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Clinical Congress 2015

Necrotizing Soft Tissue Infections: Delays in Diagnosis TIME MATTERS!

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Disclosure

- Principle investigator for multicenter RCT of AB103, novel immune modulator for NSTI patient
- Previously a consultant for AtoxBio Ltd, Israel for clinical trial design for Phase 3 study

Case

- 27y/o M presents to community hospital with c/o severe pain right shoulder, denies h/o injection drug use
- SBP 120/70 HR 110 T 38.5
- WBC 25K, Na 130, HCT 50, Cr 2.0
- Erythema over deltoid with punctate areas of blue discoloration
- Admitted 3pm on Vancomycin for cellulitis

Next day

- Persistent erythema now extending onto chest wall
- Increased areas of blue discoloration over deltoid and upper back
- WBC 30K
- SBP 90/50 HR 120 after 4 liters crystalloid

Taken to OR

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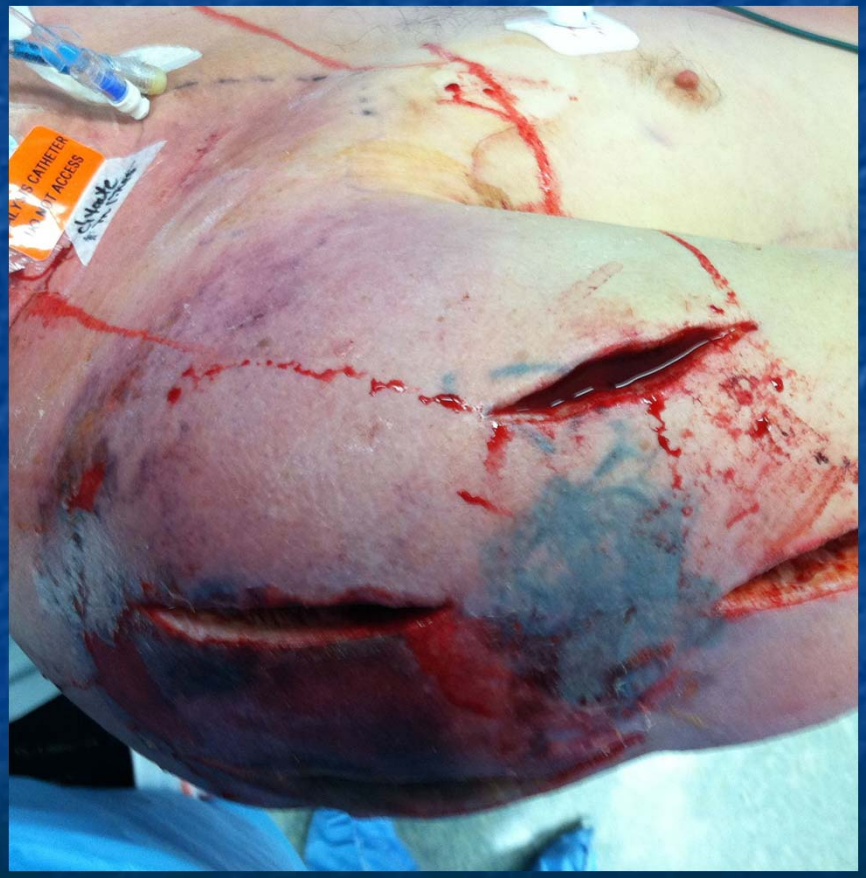
OR at Community Hospital



- Multiple incisions made to assess the fascia
- NO DEBRIDEMENT
- Call to transfer to tertiary referral center
- Now on vasopressors

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Transfer

- Transport via fixed wing aircraft (2hrs)
- Admission labs: wbc 9.5 (84%PMN), Na 132, BUN 91, Cr 3.17, Lactate 2.8, Plt 66
- Wound evaluated and scheduled for emergent debridement
- Started on antibiotics per our NSTI protocol

Post-op: Posterior

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Post-op: Anterior

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Post-op course

- Admitted to ICU with ongoing coagulopathy, transfused for post-op anemia
- Post-op labs: wbc 18.4, lactate 6.3 despite aggressive fluid resuscitation
- Levophed and Vasopressin for septic shock
- Returned to the OR 8 hours later: progression of necrosis to intercostal muscle
- Discussions with family led to decision for comfort care and died the evening of 7/31

Objectives

- Challenges in making the Diagnosis
- Impact of Delay in Diagnosis

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
- 4 cases/100,000 population/yr

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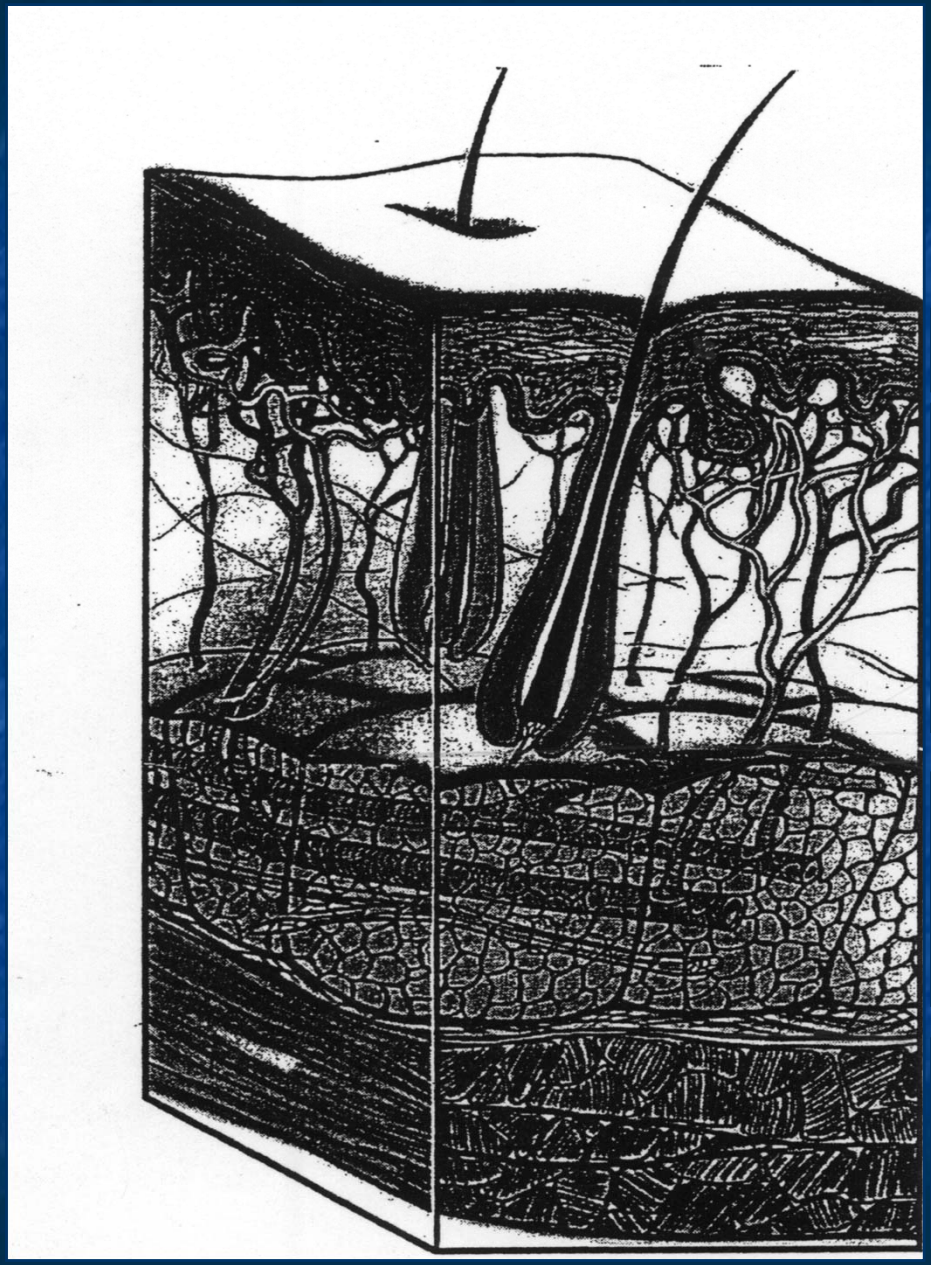
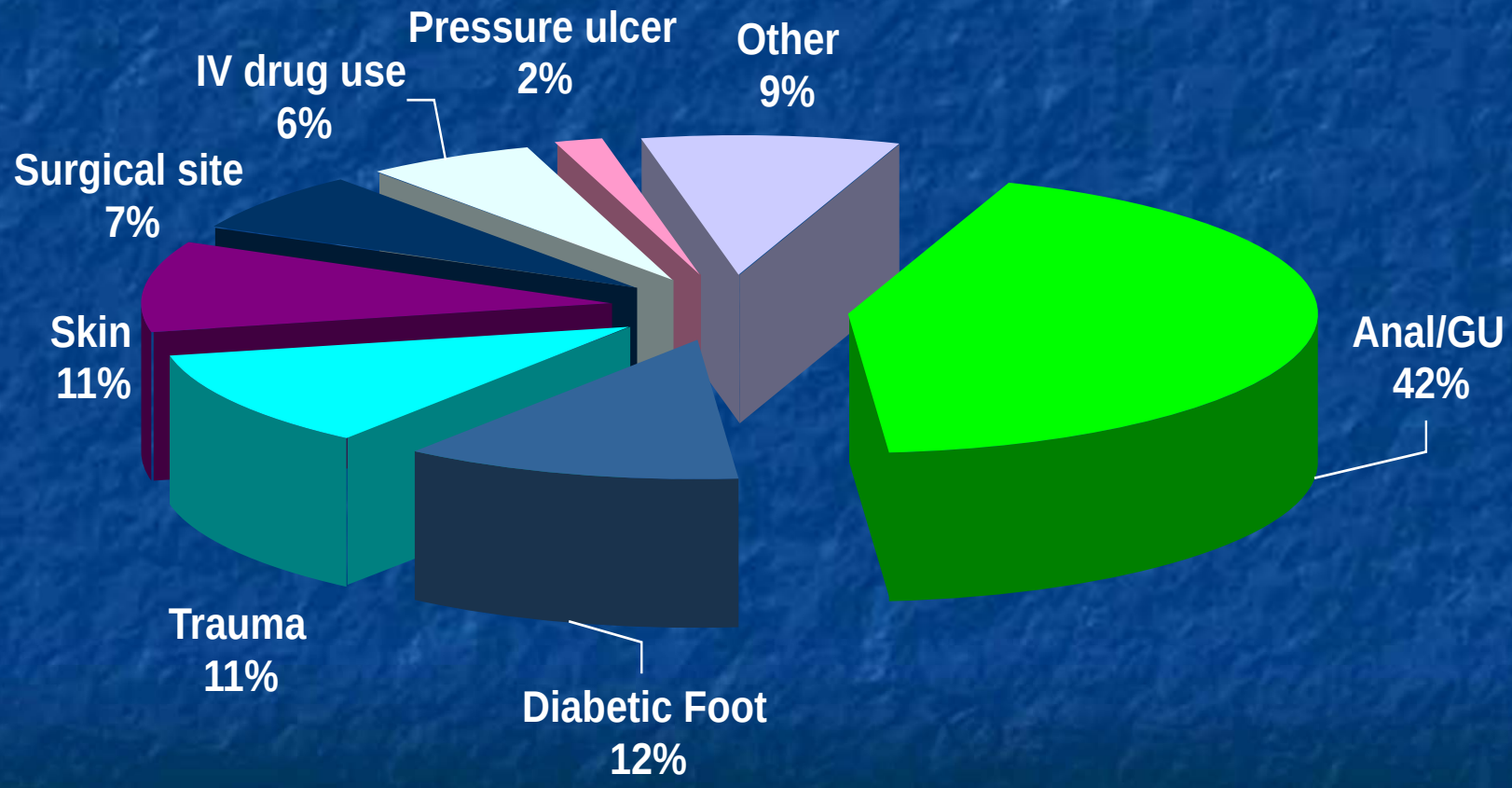


Anatomic layer	Necrotizing….
Epidermis	
Dermis	Cellulitis
Superficial fascia	
Subcutaneous fat, arteries, veins	Fasciitis
Deep fascia	
Muscle	Myonecrosis

Etiology of NSTI
Elliott, Ann Surg, 1996



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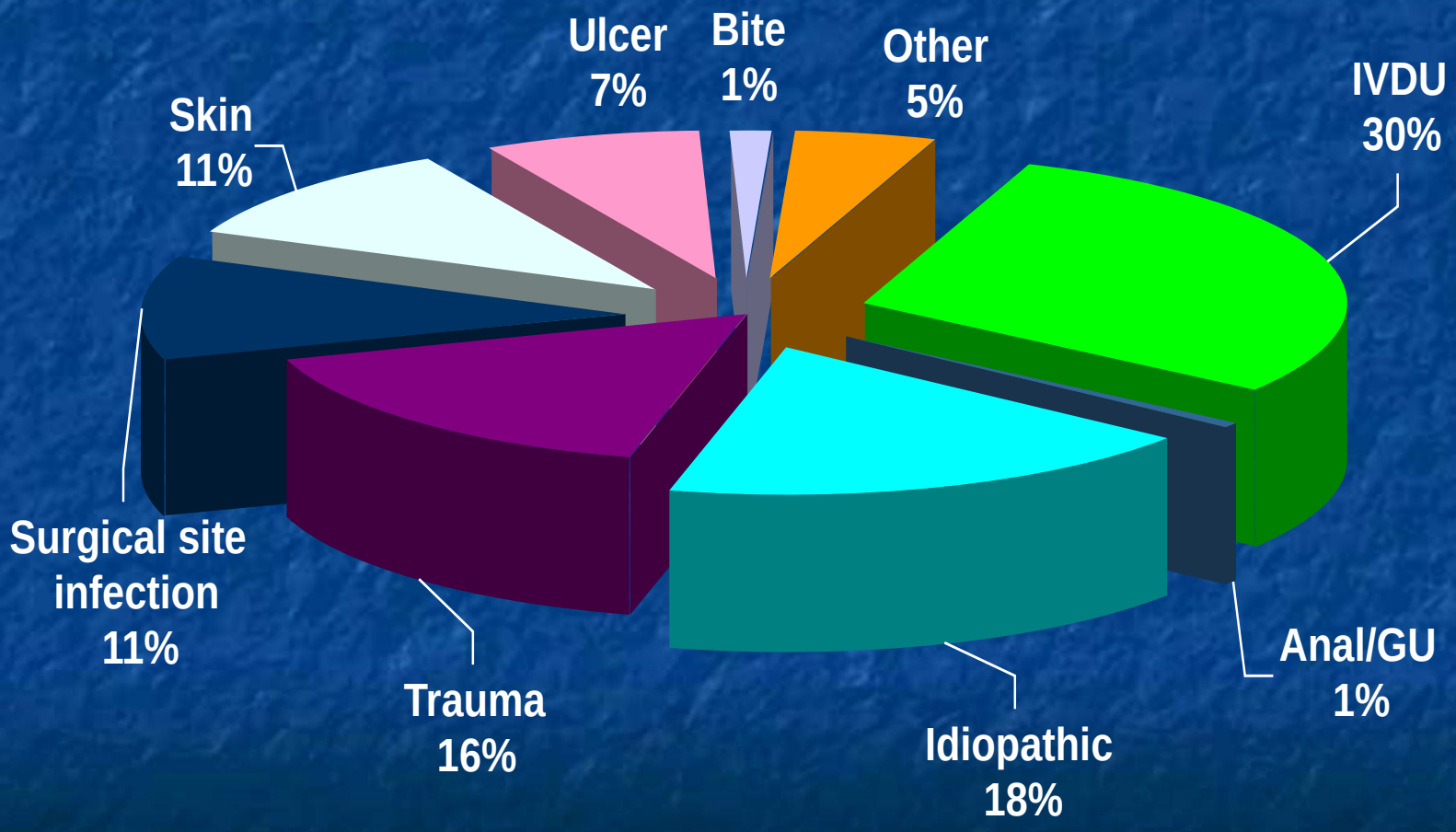
Etiology of NSTI
Anaya, Arch Surg, 2004



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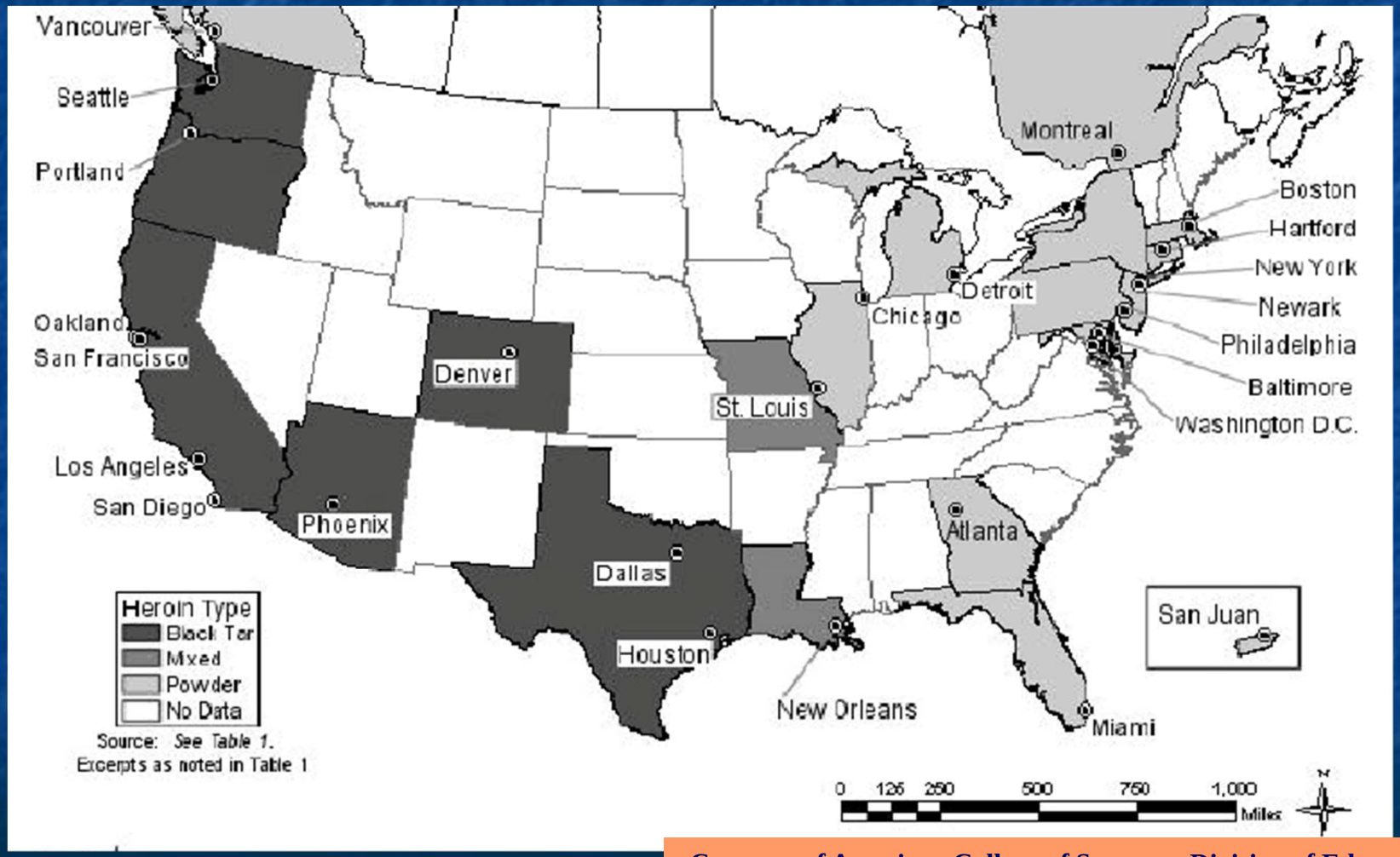
Distribution of Black Tar Heroin



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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, immunosuppressed

Hard Signs

- Gas on radiograph

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Diabetic foot?

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Tense edema

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- Tense edema
- Purple discoloration
- Cutaneous gangrene

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Pannus Infections

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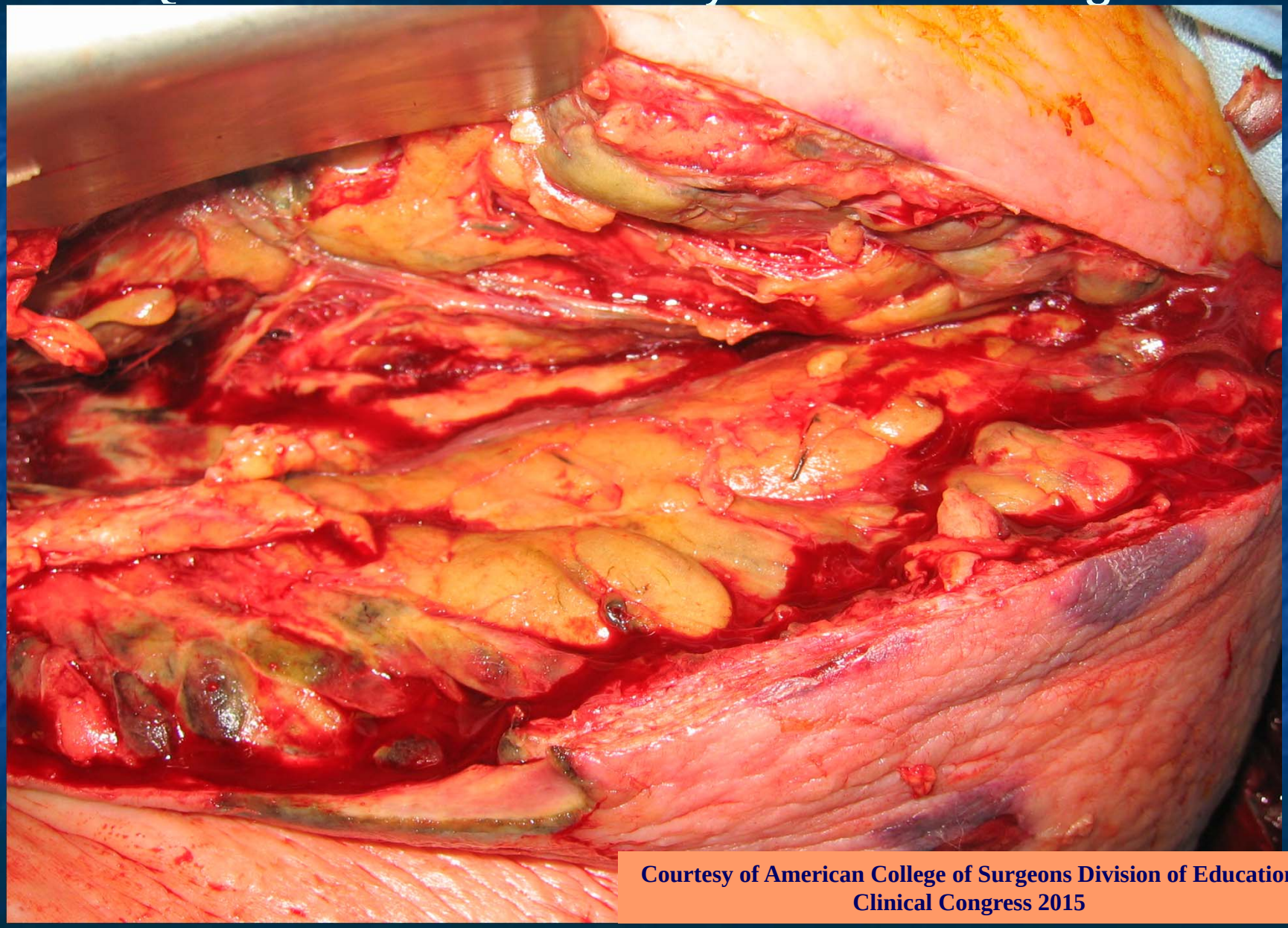
SQ Necrosis extends beyond Skin changes



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Diagnostic assessment
Wall, J Am Coll Surg, 2000

- Necrotizing fasciitis (n=31)
- Controls: soft tissue infections without necrosis or not requiring surgical intervention (n=328)
- 71% of NSTI due to IV drug use

“Hard Signs” in NSTI
Wall, J Am Coll Surg, 2000

	NSTI (%)	Non-NSTI (%)
Tense edema	23	3*
Bullae	16	3*
Purplish skin discoloration	10	1*
Sensory/motor deficit	13	3*
Cutaneous necrosis	6	2
Gas on xray	32	3*
Any hard sign	39	7

Predictive model for diagnosis of NSTI Wall, J Am Coll Surg, 2000

- Best predictors: Admission Na<135 OR WBC>15.4
- Sensitivity: 90%, Specificity: 76%
- Positive predictive value: 26%, Negative predictive value: 99%
- 95% of those without hard signs were predicted to have NSTI using this approach

LRINEC – Laboratory Risk Indicator for NSTI
Wong, Crit Care Med, 2004

- NSTI – 89 patients
- Controls (n=225) - Severe soft tissue infections
  - IV antibiotics >48 hrs OR surgical drainage
- Validated at second institution

LRINEC for diagnosis of NSTI
Wong, Crit Care Med, 2004

Variable	Score
C-reactive protein	
<150	0
>150	4
WBC	
<15	0
15-25	1
>25	2
HgB	
>13.5	0
11-13.5	1
<11	2

Variable	Score
Sodium	
≥135	0
<135	2
Creatinine	
≤1.6	0
>1.6	2
Glucose	
≤180	0
>180	1

LRINEC for diagnosis of NSTI Wong, Crit Care Med, 2004

- Stratified likelihood of NSTI by LRINEC score
  - Low (≤5): <50%
  - Moderate (6-7): 50-75%
  - High (≥8): >75%
- Using a cutoff of ≥6
  - Positive predictive value: 92%
  - Negative predictive value: 96%

What about imaging?

- Primarily a clinical diagnosis and imaging should not delay surgical intervention.
- Visible gas in the soft tissues is a late finding and not present in the majority of cases
- CT/MRI: may be useful in identifying deep abscesses when the diagnosis is not clear but fat stranding or fascial thickening is non-specific

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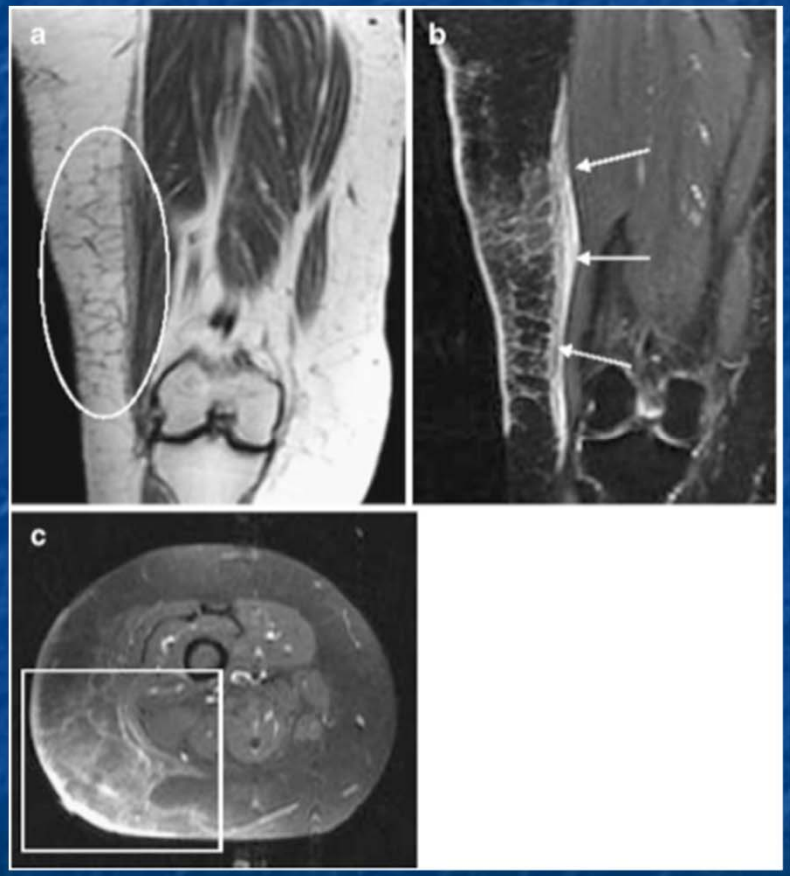
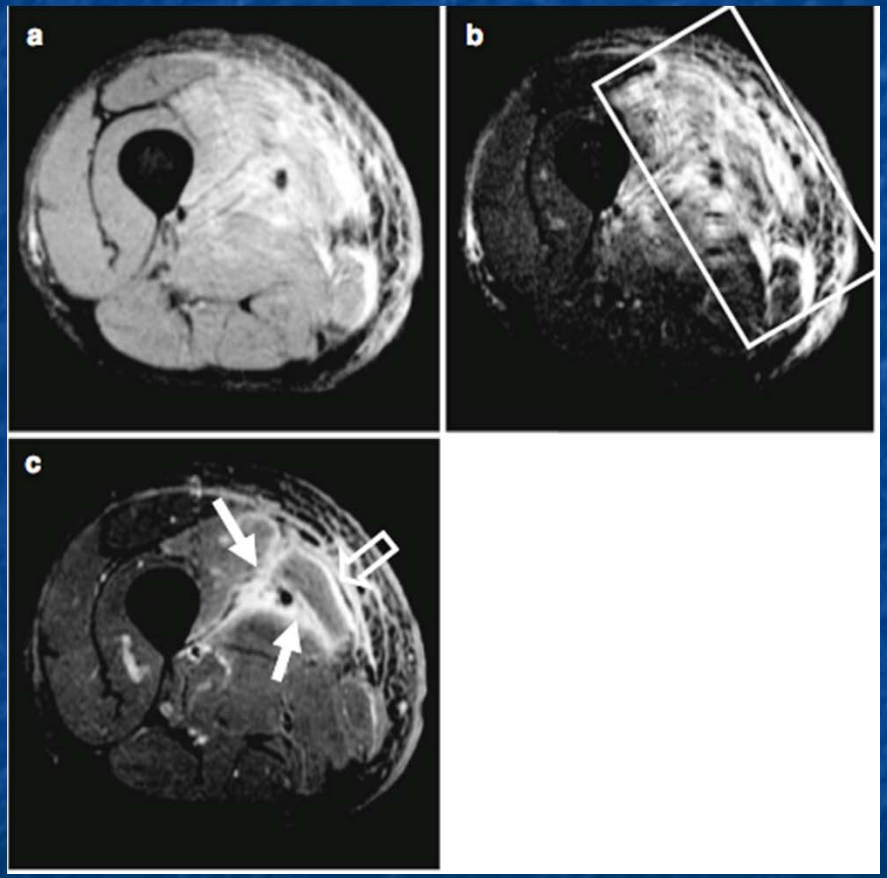
Are 16-64 slice CT scans better?

- Retrospective review 67 patients who had Contrast CT for possible NSTI
  - Obvious NSTI/ cellulitis excluded
  - Positive scan:
    - Asymmetrical and diffuse areas soft tissue inflammation and ischemia
    - Muscle necrosis
    - Gas across tissue planes
    - Fluid collections
  - Reported sensitivity 100%, Specificity 81%
  - Delay in diagnosis at least one case, not described

Zacharias et al, Arch Surg 2010

MRI?





Yu et al, Emerg Rad 2009

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The “Finger Test”?

- Area infiltrated with local anesthetic
- 2 cm incision down to fascia
  - Lack of bleeding, dishwater fluid ominous
- Push finger along deep fascia – if no resistance, nec fasciitis

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Bottom Line

- Need to look at the constellation of risk factors, exam, and lab results
- Making the diagnosis of NSTI requires a high index of suspicion and when in doubt proceed to OR for exploration

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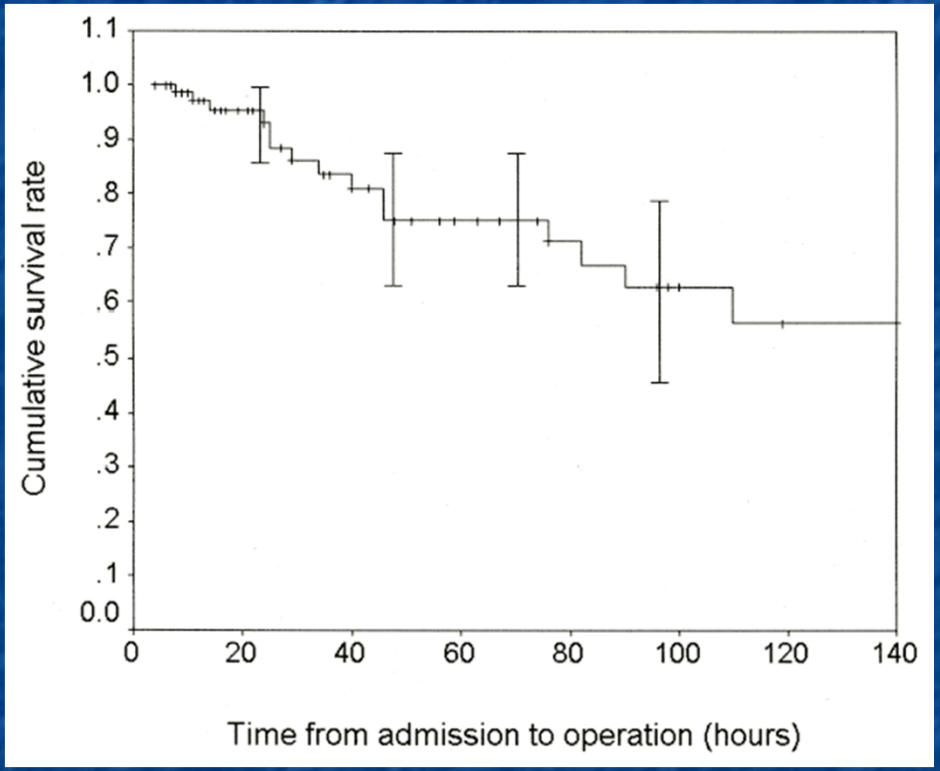
Delay in Diagnosis Increases Mortality

- Freischlag et. al
  - Early diagnosis and treatment (< 24hr): 36%
  - Late diagnosis and treatment (>24hr): 70%
- Wong et al.
  - Delay of > 24 hrs from admission to surgery was the only independent predictor of mortality



Wong et al, J Bone Joint Surg Am, 2003

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

Challenges

- Rare disease
- Limited experience for most surgeons
- Rapidly progressive
- Subtle skin changes
- Shock is a late manifestation