MSS | lec. 7 micro sum.
Done by: Ola Alahdab

• Osteomyelitis: التهاب العظم ونخاعه

- infection of bone, leads to tissue destruction, debilityضعف and formation of sequestra (dead necrotic bone).

• **Caused by:** mycobacteria, fungi, viruses.

• Management is tailoredمضبوط for each individual.

• Tailored management depends on (factors):

• Causative organism

• Which bone is involved

• State of the vascular supply

• State of nerve function

• Presence of foreign bodies

• Recent injury

• The status of the host and any associated comorbidities.

- **The spectrum**: range from extensive (tibial/vertebral) to localized (bone invasion following a tooth abscess).

- **routes of pathogenicity:**

A) Haematogenous seeding

B) Contiguous spread from adjacent infected tissues

C) Traumatic or surgical inoculation of microorganisms.

• Collection of inflammatory exudates in the bone marrow leads to increased the bone medulla pressure ➡️ extension of the exudate to bone cortex ➡️ rupture through the periosteum.

↓

1. periosteal rupture

↓

2. interruption of the blood supply

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3. necrosis and separation of dead bone (sequestrum).

↓

4. The site of periosteal damage then becomes site for new bone formation (involucrum).

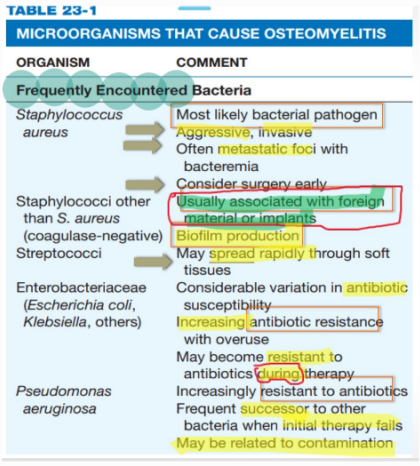
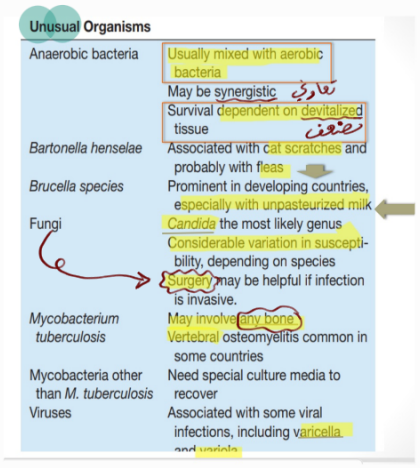


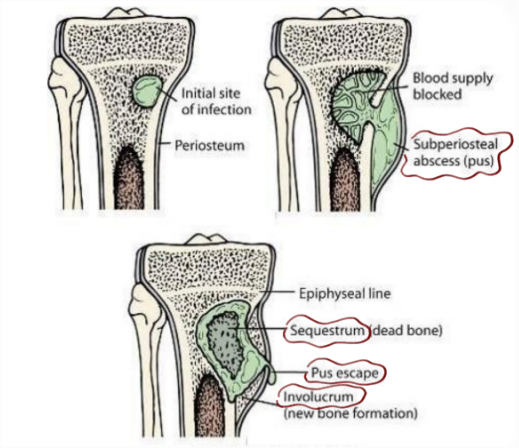
TABLE 23-1
MICROORGANISMS THAT CAUSE OSTEOMYELITIS

ORGANISM	COMMENT
Frequently Encountered Bacteria	
Staphylococcus aureus	Most likely bacterial pathogen Aggressive, invasive Often metastatic foci with bacteremia Consider surgery early
Staphylococci other than *S. aureus* (coagulase-negative)	Usually associated with foreign material or implants Biofilm production
Streptococci	May spread rapidly through soft tissues
Enterobacteriaceae (*Escherichia coli*, *Klebsiella*, others)	Considerable variation in antibiotic susceptibility Increasing antibiotic resistance with overuse May become resistant to antibiotics during therapy
Pseudomonas aeruginosa	Increasingly resistant to antibiotics Frequent successor to other bacteria when initial therapy fails May be related to contamination

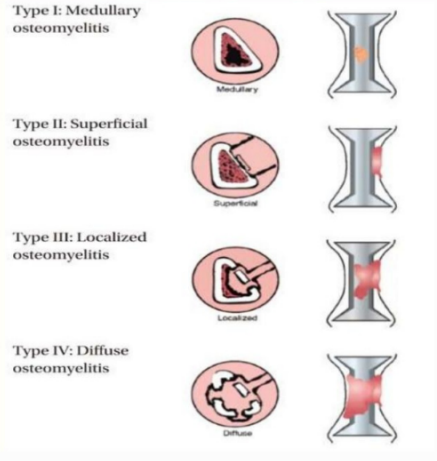


Unusual Organisms

Anaerobic bacteria	Usually mixed with aerobic bacteria May be synergistic تعاوني Survival dependent on devitalized tissue ضعيف
Bartonella henselae	Associated with cat scratches and probably with fleas
Brucella species	Prominent in developing countries, especially with unpasteurized milk
Fungi	*Candida* the most likely genus Considerable variation in susceptibility, depending on species Surgery may be helpful if infection is invasive.
Mycobacterium tuberculosis	May involve any bone Vertebral osteomyelitis common in some countries
Mycobacteria other than *M. tuberculosis*	Need special culture media to recover
Viruses	Associated with some viral infections, including varicella and variola



• the syndrome is identified as a spectrum (due to the mentioned factors) and two major **classification** systems are used (to make therapeutic decisions):
• 1) **Lee and Waldvogel system,** used three main criteria:
• a) acute or chronic
• b) hematogenous or contiguous
• c) with or without vascular compromise.
• 2)The **Cierny and Mader system:** used for long bone osteomyelitis takes into account the location and extent of infection (+other factors), it is a functional classification, based on the affected **portion of bone** and **physiological status of the host,** and is useful in guiding therapy
- There are four anatomical types:
stage 1 = **medullary** osteomyelitis, made
stage 2 = **superficial** osteomyelitis, a super
stage 3 = **localized** osteomyelitis, local
stage 4 = **diffuse** osteomyelitis. difference !!



- There are three physiological classes:
A = normal host
B = host with local (Bl) or systemic (Bs) compromise (Bl → local; Bs → systemic)
C = treatment worse than disease.

Causes:
• Haematogenous osteomyelitis: monomicrobial. Hematogenous → monomicrobial
• Contiguous osteomyelitis: monomicrobial or polymicrobial.
• The most common cause is Staphylococcus aureus and CoNS (>50%) (CoNS: coagulase -ve staph)
• others: 1. Gram-ve organisms such as Pseudomonas aeruginosa and Escherichia coli, enterococci, and propionibacteria.
2. Mycobacterium tuberculosis (a common cause in countries with limited medical resources)
3. other mycobacterial species that infect bone: M. marinum, M. chelonei, and M. fortuitum.
4. Fungi may include Candida, Coccidioides, Histoplasma, and Aspergillus species.

• In patients with sinuses, the superficial flora may not represent the true pathogen.

- **precipitating factors** (vary according to route of infection):

1- Prosthetic joint/stabilization devices and S. aureus (all foreign objects) are being used more frequently in orthopedic surgery and are associated with complex infections, S. aureus bacteremia causes a rate of metastatic osteomyelitis, & 28% if there is a prosthetic joint in place, complicated by MRSA involvement.

- Any type of instrumentation may lead to infection in a small proportion of cases.

2- Trauma if a wound is involved with trauma that leads to contamination of bone or surrounding tissue - with significant tissue damage.

• It's **NOT necessary to have an open wound or a compound fracture.** In a similar fashion to what is seen in pyomyositis:

*damaged tissue and internal bleeds slows down the circulation which creates favorable condition for bacterial growth, in these damaged tissues, bacteria from peripheral veins or lymphatic channel (low level bacteremia) may cause infection, in otherwise situation, circulation would prevent that from occurring.

3. **Bacteremia:** a frequent cause of osteomyelitis, maybe arising from **endocarditis** or from **seeding of other infection sites** (abscess, boils..etc)

4. Urinary tract circulation: (especially due to UTI causing pathogens **(E. coli and Klebsiella)**),The overlapping circulations of the urinary tract and the spine is a source of **vertebral osteomyelitis.**

E. coli and Klebsiella → (May Cause) **vertebral osteomyelitis**

5. Limited vascular supply: limited blood supply causes limit perfusion to bone to the point of an inadequate response and poor healing.

6. Diabetes and other host factors (aging/obesity) may cause osteomyelitis through impaired immunity with hyperglycemia, loss of sensation, vascular disease, and renal failure.

- After a foot puncture, 30–40% of adults with diabetes develop osteomyelitis.

- Diabetes in adults poses the most significant risk (and further accentuates the above factors).

-Diabetic neuropathy makes progression of the disease much worse, as the patient would be unaware or any symptoms (pain sensation reduced).

7. immunosuppression causes more infections, thus more osteomylitis.

- MRSA has been steadily replacing MSSA & causes more morbidity.

- Is MRSA more aggressive because it can evade antimicrobials so has more time to cause damage? Or is it cause there bugs survive longer and get more virulence factors??

- Richer countries have more orthopedic-related Osteomyelitis, whereas poorer countries have more TB and brucella or significant wounds in the society (wars, accidents), & less healthcare service (micro labs, Abx..etc).

Pathogenesis: (can be applied to all pathogens mentioned in this module)

تقريبا نفس أفكار الصفحة السابقة

The most common predisposing factor for osteomyelitis is an area of bone (or contiguous surrounding tissue) that is defective in in viability, blood supply, sensation.

This damaged tissue suffers from reduced oxygenated arterials supply and hindered venous and lymph out flow (less in, less out), these are prime factors that provide bacteria with optimal growth conditions (O2, nutrients, less inflammatory cytokines and WBC..etc).

• Host factors such as poor nutrition and immunosuppression may also be relevant.

Bacterial pathogenesis: Bacteria that cause OM perpetuateتخلد themselves (they maintain their presence) by secreting toxins that continually damages surrounding tissue.

S. aureus is especially strong in this respect, where it colonizes the **nasal area** and produce toxins that destroy tissue and affect neutrophil response.

- Certain strains of S. aureus can survive uptake into the phagocytic vacuoles of macrophages, thus keep causing tissue damage by consistently evading host defenses.

• Basically, two populations of S. aureus, *intra and extra cellular*, where *intra* cellular keeps replenishing the extra cellular pathogens.

• S. aureus can **remain dormant** (called **NCBV-viable but not culturable form**), these are **resistant forms** that hibernateتدخل في سبات and remain inactive for decades before infection erupts at sites of old injuries (especially penetrating wounds, shrapnel..).

• Although **CoNS are less virulent than S. aureus**, but they persist many years on prosthetic joints (with minimal symptoms) by producing a biofilm that protects them from the host.

• **In CoNS it is common for prosthetic joints to show no symptoms and suddenly show infection a year or even more later.**

• How much other organisms use their biofilm to their advantage is not fully understood, but **biofilm production** probably plays an important role in osteomyelitis, especially in **chronic** forms.

• Multiple bacteria may be recovered from cultures, especially when there is an entry wound,This makes the decision which one to target in antibiotic therapy difficult.

- common skin flora and colonizing bacteria are not targeted (if they are, it might make them more aggressive and resistant).

• Anaerobic bacteria can often be recovered and can play synergistic role with other pathogens. تعاوني

*** Acute osteomyelitis** is usually in **pediatric patients** and due to **hemtogenous spread.** Hematogenous → monomicrobial → acute

*** subacute to chronic is** usually in **adults.**

- Clinical features:

• pain around the affected site.

• Local and systemic signs of inflammation such as swelling, tenderness, warmth, and *erythema may or may NOT be present! (especially in vertebra, hip or pelvis-not long bones).*

Chronic osteomyelitis presentation may begin local signs of inflammation and/or presence of a sinus tract, or fracture).

• prolonged skin ulcers that fail to heal with antibiotic therapy may indicate underlying osteomyelitis, in such case, if bone is felt when palpating an ulcer this can be sufficient to diagnose osteomyelitis.

Diagnosis 1:

• **clinical** suspicion اشتباه, confirmed by a **radiology, microbiology and pathology.**

• **Blood tests.**

• **Blood cultures** are more likely positive in **vertebral** infection and in **haematogenous** spread (clavicle, pubis). Hematogenous → monomicrobial → acute → Blood culture

• **White cell count** may be raised but can be normal.

• **Inflammatory markers** (ESR and CRP) are usually high, but they are not specific and can be elevated in other conditions other than osteomyelitis (CRP changes occur earlier in bacterial infection). ©comes before Ⓔ in alphabets :

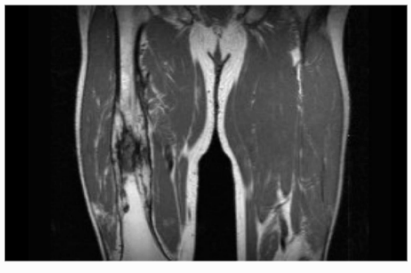
Diagnosis 2

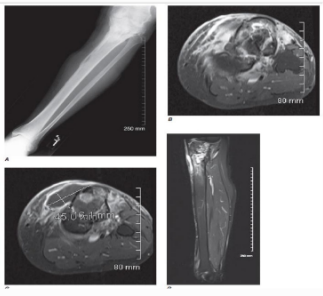
• **Radiology**: plain X-ray may show changes after 1-2 weeks, & may eliminate the need for further imaging studies.

***Hallmarks of bone infection:** Bone loss, sequestra, periosteal elevation or swelling (which can develop early on), and shadows around foreign bodies.

• **CT (computed tomography) or MRI** scans (MRI is specific and sensitive).

• MRI is contraindicated in patients with metalware; these may cause artefacts on CT.





Diagnosis 3:

• **Biopsy**: open or percutaneous bone biopsy, it can be taken in open surgery with debridment of all necrotic tissue, which is both Rx and Dx.

• **Needle aspiration** of pus collection is also both Rx and Dx for the pathogen.

• antibiotics should be stopped 48-72 hours prior to biopsy to improve the yield of culture.

• **Swabs from sinus tracts** are of questionable value, and may be presenting the local flora.

• **PCR and sequencing technologies** detect and identify specific organisms

• (even their sensitivity to **Abx**) within hours instead of days or weeks.

Management: (General principles)

• The aim of treatment is to eradicate the agent and restore/preserve function of the bone.

• OM in adults is usually treated with a combination of surgical debridement and antibiotic therapy.

• Surgery: the principles of surgical therapy are debridement of infected tissue, removal of metalware, management of dead space (using a flap), wound closure, and stabilization of infected fractures.

Antimicrobial therapy:

• Choice of ABx therapy is based on **culture** and **sensitivity results,** duration is unknown and most experts treat for 4-6 weeks IV therapy that is increased for

more extensive disease or with patients with additional comorbidity (see previous classification-Cierny Mader) + vertebral OM.

1. The addition of rifampicin to β-lactams was effective in certain staphylococcal OM animal models & used in infections, (particularly that involve prosthetic material).
   • Patients are usually discharged once they are clinically stable and treated as outpatient with an IV antimicrobial catheter.
2. **Hyperbaric oxygen** was effective in animal studies (no data in humans) and can be used as adjunctive therapy.
3. **Negative pressure wound therapy** (vacuum-assisted closure) is used and may accelerate wound healing in complex wounds and in diabetic patients.
   • There is still controversy about the optimal route and duration of therapy.
   - in pediatric population, adequate treatment with shorter duration + oral therapy is suggestive, & Because some of the active agents reach comparable levels when given by mouth, a switch from IV administration to oral therapy may be appropriate in some situations.

Complications:

1. Sinus tract formation.
2. Pathological fractures, as the sequestra make that area of bone less able to bear weight and is prone to fracture.
3. Haematogenous spread and sepsis, especially in aggressive disease.
4. Tumours in patients with long-standing (4–5 years)
5. Rarely, chronic inflammation and infection may lead to malignant transformation into squamous cell carcinoma or sarcoma

Osteomyelitis, e.g. squamous cell carcinoma (commonest), fibrosarcoma, myeloma, lymphoma, plasmacytoma, angiosarcoma, rhabdomyosarcoma, and malignant fibrous histiocytoma.

Prognosis:

• Varies, on all the factors that are included in the classfication systems.
• Veretbral: immunecompromised-late Dx..etc, **poorer prognosis**
• Mandible following tooth extraction, early proper treatment: **better prognosis**.

Prevention:

• mupirocin and chlorhexidin (in preventing operative infections, which are a common cause in prosthetic joins OM).
• **Early Dx and treatment** of other infection routes (abscess, bactermia, boil…etc).
• **Early surgical treatment** of wounds (esp extensive ones).
• Sacral ulcers, can be often a point of infection –bed ridden patients- and easily overlooked.

TABLE 23-2

ANTIBIOTICS FOR THE TREATMENT OF OSTEOMYELITIS

ORGANISM	ANTIMICROBIAL AGENT	DOSING	COMMENTS
Methicillin-susceptible *Staphylococcus aureus*	Oxacillin or nafcillin	2 g IV q6h	May be more active than cephalosporins More difficult than cephalosporins to administer for long periods
	Cephalosporins	Cefazolin: 2 g IV q8h Ceftriaxone: 1–2 g IV q24h	Ceftriaxone advantageous with OPAT
	Clindamycin[a]	600–900 mg IV q8h	Not well studied for osteomyelitis Oral form possible (300–600 mg q8h) Resistance significant and increasing Toxicity different from that of β-lactam antibiotics
Methicillin-resistant *S. aureus*	Vancomycin	15 mg/kg IV q12h	Strains with an MIC of ≥2 μg/mL may not respond well.
	Daptomycin[a]	4–6 mg/kg IV q24h	Promising, but concern about adverse effects with prolonged therapy
	Linezolid[a]	600 mg IV or PO q12h	Effectiveness and adverse effects with prolonged therapy unclear Bacteriostatic
Streptococci	Penicillin	5 mU IV q6h or 20 mU/d by continuous infusion	Not all streptococci are susceptible. Ceftriaxone (1 g/d IV or IM) and ampicillin (12 g/d IV) are alternatives.
Enterococci	Penicillin plus gentamicin	As above 5 mg/kg daily IV	If strain is susceptible
	Vancomycin	As above	If strain is susceptible
Enterobacteriaceae (*E. coli*, *Klebsiella*, other)	Ceftriaxone or another cephalosporin	As above	If strain is susceptible
	Ciprofloxacin	400 mg IV q8–12h	500–750 mg q8–12h if strain is susceptible
Pseudomonas aeruginosa	Ciprofloxacin	As above	Resistance may develop during therapy; if strain is resistant, drugs to consider include cefepime and ceftazidime.

[a]Not approved for use in osteomyelitis by the U.S. Food and Drug Administration.
Abbreviations: MIC, minimal inhibitory concentration; OPAT, outpatient parenteral antimicrobial therapy.

Septic Arthritis: التهاب المفاصل الجرثومي/العدائي

- An **inflammatory reaction** of the **joint space** caused by an infectious agent.
- caused by bacteria(usually), mycobacteria, or fungi.
- Very common, hard to treat. Due to use of prosthetic joints(2-10%), immuno compromission and eldery.
- (45% of ppl with Septic arthritis are above 65 years and 56% are male)

Caused by:

• **S. aureus:** *commonest overall*, especially in **acute** cases, increase use of Prosthetic joints increase their incidence.

• Streptococci: groups A, B, C, and G streptococci, + S. pneumoniae and viridans groups.

• CoNS • E. coli • H. influenzae • N. meningitidis • Salmonella spp • other causes, brucella, polymicrobial.

☆ • N. gonorrhoeae (the *commonest cause in sexually active young adults).*

☆ • P. aeruginosa (sternoclavicular joints, sacroilliac joints).

- Prosthetic join infection:

According to presentation:

• Acute (S. aureus) within 3 months

• Subacute within 3-24 months

• Chronic >24 months
• **S.aureus cause the delayed cases more.**

- Risk factors:

• **Age** >80 years • **Diabetes** mellitus • **Rheumatoid arthritisn** • **Prosthetic joint** • Recent **joint surgery** • **Skin infection/ulcers** • **Intra-articular corticosteroid infection** • **injection drug use, and alcoholism.**

Pathogenesis:

1. *the most common route*: after haematogenous seeding of pathogenic bacteria.
2. contiguous spread or direct inoculation like osteomyelitis.

Note: Healthy synovial cells have phagocytic activity and normally able to clear any seeding from outside sources.

3. weakness to immune system (SLE (Systemic lupus erythematosus), Rhuematoic arthritis..etc) increases risk.
4. Previously damaged joints (These joints show neovascularization and adhesion factors, which promote bacteremia and consequent infection).
5. S. aureus especially binds to articular sialoprotein, collagen, elastic and prosthetic materials visa tissue adhesion factors that they possess.

* chondrocyte proteases of S. aureus Infection damage the cartilage, the inflammation causes further damage to it.

* **Gonococcal arthritis exhibits much less influx of WBC into the joint, which explains why it is not as destructive to joints as other bacteria.**

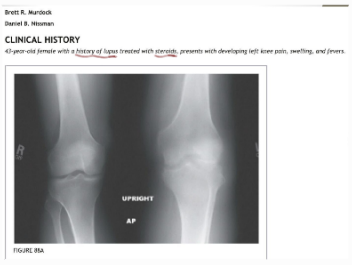
Clinical features:

• Children and adults with acute septic arthritis usually present with **fever** and **monoarticular involvement.**
• The knee is the most commonly affected joint, followed by the hip.
• Clinical features include pain, swelling, and reduced mobility in the joint.
• **Polyarticular infections occur especially in rheumatoid arthritis and viral causes patients.**
• **Infections with mycobacteria or fungi usually have an insidious onset.**

Diagnosis:

• Laboratory: shows a raised WCC and inflammatory markers.
• Joint aspiration: shows purulent synovial fluid, with an elevated WCC, mostly neutrophils.
• Gram stain is positive in 29–50%, and culture is positive in 80–90% of cases (synovial fluids in blood culture bottles may improve yield)
• Samples should also be sent for microscopy for crystals. BCs are positive in 75% of cases.

Imaging:



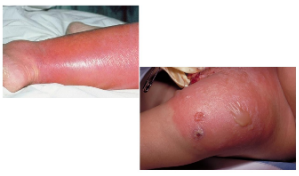
• Radiographs of the affected joint may be normal at presentation.
• Typical changes are periarticular **soft tissue swelling, fat pad edema, periarticular osteoporosis, loss of joint space, periosteal reactions, erosions, and loss of subchondral bone.**
• Ultrasound can be used to confirm an effusion and guide aspiration.
• CT and MRI are highly sensitive for imaging early septic arthritis. CT is better for imaging bone lesions.
• MRI may not distinguish septic arthritis from inflammatory arthropathies.

Management:

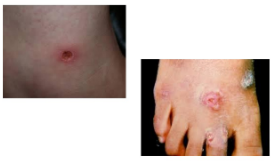
• Drainage of the joint, either by closed aspiration or arthroscopic washout, should be performed urgently.
• Open drainage may be required either when repeated drainage has failed to control the infection or for drainage of hip joints.
• Prosthetic joint infections often require removal of the prosthesis.

Antimicrobial therapy:

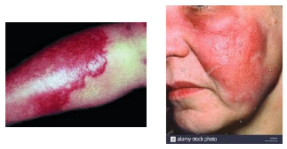
According to the initial Gram stain findings.
Empirically: IV piperacillin–tazobactam ± vancomycin.
• Definitive therapy is tailored to culture and sensitivity results
• Adjunctive therapy with a short-course systemic corticosteroid treatment has been shown to be of benefit **in children with haematogenous bacterial arthritis.**



CELLULITIS



ECTHYMA



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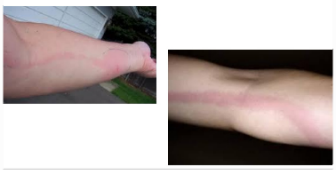
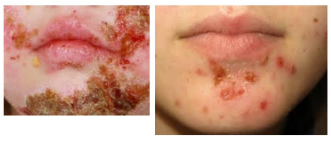
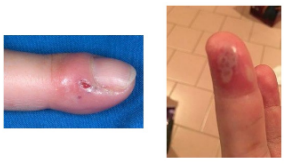


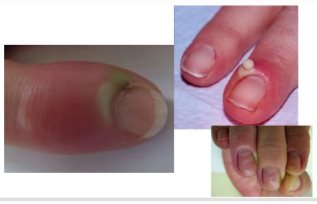
LYMPHANGITIS



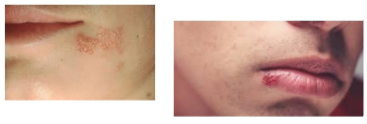
IMPETIGO



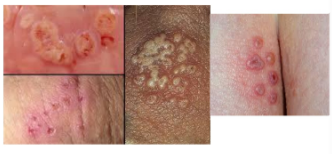
WHITLOW



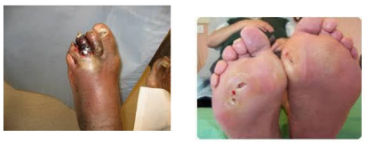
PARONYCHIA



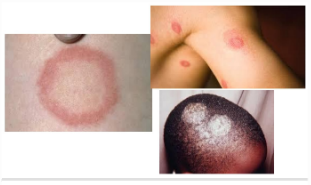
HERPES LABIALIS



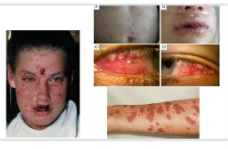
HERPES GENITALIS



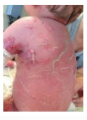
GAS GANGRENE AND DIABETIC FOOT



RING WORM



STEVEN JOHNSONS



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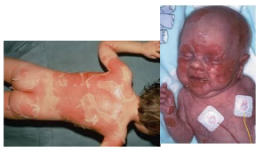
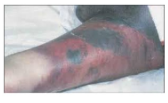


SSSS



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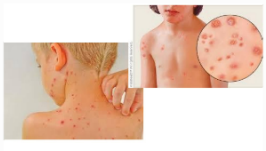

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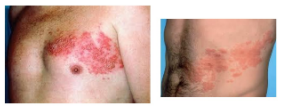

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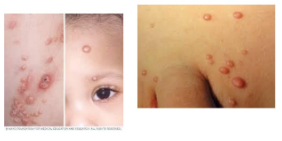
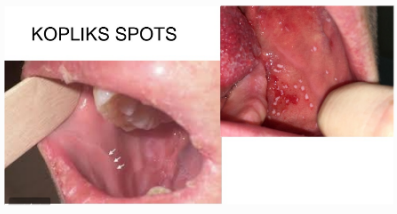


MOLLUSCUM

KOPLIKS SPOTS



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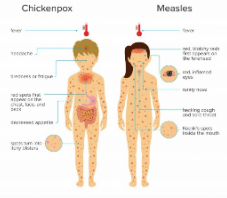

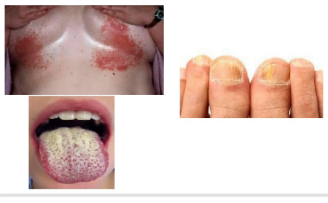

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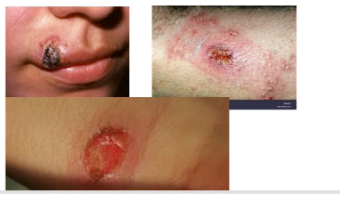

CUTANEOUS LEISHMANIASIS