Musculoskeletal Infections Update

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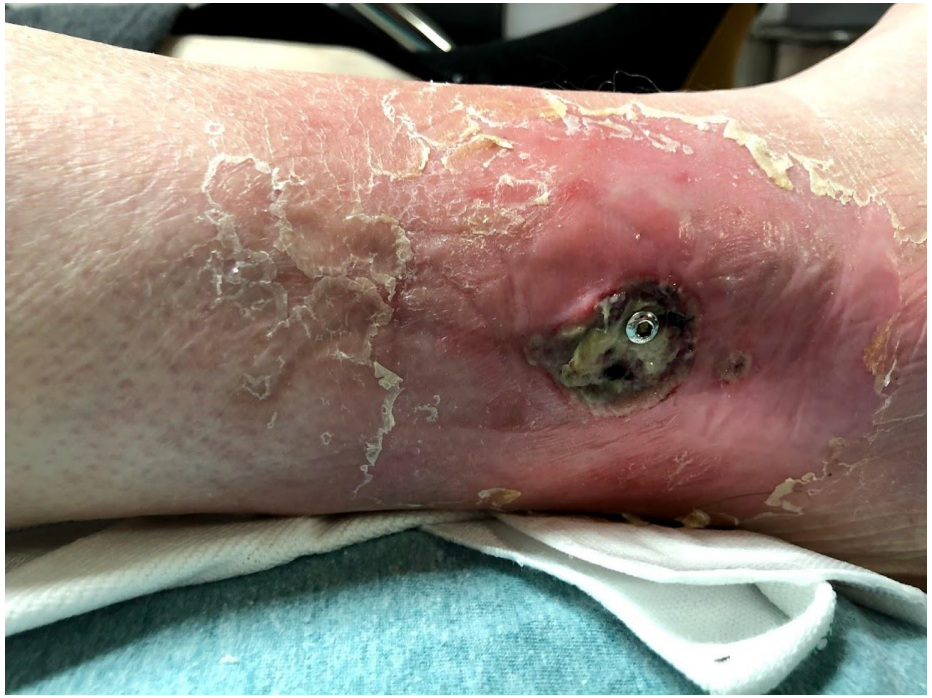
Objective

- To discuss recent research in the treatment, diagnosis, and prevention of musculoskeletal infections



Overview

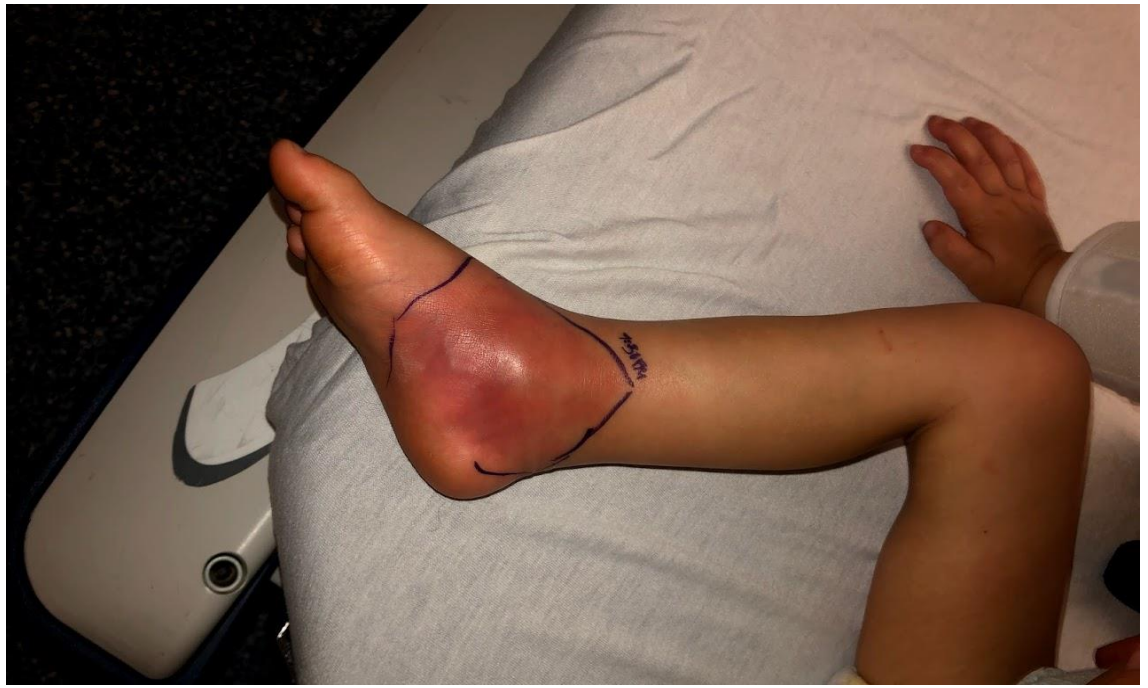
- Musculoskeletal infections are unfortunately common
- Range from mild to life and limb threatening
- Place an immense burden on healthcare resources
- Result in loss of function and productivity
- Often require multidisciplinary team to treat effectively

Outline

- Pediatrics
  - Osteoarticular Infections
  - *Kingella kingae*
- Hand
  - Flexor Tenosynovitis
  - Deep Infections
  - Open Fractures
  - Surgical Site Infection (SSI)
- Trauma
  - Open Fractures
- Spine
  - Native Spine
  - SSI
- Total Joint Arthroplasty
  - PJI Diagnosis, Treatment, Prevention

Pediatrics

- Metaphysis of children uniquely susceptible to hematogenous seeding
- 30% report history of trauma
- *Staph aureus* most common organism
- Missed or delayed diagnosis can have devastating long term sequalae

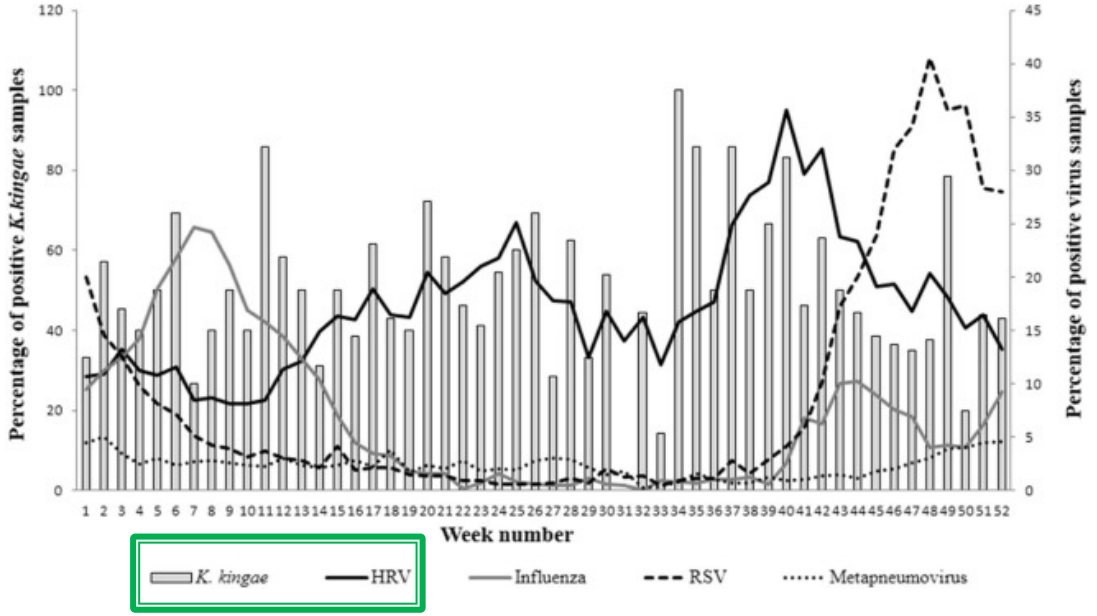


Pediatrics

- Osteoarticular infections
  - MRSA associated with more surgical procedures, more complications, longer hospital stays, and more ICU admissions when compared to MSSA
  - Patients discharged on PO antibiotics not more likely to have complications related to infections than those discharged on IV
    - In this study those discharged on PO less likely to have MRSA
  - Admissions for osteoarticular infections at one hospital decreased by 35% since introduction of pneumococcal vaccination
    - Decreased by 87% for osteoarticular disease caused by vaccine serotypes

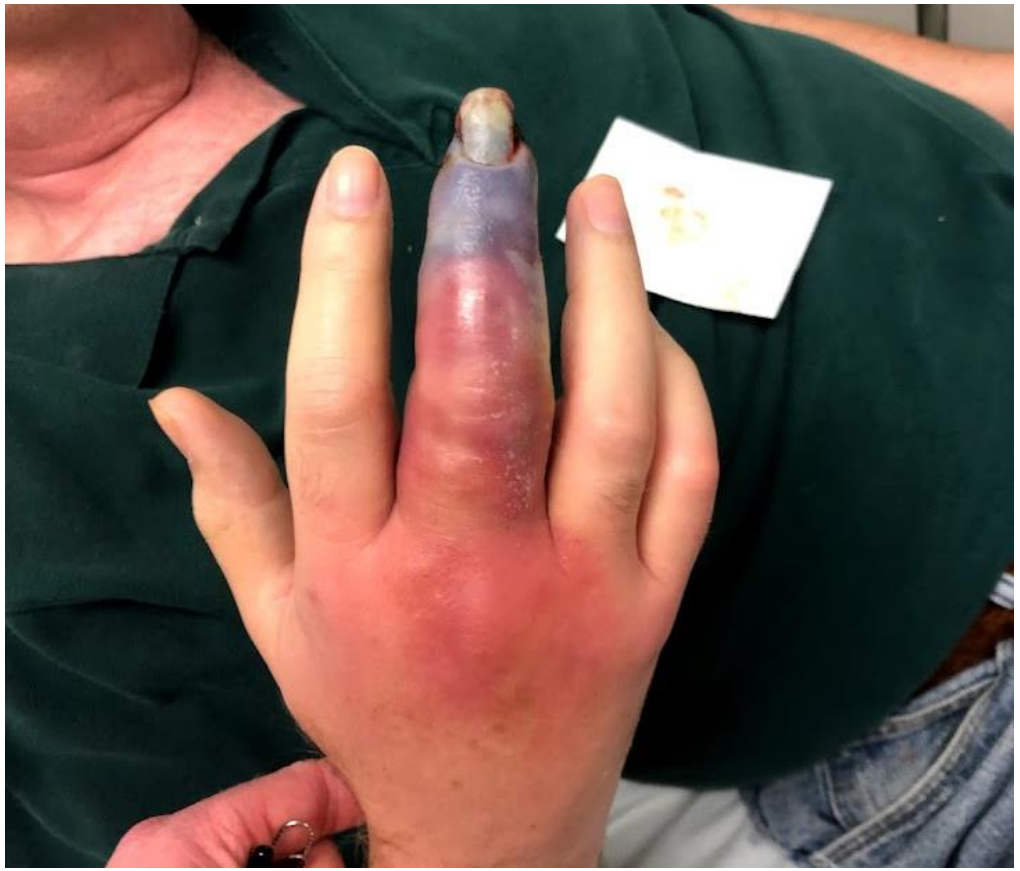
Pediatrics

- *Kingella kingae* is an emerging pathogen in patients 6 months – 4 years old
- Children with *K. kingae* osteoarticular infection 38 times more likely to have oropharyngeal carriage of *K. kingae*
- Risk for *K. kingae* associated with presence of rhinovirus



Hand

- Flexor Tenosynovitis
- Deep Infections
- Surgical Site Infections
- Open Fractures



Flexor Tenosynovitis

- Deep infection of flexor tendon sheath
- Kanavels Signs
  - Fusiform swelling
  - Tenderness over flexor tendon sheath
  - Pain with passive extension
  - Digit held in flexed posture
- Kanavels signs are sensitive (71%) but not specific
- Can be polymicrobial, but most common pathogens are *Staphylococcus* and *Streptococcus*

Flexor Tenosynovitis

- Treatment for flexor tenosynovitis includes antibiotic therapy and surgical debridement
- Delay in antibiotic therapy or infection due to *Staph aureus* associated with worse outcomes
  - Treat hospitalized patients with IV Vancomycin plus PO Quinolone or IV Ceftriaxone
    - Use Ceftriaxone if suspect gonorrhea
- 90% of patients with flexor tenosynovitis will require more than one debridement

Hand Deep Infection

- Can be caused by common pathogens like *Staph/Strep*
- Atypical infections such as *Mycobacterium tuberculosis* (TB), nontuberculous mycobacteria, and fungi also seen
  - Associated with delayed diagnosis
    - Delay of greater than 4 months associated with treatment failure
  - Some studies show that half of cases occur in healthy individuals with no obvious portal of entry or causative event
  - Treat with antimicrobials and surgery
  - Ultimately outcomes similar between immunocompromised and immunocompetent patients

Hand Deep Infection

- Order AFB cultures if…
  - Significant immunosuppression
  - Chronic or indolent infections
  - Infection not responding to antibacterials
  - Prior history of mycobacterial infection
- Consider fungal cultures if…
  - Prior open trauma
  - Significant immunosuppression
  - Chronic or indolent infections
  - Infection not responding to antibacterials
  - A prior history of fungal infections

Hand Deep Infection

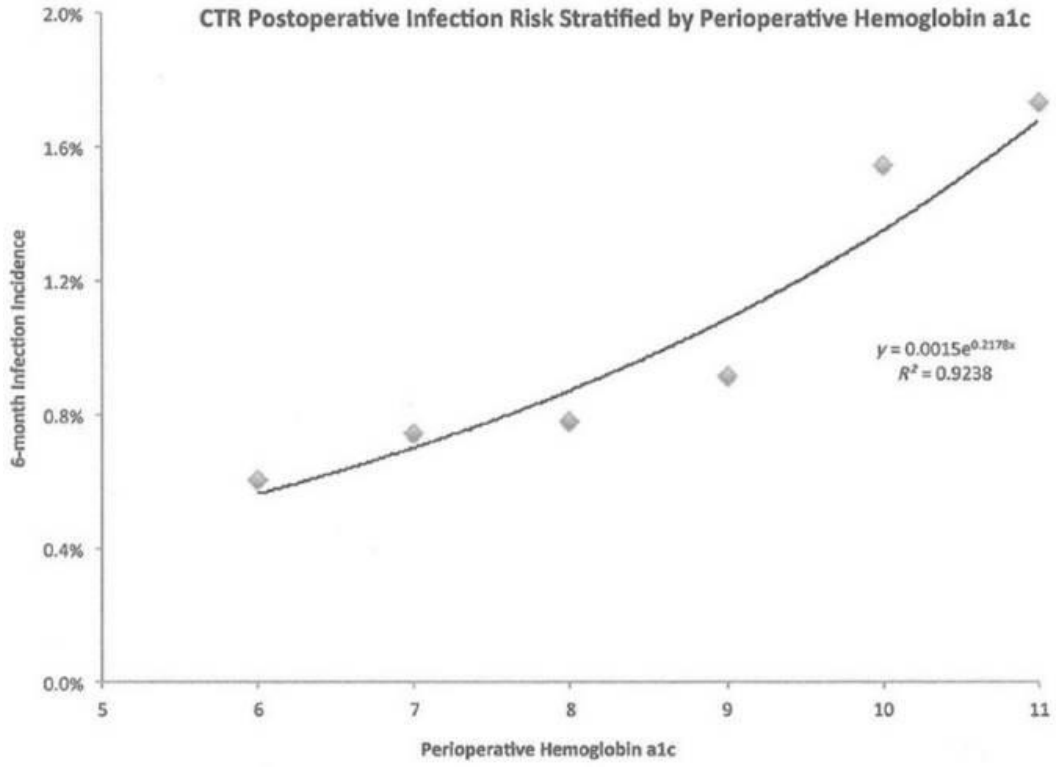
- Patients with poorly controlled diabetes more likely to have deep infections and at risk for:
  - Requiring repeat debridement
  - Amputations
  - Osteomyelitis
  - Septic arthritis
  - Necrotizing fasciitis
  - Polymicrobial infections

Hand Surgical Site Infection

- SSI after Carpal Tunnel Surgery has been shown to be .4% regardless of where performed
  - Equivalent infection rates if done in ED, office, procedure room, or OR
- Risk Factors for SSI include: young age, male sex, BMI >30, tobacco and alcohol use, peripheral vascular disease, chronic disease of kidney, liver, or lung, depression, and poorly controlled diabetes

Hand Surgical Site Infection

- Werner, et. al
  - Retrospective study
  - 7958 pts with diabetes who underwent open Carpal Tunnel Release (CTR)
  - Patients with an Hbg A1c > 8 at a significantly increased risk of SSI (p<.001)



Hand Open Fractures

- Open hand fractures not associated with greater 30-day infection risk compared with closed fracture
- Operative management of open hand fractures >1 day from presentation not associated with increased risk of infection
- Early antibiotic prophylaxis remains mainstay of open hand fractures
- Data supports decisions to delay debridement and fixation beyond traditionally held 6 hours

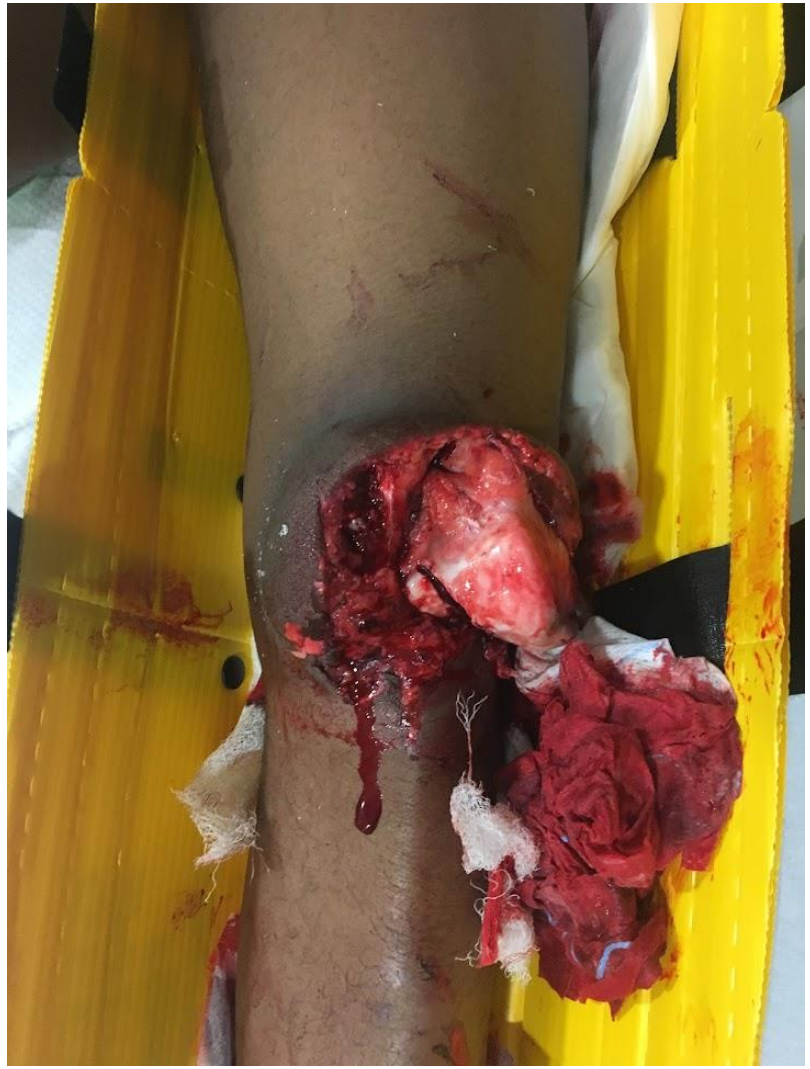
Trauma

- Open fracture treatment has dominated recent literature
- Often result of high energy trauma
- Signifies extensive soft tissue injury
- Gustillo Classification helps guide treatment and prognosis
- Type 1 infections <1% compared to as high as 30% in Type III

Gustilo classification	Description
Type I	An open fracture with a wound <1 cm long and clean.
Type II	An open fracture with a laceration >1 cm long without extensive soft tissue damage, flaps, or avulsions.
Type III	Massive soft tissue damage, compromised vascularity, severe wound contamination, marked fracture instability.
Type IIIA	Adequate soft tissue coverage of fracture despite extensive soft tissue laceration or flaps, or high-energy trauma irrespective of the size of the wound.
Type IIIB	Extensive soft tissue injury loss with periosteal strippingand bone exposure; usually associated with massive contamination.
Type IIIC	Open fracture associated with arterial injury requiring repair.

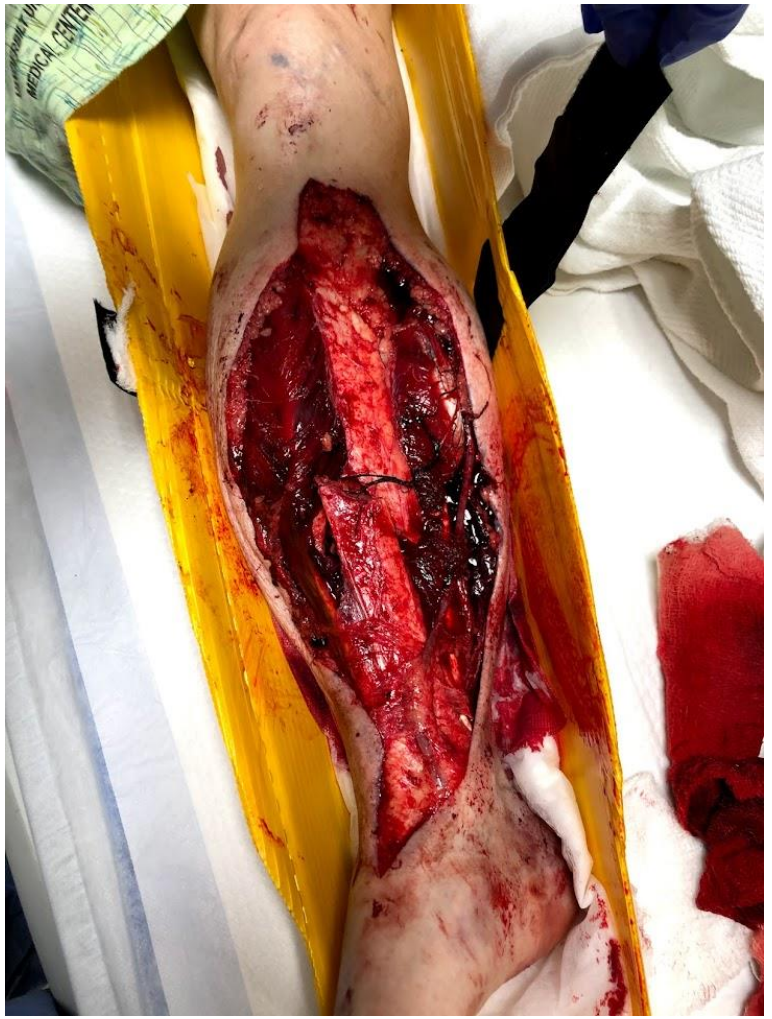
Long Bone Open Fractures

- Treatment of open fractures evolving paradigm
- Treatment begins as soon as patient presents to ED
- Early antibiotic administration important especially for severe open injuries
- 24-48hr antibiotic regimens equivalent outcomes to >72hr antibiotic regimens



Open Long Bone Fractures

- Debridement essential for open fractures
- Low pressure irrigation results in lower infection rates compared to pulsatile lavage
- Hydrojet or ultrasonic devices have been demonstrated to scatter over operative field
- New data favors early closure of wounds over delayed closure
- Coverage by 7 days results in better outcomes



A Word on Negative Pressure Wound Therapy

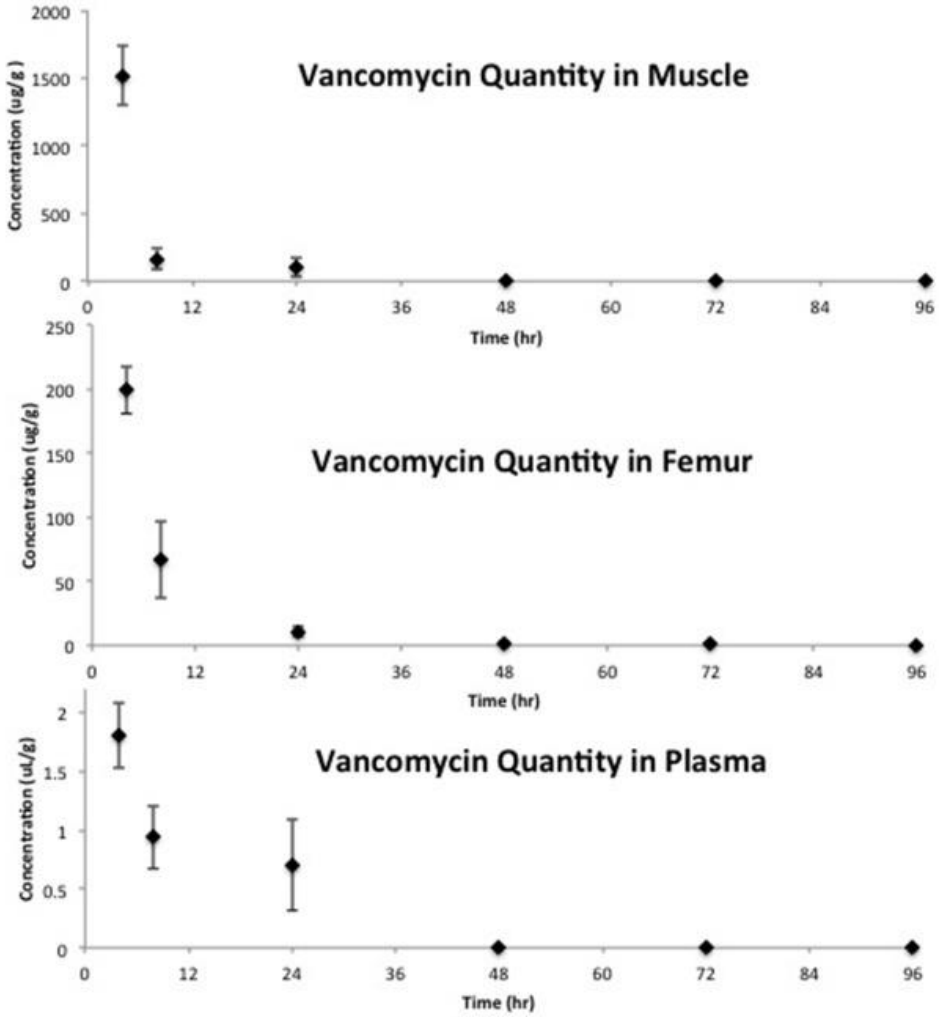
- Grant-Freemantle, et al
  - Level 1 Meta-Analysis
  - Compared NPWT with conventional dressing
  - Primary outcome of interest was deep infection
  - 9 studies and 1095 patients
  - Found significantly decreased rates of deep infection in patients with open fractures treated with NPWT
    - Decreased rates of flap failure due to infection

Local Antibiotics

- Renewed interest in using local abx in open fracture treatment
- Can consider combination systemic and local antibiotics in a carrier like polymethylmethacrylate or calcium sulfate beads, gels, or aqueous solutions
- Antibiotics can also be placed directly in the wound via Vancomycin or Tobramycin powder
  - Use topical Tobramycin with caution in patients with renal insufficiency
- Standardized use in open fractures still needs further investigation

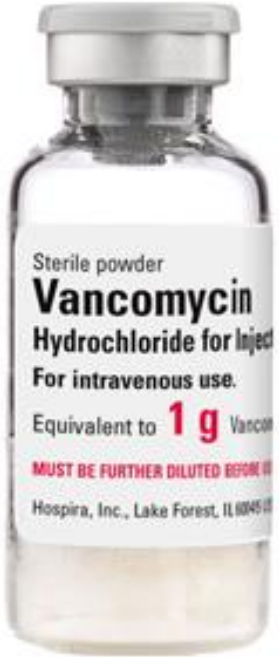
Vancomycin Powder

- Commonly used local antibiotic
- Extensive spine literature demonstrating its effectiveness at decreasing rates of infection
- In rat models: very high levels in local tissue initially, but undetectable at 96hrs after administration



Vancomycin Powder

- Patients who received intraoperative vancomycin more likely to have gram negative or polymicrobial SSI
- Increased risk of culture-negative fluid collection
- No increased risk of vancomycin resistant organisms

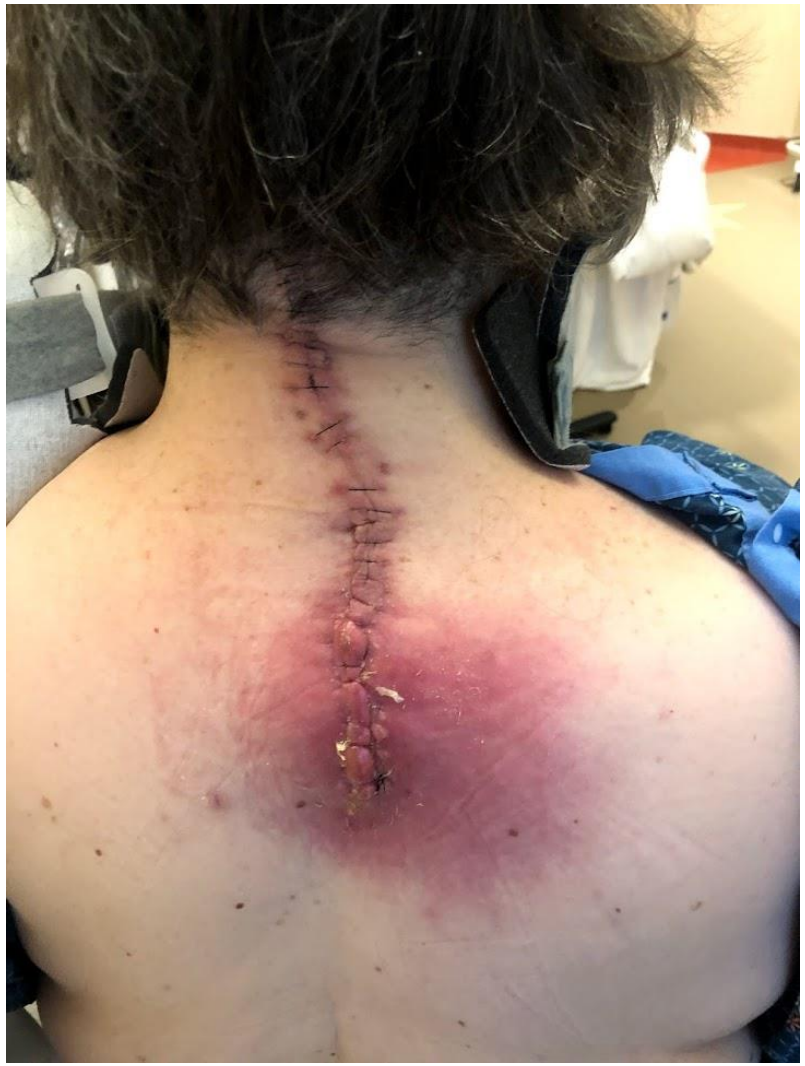


Vancomycin Powder

- Questionable benefits outside of spine
- No benefit in acetabulum ORIF
- Studies show decreased risk of PJI after total knee arthroplasty, however:
  - Questions about confounding variable
  - Possible increase in sterile wound complications
  - Authors agree that more study is needed to determine efficacy in preventing PJI

Spine

- Both native spine infections and surgical site infections can cause neurologic deficits and life-long sequelae
- Current research focusing on prevention, diagnosis, and treatment

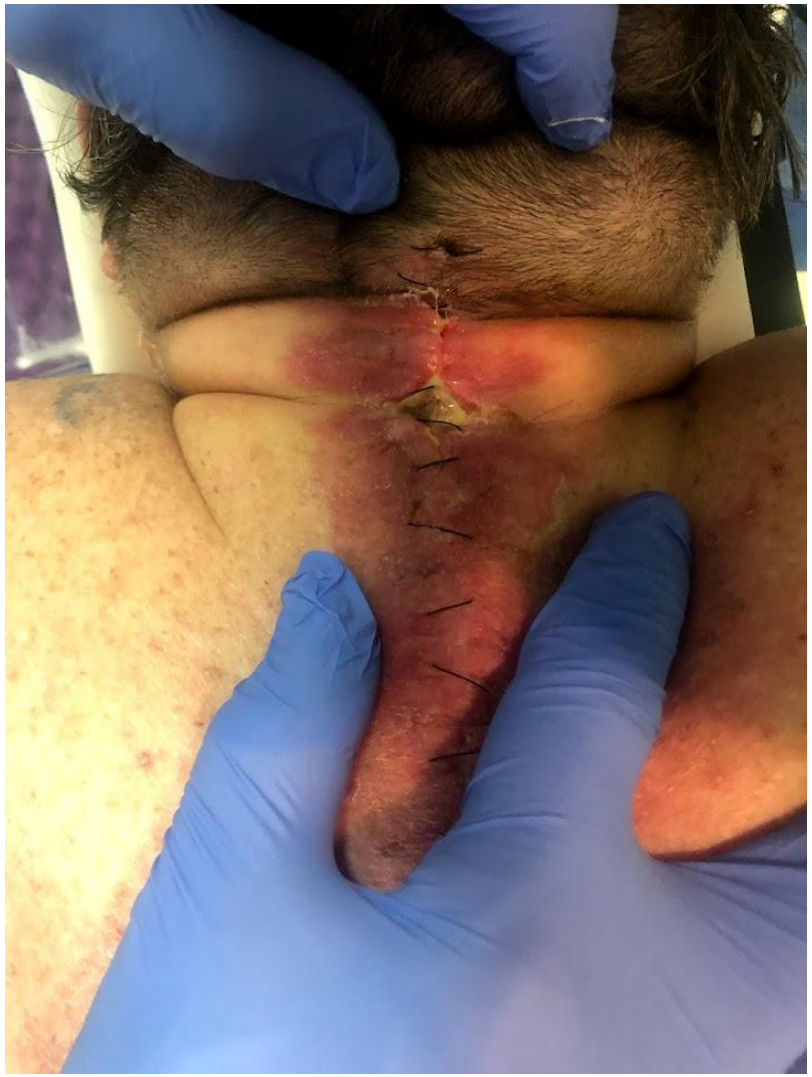


Native Spine Infections

- MRI remains gold standard but new data suggests PET may have similar sensitivity/specificity and can help identify other areas of infection
- Identification of organism very important
- CT guided biopsy identified pathogen in only 33% of cases
  - Open biopsy much better yield (91%)
- High degree of concordance between blood cultures and spine biopsy cultures
- Debate over treatment
  - Some new evidence suggests that antibiotics + surgery to drain epidural or paravertebral abscess are protective against pain and disability at 12 months

Post-op Spine Infections

- Usually occur within 3 months of index procedure
- Infection increases risk of failure of fusion up to 12 fold
- Retention of implants and MRSA infection independent risk factors for treatment failure
  - Use of rifampin when hardware retained protective against failure

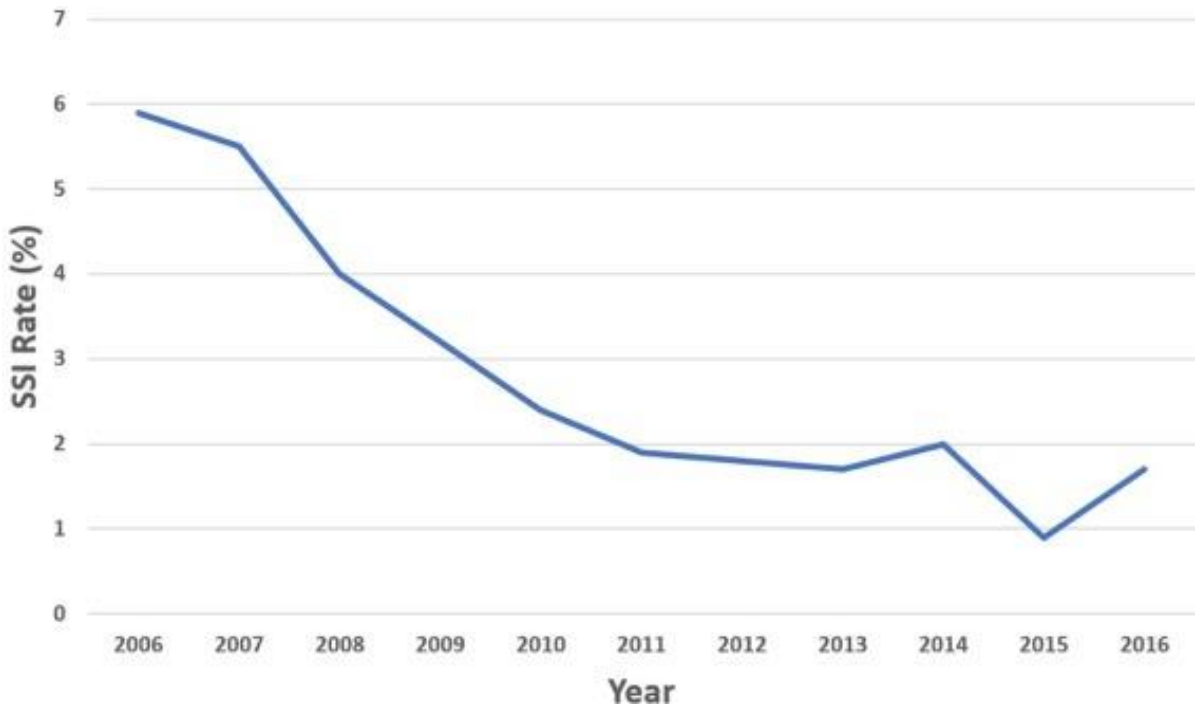


Post-op Spine Infections

- Prevention is key
- Recent study identified 5 preventative techniques:
  - Intrawound vancomycin powder
  - Dilute betadine irrigation
  - Preoperative chlorhexidine scrubs
  - Preoperative nasal screening and decolonization of *S. aureus*
  - Perioperative antibiotic administration

Post-op Spine Infections

- Tomov, et al
  - Single center study implemented 5 techniques
  - Saw a decrease in surgical site infections for laminectomy and fusions
  - Authors argue that trend of decreasing infections demonstrates that these simple, cost-effective interventions can decrease the rate of spine infections

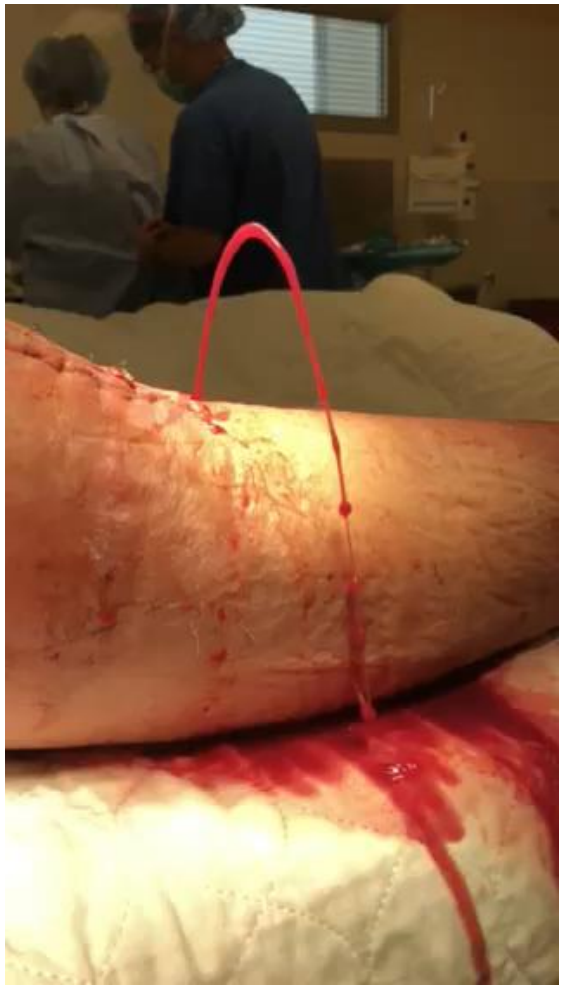


Prosthetic Joint Infection (PJI)

- Increasingly important as number of total joint replacements continues to rise precipitously and with it associated costs
  - Predicted 1.26M TKA and 635K THA by 2030
  - Cost of PJI approaching 2 billion yearly
- Presents a huge burden on the healthcare system and patients

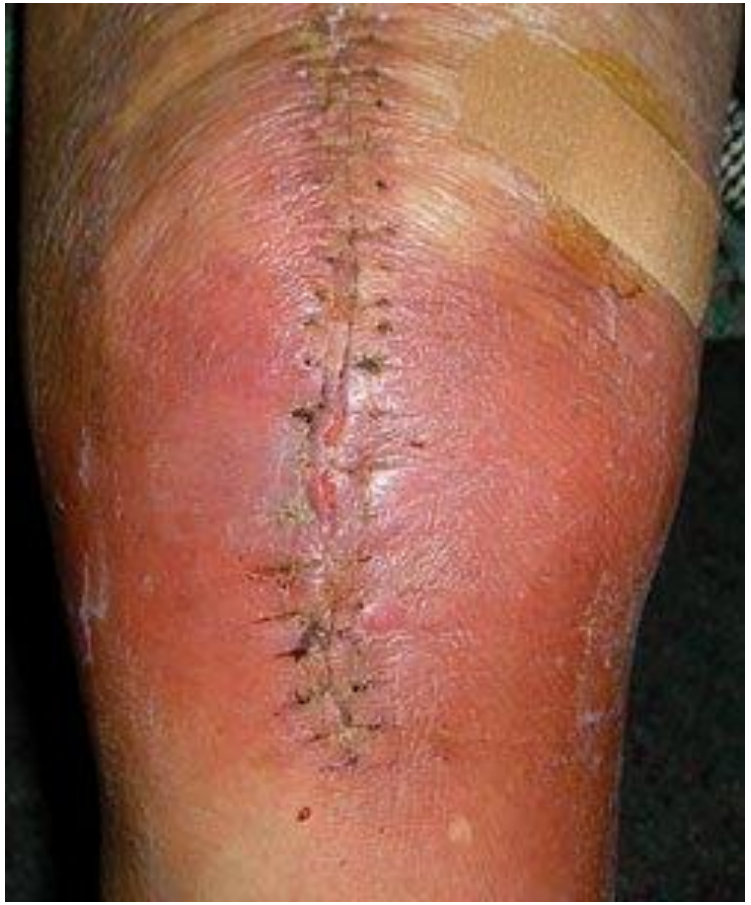
Prosthetic Joint Infection

- Rate of PJI remains largely unchanged over last 15 years
- Important to discern between acute and chronic infection, which present and are treated differently



Acute Prosthetic Joint Infection

- Defined as <90 days post op by CDC
- Confined to joint space
- No bone-implant interface invasion
- Stereotypical red, hot, swollen knee
  - Fevers, increasing erythema, wound drainage
- No biofilm formation

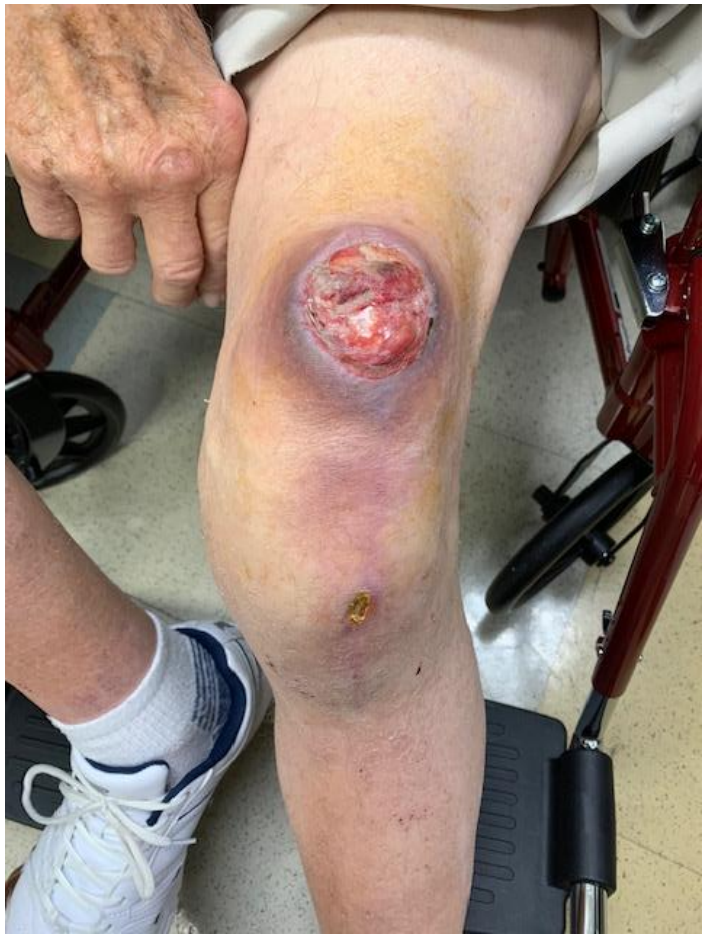


Acute Hematogenous PJI

- Similar presentation to acute PJI
- Same diagnostic criteria
- Can occur anytime post op
- Symptoms present <10-14 days
  - Fevers, chills, rapidly progressive pain/inability to bear weight
- No biofilm formation

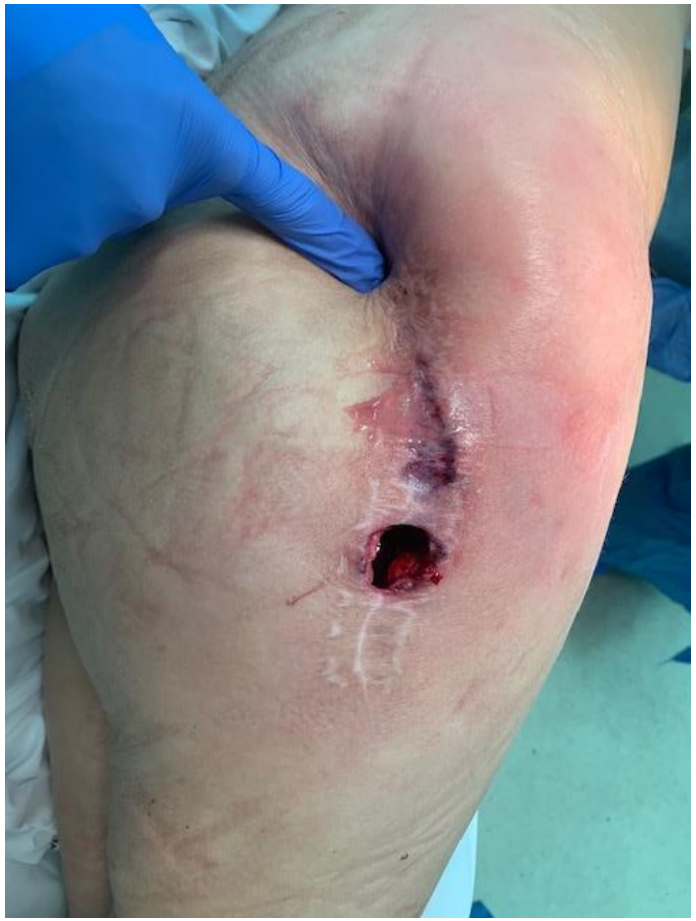
Chronic PJI

- Greater than 3 months post op
- Longer duration of symptoms
  - >2-4 weeks
- Biofilm has formed
- Invasion of bone/implant interface



Diagnosing PJI

- Evaluation
  - Acute post-op infection
    - Fevers, increasing erythema, prolonged wound drainage
  - Acute hematogenous infection
    - Fevers, chills, rapidly progressive pain/inability to bear weight
  - Chronic
    - Draining sinus
    - Pain, recurrent effusions, refractory stiffness
    - Component loosening/dislocation on x-ray



Diagnosing PJI

- Work has been done to develop better yield from cultures as well as develop biomarkers for diagnosis
- Alpha Defensin has been shown to be the most accurate biomarker currently available
  - 90% sensitivity and 95% specificity
- Use of saline solution lavage has been demonstrated to be beneficial in dry taps
  - Both for cultures and %PMN's

Current Criteria for Diagnosing PJI

- 2018 ICM/MSIS Criteria
- Simplified thresholds from previous criteria
  - 3000 PMN's on aspirate for chronic
  - 10,000 PMN's for acute infection (first 6 weeks)
  - CRP >1 mg/dl, ESR >30, %PMN>80%
- Added Alpha Defensin as criterion

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	

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

	*Inconclusive pre-op score *or* dry tap	Score	Decision
Postoperative Diagnosis	Preoperative score	-	≥6 Infected
	Positive Histology	3	4-5 Inconclusive**
	Positive Purulence	3	
	Positive Single Culture	2	≤3 Not Infected

* For patients with inconclusive minor criteria, operative criteria can also be used to fulfill definition for PJI for PJI.
**Consider further molecular diagnostics such as Next-generation sequencing.

Fig. 2

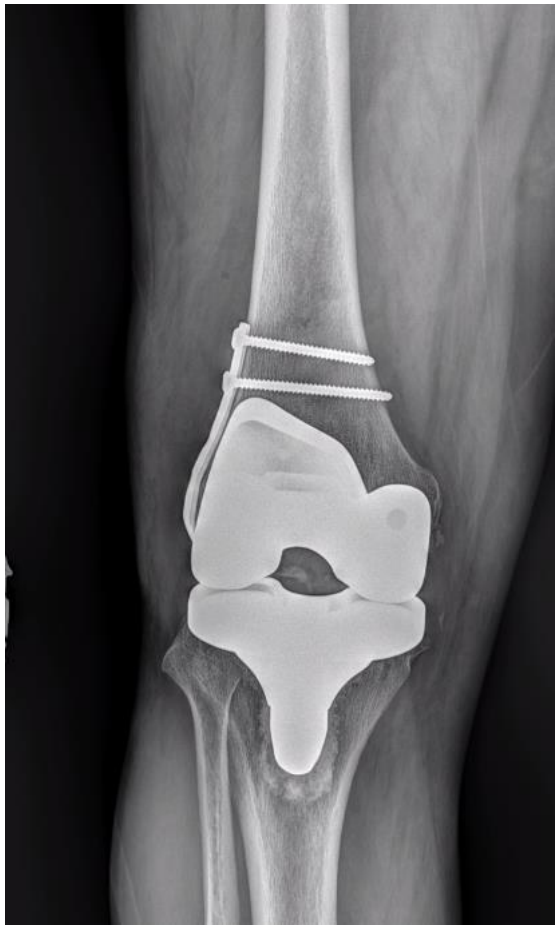
The 2018 validated and score-based ICM definition for PJI [15] (Reprinted with permission from "The 2018 Definition of Periprosthetic Hip and Knee Infection: An Evidence-Based and Validated Criteria." The Journal of Arthroplasty. Elsevier; 2018; License Number 4332741333898)

PJI Treatment

- Acute Post-op/Acute Hematogenous
  - Irrigation and debridement with liner exchange
  - Targeted IV antibiotic therapy
  - Course of oral antibiotics
- Chronic
  - Gold Standard is 2 stage revision
  - Stage 1 is removal, extensive debridement and irrigation, placement of antibiotic spacer
  - Treat with 6 weeks IV abx, followed by 2 week antibiotic holiday and confirmation of infection free knee by ESR/CRP and aspiration
  - Stage 2: reimplantation
  - Follow reimplantation with 3 months of oral prophylaxis

PJI Future Treatment

- 1 stage revision for chronic PJI a major focus right now
- Done in Europe
- Combines 2 stages into one OR day
- Randomized control trial currently underway in the United States



1 Stage Revision for PJI

- Involves 2 OR set ups
- Establish culture and sensitivity pre-op
- Step 1 first OR setup
  - Removal of hardware and I&D of soft tissue and bone
  - Intensive irrigation protocol involving 9L of NaCl, H_2O_2, and dilute betadine
  - Close over a betadine soaked lap
  - Take down drapes and remove first setup

1 Stage Revision for PJI

- Step 2
  - Completely new set up with new instruments
  - Re-prep and re-drape
  - Implant new implants
  - Irrigate again with 3L NaCl, H_2O_2, dilute betadine
  - Antibiotic course based on pre-op culture and sensitivity

1 Stage Revision for PJI

- Multicenter RCT is ongoing comparing 1 and 2 stage revisions
- Other studies have shown positive results for 1 stage revisions
  - Ji et al showed 89.2% of patients infection free at 58 month follow up
  - Zahra et al showed 10yr infection free survival of 94% of patients
  - Abdelaziz et al showed 89% of patients infection free at mean follow up of 4 years
- Risk factors for failure include
  - Previous revision for PJI
  - *Streptococcus* and *Enterococcus* species

Risk Factors for PJI

- Huge body of literature dedicated to identifying risk factors for PJI
  - Increased BMI
  - Uncontrolled diabetes
  - Lower socioeconomic status
  - Pre-op albumin below 3.5mg/dl
  - Previous PJI in a different joint
  - Transfusion
  - Longer surgical time
  - Foley catheter use

Prevention of PJI

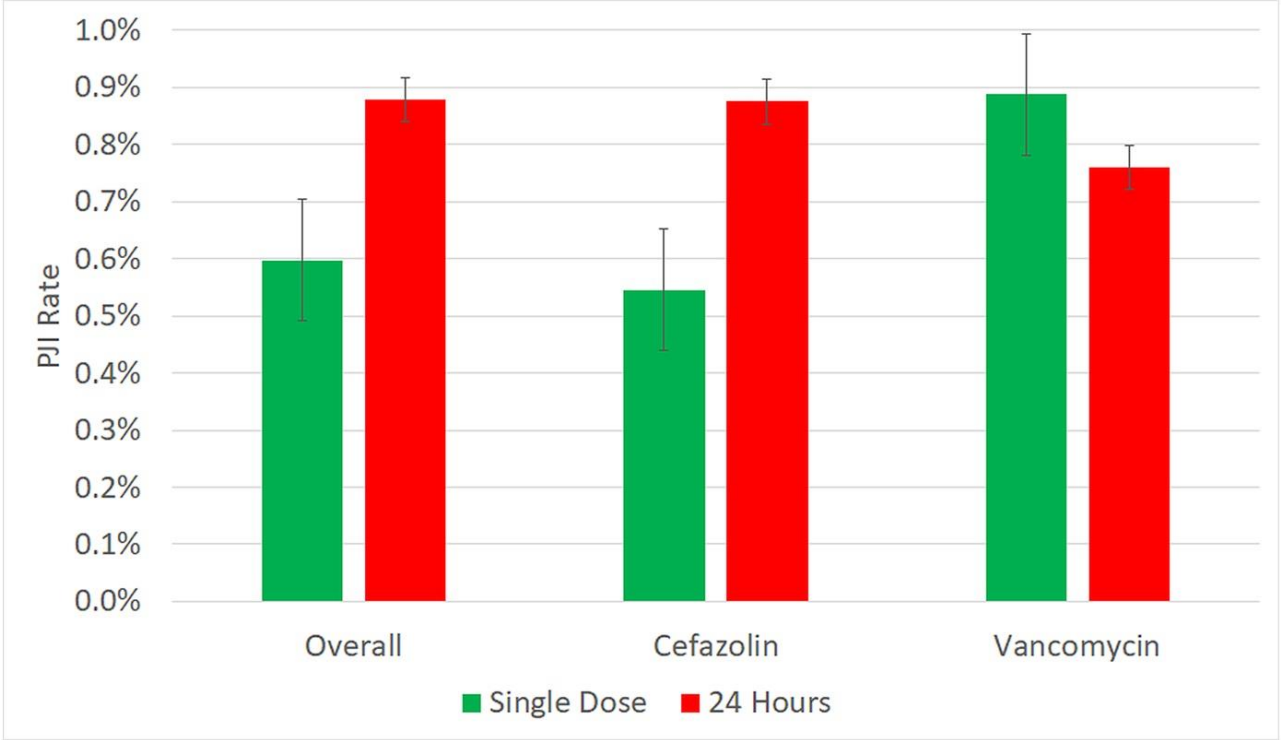
- Equally large body of work gone into preventing infection
- Changing patient modifiable risk factors
- Studies show long term glycemic control important
- Perioperative dexamethasone has been shown to have a significant increase in postoperative glucose levels in diabetics
  - Has not yet been tied to increased rates of infection

Prevention of PJI

- A great deal of effort has gone into studying irrigants
  - One study compared providone-iodine, chlorhexidine, H2O2, Dakins, and chlorine dioxide and their effectiveness in reducing *S. aureus* colonies on common orthopaedic materials
    - Found that H2O2 and providone iodine were most effective, removing 97% and 98% of colonies respectively
  - Other studies have shown that chlorhexidine, dilute providone-iodine, and saline solution were effective and safe for infection prevention
  - Real world data on the efficacy of additives, especially dilute providone-iodine, is mixed

Prevention of PJI

- Data supports use of preoperative antibiotics
  - Strong recommendation for pre-op antibiotics
  - Post operative antibiotics not recommended
  - Tan et. Al
    - Large scale metanalysis shows one dose of preop antibiotics as effective as 24 hrs of perioperative antibiotics



Prevention of PJI

- Multiple studies show that increased length of surgery associated with increased rates of PJI
- Low rates of bacterial burden on OR field in cases less than 120 minutes
- Cases over 90 minutes associated with increased rate of PJI
- Wang et al suggests 25% increase in PJI risk for every 20 additional minutes of OR time

Prevention of PJI

- Data suggest that antibiotic cement is effective for decreasing infection after revision but is mixed on its utility during primary TJA
- Use of a joints hood has no effect on rates of PJI
- Tranexamic acid, which reduces blood loss and transfusion requirements, has been shown to reduce rates of PJI

Conclusion

- Despite advances, musculoskeletal infections continue to be a burden on patients and the health care system
- Altering modifiable risk factors, strict sterile technique, correct diagnosis, thorough debridement, and appropriate antibiotic selection are essential to combating infection

Many Thanks to Dr. Thomas Freeman!

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Questions?

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