Courtesy of American College of Surgeons Division of Education
Clinical Congress 2015

Necrotizing Soft Tissue Infections: Emerging Bacterial Resistance

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Objectives

- Review definition & diagnostic criteria for NSTI
- Identify the most common bacterial organisms & toxin profile
- Discuss emerging resistance patterns
- Discuss antibiotic management strategies

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Necrotizing Soft Tissue Infections (NSTI)

- First described by Jones (1871), US Civil War
  - group A, ß-hemolytic strep. & *Staph aureus*
  - "Hospital gangrene"
- Involvement of the male genitalia described by Fournier (1883)
- "Hemolytic streptococcal gangrene" (Meleney 1924)
- "Necrotizing fasciitis" (Wilson 1952)
- TODAY: Necrotizing soft tissue infections
  - An infection of the soft tissue with associated necrosis requiring operative intervention
  - Usually in the context of a critically ill patient
  - IVDU, Morbid obesity, emerging resistance

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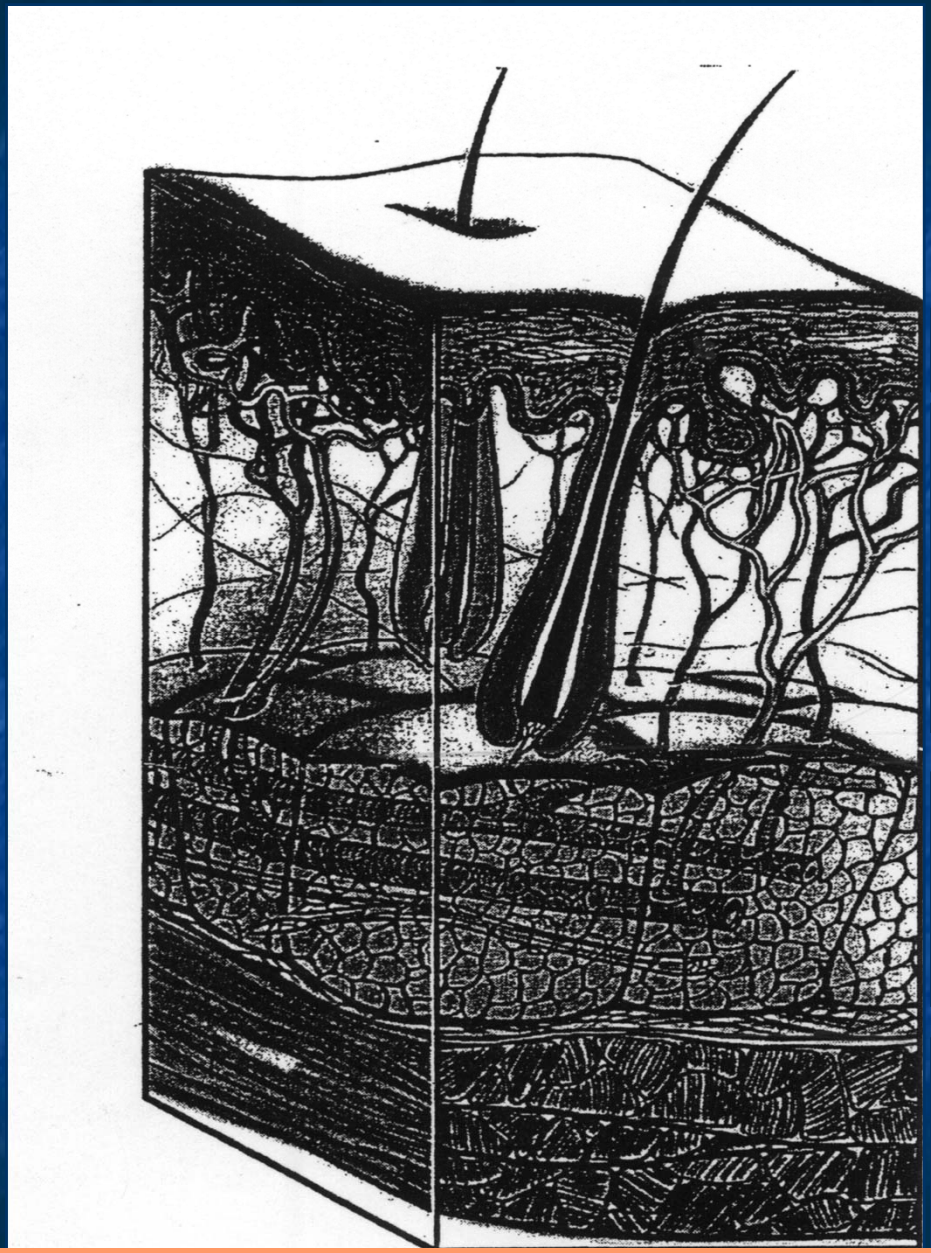

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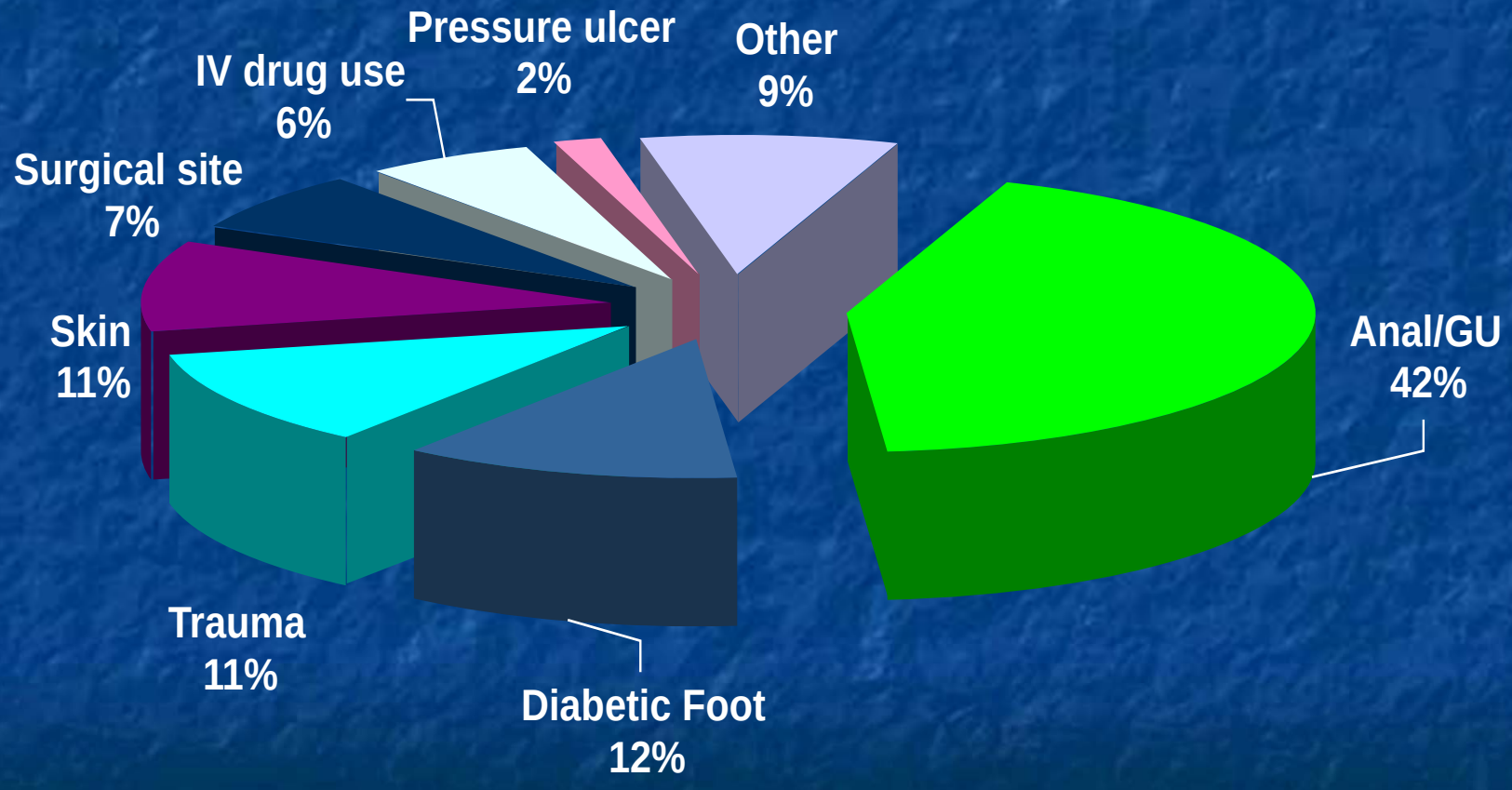
Anatomic layer	Necrotizing….
Epidermis	
Dermis	Cellulitis
Superficial fascia	
Subcutaneous fat, arteries, veins	Fasciitis
Deep fascia	
Muscle	Myonecrosis

Etiology of NSTI
Elliott, Ann Surg, 1996



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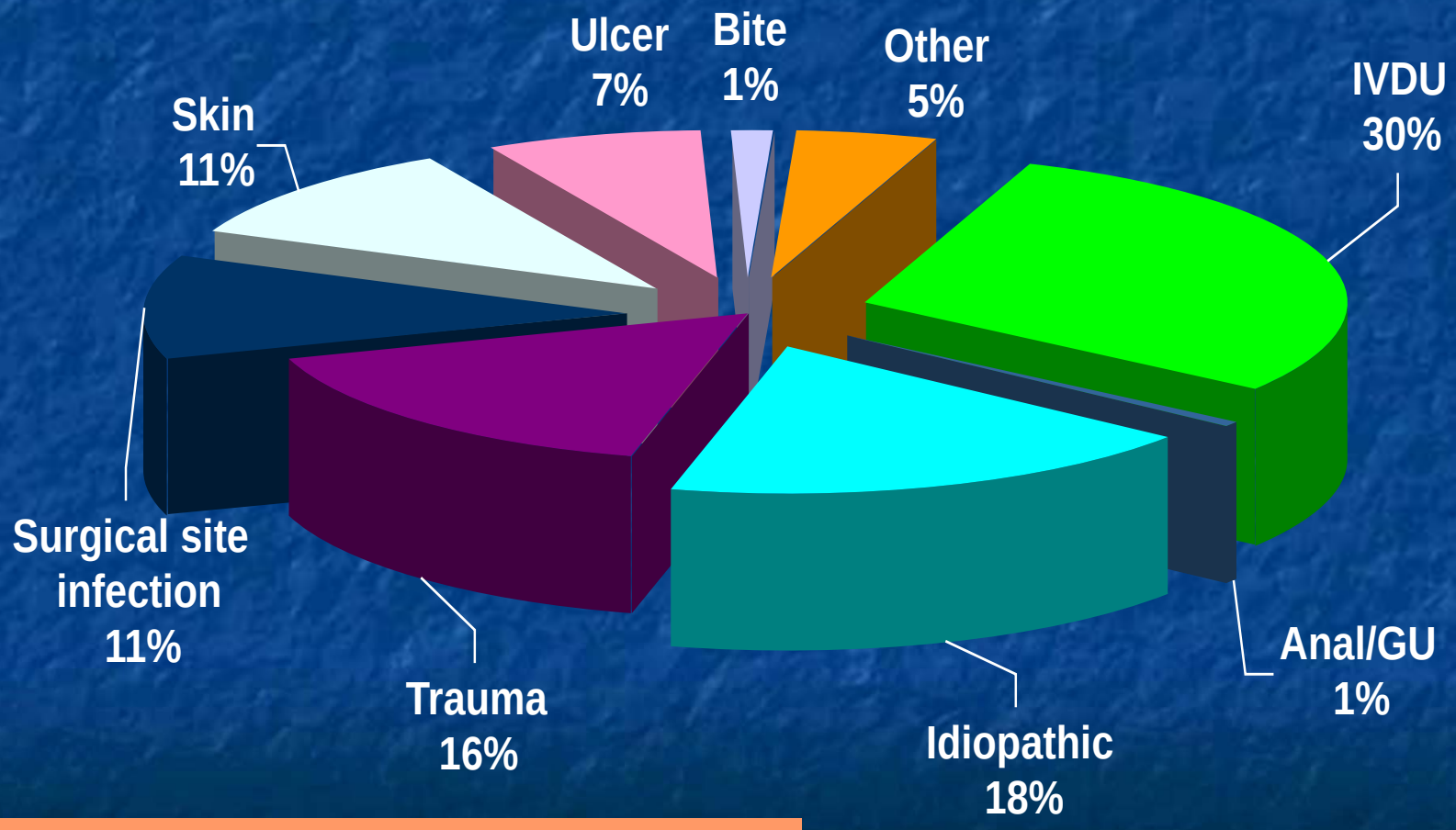
Etiology of NSTI
Anaya, Arch Surg, 2004



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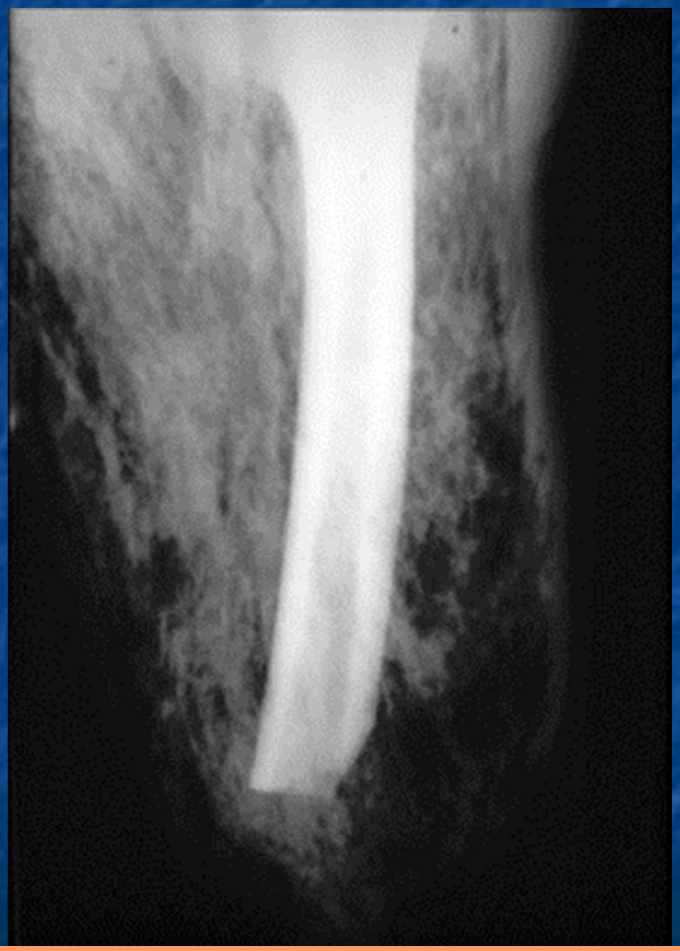
Making the diagnosis of NSTI

- Constellation of symptoms, physical signs and laboratory assessment
- Symptoms
  - Pain out of proportion to physical findings
- Signs
  - Shock, organ dysfunction if late presentation
  - Local – “hard signs”
  - WBC, Na
- High risk population?
  - IVDU, Diabetes, obesity

Hard Signs



- Gas on radiograph

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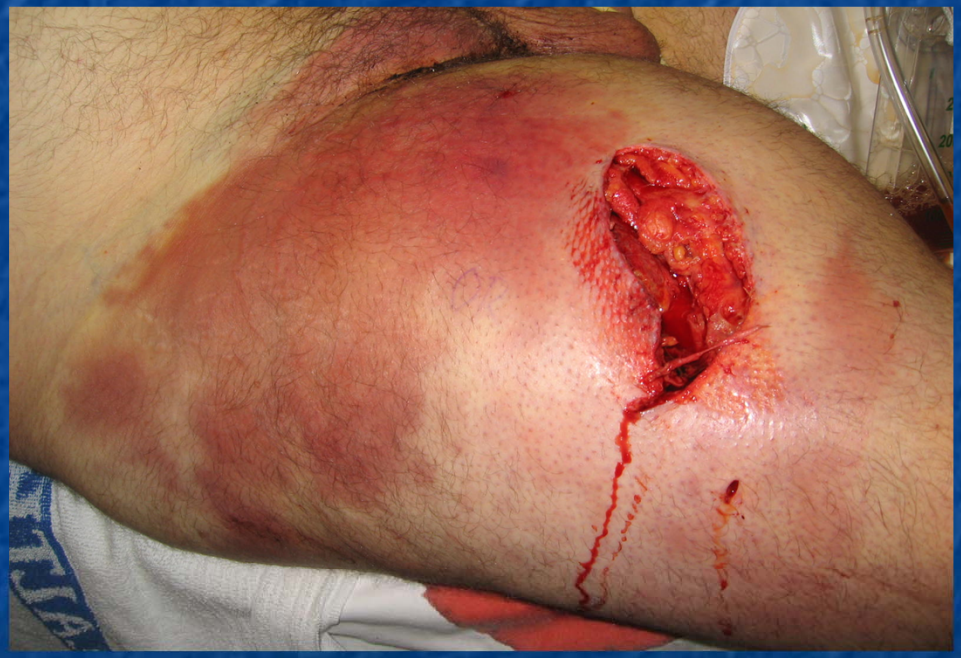

Tense edema

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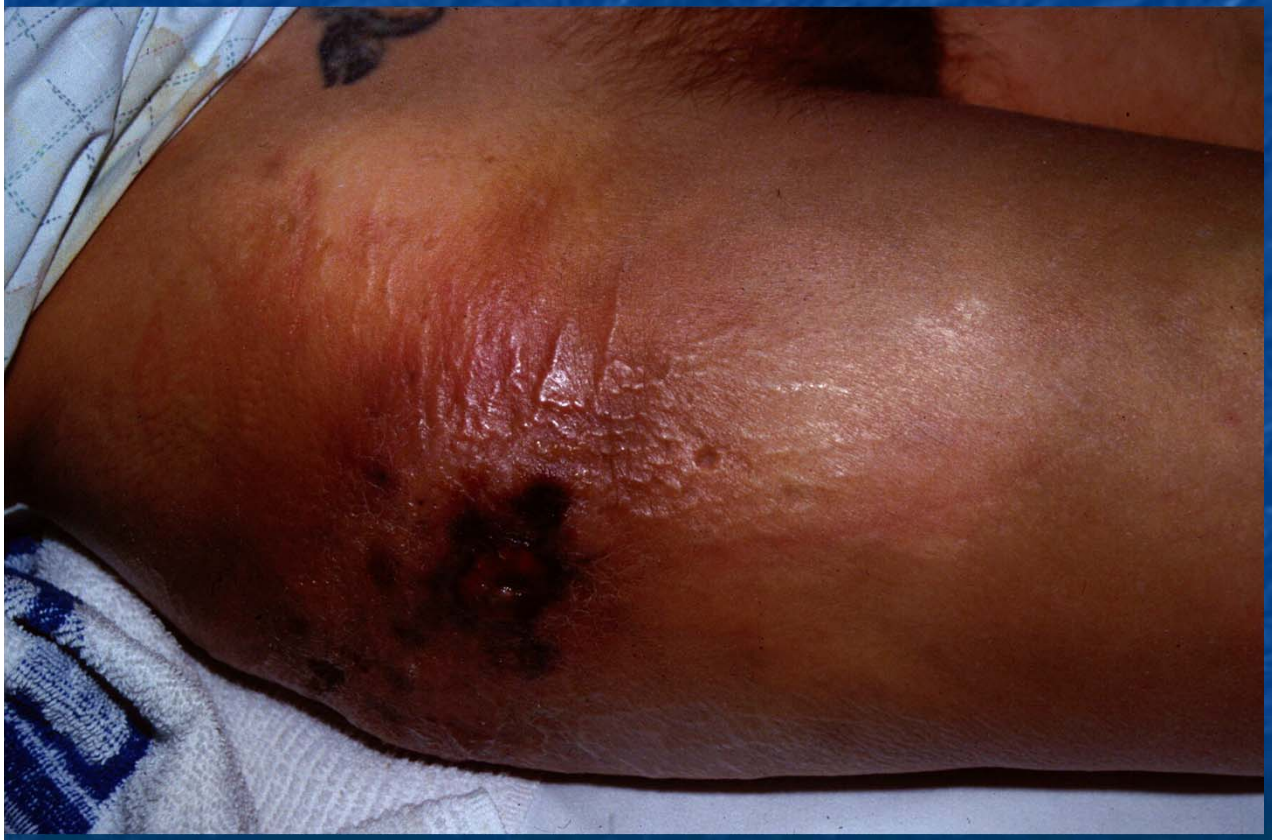

- Tense edema
- Purple discoloration
- Cutaneous gangrene

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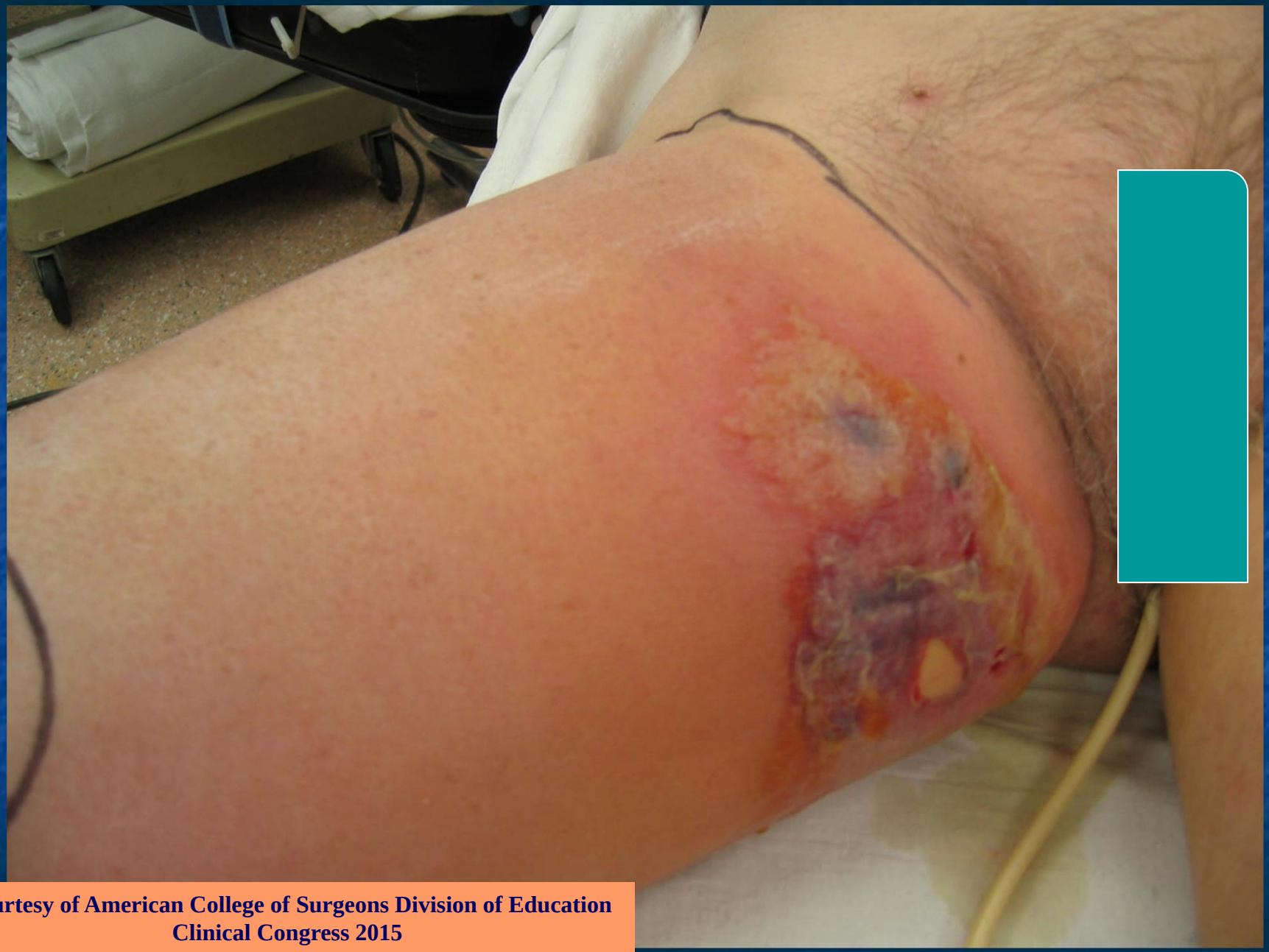

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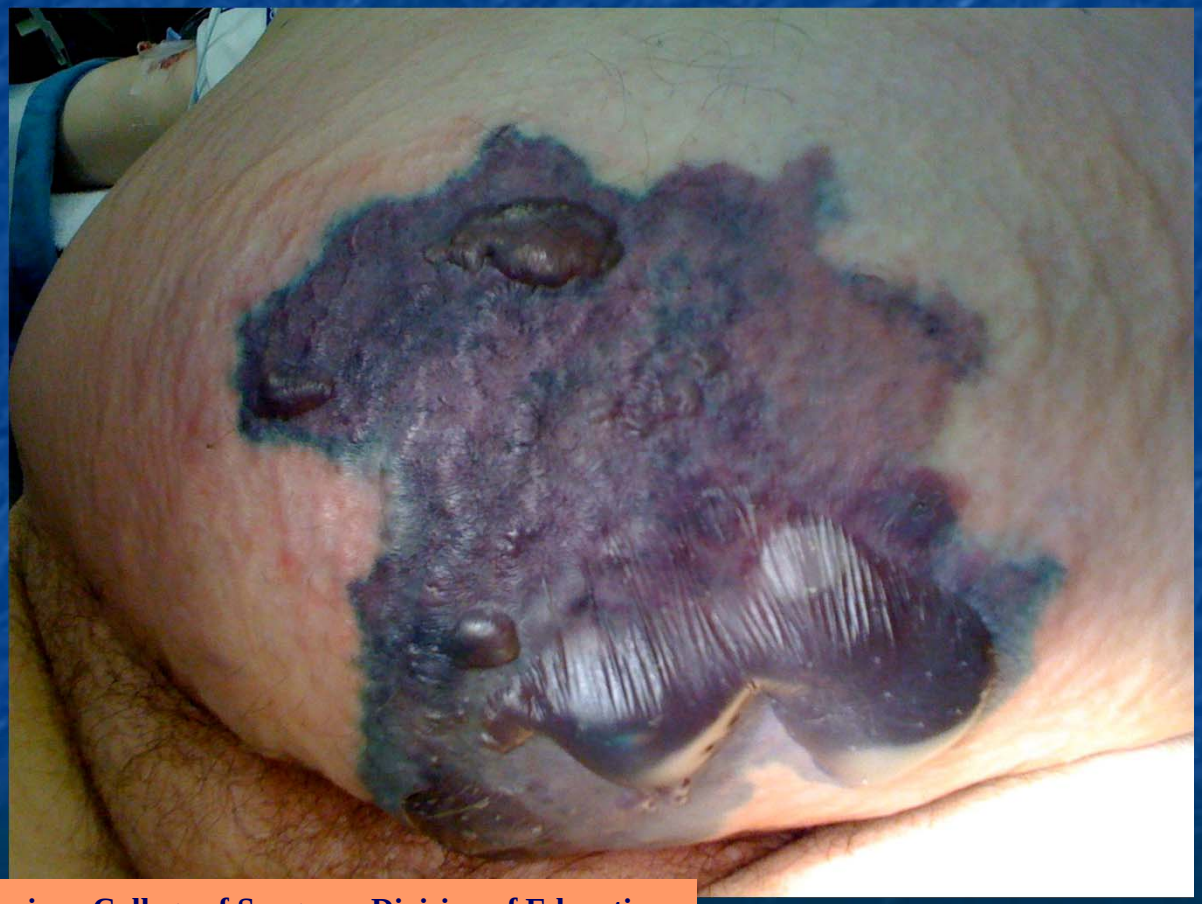
Pannus Infections



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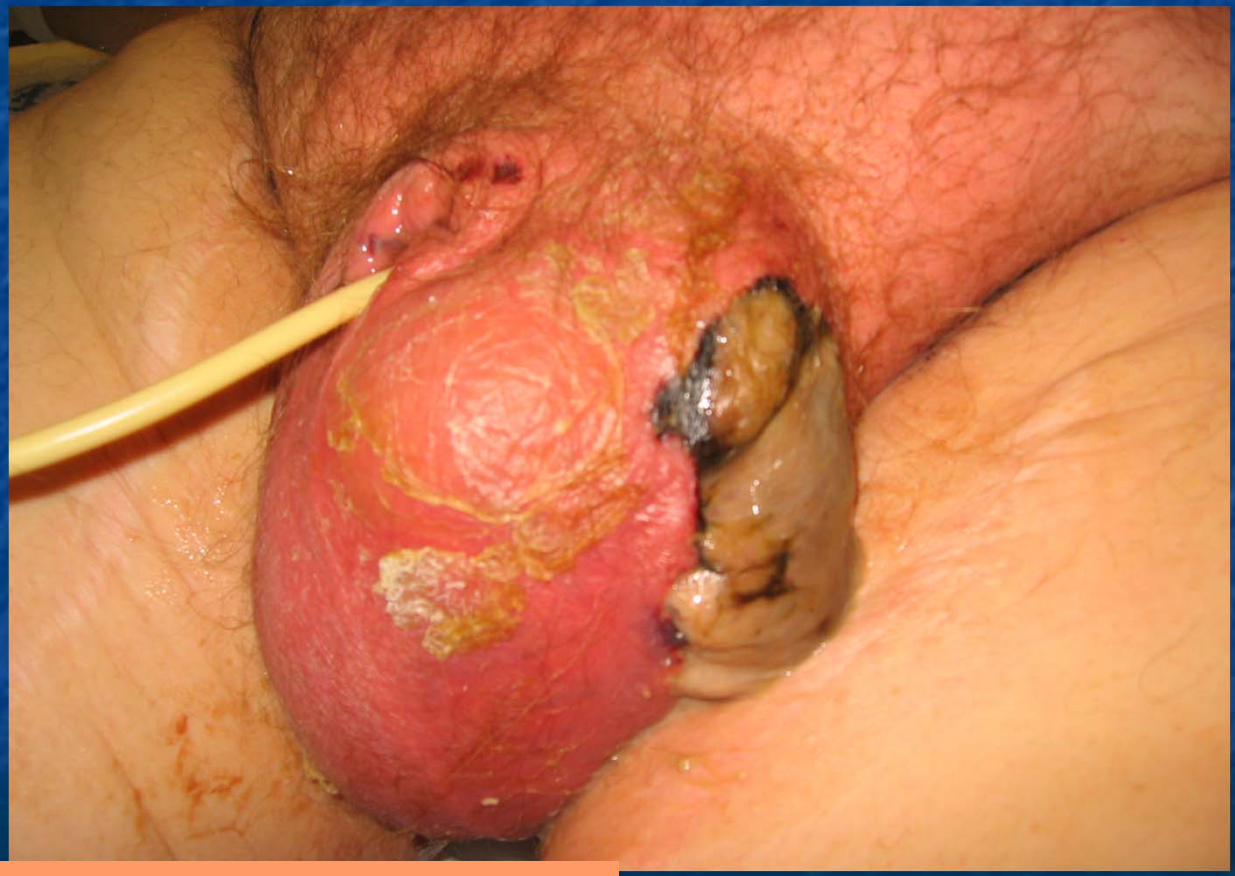
Fournier's Gangrene,
skin changes often an understatement



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Delay Associated with Increased Morbidity & Mortality

- UCLA series 2010
  - Debridement >12 hrs after ED arrival
    - Higher mortality
    - Increase in incidence of septic shock
    - Increase in incidence of renal failure
    - Increase in number of debridments required
      - Mean 7.4 vs 2.3

J Trauma epub 2011

Most common organisms?

- Monomicrobial infections
  - Clostridium perfringens (rarely others)
  - Group A streptococci
  - Methicillin resistant staph aureus
- Polymicrobial infections
  - All of the above plus gram negative rods and anaerobes
- Rare but reported
  - Vibrio vulnificus (exposure to warm sea water)
  - Aeromonas Hydrophilia (warm, brackish fresh water)

Group A streptococcus

- Rapidly progressive, may lead to Toxic Shock Syndrome
- May be seeded from remote pharyngeal infection
- M proteins
  - Filamentous cell membrane protein, antiphagocytic
  - Associated with increased virulence
- Toxins:
  - Pyrogenic exotoxin A,B,C
  - Steptococcal superantigen

Antimicrobial Coverage for Group A Strep

- High dose Penicillin remains highly effective
- DOSE: 4-6 million units q 4hrs
- Clindamycin recommended for potential anti-toxin effects
- PCN allergy: Vancomycin, Linezolid

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Clindamycin for Group A Strep

- Carpetis et al, Clinical Infectious Diseases 2014
  - 84 cases severe GAS infections in Australia
  - Clindamycin treated patients had more severe disease but lower mortality
    - 15% vs 39%
    - Adjusted OR 0.31, 95%CI 0.09-1.12)
    - Addition of IVIG appeared to provide additional benefit

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Community Acquired MRSA

- Recent CDC report: 60% of community isolates of staph aureus are methicillin resistant; some communities have reported > 70%
- Majority of these are skin and soft tissue infections
- Panton-Velentine leukocidin gene: more virulent infections
- NSTI due to CA-MRSA have been reported*

* NEJM 325:1145, 2005

Antimicrobial Coverage for CA-MRSA

- Oral therapy for outpatients: Bactrim, Doxycycline, Fluoroquinolones (moxifloxacin most potent),
  - Avoid Erythromycin (emerging resistance 5-64%)
- IV therapy: Vancomycin,, Linezolid, Daptomycin(monitor CPK), Rifampin (synergy only)
  - More recent strains with Clindamycin

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Clostridial Infections

- 70-80% *C. Perfringens*, germination time 8 minutes
- Invade and rapidly destroy healthy muscle
- α toxin (phospholipase C) and θ toxin (perfringolysin)
  - Hemolysis, microvascular thrombosis, muscle necrosis
  - Destruction of PMNs and impaired migration
  - Direct inhibition of myocardial contractility
  - Indirect induction of systemic cytokine expression

Clindamycin

- Excellent first line therapy due to coverage of streptococci, clostridia, and MRSA as well as anaerobic coverage for mixed infections
- High doses recommended to bind toxin & reduce toxin production
  - 900-1200 mg every 6 hours
- 5% of C. perfringens strains are clindamycin resistant thus used in combination with PCN
- Do not use alone for MRSA due to emerging resistance

Rare but Reported

- Vibrio Vulnificus
  - Exposure of an open wound in warm sea water
  - Doxycycline plus Ceftazidime
- Aeromonas Hydrophilia
  - Exposure to warm fresh water/brackish water
  - Doxycycline plus Cipro or ceftriaxone

Summary: Antimicrobial Therapy

- Empiric antimicrobial spectrum should cover streptococci, MRSA, clostridia, and gram negatives
- Empiric therapy
  - Penicillin 6 million units q4h
    - Strep, clostridium
  - Clindamycin 1200 mg q6h
    - Anaerobic coverage (clostridium)
    - Protein synthesis inhibitor – reduces toxin production
  - Vancomycin for endemic MRSA
  - Gram negative coverage: Fluoroqinolones, gentamicin
- Mixed infections (diabetic foot/Fourniers): VANCOMYCIN PLUS: Piperacillin/tazobactam, ertapenem, meropenem, imipenem-cilastin

IDSA Guidelines, updated 2014

Surgical Management

- Early intervention, prioritize OR availability
- Wide debridement of all necrotic tissue
  - Decompress facial planes
  - May require amputation
- Scheduled return to OR 12 to 24 hours, repeated debridement based on patient condition and progression of necrosis
- Reconstruction: Team Approach

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