



# Infectious Disease for the Orthopedics Team

LAURA DAMIOLI, MD

DIRECTOR OF ORTHOPEDIC INFECTIOUS DISEASES

ASSOCIATE PROFESSOR

UNIVERSITY OF COLORADO

# Disclosures

▶ None

# Objectives

Learn

Pre-op optimization to prevent infection

Improve

Choosing appropriate antibiotics

Improve

Approach to DFI

Understand

Treatment options for joint infections

# Overview

- ▶ Orthopedic Infections have extremely high morbidity and mortality
  - ▶ PJI – 5-yr – 20% mortality (Stanton, 2017)
  - ▶ Spine – 10-20% (Geisler Crone et al., 2021)
  - ▶ DFI >25% at 5 yrs (Armstrong et al., 2020)

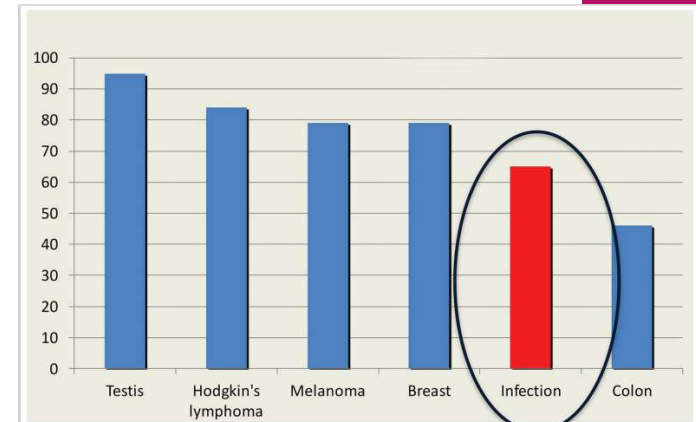


Fig. 2 Five-year survival rate for PJI and the five most commonly diagnosed (U.S.) cancers. COURTESY OF JAVAD PARVIZI, MD, FRCS/ROTHMAN INSTITUTE AT THOMAS JEFFERSON UNIVERSITY

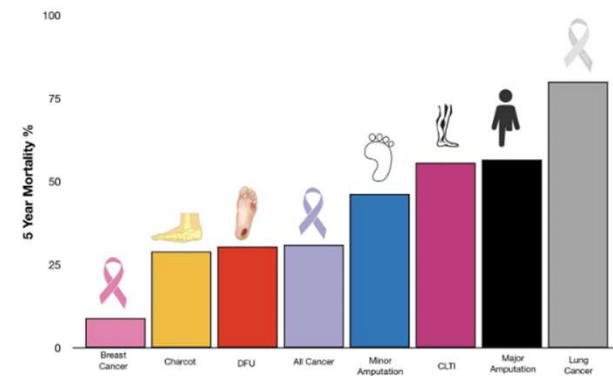


Fig. 1 Five Year Mortality of Diabetic Foot Complications and Cancer. Diabetic foot complications compared to cancer. DFU = diabetic foot ulcers [11] = 30.5%. Charcot = Charcot neuroarthropathy of the foot [14]. All Cancer = pooled 5 year survival of all cancers [11]. CLTI = chronic limb threatening ischemia [28, 29]. Major Amputation = above foot amputation [20-22, 26, 27]. Minor Amputation = foot level amputation [17, 27]



# Prevention

# Risk Factors for Post-op Infection (just a few)

## Modifiable

- ▶ Tobacco abuse
- ▶ Obesity/metabolic syndrome (1.5x)
- ▶ A1c>7
- ▶ Malnutrition (alb<3.5)
- ▶ Poor oral health
- ▶ Vit D deficiency
- ▶ Iron Def Anemia (1.75-2.5x)

## ? modifiable

- ▶ PCN Allergy
- ▶ Immunosuppressant use

## Non-modifiable

- ▶ Prior surgery (2.4x)
- ▶ Auto-immune disease (1.5x)
- ▶ Age
- ▶ Male gender (1.5-2x)

# Dental Screening

- ▶ Incidence of dental pathology in TJA patient population is 8-23%
- ▶ Patients who need dental clearance
  - ▶ Tobacco use
  - ▶ Narcotic use
  - ▶ Not having seen a dentist in 12 months
  - ▶ H/o extracted teeth
  - ▶ Older age
  - ▶ Flossing <1x per day



Lampley et al Arthroplasty 29(6): 1087, 2014  
Tokarski et al J Arthroplasty 29(9): 1729, 2014

# Dental Screening



Transient bacteremia occurs following oral hygiene activities such as tooth brushing and flossing.



PJI due to oral bacteria have been reported in the literature however a direct association with periodontal disease and PJI is controversial



Most authors advocate for preoperative dental treatment in patients with known dental pathology, though routine dental screening has not been supported in the literature



# Dental Screening: Recommendations

- ▶ Author Recommendations:

- ▶ Screen for high-risk patients with specific risk factors for dental pathology
- ▶ Require pre-operative dental clearance in these patients

- ▶ ICM Philly 2018:

- ▶ “There is a small yet real risk of hematogenous spread of oral pathogens to patients undergoing arthroplasty. Patients with poor oral hygiene undergoing arthroplasty are at increased risk of subsequent SSI/PJI. Therefore, patients with oral disease and poor dentition should be identified and optimized prior to elective arthroplasty.”
- ▶ 92% agreement

# PCN Allergy

- Reported penicillin and/or  $\beta$ -lactam allergy is very common (10% of the population)
  - Majority are not true allergies (GI upset, headache, etc.)
  - 95% do not have an IgE mediated allergy
  - Most patients with  $\beta$ -lactam allergy can safely receive cefazolin
- Multiple studies have demonstrated an increased risk of SSI in patients who are PCN-allergic
  - Up to 50% increased risk
- Preoperative allergy evaluation and penicillin skin testing is useful!
  - 97% of allergic pts cleared to use cefazolin
  - Preoperative allergy evaluation is cost effective



Blumenthal *et al.* Clin Infect Dis 2018; 66: 329  
Wyles *et al.* Bone Joint J 2019;101-B:9–15.  
Spangehl. J Arthroplasty 2022; 37:1432-1434  
(Liu *et al.*, 2023)

# Why Does PCN Allergy Matter?

- Alternative: Vanc or Clinda
- Multiple studies have demonstrated the inferiority of vancomycin
  - Vancomycin often dosed and timed incorrectly
    - ▶ Only 28% of patients receiving vancomycin prophylaxis for TJA received appropriate doses in one study
    - ▶ Majority do not receive vancomycin in the recommended time frame
      - ▶ PJI rate is higher when vancomycin started late and/or not completed
  - Higher rate of nephrotoxicity



Kheir *et al.* CORR 2017; 475: 1767–1774  
Blumenthal *et al.* Clin Infect Dis 2018; 66: 329-36  
Burger *et al.* J Arthroplasty 2018; 33: S213  
Ponce *et al.* JBJS 2014; 96: 970-7  
Zastrow *et al.* J Arthroplasty 2020; 35(9): 2581-2589  
Marigi *et al.* J Bone Joint Surg Am. 2022;104:872

# What about Clindamycin?

- Better pharmacokinetics than vancomycin
- Mayo case series, 2000-2019 (7713 TSA)
  - ▶ Odds of PJI vs cefazolin: HR 5.07 for all-cause PJI (8.01 for *C. acnes*)
- Major issue is the antimicrobial spectrum as well as resistance
  - ▶ Resistance in *Staphylococcus aureus*, *Staphylococcus epidermidis*, beta-hemolytic streptococci

# PCN Allergy Recommendations

- ▶ Question the allergy
  - ▶ Childhood reactions, family reactions, do they remember it?
  - ▶ Remove the allergy for non IgE mediated reactions – can list as intolerance
- ▶ Refer to Allergy prior to surgery





# Antibiotic Selection

# How to Pick an Antibiotic

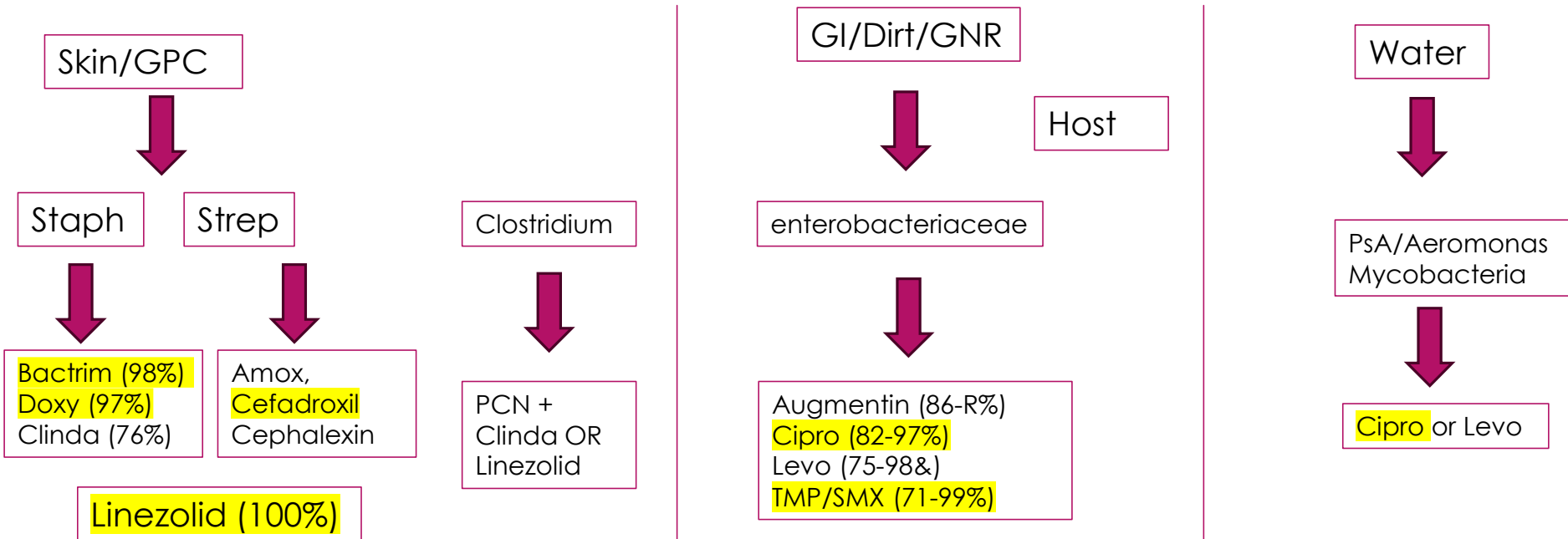
What are you trying to cover?

- Skin flora, GI flora/dirt contamination, water

Consider the Host

Potential Side Effects

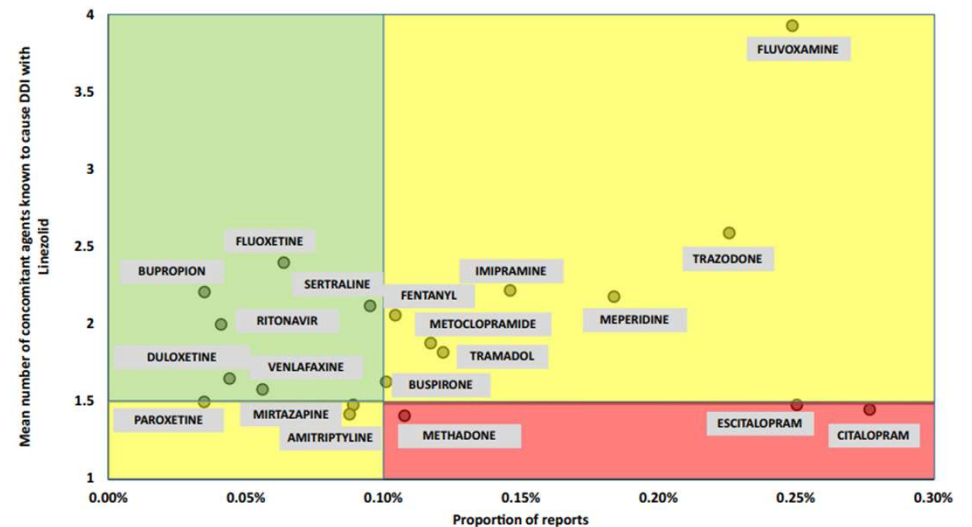
# My Algorithm





# Linezolid and Serotonin Syndrome

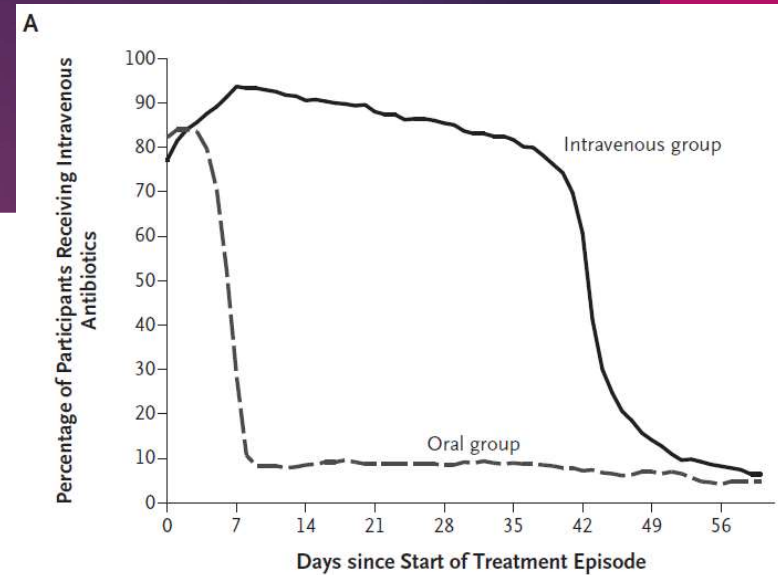
- ▶ Incidence is rare
- ▶ Karkow 2017 reported on 348 pts
  - ▶ 87 with combo, 261 received linezolid alone
  - ▶ 1 pt in each group developed serotonin syndrome
- ▶ Risk increases if >2 serotonergic agents used
- ▶ Warn patients of early s/s
  - ▶ agitation, restlessness, shivering, HA, diarrhea



(Catti et al., 2021)

# OVIVA

- ▶ Prospective randomization to IV or PO abx at 26 centers in UK
  - ▶ 1054 participants -> 527 each group
    - ▶ ~1/3 chronic OM without HW
    - ▶ 23% DAIR
    - ▶ ~20% HW removed
    - ▶ ~4% vertebral OM
- ▶ Primary Endpoint: definitive treatment failure within 1 year
- ▶ Secondary Endpoint: Adverse Events

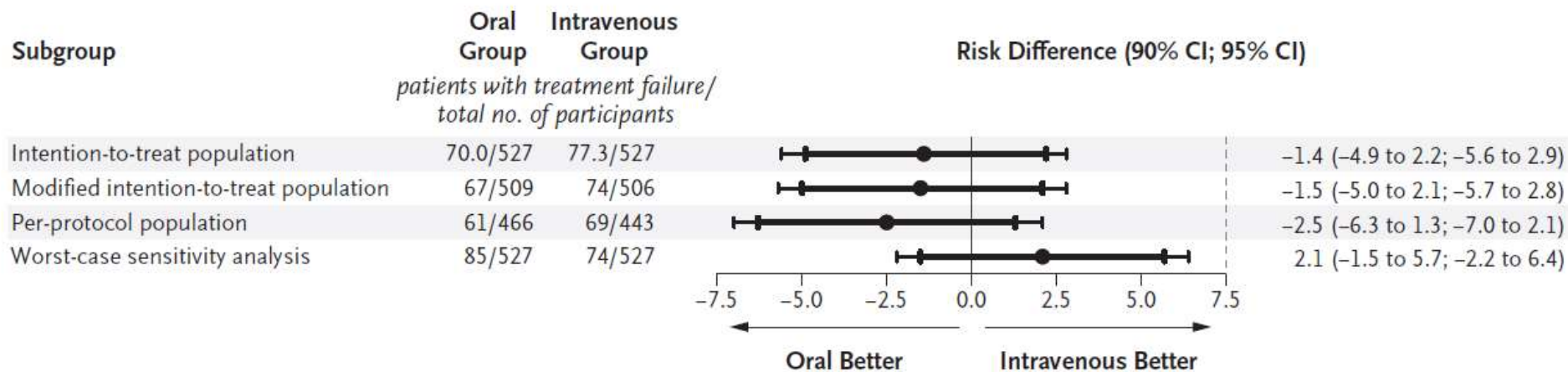


- ▶ Sinus tract or purulence near bone/prosthesis
- ▶ Isolation of identical bacterial isolate
- ▶ Inflammatory infiltrate or bacteria noted on path

# OVIVA con't

► **PO is noninferior to IV**

- 74 failures in IV group => 14.6%
- 67 failures in PO group => 13.2%



# Real World OVIVA

- ▶ Patients with PJI 12 months pre and post implementation of OVIVA
  - ▶ Guided by ID physician, followed by OPAT team
  - ▶ 145 pre patients
  - ▶ 183 post patients -> 66.1% switched to po

# Real World OVIVA

**Table 3. Clinical Outcome Defined as Definite Failure at 1 Year**

Clinical Outcome	Preimplementation (n = 145)	Postimplementation (n = 183)	Postimplementation Subgroups	
			IV (n = 62)	Oral (n = 121)
Lost to follow-up, No.	0	0	0	0
Deaths, No.	4	5	1	4
Not curative intent, No.	1	6	1	5
Evaluable patients, No.	140	172	60	112
Definite failures at 1 y, % (No.)	13.6 (19)	18.6 (32)	26.7 (16)	14.3 (16)

▶ Failure at one year

▶ Pre: 13.6%

P=0.154

▶ Post: 18.6%

▶ More common with lack of good oral options

▶ Median LOS reduced by 4 days -> \$3756.24 saved per patient

INFECTED DFI



**I. Neuropathic uninfected ulcer**

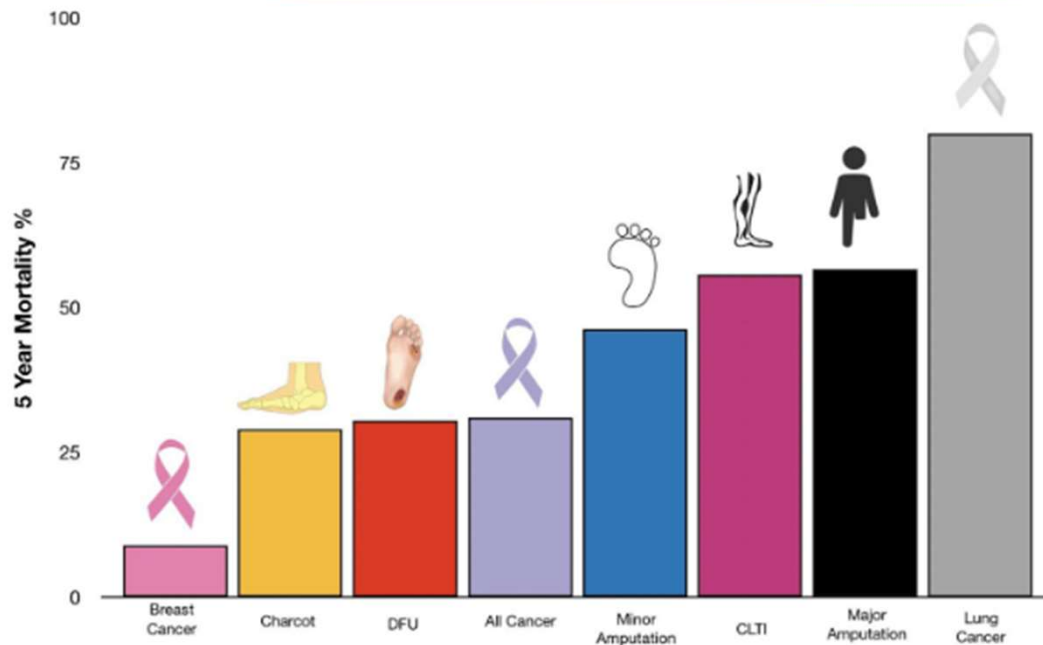


# Diabetic Foot Infections

<http://www.antimicrobe.org/e26.asp>;

<http://www.antimicrobe.org/printout/e26printout/e26causes.htm>

# Why DFI Matters



**Fig. 1** Five Year Mortality of Diabetic Foot Complications and Cancer. Diabetic foot complications compared to cancer. DFU = diabetic foot ulcers [11] = 30.5%. Charcot = Charcot neuroarthropathy of the foot [14]. All Cancer = pooled 5 year survival of all cancers [11]. CLTI = chronic limb threatening ischemia [28, 29]. Major Amputation = above foot amputation [20–22, 26, 27]. Minor Amputation = foot level amputation [17, 27]

D. G. Armstrong et al.  
*Journal of Foot and Ankle Research*(2020)

## Comprehensive approach to diabetic foot infections



\*Society for Vascular Surgery Wound, Ischemia, foot Infection (WIFI) score

(Cortes-Penfield et al., 2023)



# DFI – Key Points

- ▶ Aseptic Culture
- ▶ Imaging (xray, mri), Probe-to-bone
- ▶ CRP, ESR
- ▶ 1-2 weeks for soft tissue; if improving but slowly can extend to 3-4 weeks
- ▶ 6 weeks for OM; can shorten if debrided without source control
- ▶ Consider the Pathogens
  - ▶ Mild Infection: *Staph*, *Strep*
  - ▶ Moderate/Severe: Gram negative, PsA if wet environment
    - ▶ Anaerobes?

(Senneville et al., 2024)

# How to Culture per IDSA

## ▶ Do

- Culture almost all infected wounds
- Cleanse and debride the wound before obtaining specimen(s) for culture
- Obtain a tissue specimen for culture by scraping with a sterile scalpel or dermal curette (curettage) or biopsy from the base of a debrided ulcer; **E-swab**

• **Aspirate any purulent secretions** using a sterile needle and syringe

• **Promptly send specimens**, in a sterile container or appropriate transport media, for aerobic and anaerobic culture

## ▶ Do not

- Culture a clinically uninfected lesion, unless for specific epidemiological purposes
- **Swab the wound or wound drainage**
- **Culture without cleansing or debriding**

## Probe To Bone

Technique, experience, the ulcer's location, and its etiology may affect reliability.

Sensitivity = 87%

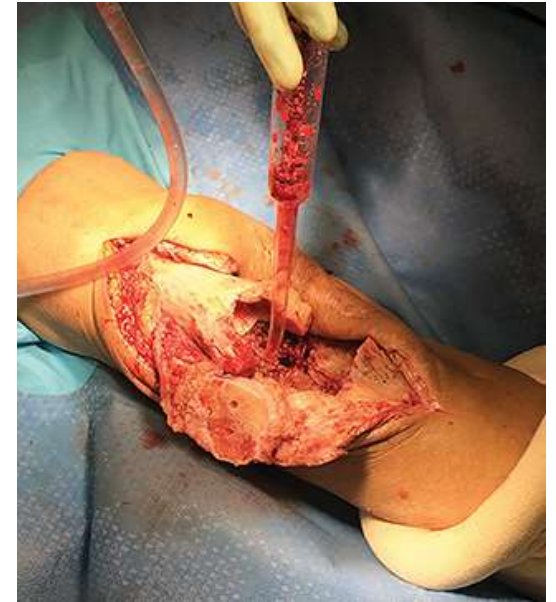
Specificity = 83%



# PJI/Septic Arthritis

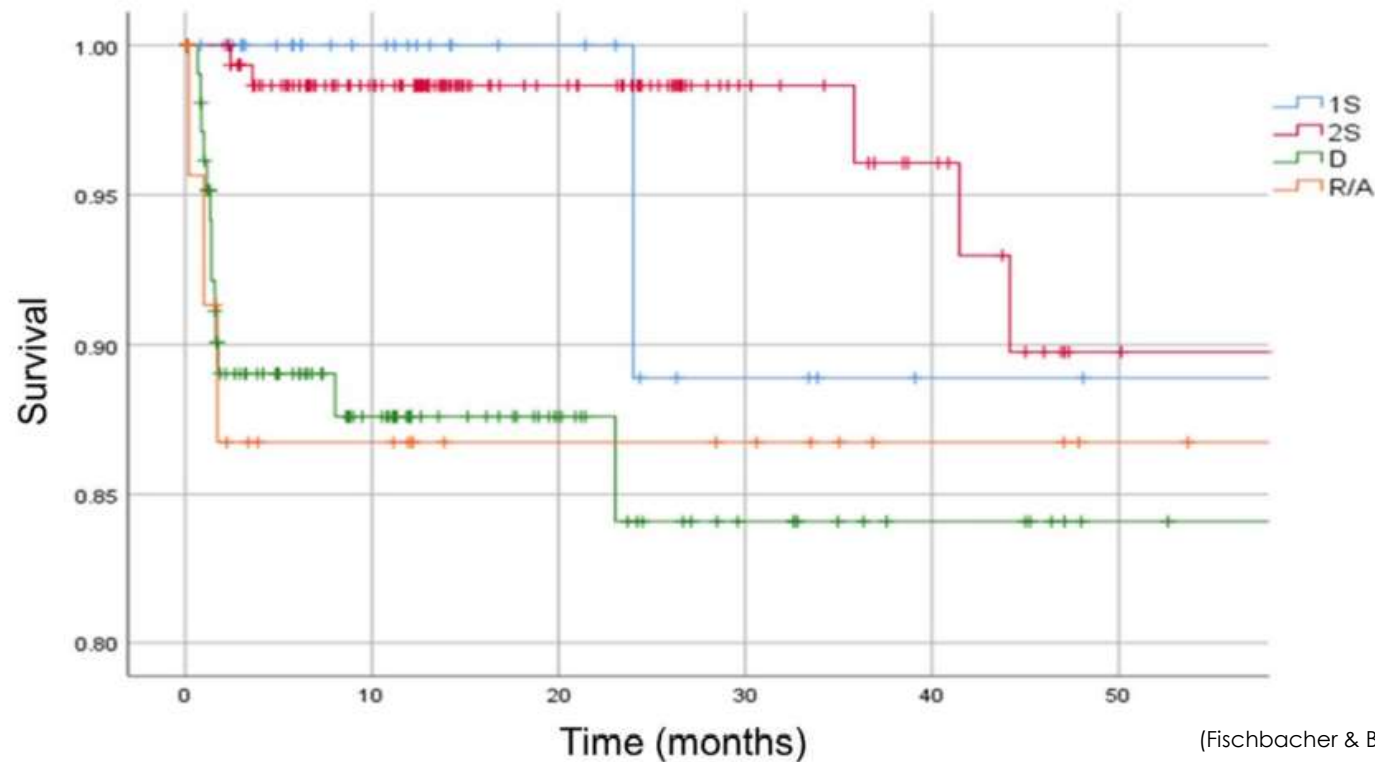
# PJI Surgical Treatment Options

- ▶ DAIR/washout/poly-swap
  - ▶ success rate of 14%–100%
  - ▶ Thought better if from hematogenous spread
  - ▶ Worse outcomes with MRSA, GNR, MSSA without rif use
- ▶ 1 stage
  - ▶ 80-90% success, linked to extent of debridement
- ▶ 2 stage
  - ▶ 87% success



(Stanton, 2017)

# What's the Best Surgical Approach?

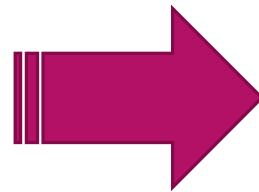


(Fischbacher & Borens, 2019)

**Figure 7.** Kaplan-Meier survival curve. The analysis is separated in different types of surgical treatment. Vertical marks indicate censoring. 1S = one-stage exchange, 2S = two-stage exchange, D = debridement, R/A = removal or arthrodesis.

# PJI Treatment Options

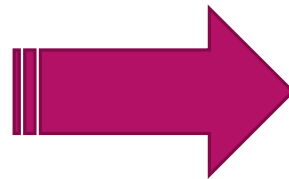
- ▶ Washout/DAIR/Poly-swap
- ▶ 1-stage



6 weeks IV abx with rifampin (if staph)  
followed by orals with rif

- ▶ TKA: total 6 months
- ▶ THA and others: total 3 months
- ▶ Consider indefinite suppression

- ▶ 2-stage



6 weeks IV abx

**GONORRHEA CAUSES  
BLINDNESS - ARTHRITIS  
INVALIDISM AND MISERY  
IT CAN BE PREVENTED AND CURED**

For Examination and Free Pamphlets  
Consult your Doctor or Dept. of Health Clinic  
ST. GEORGE 6 STUYVESANT PLACE  
STATEN ISLAND CASE F. NO. NC PROJECT



# Septic Arthritis

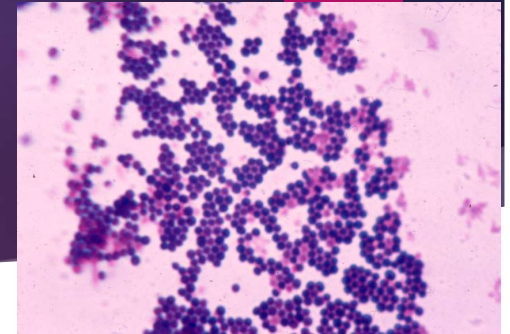


# Gonococcal Septic Arthritis

- ▶ *Neisseria gonorrhoea* and monitor the shoulder
  - ▶ Gram stain and culture are negative in 50% cases
    - ▶ Consider triple site GC/CT testing in work-up of high risk patients
      - ▶ 80% patients with gonococcal septic arthritis have a positive mucosal test NAAT
    - ▶ Unable to get NAAT of synovial fluid performed
  - ▶ Treatment: 10 days of IV Ceftriaxone *after* clinical improvement is noted
    - ▶ If you cannot get an urgent ID appointment then send pt to the ER
    - ▶ Oral therapy can only be used if you have sensitivities (rare)
    - ▶ Surgery is rarely needed

(Bardin, 2003)

# Non-gonococcal Septic Arthritis



- ▶ *Staph aureus* septic joint -> urgent surgery
  - ▶ >50k wbc's with hot/painful joint, GPCs on gram stain are most likely SA
  - ▶ Even though this is fairly chronic SA is always an urgent manner; joint destruction and risk of bacteremia (Elsissy et al., 2020)
    - ▶ SA bacteremia has a 90-day mortality of 33% (van der Vaart et al., 2022)
  - ▶ Treatment: 2-6 weeks antibiotics (traditionally IV but PO becoming more popular – more to come on this)
- ▶ If Synovial WBC was less, ~30k, depending on the story you should wait for more culture information -> this could be a CoNS and gout for example

# Abx effect on Arthrocentesis

Median Laboratory Values of Treated and Untreated Patients.

Diagnostic Test	Treated (n = 13)		Untreated (n = 36)		P-Value
	Median	IQR (Q2-Q3)	Median	IQR (Q2-Q3)	
Inflammatory markers					
CRP (mg/L)	22	13-61	105	49-196	.006 <sup>a</sup>
ESR (mm/h)	45	36-63	47	30-61	.931
Synovial fluid					
Synovial WBC count (cells/ $\mu$ L)	4,473	1,664-15,288	57,591	15,200-101,189	.003 <sup>a</sup>
Synovial neutrophil percentage (%)	76	56-86	94	88-97	.004 <sup>a</sup>
Synovial ANC (cells/ $\mu$ L)	2,804	634-8,605	50,748	14,572-93,270	<.001 <sup>a</sup>

- ▶ Median duration of abx = 4 days
- ▶ Normal cut-offs don't apply

(Dugdale et al., 2022)

Thanks!



# References

- ▶ Alamanda, V. K., & Springer, B. D. (2018). Perioperative and Modifiable Risk Factors for Periprosthetic Joint Infections (PJI) and Recommended Guidelines. *Current Reviews in Musculoskeletal Medicine*, 11(3), 325-331. <https://doi.org/10.1007/s12178-018-9494-z>
- ▶ Armstrong, D. G., Swerdlow, M. A., Armstrong, A. A., Conte, M. S., Padula, W. V., & Bus, S. A. (2020). Five year mortality and direct costs of care for people with diabetic foot complications are comparable to cancer. *J Foot Ankle Res*, 13(1), 16. <https://doi.org/10.1186/s13047-020-00383-2>
- ▶ Bardin, T. (2003). Gonococcal arthritis. *Best Practice & Research: Clinical Rheumatology*, 17(2), 201-208. [https://doi.org/10.1016/s1521-6942\(02\)00125-0](https://doi.org/10.1016/s1521-6942(02)00125-0)
- ▶ Cortes-Penfield, N. W., Armstrong, D. G., Brennan, M. B., Fayfman, M., Ryder, J. H., Tan, T. W., & Schechter, M. C. (2023). Evaluation and Management of Diabetes-related Foot Infections. *Clinical Infectious Diseases*, 77(3), e1-e13. <https://doi.org/10.1093/cid/ciad255>
- ▶ Dugdale, E. M., Uvadich, M. E., Osmon, D. R., Pagnano, M. W., Berry, D. J., & Abdel, M. P. (2022). Recent Antibiotic Treatment Impacts Serum and Synovial Laboratory Values in Early Periprosthetic Joint Infection Workup. *Journal of Arthroplasty*, 37(6s), S286-s290. <https://doi.org/10.1016/j.arth.2022.02.064>
- ▶ Fischbacher, A., & Borens, O. (2019). Prosthetic-joint Infections: Mortality Over The Last 10 Years. *J Bone Jt Infect*, 4(4), 198-202. <https://doi.org/10.7150/ijbji.35428>
- ▶ Frey, C., Navarro, S. M., Blackwell, T., Lidner, C., & Del Schutte, H., Jr. (2019). Impact of dental clearance on total joint arthroplasty: A systematic review. *World J Orthop*, 10(12), 416-423. <https://doi.org/10.5312/wjo.v10.i12.416>
- ▶ Gatti, M., Raschi, E., & De Ponti, F. (2021). Serotonin syndrome by drug interactions with linezolid: clues from pharmacovigilance-pharmacokinetic/pharmacodynamic analysis. *European Journal of Clinical Pharmacology*, 77(2), 233-239. <https://doi.org/10.1007/s00228-020-02990-1>
- ▶ Geisler Crone, C., Mose Tefens, M., Bengaard Andersen, A., Obel, N., & Lebech, A.-M. (2021). Clinical characteristics of pyogenic vertebral osteomyelitis, and factors associated with inadequate treatment response. *International Journal of Infectious Diseases*, 108, 487-493. <https://doi.org/10.1016/j.ijid.2021.05.078>
- ▶ Karkow, D. C., Kauer, J. F., & Ernst, E. J. (2017). Incidence of Serotonin Syndrome With Combined Use of Linezolid and Serotonin Reuptake Inhibitors Compared With Linezolid Monotherapy. *Journal of Clinical Psychopharmacology*, 37(5), 518-523. <https://doi.org/10.1097/jcp.0000000000000751>
- ▶ Liu, M. Y., McCoul, E. D., Brooks, E. G., Lao, V. F., & Chen, P. G. (2023). Inaccurate penicillin allergy labels: Consequences, solutions, and opportunities for rhinologists. *Int Forum Allergy Rhinol*, 13(6), 973-978. <https://doi.org/10.1002/alr.23173>
- ▶ Osmon, D. R., Berbari, E. F., Berendt, A. R., Lew, D., Zimmerli, W., Steckelberg, J. M., Rao, N., Hanssen, A., Wilson, W. R., & Infectious Diseases Society of A. (2013). Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. *Clinical Infectious Diseases*, 56(1), e1-e25. <https://doi.org/10.1093/cid/cis803>
- ▶ Seok, H. G., Park, J. J., & Park, S. G. (2022). Risk Factors for Periprosthetic Joint Infection after Shoulder Arthroplasty: Systematic Review and Meta-Analysis. *J Clin Med*, 11(14). <https://doi.org/10.3390/jcm11144245>
- ▶ Senneville, É., Albalawi, Z., van Asten, S. A., Abbas, Z. G., Allison, G., Aragón-Sánchez, J., Embil, J. M., Lavery, L. A., Alhasan, M., Oz, O., Uçkay, I., Urbančič-Rovan, V., Xu, Z. R., & Peters, E. J. G. (2024). IWGDF/IDSA guidelines on the diagnosis and treatment of diabetes-related foot infections (IWGDF/IDSA 2023). *Diabetes/Metabolism Research and Reviews*, 40(3), e3687. <https://doi.org/10.1002/dmrr.3687>
- ▶ Stanton, T. (2017). PJI and Cancer: More Similar Than Different? AAOS Now[Aug 2017].
- ▶ Tokarski, A. T., Patel, R. G., Parvizi, J., & Deirmengian, G. K. (2014). Dental clearance prior to elective arthroplasty may not be needed for everyone. *Journal of Arthroplasty*, 29(9), 1729-1732. <https://doi.org/10.1016/j.arth.2014.04.018>
- ▶ Walocha, D., Bogdan, P., Gordon, A. M., Magruder, M. L., Conway, C. A., Razi, A. E., & Choueka, J. (2023). Risk factors for the development of a peri-prosthetic joint infection up to 2 Years following primary reverse shoulder arthroplasty. *J Orthop*, 35, 69-73. <https://doi.org/10.1016/j.jor.2022.11.007>