Necrotizing Fasciitis

Basem Attum, MD

Megan Mignemi, MD

Jonathan G. Schoenecker, MD

Addison K. May, MD, FACS, FCCM

William Obremskey, MD, MPH, MMHC

Vanderbilt University Medical Center

Created August 2017

Necrotizing Soft Tissue Infections- Epidemiology

500 – 1,000 cases annually

Necrotizing Soft Tissue Infections- Epidemiology

500 – 1,000 cases annually

20-30% mortality rate

Necrotizing Soft Tissue Infections- Epidemiology

500 – 1,000 cases annually

20-30% mortality rate

4% increase in mortality every year of life

Necrotizing Soft Tissue Infections- Epidemiology

500 – 1,000 cases annually

20-30% mortality rate

4% increase in mortality every year of life

Time from admission to initial debridement most important variable determining mortality

Independent Predictors for Mortality

Retrospective reviews identify several factors:

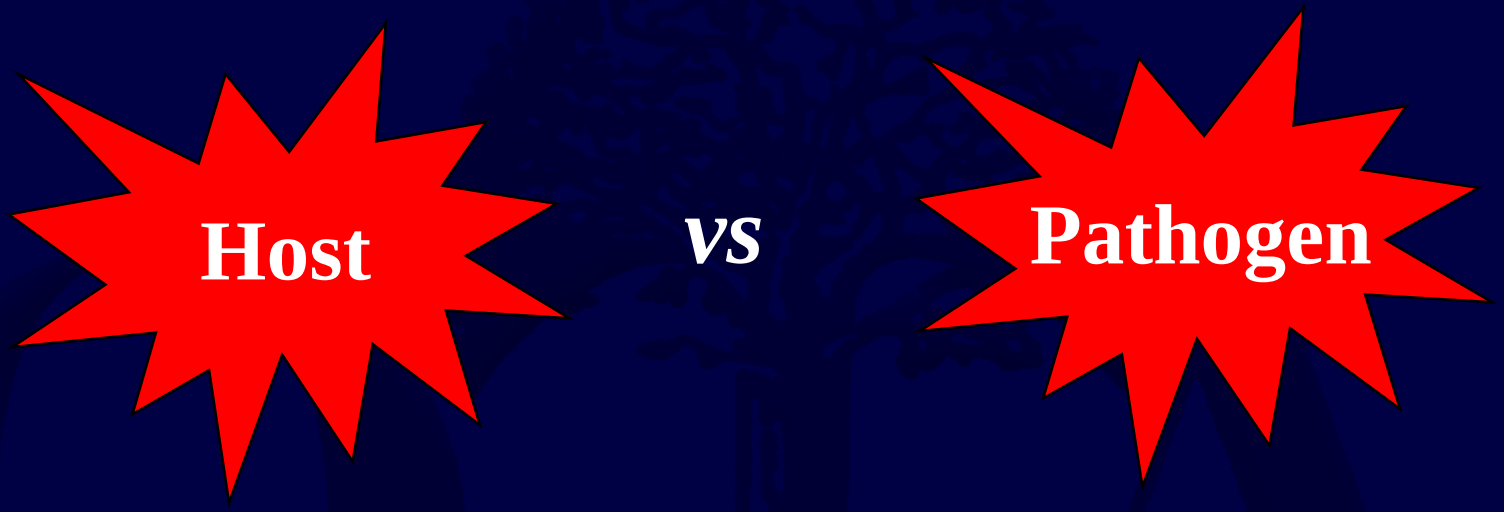
- **Time to first debridement**
- **Inadequate first debridement**
- **Extent of tissue involvement**
- **Age > 60 years**
- **Bacteremia**
- **# Failed organs on admission**
- **Elevated lactate**

Bosshardt TL. *Arch.Surg*. 1996;131:846-52
Elliott DC. *Ann.Surg*. 1996; 224:672-83
Bilton BD. *Am.Surg.* 1998; 64:397-400

Necrotizing Soft Tissue Infection (NSTI)Tissue layers and infection

- **Dermis and subcutaneous fat**
  - **Good resistance to bacterial invasion, proliferation**
  - **Infection: NECROTIZING CELLULITIS**
- **Fascia (deep or muscle)**
  - **Tentative blood supply, poor lymphatic drainage, and low resistance to bacterial invasion, growth, and spread**
  - **Infection: NECROTIZING FASCIITIS**
- **Muscle**
  - **Very good blood supply and good resistance to bacterial invasion and proliferation**
  - **Infection: MYOSITIS and MYONECROSIS**

Determinants of Infection



HOST TISSUE RESISTANCE

BACTERIAL VIRULENCE GROWTH CHARACTERISTICS

… Presentation and severity of infection determined by a balance between these factors …

Necrotizing Soft Tissue Infections- Risk Factors

- **Risk Factors**
  - **Any condition causing a decrease in immune function**
    - **Diabetes and IVDA are most common.**
    - **Others include:**
      - **obesity,**
      - **peripheral artery disease**
      - **corticosteroid therapy**
      - **malnutrition**
      - **Smoking**
      - **chronic cardiac disease**
      - **chronic immunosuppression and cancer**

1.
Giannoudis PV. Necrotizing fasciitis of upper and lower limb: a systematic review. Injury. 2007;38(suppl 5):S18eS25)
Childers BJ, Potyondy LD, Nachreiner R, et al. Necrotizing fasciitis: a fourteen-year retrospective study of 163 consecutive patients.Am Surg. 2002;68(2):109e116.)

Necrotizing Soft Tissue Infections- Risk Factors

- Risk Factors
  - **NSAIDs**
    - risk factor as use may initially mask the symptoms.

MOST COMMON

+/- trauma

Diabetes present in 18-60%

>50% cases in healthy individuals

Bellapianta, Joseph M., et al. "Necrotizing fasciitis." *Journal of the American Academy of Orthopaedic Surgeons* 17.3 (2009): 174-182.)

Necrotizing Soft Tissue Infections- Signs and Symptoms

Necrotising fasciitis of upper and lower limb: A systematic review

A.G. Angoules [a], G. Kontakis [b], E. Drakoulakis [a], G. Vrentzos [c], M.S. Granick [d], P.V. Giannoudis [a,*]

- Review of 12 studies totaling 317 limbs found that **erythema (73%), pain (63%) and edema were the most common physical exam findings.**

Angoules AG, Kontakis G, Drakoulakis E, Vrentzos G, Granick MS, Giannoudis PV. Necrotizing fasciitis of upper and lower limb: a systematic review. Injury. 2007;38(suppl 5):S18eS25

Necrotizing Soft Tissue Infections- Signs and Symptoms

J Bone Joint Surg Am. 2003 Aug;85-A(8):1454-60.

Necrotizing fasciitis: clinical presentation, microbiology, and determinants of mortality.

Wong CH[1], Chang HC, Pasupathy S, Khin LW, Tan JL, Low CO.

- Study among 89 consecutive patients with necrotizing fasciitis
  - Most common physical examination findings
    - **erythema (100%)**
    - **pain out of proportion to physical findings (97.8%)**
    - **warm skin (96.6%)**

Necrotizing Soft Tissue Infections- Signs and Symptoms

Am Surg. 2002 Feb;68(2):109-16.

Necrotizing fasciitis: a fourteen-year retrospective study of 163 consecutive patients.

Childers BJ[1], Potyondy LD, Nachreiner R, Rogers FR, Childers ER, Oberg KC, Hendricks DL, Hardesty RA.

- 163 patients with NF
  - **pain was present in all patients**
  - **erythema in (95%)**
  - **edema in (82%)**

Necrotizing Soft Tissue Infections-Diagnosis

Objective Criteria to Distinguish Necrotizing from Non-necrotizing Infection

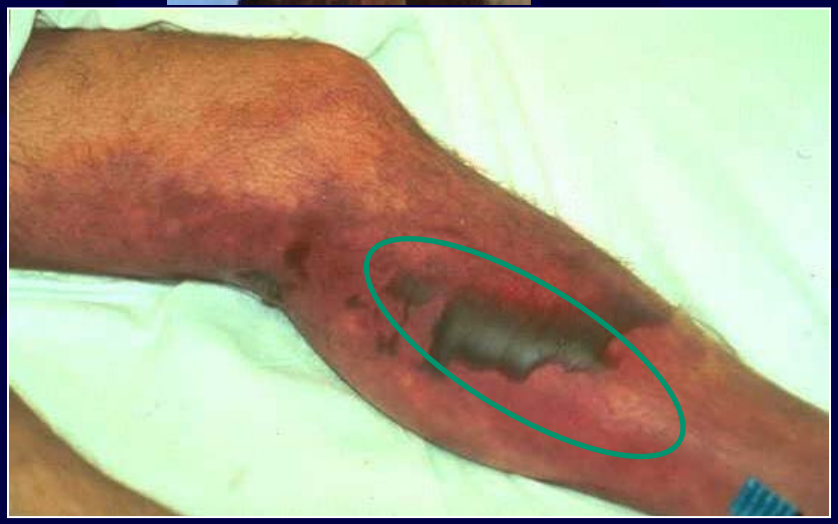
	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
Tense Edema	38	100	100	62
Gas on XR	39	95	88	62
Bullae	24	100	100	57
WBC > 14 x 10^9/L	81	76	77	80
Sodium < 135 mmol/L	75	100	100	77
Chloride < 95 mmol/L	30	100	100	55
BUN > 15 mg/dL	70	88	88	71

Wall DB et al. *Am J Surg*. 2000;179:17-21.

Necrotizing Soft Tissue Infections- Diagnosis

Diagnosis of Necrotizing STI:

- **"Hard signs" for the presence of a necrotizing process:**
  - **bullae**
  - **skin ecchymosis preceding skin necrosis**
  - **gas in tissues by exam or on radiographs**
  - **cutaneous anesthesia**
    - **present in 7- 44% of cases**

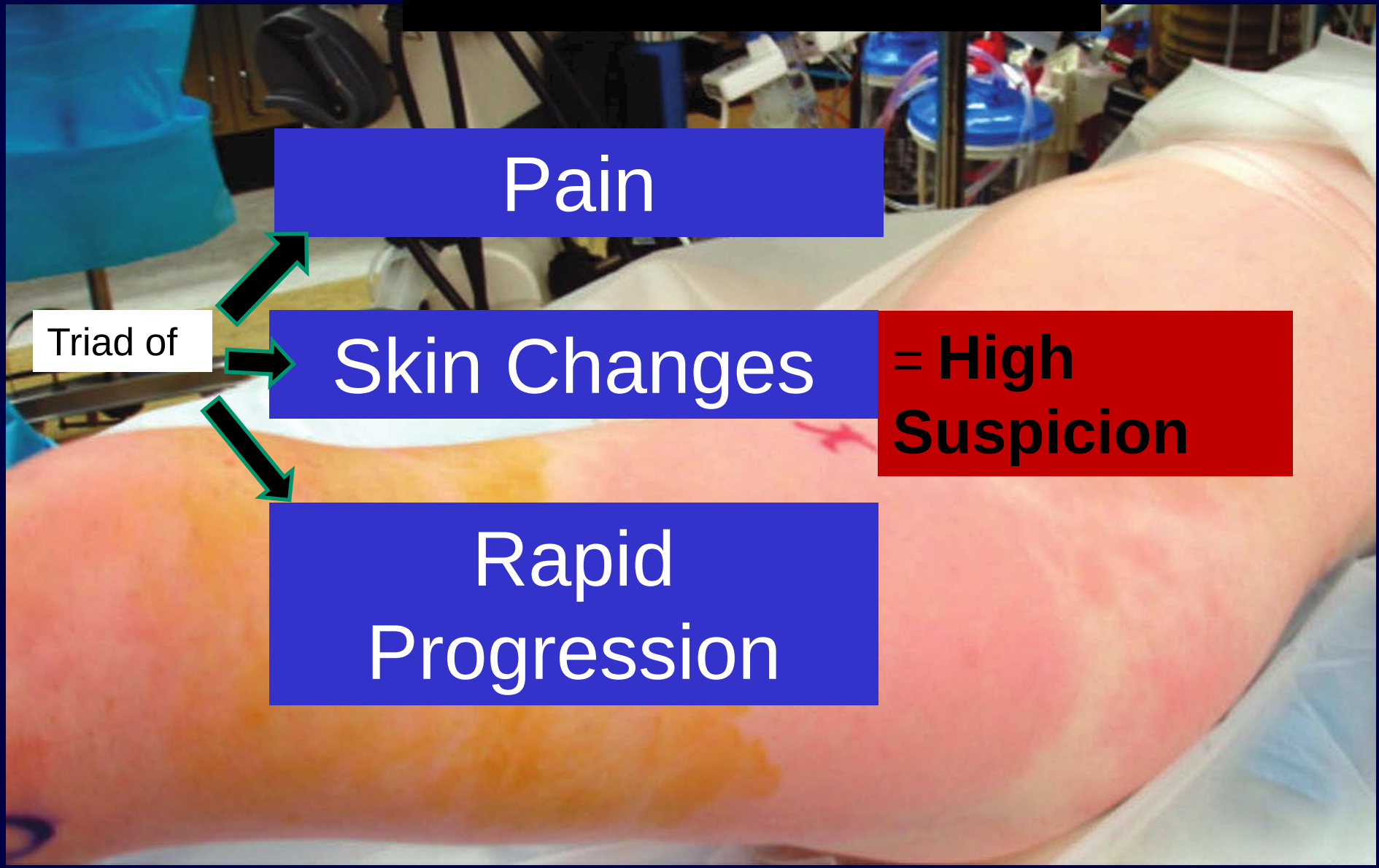


Necrotizing Soft Tissue Infections- Diagnosis

Diagnosis of Necrotizing SSTI:

- **Suggestive signs:**
  - **pain disproportionate to examination**
  - **edema extending beyond skin erythema**
  - **systemic toxicity**
  - **progression of infection despite antibiotic therapy**

Clinical Diagnosis!



Triad of

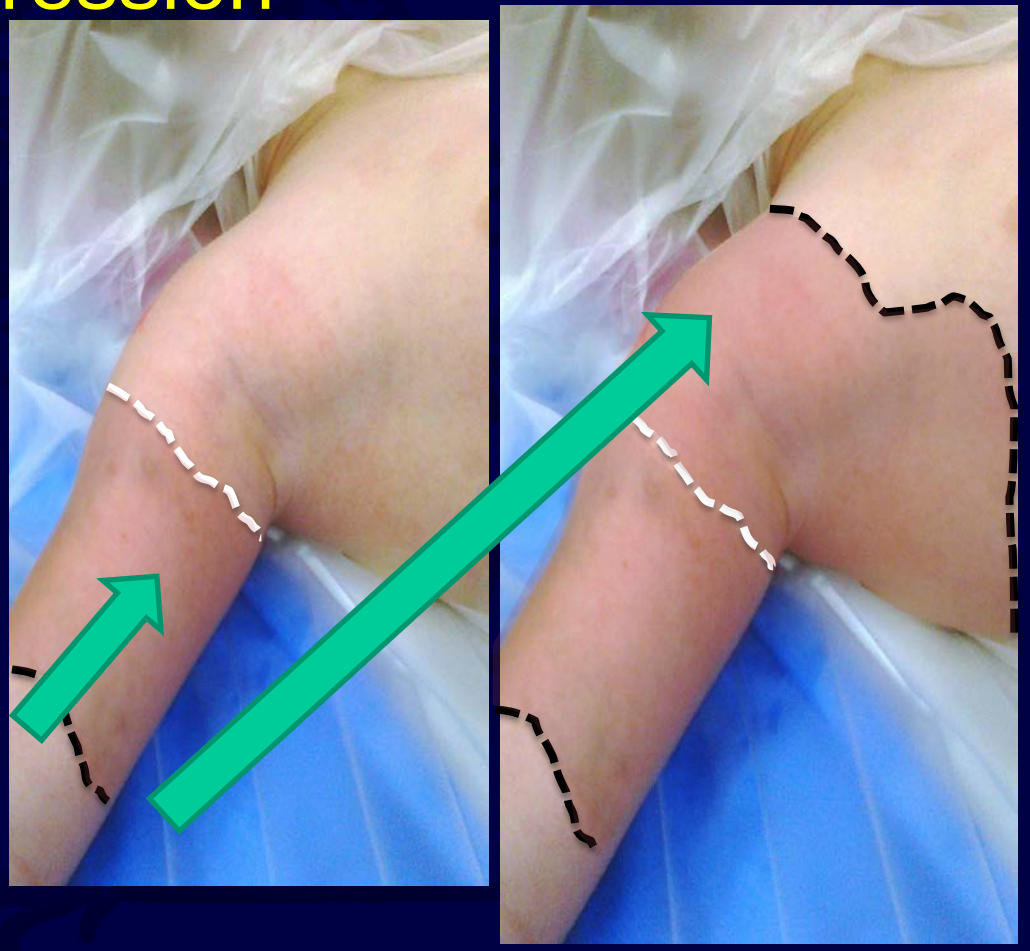
- Pain
- Skin Changes
- Rapid Progression

= **High Suspicion**

Necrotizing Soft Tissue Infections- Progression

- Necrotizing infection
  - Early in disease process may present identical to cellulitis and erysepilas

- Fever **may or may not be** present.

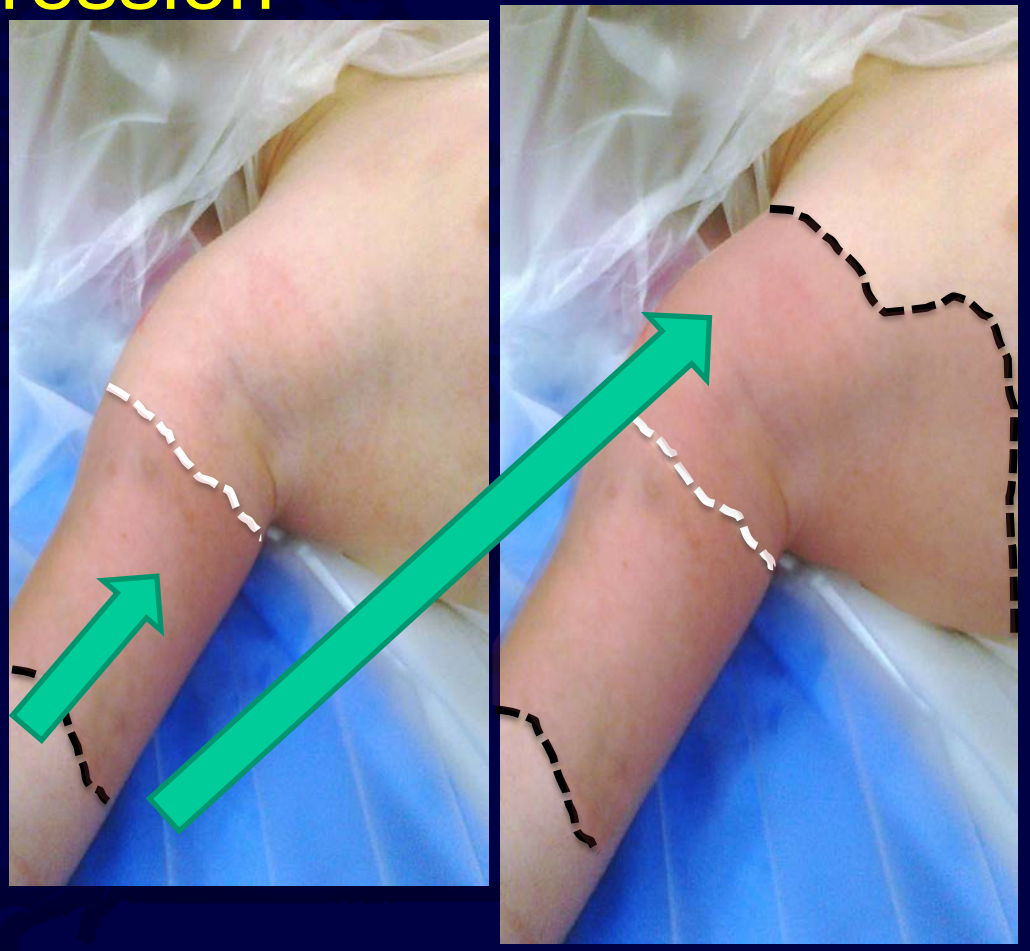


Fontes Jr, Roger A., Christian M. Ogilvie, and Theodore Miclau. "Necrotizing soft-tissue infections." *Journal of the American Academy of Orthopaedic Surgeons* 8.3 (2000): 151-158.)

Bisno, A. L., & Stevens, D. L. (1996). Streptococcal infections of skin and soft tissues. *New England Journal of Medicine*, *334*(4), 240-246.

Necrotizing Soft Tissue Infections- Progression

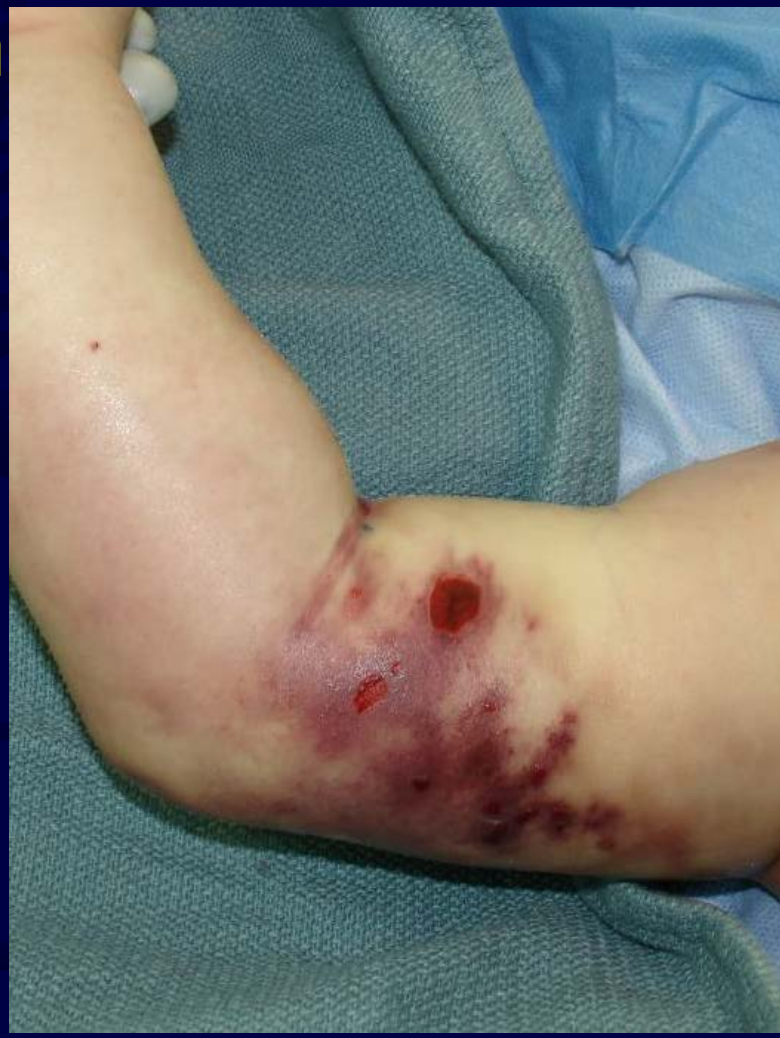
- With disease progression, systemic signs of **sepsis** may present:
  - **hypotensive acidosis,**
  - **leukocytosis**
  - **Tachycardia**
  - **hypo or hyperthermia.**



Fontes Jr, Roger A., Christian M. Ogilvie, and Theodore Miclau. "Necrotizing soft-tissue infections." *Journal of the American Academy of Orthopaedic Surgeons* 8.3 (2000): 151-158.)

Necrotizing Soft Tissue Infections- Progression

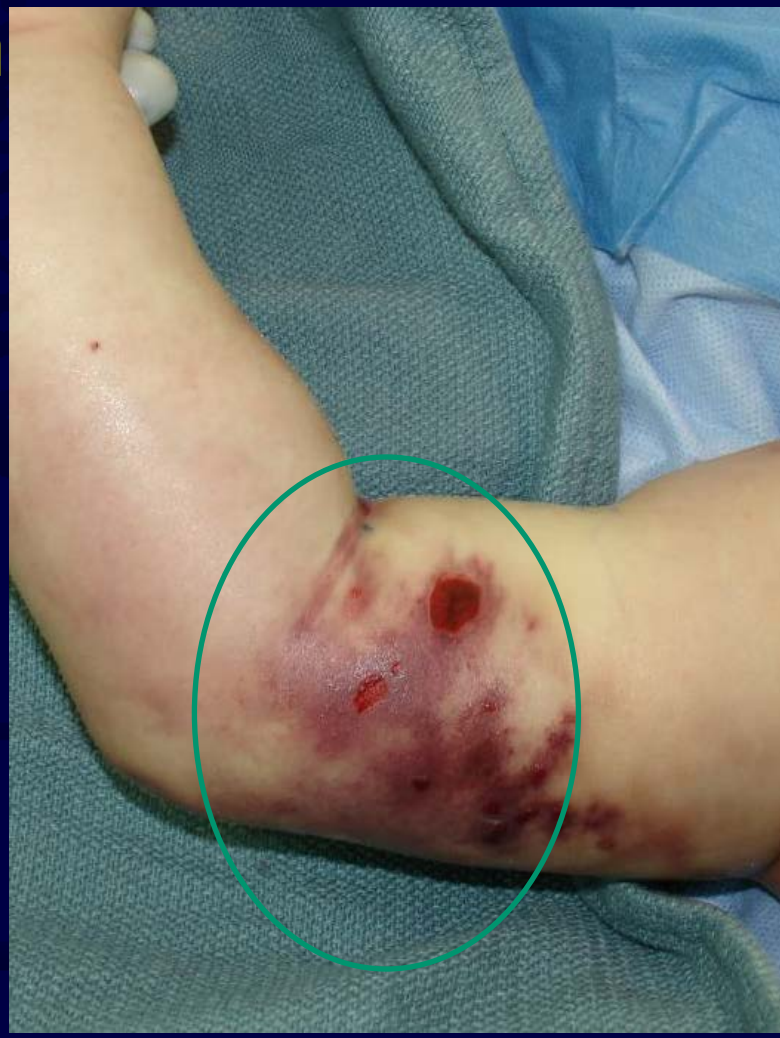
- Variable depending on the size of
  - bacterial inoculum
  - organism involved
  - location of the infection
  - health of the patient.



Fontes Jr, Roger A., Christian M. Ogilvie, and Theodore Miclau. "Necrotizing soft-tissue infections." *Journal of the American Academy of Orthopaedic Surgeons* 8.3 (2000): 151-158)

Necrotizing Soft Tissue Infections- Progression

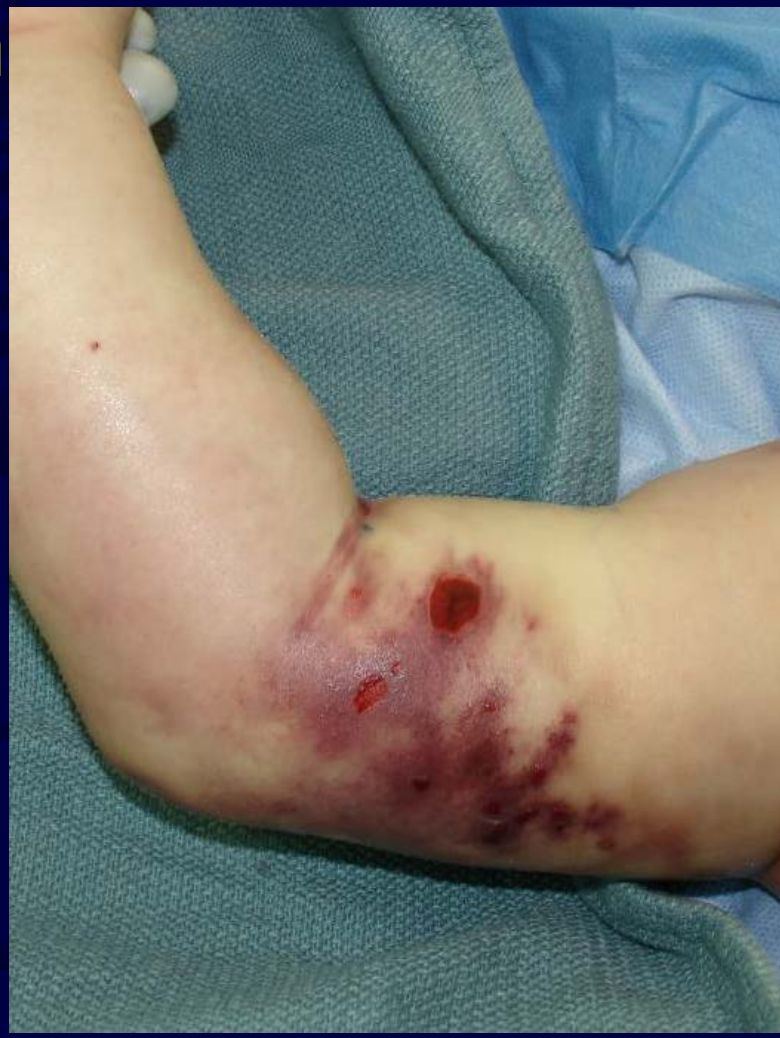
- Progression
  - Generally speaking, edema, erythema and necrosis progress slowly over a 2-4 day period.
  - With **group A streptococcal infection**
    - progression rapid presenting with **dark red bullae**.



Fontes Jr, Roger A., Christian M. Ogilvie, and Theodore Miclau. "Necrotizing soft-tissue infections." ***Journal of the American Academy of Orthopaedic Surgeons*** **8.3 (2000): 151-158)**

Necrotizing Soft Tissue Infections- Progression

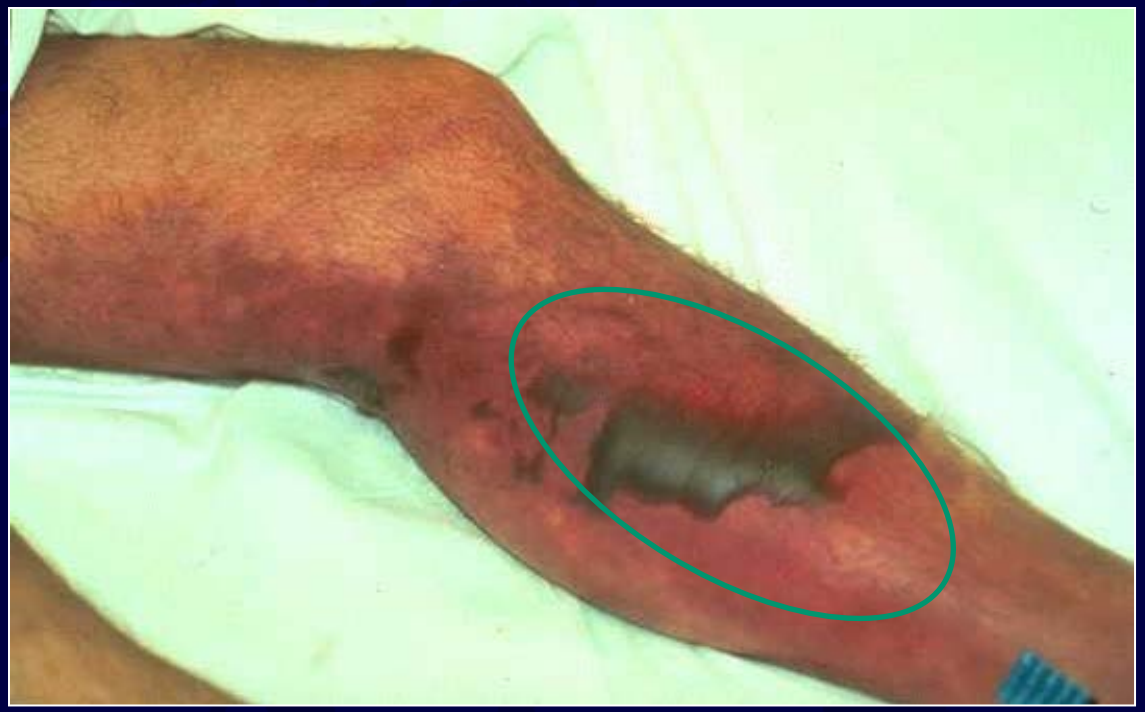
- Level of suspicion should be heightened when
  - patients diagnosed with cellulitis have **pain out of proportion to lesion**.
  - rapid progression of erythema and **skin induration (>1 cm/hr) in spite of IV antibiotic treatment**.



Fontes Jr, Roger A., Christian M. Ogilvie, and Theodore Miclau. "Necrotizing soft-tissue infections." ***Journal of the American Academy of Orthopaedic Surgeons*** **8.3 (2000): 151-158)**

Necrotizing Soft Tissue Infections- Progression

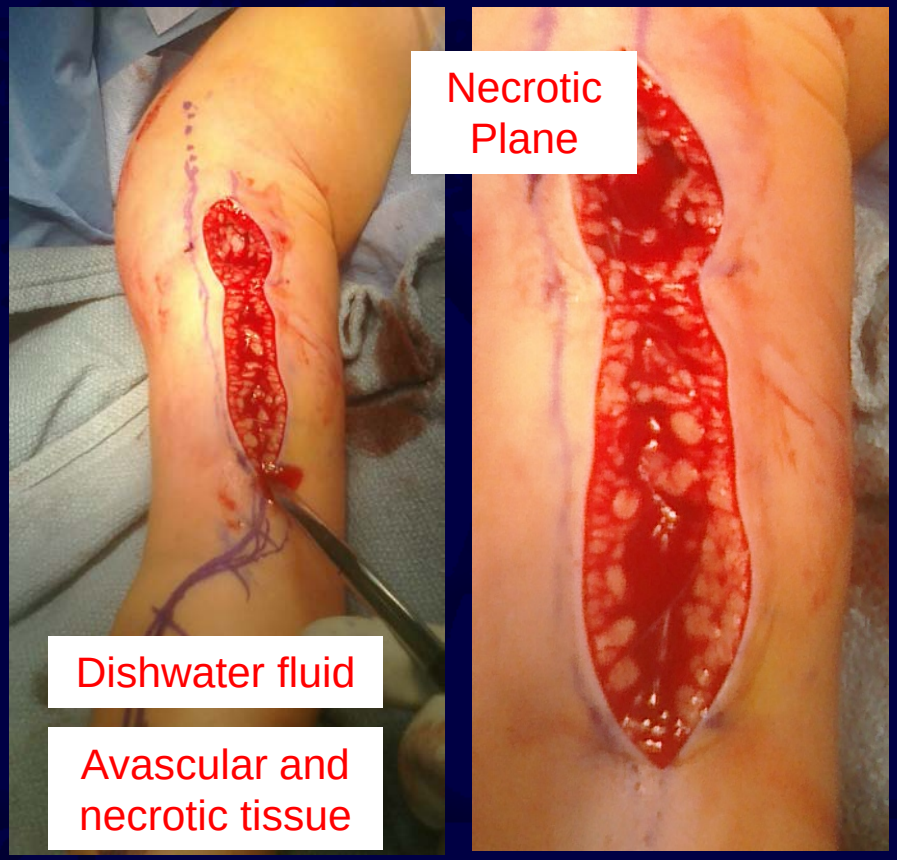
- **Blisters and Bullae**
  - initially drain serosanguinous fluid then drain hemorrhagic fluid
- **Crepitus**
  - present when soft tissue in gas
- **Pain dulls**
  - cutaneous nerves destroyed



Green, R. J., Dafoe, D. C., & Rajfin, T. A. (1996). Necrotizing fasciitis. *Chest*, *110*(1), 219-229.

Necrotizing Soft Tissue Infections- Progression

- Later stage disease may present with a
  - **watery, grayish , foul smelling "dishwater pus"** due to superficial fat and fascial necrosis



Green, R. J., Dafoe, D. C., & Rajfin, T. A. (1996). Necrotizing fasciitis. *Chest*, *110*(1), 219-229.

Improvement of a Clinical Score for Necrotizing Fasciitis: 'Pain Out of Proportion' and High CRP Levels Aid the Diagnosis

Thomas Borschitz[1☯], Svenja Schlicht[2☯], Ekkehard Siegel[3], Eric Hanke[4], Esther von Stebut[2*]

- Diagnosis often delayed due to similar presentation with cellulitis
  - Compared 59 pts with NF to matched cohorts
    - **NF group had**
      - **stronger complaint of pain**
      - **5 fold increase in CRP levels**
      - **LRINREC scores were significantly higher.**

Necrotizing Soft Tissue Infections-Lab Studies

(LRINEC) Score

Laboratory parameter, units	LRINEC points	Laboratory parameter, units	LRINEC points
CRP, mg/L		Sodium, mmol/L	
<150	0	≥135	0
≥150	4	<135	2
Total WBC, k/mm^3		Creatinine, mg/dL	
<15	0	≤1.6	0
15-25	1	>1.6	2
>25	2	Glucose, mg/dL	
Hb, g/dL		≤180	0
>13.5	0	>180	1
11–13.5	1		
<11	2		

Modified from Abrahamian FM, et al. *Infect Dis Clin North Am*. 2008;22:89-116; Wong CH, et al. *Crit Care Med.* 2004;32:1535-1541.

Necrotizing Soft Tissue Infections- Lab Studies

Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) Score

- The maximum cumulative score 13.
- A score greater than or equal to 6
  - positive predictive value of 92% (95% CI, 84.3–96.0)
  - negative predictive value of 96% (95% CI, 92.6–97.9)

- The probability of necrotizing SSTI increased to more than 75% when the LRINEC score was **greater than or equal to 8.**

Necrotizing Soft Tissue Infections- Lab Studies

- Initial lab workup of a suspected necrotizing infection should include:
  - **CBC**
  - **serum albumin**
  - **electrolyte panel (including calcium)**
  - **BUN**
  - **liver function tests**
  - **PT and PTT.**
  - **ESR**
  - **CRP**

- **1 (Elliott DC, Kufera JA, Myers RA: Necrotizing soft-tissue infections: Risk factors for mortality and strategies for management. Ann Surg 1996;224: 672-683).**

Ann Surg. 1996 Nov; 224(5): 672–683. PMCID: PMC1235444

Necrotizing soft tissue infections. Risk factors for mortality and strategies for management.

D C Elliott, J A Kufera, and R A Myers

- Decreased
  - **platelets**
- Elevated
  - **BUN**
  - **creatinine**
  - **bilirubin**
  - **blood lactate levels**

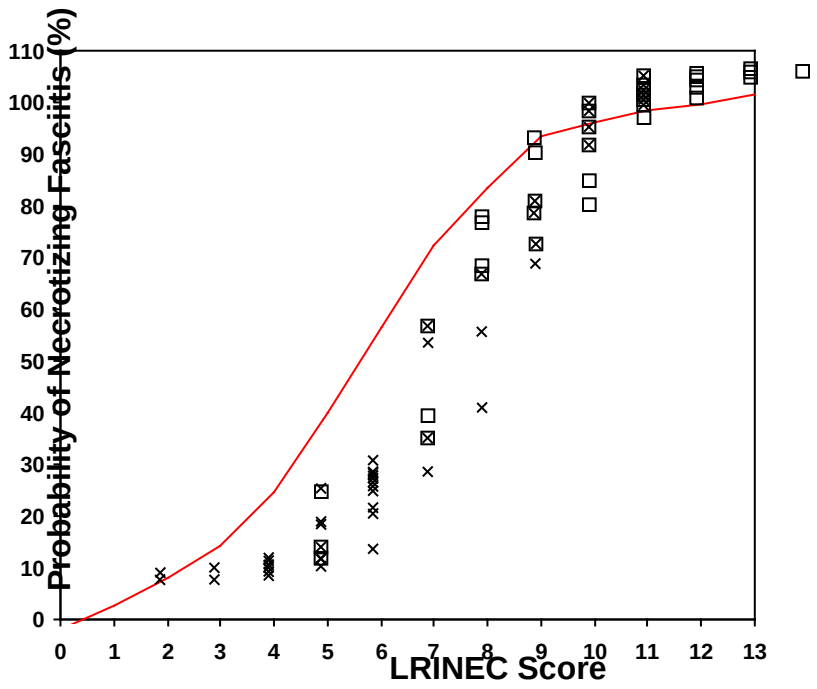
Associated with Death!

Necrotizing Soft Tissue Infections-Lab Studies

Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) Score

- **Caveats:**
  - Not been prospectively validated in patients for whom the diagnosis of necrotizing SSTI is **not** apparent on initial history and physical examination.
  - It is also unclear if the LRINEC score can be applied to **all age groups** (the youngest patients were 13 and 27 years old in the study cohort).

Necrotizing Soft Tissue Infections-Lab Studies

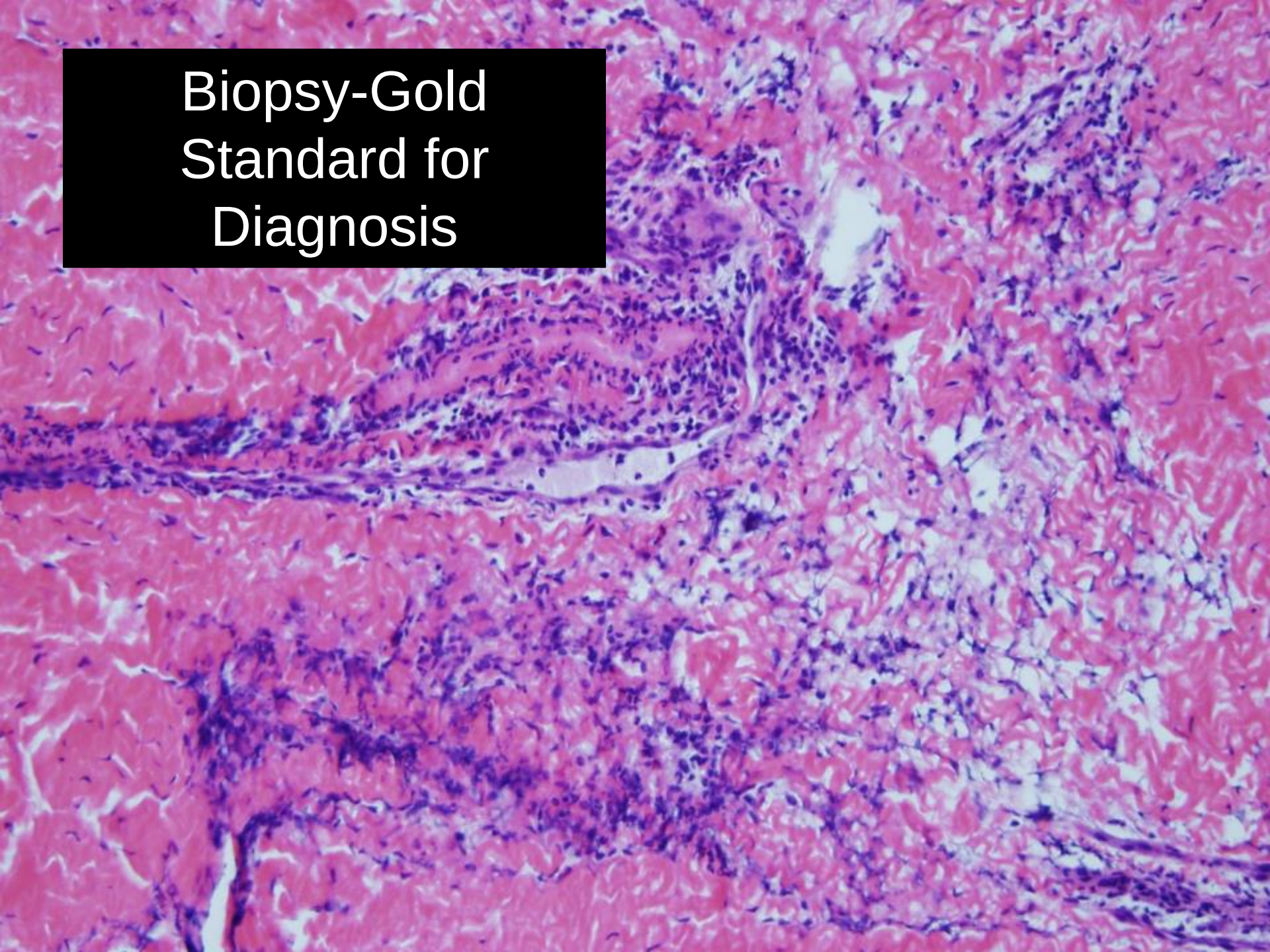


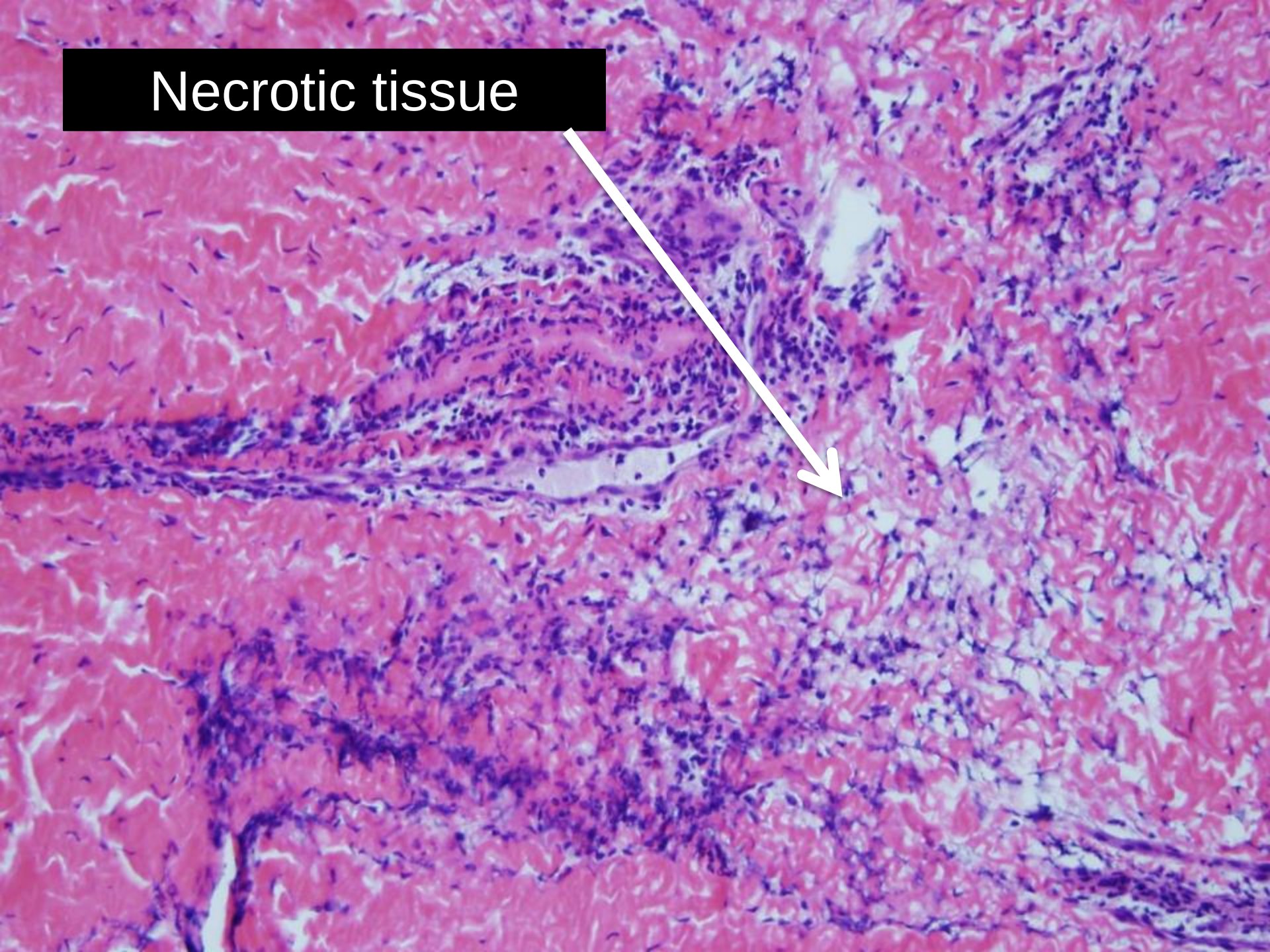
LRINEC Score		
LRINEC score	**Risk category**	**Probability of necrotizing SSTI**
≤5	**Low**	**<50%**
6–7	**Intermediate**	**50%–75%**
≥8	**High**	**>75%**

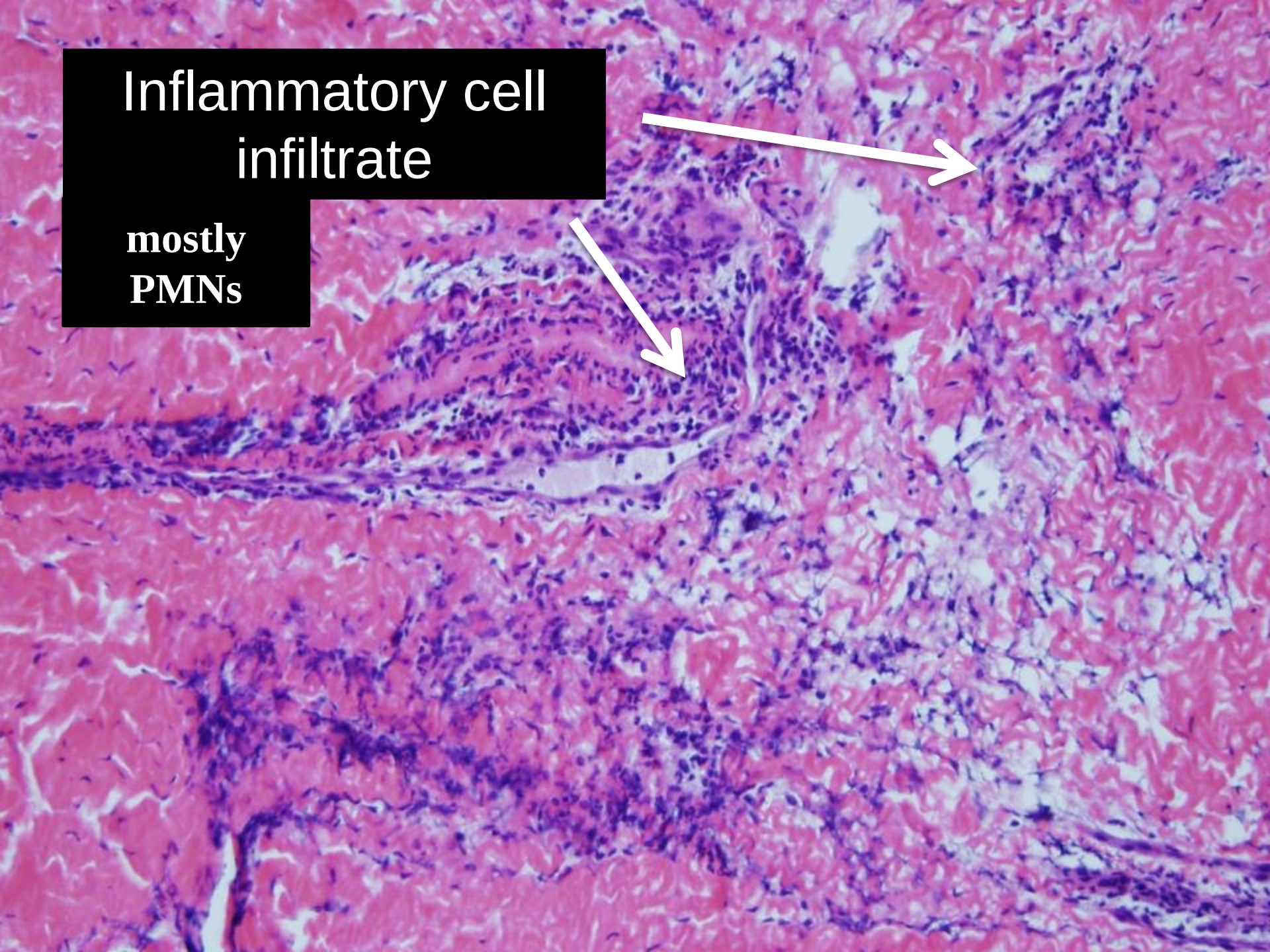
Finding abnormalities that make up the LRINEC score in patients with SSTI should increase suspicion of a necrotizing infection such that further observation and evaluation should be considered

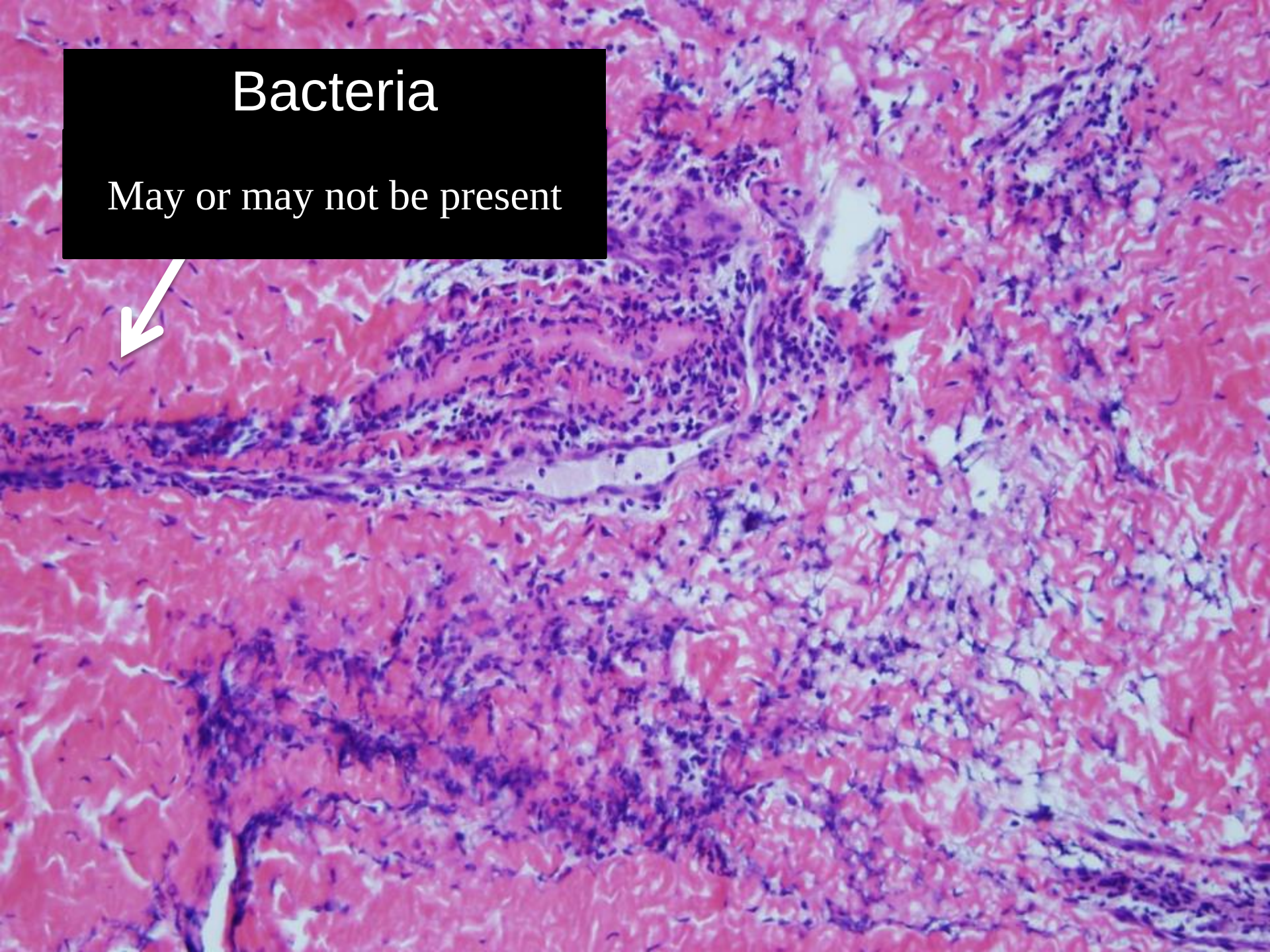
Wong CH, et al. *Crit Care Med*. 2004;32:1535-1541.
Abrahamian FM, et al. *Infect Dis Clin North Am.* 2008;22:89-116, vi.

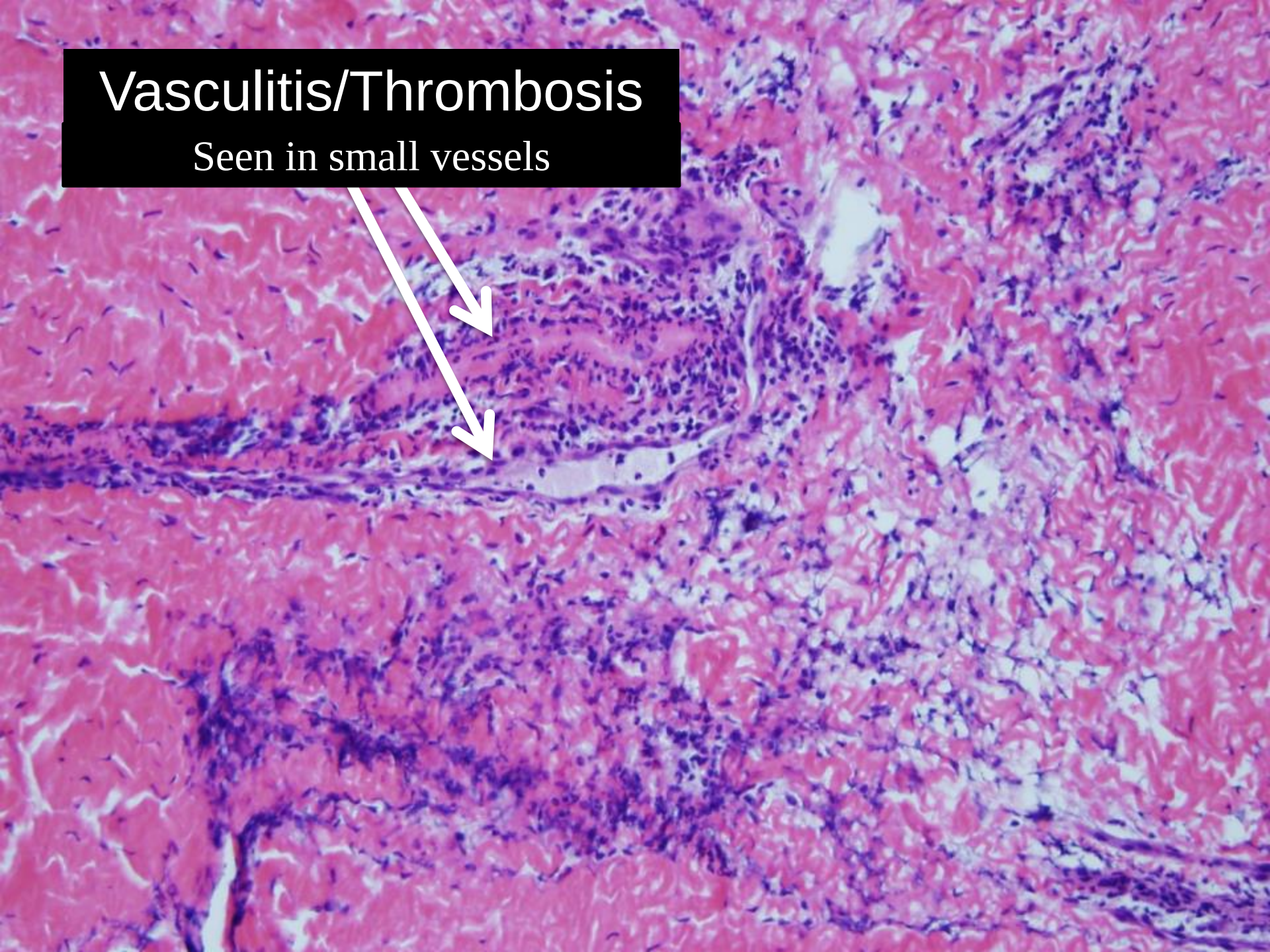
31


Biopsy-Gold Standard for Diagnosis

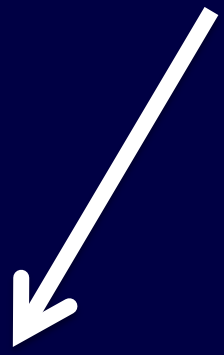

Necrotic tissue


Inflammatory cell infiltrate
mostly PMNs


Bacteria
May or may not be present


Vasculitis/Thrombosis
Seen in small vessels

Necrotizing Soft Tissue Infections- Biopsy Summary



Necrotic tissue

Bacteria

Inflammatory cell infiltrate

Vasculitis and Thrombosis

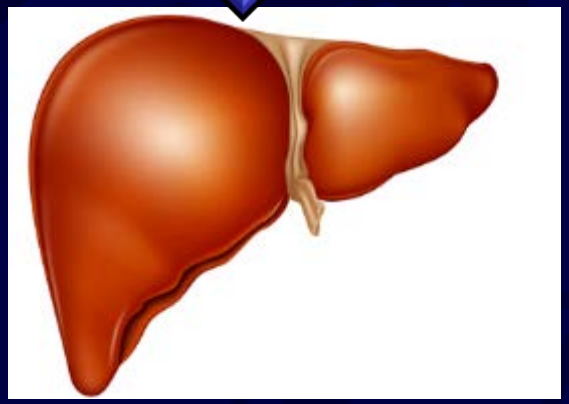
Pathophysiology-Infection Provoked Acute Phase Response

- NF
  - represents sustained injury from infection

Pathophysiology-Infection Provoked Acute Phase Response

- Sustained tissue injury elicits an acute phase response
  - myokine IL-6 released from damaged tissue
- IL-6 travels to the liver and affects the expression of over 1000 different genes.

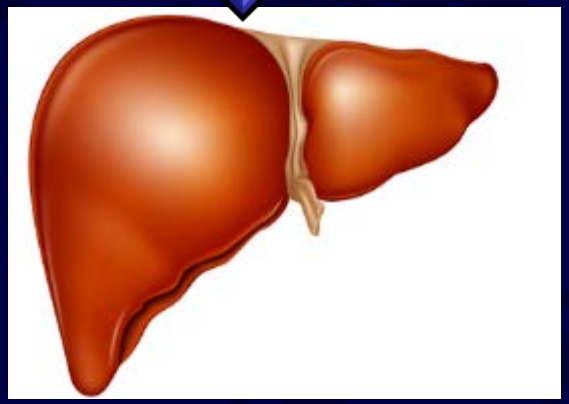
IL-6



Pathophysiology-Infection Provoked Acute Phase Response

- Most genes expressed make proteins involved in coagulation and inflammation leading to persistent tissue injury and sustained acute phase response

IL-6

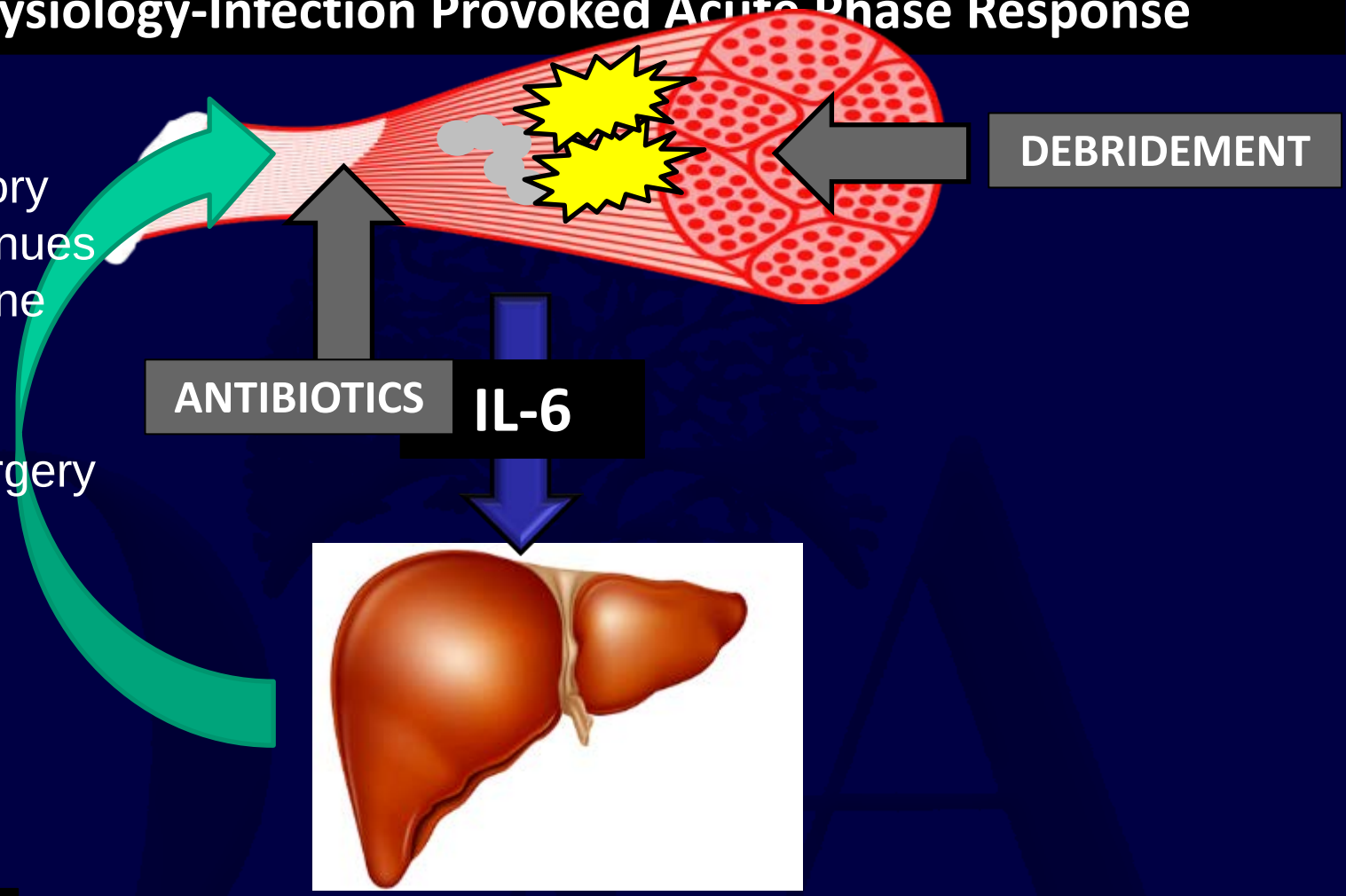


Hemostasis
Antimicrobial

PERSISTENT INJURY

Pathophysiology-Infection Provoked Acute Phase Response

- Constant inflammatory state continues until immune system, antibiotics and/or surgery ends the infection

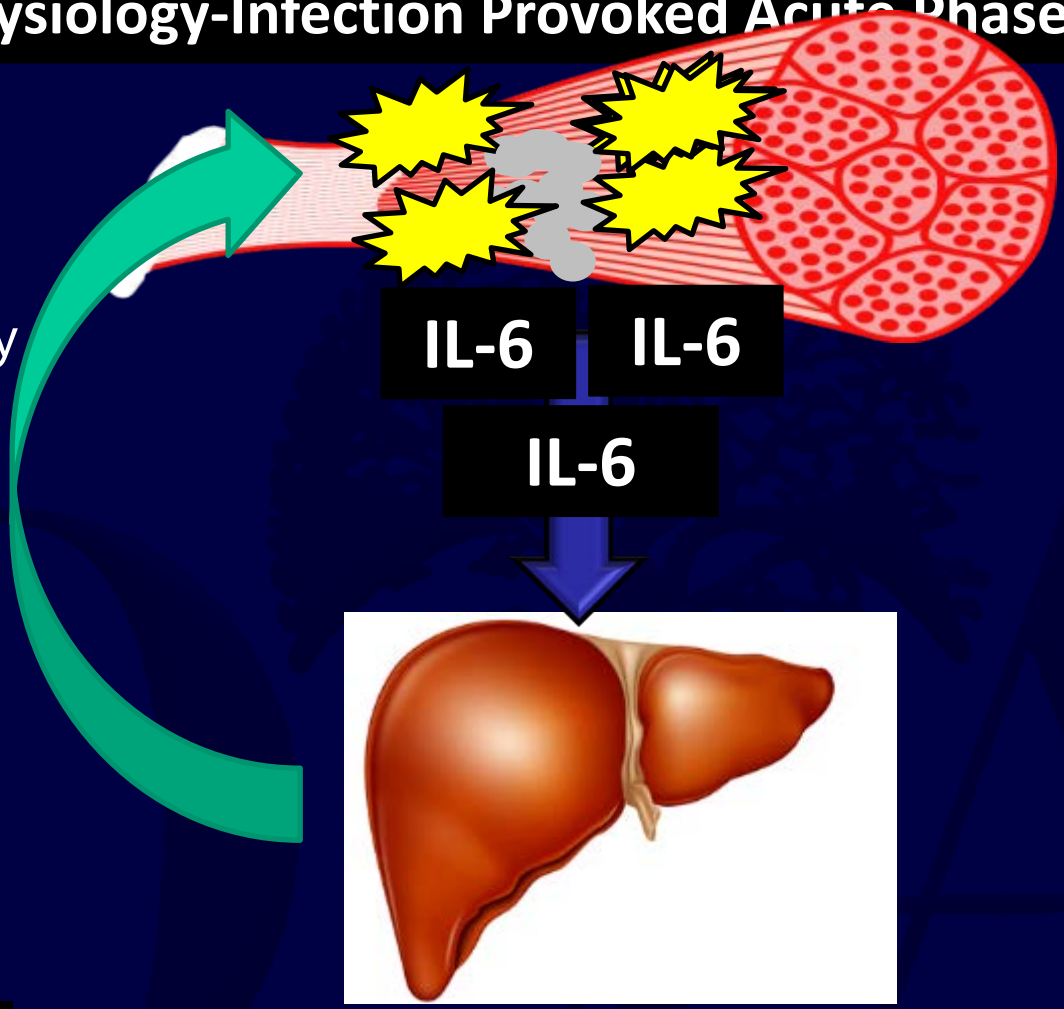


Hemostasis
Antimicrobial

PERSISTENT INJURY

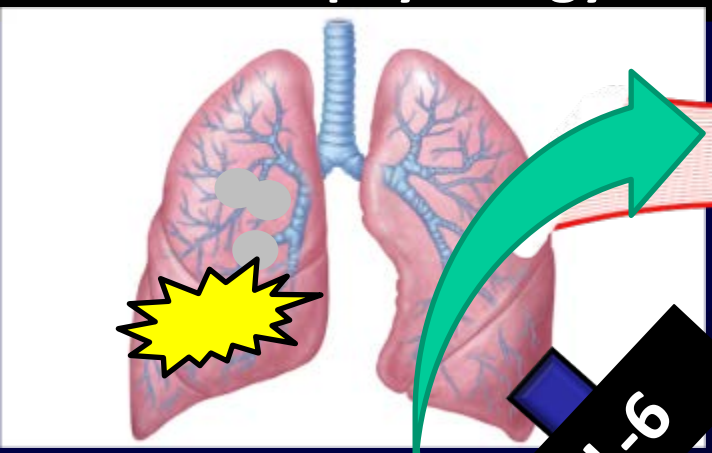
Pathophysiology-Infection Provoked Acute Phase Response

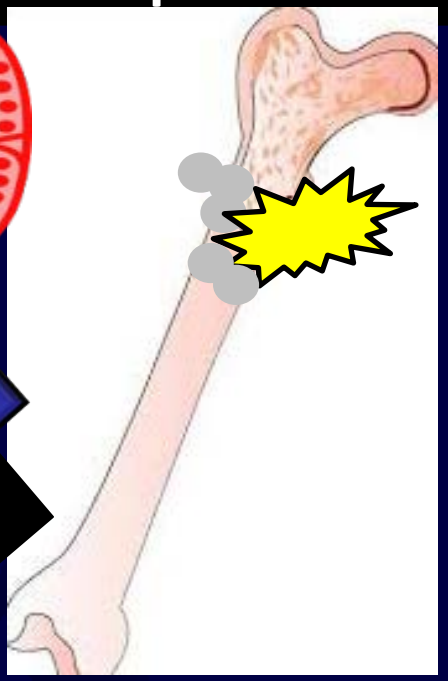
- Without prompt treatment tissue injury continues



Hemostasis
Antimicrobial

Pathophysiology-Infection Provoked Acute Phase Response



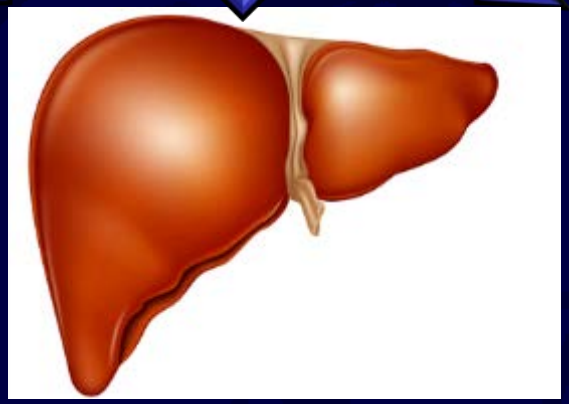


IL-6

IL-6

IL-6

IL-6



Hemostasis
Antimicrobial

- Amplified acute phase causes development of SIRS, DIC, MSOF, and eventual death.

SIRS

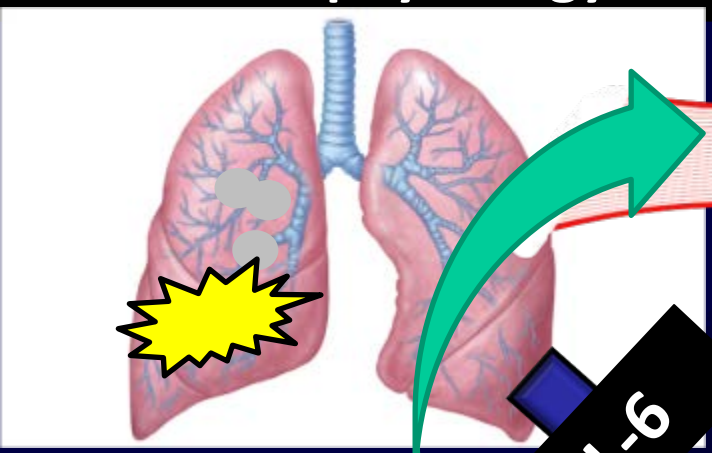
MSOF

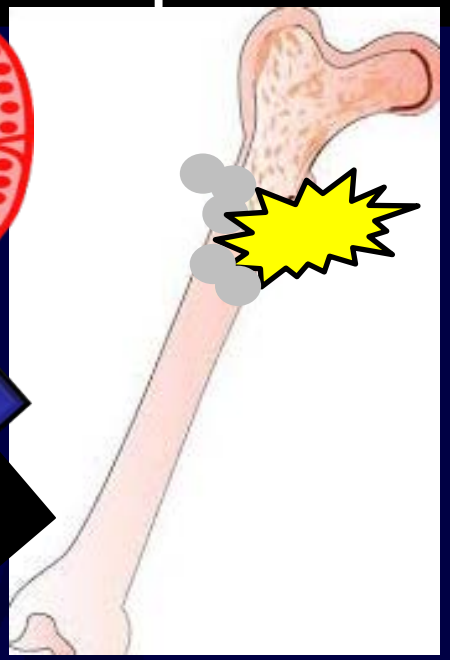
DIC

Death

Systemic Complications

Pathophysiology-Infection Provoked Acute Phase Response



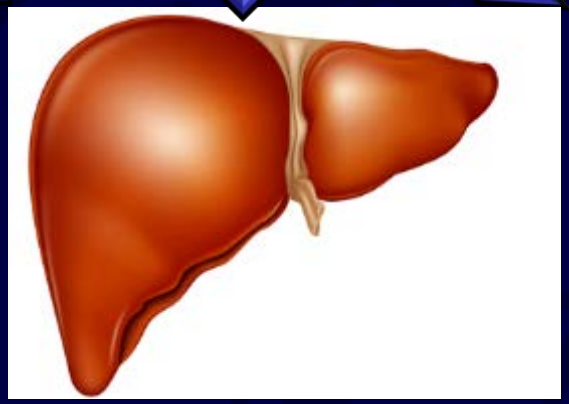


IL-6

IL-6

IL-6

IL-6



Hemostasis
Antimicrobial

CRP

SIRS

MSOF

DIC

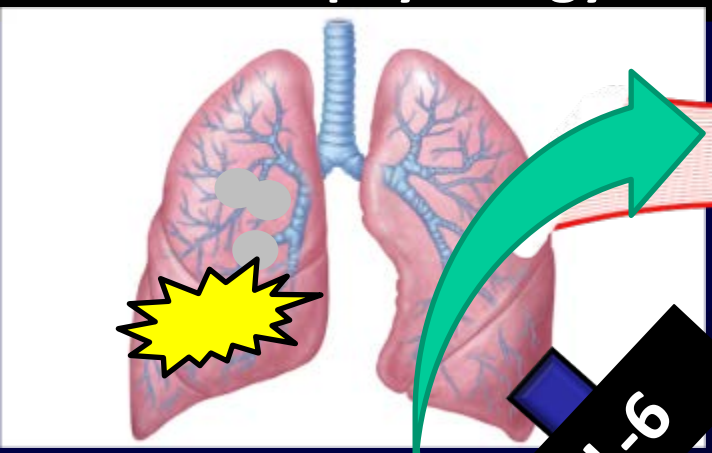
Death

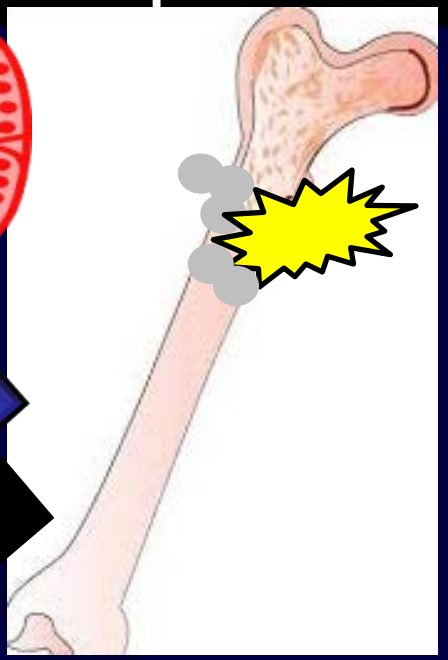
Systemic Complications

CRP

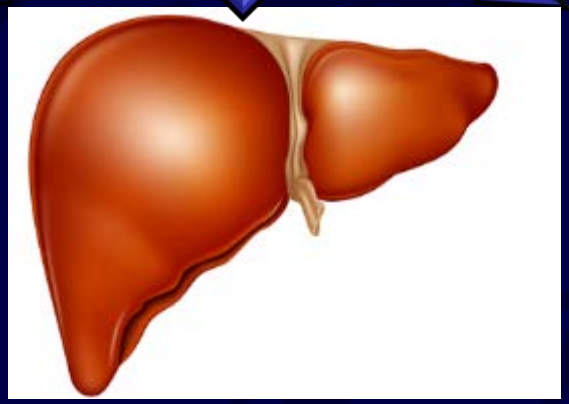
- rapid acute phase reactants which increases significantly in response to tissue from nec fasc

Pathophysiology-Infection Provoked Acute Phase Response





IL-6 IL-6 IL-6 IL-6 IL-6



Hemostasis
Antimicrobial

CRP

Ptn c

Ptn s

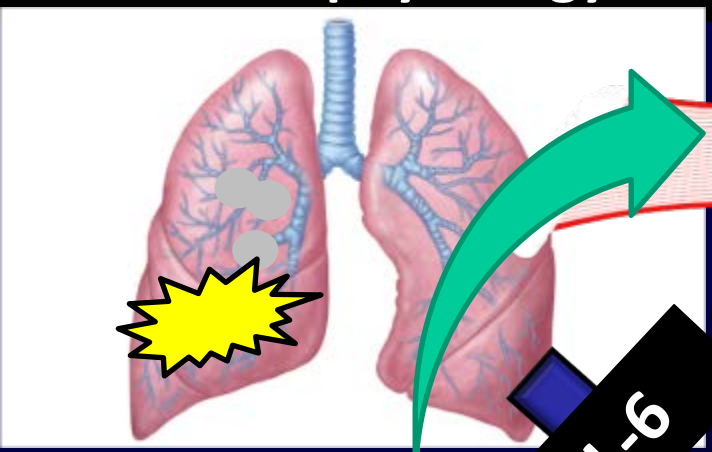
SIRS MSOF

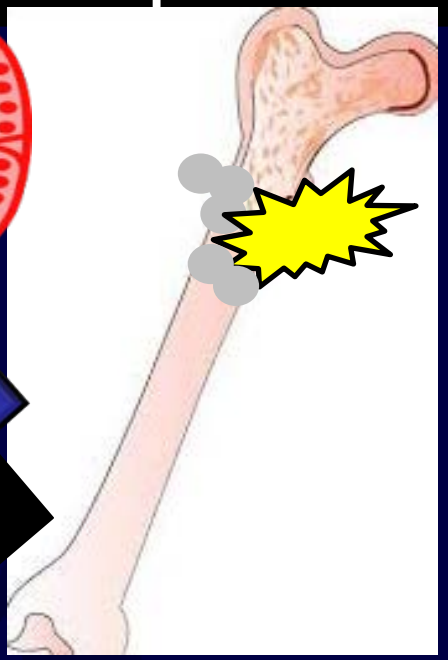
DIC Death

Systemic Complications

- During increasing hyperinflammatory state protein C and S become activated to buffer this effect.

Pathophysiology-Infection Provoked Acute Phase Response



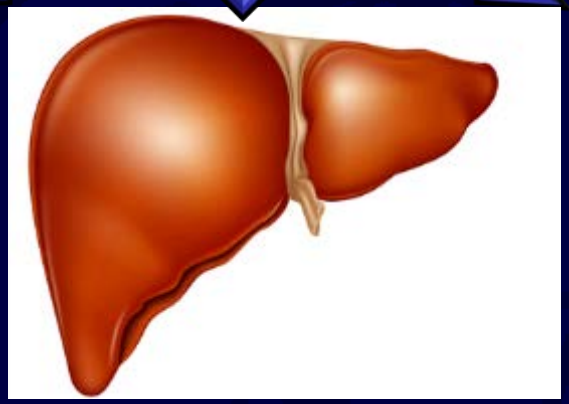


IL-6

IL-6

IL-6

IL-6



Hemostasis
Antimicrobial

CRP

Ptn c

Ptn s

SIRS

MSOF

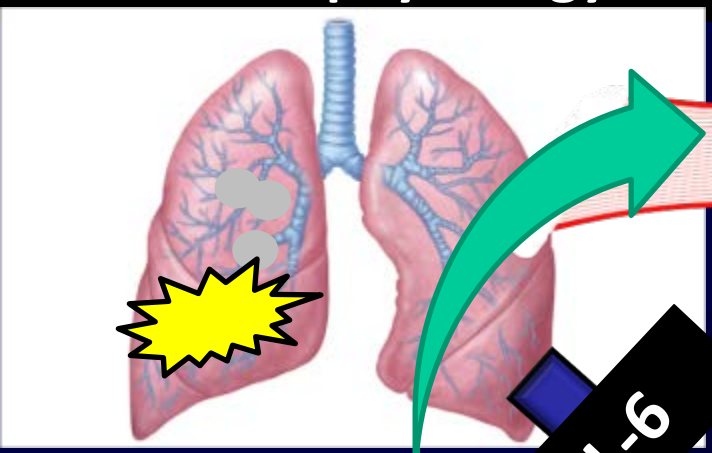
DIC

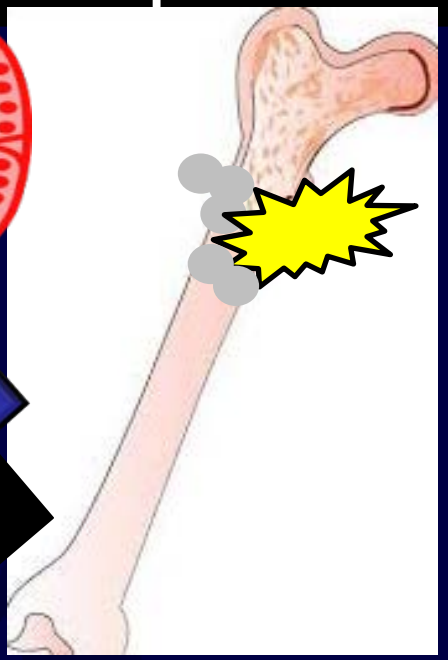
Death

Systemic Complications

- Longer the hyperinflammatory state persists, the more ptn c and s are consumed.

Pathophysiology-Infection Provoked Acute Phase Response





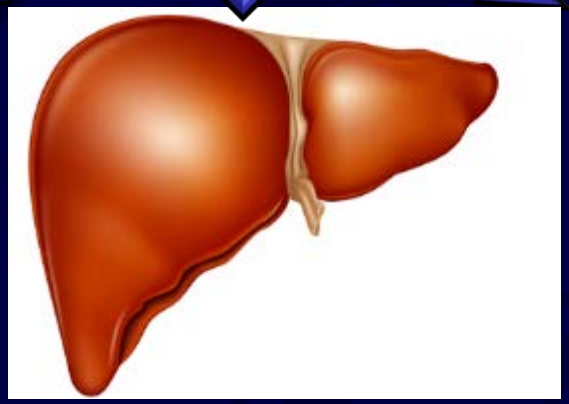
IL-6

IL-6

IL-6

IL-6

IL-6



Hem tasis

Anti ic obial

X

CRP

Ptn c

Ptn s

SIRS

MSOF

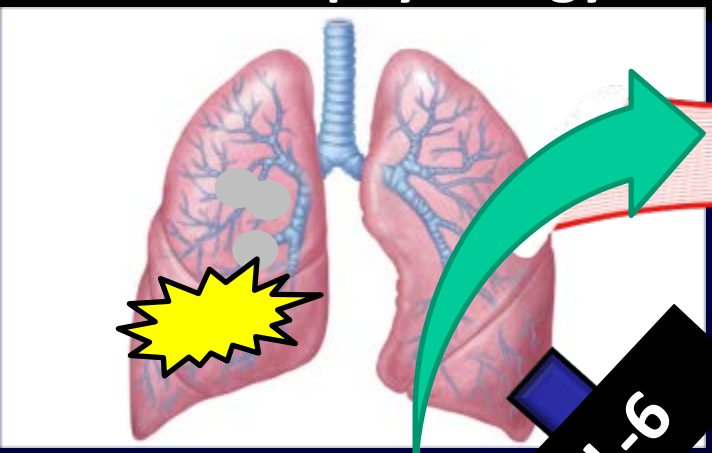
DIC

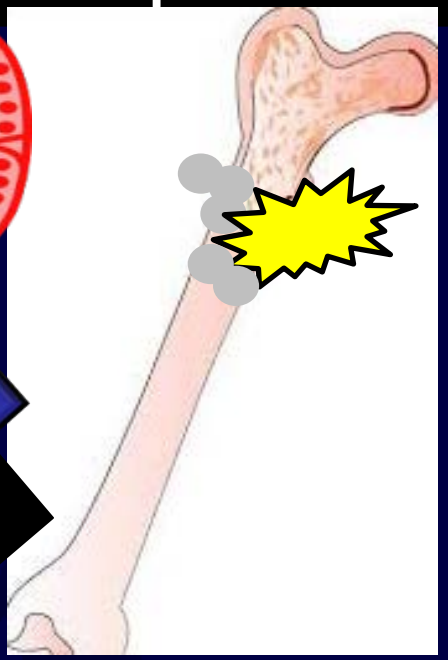
Death

Systemic Complications

- As proteins consumed, ability to buffer coagulation decreases

Pathophysiology-Infection Provoked Acute Phase Response





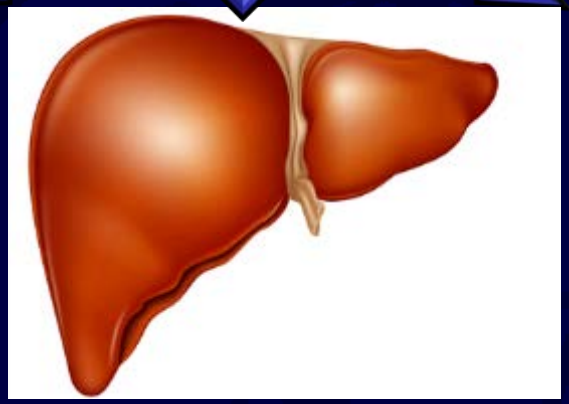
IL-6

IL-6

IL-6

IL-6

IL-6



Hem tasis

Anti ic obial

X

CRP

Ptn c

Ptn s

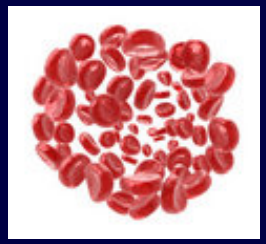
SIRS

MSOF

DIC

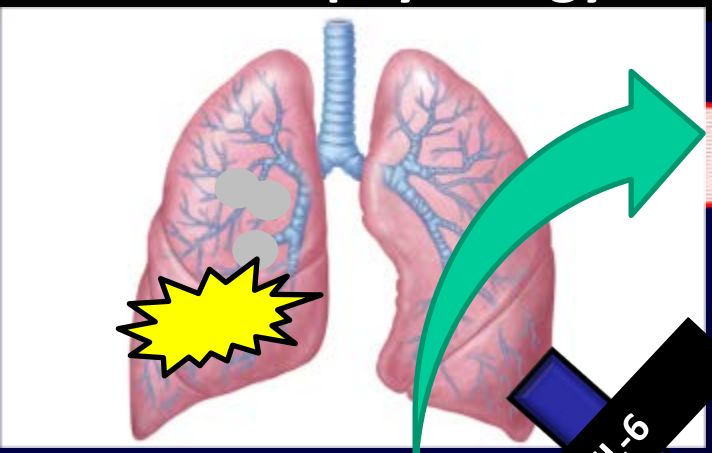
Death

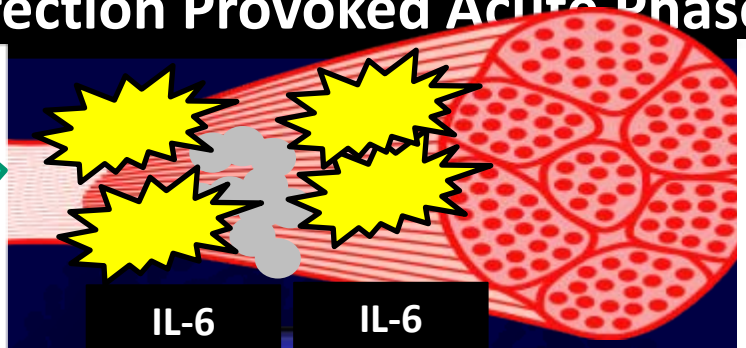
Systemic Complications

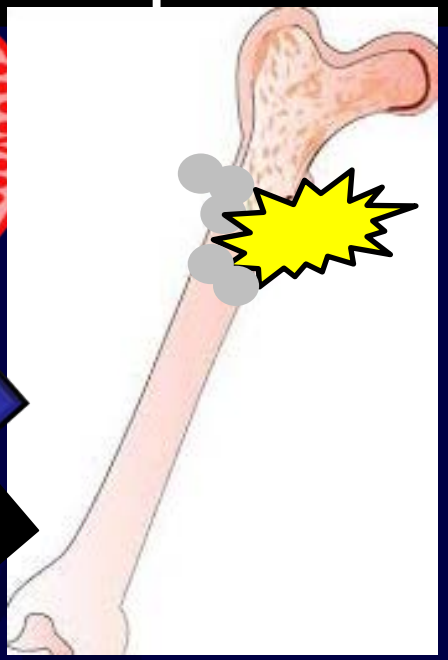


- As this proceeds unchecked patients develop thrombus once they begin to consume their clotting factors

Pathophysiology-Infection Provoked Acute Phase Response





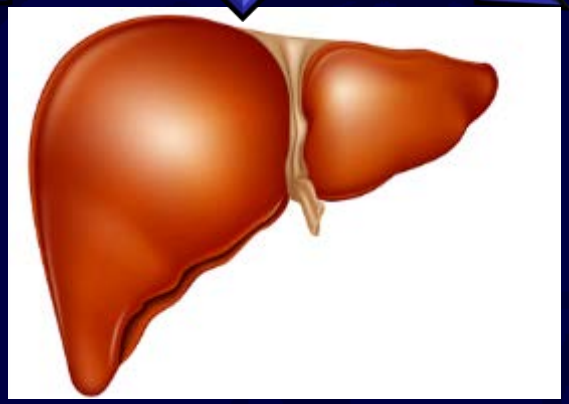


IL-6

IL-6

IL-6

IL-6



Her stasis

Ant bial

CRP

- Hemorrhage occurs due to DIC

Ptn c

Ptn s

SIRS

MSOF

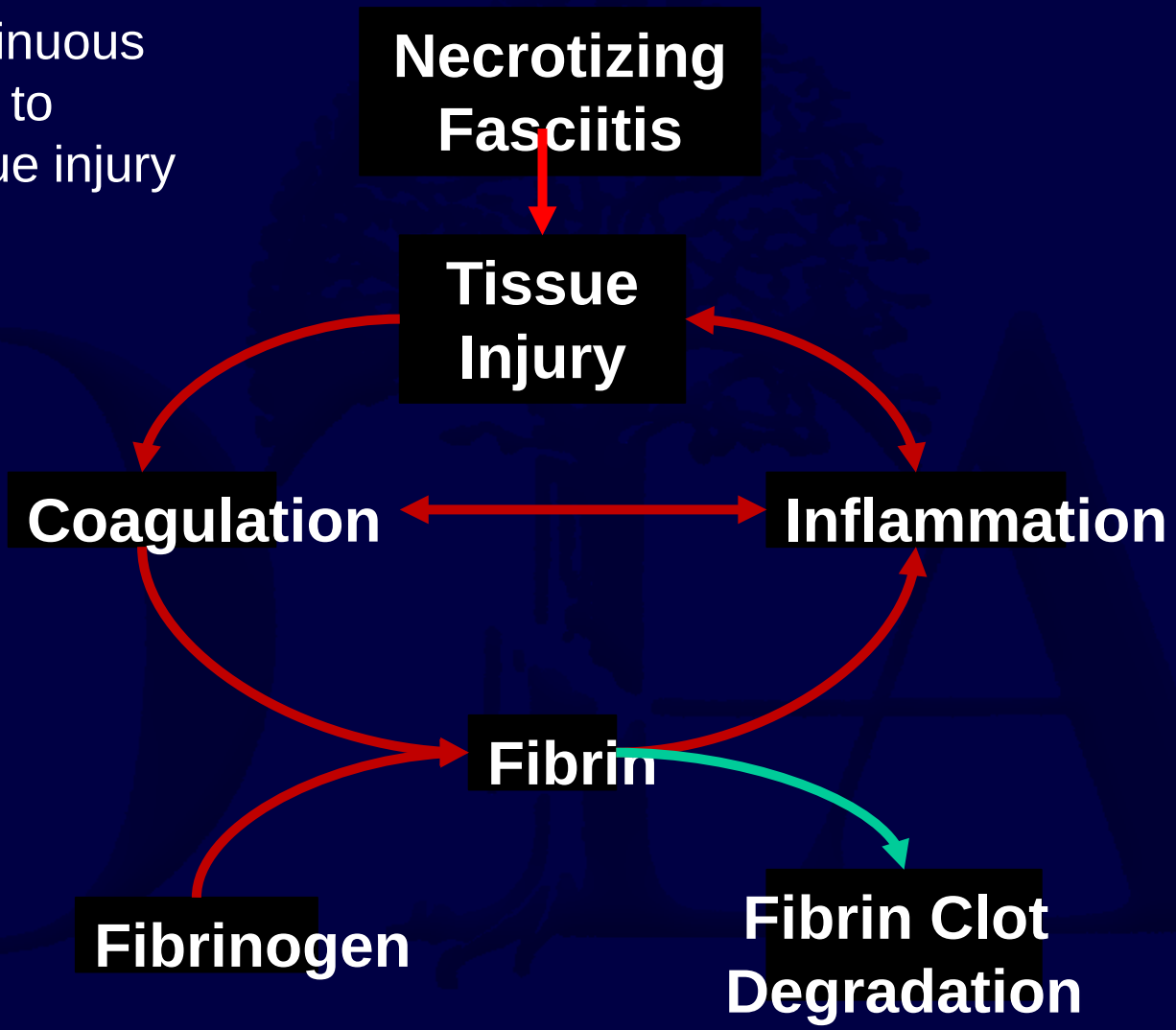
DIC

Death

Systemic Complications

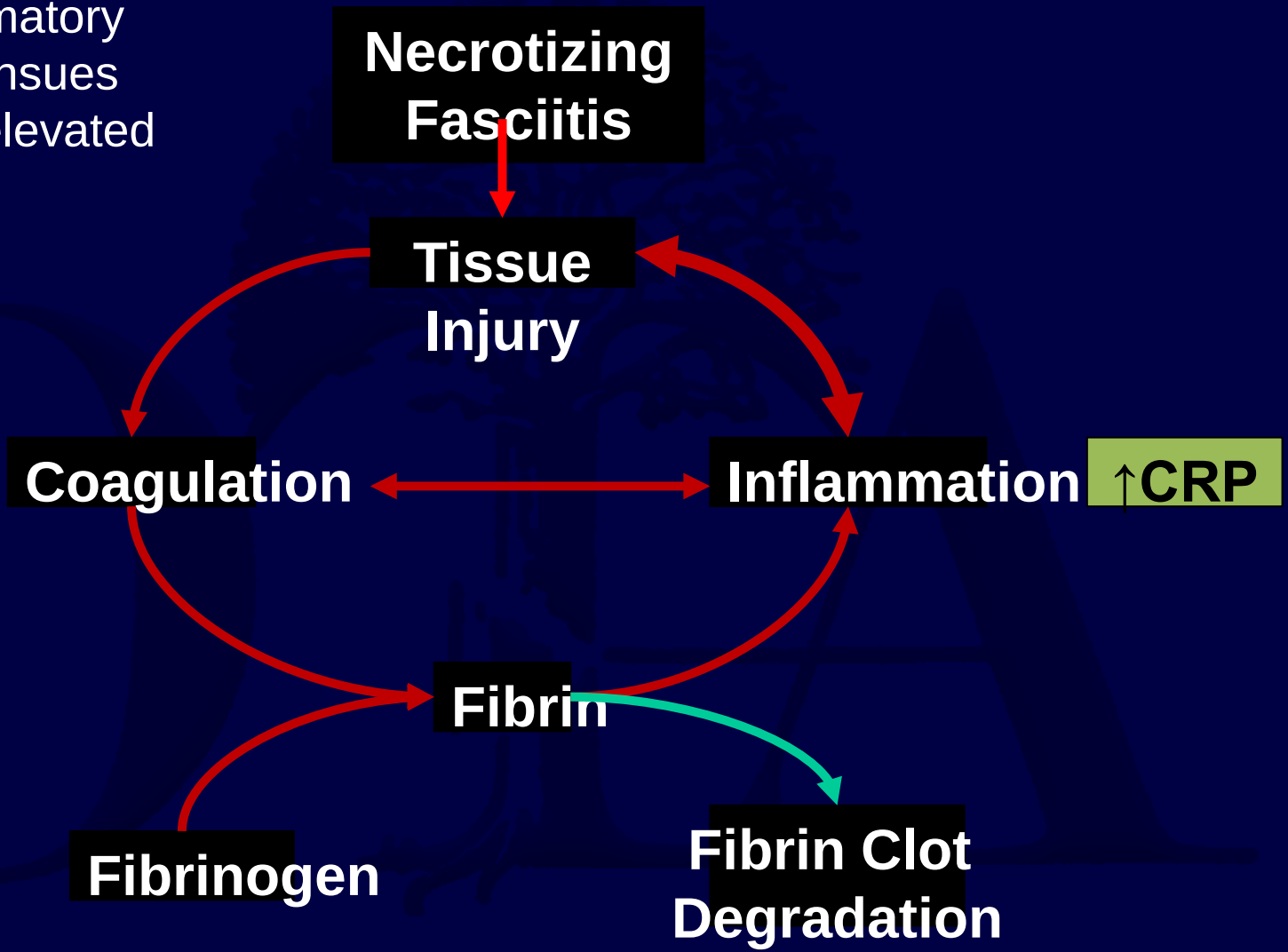
Coagulation Inflammation Cycle

Clinically, continuous cascade leads to persistent tissue injury



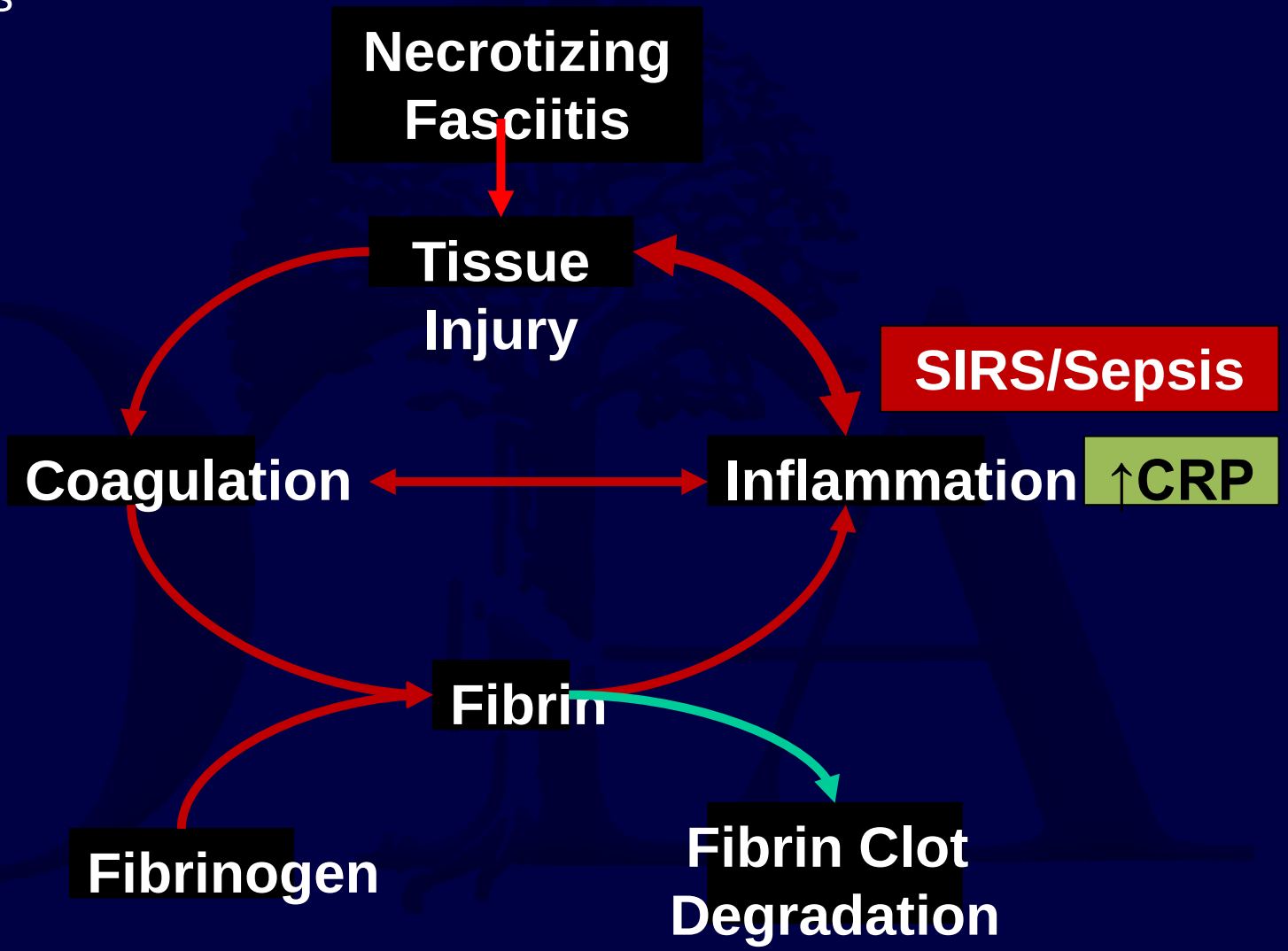
Coagulation Inflammation Cycle

A hyperinflammatory environment ensues leading to an elevated CRP



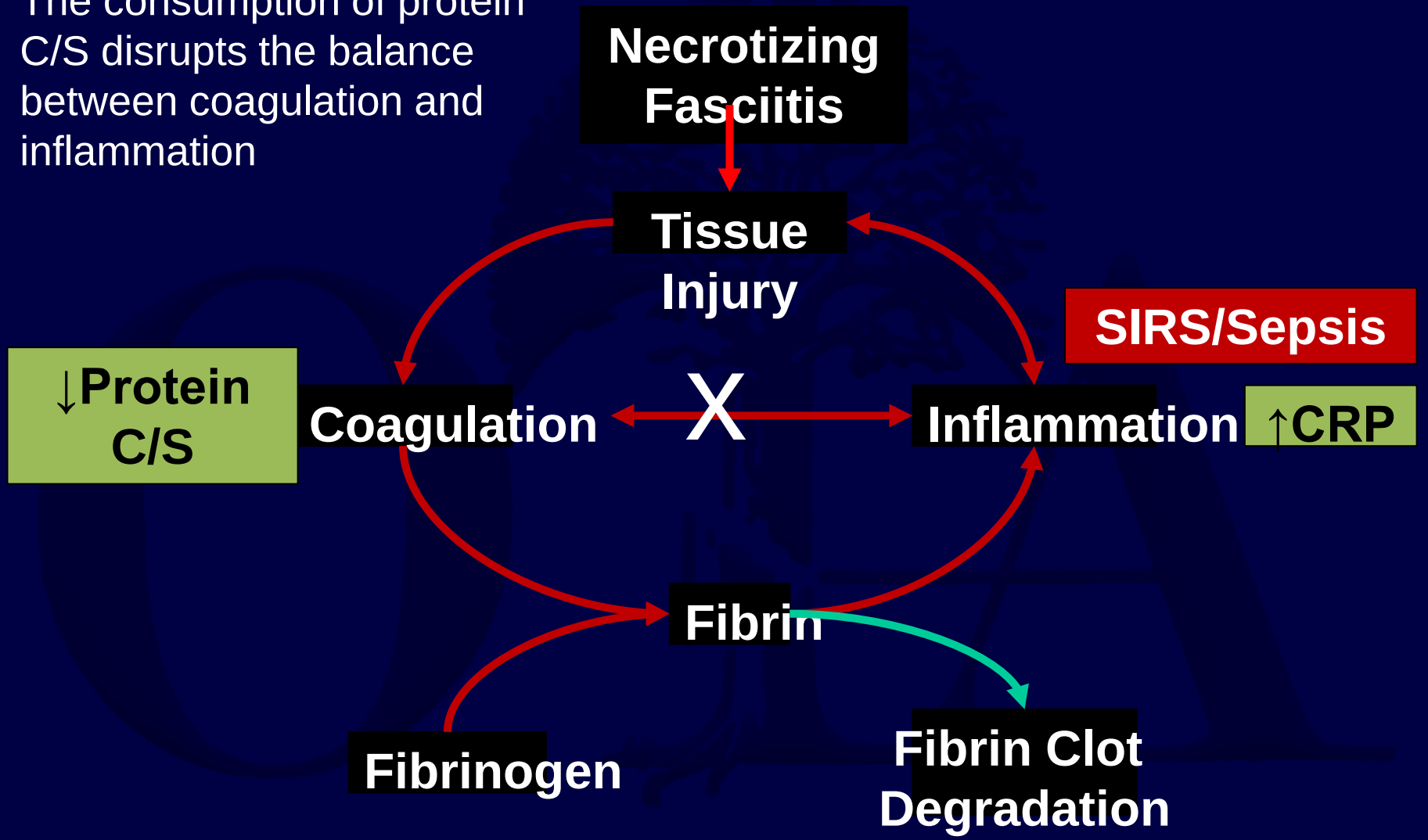
Coagulation Inflammation Cycle

Clinically this is recognized as SIRS/sepsis



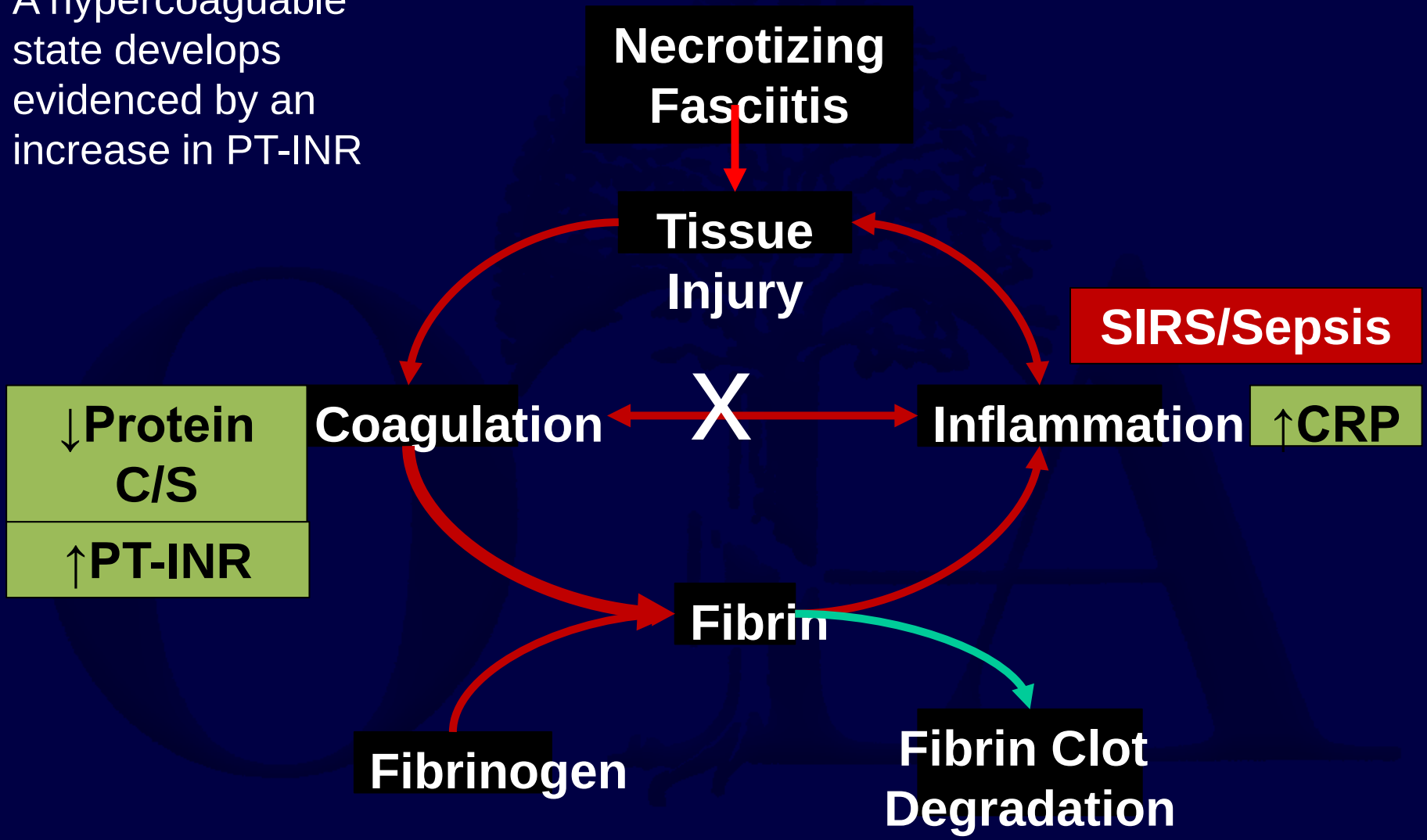
Coagulation Inflammation Cycle

The consumption of protein C/S disrupts the balance between coagulation and inflammation



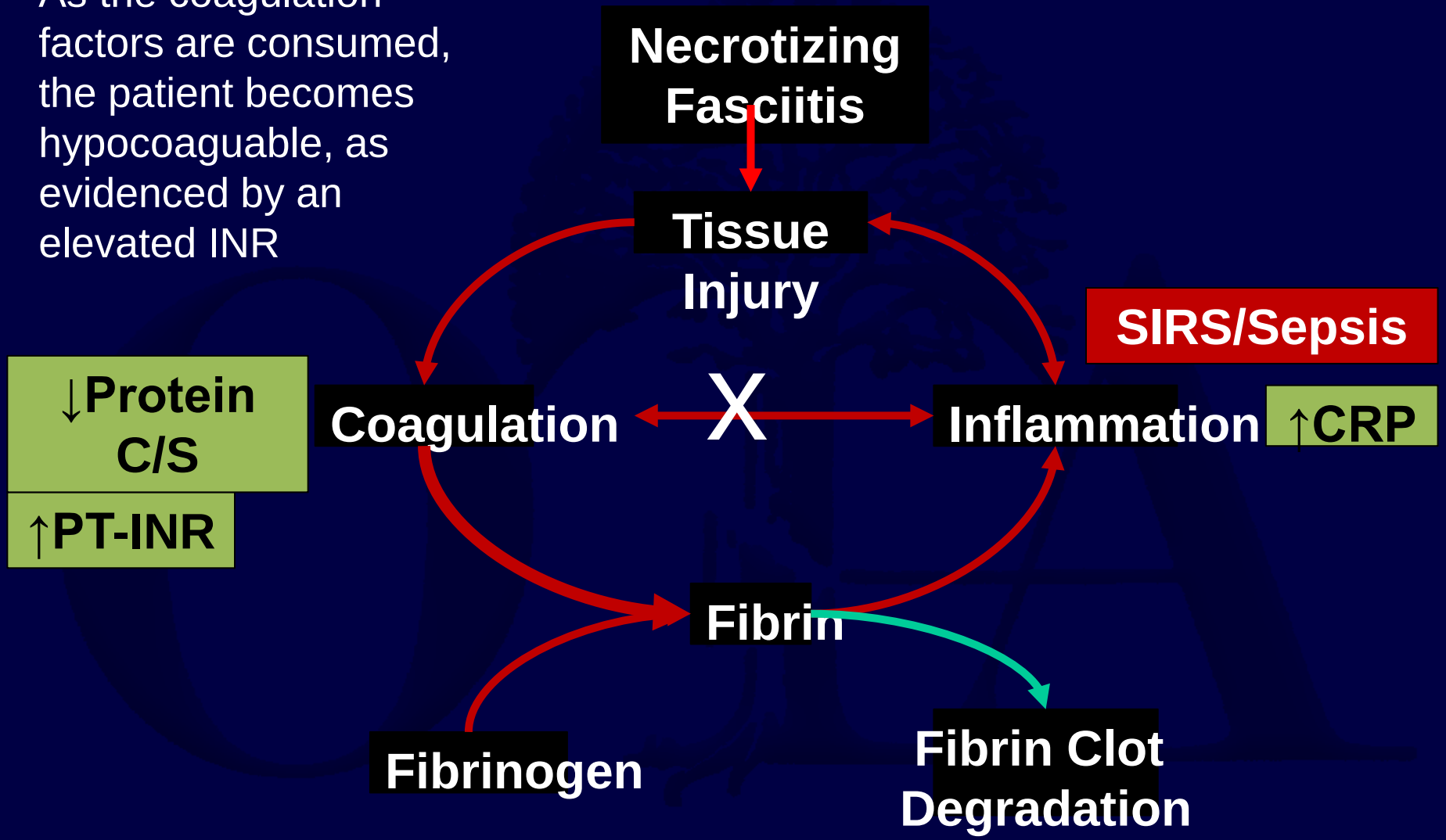
Coagulation Inflammation Cycle

A hypercoaguable state develops evidenced by an increase in PT-INR



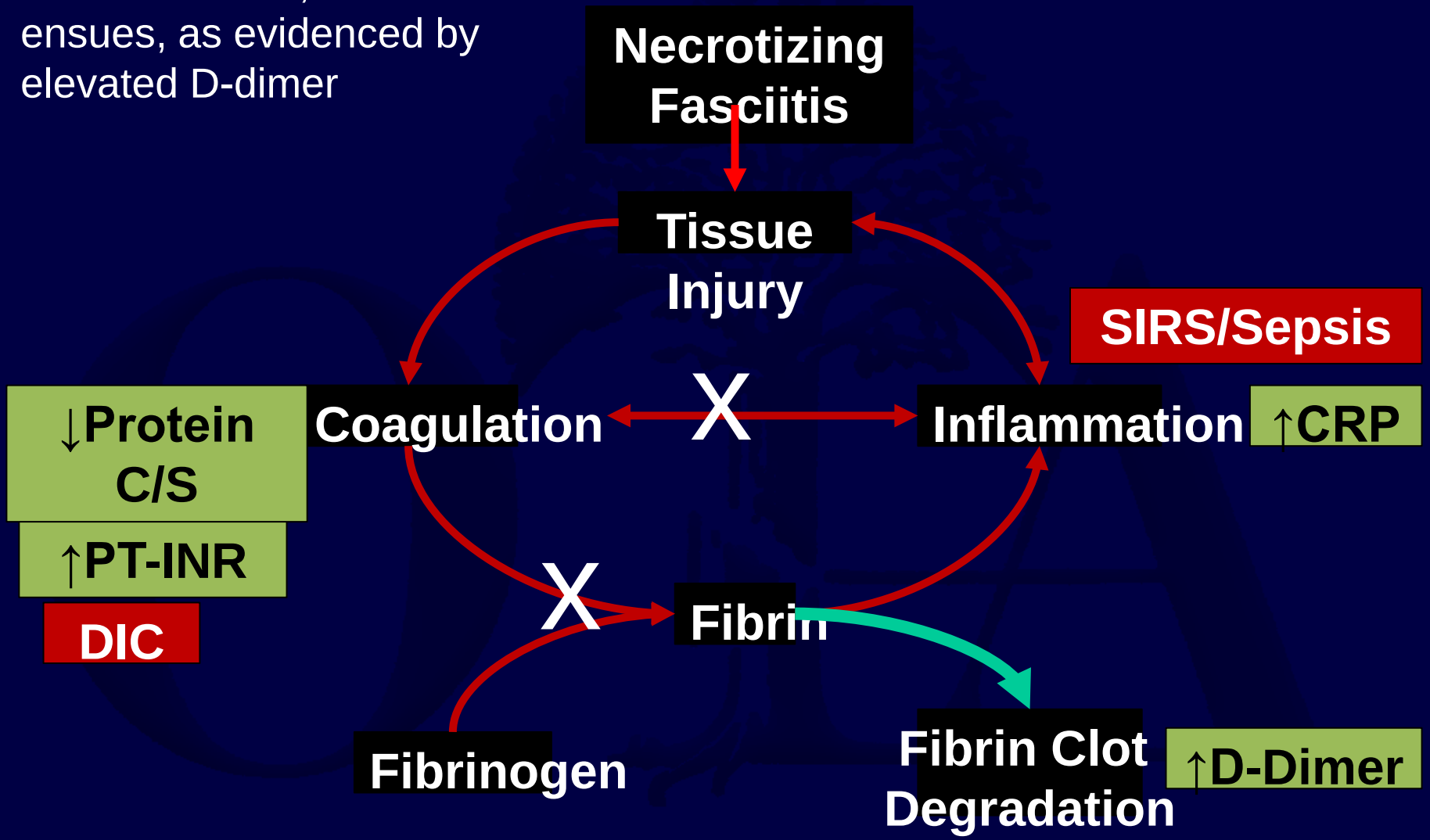
Coagulation Inflammation Cycle

As the coagulation factors are consumed, the patient becomes hypocoaguable, as evidenced by an elevated INR



Coagulation Inflammation Cycle

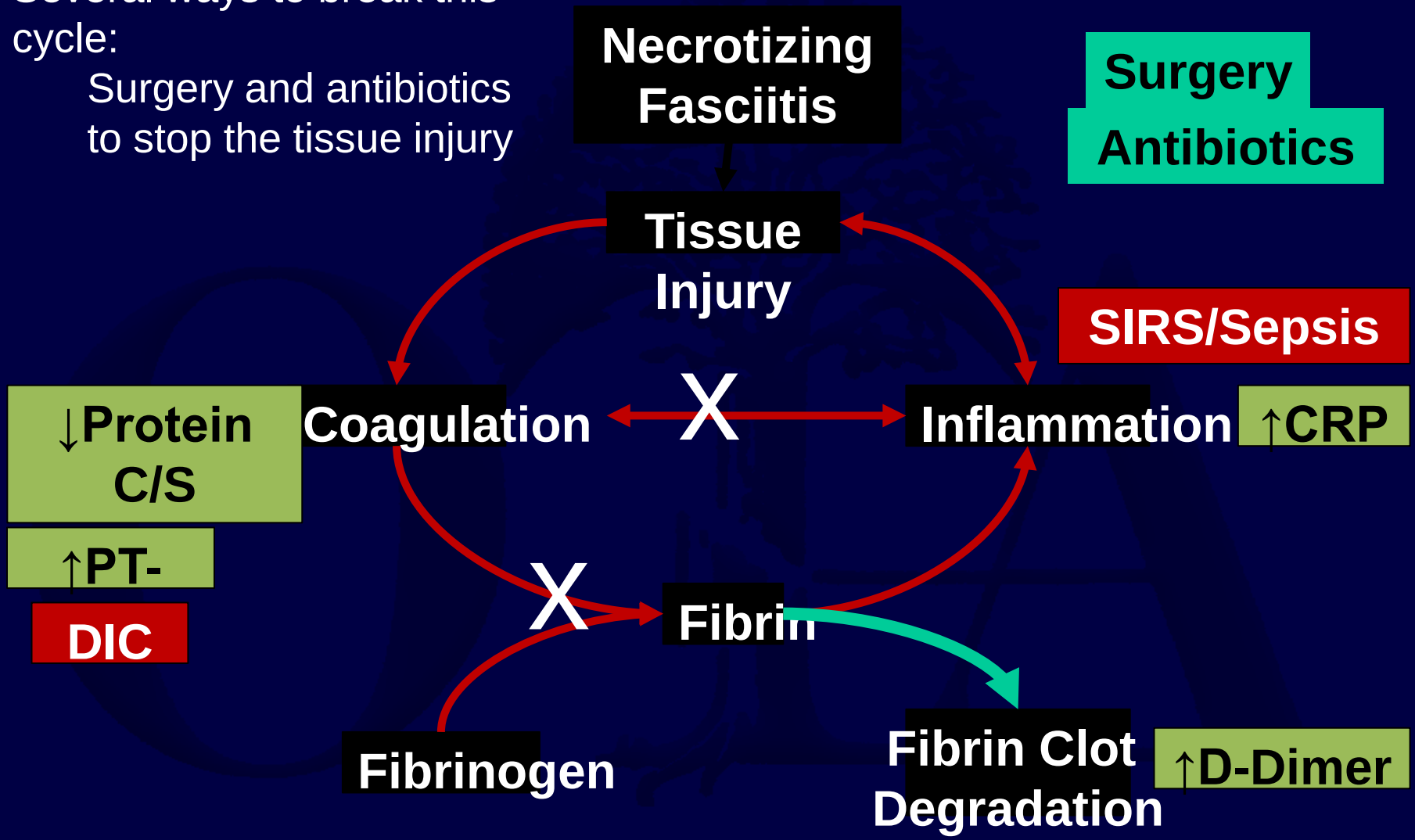
If left untreated, DIC ensues, as evidenced by elevated D-dimer



Coagulation Inflammation Cycle

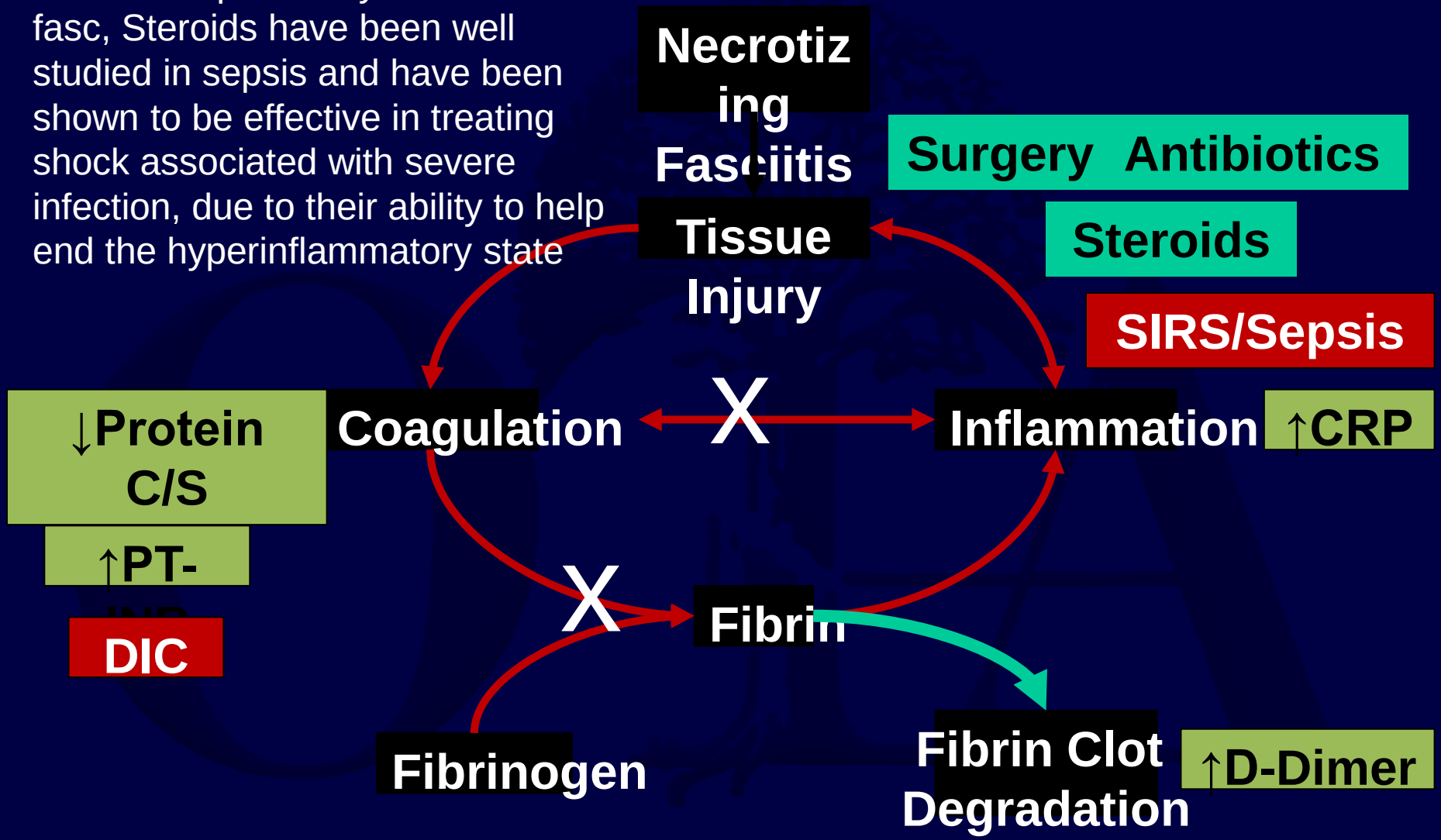
Several ways to break this cycle:

- Surgery and antibiotics to stop the tissue injury



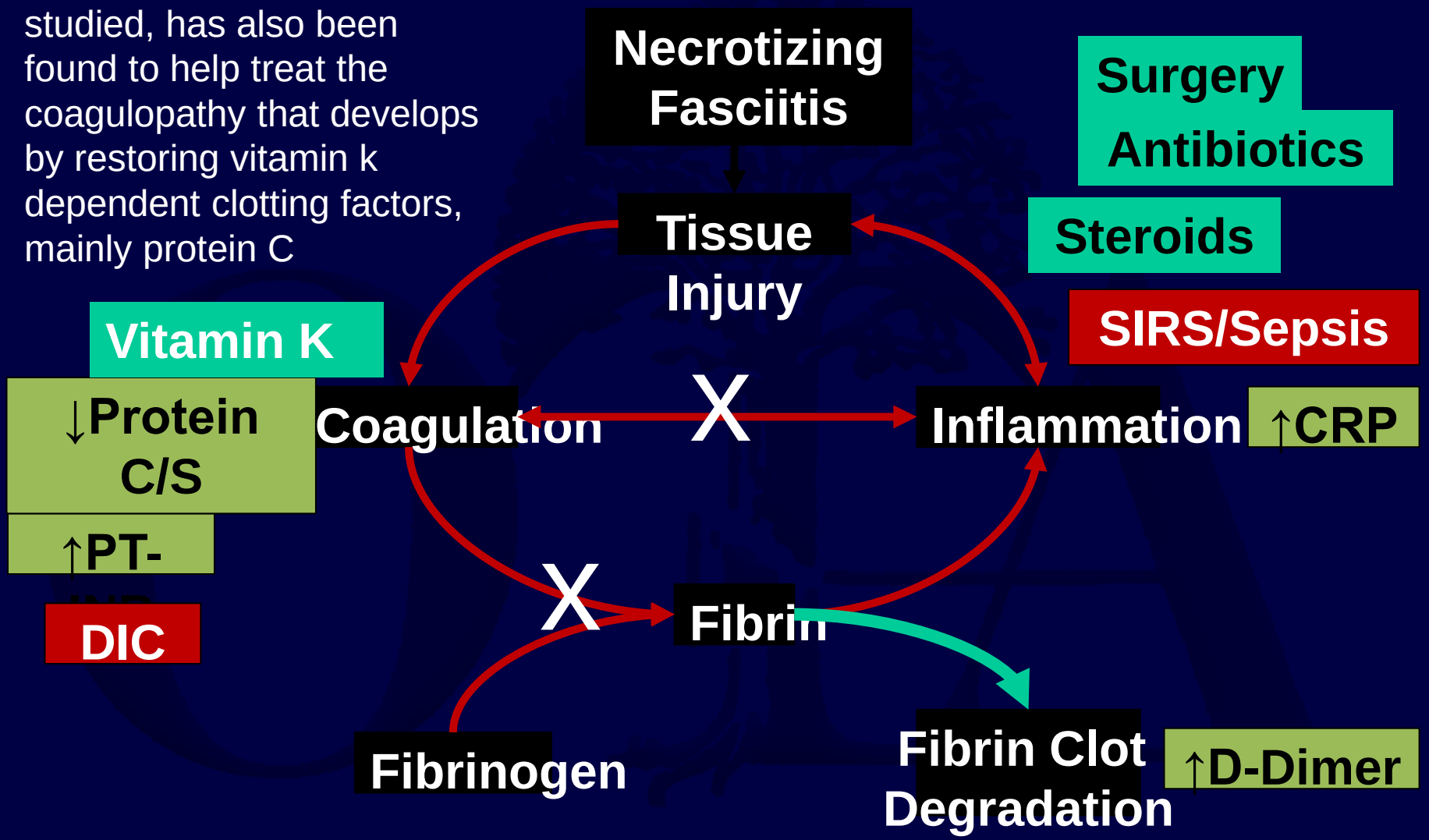
Coagulation Inflammation Cycle

While not specifically studied in nec fasc, Steroids have been well studied in sepsis and have been shown to be effective in treating shock associated with severe infection, due to their ability to help end the hyperinflammatory state



Coagulation Inflammation Cycle

Vitamin K, while not as well studied, has also been found to help treat the coagulopathy that develops by restoring vitamin k dependent clotting factors, mainly protein C



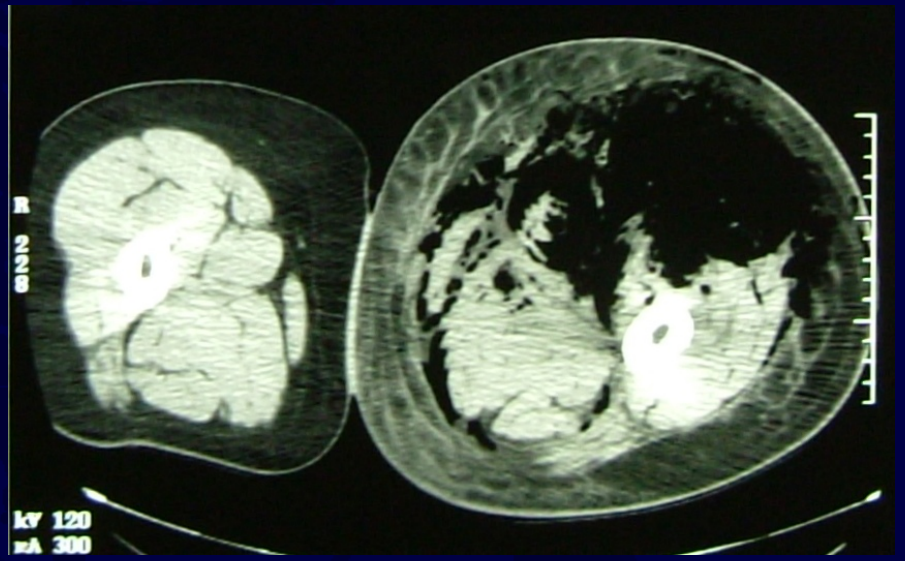
Necrotizing Soft Tissue Infections- Imaging

- Radiographs not normally indicated in the work up in necrotizing fasciitis.
  - In clostridial myonecrosis
    - gas in the muscle bellies

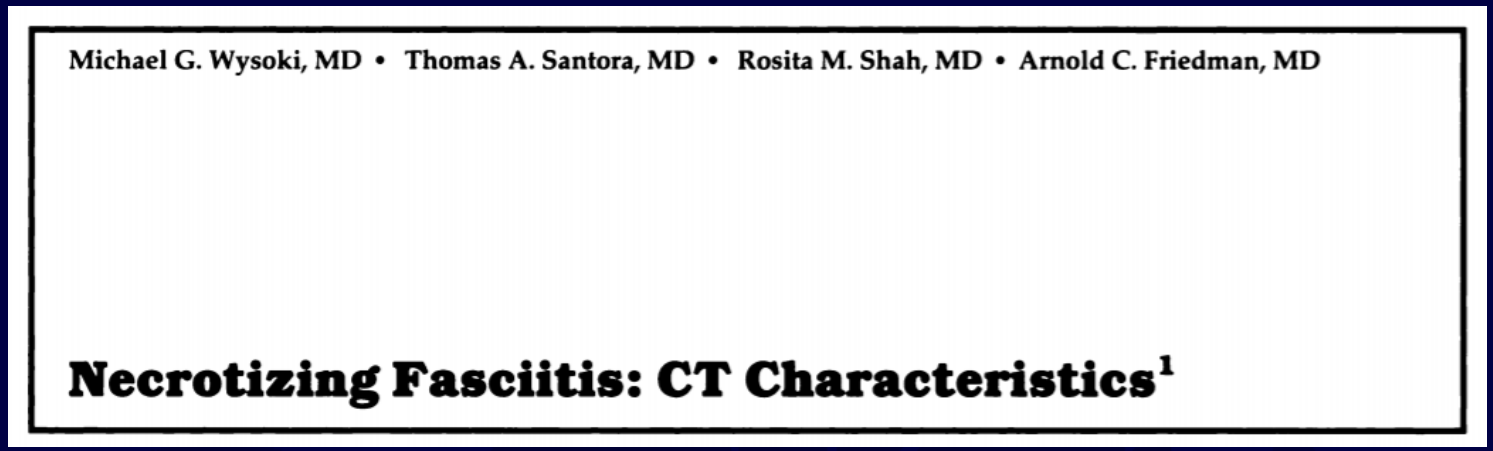
Chapnick, E. K., & Abter, E. I. (1996). Necrotizing soft-tissue infections. Infectious disease clinics of North America, 10(4), 835-855.

Necrotizing Soft Tissue Infections- Imaging

- CT scan
  - may be more sensitive than plan radiographs for
    - air in the soft tissues
    - findings
      - **gas within the superficial fascia distributed linearly**
      - predominance of fascial involvement.



Beauchamp, N. J., Scott, W. W., Gottlieb, L. M., & Fishman, E. K. (1995). CT evaluation of soft tissue and muscle infection and inflammation: a systematic compartmental approach. *Skeletal radiology*, *24*(5), 317-324



- CT scans of 20 patients with biopsy proven necrotizing fasciitis
  - 80% had asymmetric subcutaneous fat or fascial stranding
  - 55% had superficial or deep tracking of air
  - 35% had a loculated abscess

Diagnosis of Necrotizing Soft Tissue Infections by Computed Tomography

Nikos Zacharias, MD; George C. Velmahos, MD, PhD; Ahmed Salama, MD; Hasan B. Alam, MD; Marc de Moya, MD; David R. King, MD; Robert A. Novelline, MD

- Looked at CT scans before surgery in patients with suspected necrotizing fasciitis.
  - 25 diagnosed with necrotizing fasciitis based on pathology
  - All 25 of these patients had enhanced soft tissues consistent with inflammation and necrosis.
  - 9 had subcutaneous gas and 7 had fluid collections.
  - CT
    - 100% sensitive and 81% specific
    - PPV 76%
    - NPV 100% in identifying soft tissue infections

Radiology. 1994 Aug;192(2):493-6.

MR imaging in acute infectious cellulitis.

Rahmouni A[1], Chosidow O, Mathieu D, Gueorguieva E, Jazaerli N, Radier C, Faivre JM, Roujeau JC, Vasile N.

- MRI differentiates cellulitis from necrotizing soft tissue infection
  - distinguished surgically proven necrotizing fasciitis and cellulitis in all 33 patients
  - On MRI
    - both cellulitis and NF show decreased T1 signal and increased T2 signal in subcutaneous tissue
    - NF shows increased T2 signal in the fascia itself.

Radiology. 1994 Aug;192(2):493-6.

MR imaging in acute infectious cellulitis.

Rahmouni A[1], Chosidow O, Mathieu D, Gueorguieva E, Jazaerli N, Radier C, Faivre JM, Roujeau JC, Vasile N.

- Main drawbacks of MRI is the length of time needed for the study
- **Should not be used if it slows down time to surgical treatment.**

Necrotizing Soft Tissue Infections- Bacteriology

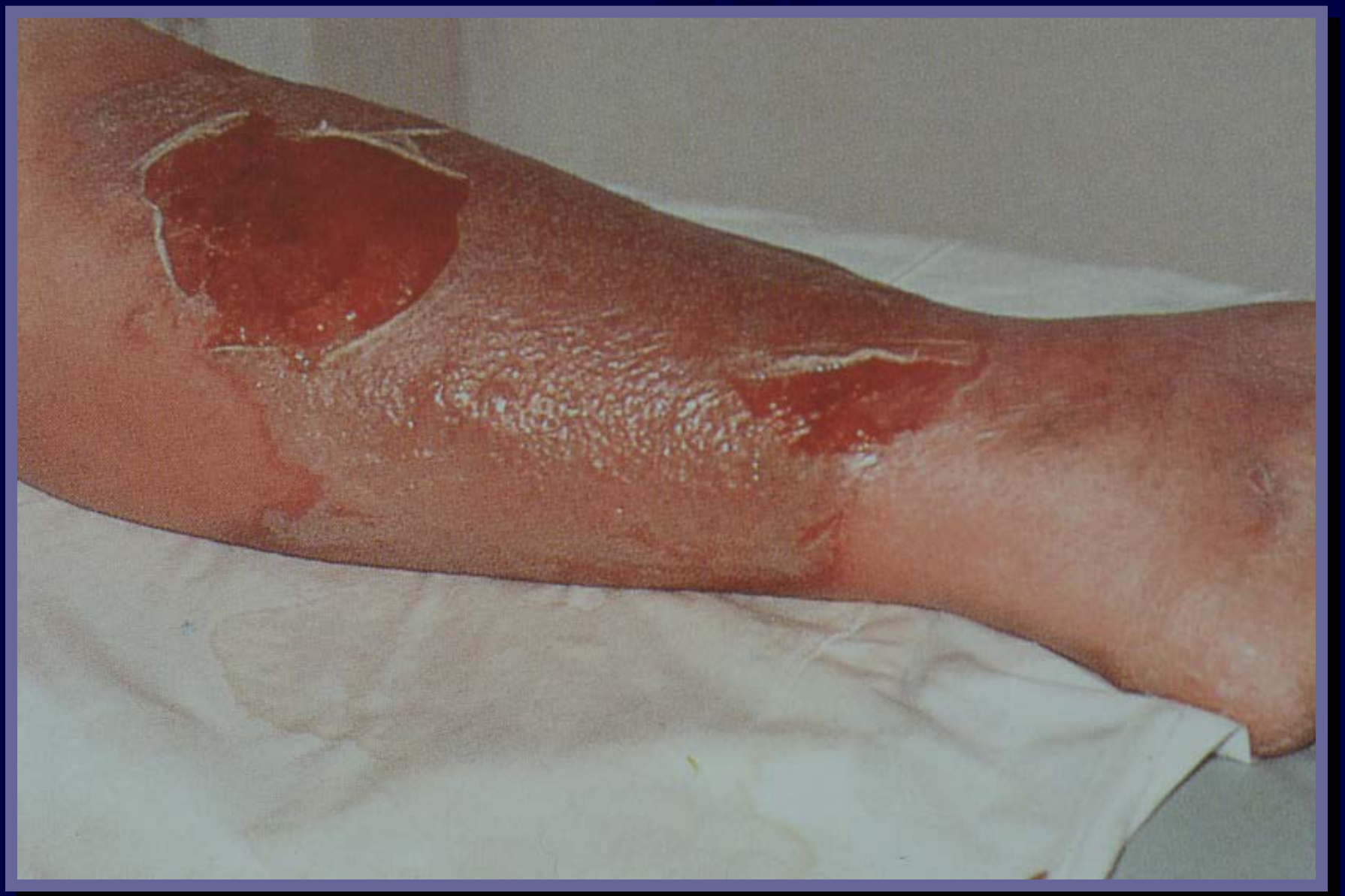
Streptococcal

Group A strep *(Strep. pyogenes)*

- **incubation period 1-3 days**
- **fulminant course due to streptolysin / hemolysins / hyaluronidase**
- **“flesh-eating” bacteria – streptococcal pyrogenic exotoxin (*speA, speB, speC*)**

Feingold DS *Arch Dermatol* 1996; 132:67-70

Necrotizing Streptococcal Cellulitis



Necrotizing Soft Tissue Infections- Bacteriology

Streptococcal

Group B strep *(Strep. Agalacitiae)*

a. **More common in pts with altered resistance**
   - **diabetes, cancer, neonatal, etc**

b. **Short incubation period**

Necrotizing Soft Tissue Infections- Bacteriology

Clostridial species

a. **incubation period 1-2 days**

b. **very fulminant course due to toxins**
   - ***C. perfringens* – 20 known exotoxins**

c. **local gas, brownish discharge, high fever, high mortality**

d. ***C. perfringens, C. septicum***

Stevens DL *Clin Inf Dis* 1997; 25:S160-64

Necrotizing Soft Tissue Infections- Bacteriology

Gram negative bacillary

E. coli, Kleb, Proteus, others

- **incubation period 7-14 days**
- **fever (FUO), local symptoms, sepsis**
- **may be mixed**

Necrotizing Soft Tissue Infections- Bacteriology

<u>Pathogenic gram negative bacteria</u>

- **Vibrio vulnificus - shellfish**
- **Aeromonas hydrophila – fresh water**
- **Pasteurella multocida – dog/cat bites**
- **Eikenella corrodens – human bites**
  - ***Treat with tetracycline class + beta-lactam***

Necrotizing Soft Tissue Infections- Bacteriology

Mixed aerobic / anaerobic

a. **incubation period 10-14 days**

b. **local pain, edema, purplish discoloration**

c. **Meleny's progressive cutaneous gangrene**

d. **Fournier's gangrene**

e. **Necrotizing fasciitis**

Necrotizing Soft Tissue Infections-Bacteriology

Others – "high-risk" for unusual or resistant pathogens

a. **Special exposures**
   - **Bites and environmental**

b. **Nosocomial**
   - **LOS > 4d, AB use, high APACHE II**

c. **Chronic**
   - **Previous AB use, altered tissue resistance**

The “Eagle effect”

- 1952 – Harry Eagle demonstrated failure of cell-wall agents in *S. pyogenes* myositis model with high inoculum
- Clindamycin >> erythromycin > penicillin
- Believed related to stationary phase of growth and PBP↓
- Also demonstrated in *C. perfringens* and *S. aureus* models
- Retrospective human studies suggest outcome from *S. pyogenes* infection better with clindamycin

1. Eagle H *Am J Med* 1952; 13:389-99
2. Stevens DL *J Infect Dis* 1988; 158:23-8
3. Stevens DL *J Infect Dis* 1987; 155:220-8
4. Zimbelman J *Ped Infect Dis J* 1999; 18:1096-1100

Protein synthesis-inhibiting antibiotics

- **Shown to decrease production of toxins, superantigens, and enzymes from:**

Gram positive:

- ***S. aureus***
- ***S. pyogenes*** — **Clindamycin (linezolid)**
- ***C. perfringens***

Gram negative:

- ***Vibrio sp***
- ***Aeromonas sp*** — **tetracycline class**
- ***Pasteurella sp***

- **No prospective human studies**

Zimbelman J *Ped Infect Dis J* 1999; 18:1096-1100

Antibiotic Rx for necrotizing SSTI due to virulent pathogens:

Group A strep *(Strep. pyogenes)*

- **incubation period 1-3 days**
- **fulminant course due to streptolysin / hemolysins / hyaluronidase**
- **“flesh-eating” bacteria – streptococcal pyrogenic exotoxin (*speA, speB, speC*)**
- **High dose penicillin + clindamycin (2.4 g/d)**

Feingold DS *Arch Dermatol* 1996; 132:67-70

Antibiotic Rx for necrotizing SSTI due to virulent pathogens:

Clostridial species ***(C. perfringens, C. septicum)***

a. **incubation period 1-2 days**

b. **very fulminant course due to toxins**
   - ***C. perfringens*** **– 20 known exotoxins**

c. **local gas, brownish discharge, high fever, high mortality**

d. **penicillin (24 million U/day) or carbapenems + clindamycin (2.4 g/d)**

Antibiotic Rx for necrotizing SSTI due to virulent pathogens:

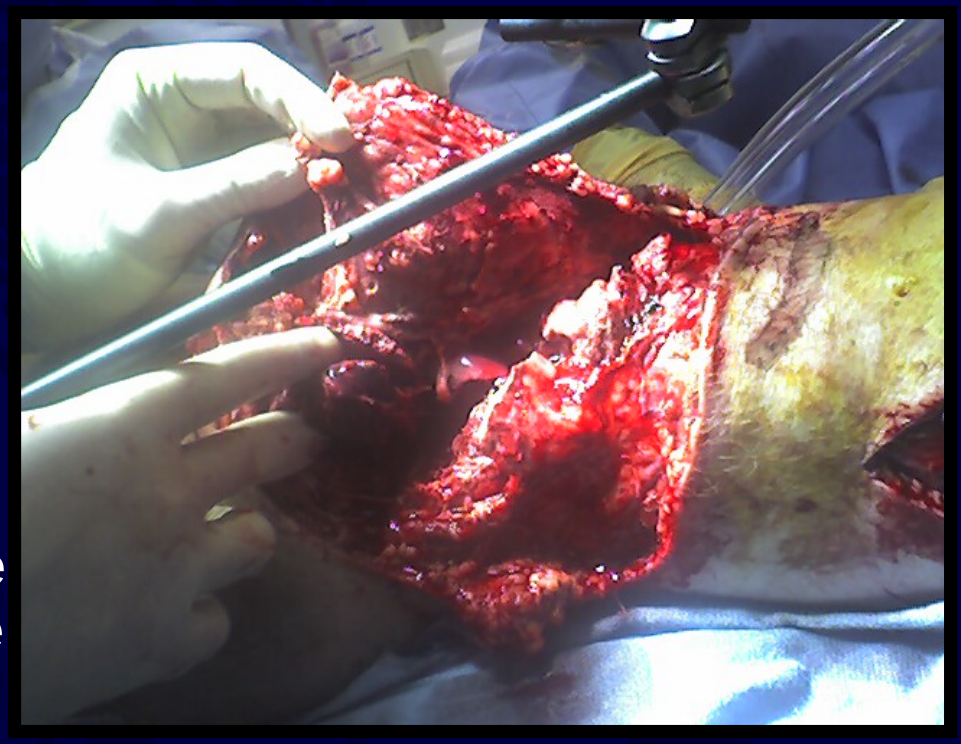
Highly virulent gram negative bacteria:

- *Vibrio vulnificus*
- *Aeramonas* sp.

- **Both associated with contaminated water exposure**
- **Both highly virulent with fulminate course**
- **Antibiotic Rx –**
  - **3rd generation cephalosporins, imipenem/meropenem, and ciprofloxacin/oflaxacin – in combination with**
  - **Tetracycline/minocycline**

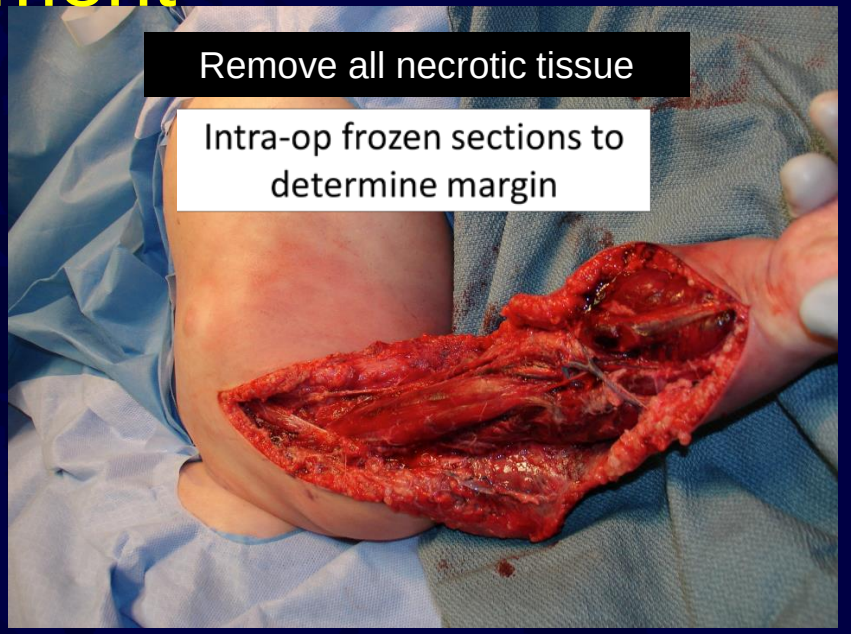
Necrotizing Soft Tissue Infections- Management

- Surgical Management
  - After patient anesthetized perform follow up exam
    - important due to rapid progression
    - some areas such as the posterior aspects of the thigh and trunk are difficult to examine while the patient is awake due to pain.



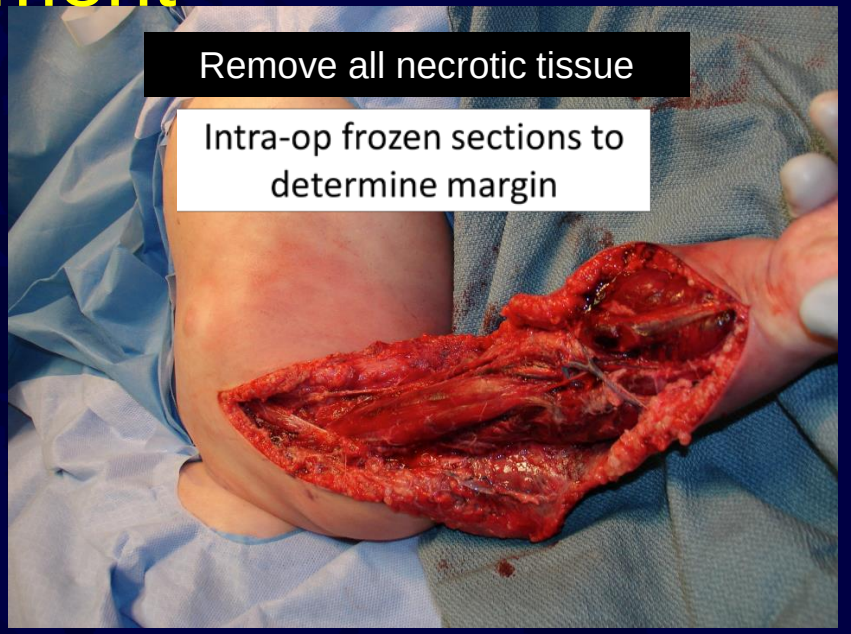
Necrotizing Soft Tissue Infections- Management

- Surgical Management
  - The zone approach is often used during surgical debridement.
    - Zone I:
      - Area clearly defined as necrosis presenting with induration and erythema.



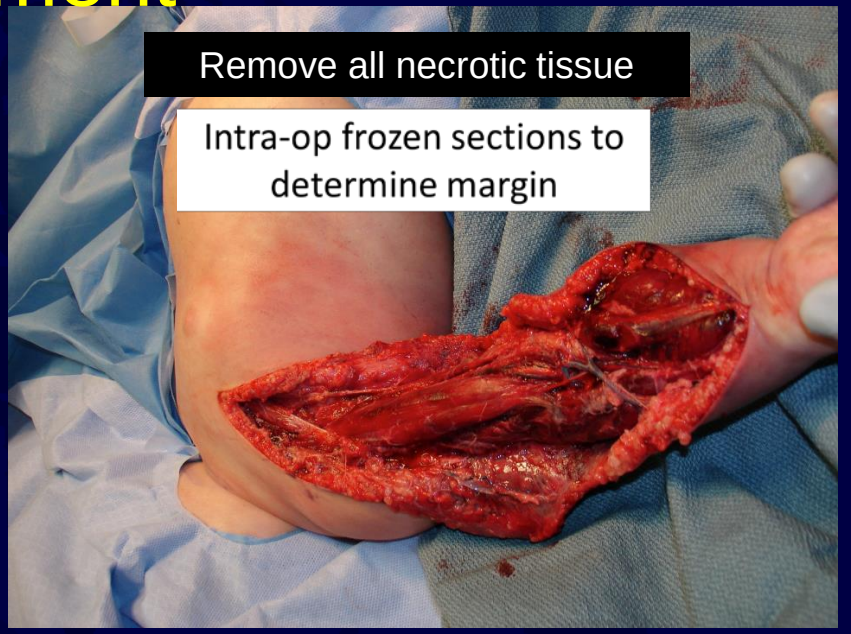
Necrotizing Soft Tissue Infections- Management

- Surgical Management
  - The zone approach is often used during surgical debridement.
    - Zone II:
      - reactionary zone
      - zone surrounding the area of necrosis and presents with induration and erythema.



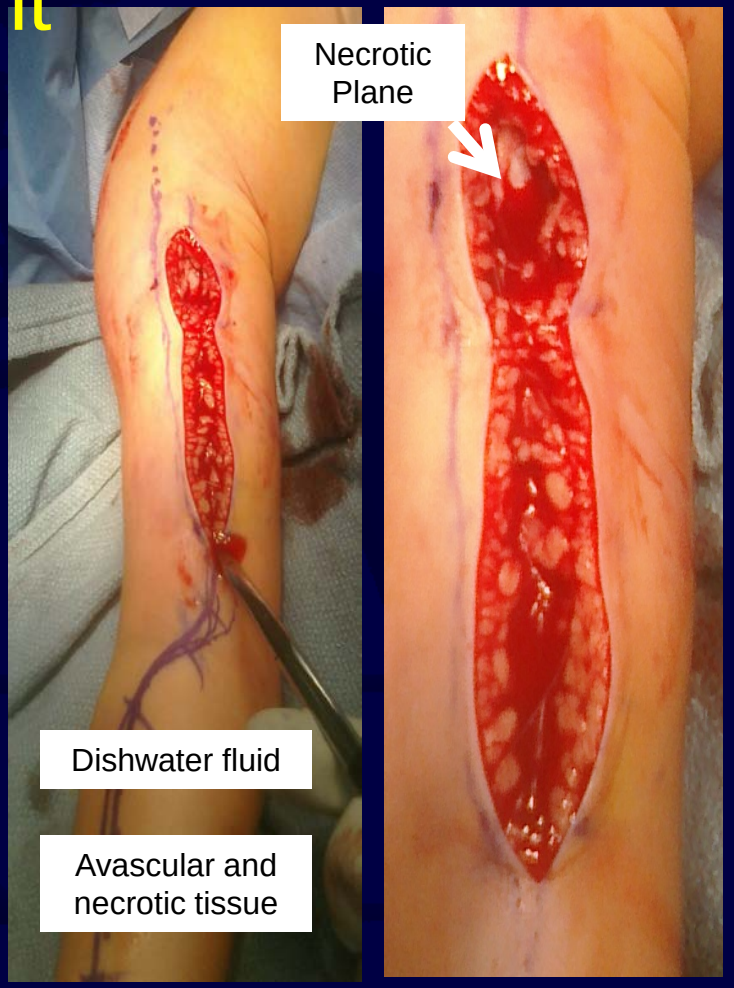
Necrotizing Soft Tissue Infections- Management

- Surgical Management
  - The zone approach is often used during surgical debridement.
    - Zone III is considered healthy tissue.



Necrotizing Soft Tissue Infections- Management

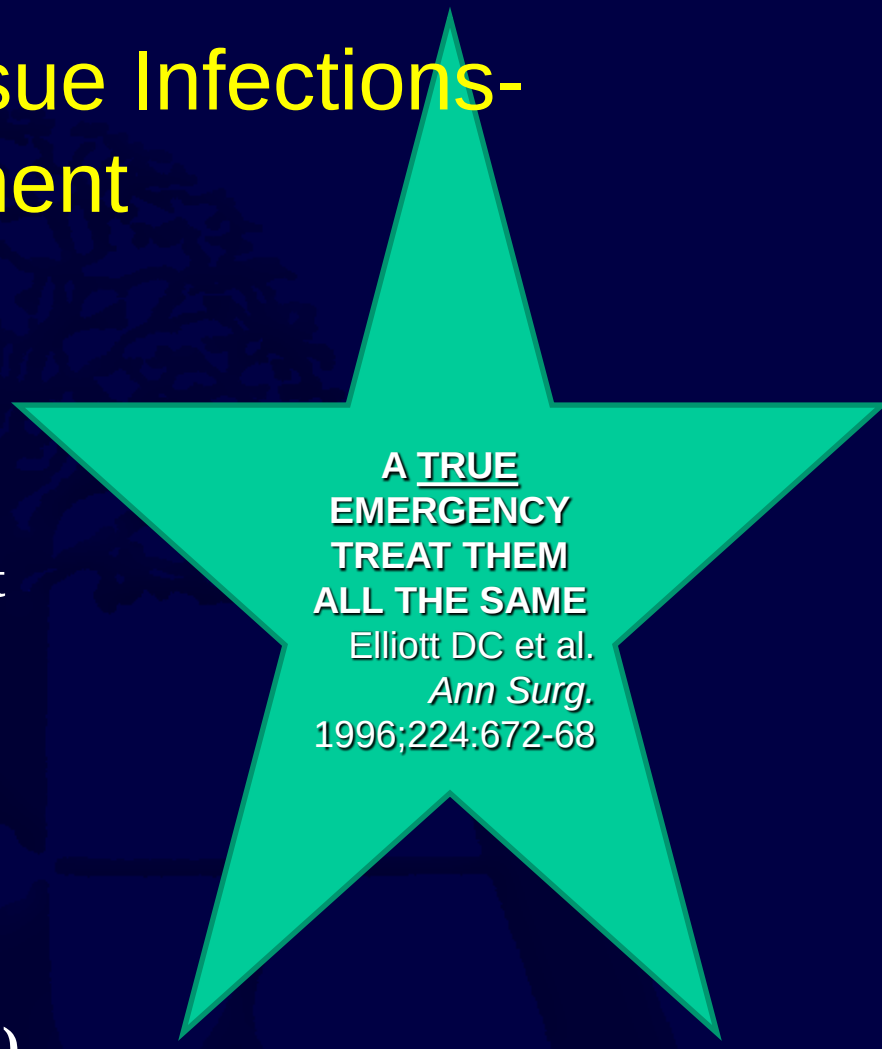
- Surgical Management
  - Completely debride all **necrotic** tissue in zone I
  - Make exploratory incisions in zones II and III. Get ahead of the disease!
  - Perform the finger sweep test
    - Run a finger between the fascia and the subcutaneous tissue in a forward sweeping manner
  - Necrotic tissue in the subcutaneous tissue will peel away from fascia
  - Use wound vac for dressings



Harrison, W. D., & Kapoor, B. (2016). Necrotizing soft tissue infection: principles of diagnosis and management. Orthopaedics and Trauma, 30(3), 223-231.

Necrotizing Soft Tissue Infections-Management

- **Resuscitate the patient in shock**
- **Physiologic Support (O2, Fluids)**
- **Begin broad-spectrum antibiotic coverage**
- **Early aggressive surgical debridement**
  - **Obtain gram stain and culture**
  - **Histology, if necessary**
- **Repeat debridement every 24-48 h as necessary**
- **Adjust antibiotic therapy based on culture**
- **Nutritional support (enteral preferred)**



Laucks SS et al. *Surg Clin N Am*. 1994;74:1339-1352.

Elliott D et al. *Am J Surg*. 2000;179:361-366.

Necrotizing Soft Tissue Infections-Management

- **Surgical debridement is mainstay of therapy**
- **Aggressive EARLY incision or debridement of all involved tissues**
- **Average number of débridements 3-4 / patient**
- **Primary Closure of wounds once tissue improves**
- **STSG or flap coverage most commonly used for coverage of tissue defects**
- **Studies suggest that early and aggressive surgical therapy can reduce mortality to < 10%**

Gunter OL *Surg. Infect.* 2008; 9:443-450
Bilton BD. *Am.Surg.* 1998; 64:397-400
Bosshardt TL. *Arch.Surg*. 1996;131:846-52
Elliott DC. *Ann.Surg*. 1996; 224:672-83

Adjuvants

- IGG
- Steroids

Intravenous Immunoglobulin as Adjunctive Treatment for Streptococcal Toxic Shock Syndrome Associated with Necrotizing Fasciitis: Case Report and Review

Michael J. Cawley, Pharm.D., Michael Briggs, Pharm.D., Linwood R. Haith, Jr., M.D., FACS, Kathleen J. Reilly, M.D., Robert E. Guilday, M.D., Gayna R. Braxton, B.A., and Mary Lou Patton, M.D., FACS, FICS

- IGG
  - Experimental data on streptococcal toxins suggest that normal polyspecific immunoglobulin given intravenously may inhibit T cell proliferation
  - may bind to a toxin itself neutralizing
  - neutralizing mitogenic and cytokine-inducing activities of group A streptococcal superantigens.
  - Also causes down regulation of TNF-a and IL-6

Original Research: Critical Care

Hydrocortisone, Vitamin C, and Thiamine for the Treatment of Severe Sepsis and Septic Shock: A Retrospective Before-After Study

Paul E. Marik MD, FCCP [a], Vikramjit Khangoora MD [a], Racquel Rivera PharmD [b], Michael H. Hooper MD [a], John Catravas PhD, FCCP [c, d]

- Steroids
  - not specifically studied in nec fasc
  - well studied in sepsis
  - effective in treating shock associated with severe infection, due to ability to help end the hyperinflammatory state

Original Research: Critical Care

Hydrocortisone, Vitamin C, and Thiamine for the Treatment of Severe Sepsis and Septic Shock: A Retrospective Before-After Study

Paul E. Marik MD, FCCP [a], Vikramjit Khangoora MD [a], Racquel Rivera PharmD [b], Michael H. Hooper MD [a], John Catravas PhD, FCCP [c, d]

- 47 patients in both treatment and control group
- Hospital mortality 8.5% (4 of 47) treatment group vs. 40.4% (19 of 47) in the control group ($P < .001$).
- Sepsis-Related Organ Failure Assessment score decreased in all patients in the treatment group, none developing progressive organ failure.
- All patients in the treatment group weaned off vasopressors, a mean of 18.3 ± 9.8 h vs. 54.9 ± 28.4 h in the control group ($P < .001$).

Treatment

- Steroids
  - Inhibit T cell activation
  - Inhibit cytokines
- Four case reports

- Alwattar BJ, Strongwater A, Sala DA. Streptococcal toxic shock syndrome presenting as septic knee arthritis in a 5-year-old child. *J Pediatr Orthop*. 2008;28:124-127.
- Chiu CH, Ou JT, Chang KS, Lin TY. Successful treatment of severe streptococcal toxic shock syndrome with a combination of intravenous immunoglobulin, dexamethasone and antibiotics. *Infection*. 1997;25:47-48.
- Shoji F, Yoshino I, Osoegawa A, Yano T, Maehara Y. Toxic shock syndrome following thoracic surgery for lung cancer: report of a case. *Surg Today*. 2007;37:587-589.
- Stegmayr BG. Plasmapheresis in severe sepsis or septic shock. *Blood Purif*. 1996;14:94-101.

First and ONLY Report of this Transmission

Steroids in the Treatment of Group A Streptococcal Necrotizing Soft Tissue Infection

Addison K. May,[1] Titus L. Daniels,[2] William T. Obremskey,[3] Allen B. Kaiser,[2] and Thomas R. Talbot, III[2]

- **Case report**
  - **47 y/o male surgeon with hx of right THA**
    - **In-hospital exposure to index patient while assisting in hip disarticulation in patient with necrotizing fasciitis**
    - **10 day later developed necrotizing infection at site of chronic tinea capitis in right foot with ecchymosis migrating to the medial thigh**
      - **10 mg IV dexamethasone given followed by 4 mg given q6 hrs for 48 hours**

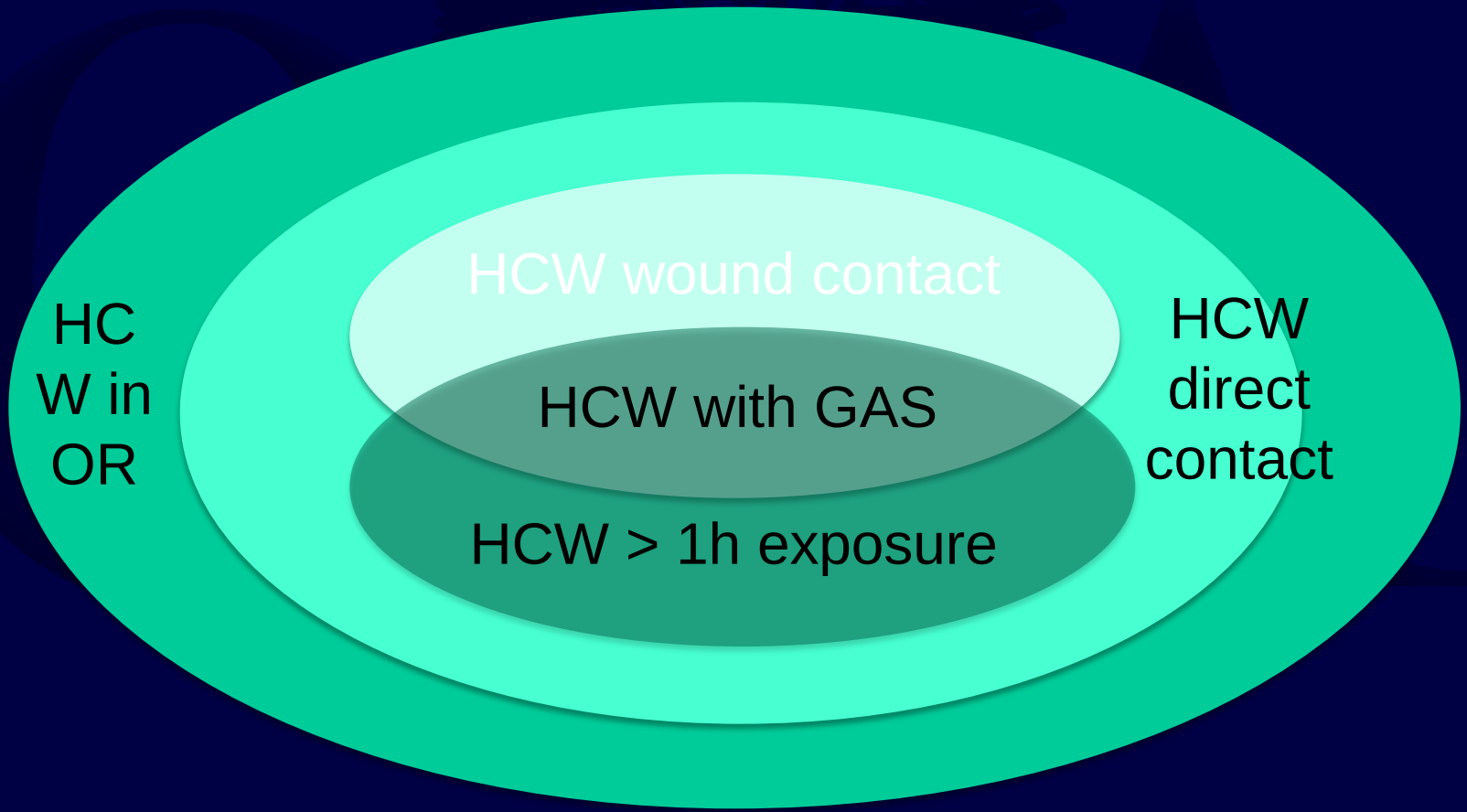
How to Avoid Transmission?

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY NOVEMBER 2006, VOL. 27, NO. 11

ORIGINAL ARTICLE

Transmission of Group A *Streptococcus* Limited to Healthcare Workers with Exposure in the Operating Room

Rebecca E. Chandler, MD; Lore E. Lee, MPH; John M. Townes, MD; Randy A. Taplitz, MD



INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY NOVEMBER 2006, VOL. 27, NO. 11

ORIGINAL ARTICLE

Transmission of Group A *Streptococcus* Limited to Healthcare Workers with Exposure in the Operating Room

Rebecca E. Chandler, MD; Lore E. Lee, MPH; John M. Townes, MD; Randy A. Taplitz, MD

Prolonged intraoperative exposure

GAS aerosolized in OR setting

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY NOVEMBER 2006, VOL. 27, NO. 11

ORIGINAL ARTICLE

Transmission of Group A *Streptococcus* Limited to Healthcare Workers with Exposure in the Operating Room

Rebecca E. Chandler, MD; Lore E. Lee, MPH; John M. Townes, MD; Randy A. Taplitz, MD

Prolonged intraoperative exposure

GAS aerosolized in OR setting

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY NOVEMBER 2006, VOL. 27, NO. 11

ORIGINAL ARTICLE

Transmission of Group A *Streptococcus* Limited to Healthcare Workers with Exposure in the Operating Room

Rebecca E. Chandler, MD; Lore E. Lee, MPH; John M. Townes, MD; Randy A. Taplitz, MD

Prolonged intraoperative exposure

GAS aerosolized in OR setting

Nosocomial Transmission of Invasive Group A Streptococcus from Patient to Health Care Worker

Mark D. Lacy and Kim Horn

Infectious Disease Service, Flagstaff Medical Center, Flagstaff, Arizona

Index patient: 34 yo M LE nec fasc, taken to OR for debridement

Nosocomial Transmission of Invasive Group A Streptococcus from Patient to Health Care Worker

Mark D. Lacy and Kim Horn

Infectious Disease Service, Flagstaff Medical Center, Flagstaff, Arizona

Index patient: 34 yo M LE nec fasc, taken to OR for debridement

48 h postop HCW 1 (resp therapist):
+ GAS pharyngitis

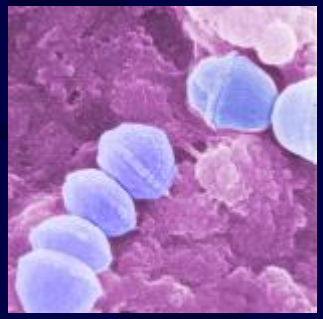
Nosocomial Transmission of Invasive Group A Streptococcus from Patient to Health Care Worker

Mark D. Lacy and Kim Horn

Infectious Disease Service, Flagstaff Medical Center, Flagstaff, Arizona

Index patient: 34 yo M LE nec fasc, taken to OR for debridement

48 h postop HCW 1 (resp therapist):
+ GAS pharyngitis



Nosocomial Transmission of Invasive Group A Streptococcus from Patient to Health Care Worker

Mark D. Lacy and Kim Horn

Infectious Disease Service, Flagstaff Medical Center, Flagstaff, Arizona

Transmission through aerosols:
Open wounds
Secretions

Nosocomial Transmission of Invasive Group A Streptococcus from Patient to Health Care Worker

Mark D. Lacy and Kim Horn

Infectious Disease Service, Flagstaff Medical Center, Flagstaff, Arizona

Transmission through aerosols:
Open wounds
Secretions

Nosocomial Transmission of Invasive Group A Streptococcus from Patient to Health Care Worker

Mark D. Lacy and Kim Horn

Infectious Disease Service, Flagstaff Medical Center, Flagstaff, Arizona

Transmission through aerosols:
Open wounds
Secretions

The best treatment places healthcare workers at risk

Protect your oropharynx!

Summary

- **HARD signs = necrotizing infection and require OR**
  - **Bullae, cutaneous anesthesia, ecchymosis, tense edema, gas**
- **Early and aggressive surgical debridement improves outcome with achievable mortality of < 10%**
- ***Empiric surgical exploration if in doubt!***
- ***Protect your oropharynx***
- ***Consider Steroids or IGG in "Toxic" patient (Strep)***
- ***Transfer patient AFTER initial debridement***