Microbiology of joints and bone infections

- Important
- Doctor Notes
- Extra

Editing File
Objectives:

- Recognize the differences between osteomyelitis and arthritis.
- Know how infection reaches the bone/joint.
- Recognize the epidemiology, risk factors, and pathogenesis of both osteomyelitis and arthritis.
- Recall the route of infection of bone and joint.
- Know the commonest causative organisms of acute and chronic osteomyelitis and arthritis.
- Recall the differential diagnosis of both conditions.
- Know the laboratory diagnosis and investigation of osteomyelitis and arthritis.
- Recognize the management and treatment of both osteomyelitis and arthritis.
- Recall the complications of both conditions.
- Know the causative organisms, diagnosis, management, and treatment of infection of the joint prosthesis.
Introduction:

- Bone & joint infections may exist separately or together.
- Both are more common in infants and children.
- Often associated with foreign body at the primary wound site.
- If not treated lead to devastating effect.

(metaphysis: most serious (has most of blood supply) most infection starts there and usually spread)
Acute Osteomyelitis

● Definition: An acute infectious process of the bone and bone marrow.

● How the pathogen reaches the bone:
  ○ 1. Hematogenous route (blood)
  ○ 2. Contiguous soft tissue focus (postoperative infection, contaminated open fracture, soft tissue infection, puncture wounds)
  ○ 3. In association with peripheral vascular disease “chronic diseases” (diabetes mellitus, severe atherosclerosis, vasculitis)

● Duration:
  ○ short duration (few days for hematogenously acquired infection).
  ○ last several weeks to months (if secondary to contiguous focus of infection).
<table>
<thead>
<tr>
<th>How they reach</th>
<th>Risk Group</th>
<th>Etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Hematogenous route</strong>&lt;br&gt;site: (Metaphysis of long bones)</td>
<td>• Children and infants common&lt;br&gt;• Adult less common (may occur due to reactivation of a quiescent focus of infection from infancy or childhood) →&lt;br&gt;  • most cases are due to S. AUREUS&lt;br&gt;  • S. Aureus is common as the infection begins in the diaphysis.&lt;br&gt;  • Septic infection can be in the beginning of infection (in diaphysis) and then it can spread to metaphysis.</td>
<td>Infant: S. aureus, group B streptococci, gram –ve rods like (E. coli, Klebsiella)&lt;br&gt;Children: S. aureus, group A streptococci, Haemophilus &quot;(H.)influenzae.&quot;&lt;br&gt;Adults: S. aureus, Salmonella species</td>
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<tr>
<td><strong>Other cases – special clinical situations:</strong></td>
<td>Infection after puncture wound of foot.</td>
<td>Pseudomonas aeruginosa → common in water, S. aureus.</td>
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<tr>
<td>Fist injuries, and diabetic foot and decubitus ulcers,</td>
<td>Streptococci „ anaerobes</td>
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<tr>
<td>in sickle cell patients (phagocytosis will be affected because they have Autosplenectomy → infection of spleen)</td>
<td>Salmonella or S. pneumoniae (Salmonella and other capsulated organism) , and S. aureus</td>
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</tbody>
</table>
| Immunocompromised patients → AIDS patients. | M. tuberculosis or M. avium
(Mycobacterium tuberculosis (MTB) or Mycobacterium avium) |
| Infection after trauma, injury or surgery | S. aureus, group A Streptococcus, Gram negative rods, anaerobes. |
Clinical presentation & investigation findings

Acute osteomyelitis usually of abrupt “sudden” onset

<table>
<thead>
<tr>
<th>Clinically Usually Quick</th>
<th>Blood findings</th>
<th>X-ray findings</th>
<th>Ultrasound findings</th>
<th>CT scan findings</th>
<th>MRI findings (the most sensitive)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- fever</td>
<td>-leukocytosis</td>
<td>Early stages: normal</td>
<td>Fluid collection (abscess) and surface abnormalities of bone. (Good for pediatrics)</td>
<td>Reveal small area of osteolysis in cortical bone.</td>
<td>In early detection, help in unclear situation (Define bone involvement in patients with negative bone scan). (Baseline)</td>
</tr>
<tr>
<td>- localized pain - heat</td>
<td>-High ESR</td>
<td>Later stages: Swelling of soft tissues followed by elevation of periosteum, demineralization and calcification of bone. (lytic bone lesion)</td>
<td></td>
<td></td>
<td>- you use it in complicated cases, if you highly suspected in infections, but all the investigations are normal.</td>
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<tr>
<td>- swelling</td>
<td>-High C-reactive protein.</td>
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<tr>
<td>- tenderness of affected site (one or more bones or joints affected in hematogenous spread)</td>
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<tr>
<td>- May be local tissue infection (abscess or wound)</td>
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Diagnosis of acute osteomyelitis:

**Blood culture:** Bacteremia “presence of bacteria in blood” common

If blood culture is negative: biopsy of periosteum or bone, or needle aspiration of overlying abscess

**Blood test:**
- complete blood and differential counts

**Erythrocyte sedimentation rate (ESR):** elevated but could be normal

**C-reactive protein**

**Imaging studies:**
- X-RAY, MRI, CT-SCAN

Differential diagnosis includes:

- Rheumatoid arthritis
- Septic arthritis
- Fractures (esp pathological fracture)
- Sickle cell crises (hypoxia ----> sickling of RBCs ----> Thickened blood ----> hypoxia ------> severe pain)

Complications of acute osteomyelitis include:

- Septic arthritis
- Chronic osteomyelitis
- Metastatic infection to other bones or organs (especially staph.aureus)
- Pathological fractures
# Management and treatment

<table>
<thead>
<tr>
<th>Organisms</th>
<th>Antibiotics</th>
<th>Duration/Surgery/complication and follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methicillin sensitive (MSSA) Ex: Staph. aureus</td>
<td>Cloxacillin, cefazolin or Clindamycin.</td>
<td>• Early treatment is critical</td>
</tr>
<tr>
<td>Methicillin resistant (MRSA) Ex: Staph. aureus</td>
<td>Vancomycin followed by Clindamycin, Linezolid, or TMP-SMX (cannot use Beta-Lactam antibiotics)</td>
<td>• Treat for 2-4 weeks parenteral (I.V) followed by oral therapy for a total of at least 6 weeks.</td>
</tr>
<tr>
<td>Polymicrobial* infection:</td>
<td>Ampicillin-Sulbactam, Piperacillin-Tazobactam or Quinolone with Metronidazole.</td>
<td>• Surgery for neurological complications, paravertebral abscess &amp; hip joint involvement.</td>
</tr>
<tr>
<td>S. epidermidis:</td>
<td>Vancomycin and Rifampicin</td>
<td>• Complications: septicemia, metastatic abscesses, septic arthritis, chronic osteomyelitis, loss of limb, or paravertebral abscess.</td>
</tr>
<tr>
<td>Enterobacteriaceae:</td>
<td>Ceftriaxone</td>
<td>• Monthly ESR for 3 months and at 6 months useful to document treatment.</td>
</tr>
<tr>
<td>Other Gram negative bacilli:</td>
<td>Quinolones</td>
<td>• Cases due to contiguous source more difficult to eradicate, Relapse common (50%), surgery indicated.</td>
</tr>
<tr>
<td>P. aeruginosa:</td>
<td>Cefepime, Meropenem, or Piperacillin +/- Aminoglycoside.</td>
<td>- Duration: 4 - 6 weeks to ensure cure and prevent progression to chronic osteomyelitis.</td>
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<tr>
<td>Anaerobes:</td>
<td>Metronidazole or Clindamycin</td>
<td>- Surgical drainage: (as needed) if there is local purulent process.</td>
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</table>
Chronic Osteomyelitis

- A chronic infection of the bone and bone marrow usually secondary to inadequately treated or relapse of acute osteomyelitis or foreign body.
- Difficult management and Poor prognosis
- Infection may not completely cured.
- May recur many years or decades after initial episode.
- Most infections are secondary to a contiguous focus or peripheral vascular disease.
- Chronic infection due to hematological spread is rare.

The blood vessels coming in and out of the bone will be obstructed from the pus ⇒ No or small amount of antibiotics can enter the bone ⇒ Difficult management + poor prognosis.
Pathogens:

- **S.aureus**: is the most common pathogen
- **Other microorganisms**: S.epidermidis, Enterococci, streptococci, Enterobacteriaceae, *Pseudomonas* and anaerobes
- **Tuberculosis and fungal**: clinically have indolent “chronic” course
- **Immunosuppressed patients**: Mycobacteria and fungi
- **Polymicrobial infection**: common with decubitus ulcers and diabetic foot infections.

Diabetic patients lose sensation of pain due to nerve damage, so they will not feel the pain when they get a cut and may not clean the wound early, which can increase the chances of more microbes to infect the patient.
Tuberculous and Fungi Osteomyelitis

**Tuberculous osteomyelitis:**
- primarily results from:
  1. hematogenous spread from lung foci
  2. caseating lymph bone (50% in spine).
- It resembles Brucella osteomyelitis.

**Fungi Osteomyelitis:**
- Hematogenous osteomyelitis due to fungi

Examples:
- Candida species, Aspergillus species and other fungi may occur.

TB and Brucella are common in KSA.
Diagnosis of chronic osteomyelitis:

1- Blood:
   . Blood culture: is not very helpful because bacteremia is rare.
   . WBC: usually normal.
   . ESR: elevated but not specific.

2- radiology:
   . MRI: helpful for diagnosis and evaluation of the extent of disease. (*MRI excellent for chorionic osteomyelitis*)
   . Radiological changes are complicated by the presence of bony abnormalities.
Management & Treatment of chronic osteomyelitis:

★ Extensive surgical debridement (and then start) with antibiotic therapy. (because of long time infection & abscess formation)

★ Antibiotics:

- Parenteral antibiotics for 3-6 weeks followed by long term oral suppressive therapy.
- MSSA: Cloxacillin
- MRSA & S.epidermidis: Vancomycin then oral Clindamycin or TMP-SMX.
- Other bacteria: treat as acute osteomyelitis.
- Brucella: Tetracycline and Rifampicin for 2 to 3 months (6 Weeks)
- MTB: combination of 4 drugs: INH+RIF +Pyrazinamide & Ethambutol for 2 months followed by RIF + INH for additional 4 months. (Please Know them this is a possible question different between Brucella and TB)
- Some patients may require lifelong antibiotic, others for acute exacerbations.
Septic (infectious) arthritis

- an **acute inflammation** of the **joint space** secondary to infection.
- Generally affects a **single joint** and results in **suppurative inflammation**.
- May caused by bacteria or viruses commonly by **haematogenous seeding**

Haematogenous seeding = Blood borne spread = transmitted by blood circulation
**Septic arthritis**

- **Symptoms:**
  - pain, swelling, limitation of movement. *(esp; in children)*
- **Diagnosis by:**
  - Arthrocentesis to obtain synovial fluid analysis, Gram stain, culture & sensitivity.
- **Management:**
  - Drainage & antimicrobial therapy

How it happen? When the joint space is blocked and there is contact of bones. Then inflammation will take place and the synovial membrane will swallow.

Arthrocentesis is a procedure to maintain synovial fluid of the joint.
# Septic arthritis caused by:

## Bacteria

<table>
<thead>
<tr>
<th>Age / special condition</th>
<th>Common organisms</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neonates</strong></td>
<td>S.aureus, group B streptococcus, -Gram rods ( eg. E.coli, klebsiella, proteus, pseudomonas )</td>
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<tr>
<td><strong>Infants / children</strong></td>
<td>S.aureus, group A streptococcus, S.pneumoniae, H.influenzae type b</td>
</tr>
<tr>
<td><strong>Adults</strong></td>
<td>S.aureus, (Neisseria gonorrhoeae)</td>
</tr>
<tr>
<td><strong>Sickle cell disease</strong></td>
<td>Salmonella species, S.aureus</td>
</tr>
<tr>
<td><strong>Trauma / surgery</strong></td>
<td>S.aureus</td>
</tr>
<tr>
<td><strong>Chronic arthritis</strong></td>
<td>MTB, Fungi</td>
</tr>
<tr>
<td><strong>Prosthetic arthritis</strong></td>
<td>Skin flora; S.epidermidis</td>
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</tbody>
</table>

Chronic is always associated with TB or Fungi

Sexually transmitted disease
Other causes of Septic arthritis:

**Viruses**

*Include:* Rubella *(rash)*, Hepatitis B, mumps, Parvovirus B19 *(common)*, Varicella, EBV, Adenovirus, etc.

These are self limiting.

It doesn't need treatment.

**Reactive arthritis due to (antigen-antibody complex):**

- Campylobacter jejuni
- Yersinia enterocolitica
- Some Salmonella species

**Non infectious causes of arthritis:**

- Rheumatoid arthritis
- Gout
- Traumatic arthritis
- Degenerative arthritis
## Risk Factors

<table>
<thead>
<tr>
<th>Gonococcal (Maybe reactive)</th>
<th>Nongonococcal</th>
<th>Trauma procedures (arthroscopy) contiguous soft tissue</th>
<th>Lyme disease</th>
<th>Sickle cell disease</th>
<th>Chronic arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Most common in <strong>young</strong>, sexually active adults</td>
<td>- Most common in <strong>older adults</strong></td>
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<tr>
<td>- Caused by <em>Neisseria gonorrhoeae</em></td>
<td>- Caused by introduction of organisms into joint space as a result of bacteremia or fungaemia from infection at other body sites.</td>
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<tr>
<td>- Leads to disseminated infection secondary to urethritis/cervicitis</td>
<td>- Initially present with polyarthritis, tenosynovitis, fever, skin lesions</td>
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<tr>
<td>- If untreated leads to suppurative monoarthritis</td>
<td>- Most common cause <em>S. aureus</em></td>
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<tr>
<td></td>
<td>Other organisms: streptococci and aerobic Gram negative bacilli</td>
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</table>

- Due to tick bite in endemic areas (skin rash) uncommon in KSA

- Caused by *Salmonella species*

- Due to *MTB* or fungi
# Diagnosis of septic Arthritis

**History/examination** to exclude systemic illness. Note history of tick exposure in endemic areas

**Arthrocentesis** should be done as soon as possible;

1. Synovial fluid is cloudy and purulent (normally is transparent)
2. Leukocyte count generally > 25,000/mm³, with predominant neutrophils (because it’s acute inflammation)
3. Gram stain and culture are positive in >90% of cases. (except in gonococal the percentage is smaller)
4. Exclude crystal deposition arthritis or noninfectious inflammatory arthritis.

**Blood cultures** indicated

If Gonococcal infection suspected; **take specimen** from cervix, urethra, rectum & pharynx for culture

Investigation for other sexually transmitted diseases; **DNA testing** for N.gonorrhoeae

**Culture** of joint fluid and skin lesions
Management & Treatment

1. Surgical drainage / debridement
   In some cases.

2. Antimicrobial therapy

**Gonococcal arthritis**
- IV Ceftriaxone (or Ciprofloxacin or Ofloxacin) then switch to oral Quinolone or Cefixime for 7-10 days.

**Nongonococcal arthritis**
- MSSA: Cloxacillin or Cefazolin
- MRSA: Vancomycin
- Streptococci: Penicillin or Ceftriaxone or Cefazolin
- Enterobacteriaceae: Ceftriaxone or Fluroquinolone
- Pseudomonas: Piperacillin and Aminoglycoside
- Animal bite: Ampicillin-Sulbactam

**Lyme disease arthritis**
- Doxycycline for one month

Depends on:
- 1. suspected organism
- 2. sensitivity results
Prognosis & complication

Gonococcal arthritis

Excellent outcome

Nongonococcal arthritis

hip or shoulder involvement

Risk factors for long term adverse sequelae include:

Age - prior rheumatoid arthritis - polyarticular joint involvement - hip or shoulder involvement - virulent pathogens - delayed initiation or response to therapy
Infections of Joint Prosthesis

- Occur in 1 - 5 % of total joint replacement.
- Most infections occur within 5 years of joint replacement.
- Often caused by skin flora.
- Diagnostic aspiration of joint fluid necessary.
- Result in significant morbidity and health care costs.
- Successful outcomes result from multidisciplinary approach.
Diagnosis of Prosthetic Arthritis

1- Aspiration & surgical exploration to obtain specimen for culture, sensitivity testing & histopathology.

- Skin flora regarded as pathogens if isolated from multiple deep tissue cultures.

2- Radiology:
- Plain X-ray: may not be helpful.
- Arthrography: may help define sinus tracts. (A series of joint infection after injection of contrast media)
- Bone scan: not specific for infection.

3- Blood:
ESR and C-reactive protein (CRP) may be high.
1- **Surgery:** removal of prosthesis.

2- **Antibiotics:**
   - Impregnated cement during re-implantation
   - Antimicrobial for 6 weeks:
     - Begin empiric IV antibiotic to cover MRSA and Gram negative rods (Vancomycin, Cefepime, Ciprofloxacin, or Aminoglycoside)
     - Chronic therapy with oral drug if removal of prosthesis not possible.

Empiric therapy: is therapy based on experience and, more specifically, therapy begun on the basis of a clinical educated guess in the absence of complete or perfect information.

Spacers are made with bone cement that is loaded with antibiotics. The antibiotics flow into the joint and surrounding tissues and, over time, help to eliminate the infection.
<table>
<thead>
<tr>
<th>Summary</th>
<th>Acute osteomyelitis</th>
<th>Chronic osteomyelitis</th>
<th>Septic arthritis</th>
<th>Joint Prosthesis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of infection ;</strong></td>
<td>Acute</td>
<td>Chronic</td>
<td>Acute</td>
<td>-</td>
</tr>
<tr>
<td><strong>Infection of ;</strong></td>
<td>Bone and bone marrow</td>
<td>Bone and bone marrow</td>
<td>Joint space</td>
<td>Joint due to joint replacement</td>
</tr>
</tbody>
</table>
| **Caused by ;** | S.aureus : is the most common pathogen | S.aureus : is the most common pathogen  
- Tuberculosis and fungal: clinically have indolent “chronic” course.  
- Immunosuppressed patients: Mycobacteria and fungi  
- Polymicrobial infection: common with decubitus ulcers and diabetic foot infections | Bacteria /viruses | skin flora: S.epidermidis |
| **Significant Symptom ;** | - | - bony abnormalities.  
- sinus tracts | limitation of movement | sinus tracts |
| **Diagnosis ;** | Blood culture,  
Ultrasound findings for pediatrics, MRI in complicated cases. | MRI | Arthrocentesis | Arthrography |
| **Management ;** | Antibiotics , surgical drainage if needed | Extensive surgical debridement with antibiotic therapy | Drainage & antimicrobial therapy | Surgical debridement and prolonged antimicrobial therapy |
In general Staph. Aureus is the most common cause of these infections,
  - Except in joints, paediatrics, and ( adult patients sexually active → Neisseria gonorrhoeae ).
Infants have diff type of organisms → ( Gram -ve, group B strepto ) besides S.aureus .
  - When they grow little bit older (children), they will have (Haemophilus influenzae, S.aureus, group A).
Acute Osteomyelitis:
  - Generally the infection common in children.
  - The routes of infection are blood borne, foreign body, animals bites, and deep injury, so by this the organism can inter the bone.
  - Metaphysis is the most serious part in infections, WHY?
    - Because lots of blood supplies there, so the infection can start there then spread to joints.
    - And it will affect the growth plate (growth of bone).
  - Acute infection will affect the bone and bone marrow, how the pathogen will reach there?!
    - 1- throw blood (hematogenous route)
    - 2- Contiguous → means from skin and soft tissue or by near organ, then the organism can reach the bone.
    - 3- it’s associated more with people who has vascular diseases → it will decrease blood supply and this create good environment for the bacteria to pass, SPECIALLY anaerobes.
  - The infection might be gradual onset or acute onset.
  - Duration range between days to weeks.
  - Primary hematogenous infection mainly in children and infants:
    - In case of infants think about group B & E.coli as the causes.
    - In case of children H. influenzae is there because the child will lose the immunity (IgG) that coming from his/her mother.
  - Long bones mainly are the site of infection (in diaphysis), other bones can be affected but it’s less common.
  - This infection is less common in adults, however the most causes here is S. aureus .
Bacteremia: means the infection of blood.
  - Duration of treatment is long (4-6 weeks) → majority of infections (2 weeks mostly) → except few reach to (4-6 weeks) e.g joint infections, bone infections, and then TB is the long one (6-9 months) → so acute osteomyelitis is one of the serious infections.
Chronic osteomyelitis:
- An acute osteomyelitis that didn’t treated or wound infection that didn’t treat well → it will develop to a chronic osteomyelitis → where there will be pus formation, and it’s difficult to treat it.
- S. aureus is the champion, and it’s the most causes here.
- Rifampicin used to treat MTB & brucella.
  - If you treat a patient that you suspect he have brucella by Rifampicin, but he have MTB → it will develop to resistance.
  - In KSA both of MBT & brucella are common, and Rifampicin was sold in pharmacies and described by doctors a lot → so TB became resistance.

Septic arthritis:
- Affect a single joints, not like inflammatory diseases (e.g. Rheumatoid arthritis) → which usually affect multiple joints, but Septic arthritis means that cause by microbes (bacteria and viruses)
- Joint infections is very serious, bacteria can cause liquidation of the joint → joint become like liquid → then the joint will lose its function → so you need to act quickly.
- Will be swilling in synovial space due to accumulation of the suppurative fluid (suppurative inflammation), there will be lots of pus cells.
- Prosthetic arthritis → caused by the normal flora of the skin (s.epidermidis, propionibacterium acnes, corynebacteria, s.aureus, bacillus. → these are the organism that can cause joint infection in case of prosthetic joints
- The common virus that cause septic arthritis is Parvovirus B19 (and other hilarious viruses you can memorise it S.17)
  - The patient will have a systemic disease (rash, fever, etc.) in viruses cases.
1) joint and bone infections are more common in?
A) infants and children   B) young.   C) older people.   D) in female

2) arthrocentesis is diagnostic procedure for?
A) acute osteomyelitis.   B) septic arthritis.   C) chronic osteomyelitis.   D) atherosclerosis

3) animal bite leads to nongonococcal arthritis is treated by?
A) ampicillin.   B) vancomycin.   C) cloxacillin   D) IV ceftriaxone

4) In case of Prosthetic Arthritis the doctor should use an empiric antibiotics that must cover which type of bacteria?
A) MRSA and aerobics   B) Gram negative and aerobics   C) Gram positive and anaerobics   D) Gram negative and MRSA

5) the most common pathogen that can cause chronic osteomyelitis in immunosuppressed patients?
A) fungi   B) streptococci   C) Enterobacteriaceae   D) Pseudomonas

1-A  2-B  3-A  4-D  5-A
1) Patients come with severe pain and fever a blood test showed -ve. Physician had followed this by a biopsy to the periosteum abscess and culture the organism of the cause was identified as MSSA what is your treatment plan? (please note it is acute OM)

A) Give Cloxacillin.

2) Patients come with severe pain and fever a biopsy a blood test showed -ve. Physician had followed this by a biopsy to the periosteum abscess and culture the organism of the cause was identified as MRSA what is your treatment plan? (please note it is acute OM)

A) Give Vancomycin.

3) 25 Yr old patient present with joint swelling and pain, other complains includes urethral discharge. The patient is not married, has travelled lately, lymes disease test showed -ve. What is the disease and what is the organism of the cause and what treatment should be given?

Disease: Gonococcal infectious arthritis.

Organism: Neisseria Gonorrhoeae, treatment: Ceftriaxone
“We cannot fathom the marvelous complexity of an organic being; but on the hypothesis here advanced this complexity is much increased. Each living creature must be looked at as a microcosm--a little universe, formed of a host of self-propagating organisms, inconceivably minute and as numerous as the stars in heaven.”

— Charles Darwin