

### primed

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The following relationships exist related to this presentation:

 Daniela Kroshinsky, MD, MPH: No financial relationships to disclose.

### **Off-Label/Investigational Discussion**

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### Overview

- · Cellulitis & Pseudocellulitis: Background
- · Typical cellulitis
- · Cellulitis variants
- · Diagnosis: Typical vs. Variant vs. Pseudocellulitis
- Pseudocellulitis

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### Cellulitis

- Deep skin and subcutaneous fat infection
- Poorly-demarcated erythema, warmth, tenderness, edema
   Rubor, calor, dolor, tumor: *inflammation*
- 2.2% of all general practitioner office visits
- 400,000 bed days per year in the English National Health Service, cost of £96 million (\$157.2 million)
   US: \$98 million for US hospitalization for *mouth* cellulitis alone
- One of the most common infections resulting in hospitalization
  - Diagnostic criteria are poorly defined, variably applied

- Pseudocellulitis
- Dozens of clinical mimickers of cellulitis: 'pseudocellulitis'
- Very little literature on pseudocellulitis, prevalence or outcome measures
- Empiric use of aggressive antibiotics → rising rates of resistance in soft tissue infections
   - '98 -'04: MRSA soft tissue infections 26.2 → 47.4%

### **Pseudocellulitis: The Problems**

- Preliminary data: 7% of 500 inpatient consults over nine months for unresponsive cellulitis

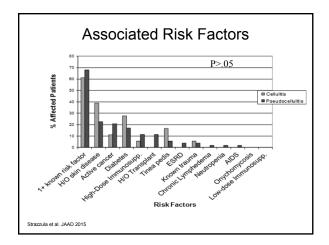
   85% = pseudocellulitis
- Very little agreement on the 'gold standard' – No laboratory criteria exist to confirm dx
- Dermatologist expertise facilitates the identification and proper treatment of actual mimicking diagnoses

### David CV et al. Diagnostic accuracy in patients admitted to hospitals with cellulitis. Dermatol Online J. 2011 Mar 15;17(3):1.

- · Prospective evaluation at two institutions
- Dermatology or infectious disease attending evaluation of all consecutive patients hospitalized for "cellulitis" by the ED (n= 145)
  - Misdiagnosis: 28% patients
  - Most common cause: stasis dermatitis (37%)

### Levell et al. Severe lower limb cellulitis is best diagnosed by dermatologists and managed with shared care between primary and secondary care. Br J Dermatol. 2011 Jun;164(6):1326-8.

- 210/ 635 referrals for lower limb cellulitis (33%) had other diagnoses which did not require admission
- 96% true cellulitis pts managed entirely as outpatients, many at home
- 28% patients with cellulitis had an underlying skin disease identified and treated → reduced the risk of recurrent cellulitis, leg ulceration and lymphedema
- 18 /635 patients referred with lower limb cellulitis required hospital admission for conventional treatment (3%)



### Conclusions

- Misdiagnosis of cellulitis is a significant problem in the inpatient population
- No statistical difference in identifying factors between the groups
- · Education on cellulitis mimickers may be helpful

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### **Typical Cellulitis: Presentation**

- Rubor, dolor, calor, tumor
- +/- Ascending lymphangitis, regional lymphadenopathy
- +/- Fever, leukocytosis
- · Severe: vesicles, bullae, pustules, necrosis

### Microbiology: Common Pathogens

- Adults:
  - Streptococcus pyogenes > Staphylococcus aureus
    - Methicillin-sensitive S.aureus >>>MRSA, unless traumatic
- Children: Staphylococcus aureus
   Previously Haemophilus influenza

### Microbiology: Immunosuppression

- Mild/Moderate: diabetes, end stage renal disease, cirrhosis, prednisone <20mg
  - Staphylococci, streptococci
  - Gram Negative Rods (GNR)
- Severe: neutropenic, prednisone >20mg, other immunosuppressives, AIDS
  - Staphylococci, streptococci, GNR
  - Atypical mycobacteria, deep fungal, nosocomials

Adapted from Bolognia Dermatology Fig 73.7

# Predisposing factors to cellulitis

- Trauma:
- Piercings
- IVDA/'popping'
- Bites
- Self-induced
- · Tinea pedis/ onychomycosis

Bjornsdottir S et al. Risk factors for acute cellulitis of the lower limb; a prospective case-control study. Clin Infect Dis 2005; 41: 1416-1422. Roujeau JC et al. Chronic dermatomycoses of the foot as risk factors for acute bacterial cellulitis of the leg: a case-control study Dermatology 2004; 209; 301-307.

### **Chronic Ulcers & Infection**

- Diabetic, stasis, decubitus
- Culture usually not helpful, can be confusing

### **Chronic Ulcers & Infection**

- · Signs of infection:
  - New onset pain
  - Increased erythema
- Usually multiorganism
   Anaerobes, Gram-negative aerobes

### Predisposing Factors for Recurrence

- Peripheral vascular disease
- Lymph Node dissection
- Radiation therapy
- Liposuction
- Leg vein harvesting for CABG
- Intravenous drug abuse, skin popping
- Tinea pedis, onychomycosis
- Underlying vascular and lymphatic disease due to prior episodes

### Possible Complications of Typical Cellulitis

- Bacteremia
- Lymphadenitis
- · Subacute bacterial endocarditis
- Glomerulonephritis
- · Elephantiasis verrucosa nostra

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### **Cellulitis Variants**

- Erysipelas
- · Perianal streptococcal infection
- · Preseptal cellulitis/ orbital cellulitis

### Erysipelas

- Superficial cellulitis of the skin with marked lymphatic involvement
- Usually Group A B-hemolytic Strep, +/- coinfection w S.aureus
- Direct inoculation through a break in the skin, occasionally hematogenous

# Erysipelas

- Small area of erythema, gradually enlarges
- Warm, painful, <u>well-</u> <u>demarcated</u>, shiny, bright red plaque
- · Face, scalp, hands

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### **Evaluation**

- History
  - Onset and duration: first or recurrent episode
  - Local sx: pain/ pruritus/ burning/ dysesthesia
  - Associated symptoms: SOB, arthritis, diarrhea, headache, cough, chills, fever
  - Course/ progression
- PMHx, FHx, SHx, Meds

### **Evaluation: Objective**

- General appearance
- · Vital Signs:
  - Fever: infection or systemic inflammation
     Pattern of fever (ie diurnal- Still's disease)
  - Tachycardia, hypotension
- LAD: infectious, inflammatory, neoplastic

### Atypical Features or Unresponsive to Treatment:

- · Resistant pathogens
- · Cellulitis variant (ie- necrotizing, fungal)
- Pseudocellulitis

### **Diagnostic Testing for Cellulitis**

- Labs
- Cultures
- Biopsy
- Imaging
- Special tests directed at pseudocellulitides

### **Diagnostic Testing for Cellulitis**

- · Labs: CBC w/ differential, CMP
- · Cultures:
  - Blood: usually negative and not helpful
  - Skin swabs, biopsy culture, aspirate usually not helpful

### When to Biopsy

- Immunosuppression - Bacterial, fungal, viral, parasitic, mycobacterial
- · Other concern about non-bacterial etiology - Special stains, cultures
- · Concern for pseudocellulitis

### Imaging & the DDx

- Osteomyelitis(chronic), foreign body Ultrasound - Abscess, pyomyositis

X-ray

• CT - Osteomyelitis, pyomyositis\*, necrotizing fasciitis\*

 MRI - Osteomyelitis\*, pyomyositis, necrotizing fasciitis Gold, RH, Hawkins, RA, Katz, RD. Bacterial osteomyelitis: Findings on plain radiography, CT, MR, and scintigraphy. AJR Am J

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### Pseudocellulitis DDx

- Cutaneous infections · Vascular
- Non-cutaneous Metabolic infections
- Inflammatory non-· latrogenic, Factitious, infectious Exogenous
- Neoplastic Contact Dermatitis

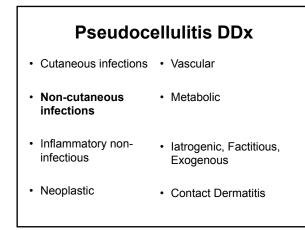
### Pseudocellulitis DDx

· latrogenic, Factitious, Exogenous

- Cutaneous infections 
   Vascular - Superficial Metabolic
  - Deep
- · Non-cutaneous infections
- · Inflammatory non
  - infectious · Contact Dermatitis
- Neoplastic

### Erysipeloid

- · Erysipelothrix rusipathiae, Gram+ rod
- Erythematous to violaceous painful plaque, usually hand
- · Severe pain, no edema, rarely systematizes
- · Clue: contact w farm animals
- Tx: PCN or cephalosporin, PCN allergic: cipro or erythromycin + rifampin; resistant to vancomycin



### **Cutaneous Sinus of Dental Origin**

- Bacterial infections of dental carries → osteomyelitis
- Immune compromise or virulent organisms spread from bone to skin → cellulitis
- Moderate virulence: infection contained but inflammation → erosion through facial skin

### Non-cutaneous Infectious DDx

- Contiguous spread of subcutaneous infection
  - Osteomyelitis
  - Dental infections
  - Perforated sigmoid diverticula
  - Infected implanted devices

### Pseudocellulitis DDx

- Cutaneous infections · Vascular
- Non-cutaneous
   Metabolic
   infections
- Inflammatory noninfectious
   Iatrogenic, Factitious, Exogenous
- Neoplastic
   Contact Dermatitis

### Inflammatory, Non-Infectious

- Panniculitis
  - Erythema Nodosum
  - Subcutaneous fat necrosis of newborn
  - Cold panniculitis
  - Alpha-1-antitrypsin deficiency
- · Clue: multiple sites, recurrence, hx

### **Neutrophilic Diseases**

- Acute Febrile Neutrophilic Dermatosis (Sweet's syndrome)
- · Neutrophilic eccrine hidradenitis

### Clues:

- Neutrophilia
- Association with underlying condition/exposure
  - Malignancy
  - Upper respiratory/GI infections, HIV
  - Vaccinations
  - Drugs (G-CSF, ATRA)
  - Inflammatory bowel disease, GI
  - Bypass – Pregnancy
  - Pregnancy
- Rapid Response to prednisone

### Pathergy

- Response to dermal trauma, usually elicited with needle insertion 24-48 hours later
- · Behcet's disease
- · Bowel-associated dermatosis-arthritis syndrome
- Sweet's syndrome
- Pyoderma gangrenosum
- Rheumatoid arthritis

# Pseudocellulitis DDx • Cutaneous infections • Vascular • Non-cutaneous infections • Metabolic • Inflammatory non-infectious • Iatrogenic, Factitious, Exogenous • Neoplastic • Contact Dermatitis

# Carcinoma Erysipeloides

- Well-circumscribed, erythematous, warm, firm plaques
- · Underlying malignancy
- Breast\*, gastric, uterine, cervical, colon, GU, prostate, nasopharyngeal, mesothelioma, idiopathic

### Carcinoma en cuirasse

Bolognia Dermatology Fig 122.3

- Fibrosis
- Induration
- Peau d'orange
- H/o nearby cancer (breast)

# Pseudocellulitis DDx • Cutaneous infections • Vascular • Non-cutaneous infections • Metabolic • Inflammatory non-infectious • latrogenic, Factitious, Exogenous • Neoplastic • Contact Dermatitis

### **Calciphylaxis Risk Factors:**

- Renal Impairment
- White Race
- Obesity
- Warfarin
- Hypercoagulable States
- Diabetes
- Liver Disease
- Dialysis
- Ca, Phos, PTH abnormalities

### Vascular

- Calciphylaxis
- Deep Vein Thrombosis
- Lymphedema
- Stasis dermatitis
- Lipodermatosclerosis

### Venous Stasis Dermatitis

- · Venous hypertension, upright position
- Incompetence of the deep leg vein valves
- · Slowed blood flow in the microvasculature

### **Pathogenesis**

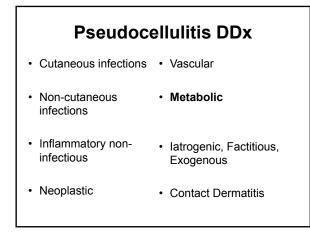
- Chronic venous insufficiency of the legs
- · Capillary distension
- Damaged capillary permeability barrier
   Leakage of RBCs, fluid, plasma proteins, neutrophils, macrophages

### Pathogenesis

- Platelets accumulate  $\rightarrow$  focal thrombosis
- Fibrosis and tissue remodeling
- Venous ulcers
   especially medial malleolus

### **Stasis Dermatitis**

- Bilateral cellulitis is exceedingly unlikely unless h/o trauma to B LE
- H/O acute or chronic leg swelling
- Post-inflammatory hyperpigmentation, hemosiderin
- · Treat the edema/ active stasis



### Metabolic

- Gout
  - Joint inflammation w acute painful erythematous overlying skin changes
  - Can extend beyond joint, +/- fever and systemic symptoms
  - Joint aspiration or smear demonstrates crystals
  - Ethanol-based fixative

# Pseudocellulitis DDx • Cutaneous infections • Vascular • Non-cutaneous infections • Metabolic • Inflammatory non-infectious • latrogenic, Factitious, Exogenous • Neoplastic • Contact Dermatitis

### latrogenic, Exogenous, Factitial

- · IM vaccination placement
- · Injection site reactions
- · Fixed drug eruption
- Atypical drug eruptions

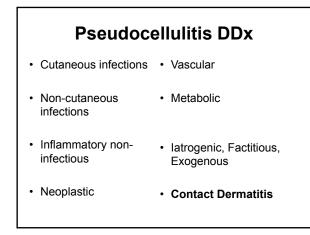
### latrogenic, Factitial, Exogenous

- Injection site reactions: subcutaneous or IM

   Hypersensitivity reactions within 2-4 weeks of
   injection
  - Pruritic, expanding erythematous patches, can vesiculate or be tender and edematous
- IM Vaccination reaction given sub Q – Erythema, extremity swelling

# **Fixed Drug Eruption**

- Recurrent, round to oval, erythematous edematous plaques in the **same** locations
- Pruritic or painful, can vesiculate, heal w PIH
- · Genitalia, lips, hands/feet- but really anywhere
- NSAIDs, sulfonamides, barbituates, tetracyclines, carbamazepine



### **Contact Dermatitis**

- · Can be tender 2/2 degree of edema
- · Rapid response to topical or systemic corticosteroids
- Caution: contact dermatitis w secondary infection

### Conclusions

- · Broad differential for erythematous skin
- · Consider dermatology consultation for atypical or unresponsive cases
- Inpatient study

### References

- Hepburn MJ, Dooley DP, Ellis MW. Alternative diagnoses that often mimic cellulitis. Am Fam Physician. 2003 Jun 15677(12):2471.
   Roberts R. Management of patients with intercloue diseases in an emergency department observation unit. Emerg Med Clin North Am. 2001 Feb; 16(1):1672-207.
   Roberts J. Consaman ME. Fox LP. Approach to the patient with presume cellulitis. Semin Cutatin Med Surg. 2007 Sep;26(3):168-76.
   Stevens DL et al. Practice guidelines for the diagnosis and management of skin and soft-lissue infections. Clin Infect Dis. 2005 Nov 1534(15):173-466. Inserve to an intervent optimiser of the diagnosis and management of skin and soft-lissue infections. Clin Infect Dis. 2005 Nov 15:541(10):1737-406.
   Stulle DL, Penrod MA, Blatry RA. Common bacterial skin infections. Am F am Physicalar 2002;66:119-24.
   Wing AK, Skin and soft sasue infections. Sing Clin N Am. 2008;8:043-20.
   Biodgina, Dematology
   Biodgina, Dematology
   Rolegau JC et al. Chronic dematomycoses of the foot as risk factors for acute bacterial cellulits of the leg: a case-control study. Clin Infect Dis. 2005; 11:416-1422.
   Rolegau JC et al. Chronic dematomycoses of the foot as risk factors for acute bacterial cellulits of the leg: a case-control study. Demator 2006; 200; 30:307 Rogeau JC et al. Chonic demaktingcoses of the loot as risk factors for acute bacterial cellulitis of the leg: a case-control study. Demaktology 2004; 200; 301-307
   Lethwaite P et al. Group G streptococal bacteriaremic: an opportunistic infection associated with immune senescence. Scand J Infect Dis. 2002;34(3):53-71
   Hunkitz, Pedalinic Demaktogy
   Hann C et al. Recent microbiological antihin periaral bacterial demaktis. Infection associated with immune senescence. Scand J Infect Dis. 2002;34(3):53-71
   Hunkitz, Pedalinic Demaktogy
   Hann C et al. Recent microbiological antihin periaral bacterial demaktis. Staphylococcal preformance. Ped Dem 26(6): 686-700, 2009.
   Hann C et al. Recent microbiological antihin periaral bacterial demaktis. Staphylococcal preformance. Ped Dem 26(6): 686-700, 2009.
   Hann C et al. Recent microbiological antihin periaral bacterial demaktis. Exployhococcal preformance. Ped Dem 26(6): 686-700, 2009.
   Roncell E, Mankitz R, Bosterial celecomyetilis. Findings on plain radiography. CT, MR, and scintgraphy. AIR Am J Reentgenol 1991; 157:356.
   Rockam et al. Levieemia actis in acide myetiononocytic leukemia: infiltration to minor traumas and scars. J Dermatol. 1991 May; 18(5):281-5.
   Lebolt, Pahology and genetics of thin kmnsry. vid 6
   Mankin, M. Otsomy Wound Managemett
   Ringar H, Breandex-medinate demating. Europace. 2008 Nov;10(11):1354.
   Annas Vest J. Emeg Med. 2008 May; 6(2): 128
   Schart J. Emeg Med.