Systemic toxicity and laboratory derangements: rise in CPK, creatinine, leukocytosis, thrombocytopenia, acidosis
  - Laboratory Risk Indicator (LRINEC) score insufficiently sensitive

Fernando *et al*. Ann Surg 2019;269:58

Necrotizing Fasciitis: Management

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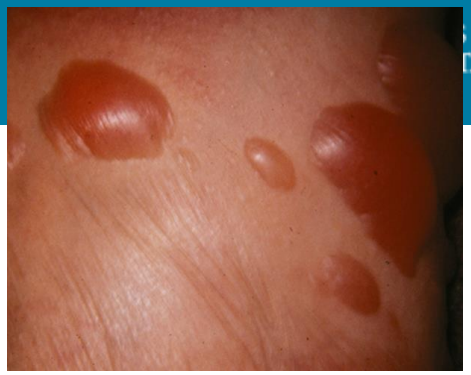
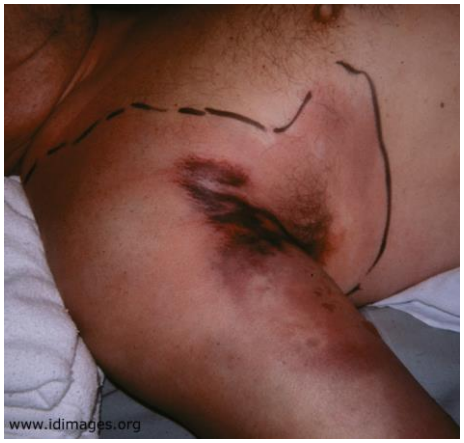
- Surgery to confirm diagnosis
  - Swollen fascia; gray necrotic tissue, dishwater pus, lack of bleeding, lack of resistance to dissection, non-contractile muscle
- Surgical Debridement
  - Numerous retrospective studies confirm early surgery increases survival
  - Surgical reassessment at 24-36 hours and as needed thereafter
- Antimicrobial Therapy
  - Empiric: broad and include coverage against gram-positive (including MRSA), gram negative, and anaerobes
  - Clindamycin if GAS or clostridium suspected
  - Narrow based on cultures
- Intravenous immunoglobulin (IVIG), hyperbaric oxygen not currently recommended

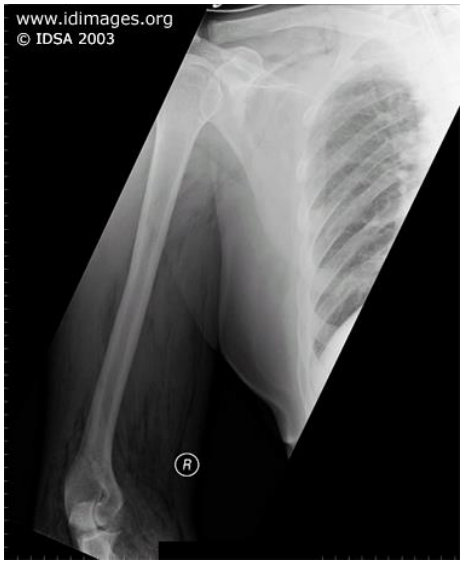
Stevens and Bryant. New Engl J Med 2017;377:2253
Kadri *et al* Clin Infect Dis 2017;64:877
Madsen *et al* Intensive Care Med 2017;43:1585

Clostridial Myonecrosis

- Necrotizing Myositis; a clinical emergency
- Pathogenesis:
  - Hematogenous (*C. septicum*)
  - Traumatic (*C. perfringens*)
  - Anaerobic infection: toxin and gas production lead to ischemia through vascular compromise and pressure necrosis
- Clinical:
  - Rapid progression of skin changes
    - pallor, discoloration (bronze, purple), bullae
  - Gas in soft tissues (crepitus, radiographically)
  - Systemic toxicity and shock
- Management: aggressive surgical debridement
  - Including amputation / disarticulation
  - Penicillin plus clindamycin

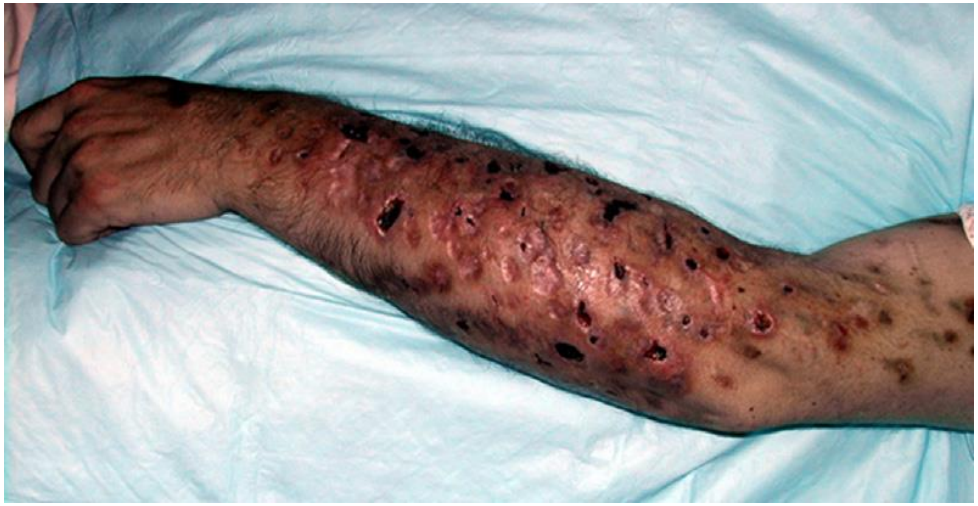






SSTIs in PWID: Epidemiology

- Skin and soft tissue infections are common
  - 10-40% per year by self-report
- Self-treatment is common
  - Self-lancing
  - Antibiotics on street
- Present to medical care at a later stage of infection
- Most common reason PWID engage with medical system
- A risk for subsequent hospitalization and death

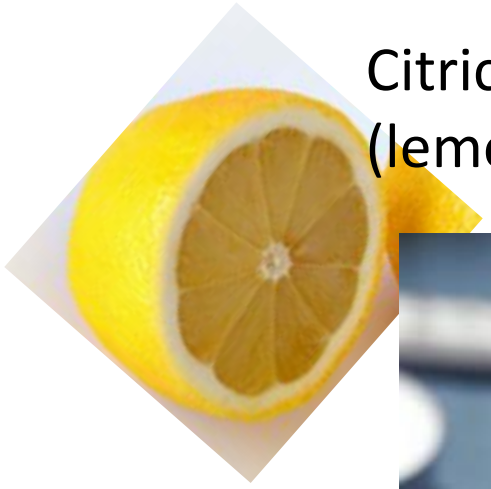


Binswanger et al. J Stud Alcohol Drug 2008
Bearnot et al. J Subst Abuse Treatment 2019
Image: Saldana et al. Infect Dis Clin N Am 2020

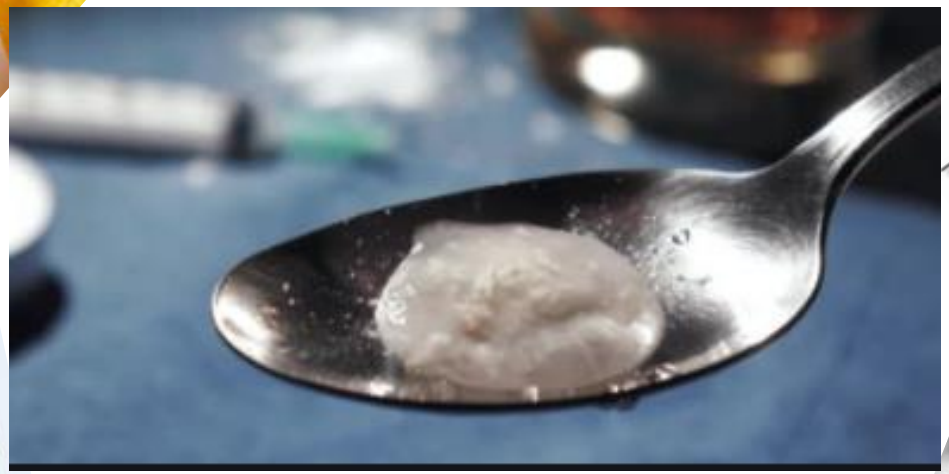
SSTIs in PWID: Risk factors

- Site of injection
  - Antecubital lowest risk
- Frequency of injection
- Needle contamination (re-use, licking, sharing)
- Lack of skin preparation (skin flora)
- Skin popping (subcutaneous, intramuscular)
- Co-injection of stimulants and opioids

SSTIs in PWID: Microbiology



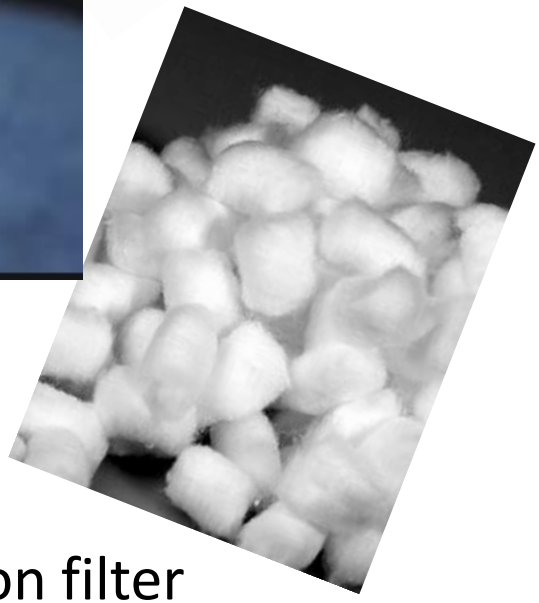
Citric acid
(lemon juice, vinegar)



Cooker

Needle and syringe

Water source



Cotton filter

SSTIs in PWID: Microbiology

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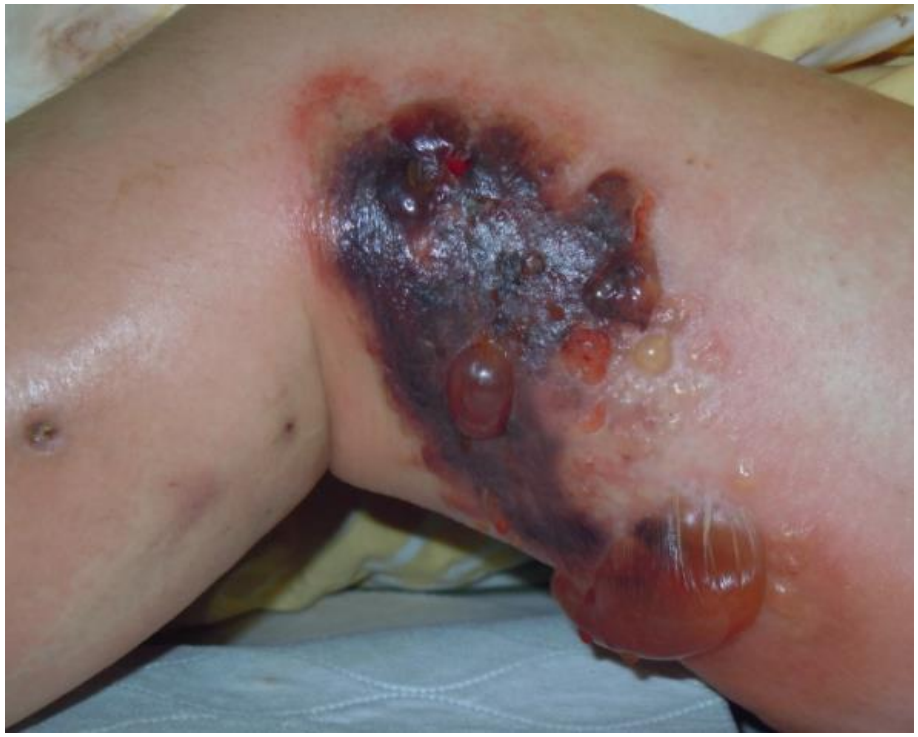
- Skin Flora
  - *Staph aureus*
  - Group A Streptococcus
- Oral Flora
  - Anaerobes (*Eikenella corrodens*)
  - Viridans Streptococci
- Cotton filter
  - Enterobacter species
- Acidifier (heroin, crack)
  - Lemons: Candida species
- Water
  - *Pseudomonas aeruginosa*
  - *Serratia marcescens*
- Contamination of drugs
  - Bacillus and Clostridiodes
  - Esp. black tar heroin (west coast)

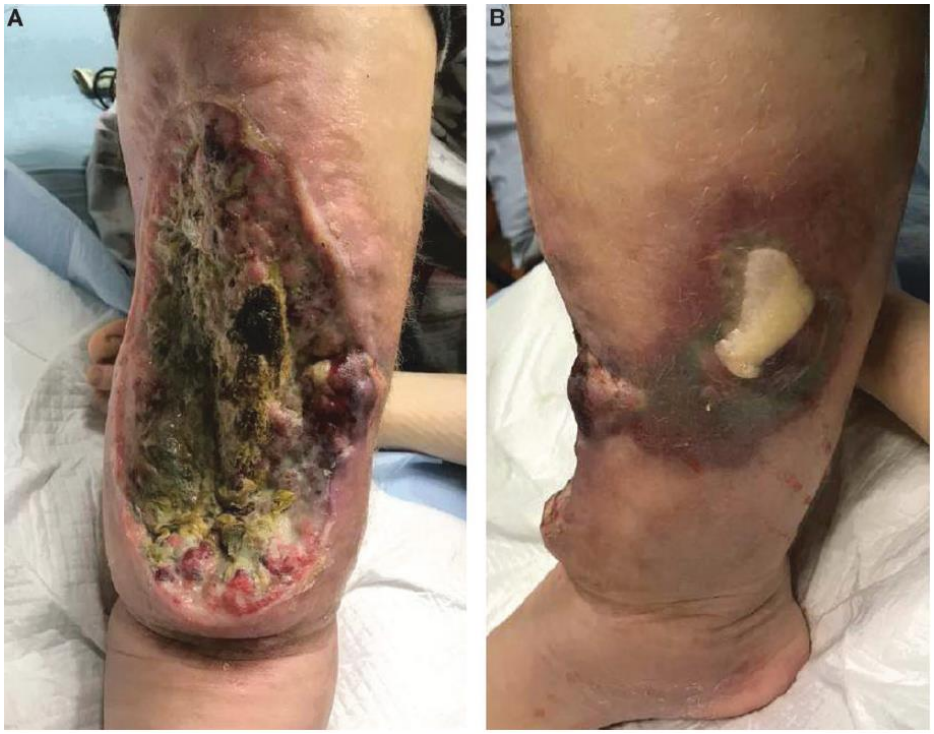
SSTIs in PWID: Examples

- Cutaneous Anthrax



Grunow et al. Dtsch Arztebl Int 2012

- Clostridium myonecrosis

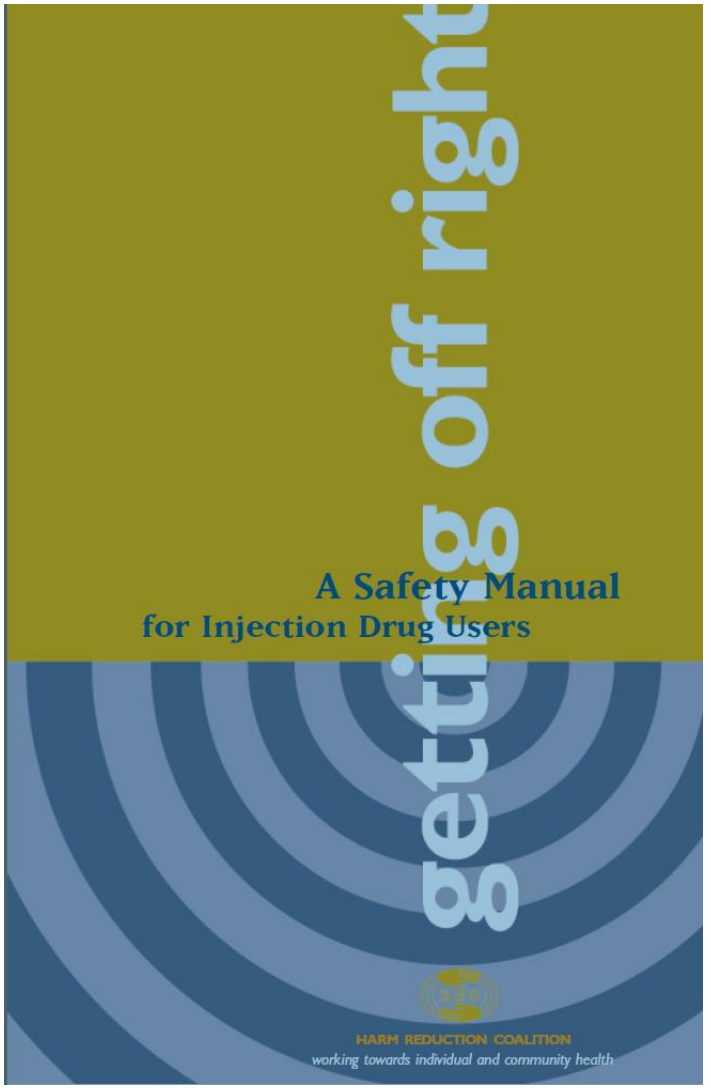


Cardinal et al. Surg Infect 2020

Harm Reduction

- New needles and syringes
  - If re-use: rinse with bleach, cold water
  - Smaller gauge better
- Vitamin C powder as acidifier
- New cotton balls and swabs
  - preferable to cigarette filters
- Skin preparation
  - handwash, alcohol skin prep
- Avoid needle-licking and skin popping
- Rotate injection sites

- Also:
  - Don't inject alone; naloxone



harmreduction.org

Harm Reduction for Clinicians: Six Moments

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1. CONTAMINATED NEEDLE BEFORE STARTING INJECTION

RISKS | HIV, HBV, HCV, delta agent

! ALWAYS use a clean, fresh needle. NEVER share needles. Do not reuse needles. NEVER lick your needle.

! GET VACCINATED to prevent HAV & HBV.

2. CONTAMINATED ACIDIFICATION AGENT/WATER

RISKS | *Candida* and others

3. DIRTY/SHARED SPOON

RISKS | HIV, HBV, HCV, delta agent

! ALWAYS use a clean spoon and NEVER share spoons

4. DIRTY FILTER

! ALWAYS use fresh, clean cotton.

! NEVER use cigarette filters – they can contain glass particles.

5. UNCLEANED SKIN

RISKS | Skin organisms can lead to MRSA endocarditis, skin abscesses.

! ALWAYS clean your skin beforehand.

! Twist alcohol swab in a circular, outward motion for 30 seconds – about the length of "Twinkle, Twinkle, Little Star" – on dry skin.

6. CONTAMINATED NEEDLE AFTER FILLING SYRINGE (USUALLY FROM LICKING)

RISKS | Oral organisms can lead to strep endocarditis.

Harvey et al. Open Forum Infect Dis 2022; https://doi.org/10.1093/ofid/ofab631

Take-home Points

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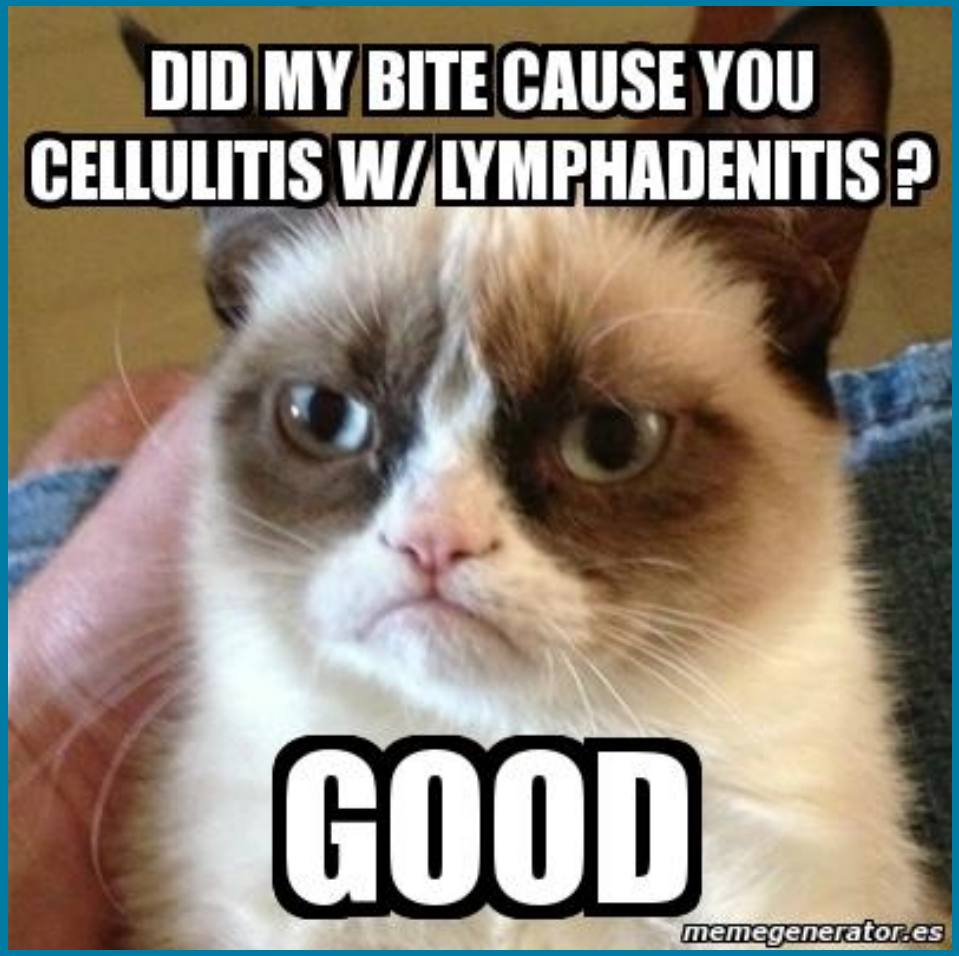
- The epidemiology of skin and soft tissue infections is evolving
- Cellulitis is a frequent misdiagnosis
  - Pseudocellulitis leads to unnecessary costs and toxicities
  - Strategies to reduce misdiagnosis are being developed
- Compression is better than antibiotic therapy to prevent recurrent lower extremity cellulitis
- For individuals who inject drugs, every SSTI is an opportunity for harm reduction



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