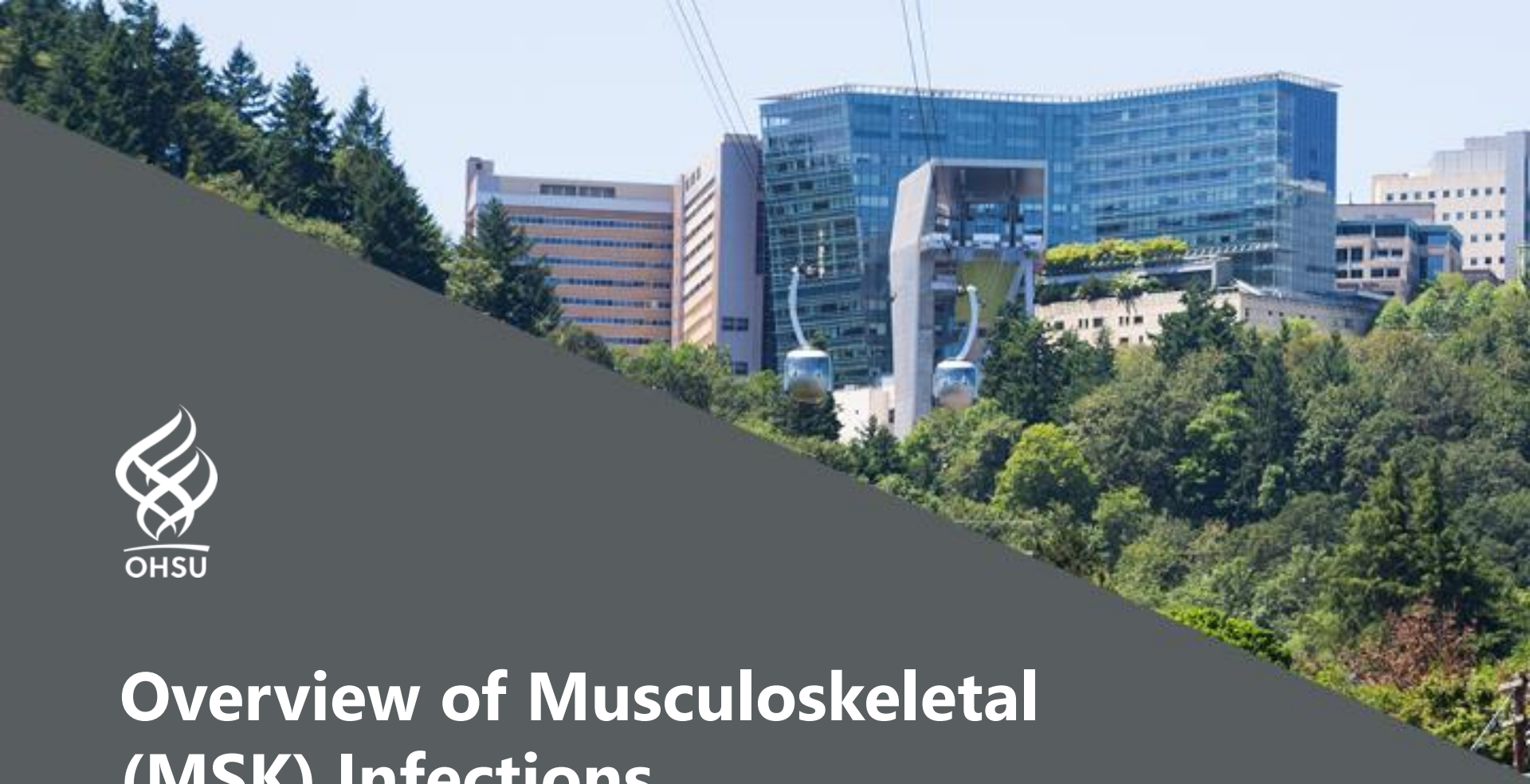


Overview of Musculoskeletal (MSK) Infections

AAPA/AAOS 2021 Musculoskeletal Galaxy Conference

DATE: June 21, 2021

PRESENTED BY: Ryland Kagan, MD

Disclosures

- OrthoDevelopment Corporation
  - Research Support
- KCI Acelity
  - Research Support
  - Consulting Fees

Learning Objectives

- At the conclusion of the session, participants should be able to:

- Recognize and diagnose common MSK infections

- Understand basic epidemiology, imaging and treatment of common MSK infection

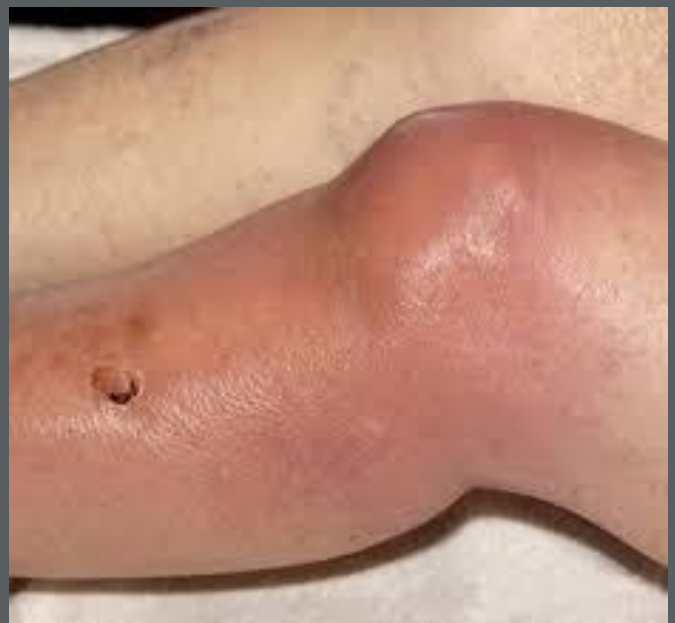
- Triage urgent and emergent MSK infections

MSK Infections

- Septic Arthritis
- Pyomyositis
- Necrotizing soft tissue infections
- Cellulitis and skin abscess
- Biofilms and Surgical Site Infection
- Prosthetic Joint Infection
- Infections after Fracture

Septic Arthritis

- Infectious Arthritis
  - Joint inflammation caused by a microbe
  - Most commonly from bacterial infection of the joint
  - Can occur from hematogenous spread or direct inoculation (penetrating injury, injection, trauma)



Septic Arthritis

- Demographics
  - Children or older adults are most likely to develop septic arthritis
  - Immunosuppressed patients or patients with autoimmune disease

Septic Arthritis

- Key Principles
  - Failure to initiate treatment within the first 24-48 hours of onset of symptoms can cause subchondral bone loss and permanent joint dysfunction. [Matthews et al. Lancet 2010 & Goldenberg et al Lancet 1998]
  - Most common route of entry into joint is hematogenous spread during bacteremia. [Margaretten et al JAMA 2007]

Septic Arthritis

- Diagnosis
  - History
    - Acute joint swelling
    - Pain
    - Erythema
    - Warmth
    - Joint immobility
    - Recent injection or arthrocentesis
  - Past Medical History
    - Evaluation for open wounds or ulcerations
    - Diabetes
    - HIV
    - Immunosuppressive medications
    - Intravenous (IV) drug abuse
    - Osteoarthritis
    - Prosthetic Joint
    - Rheumatoid Arthritis
    - Sexual activity (Specifically gonoccal arthritis)

Septic Arthritis

Table 1. Risk Factors for Septic Arthritis

Contiguous spread

Skin infection, cutaneous ulcers[8,9]

Direct inoculation

Previous intraarticular injection[8,10]

Prosthetic joint: early and delayed[8] (Table 6)

Recent joint surgery[8,10]

Hematogenous spread

Diabetes mellitus[8,10]

Human immunodeficiency virus infection[11]

Hematogenous spread *(continued)*

Immunosuppressive medication[9,11]

Intravenous drug abuse[11]

Osteoarthritis[9]

Other cause of sepsis[9]

Prosthetic joint: late[8] (Table 6)

Rheumatoid arthritis[8,9]

Sexual activity (specifically for gonococcal arthritis)[12]

Other factors

Age older than 80 years[8]

- [Horowitz et al AFP 2011]

Septic Arthritis

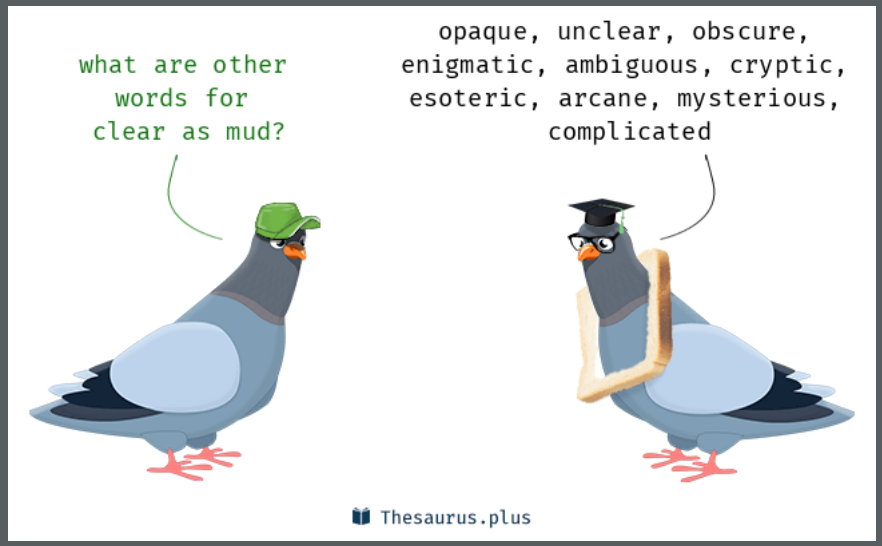
- Diagnosis
  - Physical Exam
    - Careful evaluation of joint
    - Evaluation mono-articular or poly-articular
      - Up to 20% of cases involve other joints [Matthews et al. Lancet 2010]
    - Limited range of motion
    - Erythema and warmth
  - Most Common Joints Infected [Morgan et al Epidemiol Infect 1996]
    - #1 Knee
    - #2 Hip
    - #3 Shoulder
    - #4 Ankle
    - #5 Elbow
    - #6 Wrist
    - Infection of non-axial joints (sternoclavicular, sacroiliac) should prompt investigation of IV drug abuse.

Septic Arthritis

- Diagnosis
  - Imaging
    - Radiographs
      - Key first step, identify fractures, foreign bodies, chondrocalcinosis or erosions.
    - Ultrasound [Zieger et al Skeletal Radiol 1987]
      - More sensitive for detecting effusions particularly in difficult to examine joints such as the hip.
      - User dependent and may not be readily available
    - MRI
      - Can potentially detect associated osteomyelitis or marrow edema
      - Often not feasible with time and cost limitations and should not delay diagnosis in most cases.

Septic Arthritis

- Diagnosis
  - Can be clear
  - Other bad actors
    - Crystaline arthropathy: Gout, pseudogout
    - Hemarthrosis
    - Toxic Synovitis
    - Other rheumatic diseases



Septic Arthritis

Table 2. Differential Diagnosis of Acute Arthritis

Diagnosis	*Etiology*
Crystal-induced arthritis	Calcium oxalate, gout, cholesterol, pseudogout, hydroxyapatite crystals
Infectious arthritis	Bacteria, fungi, mycobacteria, spirochetes, viruses
Inflammatory arthritis	Behçet syndrome,* rheumatoid arthritis,* sarcoid, systemic lupus erythematosus,* Still disease,* seronegative spondyloarthropathy (e.g., ankylosing spondylitis, psoriatic arthritis, reactive arthritis, inflammatory bowel disease–related arthritis), systemic vasculitis*
Osteoarthritis	Erosive/inflammatory variants*
Other	Amyloidosis, avascular necrosis, clotting disorders/anticoagulant therapy, familial Mediterranean fever,* foreign body, fracture, hemarthrosis, hyperlipoproteinemia,* meniscal tear
Systemic infection	Bacterial endocarditis, human immunodeficiency virus infection
Tumor	Metastasis, pigmented villonodular synovitis

- [Horowitz et al AFP 2011]

Septic Arthritis

- Diagnosis
  - Laboratory Evaluation
    - White Blood Cell Count (WBC)
    - Erythrocyte Sedimentation Rate (ESR)
    - C-Reactive Protein (CRP)
    - Blood Cultures
      - Key initial lab tests should include above
      - Important for initial diagnoses but also for monitoring therapeutic response

Septic Arthritis

- Synovial Fluid Analysis
  - Arthrocentesis indicated to confirm diagnosis and may identify infectious agent.
    - Use image guidance as needed, US, CT, or Fluoroscopic
  - Synovial fluid testing
    - Evaluate at bedside appearance of fluid
    - Synovial WBC count
    - Synovial polymorphonuclear (PMN) cell count %
    - Gram stain and culture should be sent but sensitivities of these vary based on pathogenic organism
  - Future
    - Synovial alpha-defensing (Synovasure)
    - Synovial esr, crp
    - Broad spectrum PCR

Septic Arthritis

Table 3. Synovial Fluid Analysis

Arthritis diagnosis	*Color*	*Transparency*	*Viscosity*	*WBC count (per mm³)*	*PMN cell count (%)*	*Gram stain*
Normal	Clear	Transparent	High/thick	< 200	< 25	Negative
Noninflammatory	Straw	Translucent	High/thick	200 to 2,000	< 25	Negative
Inflammatory: crystalline disease	Yellow	Cloudy	Low/thin	2,000 to 100,000	> 50	Negative
Inflammatory: noncrystalline disease	Yellow	Cloudy	Low/thin	2,000 to 100,000	> 50	Negative
Infectious: Lyme disease	Yellow	Cloudy	Low	3,000 to 100,000 (mean: 25,000)	> 50	Negative
Infectious: gonococcal	Yellow	Cloudy-opaque	Low	34,000 to 68,000	> 75	Variable (< 50 percent)
Infectious: nongonococcal	Yellow-green	Opaque	Very low	> 50,000 (> 100,000 is more specific)	> 75	Positive (60 to 80 percent)

NOTE: *These are general guidelines in the interpretation of synovial fluid. Many parameters vary widely and must be interpreted in the clinical context. Three bedside observations (color, transparency, and viscosity) are quick and easy to assess. With normal transparent fluid, words can be read clearly through the fluid. The words become less crisp and gradually obscured with increasing turbidity. Viscosity is assessed by observing the fluid dropping from the syringe. Normal viscosity has a long, stringy tail.*

PCR = polymerase chain reaction; PMN = polymorphonuclear; WBC = white blood cell.

**—Crystalline disease can coexist with septic arthritis. A positive result does not exclude infection.*

- [Horowitz et al AFP 2011]

- Organisms [Horowitz et al AFP 2011]
  - Staphylococci (S. aureus)
    - 40%
  - Streptococci
    - 28%
  - Gram-negative bacilli (Pseudomonas aeruginosa & Escherichia coli)
    - Think chronic UTI, IVDA, older age, immunocompromised
    - 19%
    - Haemophilus influenza (children), more historical due to widespread H. influenza vaccination.
  - Mycobacteria
    - 8%
  - Gram-negative bacilli
    - 19%
  - Gram-negative cocci
    - 3%
  - Gram-positive bacilli
    - 1%
  - Anaerobes
    - 1%

Septic Arthritis

- Organisms

  - Staphylococci

    - Staphylococcus aureus is the most organism most commonly found in septic arthritis in the USA and other developed countries. [Ryan et al Br J Rheumatol 1997]

    - The incidence of methicillin-resistant S. aureus (MRSA) is emerging and ranges in reports of up to 25% of cases. MRSA tends to affect elderly, involve the shoulder, or health care-associated [Ross et al Rheumatology 2005]

Septic Arthritis

- Special Situations

  - Gonococcal Arthritis [Ryan et al Br J Rheumatol 1997]

    - Young, healthy and sexually think Neisseria gonorhoeae

    - Various clinical musculoskeletal presentations
      - » Migratory arthralgias
      - » Tenosynovial inflammation
      - » Nonerosive arthritis

    - Blood cultures are seldom positive

    - Synovial fluid cultures are variable (25-70% positive)

    - When suspected take cultures from other mucosal sites (Urethra, rectum, pharynx, cervix)

Septic Arthritis

- Special Situations

  - Mycobacterial Infections [Gardam et al Infect Dis Clin North Am 2005]
    - Can be indolent and delayed diagnosis
    - Mycobacterium tuberculosis typically hip, knee or spine and caused by reactivation from past dissemination
    - Synovial fluid is + in 80% of cases
    - Acid-fast smears are not helpful and often negative

  - Borrelia burgdorferi (Lyme disease) [Bacon et al MMWR Surveliill Summ 2008]
    - Late Lyme disease is caharacterized by intermittent oligoarthritis that usually involves the knee or other large joints
    - Diagnosis is made with a two-step serologic testing process
    - B. burgdorferi cannot be cultured from synovial fluid

Septic Arthritis

- Treatment
  - Urgent Surgical Debridement

Septic Arthritis

- Treatment
  - Urgent Empiric Antibiotics
    - Should be based on patient's clinical presentation and key history
    - Gram stain results

Septic Arthritis

- Treatment
  - Urgent Empiric Antibiotics
    - ***<u>Diagnostic arthrocentesis and/or debridement prior to antibiotic therapy is critical for identification of a pathogen.</u>***

Septic Arthritis

- Treatment

  - Urgent Empiric Antibiotics

Table 5. Empiric Antibiotic Therapy for Suspected Bacterial Arthritis

Gram stain result	*Antibiotic*
Gram-positive cocci	Vancomycin
Gram-negative cocci	Ceftriaxone (Rocephin)
Gram-negative rods	Ceftazidime (Fortaz), cefepime (Maxipime), piperacillin/tazobactam (Zosyn), or carbapenems If patient is allergic to penicillin or cephalosporins: aztreonam (Azactam) or fluoroquinolones
Negative Gram stain	Vancomycin plus either ceftazidime or an aminoglycoside

Septic Arthritis

- Prognosis

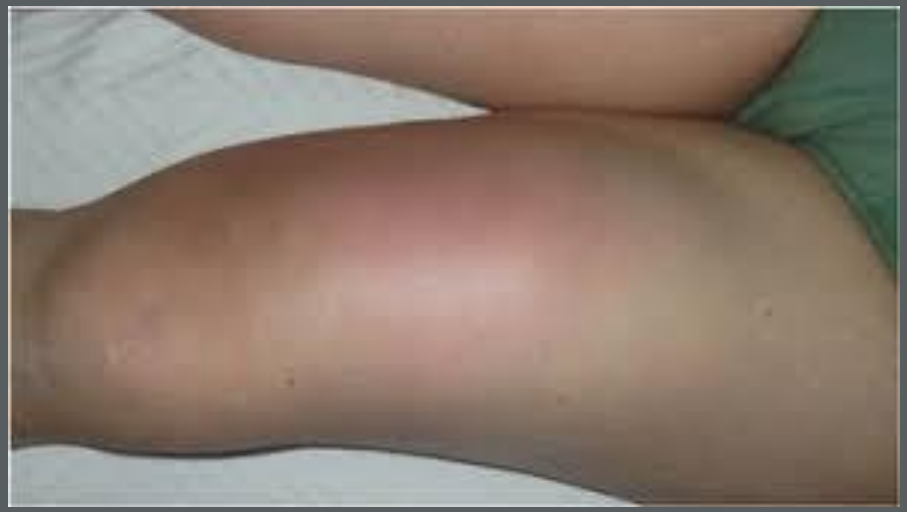
  - Prior to antibiotics 2/3rd of patients with septic arthritis died [Dickie Drugs 1986]

  - Current mortality rates range from 10-20%
    - Factors associated with death include age >65, infection in the shoulder, elbow or at multiple sites [Kaandorp Arthritis Rheum 1997]

  - Morbidity
    - Amputation, arthrodesis, prosthetic surgery, severe functional deterioration occurs in 1/3rd of patients with bacterial arthritis [Kaandorp Arthritis Rheum 1997]

Pyomyositis

- Infection of skeletal muscle
- Traditionally defined as hematogenous spread
- Most commonly from bacterial infection and usually with abscess formation



Pyomyositis

- Demographics

  [Crum Am J Med 2004]

  - Tropical pyomyositis
    - Children (age 2-5) and Adults (age 20-45)
    - Most otherwise healthy
  - Temperate pyomyositis
    - Adults
    - More likely to be immunocompromised

Pyomyositis

- Pre-disposing factors
  - Immunodeficiency
    - HIV, diabetes mellitus, malignancy, cirrhosis, renal insufficiency, organ transplantation [Belsky Am J Med Sci 1994]
  - Intravenous Drug Use [Ebright et al Infect Dis Clin North Am 2002]
    - Associated with pyomyositis-induced bacteremia
    - Local injection site infection & abscess extension into muscle should not be confused with true pyomyositis
  - Trauma [Chauhan et al Postgrad Med J 2004]
    - 25-50% of patients with pyomyositis report history of trauma
    - Possibly related to hematoma formation and favorable bacterial growth conditions.

Pyomyositis

- Clinical Presentation [Niamane et al Joint Bone Spine 2004]
  - Symptoms
    - Fevers, pain and cramping isolated to a single muscle group
  - Location
    - Most common in the lower extremity
      - Thigh, calf, gluteal, iliopsoas, para-spinal most common locations
    - 20% of cases are multifocal infections

Pyomyositis

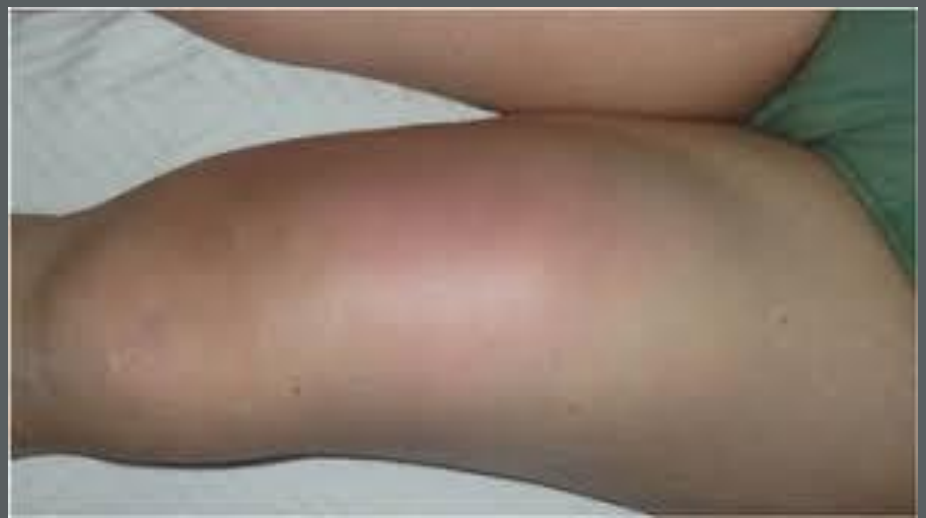
- Microbiology [Small et al Infect Dis Clin North Am 2005]
  - Staphyloccus
    - S. aureus causes up to 90% of tropical cases and 75% of temperate cases
    - MRSA may represent up to 25% of cases.
  - Streptoccoci
    - Group A beta-hemolytic streptococcus is the second most common
  - Others
    - Pneumococci, gram-negative enteric bacilli, E. coli
    - Mycobacterial pyomyositis has also been reported.

Pyomyositis

- Clinical Stage [Chiedozi Am J Surg 1979]
  - Stage 1
    - Cramping local muscle pain, swelling, low grade fever
    - Fluctuation is not present but may start to develop woody textured muscle
    - Mild leukocytosis and induration
    - Only 2% present at this stage

Pyomyositis

- Clinical Stage [Chiedozi Am J Surg 1979]
  - Stage 2
    - 10-21 days after initial onset of symptoms
    - Fever, exquisite tenderness and edema
    - Frank abscess with aspiration typically yielding purulence
    - Marked leukocytosis
    - 90%+ present at this suppurative stage



Pyomyositis

- Clinical Stage [Chiedozi Am J Surg 1979]
  - Stage 3
    - Systemic toxicity, septic shock
    - Fever, fluctuance
    - Endocarditis, septic emboli, rhabdomyolyis
    - Usually delay in presentation

Pyomyositis

- Imaging [Stevens et al Clin Infect Dis 2014]
  - Radiographs
    - Simple, rapid and useful for ruling out foreign bodies, or soft tissue air, fracture
  - US
    - Can be useful to detect abscess or to guide aspiration or drain placements
  - CT
    - Helpful for detecting muscle swelling and areas of fluid attenuation with rim enhancement. Also helpful for guided drainage or drain placement.
  - MRI
    - Highly sensitive for muscle inflammation even prior to formation of abscess and can demonstrate extent of involvement

Pyomyositis

- Laboratory Evaluation
  - White Blood Cell Count (WBC)
  - Erythrocyte Sedimentation Rate (ESR)
  - C-Reactive Protein (CRP)
  - Blood Cultures
  - Creatine kinase (CK) levels are often normal and not useful except in stage 3 disease or concern for rhabdomyolysis

Pyomyositis

- Drainage / Aspiration
  - ***Diagnostic drainage, aspiration or debridement prior to antibiotic therapy is critical for identification of a pathogen.***

Pyomyositis

- Treatment
  - Stage 1
    - Antibiotics alone
    - However most patients present with stage 2-3 disease

Pyomyositis

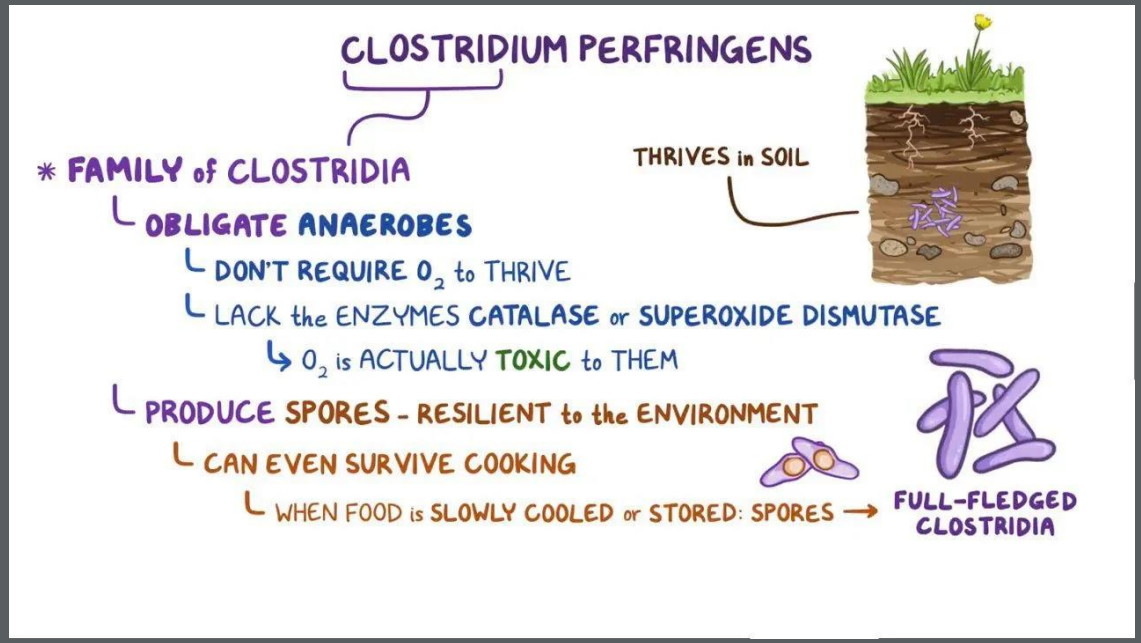
- Treatment
  - Stage 2/3
    - Drainage / Aspiration + Antibiotics
    - Image-guided percutaneous drainage is often both useful for diagnostic and therapeutic when combined with antimicrobial therapy.
    - Often CT guided but depending on your facility and availability of US this is also a good option.
    - Surgical drainage reserved for cases that fail percutaneous drainage or is certain cases where image guided drainage is no feasible or possible.

Clostridial Myonecrosis

- Aka: Gas gangrene
- Life-threatening muscle infection from EITHER an area of trauma or hematogenously spread from GI track and muscular seeding.
- Early recognition and aggressive treatment are key.

Clostridial Myonecrosis

- Traumatic
  - Most commonly caused by Clostridium perfringens



Clostridial Myonecrosis

- Spontaneous (Hematogenous spread)
  - Most commonly caused by Clostridium septicum
  - Commonly found in human and animal intestinal tracks

Clostridial Myonecrosis

- Steps in Clostridial Myonecrosis
  - Wound contamination or hematogenous spread
  - Anaerobic cellulitis
  - Myonecrosis (gas gangrene)
  - Can progress to necrotizing fasciitis

Clostridial Myonecrosis

- Contamination in the absence of devitalized tissues does not necessarily lead to infection
- Anaerobic cellulitis requires an anaerobic niche such as devitalized tissue
- Gas is produced locally and extends along fascial planes
- 30-80 percent of open traumatic wounds may be contaminated with clostridial species [Maclennan Bacteriol Rev 1962]

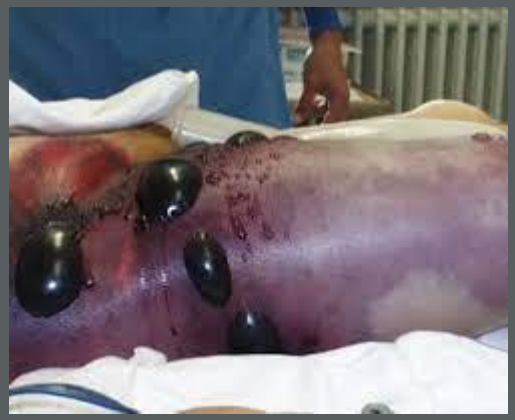
Clostridial Myonecrosis

- Traumatic wound with vascular compromise
  - Classically deep penetrating injuries that create an anaerobic environment for proliferation of Clostridia.
    - Knife wounds
    - Gunshot wound
    - Crush injuries
    - Heroin “skin popping”

Clostridial Myonecrosis

- Clinical presentation

  - Sudden onset of pain at site of surgery or trauma
  - Mean incubation period <24 hours
  - Skin over the infected area may appear pale but will rapidly develop bronze followed by purple and red discoloration
  - Often will see overlying bullae
  - Evaluate for tachycardia and fever which often can rapidly progress to shock and multi-organ failure.

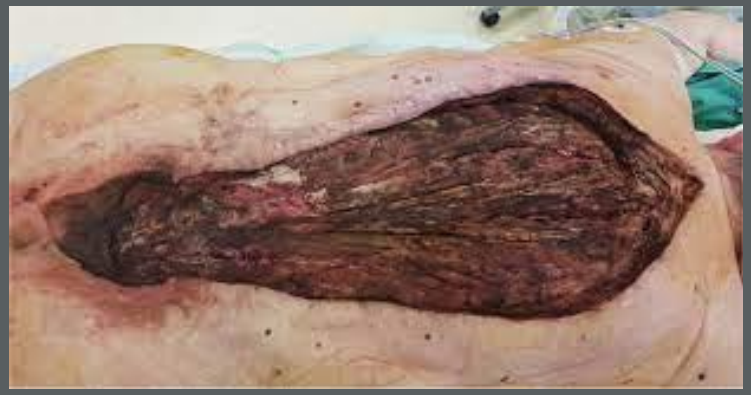


Clostridial Myonecrosis

- Imaging
  - Radiographic imaging can reveal gas in the deep tissues
  - CT or MRI can be useful for determining if infection is localized or spreading along fascial planes

Clostridial Myonecrosis

- Treatment
  - Urgent, aggressive surgical debridement of devitalized tissue is mandatory.
  - Often can require multiple surgical debridement procedures over course of days



Clostridial Myonecrosis

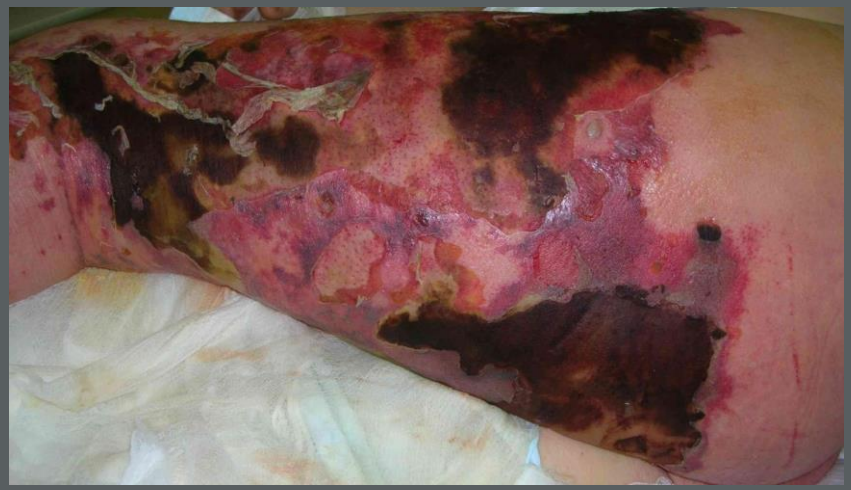
- Treatment
  - Antibiotic treatment
    - If Clostridial Myonecrosis is suspected should use Piperacillin-tazobactam (Zosyn) + clindamycin as initial therapy

Clostridial Myonecrosis

- Prognosis
  - Dependent on stage or presentation
  - Mortality is highest for patients in shock at time of diagnosis.
    - Series of 139 patients all treated with surgical debridement, antibiotics all deaths (27) were in shock at time of presentation. [Hart et al J Trauma 1983]

Necrotizing soft tissue infections

- Aka: Necrotizing fasciitis or NSTI
- NSTI's include necrotizing forms of fasciitis, myositis and cellulitis
- Characterized by fulminant tissue destruction, systemic toxicity and high mortality



Necrotizing soft tissue infections

- Risk Factors
  - Diabetes Mellitus
  - HIV/AIDS
  - Cancer
  - IV drug abuse
  - Obesity
  - Insect bites

Necrotizing soft tissue infections

- **Poly**microbial (type I) NSTI
  - Most Common (80-90%)
  - Caused by aerobic and anaerobic bacteria
  - Typically at least one anaerobic species
    - Bacteroides, Clostridium or Peptostreptoccus
  - In combination with Enterobacteriaceae (E. coli, Enterobacter, Klebsiella, Proteus) and one or more facultative anaerobic streptocci
  - Usually older or patients with comorbidities; diabetes, cancer, etc.

Necrotizing soft tissue infections

- **Mono**microbial (type II) NSTI
  - Less Common (5-10%)
  - Group A beta-hemolytic Streptocci
  - Seen in healthy patients, most commonly in the extremities
  - Infection with no clear portal of entry occurs in about ½ of cases and though to be hematogenous spread of GAS to the site of blunt trauma or muscle strain.

Necrotizing soft tissue infections

- **Mono**microbial Others
  - Marine Vibrio vulnificus and Aeromonas hyrophila
    - From traumatic injury associated with sea water or fresh water
  - MRSA

Necrotizing soft tissue infections

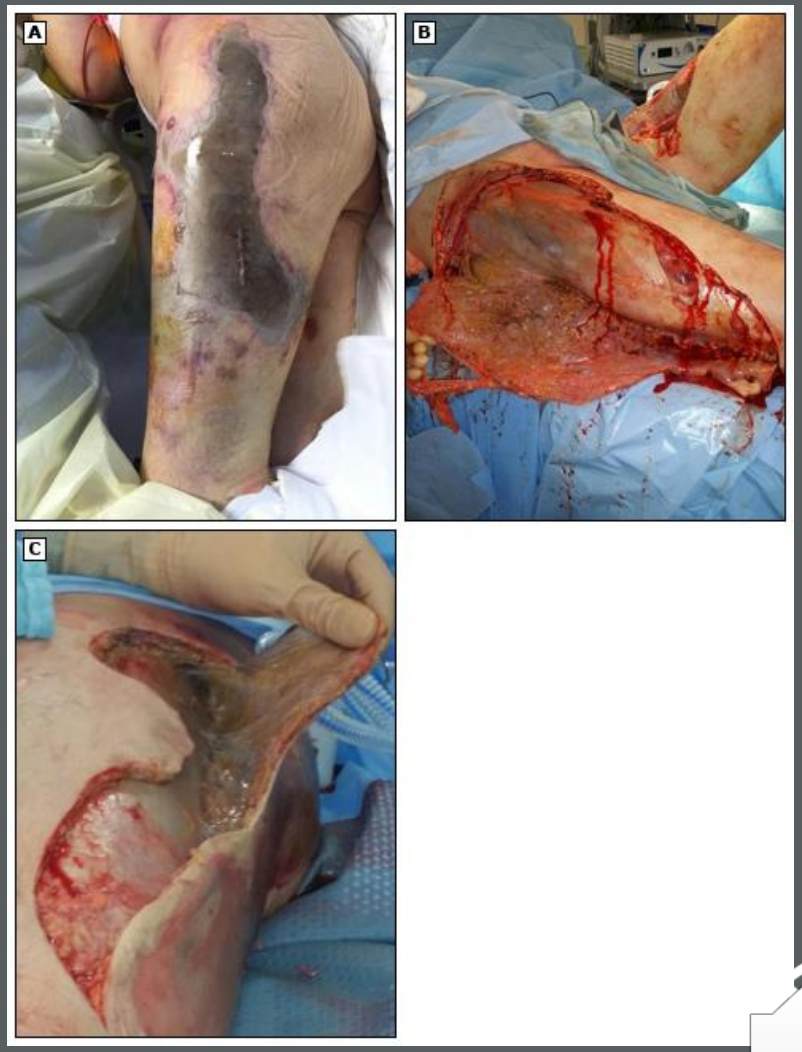
- Presentation [Stevens et al NEJM 2017]
  - Erythema (without sharp margins 72%)
  - Edema extending beyond erythema (75%)
  - Severe pain out of proportion to exam (72%)
  - Fever (60%)
  - Crepitus (50%)
  - Skin bullae, necrosis or ecchymosis (38%)

Necrotizing soft tissue infections

- Imaging = ***Not required for diagnosis or treatment***
  - Radiographs
    - If extremity and can be done rapidly may help identify gas
  - US
    - May show gas in tissue
  - CT
    - Will show presence of gas most commonly in Type I, and highly specific for NSTI.
  - MRI
    - Less useful and overly sensitive, may overestimate deep tissue involvement.

Necrotizing soft tissue infections

- Diagnosis = ***Surgical Exploration***
  - Intra-operative findings
    - Swollen, dull-gray (dish water) appearance of the fascia, with thin exudate without clear purulence and easy separation of tissue planed by blunt dissection.



[Stevens et al. Clin Infect Dis 2014]

Necrotizing soft tissue infections

- Diagnosis
  - Biopsy
    - Emergent frozen section can confirm diagnosis, especially in early cases
    - 1x1x1 cm tissue sample
    - Histology
      - » Necrosis of fascia
      - » Microorganisms within fascia layer
      - » PMN infiltration
      - » Fibrinous thrombi in arteries and veins and necrosis of arterial and venous walls

Necrotizing soft tissue infections

- Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) Score [Wong et al. Crit Care Med 2004]

  - Score >6 has PPV of 92% of having NSTI
  - Despite initial study describing high specificity and NPV subsequent studies have questioned the sensitivity, thus should ***not be used to RULE OUT NSTI***.

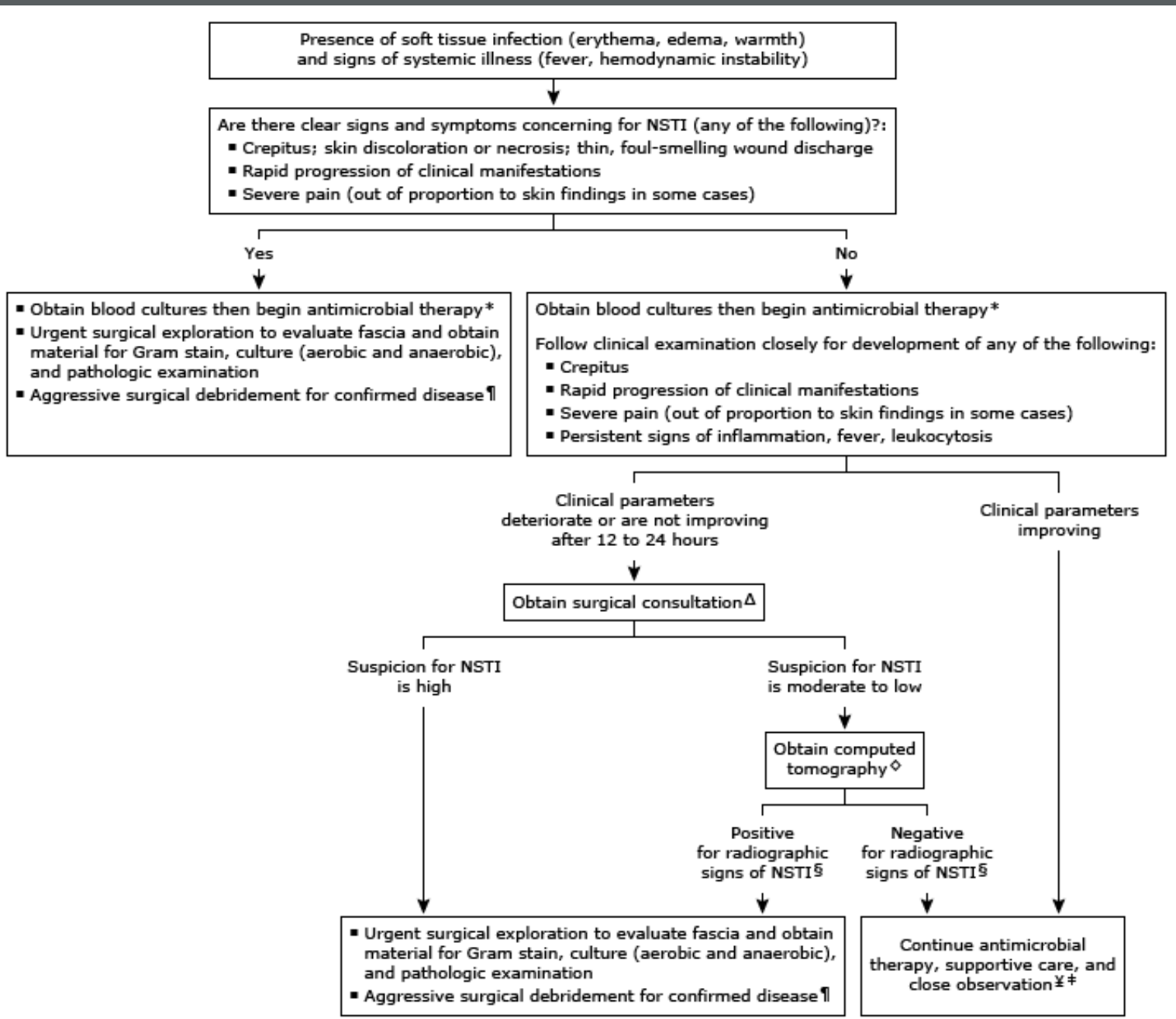
    - CRP (mg/L)
      - >150 = 4 points
    - WBC count
      - <15 = 0 points
      - 15-25 = 1 point
      - >25 = 2 points
    - Hemoglobin
      - >13.5 = 0 points
      - 11-13.5 = 1 point
      - <11 = 2 points
    - Sodium
      - <135 = 2 points
    - Creatinine
      - >141 = 2 points
    - Glucose
      - >10 = 1 point

Necrotizing soft tissue infections

- Surgical Exploration and Debridement
  - Early debridement is associated with better outcomes
    - Survival is significantly increased among patients taken to the OR within 24 hours of admission [McHenry et al Ann Surg 1995]
    - 9x increase in mortality if surgery delayed 24 hrs of admission [Wong et al. Crit Care Med 2004]
    - Survival is further increased with earlier surgical intervention (within 6 hours) [Bucca et al Anz J Surg 2013]

Necrotizing soft tissue infections

- Surgical Exploration and Debridement
  - Initial Debridement
    - Initial debridement should be performed at the facility to which they first presented. Those debrided initially at hospital to which they presented had significantly reduced mortality comparted to those transferred without debridement. [Holena et al Surgery 2011]
    - After the initial debridement, referral should be initiated to a burn center or similar tertiary referral center accustomed to managing complex wounds and for further debridement.
    - Aggressive debridement of necrotic tissues into health tissue when normal bleeding is seen. Multiple tissue biopsies and cultures should be obtained from several sites.



[Rogers et al UTD 2021]

Necrotizing soft tissue infections

- Prognosis and Outcomes
  - Mortality
    - Pooled analysis from the 1990's 34% [McHenry et al Ann Surg 1995]
    - 2010 NSQIP data mortality 12% [Mills et al Am J Surg 2010]
  - Morbidity
    - Longer hospital stays than burn patients with the same body surface involved.
    - Often complex soft tissue injuries, frequent amputations.

Cellulitis and skin abscess

- Cellulitis, abscess or both are among the most common MSK infections [Stevens et al Clin Infect Dis 2014]
- Cellulitis develops as a result of bacterial entry via breaches in the skin barrier
- A skin abscess is a collection of pus within the dermis or subcutaneous space.

Cellulitis and skin abscess

- Epidemiology
  - Most common in middle-age and older adults
  - Incidence is approx. 200 cases per 100,000 patient years. [McNamara et al Mayo Clin Proc 2007]
- Risk Factors
  - Trauma, eczema, lymphedema, obesity, venous insufficiency, immunosuppression.

Cellulitis and skin abscess

- Microbiology [Raff et al JAMA 2016]
  - Cellulitis
    - Most common beta-hemolytic streptocci
    - S. aureus is notable but less common
  - Skin abscess
    - S. aureus most common

Cellulitis and skin abscess

- Diagnosis
  - Based on clinical manifestations
    - Skin erythema edema and warmth
  - Laboratory testing
    - No required with uncomplicated infection in the absence of co-morbidities or complications
    - Blood cultures are positive in <10 percent of cases
    - Skin swab cultures are not helpful
  - Imaging
    - Not required however US may aid in identifying drainable abscess

Cellulitis and skin abscess

- Treatment
  - Cellulitis
    - Elevation
    - Empiric antibiotic therapy
  - Cellulitis and skin abscess
    - Incision and drainage
    - Empiric antibiotic therapy

Biofilms and surgical site infections

- Surgical Site Infections (SSI) [http://www.cdc.gov/nhsn/pdfs/pscmanual/]
  - The US CDC defines SSI as an infection that occurs after surgery in the part of the body where the surgery took place within 30 days of a procedure, or within 90 days if an open reduction, spinal fusion, or implantation of a hip or knee prosthesis is performed.
    - Any of the following four criteria are diagnostic for SSI
      - » Purulent drainage
      - » Positive culture
      - » Surgical reopening of an incision for pain, tenderness, localized swelling, redness or heat
      - » Diagnosis of infection by a surgeon
  - The life cycle of infecting microorganisms and their interactions with both the host and each other are important to understanding surgical site infections (SSIs)

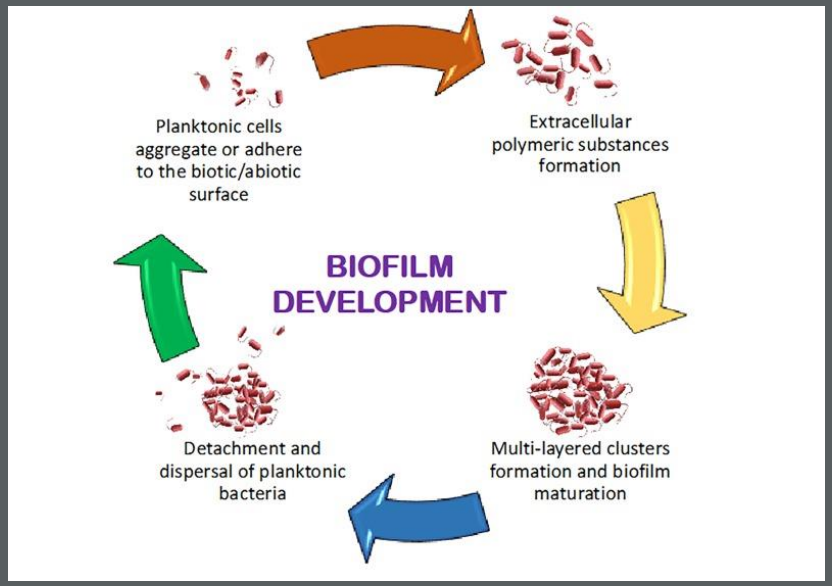
Biofilms and surgical site infections

– Surgical Site Infections

- Commensal microorganisms coexist on almost all healthy body surfaces that are covered by epithelial cells.
- The resulting biosystems have diverse symbiotic interactions between micros and host.
- Surgical sites disrupt patient defenses, providing opportunity for SSI, as these lack the host defenses specific to the locations where commensal organisms exist.

Biofilms and surgical site infections

- Biofilms & Planktonic pathogens
  - Planktonic bacteria are free-living bacteria, grow in the familiar culture medium and flask cultures
  - Conventional wisdom over the past 150 years focused on planktonic pathogens.
  - Currently most infection are no longer acute, planktonic phase infections



Biofilms and surgical site infections

- Biofilms

  - US CDC estimates that 56%-80% of infections in modern health care facilities in the US are associated with biofilms

  - Biofilms are polymicrobial, sessile, community-based aggregations within a self-secreted matrix

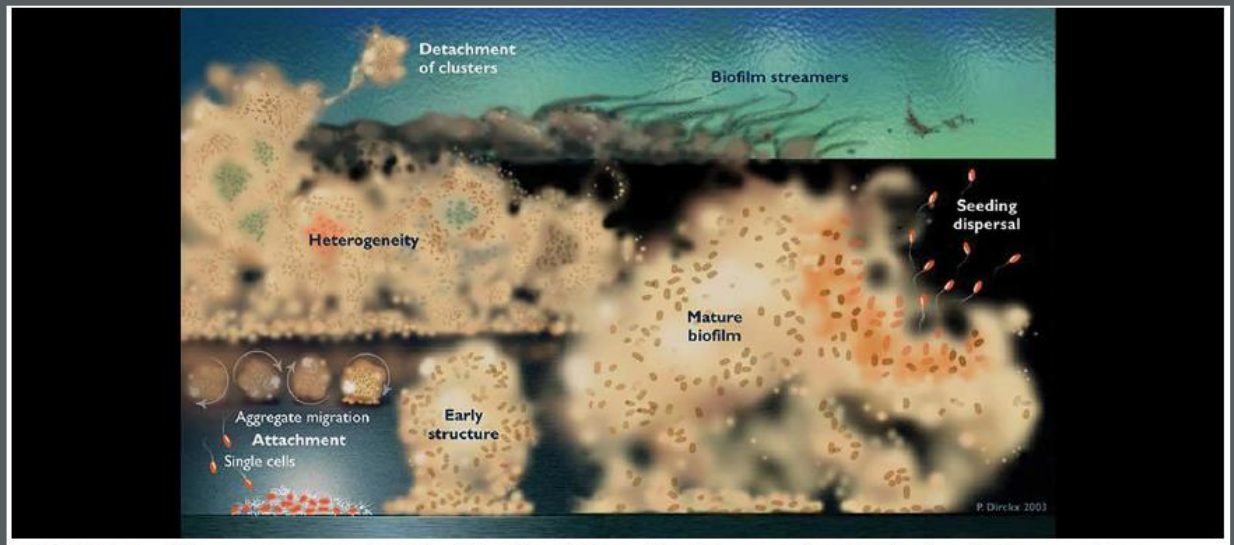


FIGURE 1 Illustration depicts the biofilm life cycle. (Copyright P. Dirckx, Montana State University, Bozeman, MT.)

Biofilms and surgical site infections

- Biofilms
  - Biofilm thickness can vary from a single cell layer to a thick community of cells with sophisticated architecture with intricate networks of channels.
  - Provide a safe environment for microbes and have several advantages over the planktonic microorganisms.
  - Resistant to antimicrobial agents and to cellular and humoral host immune effectors
    - Biofilm-embedded bacteria are up to 1,000 times more tolerant to antimicrobials. [Yasuda et al J Med Microbiol 1994]

Biofilms and surgical site infections

- Biofilms
  - A biofilm can be seen as a collective response to environmental conditions, as though it was a single living “organism”.
  - Multiple species, often multiple kingdoms, coexist within close, spatially structured regions that allow more robust signaling and exchange of genetic materials through horizontal gene transfer.
  - This exchange occurs at rates more than 10,000 times faster in a biofim mode of growth than in those between planktonic microbes.

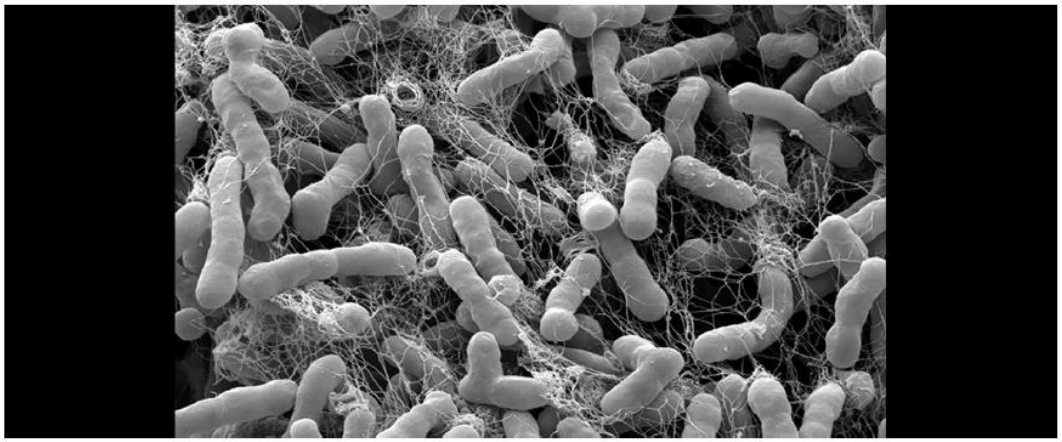


FIGURE 2 Scanning electron microscopic image of polymicrobial biofilm demonstrates nanotubes. (Reproduced with permission from Schaudinn C, Carr G, Gorur A, Jaramillo D, Costerton JW, Webster P: Imaging of endoontic biofilms by combined microscopy [FISH/cLSM-SEM]. *J Microsc* 2009;235[2]:124-127.)

Biofilms and surgical site infections

- Diagnostic Implications
  - Classically pathogen identification and antimicrobial susceptibility require propagation in microbial cultures.
  - At best, microbe recovery and ID can occur in days to weeks.
  - Biofilm infections are particularly difficult to culture and even small foci of microbes can cause inflammation in large areas of tissue because of secreted toxins and inflammatory mediators.
  - If a biopsy misses the small biofim population among the larger volume of involved tissue, then microbial cultures will be negative.

Biofilms and surgical site infections

- Diagnostic Implications

  - Due to high false-negative culture rate for biofilm microbes, many indolent biofilm infections were previously thought to be chronic inflammatory disorders.

  - Sophisticated new molecular techniques are being developed including PCR based, DNA array, RNA, fluorescent in situ hybridization probes, enzyme-linked immunosorbent assay and others. However these are largely investigational and not yet cost effective for clinic use. [Hoiby et al Clin Microbiol Infect 2015]

  - Clinicians must use clinical experience and consensus results from multiple diagnostic strategies.

Prosthetic Joint Infection (PJI)

- Incidence [Kurtz et al CORR 2010]
  - 0.5 - 2% Primary Total Knee Arthroplasty (TKA) and Total Hip Arthroplasty (THA)
  - 2.0 – 4.0% Revision THA/TKA

Prosthetic Joint Infection (PJI)

- Diagnosis and clinical presentation
  - Extremely variable clinical presentation
    - Can present with acute PJI, pain, erythema, drainage, fevers
    - Can present with subtle symptoms of pain or even just stiffness
  - All patients with pain after total joint arthroplasty should be evaluated for infection
  - Evaluation should begin with clinical history, onset, evolution of symptoms, events of concern regarding index procedure, presence of known risk factors.

TABLE 1: Risk Factors for Periprosthetic Joint Infection

Established Risk Factors	Potential Risk Factors
History of superficial SSI[a,b]	Hematoma formation
History of prior joint infection[b]	Delayed wound healing
Obesity[a,b]	Prolonged drainage
Immunosuppressive conditions[b]	Recent bacteremia
Surgical time >2.5 hours[a,b]	Skin disorders
	Intravenous drug use
	Active infection at another site
	Smoking
	Prior open surgery
	Simultaneous bilateral surgery
	Prolonged hospitalization
	Allogeneic transfusion

SSI = surgical site infection.
[a]Established risk factor following total hip arthroplasty.
[b]Established risk factor following total knee arthroplasty.
Data obtained from Cooper HJ, Della Valle C: Diagnosis of periprosthetic joint infection: An algorithmic approach to patients, in Springer BD, Parvizi J, eds: *Periprosthetic Joint Infection of the Hip and Knee*, New York, NY, Springer, 2014, pp 65-77.

Prosthetic Joint Infection (PJI)

Laboratory Evaluation

- Erythrocyte sedimentation rate (ESR)
- C-reactive protein (CRP)
  - ESR/CRP high sensitivity, good negative predictive value and are cost-effective
  - Should be initial **screening** tool

- Serum Interleuken 6
  - Potentially more specific, especially for acute PJI
  - Not readily available
- D-Dimer
  - Promising marker for diagnosis of PJI
  - May also have utility for determining optimal timing of reimplantation

Prosthetic Joint Infection (PJI)

- Synovial Fluid Evaluation

TABLE 3: Cutoff Values for Diagnosis of Periprosthetic Joint Infection

Study	WBC (cells/μL)[a]	PMN cells (%)	CRP (mg/L)	ESR (mm/h)	Patient Population	Time From Index Surgery
Spangehl et al	50,000	80	10	30	202 hips (35 infected)	Mentioned anecdotally, ≥11 years
Mason et al	2,500 cells/mL	60			86 knees (36 infected)	NR
Trampuz et al	1,700	65			133 knees (34 infected)	Greater than 6 months
Parvizi et al	1,760	73			145 knees (78 infected)	NR
Trampuz et al	1,700	65	10	30	331 joints (207 knees, 124 hips) (79 infected)	NR

CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, NR = not reported, PMN = polymorphonuclear, WBC = white blood cell count.

[a]Reprinted with permission from Bedair H, Ting N, Jacovides C, et al: The Mark Coventry Award: Diagnosis of early postoperative TKA infection using synovial fluid analysis. *Clin Orthop Relat Res* 2011; 18(12):760-770.

Prosthetic Joint Infection (PJI)

TABLE 3 *(continued)*

Study	WBC (cells/μL)	PMN cells (%)	CRP (mg/L)	ESR (mm/h)	Patient Population	Time From Index Surgery
Della Valle et al	3,000 cells/mL	65	10	30	94 knees (41 infected)	NR
Nilsdotter-Augustinsson et al	1,700		10	30	85 knees (25 infected)	Uninfected: 9 years (range, 1–22 Infected: 3 years (range, 0.2–16.0)
Ghanem et al	1,100	64	10	30	429 knees (161 infected)	1.2 years (range, 0.1–7.8)
Schinsky et al	4,200 cells/mL	80	10	30	201 hips (55 infected)	Uninfected: 8.0 years Infected: 4.5 years (including 7 with <6 weeks)
Parvizi et al	1,100	64	10	30	296 knees (116 infected)	NR
Ghanem et al			20.5	31	479 hips (127 infected)	NR
Bedair et al	27,800	89	95		146 knees (19 infected)	< 6 weeks

Prosthetic Joint Infection (PJI)

- Synovial Fluid Analysis Continued
  - α-defensin
    - [Bingham CORR 2014]
  - Leukocyte esterase
    - [Parvizi JBJA Am 2011]

Prosthetic Joint Infection (PJI)

- Imaging
  - Radiograpahs lack findings that are specific for PJI
  - Greater than expected osteolysis or implant loosening concerning
  - Radionuclide imaging may help however $$$ and lack of specificity
  - Limited indications for CT or MRI

The 2018 Definition of Periprosthetic Hip and Knee Infection: An Evidence-Based and Validated Criteria

Javad Parvizi, MD [a,*], Timothy L. Tan, MD [a], Karan Goswami, MD [a], Carlos Higuera, MD [b], Craig Della Valle, MD [c], Antonia F. Chen, MD, MBA [a], Noam Shohat, MD [a,d]

Table 2
Simple Importance Based on Random Forest and Beta Coefficients Derived From a Multivariate Regression Analysis of Each Step.

Step	Random Forest	Beta	Standard Error	*P* Value	Score
Step 1					
Serum CRP >1 mg/dL[a]	198	2.48	0.28	<.001	2
Serum D-dimer > 860 ng/mL[a]	134	2.41	0.62	<.001	2
Serum ESR >30 mm/h	112	1.39	0.29	<.001	1
Step 2					
Synovial WBC count >3000 (cells/μL)[a]	109	2.65	0.80	.001	3
Synovial alpha-defensin	79	2.64	1.24	.041	3
Synovial LE (++)[a]	63	2.56	1.02	.017	3
Synovial PMN% >80%	47	1.73	0.92	.121	2
Synovial CRP >6.9 mg/L	22	0.85	1.12	.449	1
Step 3					
Histology[b]	17	3.21	1.02	.002	3
Purulence	12	3.47	1.32	.007	3
Single culture	8	2.25	1.45	.122	2

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LE, leukocyte esterase; PMN%, polymorphonuclear %; WBC, white blood cell.

[a] The following demonstrated a high collinearity ($r > 0.7$) and thus were grouped into a single criterion in the final model.

[b] Greater than 5 neutrophils per high-power field in 5 high-power fields observed from histologic analysis of periprosthetic tissue at 400× magnification.

Major criteria (at least one of the following)	Decision
Two positive cultures of the same organism	Infected
Sinus tract with evidence of communication to the joint or visualization of the prosthesis	

Preoperative Diagnosis	Minor Criteria	Score	Decision
Serum	Elevated CRP *or* D-Dimer	2	≥6 Infected
Serum	Elevated ESR	1	
Synovial	Elevated synovial *WBC count or LE*	3	**2-5 Possibly Infected [a]**
Synovial	Positive alpha-defensin	3	
Synovial	Elevated synovial PMN (%)	2	0-1 Not Infected
Synovial	Elevated synovial CRP	1	

Intraoperative Diagnosis	Inconclusive pre-op score *or* dry tap [a]	Score	Decision
	Preoperative score	-	≥6 Infected
	Positive histology	3	**4-5 Inconclusive [b]**
	Positive purulence	3	
	Single positive culture	2	≤3 Not Infected

Validation & Performance

Table 3
Performance of the New Definition Compare With the Traditionally Used Musculoskeletal Infection Society (MSIS) and International Consensus Meeting (ICM) Criteria.

Criteria	PJI Cohort (n = 222)			Aseptic Cohort (n = 200)			Sensitivity (95% CI)	Specificity (95% CI)
	True Positives	False Negatives	Inconclusive	True Negative	False Positives	Inconclusive		
MSIS (2011)	176 (79.3%)	46 (20.7%)	-	199 (99.5%)	1 (0.5%)	-	79.3% (73.4-84.4)	99.5% (97.3-99.99)
ICM (2013)	193 (86.9%)	29 (13.1%)	-	199 (99.5%)	1 (0.5%)	-	86.9% (81.8-91.1)	99.5% (97.3-99.99)
New definition (2018)	212 (95.5%)	5 (2.3%)	5 (2.3%)	195 (97.5%)	1 (0.5%)	4 (2.0%)	97.7% (94.7-99.3)	99.5% (97.2-99.99)

CI, confidence interval; PJI, periprosthetic joint infection.

Table 4
Proposed Thresholds Based on the 2013 ICM Combined With Current Findings.

Marker	Chronic (>90 d)	Acute (<90 d)
Serum CRP (mg/dL)	1.0	10
Serum D-dimer (ng/mL)	860	860[a]
Serum ESR (mm/h)	30	-
Synovial WBC count (cells/μL)	3000	10,000
Synovial PMN (%)	80	90
Synovial CRP (mg/L)	6.9[a]	6.9
Synovial alpha-defensin (signal-to-cutoff ratio)	1.0	1.0

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; ICM, International Consensus Meeting; PMN, polymorphonuclear; WBC, white blood cell.
[a] Further studies are needed to validate a specific threshold.

Prosthetic Joint Infection (PJI)

The Future

- Newer DNA-, RNA- tests
- Broad Spectrum PCR +/- Sonication
  - Not sure how to use these results yet
- Next-Generation Sequencing
  - Ask a lot of interesting questions, not ready for broad clinical application.
  - Do knees have native microorganisms??? [Torchia Knee 2020]
  - Are all or almost all PJI's truly polymicrobial???

Prosthetic Joint Infection (PJI)

Treatment

Prosthetic Joint Infection (PJI)

Debridement Antibiotics and Implant Retention (DAIR)

- Often in combination with modular (femoral head, poly or other bearing exchange)

- Suggested Indications:
  - Acute infection, acute post – op or acute hematogenous spread. Often 2-6 wks

  - Immunocompetent immunologically functional patient in whom a non-resistant organism has been identified

Prosthetic Joint Infection (PJI)

TABLE 6: Risk Factors for Failure of Irrigation and Débridement
Older age
Duration of symptoms >4 weeks
Presence of sinus tract or prolonged wound drainage
Staphylococcus aureus
Resistant organisms (such as methicillin-resistant *S aureus*)
Immunocompromised host (such as patients with diabetes mellitus, rheumatoid arthritis)
Nutritional deficiency
Radiographic osteitis
Radiographic component loosening

Prosthetic Joint Infection (PJI)

DAIR continued

- Results
  - Success rates greatly varied
    - 15%-60% reported
    - Potentially higher failure rates of subsequent two-stage exchange [Sherrell CORR 2011]

- Unknowns???
  - What is the role of chronic suppressive PO Abx in DAIR Procedures???

  - What is your goal, infection eradication, or stable functional joint and PO suppressive therapy?

Prosthetic Joint Infection (PJI)

Two-Stage Exchange

- Often considered the gold standard for treatment of **chronic** PJI in TKA and THA

- Substantial investment of time and resources by the patient, surgeon, and healthcare system

Results of Two-Stage

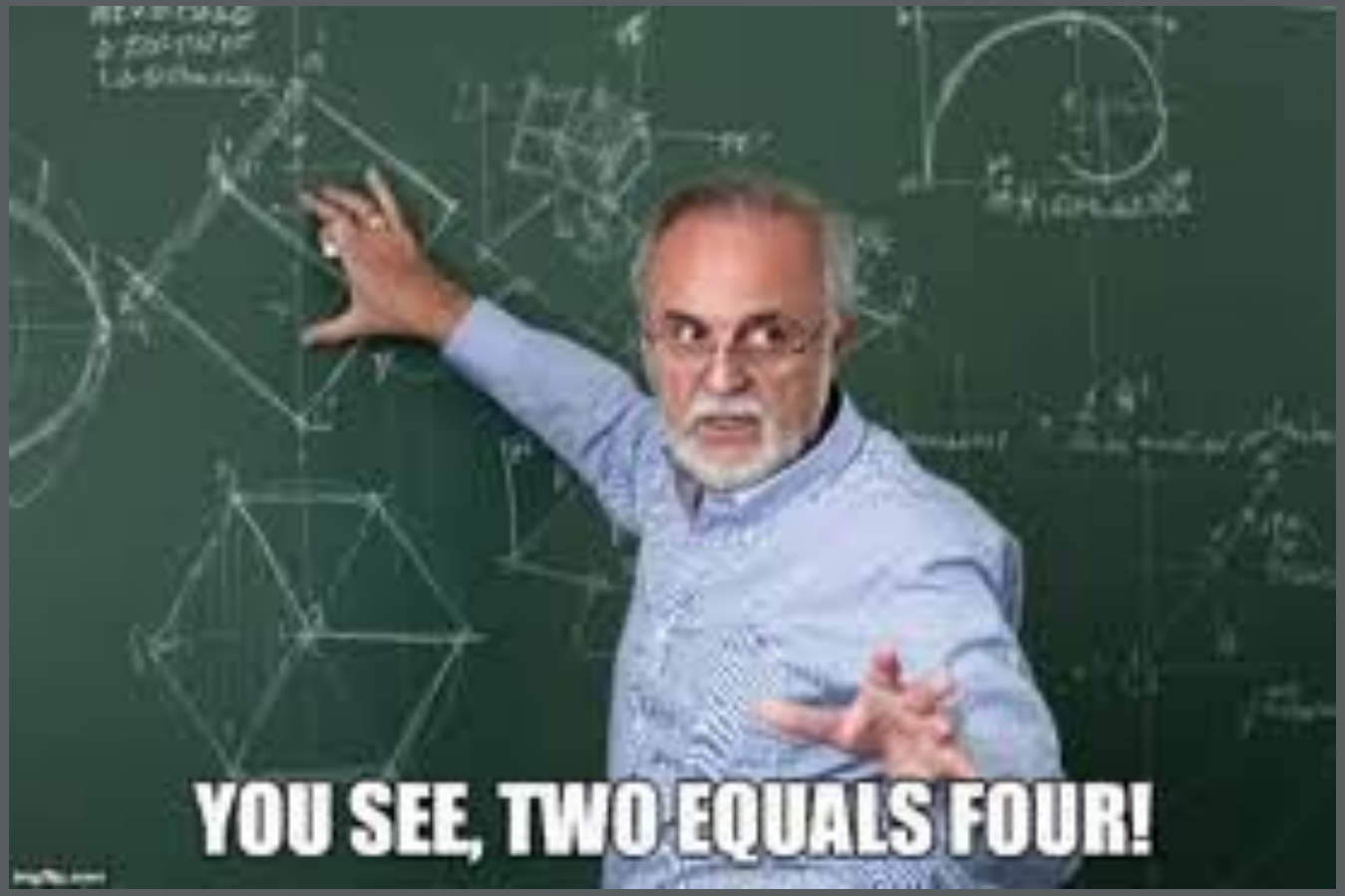
TABLE 7: Eradication Rates Following Two-Stage Revision for Periprosthetic Joint Infection

Author(s)	Year	Success Rate	Resistant Organisms	Mean Follow-up (months)
Fehring	2000	93%	NR	36.0
Durbhakula	2004	92%	20%	33.0
Haleem	2004	91%	NR	86.0
Cuckler	2005	98%	11%	NR
Hoffman	2005	88%	4%	30.0
Hart and Jones	2006	88%	2%	48.5
Kurd	2010	73%	50%	34.5
Mahmud	2012	93%	4%	48.0

NR = not reported.

Studies listed in this table originally cited in Mahmud T, Lyons MC, Naudie DD, Macdonald SJ, McCalden RW: Assessing the gold standard: A review of 253 two-stage revisions for infected TKA. *Clin Orthop Rela Res* 2012;470(10):2730-2736.

Those numbers sounded good…



Risk Factors for Repeat Debridement, Spacer Retention, Amputation, Arthrodesis, and Mortality After Removal of an Infected Total Knee Arthroplasty With Spacer Placement

Jourdan M. Cancienne, MD [a], Victor A. Granadillo, MD [a], Kishan J. Patel, DO [b], Brian C. Werner, MD [a], James A. Browne, MD [a,*]

- Medicare database patients who underwent removal of infected TKA
- Within 1 year:
  - 3.7% died
  - 4.5% knee arthrodesis
  - 3.1% amputation
  - 14.5% repeat debridement procedure without replant
  - 12.5% retained their spacer
  - 61% re-plant

Removal of an Infected Total Hip Arthroplasty: Risk Factors for Repeat Debridement, Long-term Spacer Retention, and Mortality

Jourdan M. Cancienne, MD, Brian C. Werner, MD, Surajudeen A. Bolarinwa, MD, James A. Browne, MD *

- Medicare database study patients with removal of THA for PJI

- Within 1 year
  - 6.5% died
  - 10.8% repeat debridement
  - 5.7% resection (girdlestone) arthroplasty
  - 16.8% retained spacer
  - 60.2% re-plant

Prosthetic Joint Infection (PJI)

Key Take Home Points

- If you are going to do a two stage revision with a stage 1
  - Do a good job at the stage 1 this may not be temporary
  - Consider avoiding pre-fab spacer molds
  - Do not be afraid to transfer if you do not have the resources to do this at your institution, this takes more than surgical skills, infectious disease team, outpatient coordination of IV antibiotics, social or other support, etc.

Prosthetic Joint Infection (PJI)

Single Stage Revision

- Performed in up to 85% of centers in Europe

- Pros
  - Lower overall costs
  - Faster mobilization
  - Reduced hospitalization

- Cons
  - If fails can be difficult to remove in the future
  - Radical debridement technically demanding
  - 2-set ups or other technique specific issues

Prosthetic Joint Infection (PJI)

Single Stage Revision

- Possible Contraindications
  - Culture negative PJI
  - Highly resistant organisms
  - Sepsis
  - Soft tissue flap coverage

Prosthetic Joint Infection (PJI)

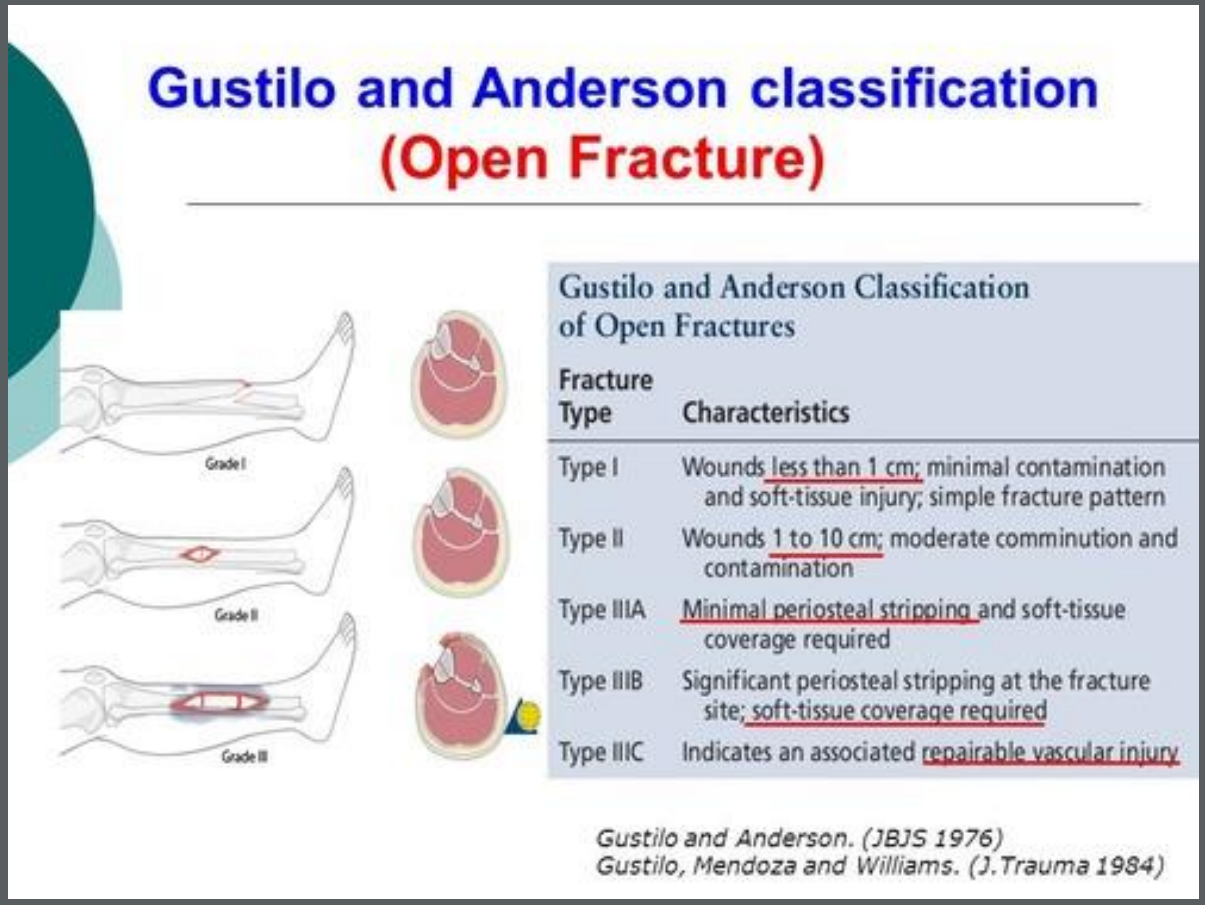
Treatment

Infections After Fracture

- Open versus Closed
  - Closed fractures are clean wounds
  - Open fractures are contaminated
    - SSI is more common in open fractures due to contamination with environmental or host microorganisms through disruption of the skin and soft-tissue envelope.

Infections After Fracture

- Classification of open fractures



Infections After Fracture

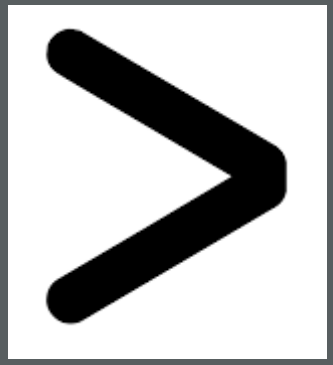
- Open fracture principles
  - Early systemic antimicrobials (single most effective intervention)
  - Thorough debridement
  - Definitive stabilization
  - Soft-tissue coverage
  - NO cultures from initial debridement

Infections After Fracture

- Open fracture principles & controversies
  - Timing of initial debridement
    - Likely short delays in surgical debridement beyond 6 hrs do no increase infection rate. [Pollak et al JBJS am 2010]
    - Severe, type IIIA and IIB preferably within 4-8 hours
    - Less severe, I&II, and some IIIA preferably within 24 hours
  - More important is timely admission to definitive trauma treatment center
  - Management of bone fragments
    - Bone fragments are likely contaminated, avascular, unprotected surfaces in an ideal environment for biofilm formation and should “generally” be removed
    - Except for large articular fragments
    - Except if you are not planning on doing the definitive fixation.

Infections After Fracture

- Irrigation
  - After a contaminated traumatic open fractures has been converted to a surgical wound with viable surfaces the remaining planktonic contamination is managed using systemic antimicrobials and irrigation
  - Irrigation is used to remove debris, excessive irrigation cannot mitigate inadequate debridement
  - Saline is preferred, if anything is added Castile soap may be considered.
  - High pressure pulsed lavage can increase the soft-tissue injury and drive contamination deeper into tissues. Gravity-flow or low-pressure irrigation is preferred. [Petrisor et al BMC Musc Disord 2008].
  - Volume
    - 3L for type 1 fractures
    - 9L For IIIB



Infections After Fracture

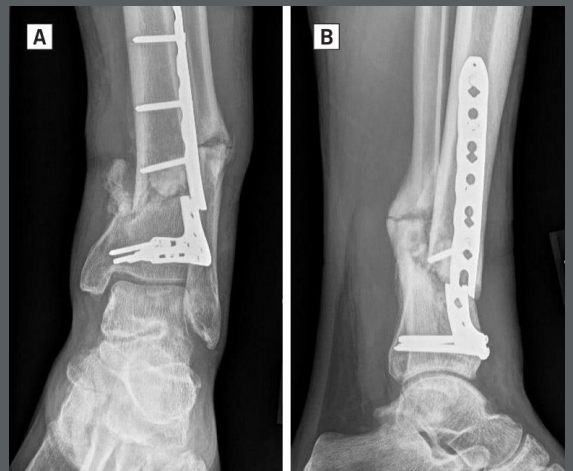
- Wound Closure / Coverage
  - Controversial
    - When soft-tissue defects exist, reconstruction with flap coverage is performed as soon as the wound is deemed ready.
    - Obtaining a reconstructed soft-tissue envelope by 1 week after injury is associated with a lower risk of infection and improved outcome. [D'Alleyrand et al JOT 2014]
  - Use and indications for negative pressure wound therapy is expanding.

Infections After Fracture

- Treatment of Infection after Fracture Fixation
  - Surgical treatment without fracture union
    - Wound debridement
    - Low-pressure irrigation
    - Stable fixation devices may be obtained until fracture union
    - If fracture union has not occurred, antimicrobial suppression and retention is recommended until fracture has united, then internal fixation devices may be removed.

Infections After Fracture

- Treatment of Infection after Fracture Fixation
  - Surgical treatment chronic infection with non-union
    - Generally 2-stage process is gold standard.
    - Wound debridement
    - Low-pressure irrigation
    - Removal of all hardware and debridement of non-union and non-viable tissue
    - Consider anti-microbial-loaded bone cement to both provide local delivery of antibiotics but to fill bone voids and add stability
    - External fixation devices or special frames can be considered additionally.



Take Home Points

- Septic Arthritis
  - Most common in children, elderly or immunocompromised
  - Early diagnosis and intervention key to reduce the risk of subchondral bone loss and permanent joint dysfunction
  - Special Situations
    - Gonococcal Arthritis
    - Crystaline arthropathy: Gout, pseudogout
    - Mycobacterial Infections
    - Borrelia burgdorferi (Lyme disease)
  - Treatment
    - Urgent surgical debridement and antimicrobial therapy

Take Home Points

- Pyomyositis
  - Infection of skeletal muscle from a hematogenous spread
  - Pre-disposing factors
    - Immunodeficiency
    - Intravenous Drug Use
    - Trauma
  - Treatment
    - Drainage, often image guided and antimicrobial therapy

Take Home Points

- Clostridial Myonecrosis
  - Urgent life / limb threatening
  - Traumatic wound with vascular compromise especially deep penetrating injuries that create an anaerobic environment for proliferation of Clostridia
  - Treatment
    - **Urgent**, aggressive surgical debridement of devitalized tissue is mandatory.
    - Anti-microbial therapy
    - Often can require multiple surgical debridement procedures over course of days

Take Home Points

- Necrotizing soft tissue infections (NSTI)
  - Urgent life / limb threatening
  - Two main types
    - **Poly**microbial (type I) NSTI, most Common (80-90%)
    - **Mono**microbial (type II) NSTI, less Common (5-10%) Group A beta-hemolytic Streptocci
  - Diagnosis is surgical debridement and biopsy
  - Treatment
    - **Emergent**, aggressive surgical debridement of devitalized tissue is mandatory.
    - Anti-microbial therapy
    - Often can require multiple surgical debridement procedures over course of days
    - Initial debridement should not be delayed for transfer to burn center

Take Home Points

- Cellulitis and Skin Abscess
  - Cellulitis
    - Most common beta-hemolytic streptocci
    - S. aureus is notable but less common
  - Skin abscess
    - S. aureus most common
  - Treatment
    - Cellulitis
      - Elevation
      - Empiric antibiotic therapy
    - Cellulitis and skin abscess
      - Incision and drainage
      - Empiric antibiotic therapy

Take Home Points

- Biofilms and surgical site infections (SSIs)
  - Conventional wisdom over the past 150 years focused on planktonic pathogens.
  - Currently most infection are no longer acute, planktonic phase infections
  - Biofilm infections are particularly difficult to culture and even small foci of microbes can cause inflammation in large areas of tissue because of secreted toxins and inflammatory mediators.
  - Clinicians must use clinical experience and consensus results from multiple diagnostic strategies.

Take Home Points

- Prosthetic Joint Infection (PJI)
  - Variable clinical presentation
  - Diagnosis can be difficult but at least we have the MSIS Criteria to help guide clinical decision making
  - Treatment (think about your patient and goals)
    - DAIR
    - Two-stage revision
    - Single-stage revision

Take Home Points

- Infections after fracture
  - Early antimicrobial administration for open fractures with prompt surgical debridement and soft tissue coverage
  - Diagnosis can be difficult but at least we have the MSIS Criteria to help guide clinical decision making
  - Treatment
    - Dependent on if union has been achieved
    - Debridement and retention of internal fixation until fracture union for acute
    - Chronic non-union = two staged process

References

- 1. Goldenberg DL. Septic arthritis. Lancet 351(9097): 197, 1998
- 2. Mathews CJ, Weston VC, Jones A, Field M, Coakley G. Bacterial septic arthritis in adults. Lancet 375(9717): 846, 2010
- 3. Margaretten ME, Kohlwes J, Moore D, Bent S. Does this adult patient have septic arthritis? JAMA 297(13): 1478, 2007
- 4. Horowitz DL, Katzap E, Horowitz S, Barilla-LaBarca ML. Approach to septic arthritis. Am Fam Physician 84(6): 653, 2011
- 5. Morgan DS, Fisher D, Merianos A, Currie BJ. An 18 year clinical review of septic arthritis from tropical Australia. Epidemiol Infect 117(3): 423, 1996
- 6. Zieger MM, Dorr U, Schulz RD. Ultrasonography of hip joint effusions. Skeletal Radiol 16(8): 607, 1987
- 7. Ryan MJ, Kavanagh R, Wall PG, Hazleman BL. Bacterial joint infections in England and Wales: analysis of bacterial isolates over a four year period. Br J Rheumatol 36(3): 370, 1997
- 8. Ross JJ, Davidson L. Methicillin-resistant Staphylococcus aureus septic arthritis: an emerging clinical syndrome. Rheumatology (Oxford) 44(9): 1197, 2005
- 9. Gardam M, Lim S. Mycobacterial osteomyelitis and arthritis. Infect Dis Clin North Am 19(4): 819, 2005
- 10. Bacon RM, Kugeler KJ, Mead PS, Centers for Disease C, Prevention. Surveillance for Lyme disease--United States, 1992-2006. MMWR Surveill Summ 57(10): 1, 2008
- 11. Dickie AS. Current concepts in the management of infections in bones and joints. Drugs 32(5): 458, 1986
- 12. Kaandorp CJ, Krijnen P, Moens HJ, Habbema JD, van Schaardenburg D. The outcome of bacterial arthritis: a prospective community-based study. Arthritis Rheum 40(5): 884, 1997
- 13. Crum NF. Bacterial pyomyositis in the United States. Am J Med 117(6): 420, 2004
- 14. Belsky DS, Teates CD, Hartman ML. Case report: diabetes mellitus as a predisposing factor in the development of pyomyositis. Am J Med Sci 308(4): 251, 1994
- 15. Chauhan S, Jain S, Varma S, Chauhan SS. Tropical pyomyositis (myositis tropicans): current perspective. Postgrad Med J 80(943): 267, 2004
- 16. Small LN, Ross JJ. Tropical and temperate pyomyositis. Infect Dis Clin North Am 19(4): 981, 2005
- 17. Niamane R, Jalal O, El Ghazi M, Hssaida R, Had A. Multifocal pyomyositis in an immunocompetent patient. Joint Bone Spine 71(6): 595, 2004
- 18. Chiedozi LC. Pyomyositis. Review of 205 cases in 112 patients. Am J Surg 137(2): 255, 1979
- 19. Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJ, Gorbach SL, Hirschmann JV, Kaplan SL, Montoya JG, Wade JC. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the infectious diseases society of America. Clin Infect Dis 59(2): 147, 2014
- 20. Maclennan JD. The histotoxic clostridial infections of man. Bacteriol Rev 26: 177, 1962

References

- 21. Hart GB, Lamb RC, Strauss MB. Gas gangrene. J Trauma 23(11): 991, 1983
- 22. Stevens DL, Bryant AE. Necrotizing Soft-Tissue Infections. N Engl J Med 377(23): 2253, 2017
- 23. Wong CH, Khin LW, Heng KS, Tan KC, Low CO. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. Crit Care Med 32(7): 1535, 2004
- 24. Bucca K, Spencer R, Orford N, Cattigan C, Athan E, McDonald A. Early diagnosis and treatment of necrotizing fasciitis can improve survival: an observational intensive care unit cohort study. ANZ J Surg 83(5): 365, 2013
- 25. McHenry CR, Piotrowski JJ, Petrinic D, Malangoni MA. Determinants of mortality for necrotizing soft-tissue infections. Ann Surg 221(5): 558, 1995
- 26. Holena DN, Mills AM, Carr BG, Wirtalla C, Sarani B, Kim PK, Braslow BM, Kelz RR. Transfer status: a risk factor for mortality in patients with necrotizing fasciitis. Surgery 150(3): 363, 2011
- 27. Mills MK, Faraklas I, Davis C, Stoddard GJ, Saffle J. Outcomes from treatment of necrotizing soft-tissue infections: results from the National Surgical Quality Improvement Program database. Am J Surg 200(6): 790, 2010
- 28. McNamara DR, Tleyjeh IM, Berbari EF, Lahr BD, Martinez JW, Mirzoyev SA, Baddour LM. Incidence of lower-extremity cellulitis: a population-based study in Olmsted county, Minnesota. Mayo Clin Proc 82(7): 817, 2007
- 29. Raff AB, Kroshinsky D. Cellulitis: A Review. JAMA 316(3): 325, 2016
- 30. Costerton W, Veeh R, Shirtliff M, Pasmore M, Post C, Ehrlich G. The application of biofilm science to the study and control of chronic bacterial infections. J Clin Invest 112(10): 1466, 2003
- 31. Yasuda H, Ajiki Y, Aoyama J, Yokota T. Interaction between human polymorphonuclear leucocytes and bacteria released from in-vitro bacterial biofilm models. J Med Microbiol 41(5): 359, 1994
- 32. Kurtz SM, Ong KL, Lau E, Bozic KJ, Berry D, Parvizi J. Prosthetic joint infection risk after TKA in the Medicare population. Clin Orthop Relat Res 468(1): 52, 2010
- 33. Parvizi J, Tan TL, Goswami K, Higuera C, Della Valle C, Chen AF, Shohat N. The 2018 Definition of Periprosthetic Hip and Knee Infection: An Evidence-Based and Validated Criteria. J Arthroplasty 33(5): 1309, 2018
- 34. Torchia MT, Amakiri I, Werth P, Moschetti W. Characterization of native knee microorganisms using next-generation sequencing in patients undergoing primary total knee arthroplasty. Knee 27(3): 1113, 2020
- 35. Cancienne JM, Werner BC, Bolarinwa SA, Browne JA. Removal of an Infected Total Hip Arthroplasty: Risk Factors for Repeat Debridement, Long-term Spacer Retention, and Mortality. J Arthroplasty 32(8): 2519, 2017
- 36. Pollak AN, Jones AL, Castillo RC, Bosse MJ, MacKenzie EJ, Group LS. The relationship between time to surgical debridement and incidence of infection after open high-energy lower extremity trauma. J Bone Joint Surg Am 92(1): 7, 2010
- 37. Petrisor B, Jeray K, Schemitsch E, Hanson B, Sprague S, Sanders D, Bhandari M, Investigators F. Fluid lavage in patients with open fracture wounds (FLOW): an international survey of 984 surgeons. BMC Musculoskelet Disord 9: 7, 2008

OHSU

Thank You