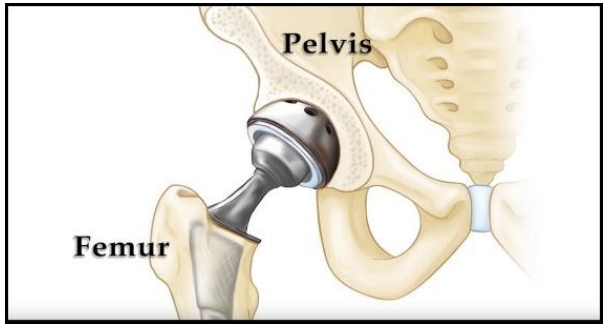
Bone and joint infections

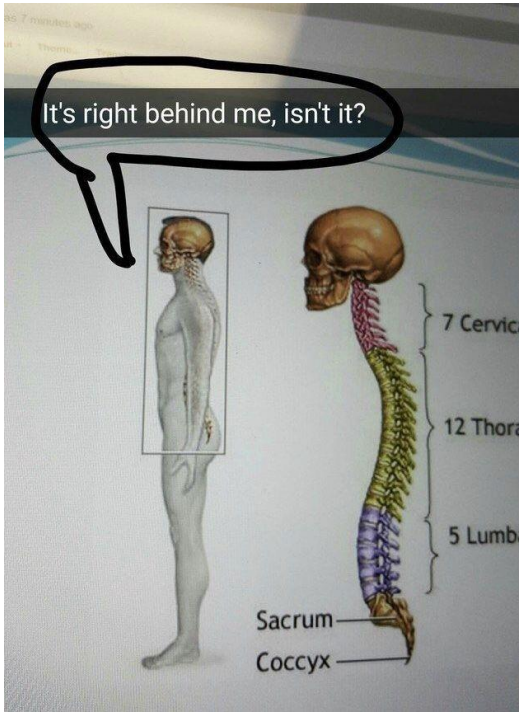
Anežka Gryndlerová

Bone and joint infections

- Poor ATB penetration into the site of infection
  - → difficult to treat
  - → long term ATB treatment
  - → combination with surgery

- Osteomyelitis
- Vertebral osteomyelitis
- Septic arthritis
- Periprosthetic joint infections

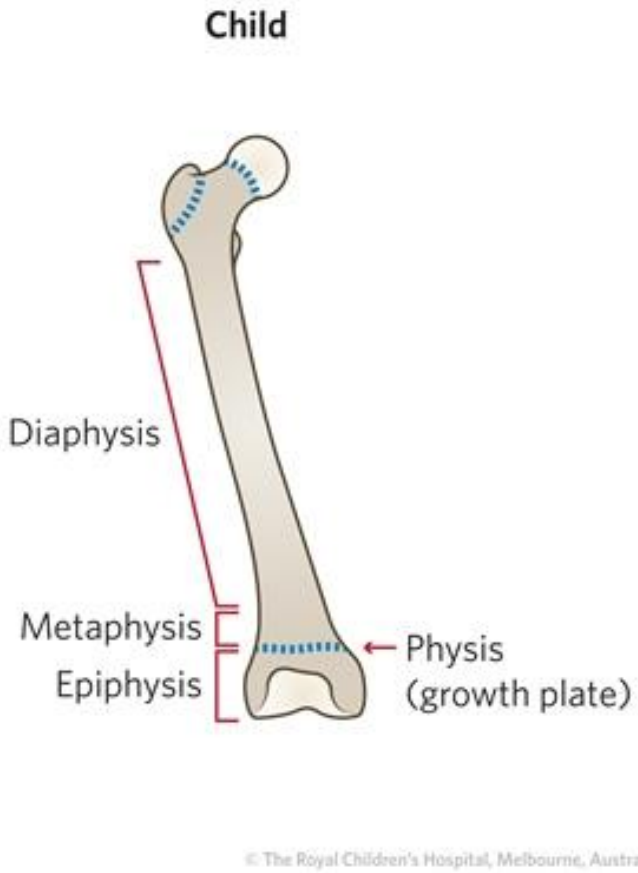


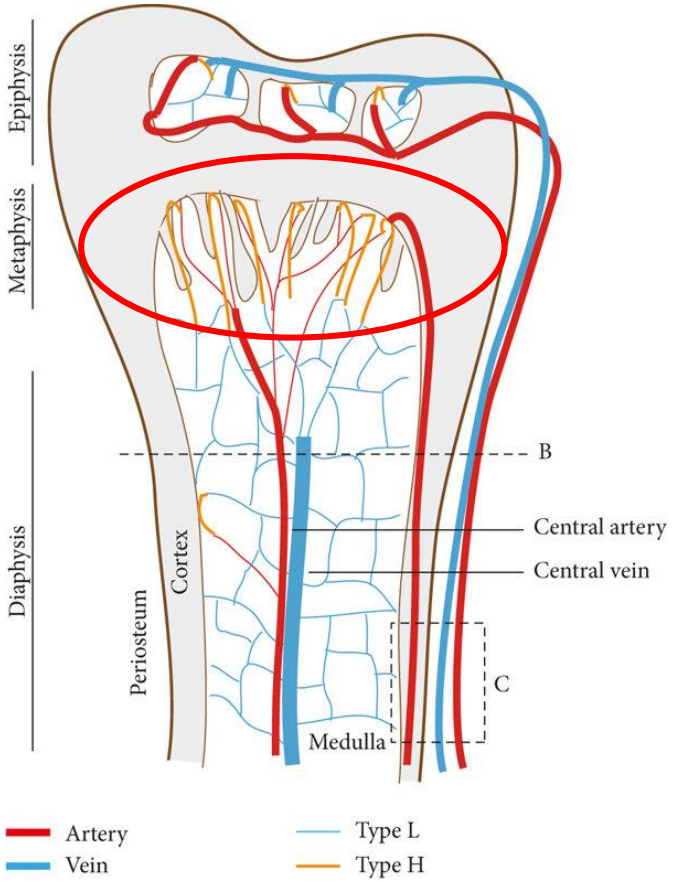


Tornado Studios
https://cz.pinterest.com/pin/674484481729139216/
https://www.kenhub.com/en/library/anatomy/the-knee-joint
https://orthoinfo.aaos.org/en/treatment/total-hip-replacement/

Bone infections

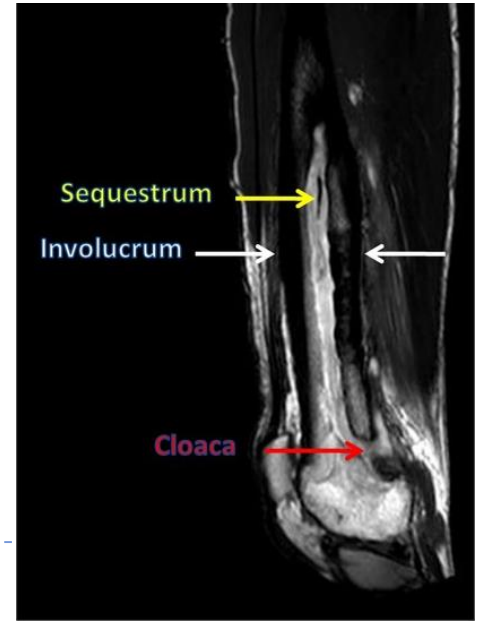
Bone anatomy





Osteomyelitis

- Bone and bone marrow infection
- Acute/chronic
  - Suppurative inflammation
  - → intramedullary pressure → disruption of periosteum
  - → impaired blood supply, ischemia, necrosis (CH)
  - Sequestrum, cloaca – drainage (CH)
- Difficult to treat:
  - Biofilm formation (native tissue, hardware)
  - Intracellular persistence ? (*S. aureus*)
  - → longer ATB treatment (vs. pneumonia), surgery

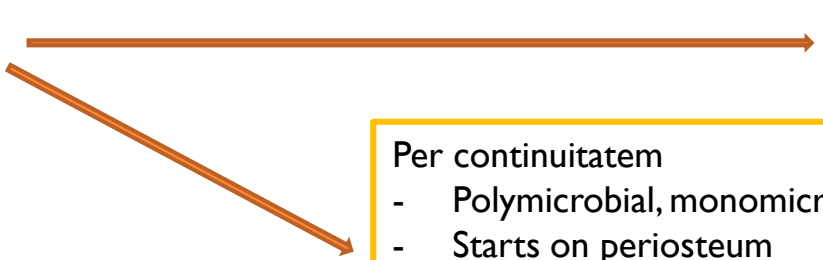


Radiopaedia.org

Osteomyelitis

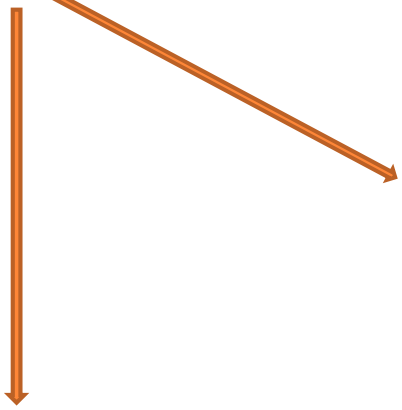
- Relatively uncommon, bones resistant to infection
  - Highly virulent pathogen, large inoculum, bone damage, foreign material, impaired blood supply

- Etiology



Direct inoculation (trauma, surgery)

Per continuitatem
- Polymicrobial, monomicrobial
- Starts on periosteum
- Sacral pressure ulcer → sacral osteomyelitis
- Osteomyelitis associated with diabetic foot: colonisation → soft tissue infection → osteomyelitis (risk of amputation)

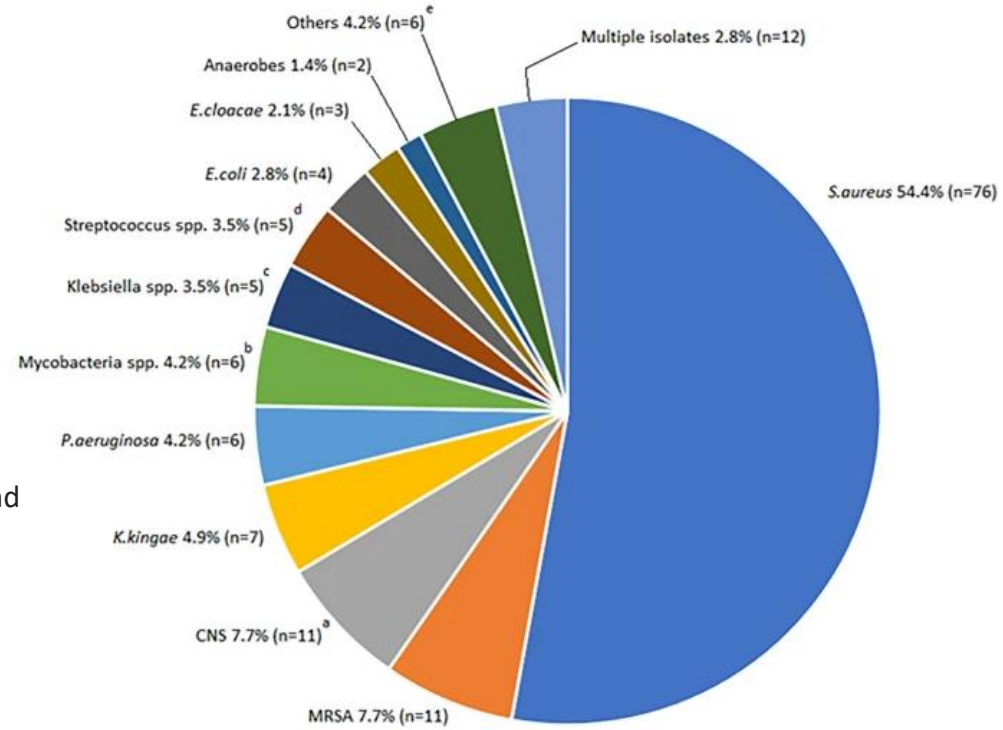


Hematogenous
- Mostly monomicrobial
- Starts in bone marrow
- Bacteriemia (endocarditis, catheter infection, transient bacteriemia - viridans streptococci, anaerobes, staphylococci, enterobacterales)
- Children – long bones
- Adults – vertebrae

S. aureus

Osteomyelitis – etiology

- ***S. aureus*** (intact bone)
- Coagulase-negative staphylococci (CNS)
  - Arteficial implants
- Enterobacteria (incl. *Salmonella*), *P. aeruginosa,* streptococci, enterococci, anaerobic bacteria
- Pediatrics: + *Kingella kingae* (6-36m.), GBS (neonates, infants), *Haemophilus influenzae*
- TBC



Krzysztofiak, A., Roversi, M., Musolino, A. *et al.* Clinical report and predictors of sequelae of 319 cases of **pediatric bacterial osteomyelitis**. *Sci Rep* 12, 14846 (2022). https://doi.org/10.1038/s41598-022-19208-2

Osteomyelitis

- Clinical presentation
  - Long bones mostly (femur, tibia, phalanx)
  - Pain, chills, fever → swelling, redness
  - Can lead to sepsis

Wael Nemattalla, Radiopaedia.org, rID: 8487

Surgical Treatment of Limb- and Life-Threatening Infections in the Feet of Patients With Diabetes and at Least One Palpable Pedal Pulse - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Osteomyelitis-accompanied-of-necrotizing-soft-tissue-infection-Extensive-debridement-did_fig6_51741915 [accessed 10 Dec, 2023]

Osteomyelitis

- Microbiological diagnosis
  - Samples?
    - Blood culture
    - Tissue/(swab) (especially during surgery!)

Methods?

Osteomyelitis

- Microbiological diagnosis
  - Samples?
    - Blood culture
    - Tissue/(swab) (especially during surgery!)

Methods?
- Microscopy (tissue/pus)
- Culture
- PCR

Osteomyelitis – diagnosis by bone biopsy

- Histology
- Microbiology

IWGDF/IDSA guidelines on the diagnosis and treatment of diabetes-related foot infections (IWGDF/IDSA 2023)

Éric Senneville ✉, Zaina Albalawi, Suzanne A. van Asten, Zulfiqarali G. Abbas, Geneve Allison, Javier Aragón-Sánchez, John M. Embil, Lawrence A. Lavery, Majdi Alhasan, Orhan Oz, Ilker Uçkay, Vilma Urbančič-Rovan, Zhang-Rong Xu, Edgar J. G. Peters ... See fewer authors ^

Recommendation 10

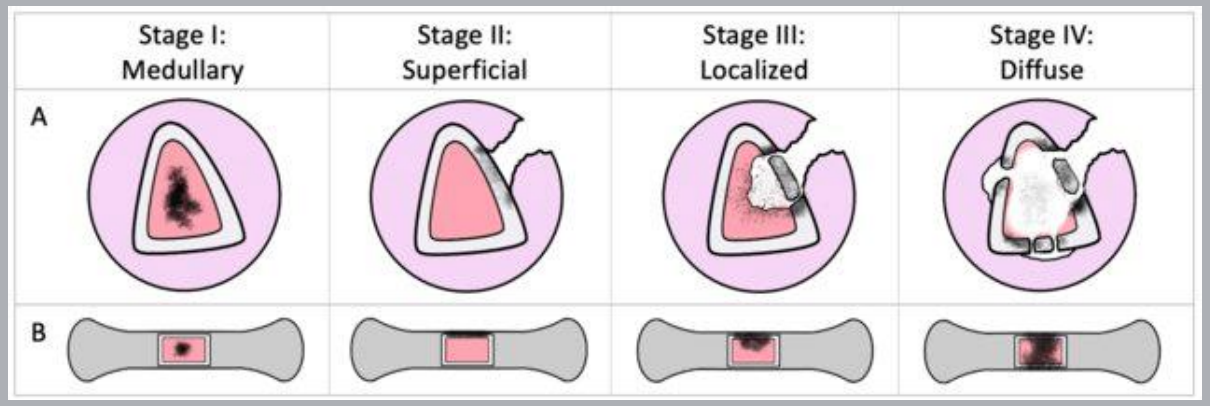
In a person for whom there is suspicion of osteomyelitis of the foot (before or after treatment), consider obtaining bone (rather than soft tissue) samples for culture, either intraoperatively or percutaneously. (Conditional; Moderate).

Rationale

Obtaining a bone specimen to diagnose osteomyelitis is the generally accepted criterion standard for diagnosing the infection, and the only definitive way to determine the causative pathogen(s). BonE BiOPsy is, however, usually not performed in most cases of suspected DFO due to the absence of a health care professional adequately trained to perform the procedure and/or the fear of possible adverse effects, especially fracture or induced infection of the bone.[114] Published studies consistently report a low correlation between

Cierny-Mader classification (**details in orthopedics**)

- Anatomical
  - 1 – monobacterial, hematogenous, arteficial material in medullary cavity
  - 2 – cortical bone, per continuitatem
  - 3 – cortical bone + medullary cavity, not full diameter affected
  - 4 – cortical bone + medullary cavity, full diameter affected – impairment of stability



- Physiological class (physiological condition of the patient)
  - DM, immune disease, malnutrition, renal or hepatic failure, extremes of age, malignancy …

- → Treatment strategy

https://www.researchgate.net/publication/340245669_Developments_in_Antibiotic-Eluting_Scaffolds_for_the_Treatment_of_Osteomyelitis/figures
Harry Kyriacou

Osteomyelitis – therapy

- Surgery – débridement (removal of necrotic and infected tissue), removal of the foreign material
- ATB
  - Long term (4-6 w. minimum)
  - Targeted, if possible (start after microbiology sampling)
  - Septic osteomyelitis – empirical treatment
    - Always cover *S. aureus*!
    - Probably *S. aureus:* oxacilin + aminoglycoside
    - Possible polymicrobial etiology – broad spectrum ATB (e.g. cefepime + aminoglycoside, cefepime + vancomycin)

2. In children with presumed AHO who are not clinically ill and for whom an aspirate or biopsy by invasive diagnostic procedure is being planned prior to initiating antibiotics, we suggest withholding antibiotics for no more than 48 to 72 hours (*conditional recommendation and very low certainty of evidence*).
Comment: The decision to implement this recommendation incorporating a reasonable delay may be influenced by local accessibility to experts and resources to perform invasive diagnostic procedures or the time required for transport to a higher level of care if appropriate. For children likely to have AHO, it is advisable that children remain hospitalized for observation while withholding antibiotics until cultures can be obtained.

IDSA

Osteomyelitis – targeted therapy

- Is´s complicated….

Suggested antimicrobial regimens for the most commonly isolated pathogens causing osteoarticular infections in infants and children when results of culture and susceptibility testing are known

Pathogen	Parenteral agents	Oral agents
Staphylococcus aureus		
Methicillin-susceptible	Cefazolin Nafcillin Oxacillin	Cephalexin Cloxacillin (not available in the United States) Dicloxacillin Clindamycin*
Methicillin-resistant		
Clindamycin-susceptible	Vancomycin Clindamycin	Clindamycin
Clindamycin-resistant¶	Vancomycin Linezolid Daptomycin$^{\Delta}$	Linezolid

UpToDate®

Osteomyelitis – targeted therapy (simplified)

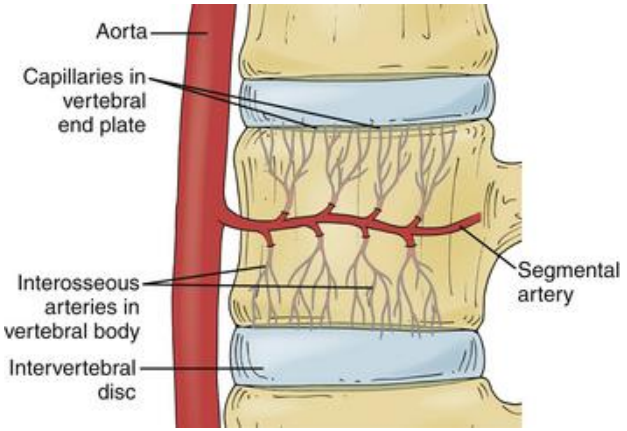
- Beta-lactam ATBs, vancomycin
  - Staphylococci – oxacilin, vancomycin (MRSA, some CNS)
  - Enterococci – ampicilin, vancomycin (*E. faecium*)
  - Streptococci – penicilin G
  - Enterobacterales – III./IV. gen. cephalosporins
  - *P. aeruginosa* – antipseudomonal beta-lactams (examples?)
- Possible to add aminoglycosides (acute phase)

Osteomyelitis – targeted therapy (simplified)

- Other antibiotics
  - Clindamycin
    - + very good bone penetration
    - - CDI, bacteriostatic, only covers G+ and anaerobes
  - Linezolide
    - + good bone concentrations
    - - llimited use (28d, toxicity), bacteriostatic, only G+ bacteria
  - Rifampin (in combination)
    - + good biofilm concentration
    - - drug interactions, mostly G+ and TBC
  - Ciprofloxacin
    - + good bone concentrations
    - - resistence development during therapy and treatment failure, mostly for G-

Vertebral osteomyelitis (spondylodiscitis)

- Intervertebral disc + vertebrae (vascularisation)
- Commonly lumbar spine
- Adults
- Pathogenesis
  - Mostly hematogenous
    - Infective endocarditis, catheter-related infections, skin and soft tissue infections
    - i.v. drugs abusers
  - Direct inoculation (surgery)
- Etiology
  - *S. aureus*
  - CNS, Enterobacteriales, *P. aeruginosa*, TBC, *Candida* spp.



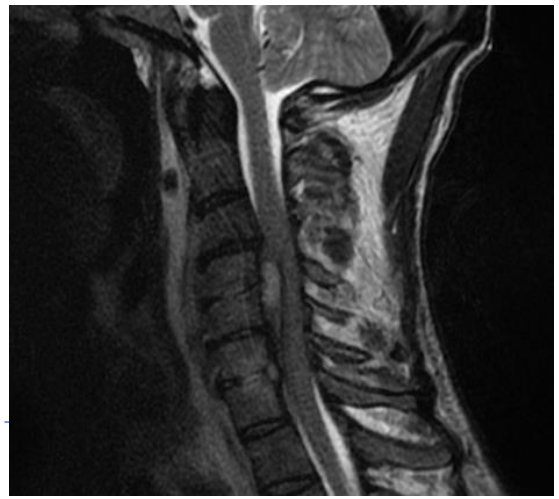
https://clinicalgate.com/intervertebral-disc-process-of-degeneration-physiology-and-pathophysiology/

Vertebral osteomyelitis (spondylodiscitis)

- Clinical presentation

Slowly progressing back pain, fever may not appear	Acute back pain, fever chills, sweating

  - Back pain: worsening with movement, percussion
  - Neurological symptoms can occur – motor and sensory impairment (epidural abscess)
- Complications
  - Epidural abscess/empyema, psoas abscess



https://radiopaedia.org/cases/epidural-abscess-spinal-1?lang=us

Vertebral osteomyelitis (spondylodiscitis)

- Diagnosis
  - MRI (details in radiology)
  - Blood culture, samples from infection site (microscopy, culture, ev. PCR)

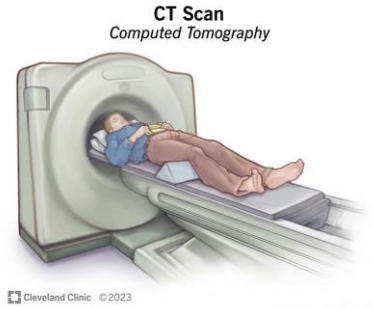
IDSA 2015 Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in Adults

Published CID, 7/29/2015

III. When Should an Image-Guided Aspiration Biopsy or Additional Workup Be Performed in Patients With NVO?

14. We recommend an image-guided aspiration biopsy in patients with suspected NVO (based on clinical, laboratory, and imaging studies) when a microbiologic diagnosis for a known associated organism (*S. aureus*, *Staphylococcus lugdunensis*, and *Brucella* species) has not been established by blood cultures or serologic tests *(strong, low)*.
15. We advise against performing an image-guided aspiration biopsy in patients with *S. aureus*, *S. lugdunensis*, or *Brucella* species bloodstream infection suspected of having NVO based on clinical, laboratory, and imaging studies *(strong, low)*.

- Therapy
  - Surgery (if needed), ATBs 6w.



Joint infections

Septic arthritis (infectious arthritis)

- Purulent infection of a joint
- Usually monoarticular (knee, hip)
- Risk factors:
  - Joint pathology: rheumatoid arthritis, gout, trauma, orthopedic surgery in history
  - Immune suppresion (DM, malignancy, older age, …)
  - i.v. drug abusers, infective endocarditis
  - Foreign body presence
- → joint damage, sepsis
- Mortality 5-18% (1 year)

› Int Orthop. 2018 Jan;42(1):1-7. doi: 10.1007/s00264-017-3565-4. Epub 2017 Jul 17.

Septic arthritis associated with systemic sepsis

Sung-Weon Jung [1], Dong-Hee Kim [2], Sung-Jin Shin [2], Byoung-Youl Kang [2], Yil-Ju Eho [2], Seong-Wook Yang [2]

Affiliations + expand

PMID: 28717843 DOI: 10.1007/s00264-017-3565-4

30 % sepsis at the time of dg.

https://www.oliveviewim.org/didactic/morning-report-septic-arthritis/

Septic arthritis

- Etiology
  - Hematogenous (synovial vascularisation), per continuitatem, direct inoculation
  - *S. aureus*, streptococci, Enterobacteriales, *P. aeruginosa*, *H. influenzae*, *Kingella kingae*, *Neisseria gonorrhoeae*
- Clinical presentation
  - Swelling, pain, redness, impaired function, fever
- Microbiological sampling
  - Synovial fluid, blood culture
  - Microscopy, culture, PCR

https://boneandspine.com/elbow-arthrocentesis/

Septic arthritis – ATB treatment

- Microscopy
  - G+ cocci in groups
    - Oxacilin
    - MRSA suspicion – vancomycin, (linezolide)
  - G- diplococci
    - 3rd gen. cephalosporins
  - G- rods
    - Cefepime, piperacillin/tazobactam
  - Negative
    - e.g. cefepime + vancomycin
- Targeted treatment
- 2-3 w. or more

Disseminated gonococcal infection

- Risk factors: immune defficiency, menstruation, pregnancy, IUD

- Urethritis, proctitis, pharyngitis, cervicitis
  → arthritis-dermatitis syndrome: bacteriemia with fever, dermatitis, tenosynovitis (hand, fingers), assymetric migratory polyarthritis
  → purulent mono-/oligoarthritis

- Microbiological sampling
  - Synovial fluid, blood culture – can be negative, especially in arthritis-dermatitis syndrome
  - ?
  -

https://www.thedermcenters.com/lesions-invasion-of-a-microorganism/

Disseminated gonococcal infection

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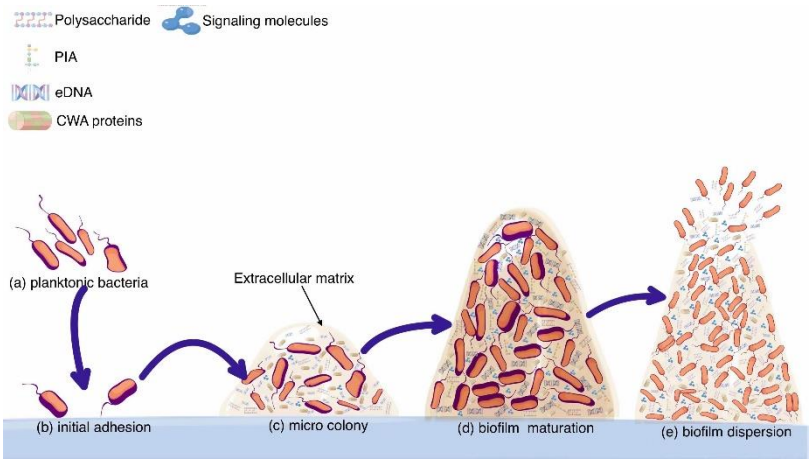
- Microbiological sampling
  - Synovial fluid, blood culture – can be negative, especially in arthritis-dermatitis syndrome
  - ?
  - Urine, swab (urethral/cervical/rectal/throat) – culture, PCR

https://www.thedermcenters.com/lesions-invasion-of-a-microorganism/

Periprosthetic joint infections

- Incidence 1-2%*
- Pathogenesis
  - Contamination of operating field, hematogenous
  - Adhesion to arteficial material and biofilm formation
  - Poor ATB penetration into a biofilm – surgery and removal often needed



*Jindrák et al.: Antibiotická politika a prevence infekcí v nemocnici
https://www.frontiersin.org/articles/10.3389/fcimb.2022.1003033/full
Wikipedia.org

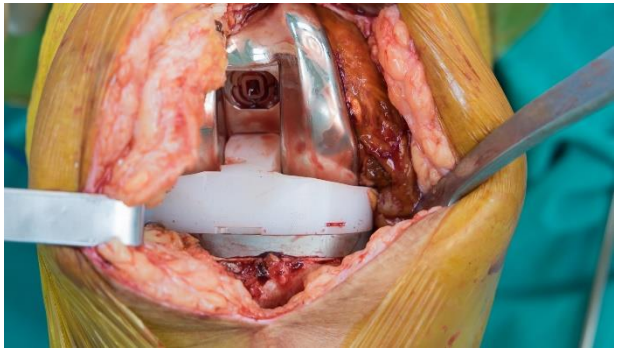
Periprosthetic joint infections - classification

- Acute infection (< 3 m.)
  - High virulence (*S.aureus*, beta-hemolytic streptococci, enterobacteriales)
  - Fever, swelling, pain, redness

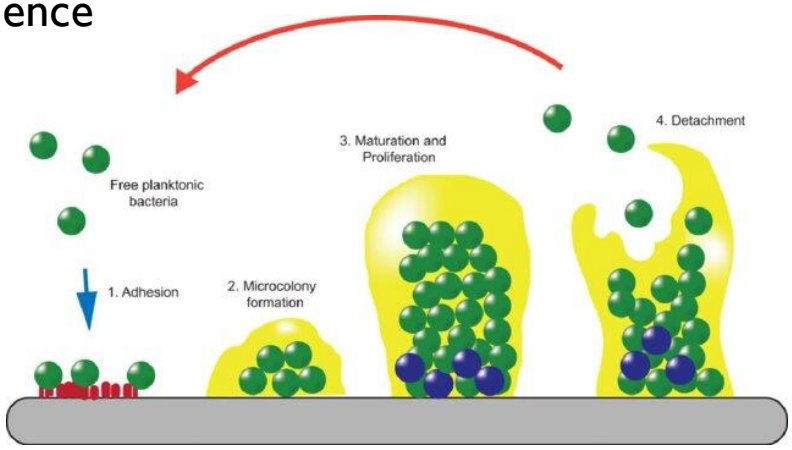
- Delayed (3-12 m.), Late (> 12 m.) infection
  - Lesser virulence (CNS, *Cutibacterium acnes*, coryneform bacteria, viridans streptococci, enterococci…)
  - Late – also hematogenous
  - Pain, loosening of implant, impaired joint function
  - Possibly without signs of systemic inflamation

Periprosthetic joint infections

- Microbiological sampling
  - Synovial fluid, tissue, (implant – sonication)
    - Microscopy, culture, PCR
  - Careful interpretation
    - Contamination by skin microbiota?
    - Synovial fluid – false negativity? (biofilm)
  - Tissue: ≥3 or more samples*
    - 1 sample positive – significant for virulent pathogens
      ≥2 samples for pathogens with lesser virulence



https://www.rheumatologyadvisor.com



*Česká společnost pro ortopedii a traumatologii pohybového ústrojí: Postup pro stanovení diagnózy infekce kloubní náhrady doporučený ČSOT

Akanda, Zarique & Taha, Mariam & Abdelbary, Hesham. (2017). Current review - The rise of bacteriophage as a unique therapeutic platform in treating peri-prosthetic joint infections. Journal of Orthopaedic Research. 36. 10.1002/jor.23755.

Periprosthetic joint infections – treatment

- Surgery + ATB therapy
  - Debridement and implant retention (DAIR)
  - One-stage exchange
  - Two-stage exchange
    - With antibiotic-impregnated spacer insertion
  - ATBs
    - min 2-6 w.
    - Targeted
    - + ATBs with good biofilm concentrations (rifampin, ciprofloxacin)
    - Empirical treatment – etiology unknown: vancomycin + fluorochinolone + rifampin → deescalation

Periprosthetic joint infections – treatment

- Surgery + ATB therapy
  - Debridement and implant retention (DAIR)

Antibiotická kurativní léčba					
Mikrobiální agens	**Úvodní/ pokračovací léčba**	**Antibiotikum: 1. volba**	**Dávka a cesta podání**	**Antibiotikum: alternativa**	**Dávka a cesta podání**
Staphylococcus aureus (MSSA) a plazma-koagulasa-negativní stafylokoky **methicilin citlivé**	úvodní terapie	oxacilin + rifampicin[1]	2-3 g à 4 hod. i.v. 450-600 mg à 12 hod. p.o.	cefazolin + rifampicin[1]	2 g à 8 hod. i.v./ 450-600 mg à 12 hod. p.o.
				při alergii k β-laktamům: vankomycin + rifampicin[1]	(15 mg/kg à 12 hod.) + dle hladin a schématu i.v./ 450-600 mg à 12 hod. p.o.
	pokračovací terapie	podávat 2 týdny a pokračovat (nelze-li podávat rifampicin, pak i.v. terapie 4-6 týdnů)			
		co-trimoxazol[3] + rifampicin[1]	960 mg à 8 hod./ 450-600 mg à 12 hod. p.o.	levofloxacin[3] + rifampicin[1]	500 mg à 12 hod. p.o./ 450-600 mg à 12 hod. p.o.
				ciprofloxacin[3] + rifampicin[1]	750 mg à 12 hod. p.o./ 450-600 mg à 12 hod. p.o.
				linezolid[2] + rifampicin[1]	600 mg à 12 hod. p.o./ 450-600 mg à 12 hod. p.o.

společnost infekčního lékařství *ČLS JEP*

Reactive arthritis

- Immune response (T-cells, cytokines)
- Young adults
- 1-4 weeks after infection
- Other symptoms can be present (conjunctivitis, urethritis)
- Triggers: *Chlamydia trachomatis, Ureaplasma urealyticum, Mycoplasma genitalium, Campylobacter, Salmonella, Shigella, Yersinia, …*
- Microbiological testing according to symptoms (urine, stool, blood serum, …)
- Treatment of infection, symptomatic therapy (NSAID – diclofenac; other drugs – rheumatology)

Thank you for your attention

- https://www.travelgeekery.com