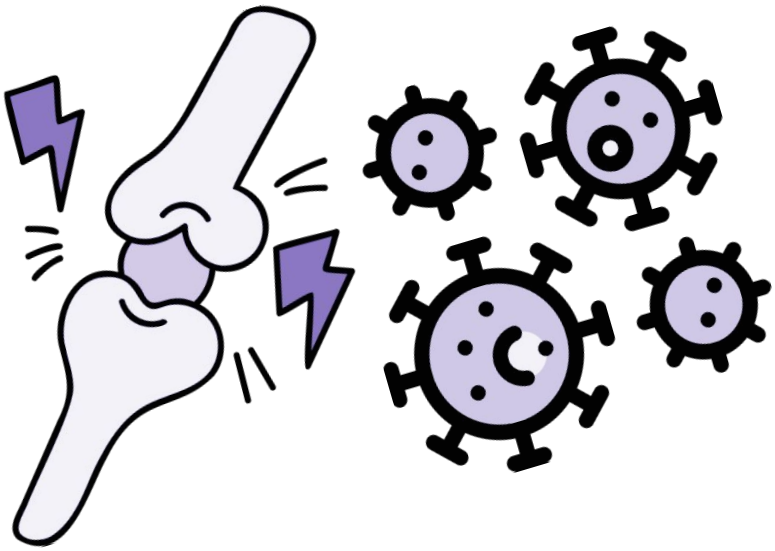

# Rheumatology & Infectious diseases

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# L31- Rheumatoid Arthritis

- **Definition:**
  - Autoimmune disease against the whole body (Joints mainly)
- **Pathogenesis:**
  - Synovitis → **Pannus → Erosions**
  - Pannus → T-cells and macrophages
  - Synovial fluid → Neutrophils
- **Clinical features:**
  - **Articular:**
    - **Symmetrical** arthritis of the small joints (**DIPJs are spared**)
    - **Deformities: Spindling**, "Z" deformity of the thumb, Swan neck (Hyperextension of PIPJ), Boutonniere (Flexion of PIPJ), ulnar deviation at the MCPJ and radial deviation at the wrist
    - ★ Cervical subaxial subluxation (**C1** and **C2**) (Do X-ray before surgery/intubation)
  - **Extraarticular:**
    - ★ **Felty syndrome:** RA + Splenomegaly + Neutropenia
    - **Caplan's syndrome:** RA + Lung nodules +Pneumoconiosis
    - **Scleritis** (cf. SpA)
    - Sjogren syndrome
    - Mononeuritis multiplex in case of **rheumatoid vasculitis**
    - Anemia of chronic disease (**Normocytic normochromic**)
    - CAD is the most common cause of death
    - Amyloidosis: Proteinuria + Edema + Carpal tunnel syndrome
- **Diagnosis:**
  - **Serology: RF** (IgM against Fc portion of IgG) and **Anti-CCP** (More specific) but both are not diagnostic
  - CBC (**Anemia** + **Thrombocytosis**)
  - ESR and CRP (Both will be high)
  - X-ray (**Erosions, periarticular osteopenia and subluxation**)
  - RFT and LFT for baseline before giving meds
  - ★ Aspiration of joint if you suspect Septic arthritis
    Note: **Suspect Septic if: Sudden + Monoarticular**; treat with aspiration and abx (Vanco or fluxo since Staph. Aureus is the most common)
- **Treatment:** (For all check CBC and LFT)
  - ***1st line:*** **NSAIDs (To relieve the pain) + MTX (To prevent progression)**
  - ***2nd line:*** NSAIDs + MTX + Leflunomide
  - ***3rd line:*** NSAIDs + MTX + Leflunomide + HCQ
  - ***Last resort:*** Anti-TNF (Check TB and fungal infxn)
    **N.B.** Use CS only for flare-ups or if NSAIDs are not working
  - ***Special cases:***
    - **If pregnant or mild non-erosive disease → HCQ (Check eye)**

# L32- Scleroderma Spectrum Disease

## Definition:

- A group of heterogeneous diseases that has a predominant feature and share other common features. They are rare, difficult to treat and associated with significant morbidity and mortality.

## 1. Scleroderma spectrum diseases

- **characterized by:**
  - **Skin thickening**
  - **Vasculopathy**
  - **Autoantibody**
- **Types of SSc**
  - **Diffuse:** (Diffuse Cutaneous Scleroderma (DcSSc) I 30% of cases)
    - Associated with **more internal organ involvement**
    - Has a **worse prognosis**
    - **Anti-topoisomerase** / RNA polymerase III antibodies.
  - **Limited:** (Limited Cutaneous Scleroderma (LcSSc) I 70% of cases)
    **also known as CREST syndrome:**
    - Calcinosis, Raynaud's phenomenon, Esophageal involvement, Sclerodactyly, Telangiectasia
    - Often more indolent (has a longer disease duration before diagnosis)
    - Has a **higher risk of pulmonary hypertension**
    - **Anti-centromere antibodies.**

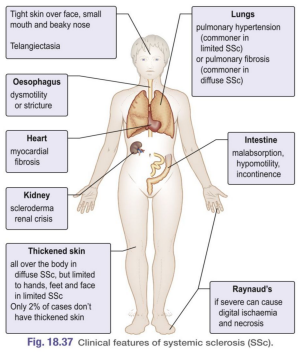


Fig. 18.37 Clinical features of systemic sclerosis (SSc).

- **AutoAntibodies in SSc**
  - **Anti-Scl-70 (topoisomerase) is associated with:**
    - **Diffuse** subset
    - The **development** of ILD
    - **Reduced** risk of PAH
  - **Anti-centromere is associated with:**
    - **limited** subset
    - **P**ulmonary **A**rterial **H**TN
    - **D**igital **u**lcer
  - **RNA polymerase III is associated with:**
    - **Scleroderma Renal Crisis**
    - **Malignancy** associated SSc
    - **Mortality.**

## Involvements in SSc

- **Skin:**
  - Skin is the Largest and Most Important Organ in SSc
  - The **level of skin involvement** predicts **severe disease and mortality.**
  - ★ **SKIN INVOLVEMENT ALWAYS STARTS IN THE FINGERS AND TOES (distally) AND EXTENDS PROXIMALLY.**
  - **Treatment:** To prevent joint contracture and disability in the hands.
    - **Methotrexate:** Avoid it if the patient has interstitial lung disease or renal failure because of its toxic effect.
    - **Mycophenolate mofetil**
    - **Cyclophosphamide**
    - **Rituximab**
    - **Steroids:** High-dose corticosteroids is a **significant risk** factor for **Scleroderma renal crisis** and is best to be avoided in patients with DcSSc.

# L32- Scleroderma Spectrum Disease

## Involvements in SSc cont.

- **Skin: Raynaud's Phenomenon(RP) and Digital Ulcers(DU)**
  - 95% and 50% of SSc have RP and DU respectively, but **RP tends to occur years before the diagnosis of SSc** unlike DU that usually occur in the first 5 years after the development of the non-RP manifestation.
  - **Treatment in RP:**
    - **Calcium channel blockers (FIRST-LINE)**
    - If the patient is not responding you can give IV prostaglandins or even Phosphodiesterase inhibitors
    - **IV iloprost better than nifedipine.**
  - **Treatment in DU:**
    - **CCB has not role in Digital ulcer**
    - **Phosphodiesterase inhibitors & IV prostaglandins: Prevent** new ulcers and **Improve** (fasten) the healing.
    - **Endothelin receptor antagonist:** Only **prevents** new ulcers and **DO NOT** improve the healing.
- **Lungs: Interstitial lung disease:**
  - ★ Interstitial Lung Disease is the number ONE cause of mortality in patients with SSc.
  - ★ Common in patients with DcSSc who have topoisomerase 1 antibodies (Scl70)
  - High-resolution lung CT is the Gold standard.
  - ★ **Clinical findings in ILD:**
    - Tachypnea - Tachycardia - Cyanosis - Clubbing - Reduced chest expansion - Fine early inspiratory crackles
  - **Treated with** cyclophosphamide
- **Lungs: Pulmonary Arterial Hypertension:**
  - **PAH is defined as Pulmonary Arterial Pressure ≥ 25 mmHg** with a normal Pulmonary wedge pressure (≤ 15 mmHg.)
  - The **First** investigation to order is **echocardiography.**
  - The **Gold** diagnostic tool is **right sided heart catheterization.**
  - ★ **Clinical findings** (It is important to look at the lung and heart together)
    - Desaturation ● Tachycardia ● Palpable P2 ● Parasternal heave ● Loud 2nd heart sound ● Signs of right sided heart failure which include: JVD, lower limb edema and ascites. ● PFT may show isolated low DLCO
  - **Treatment:**
    - **Endothelin Receptor Antagonists:** Bosentan, Ambrisentan**,** Macitentan**,** Sitaxentan
- **Gastrointestinal System:** is the most common internal organ to be involved (95-99%) which includes:
  - **Mouth,** Esophagus (most common) , Stomach, Small bowel, Large bowel, Anorectal incontinence
- **Scleroderma Renal Crisis (SRC)**
  - Patients with SSc usually have low BP, once you see high BP suspect SRC.
  - Precipitating factors include: high dose steroids, cyclosporin & pregnancy.
  - **Best (and only) drug: Angiotensin Converting Enzyme Inhibitors (ACE inhibitors)**
- **Others:**
  - **Arthritis:** similar to RA with erosions and joint destruction
  - **Myositis:** manifested by weakness with no pain and high muscle enzymes.
  - **Cardiac:** Myocardial fibrosis leading to conduction abnormalities, cardiomyopathy and accelerated coronary artery disease.

## 2. Sjogren's Syndrome

**Definition:**

- It is a systemic chronic inflammatory disorder characterized by **lymphocytic infiltrates** in **exocrine organs.** Especially the lacrimal and salivary glands. There is an association with HLA-88/DR3
- **Most individuals with Sjögren's syndrome present with sicca (dryness) symptoms, such as:**
  - **Xerophthalmia-** (dry eyes)**- Xerostomia** (dry mouth)**- Vaginal dryness- Parotid gland enlargement.**

**Diagnosis criteria of primary Sjogren's Syndrome:**

- **At least 4 of the criteria listed below (you MUST have number 1 or number 2)**
- The best initial test is Schirmer test
- the most accurate is a minor salivary gland (labial) biopsy.
- Best initial test on blood: SS-A and SS-B. These are also called "Ro" and "La" and are each present in about 65% of patients.
- Positive anti–SSA, This antibody is of particular interest because it can cross the placenta and cause congenital heart block

| | |
|---|---|
| 1 | • Positive minor salivary gland biopsy findings showing lymphocytic infiltration. |
| 2 | • Positive anti–SSA[3] anti-sjogren syndrome A or anti–SSB anti-sjogren syndrome B antibody results |
| 3 | • Oral signs (sialogram, scintigraphy or sialometry findings) |
| 4 | • Ocular signs (Schirmer test)[2] |
| 5 | • Oral dryness |
| 6 | • Ocular dryness |

**Extraglandular manifestations of Sjogren's Syndrome:**

- Arthritis - Myositis - Pancytopenia - Palpable purpura - **Renal tubular acidosis type 1** - **Severe unexplained Fatigue** - Raynaud phenomenon - Generalized osteoarthritis - Demyelinating disease **(Eg. Multiple sclerosis)** - interstitial lung disease - Interstitial nephritis - arthralgia

**Treatment:**

- The best initial therapy is to water the mouth.
- Parasympathomimetics (pilocarpine) **will increase the secretion of salivary and lacrimal glands.**

**Complications:**

- **SS patients are at risk of developing Non-hodgkin's B cell lymphoma 20 times more than the general population. Malignancy is the most common cause of death.**

## 3. Idiopathic inflammatory Myopathies

**Definition:**

- Are a group of autoimmune myopathies that are characterized by muscle weakness due to muscle inflammation and damage. they are **Mainly in the proximal muscles** but it can progress to peripheral muscles. and The onset is insidious and progressive.

**Organ involvement:**

- **Pharyngeal muscle** involvement can present as **dysphagia** and can lead to **aspiration pneumonia**.
- **Chest wall weakness** can present as **dyspnea** and lead to **type II respiratory failure.**
- Can affect the **heart** and lead to **cardiomyopathy**

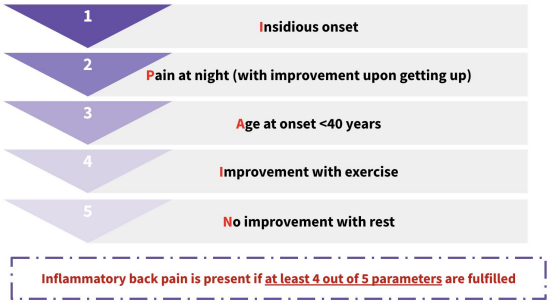
**Investigations:**

| | |
|---|---|
| Muscle enzymes | CK, LD, AST, ALT, Aldolase.<br>The **best initial test** is CPK and aldolase |
| MRI Muscle | Showing muscle edema |
| Muscle biopsy | Showing lymphocytic infiltration (Either CD4 or CD8, based on the subtype).<br>Muscle biopsy is the **most accurate test** Establishing diagnosis and excluding other causes of myopathies. |
| EMG | Myopathic changes. Not very helpful |
| Autoantibodies | **Jo-1** the most common, occurs in around 40% of patients , Non-Jo-1 antibodies, Anti-SRP, Anti-Mi2 |
| **MOST IMPORTANT:** RULE OUT OTHER CAUSES OF MYOPATHIES (Eg, hypothyroidism, hyperthyroidism, diabetes, cushing syndrome, Addison disease, statins ,etc) | |

**Treatment:**

- **Steroids (Oral prednisolone is the treatment of choice)**
- Methotrexate
- Mycophenolate mofetil
- Azathioprine
- Rituximab
- **Intravenous immunoglobulins** if the patient has dysphagia or chest wall involvement (Heart, pharyngeal muscle, etc)

- **Introduction:**
  - **Low back pain:**
    - Can be inflammatory or mechanical
    - **IPAIN** criteria for inflammatory
  - **Definition of SpA:**
    - Seronegative spondyloarthropathies
    - Associated with HLA-B27
  - **Types:**
    - AS, nr-axSpA, IBD related, Juvenile, PsA and ReA




## 1. Ankylosing spondylitis:

- **Definition:**
  - Bilateral grade ≥2 Sacroiliitis on X-ray or unilateral grade 3 and 4 sacroiliitis
  - N.B. If changes are only seen on MRI then it's nr-axSpA
- **Clinical features:**
  - ASAS criteria; Low back pain for ≥ 3mo and age of onset < 45:
    - **Sacroiliitis + ≥ 1 SPPINE-ACHEE**
      **OR**
    - **+ve HLA-B27 + ≥ 2 SPPINE-ACE*E**
      ***Acute unilateral anterior uveitis** is the most common extra-articular feature, not related to disease activity
  - Kyphosis, loss of lordosis and reduced chest expansion

**SpA features** SPINE-ACHE

1) Dactylitis (**S**ausage digit)
2) **P**soriasis
3) **P**ositive family history for SpA
4) **I**nflammatory back pain
5) Good response to **N**SAIDS
6) **E**nthesitis (heel)
7) **A**rthritis
8) **C**rohn's/colitis
9) **H**LA-B27
10) Uveitis (**E**ye)
11) **E**levated CRP

- **Diagnosis:**
  - **Best initial:** X-Ray (Will show syndesmophytes and bamboo spine)
  - **Most accurate:** MRI
- **Treatment:**
  - ***1st line:*** NSAIDs
  - ***2nd line:*** TNF-inhibitors or IL-17 inhibitors

## 2. Psoriatic arthritis

- **Definition:**
  - Usually psoriatic lesions precede the arthritis (cf. AS) and it mainly involves the small joints (cf. AS)
  - Associated with nail lesions: Pitting, Oncholysis and ridging
  - Associated with Dactylitis
- **Patterns of arthritis:**
  - **Asymmetrical (after):** Oligoarthritis involving mainly small joints
  - **Symmetrical (Concurrent):** Involves small and large joints. Similar to RA.
  - **Ps Spondylitis (after):** Looks like AS but psoriatic lesions precede the arthritis
  - **DIP synovitis:** Only DIP joint is involved
  - **Arthritis mutilans:** Deforming erosive arthritis. Telescoping of skin.
- **Diagnosis:**
  - **Best initial:** X-ray (Will show pencil in cup)
  - **Most accurate:** MRI
- **Treatment:**
  - ***1st line:*** NSAIDs
  - ***2nd line:*** MTX
  - ***3rd line:*** Sulfasalazine
  - ***4th line:*** TNF-inhibitors or IL-17 inhibitors
    N.B. (If Ps Spondylitis use TNF-inhibitors or IL-17 inhibitors as 2nd line)

## 3. Reactive arthritis

- **Definition:**
  - STERILE arthritis following GI/GU infection (usually after 2 weeks)
  - Formerly known as Reiter's syndrome: Can't see, can't pee, can't climb a tree
- **Etiology:**
  - **GI:** Shigella, Salmonella, C.diff, Campylobacter and Yersinia
  - **GU:** Chlamydia
- **Clinical features:**
  - Asymmetrical oligoarthritis and Achilles enthesitis
  - Circinate balanitis: Superficial erosions on glans penis
  - Keratoderma blennorrhagica: Yellow-brown papules on palms and sole of foot
- **Diagnosis: (Usually clinical)**
  - Tap joint: Sterile with high neutrophils
  - Radiology: Similar to PsA
- **Treatment:**
  - ***1st line:*** NSAIDs
  - ***2nd line:*** MTX or Sulfasalazine
  - ***3rd line:*** TNF-inhibitors
  - **Abx against chlamydia:** Doxycycline/Azithromycin
    N.B. Don't use abx unless an organism has been identified

# L34- SLE

**Definition:**

- Chronic, multisystem inflammatory disease characterized by autoantibodies directed against self-antigens, immune complex formation, and immune dysregulation resulting in damage to essentially any organ.

**Pathophysiology: Disturbances in the immune system:**

- **High ratio of CD4+ to CD8+ T cells.**
- **Defects in immune cell tolerance leading to:** Production of **autoantibodies targeting** antigens located in **nuclei**, **cytoplasm**, on cell surfaces, and in plasma proteins
- **Autoantibodies**

**Etiology: Specific cause(s) of SLE is unknown. Multiple factors play a role in the etiology of SLE:**

- Environmental: **Ultraviolet light**, viruses (e.g. **EBV**), drugs cause or exacerbate, silica dust, smoking.
- Genetics predisposition : **HLA-DR2** and **HLA-DR3** and other HLA genes occur more often in SLE than in the general population.
- **Female to male rations and Hormonal factors: Age at onset :**
  - ➔ 65%: between **16 and 55 (Reproductive age)**.
  - ➔ 20%: before age 16.
  - ➔ 15%: after age 55 .
- Higher prevalence in men with **Klinefelter disease**, their extra X chromosome increases their susceptibility.

**Organ involvement:**

- **Joints 90%**
- **Pleuropericardial 60%**
- **Skin**
- **Kidney 50%**
- **Raynaud's 20%**
- **CNS 15%**
- **Mucous membrane 15%**

**Clinical presentation and diagnostic criteria:**

**ANA is needed to diagnose:** found in 95%-99% of cases. A negative ANA is extremely sensitive for SLE. You need to have **at least 4** of the following: (the more you get the more definite the diagnosis is) :

- Malar rash : tending to spare the nasolabial folds.
- Discoid rash : Erythematous raised patches. Chronic, affect deeper layers.
- **Photosensitivity**
- **Oral ulcers : painless**
- **Arthritis: Nonerosive** (but maybe deforming) arthritis involving 2 or more peripheral joints, usually symmetrical. characterized by tenderness, swelling, or effusion.
- **Serositis : A. Pleuritis B. Pericarditis C. Peritonitis**
- **Renal disorder : A.Persistent proteinuria** (>0.5 g/day) **B. Cellular casts**
- **Neurologic disorder : A . Psychosis or Seizures B. Cerebral lupus feature:** visual hallucination, chorea
- Hemolytic disorder : A. **Hemolytic anemia** **B. Neutropenia C. Lymphopenia D. Thrombocytopenia E.Leukopenia**
- **Immunologic disorder either: A. +ve antiphospholipid antibodies. B. Anti-DNA:** antibody to native DNA in abnormal titer Highly associated with lupus nephritis,+ it correlates with disease activity so it's used for **monitoring**
- **Antinuclear antibody (ANA)**

**Clinical features:**

- **Bullous rash**
- **Subacute cutaneous lupus erythematosus:** associated with **Anti-SSA/RO** & neonatal lupus. **leads to complete heart block** in the fetus (2%)
- **Chronic discoid rash Discoid scarring alopecia** (Irreversible)
- **Alopecia :** usually non scarring, goes back to normal once you treat the patient.
- **Externally not distinguishable from RA :** X-ray shows **non erosive** correctable deformity
- **Lupus in the lung capillaries (Emergency):** Pulmonary alveolar hemorrhage (mortality is 50%)
- Other symptoms: constitutional symptoms: **Fever** → one of the DDx of fever with unknown origin is SLE

**Investigations:**

- Blood count :
  - Normochromic, normocytic anaemia or autoimmune hemolytic anemia
  - Neutropenia
  - Lymphopenia
  - leucopenia
  - thrombocytopenia
- ESR and CRP : ESR: **A raised ESR, leukopenia and lymphopenia are typical of active SLE**
- **Urea and creatinine.**
- **Serum :**
  - **Complement C3 and C4 levels: reduced** in active disease
  - **Autoantibodies:**
    a. **ANA:** Sensitive but not specific
    b. **Anti-ds DNA** (in 70%): highly specific (but not sensitive)
    c. **Anti-Smith** (in 30%): very specific (but not sensitive)
    d. **Antiphospholipid antibodies** (in 25% to 40%)
    e. **Antihistone** (in 70%) are present in >95% of cases of **drug-induced lupus**.

**Drug induced lupus:**

- Nephritis and CNS not common.
- No anti-native DNA or hypocomplementemia.
- Resolution on **discontinuation of drug**.
- **Drugs with definite association with lupus erythematosus :**
  - Chlorpromazine(antipsychotic)
  - **Methyldopa** (antihypertensive)
  - **Hydralazine**(antihypertensive)
  - **Procainamide** (antiarrhythmic)
  - Isoniazid (antibiotic)
  - Quinidine

**Treatment of SLE:**

- **Mild to moderate disease:**
  - **NSAIDS**
  - **hydroxychloroquine**
- **Life-threatening disease :** for the treatment of **renal, CNS, and cardiac involvement** or flares.
  - **High-dose corticosteroids and immunosuppressants**
  - immunosuppressant drugs
    - **Cyclophosphamide** we **try to avoid in patients in productive age**. If we need to give it, it is given at lower doses, then switch to mycophenolate.
    - **Mycophenolate mofetil**:
- **General considerations:**
  - Avoid UV light and sun (sunscreening)
  - Antimalarial (Hydroxychloroquine and chloroquine) to prevent **relapses**. (For those who already got Lupus to prevent relapses, not just have +ve ANA)

**Pregnancy and SLE:**

Recurrent miscarriages can occur, **especially in women with anti-phospholipid antibodies**.

**Prognosis:**

- Poor prognostic factors for survival in SLE include:
  - Renal disease
  - Hypertension
  - Central nervous system (CNS) disease
  - presence of anti phospholipids antibodies: increase the risk for thrombosis.
    - Treatment: Warfarin (DO NOT USE NOAC)

## HIV Structure

subgroup of retroviruses, and it is an RNA viruses that replicate via a DNA intermediate.
It is made of:

1. The core: contain the genetic material [ RNA ] and Reverse transcriptase [ enzyme]
2. The capsid: outer protein coat. (p24)
3. Lipid envelope (env): It's derived from infected cell, containing numerous external spikes formed by two major envelope proteins:
   a. The external gp120 which attaches to host CD4+ T-cell.
   b. The transmembrane gp41
4. Polymerase (pol)

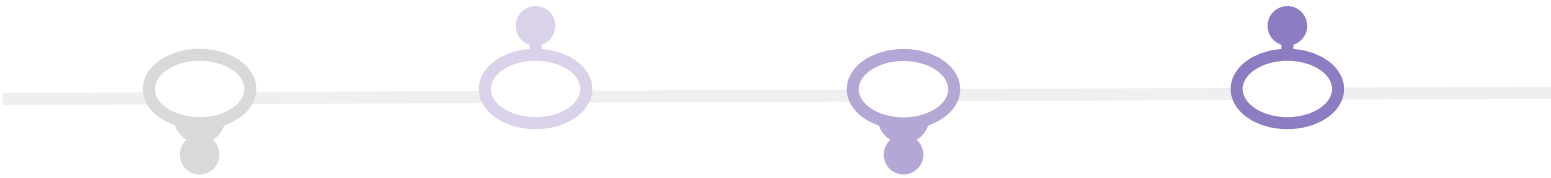
## Genetic susceptibility

**CCR5 (delta) 32 homozygotes genotype:** people who inherited the Delta 32 mutation, resulting in the genetic deletion of a portion of the CCR5 gene are **highly resistant to HIV infection.**

## Routes of Transmission

**Mother to child**
Can occur in utero (30%), although the majority of infections takes place perinatally (60%). It also can transmitted through breast milk (10%)
one-third of their babies become infected.

**Contaminated needles**
share needles and syringes. Health care workers with a needle-stick exposure are at high risk as well.



**Sexual intercourse**
heterosexual and homosexual

**Blood, blood products**

### What factors increase the risk of HIV transmission?

1. High viral load. ( Acutely infected or chronically untreated patient)
2. Certain sexual behaviours.( MSM is more )
3. Presence of ulcerative sexually transmitted infections.
4. lack of circumcision.
5. Certain other host and genetic factors.

## Complications of HIV infection

### 1. Pneumocystis jirovecii Pneumonia :

One of the leading causes of opportunistic infections among persons with HIV and low CD4 cell counts (<200 cell/mm3). It causes lower respiratory tract infection, Occurs in those who are unaware of their HIV diagnoses or are not receiving medical care.

- Pneumocystis is currently recognized as a fungus (atypical fungi).
- X-ray: typically shows bilateral perihilar interstitial infiltrates.
- Definitive diagnosis of PCP requires visualization of the cystic or trophic forms in respiratory secretions by methenamine silver stain
- Treatment: Trimethoprim-sulfamethoxazole.

**i 12.9 CD4 count and risk of common HIV-associated diseases**

| <500 cells/mm³ | |
|---|---|
| • Tuberculosis | • Kaposi's sarcoma |
| • Bacterial pneumonia | • Non-Hodgkin lymphoma |
| • Herpes zoster | • HIV-associated idiopathic thrombocytopenic purpura |
| • Oropharyngeal candidiasis | |
| • Non-typhoid salmonellosis | |
| **<200 cells/mm³** | |
| • *Pneumocystis jirovecii* pneumonia | • HIV wasting syndrome |
| • Chronic herpes simplex ulcers | • HIV-associated dementia |
| • Oesophageal candidiasis | • Peripheral neuropathy |
| • *Cystoisospora belli* (syn. *Isospora belli*) diarrhoea | • Endemic mycoses |
| **<100 cells/mm** | |
| • Cerebral toxoplasmosis | • Cytomegalovirus |
| • Cryptococcal meningitis | • Disseminated *Mycobacterium avium* complex (MAC) |
| • Cryptosporidiosis and microsporidiosis | • Progressive multifocal leucoencephalopathy |
| • Primary CNS lymphoma | |

### 2. Malignancy (AIDS-defining cancers):

**a) Kaposi sarcoma**

- associated with human herpesvirus 8 (HHV-8).
- (CD4 <500 cells/mm3).
- Diagnosis: Skin biopsy: spindle-shaped cells, leukocyte infiltration, and angiogenesis
- Management: decrease Incidence with use of antiretroviral therapy (ART).

**b) Non-Hodgkin lymphoma**

i) EBV related

**c) Cervical cancer**.

**i)** Related to HPV.

## Diagnosis

**Whom to test?**

1. **Symptoms of HIV infection:**Signs and symptoms of acute or chronic HIV infection should be tested. Testing for HIV RNA may be needed.
2. **Possible HIV exposure:** Patients after a known high-risk exposure to HIV (eg, sexual or percutaneous )
3. **Patient with sexually transmitted disease (STD).**
4. **Pregnant women** should be tested for HIV early in each pregnancy.

**Positive result** with **Third-(HIV- antibody only**, time to positivity 20-30 days**)** and/or **Fourth-generation (HIV antigen and antibody,** time to positivity 15-20 days**)** HIV serologic assays **should be confirmed by** confirmatory **HIV-1/HIV-2 antibody differentiation immunoassay**.

**What is the definition of Acquired Immunodeficiency syndrome (AIDS)?**

1. It is defined by a loss of CD4 T lymphocytes ( < 200 cell) OR
2. The occurrence of opportunistic infections or cancers in HIV infected Patient.

## Treatment

- Current ART does not cure HIV, only highly suppresses viral replication.
-Combination antiretroviral therapy (ART) declines in morbidity and mortality among persons with HIV.

**most countries start treatment if:**

1- CD4 count ≤350 : Initiating ART results in a significant decline in the risk of AIDS-related morbidity and mortality
2-CD4 count <200 cells [ AIDS ] : ART improves survival and delays disease progression.

**Treatment is initiated with three drugs:** two NRTIs in combination, with a third agent - either an NNRTI, a boosted PI or an integrase inhibitor.

## Drugs

1. **Reverse transcriptase inhibitors (-INE,-VIR)**
   a. Nucleoside Analogue RTI (NRTI): Abacavir (ABC), Emtricitabine(FTC) , Lamivudine(3TC) , Tenofovir
   b. Non-nucleoside RTI (NNRTI): Delavirdine , Efavirenz , Nevirapine.
2. **Protease inhibitors (-NAVIR):** Atazanavir, Darunavir
3. **Integrase inhibitors:** Raltegravir, Dolutegravir

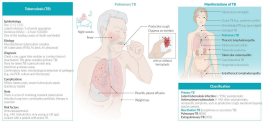
## Prevention

| Use of ARVs for prevention | |
|---|---|
| **Secondary prevention benefits of ART**<br>• Several studies confirmed that if an HIV-positive person is taking ART and is virally suppressed they do not transmit HIV to their uninfected sexual. | |
| **Pre-exposure prophylaxis for HIV-negative partner** | • Oral PrEP of HIV is the daily use of ARVs by HIV-negative people to protect themselves from high-risk sexual and needle-sharing practices with potentially HIV-infected contacts. Its effective in reducing HIV transmission. |
| **Post-exposure prophylaxis** | • **Indicated in case of:**<br>○ Sexual contact (unprotected)<br>○ Health care associated percutaneous exposure. (Needle-stick)<br>• PEP may be useful up to 72 hours after possible exposure.<br>• PEP is **not recommended when care is sought > 72 hours after potential exposure.**<br>• PEP is given for 1 month as a combination therapy |

## How to eliminate Mother to child transmission?

1. Effective antiretroviral therapy (ART)
2. Formula feeding

HIV-positive women are advised against breast-feeding, which doubles the risk of vertical transmission.



# L36- Tuberculosis



## Overview

- Tuberculosis is a bacterial infection caused by **Mycobacterium tuberculosis**
  - **Mycobacteria are acid-fast bacilli (AFB)—considered slow growing but hardy organisms.**

## Transmission

- By inhalation of **aerosolized droplets** containing the active organism from a person with active TB.
- After exposure to TB the patient will either present with an active TB or will just remain in a dormant latent phase of TB. Whether the patient had the infection or developed latent TB, **TST or IGRA will be positive.**

## Risk factors

**For TB infection:**
- Exposure to TB case & HCWs
- Homlessness or imprisonment
- From TB endemic areas
- Injection drug users

**For Progression to TB disease:**
- **Recent infection (<2 years)**
- **HIV-positive patients**
- Immunosuppression (anti TNF-a)
- ESDR - DM - Silicosis
- CXR showing prior TB
- Malnoureshment (intestinal bypass)
- Cancer (Hodgkin/Leukemia)

## Clinical Presentation

**General symptoms: - Fever - Sweats - Weight loss - Malaise - Decreased appetite**

**Pulmonary TB:**
**- Cough - Purulent sputum - Haemoptysis** in cases of cavitation - SOB
**- Subacute in onset, but can be acute in immunocompromised patients.**

**Extrapulmonary TB:**
- TB can affect any organ: (**TB lymphadenitis** (25%), Pleural TB, Skeletal TB, **TB meningitis**, GI & GU).
- It is important to obtain clinical specimens from the site affected.

**Disseminated (Miliary) TB**
- hematogenous spread TB.
- Presents with acute sepsis-like syndrome esp. in immunocompromised patients.
- Mostly nonspecific, could include lymphadenopathy or hepatosplenomegaly

**Diagnosis**: - **blood culture** and resp. specimens - CXR: multiple small nodules

## Diagnosis

Smear microscopy:
- 3 Specimens.
- ↓ Specificity and Sensitivity.

Rapid MTB PCR:
- ↑ **Specificity**, shows Rifampicin resistance.

**PPD & IGRA:**
- Don't distinguish latent from active.
- **IGRA isn't affected by prior BCG.**
- **IGRA False +ve:**
- **M. Kansasii - M. Marinum.**

Histopathology:
- Caseating granuloma

Culture:
- **Highest Sensitivity**
- **GOLD STANDARD**

**Chest Imaging (CXR):**
**Apical cavity ± lymphadenopathy.**

## Treatment & Prevention

**First line therapy: (RIPE)**
**Induction**: (2 months)
**R**ifampin **(enzyme inducer)**
**I**soniazid (INH) > **Per. Neuropathy**
**P**yrazinamide **> hyperuricaemia**
**E**thambutol > **Optic Neuritis**
**Cont.** INH & Rifampin (4 months)

**Treatment for latent TB** (i.e., +PPD skin test):
- **Rifampin daily for 4 months** or INH daily for 9 months
- **Active TB has been excluded FIRST (negative CXR, sputum, or both).**

**Extend treatment in case:**
**Pulmonary TB** is persistent (CXR/culture) (9m total)
**CNS TB** (9-12m total)
**Bone and Joint TB** (6-9m total)

**Prevention:**
**BCG Vaccine.**

## HIV & TB

**With immunosuppression:**
- **Smear -ve Pulmonary TB**
- **Extrapulmonary TB (CNS, miliary)**

Rifampin is replaced by Refabutin

**When to start ART**

**CD4< 50:**
**Within 2 weeks of TB treatment**

**CD4> 50**
**Within 8 weeks of TB treatment**

**HIV +ve pregnant w active TB:**
**As soon as feasible**

**TB meningitis:**
**After 8 weeks of TB treatment**

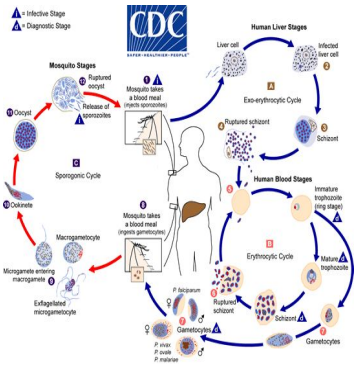
# L37- Malaria & Travel Medicine

## ◄ Definition

- Malaria is a protozoal infection that infects hepatocytes and RBCs.
- Most commonly caused by **P.falciparum** and P.vivax.
- It can be transmitted through human to human by anopheles mosquitoes, blood transfusion, contaminated needles and congenital.
- **Stable transmission: sub- Saharan Africa,**The bulk of the mortality is seen in **children**,
- **Unstable transmission:** occurs when there is **erratic, seasonal or low- level transmission** (e.g. in the Sahel belt) . Little protective immunity develops and symptomatic malaria occurs at all ages.

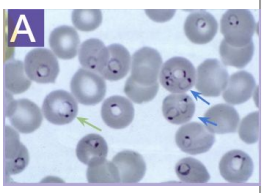
## ◄ Life cycle

- Carried by **female anopheles mosquito**. It injects the body with **sporozoites** that will reach the hepatocytes and form **Exoerythrocytic Schizonts**.
- These schizonts will rupture releasing merozoites → that will enter the erythrocytes forming **immature trophozoites** (ring stage)
- Then it will either develop into **mature trophozoite** → and again forming **erythrocytic Schizont** that will release merozoites into the bloodstream causing the **clinical attack**.
- Or the immature trophozoite develop to gametocytes.




### Plasmodium Falciparum

- **Resistant** to many antimalarial drugs.
- ★ Causes most **morbidity and mortality.**
- Infects **mature and young erythrocytes**. The surface of erythrocytes infected with late stage **trophozoites** or schizonts is altered so they stick to endothelial cells in various tissues (cytoadherence) causing multi-organ failure.
- The gametocytes are characteristically crescent-shaped
- **Pic A:** rings in peripheral blood thin film of P.Falc showing double dotted ring and multiple parasites invading one RBC. These findings are **characteristic for P.Falciparum.**




| P.vivax | P.ovale | P.malariae |
|---|---|---|
| - Only infect Duffy +ve reticulocytes.<br>- Schuffner's dots. | - Most of the biological and **clinical features are identical** to P.vivax.<br>- Can infect Duffy -ve reticulocytes. | - P. malariae can survive for a very long time in the peripheral blood (10 years or more) at a very low level of parasitaemia |

## ◄ Malaria Paroxysms

- Paroxysms associated with **synchrony of merozoite release.**
- Cold skin (1-2hr) → Hot skin (several hrs) → sweating and fatigue.
- **Between paroxysms temperature is normal and patient feels well and asymptomatic.**
- **Terian** (every 48hr) → P.vivax and P.ovale.
- **Quartan** (every 72hr) → P.malariae.
- **irregular**→ P.falciparum.

## ◄ Clinical presentation

- Hx of travel to malaria endemic area (1 year for P.falciparum and up to 10 years to P.malariae).
- **Symptoms**: Fever, **jaundice** (common in p.falc) , sweats, headache, cough diarrhea, dark urine.
- **Signs**: Splenomegaly is the most common.

## ◄ Complications

- **Cerebral malaria (Pf):**
  - ★ Risk factor for poor prognosis: **high bilirubin, high creatinine and high lactase**. if these were normal → no end organ damage.
- **Hypoglycemia -** quinn leads to insulin release.
- **Risk acute respiratory syndrome (Pf).**
- **Acute renal failure (Pf).**
- **Malaria with pregnancy will lead to abortion.**

**WHO Criteria – Severe Malaria**

History of recent possible exposure and no other recognized pathology. **EITHER** Asexual forms of (Pf) on blood smear.

**AND**

**Any one or more of the following 11 features:**

01 Impaired consciousness or coma.
02 Severe normocytic anemia.
03 Renal failure.
04 Pulmonary edema or adult respiratory distress syndrome (ARDS).
05 Hypoglycemia.
06 Circulatory collapse, shock
07 Spontaneous bleeding/disseminated intravascular coagulation.
08 Repeated generalized convulsions.
09 Acidemia/acidosis.
10 Hemoglobinuria.
11 Parasitemia of > 5% (> 250 000/microlitre) in non-immune individuals.

## ◄ Diagnosis

- **Thin and thick films:** A thin film is essential to confirm the diagnosis, to identify the species of parasite and, in P. falciparum infections, to quantify the parasite load (by counting the percentage of infected erythrocytes).
  - **Pf** → only **ring stage** asexual parasite and **gametocytes** can be seen, while RBC mature (trophozoite and schizont) stage sequestered in the peripheral microvasculature and not circulating.
  - **P.vivax & P.ovale** → **all asexual erthrocytic stages** can be seen.
- **DDx of acute ill patient:**
  - Not P.malariae because it's chronic infection.

| | | |
|---|---|---|
| Thin and Thick films[1] | Urea and Creatinine | ABG |
| CBC, Coagulation profile | LFT, Bilirubin | CXR |
| Random Blood glucose | Lactic acid | Urine analysis |

| Findings | P. Falciparum | P. Vivax & P. Ovale |
|---|---|---|
| Multiple infected RBCs | Common | Rare |
| Mature (trophozoite & schizont) parasites | Absent | Common |
| RBC enlargement with later parasite stages | Absent | Common |

## ◄ Management

- Ask lab about: species and **percent parasitemia (>1% → Pf)**.
- Complicated or uncomplicated?
- ★ **Drug of choice** is Artesunate based combination therapy (ACT), P. falciparum is now resistant to chloroquine and sulfadoxine-pyrimethamine (Fansidar) world-wide, so an ACT is recommended
- Consider admission to hospital (especially for falciparum) at least
- observe tolerance of meds in ER..

| ★ P.falciparum | | | Non P.falciparum |
|---|---|---|---|
| **Uncomplicated** | **Complicated "severe malaria"** | **Pregnant women** | |
| - **ACT** for 3 days.<br>- OR oral quinine + doxycycline or clindamycin for 7 days. | - **IV Artesunate** up to 7 days.<br>- OR IV quinine up to 7 days.<br>- OR IM Artesunate up to 7 days. | Artesunate is the drug of choice in all trimesters. | - **Chloroquine** (base).<br>- **Primaquine** for 14 days in vivax and ovale after treatment of acute infection use to **eradicate liver parasites**; **G6PD must be measured** before primaquine is given. |

## ◄ Drug toxicity

- **Quinine** → Hypoglycemia and arrhythmia .
- **Mefloquine** → Neuropsychiatric symptoms.
- **Chloroquine** → irreversible retinopathy.

**Chemoprophylaxis[1]:**

- **Start 2 days pre-travel, continue 7 days after return:**
  - → Atovaquone/ proguanil[2] (Malarone): 1 tab/d ( 250 mg atovaquone /100 mg proguanil)
- **One or 2 weeks pre-travel, continue 4 weeks after return:** less preferred
  - ★ Mefloquine 250 mg once/wk.
  - → Doxycycline 100 mg daily.
  - → Primaquine 30 mg base daily.
  - → Chloroquine[3] sensitive areas: 500 mg (300 mg base) : once/wk.

1. Choice of regimen is determined by area to be visited, length of stay, level of malaria transmission, level of drug resistance, presence of underlying disease in the traveler concomitant medication taken.
2. **Pregnant** and lactating women may take **proguanil** or **chloroquine** safely. Avoid Malarone in pregnancy.
3. **Chloroquine** should not be taken continuously as a prophylactic for more than 5 years without regular ophthalmic examination, as it may cause **irreversible retinopathy**.

**Source of infection**

- Endogenous sources: skin, nose, mouth, GI tract, or vagina
- Exogenous sources: health care workers (HCW), visitors, patient care equipment, medical devices, or the healthcare environment.

**FIRST: Catheter-Associated Urinary Tract Infections**

- **Causes**: Indwelling urinary catheter, Urinary invasive procedures.
- **Risk factors**: Advanced age, Diabetes mellitus, Pregnancy, Urolithiasis, Severe underlying disease.
- **Pathogenesis:**
  - Endogenous (meatal, rectal, or vaginal).
  - Exogenous; usually via contaminated hands of HCW during catheter insertion or manipulation of the collecting system.
  - (Formation of bio films by urinary pathogens which lead to resistance of antimicrobials and host defenses, you must remove catheter for cure).
- **Diagnostic criteria:**
  - Fever1 (38.0C or above), urgency, frequency, dysuria, or suprapubic tenderness.
  - Positive urine culture, that is more than 105 CFU per ml, with no more than 2 species of microorganisms.
  - A positive culture of a urinary catheter tip is not an acceptable laboratory test to diagnose UTI.

**SECOND: Surgical site infection**

- **causes:**
  - Inadequate antibiotic prophylaxis
  - Incorrect surgical skin preparation
  - Inappropriate wound care
- **Risk factors:** surgical duration, type of surgery, type of wound, Improper surgical aseptic preparation, poor glucose control, Malnutrition, Immunodeficiency, Hypothermia, Lack of training and supervision.
- **Causative organisms:** Staph. Aureus (30%) → most common, followed by coagulase -ve staph (13.7)
- **Surgical Wound Classification**
- **Clean:** Uninfected, no inflammation, Resp, GI, GU tracts not entered, Closed primarily.
  **Examples**: lap, mastectomy, neck dissection, thyroid, vascular, hernia,splenectomy.
- **Clean-contaminated:** Resp, GI, GU tracts entered but controlled, No unusual contamination
  **Examples:** Chole, SBR, Whipple, liver txp,gastric surgery, bronch, colon surgery, cholecystectomy.
- **Contaminated:** pen, fresh, accidental wounds, Major break in sterile technique, Gross Spillage from GI tract, Acute non purulent inflammation.
  **Examples:** Inflamed appendix, bile spillage in chole, diverticulitis, Rectal surgery, penetrating wounds.
- **Dirty:** Old traumatic wounds, devitalized tissue, Existing infection or perforation, Organisms present BEFORE procedure.
  **Examples:** Abscess I&D, perforated bowel, peritonitis, wound debridement, positive cultures pre-op.

**Superficial vs deep surgical site infection**

- **Superficial SSI**: within **30 days,** involves only **skin and subcutaneous tissue** of the incision
  - **Signs:** Purulent drainage from the superficial incision, pain or tenderness, localized swelling, redness, or heat, lack of systemic symptoms (e.g. fever). A -ve culture does not rule it out
- **Deep SSI**: **within 30 days if no implant is left in place** or **within 1 year if implant is in place and the infection appears to be related to the operative procedure**, Involves **deep soft tissues** (e.g. fascial and muscle layers) of the incision,
  - Clinically may have abscess and fever.

**SSI Epidemiology**

- Modifiable Risk Factors: Antimicrobial prophylaxis(Inappropriate choice, Improper timing, Inadequate dose based on body mass index, procedures >3h).
- Skin or site preparation ineffective.
- Colorectal procedures; Inadequate bowel prep/antibiotics.
- Inadequate wound dressing protocol.
- Improper glucose control.
- Colonization with preexisting microorganisms.

**SSI Prevention strategies:**

- **Preoperative Measures:** Administer antimicrobial prophylaxis in accordance with evidence based standards and guidelines: Administer within **30-45 minutes to incision** (**1-2hr for vancomycin and fluoroquinolones**), Select appropriate agents on basis of: Surgical procedure, Most common SSI pathogens for the procedure, Published recommendations, Consider Redosing in long procedures (>3hrs) and increasing dose in obese patients.
- **Nasal screen and decolonize only Staphylococcus aureus (MRSA) carriers** undergoing: Elective cardiac surgery, Orthopaedic surgery, Neurosurgery procedures with implants, Using preoperative mupirocin ointment therapy known as decolonisation.

**THIRD: Central line Associated Bloodstream Infections**

- Direct: in IJV or femoral or subclavian veins.
- Tunneled: for dialysis and chemotherapy.
- Laboratory-confirmed bloodstream infection by a positive blood culture that's not secondary to any infection.
- Develops at least after 48 hours of a central line placement
- The most common site is the **femoral central lines**

**CLABSI Microorganisms**

1. **Gram +ve cocci**: **Coagulase -ve staphylococcus** **(most common)**, Enterococci, Staph. aureus.
2. **Gram -ve bacilli:** Klebsiella pneumoniae, E.coli, Enterobacter spp, Pseudomonas aeruginosa, Acinetobacter baumanii.

**CLABSI Treatment**

- Removal of central line
- Antimicrobial therapy: Type and duration depends on culture results, type of organism, complicated disease (Vancomycin, cloxacillin, cefazolin, piperacillin/ tazobactam).

**CLABSI prevention**

1. **Prevention Guidelines During Insertion:**
   - Hand hygiene before wearing gloves
   - Strict aseptic technique by maximal sterile barrier precautions including a full-body drape
   - Use of 2% chlorhexidine skin preparations for disinfecting/ cleaning skin before insertion
   - Ultrasound guidance by an experienced personnel and reduce the number of attempts
   - Avoid the femoral vein, prefer the subclavian vein
   - Promptly remove any central line that is no longer required
   - Replace central lines placed during an emergency (asepsis not assured) as soon as possible or at least within 48 hours
   - Use a checklist
2. **Prevention Guidelines During Maintenance:**
   - Disinfect catheter hubs injection ports, and connections before accessing line
   - Replace administration sets other than sets used for lipids or blood products every 96 hours
   - Assess the need for the central line daily

## Pathogenesis and risk factors for ventilator Associated Pneumonia (VAP)

- Aspiration of secretions
- Colonization of the aerodigestive tract
- Use of contaminated equipment

## VAP prevention bundle

1. **Prevent Aspiration of Secretions:**
   - Maintain elevation of head of bed (HOB) 30-45 degrees
   - Avoid gastric over distention
   - Avoid unplanned extubation and re-intubation
   - Use cuffed endotracheal tube with in-line or subglottic suctioning
   - Encourage early mobilization of patients with physical/occupational therapy
2. **Reduce Colonization of Airway and Digestive Tract:**
   - Use cuffed Endotracheal Tube with inline or subglottic suctioning
     - Minimizes secretions above cuff; prevents contamination of lower airway.
   - Avoid acid suppressive therapy for patients not at high risk for stress ulcer or stress gastritis
     - Increases colonization of the digestive tract.
3. **Reduce Duration of Ventilation:**
   - Conduct "sedation vacations"
   - Assess readiness to wean from vent daily
   - Conduct spontaneous breathing trials
4. **Prevent exposure to contaminated equipment by using closed-circuit for ventilator.**

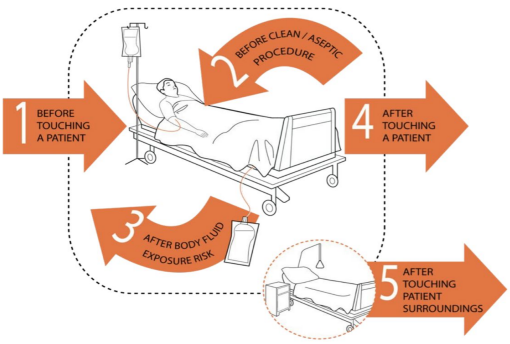
**Modes of transmission:** A microorganism may be spread by a single or multiple routes(Contact, direct or indirect, Droplet, Airborne, Vector-borne (usually arthropod) and, food-borne and waterborne, medications e.g., contaminated IV fluids).
**Hand transmission:** Hands are the most common vehicle to transmit healthcare associated pathogens.

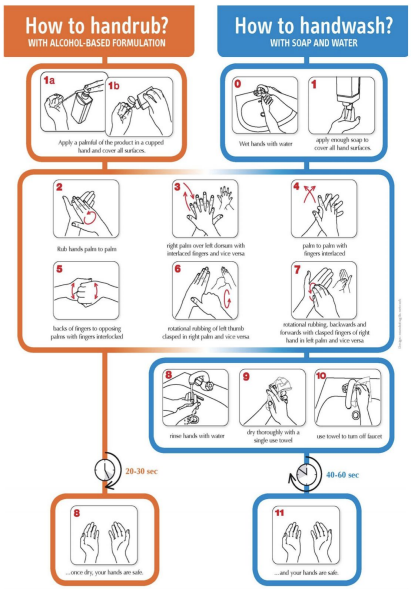
### Five Moments of Hand Hygiene

How to Clean Your Hands?

1. Handrubbing with alcohol-based handrub is the preferred routine method of hand hygiene if hands are not visibly soiled

2. Handwashing with soap and water – essential when hands are visibly dirty or visibly soiled (following exposure to body fluids) and after certain diseases e.g. C. difficile as they are spore forming bacteria that don't get disinfected by alcohol.



**Types of Isolation Precautions**

- Standard precautions.
- Transmission-based precautions:(Contact isolation, Droplet isolation, Airborne isolation).

**Contact Precautions**

- C. difficile, MRSA, VRE, ESBL, CRE and MDR GNR.
- Limit patient movement.
- Private/single room or cohort with patients with same infection.
- Wear **disposable gown and gloves** when entering the patient room.
- Remove and discard used gown and gloves inside the patient room.
- Wash hands immediately after leaving the patient room.
- Use dedicated equipment if possible (e.g., stethoscope)

**Droplet Precautions**

- E.g.MERS-CoV, SARS-CoV-2, influenza.
- A private/single room or cohort with patient with active infection with same microorganism.
- Use a **mask** when entering the room especially within 3 feet of patient.
- Limit movement and transport of the patient. Use a mask on the patient if they need to be moved and follow respiratory hygiene/cough etiquette.

**Airborne Precautions**

- **Tuberculosis,** measles, varicella, MERS-CoV (severe), COVID-19 or AGP.
- Place the patient in an airborne infection isolation room (AIIR)
- **Negative Pressure** should be monitored with visible indicator
- Use of respiratory protection (e.g., fit tested **N95 respirator**) or powered air-purifying respirator (PAPR) when entering the room
- Limit movement and transport of the patient.
- Use a mask on the patient if they need to be moved.
- Keep patient room door closed, do not open anteroom door till other door closed

**Serologies and Vaccination**

- HBSAB titre (above 10)
- VZV
- MMR
- Td
- Seasonal Influenza Vaccine
- COVID-19 vaccine

## ◄ Summary of precautions for patients with COVID-19

| Personal Protective Equipment | Close patient contact (within 2m) | Enter room but no contact with patient or environment | Cleaning room/area (Domestic staff) | ★ Aerosol generating procedures |
|---|---|---|---|---|
| Gown | ✅ | ❌ | ✅ | ❌ |
| Surgical mask | ✅ | ✅ | ✅ | ❌ |
| Long sleeved disposable gown | ❌ | ❌ | ❌ | ✅ |
| Fit Tested N95 respirator | ❌ | ❌ | ❌ | ✅ |
| Eye protection (goggles, face shield) | Risk assess | ❌ | ❌ | ✅ |
| Gloves | ✅ | ❌ | ✅ | ✅ |

# L40- Endemic infections in The middle east



| | Typhoid fever | Brucellosis | Dengue | Rift Valley |
|---|---|---|---|---|
| **Introduction/ Epidemiology** | -Severe **systemic illness with fever and abdominal pain**<br>-Caused by **Salmonella typhi** and paratyphi<br>-Common in children and young adults | -**Systemic febrile illness**<br>**-(Brucella) Aerobic intracellular gram negative coccobacilli**<br>-Mostly **Mediterranean basin and Arabic peninsula**<br>**-uncommon in infants** | -Dengue fever and Hemorrhagic fever **caused by dengue virus**<br>-Mosquito borne (**Aedes aegypti**)<br>- in **Tropical and subtropical areas** | -**Acute fever** causing **zoonotic and human disease**<br>-Phlebovirus, **transmitted by mosquitoes or infected mammals** |
| **Pathogenesis** | 1-Organism enters the blood through **fecal oral route**<br>2- **multiply in mesenteric lymph nodes**<br>3- infect the **reticuloendothelial system** (spleen, liver, bone marrow) | -**Zoonotic infection** transmitted through **contact with fluids** (Aerosols inhalation, **unpasteurized dairy**, undercooked meat, lab workers)<br>- survives phagocytosis<br>- replication in reticuloendothelial system and other organs | **Clinical features:**<br>1-**Dengue fever:**<br>-Incubation period (3-14 days)<br>-Symptoms appear (4-7 days after bite)<br>-acute febrile illness with **fever** and 2 symptoms of: **(**Headache, **retro-orbital pain,** myalgia, arthralgia, rash)<br>2- **hemorrhagic fever:**<br>-hemorrhagic manifestations, positive tourniquet test<br>3- **Dengue shock syndrome**:<br>(Cold skin, rapid pulse) | **Clinical features:**<br>**•low to moderate fever**<br>**•bleeding and disseminated intravascular coagulation**<br>•Abdominal pain<br>•malaise<br>•Encephalopathy or Encephalitis<br>•nausea and vomiting<br>•Diarrhea<br>•Renal failure<br>•Liver failure<br>•muscle pain, back pain, and joint pain |
| **Clinical features** | (Diarrhea or constipation)<br>1st week: **fever, chills**, relative bradycardia<br>2nd week: **rose spots**<br>3rd week: **hepatosplenomegaly** | **•Undulant fever**<br>**• Night sweats**<br>**•Fatigue**<br>•Anorexia<br>•Weight loss<br>•Arthralgia | | |
| **Diagnosis** | 1-**WBC: leukopenia**<br>2-**Culture**:<br>**-Blood: most important at onset**<br>-Bone marrow: most sensitive but invasive<br>-stool culture:<br>2nd,3rd weeks | 1-Culture: sensitivity<br>-blood (15%-70%)<br>-bone marrow( 80%-90%) but invasive<br>2- **Serology**:<br>Standard agglutination test (SAT)<br>Very sensitive and specific | **-RT-PCR (best)**<br>-Detection of viral antigen<br>-Serology | **-PCR**<br>-ELISA for IgM |
| **Treatment and prevention** | **•Ciprofloxacin (1st choice, empiric)**<br>**•Ceftriaxone (2nd choice)**<br>Prevention by:<br>Food and water safety, vaccination, education | **1st line: doxycycline + streptomycin** (avoid if above 65 of age)<br>2nd line: doxycycline + rifampicin<br>Prevention: avoid contact with animal fluids, pasteurization of milk, well cooked meat | **-Symptomatic treatment (use acetaminophen)**<br>-Hydration<br>- Avoid NSAIDs in children<br>Prevention: elimination of mosquito's habitat, protection from bites | -**Symptomatic** treatment<br>Prevention:<br>Vaccine for veterinary |
| **Complications** | **•Pneumonia**<br>**•Meningitis**<br>**•Osteomyelitis**<br>**•Small bowel perforation** | 1-**Osteoarticular** diseases are the most common form of focal brucellosis (Sacroiliitis, spondylitis)<br>2-**Neurobrucellocis**<br>3-**Endocarditis (the main cause of death)** | **Dangerous signs in hemorrhagic fever:**<br>**•Intense abdominal pain**<br>**•persistent vomiting**<br>**•restlessness**<br>**•sudden change from fever to hypothermia** | |

# L40- Endemic infections in The middle east



<table>
<tr><th></th><th>Cutaneous leishmaniasis</th><th>Visceral leishmaniasis</th><th>MERS-Cov</th><th>COVID-19</th></tr>
<tr><td>Introduction/ Epidemiology</td><td colspan="2">-Protozoal disease caused by leishmania parasite<br>-Transmitted by sand fly (phlebotomus papatasi) bite<br>1-cutaneous 2-muco-cutaneous 3-visceral<br>-Promastigotes injected > become Amastigotes in macrophages > multiply and infect other cells</td><td>-Betacoronavirus<br>-Transmission most likely from camel to human, also human to human<br>-incubation period (5 days)</td><td rowspan="2">-incubation period within 14 days of exposure (mostly 4-5 days):<br>1. Viral response phase: high viral replication.<br>2. Pulmonary phase: decrease in viral replication and increase immune reaction.<br>3.Hyperinflammation phase: immune reaction is high and is associated with ARDs and shock.</td></tr>
<tr><td>Pathogenesis</td><td>-males more than females<br>-L.major, L.tropica<br>-concentrated in six regions: Al-Qaseem, Riyadh, Al-Hassa, Aseer, Ha’il, and Al-Madinah</td><td>-Kala Azar<br>- L.donovani, L.infantum, rattus rattus<br>-replicate in reticulo-endothelial system ( hepatosplenomegaly)</td><td></td></tr>
<tr><td>Clinical features</td><td>-Pink papule leading to painless ulceration with indurated borders<br>-most common to the face</td><td>-asymptomatic or fever, malaise and weight loss<br>-splenomegaly<br>-Anemia , Leukopenia, Thrombocytopenia,<br>-Hyper-gammaglobulinemia<br>-Hypoalbuminemia, and edema.</td><td>1-Asymptomatic<br>2 -Fever (>38°C)<br>3 SOB<br>4 Cough<br>-CBC: lymphocytosis, pancytopenia..<br>-LFT: Elevated enzymes and LDH.<br>-RFT- Rising blood urea nitrogen and creatinine.)<br>-imaging: Ground-glass opacity, Airspace patchy infiltrates or consolidation.</td><td>●Mild case:<br>-fever, headache and dry cough<br>- loss of taste and smell<br>●Severe cases:<br>-respiratory failure<br>-cardiac (arrhythmia)<br>-neurologic ( Encephalopathy)<br>-Thromboembolic ( deep vein thrombosis and stroke)<br>●Risk factors for poor outcome:<br>-Increased age.<br>-Presence of chronic illnesses</td></tr>
<tr><td rowspan="2">Diagnosis</td><td>Aspiration From ulcer margins</td><td>Bone marrow/spleen aspiration</td><td rowspan="2">●RT-PCR<br>-Nasopharyngeal swab<br>Lower respiratory tract</td><td rowspan="2">●RT-PCR<br>-Nasopharyngeal swab, Lower respiratory tract (Optimal time 5-7 days post exposure)</td></tr>
<tr><td colspan="2">-Histopathology with Giemsa stain ( Amastigotes)<br>- culture in Schneider's drosophila or NNN media<br>- PCR</td></tr>
<tr><td rowspan="2">Treatment and prevention</td><td>●Cryotherapy<br>●paromomycin,imidazole.<br>● (sodium antimony gluconate; Pentostam).<br>● sodium stibogluconate (SSG)</td><td>●Amphotericin B (even in pregnancy)<br>●paromomycin<br>●sodium stibogluconate (SSG)</td><td rowspan="2">●Supportive<br>Prevention: avoiding camels</td><td rowspan="2">●Supportive<br>●Low dose dexamethasone:</td></tr>
<tr><td colspan="2">Prevention: clothing, insect repellent, educate</td></tr>
</table>

# L41-Osteoarthritis

## ◄ Definition

- Mechanical **wear and tear** destroys articular cartilage **(degenerative joint disorder)**

## ◄ Etiology

- **Heritable metabolic causes:** alkaptonuria, **hemochromatosis**, wilson disease
- **Hemoglobinopathies** : sickle cell disease, thalassemia
- **Neuropathic disorders leading to a Charcot joint**
- **Underlying morphological risk factors:** Congenital hip dislocation and slipped femoral capital
- **Disorders of bone:** Paget disease, avascular necrosis
- **Previous surgical procedures:** meniscectomy
- **Diabetes mellitus**

## ◄ Risk Factors

- **Age, obesity, trauma,** women gender, hypogondism (estrogen has protective role) muscle weakness, repetitive use, septic arthritis and crystal deposition

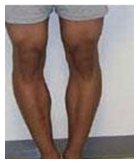
## ◄ Pathogenesis

- Degeneration of articular cartilage: is the defining feature of OA
- Consequent structural changes include **surface fibrillation** and **ulceration** with loss of cartilage that exposes underlying bone to increased stress, producing **microfractures** and **cysts** leading to abnormal **sclerotic subchondral bone** and overgrowths at the joint margins, called **osteophytes.**

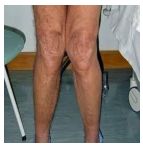
## ◄ Clinical Presentation

- **Pain**: Insidious onset, worse **with movement**, relieved by rest /**Brief (< 15 mins) morning stiffness**/ **Coarse crepitus** / **Asymmetric** joint involvement targeting the **hips, knees**, PIP, DIP, neck and lumbar spine/ Functional restriction/ No systemic symptoms

➔ Before labelling any pt to have OA you need to exclude inflammatory causes.



**Genu Varum deformity**
**Primary OA** ,The angle is **outward**



**Genu Valgum deformity**
indicates secondary OA (RA usually)

## ◄ Types of OA

- **Nodal OA:** Female preponderance. Pain, stiffness and swelling of **one or more PIP and DIP joints,** leaving painless bony swellings **Heberden's nodes (DIPs) and Bouchard's nodes (PIPs).** Involvement of the **first CMC joint** is also common causing **squaring of the thumb** base
- **Knee OA:** strong relationship with **obesity, bilateral with symmetrical** involvement, targets the patellofemoral and **medial tibiofemoral compartments** leads to a **varus "bow-legged" deformity**.
- **Hip OA:**
  - **Superior-pole hip OA :**
    - Most common, **unilateral**.
    - Affect the **upper surface of the femoral head** and adjacent acetabulum.
  - **Medial cartilage (central) loss:**
    - Usually affect women, **bilateral**.
    - Associated with hand involvement (NGOA). Has better prognosis.
- **Spine OA:** Cervical (cervical spondylosis) and lumbar spine (lumbar spondylosis) are the most common targeted sites. May be complicated with spinal stenosis or nerve root compression → neurological signs and radiation of pain.
- **Erosive OA:** an unusual group of patients with hand OA who have a more prolonged symptom phase and inflammation, more disability and worse outcome. Distinguishing features **subchondral erosions on X-rays,** occasional **ankylosis** of affected joints.

## ◄ Work up

- **X-ray:** Only abnormal when the damage is advanced.**narrowing joint space, Osteophytes, Subchondral sclerosis, and Cyst formation**
- **MRI of spine:** should be done **if nerve root compression or spinal stenosis are suspected.**
- **Bone scintigraphy:** to rule out malignancy
- **Arthrocentesis**: On suspicion of **septic arthritis. WBC : >100 OA, > 1000 Inflammatory**

# L41-Osteoarthritis

## ◄ Treatment

**Non pharmacological:**

- Lifestyle modification: Physical and rehab therapy (OA of the knee you should exercise the quadriceps) , weight loss , medical shoes with lateral and medial wedged
- insoles.

**Pharmacological:**

- First choice: **Topical (NSAID)** due to less systemic side effects and it can be added at any step.
- **Topical capsaicin:** very irritating substance , pt should avoid touching the eyes after putting the cream, bc it may lead to conjunctivitis

*If the topical therapy is failing, start oral therapy:*

- First choice: **Acetaminophen**
- **Solpadeine**: Combination of acetaminophen and low dose codeine.

*If all of above are failing even with combining oral and topical therapy go to the next step:*

- Second choice: **NSAIDs (ibuprofen, meloxicam)**
- Third choice: **Tramadol** These aren't usually used can cause addiction, bc at this level (advanced OA) the only solution is arthroplasty
- **Duloxetine:** used in depression
- **Intra-articular corticosteroid injections** produce short-term improvement when there is a **painful joint effusion.**

# L42- Gout

## ◄ Definition

- Gout is an inflammatory-arthritis **associated with hyperuricemia** and reaction to intra-articular monosodium urate crystals.
- Most commonly seen in elderly, men, and postmenuposal women due to the loss of estrogen induced uricosuric effect.

## ◄ Predisposing factors

- **Obesity & excessive weight gain.**
- **Increased intake** → Purine rich foods.
- **Diminished renal excretion** → Abnormal kidney function, alcohol intake, drugs (Thiazide & ASA, loop diuretics) Moderate to heavy alcohol intake (beer specially)
- **Generalised OA.**
- **Chemotherapy: Tumour lysis syndrome**
- **Increased production** → Inherited disorders: Lesch–Nyhan syndrome (X-linked recessive form of gout that is also associated with mental retardation) , High fructose intake

## ◄ Clinical Presentation

- **Acute monoarthritis:**
  - Sudden onset severe pain, extreme tenderness, and swelling of **the first MTP joint of the big toe.** Other common sites are the ankle, midfoot, knee, small joints of hands, wrist and elbow. The axial skeleton and large proximal joints are rarely involved.
  - Sudden onset, severe pain, extreme tenderness and marked swelling ( giving impression of cellulitis).
  - Self limiting over 5-14 days.
  - Acute attacks may be precipitated by **dietary or alcoholic excess**, by **dehydration** or by **starting a diuretic.**
- **Chronic tophaceous gout:**
  - Chronic pain and joint damage.
  - Characterised with **Tophi**: irregular firm white nodules produced when crystals are deposited in the soft tissue on **extensor surfaces** of fingers, hands, forearm, elbows (difficult to differentiate from RA nodules), Achilles tendons and sometimes the helix of the ear.

# L42- Gout

## ◄ Diagnosis

- Clinically or by rapid response to NSAIDs or colchicine.
- **Biochemical screen** → RFT, uric acid (can be normal or high), glucose and lipid profile, high ESR and CRP and neutrophelia.
- **Joint aspiration** (Synovial fluid analysis) → Cell count, polarized microscopy and culture to exclude septic arthritis and confirm the diagnosis.
  - Microscopy shows needle-shaped uric acid crystals (negatively birefringent).
- **X-ray** → normal in acute gout , well demarcated erosions in chronic gout.

## ◄ Management

- Patient presenting with acute monoarthritis: Give **antibiotics** and do not stop until the culture comes back negative.

- **Terminate acute attacks →**
  - **NSAIDS:** Fast onset of action, effective even after a few days of symptoms onset.
  - **Colchicine:** Slower onset, weak effect after 24-36 hours after symptoms onset, **narrow therapeutic index,** D/C if GI distress develops e.g. diarrhea or colicky abdominal pain.
  - **Corticosteroids:** for intolerant of NSAIDs or colchicine and Comorbidities.
  - **In renal impairment:**
    - Steroids are preferred, either intra-articular or systemic.
    - **Cr clearance < 50: Colchicine and NSAIDs are contraindicated.**
  - **Joint involvement:**
    - **Monoarthritis** → Intra-articular steroid injection is preferred, contraindicated in septic arthritis.
    - **Polyarthritis** → NSAIDs or Colchicine.

- **Prevent recurrence & reverse complications →**
  - **Use in :** tophi or radiographic changes or >2 attacks per year
  - **Xanthine oxidase inhibitors "decrease production":** Recommended urate levels <360 umol/L
    - **Allopurinol**: first choice, Start low, go slow, Dose adjust for renal function.
    - **Febuxostat**: more potent, there's a concern about **sudden cardiac death,** undergoes hepatic metabolism( CrCL > 30 mL/min - no dose adjustment)
  - **Uricosuric Agents "increase excretion":**
    - **Probenecid and Sulfinpyrazone:** have weaker action.
  - **Conjugated uricase enzyme:**
    - **Pegloticase:** treat **tophaceous gout resistant to standard therapy,** Used preventatively in people undergoing chemotherapy for **malignancies (tumour lysis syndrome).**

- **Address co-morbid conditions →**
  - Weight loss and decrease alcohol consumption.
  - Avoid if Possible organ meats e.g. liver, kidney and heart.
  - Limit Seafood sardines, tuna, mushrooms and high fructose corn syrup.
  - If possible, substitute the antihypertensive drugs that increase uric acid (e.g. thiazides, β-blockers and ACEI) with **losartan** which has uricosuric effect

# L43: Use of Antibiotic

## ◄ Important considerations when prescribing antibiotics:

**1. Obtain accurate diagnosis of infection**

- Establishing a microbiological diagnosis, Especially for: **Endocarditis, Septic arthritis, and Meningitis**
- The most likely microbiological etiology can be inferred from the clinical presentation:
  - **Cellulitis** (streptococci or staphylococci) No need for positive culture → Empirical therapy
  - **Cellulitis with wound** and the patient has diabetic foot then probably it's **secondary cellulitis** from the wound itself, so organism will be the one in the wound not the usual ones.
  - Erysipelas (has demarcated margins unlike cellulitis, affecting the upper layers of the skin, while cellulitis affects the deeper tissues)
    - Erysipelas → Most common Strep
    - Cellulitis → Most common Staph
  - CA pneumonia with no risk factors can be treated empirically with **macrolide or cephalosporins antibiotic**
  - Community-onset UTI E.Coli: bactrim/fluoroquinolones or just nitrofurantoin if patient has cystitis only**.**
  - Identification of the infecting organism:
    - **Gram stain:** the simplest, least expensive, and most useful of all the rapid methods of identification of bacterial
      - Gram +ve cocci in clusters → staph. (coagulase -ve or coagulase +ve)
      - Gram +ve cocci in chains → enterococcus or streptococcus
      - Gram +ve diplococci → pneumococcal
      - Gram -ve diplococci → neisseria
      - Gram -ve rods → many
      - Gram -ve coccobacilli → brucella
    - **Direct detection of organisms:** Microscopy and Nucleic acid amplification (PCR)
    - **Tests of the host's specific immune response:** Antibody detection
    - **Culture of organisms:** shows the organism and its susceptibility, limitation results are not immediate, even for organisms that are easy to grow.

**2. Empiric and definitive therapy**

- **Susceptibility Testing:** the ability of a specific organism to grow in the presence of a particular drug; susceptible, resistant, and intermediate. Data are reported in the form of minimum inhibitory concentration
- **Timing of initiation of antimicrobial therapy:**
  - **Urgent cases:** Acute meningitis, Septic shock, Febrile neutropenia
    - Empiric therapy (broad-spectrum antimicrobial agents) should be initiated immediately after or concurrently with collection of diagnostic specimens.
  - **Non-Urgent cases:** hold antibiotics until appropriate specimens have been collected and submitted. Example**:**
    - subacute bacterial endocarditis → multiple sets of blood cultures
    - Wound infection, diabetic foot, chronic ulcers. Patient's discharging for 2-3 weeks and stable → debridement → then deep tissue culture
    - Febrile and stable patient with fever for several days with no clue to diagnosis.

**3. Identify opportunities to switch to narrow-spectrum**

- Every attempt should be made to narrow the antibiotic spectrum to reduce cost and toxicity and Prevent the emergence of resistance. **switch to oral agents as soon as possible.**

**4. Cost-effective oral agents for the shortest duration necessary**

- **Antimicrobial stewardship:** refers to the systems and processes applied to a population to optimise the use of antimicrobial agents. aims to improve patient outcomes and reduce antimicrobial resistance (AMR).
  - The appropriate **selection, route & duration, and dosing** of antimicrobials:
    - **The lowest effective dose** → avoid subtherapeutic doses
      - Serious vs non-serious infections
      - Drug PK/PD properties
      - Site of infection
      - Other host factors (e.g. renal function)

# L43: Use of Antibiotic

## ◄ Important considerations when prescribing antibiotics cont':

**4. Cost-effective oral agents for the shortest duration necessary**

- **Antimicrobial Combinations: (Exhibits synergistic activity)**
  - **Rapid killing:** endocarditis caused by **enterococcus species** with a combination of **penicillin and gentamicin**.
  - **Shorten the course:** due to **viridans** group streptococci with a combination of **penicillin** or **ceftriaxone** with **gentamicin for 2 weeks.**
  - **Critical ill patient**
  - **Polymicrobial infections:** Intra-abdominal infections, diabetic foot such as third-generation cephalosporin or a fluoroquinolones **plus** metronidazole
  - **To prevent resistance:** combination of 4 anti-TB drugs in the first 2 months, then 2 anti-TB drugs for the rest of the course of treatment,

**5. Understanding drug pharmacodynamics and efficacy at the site of infection.**

| Bactericidal | Bacteriostatic |
|---|---|
| Cause death by cell rupture and disruption of the bacterial cell. **Drugs act on:**<br>1) **The cell wall** (b-lactams most famous) eg. penicillins & cephalosporins & carbapenems & monobactams → they own b-lactam rings → antibiotic works on the cell wall production of bacteria.<br>2) **Cell membrane** (daptomycin)<br>3) **Bacterial DNA** (fluoroquinolones)<br>- Preferred in the case of serious infections such as:<br>- endocarditis<br>- meningitis to achieve rapid cure | - Inhibit bacterial replication without killing the organism. Most common MOA<br>- Act by inhibiting protein synthesis such as:<br>1) Sulfonamides<br>2) Tetracyclines<br>3) Macrolides |

- **Oral** → for more stable patients providing that patient is tolerant to oral medications.
- IV → bacteremia, septic shock, infective endocarditis, severe meningitis.
- Candidates for treatment mild to moderate infections, well-absorbed oral antimicrobial agents :
  - **Pyelonephritis:** Fluoroquinolones
  - **Community-acquired pneumonia:** Augmentin and macrolides coverage
- The efficacy of antimicrobial agents depends on their capacity to achieve : Concentration equal to or greater than the MIC at the site of infection.
- **Ocular** fluid, **CSF**, abscess cavity, prostate, and bone are often much lower than serum levels
  - **First- and second-generation cephalosporins:** do not cross the blood-brain barrier. should **not** be used to treat them. eg. meningitis, endophthalmitis (similar to BBB)
  - **Aminoglycosides:** less active low-oxygen, low-pH, of Abscesses
  - **Fluoroquinolones** achieve high concentrations in the prostate preferred oral agents for the treatment of **Prostatitis**
    - **Moxifloxacin** does not achieve significant urinary concentrations therefore not suitable for treatment of UTIs because it is not excreted in the urine.
- Assessment of response to treatment: Clinical parameters, Laboratory values, Decreasing leukocyte count, Radiologic decrease in the size of an abscess.

**6. Host characteristics that influence antimicrobial activity**

- **Renal and Hepatic Function** (Adjust dose)
- **Pregnancy and Lactation**
  - **Sulphonamides**: A risk to develop **kernicterus** It can be used in the 2nd trimester. However, it's contraindicated in the 3rd trimester
  - **Tetracycline: Staining of the teeth**
  - **Fluoroquinolone: Cartilage damage**
  - **Thalidomide: Phocomelia**
- **History of Allergy or Intolerance: Penicillin and anaphylaxis**
- Genetic e.g, G6PD → avoid sulfa group in G6PD patients as it may lead to hemolysis
- Drug interactions

# L43: Use of Antibiotic

| Organism | Antibiotics |
|---|---|
| **MRSA Methicillin Resistant Staph. Aureus (R mechanism: PBP2a penicillin binding protein)** | • Vancomycin (Glycopeptide)<br>• Teicoplanin (Glycopeptide)<br>• Linezolid, Tedizolid<br>• Daptomycin (Lipopeptide)<br>• Telavancin (Glycopeptide)<br>• Dalbavancin (Glycopeptide)<br>• Oritavancin (Glycopeptide)<br>• Ceftaroline (5th generation cephalosporins)<br>• Tigecycline: cannot be used for pneumonia or bacteremia, only for intra-abdominal infections and skin and soft tissue infections<br>• Delafloxacin: new fluoroquinolone agent<br>• **Ceftobiprole** : 5th generation cephalosporins |
| **VRE Vancomycin Resistant Enterococcus** (common inside hospitals) | • Teicoplanin<br>• Linezolid<br>• Oritavancin<br>• Tedizolid Daptomycin<br>• Tigecycline and Eravacycline (new agents used only for intra-abdominal infections and skin and soft tissue infections, not UTIs since it isn't excreted in urine) |
| **ESBL Extended Spectrum Beta-Lactamase** ★ | • **Carbapenems: drug of choice**<br>• Piperacillin/tazobactam: increases mortality if given to severe infections.<br>• Nitrofurantoin and fosfomycin (**UTI**): for very mild infections only.<br>• Tigecycline and Eravacycline: for intra-abdominal infections and skin and soft tissue infections only<br>• Colistin<br>• Plazomicin<br>• fluoroquinolones: like cipro and bactrim (depends on what you're treating) |
| **CRE Carbapenem-Resistant Enterobacteriaceae** Challenging infection, that carries high mortality and morbidity, need to produce new agents for treatment | • Nitrofurantoin and fosfomycin (UTI): for simple cystitis<br>• Tigecycline and Eravacycline: for intra-abdominal infections and skin and soft tissue infections only.<br>• **Colistin**: only one used for **NDM and OXA-45** → MOA of bacteria (covers BOTH MOAs)<br>• Ceftazidime/avibactam and Meropenem/vaborbactam (new agents for OXA-45)<br>• Plazomicin (used for OXA-45 only)<br>Perform PCR to see what's the mechanism of resistance, based on this we choose the abx |
| **Actinobacter** Very bad, fast growing problem, especially in ICU pt and it has very limited choices of abx | • Carbapenems: 70% of actinobacter are carbapenem resistant, use if sensitive<br>• Tigecycline and Eravacycline : for intra-abdominal infections and skin and soft tissue infections only (This organism mostly causes pneumonia in ICU, these two abx cannot be used for pneumonia)<br>• Aminoglycosides, Colistin (only saving agent, but has many problems including dosing, they are nephrotoxic and not enough alone) |
| **Pseudomonas aeruginosa** Very famous hospital acquired infection ★ | • Piperacillin/tazobactam: From all penicillins this is the only one that cover psuedomonas.<br>★ Ceftazidime (3rd) and cefepime (4th) and **Ceftobiprole** (5th generation cephalosporins) These are the only cephalosporins that cover pseudomonas<br>• Meropenem, imipenem and Doripenem (carbapenem group)<br>• Aztreonam<br>• Some fluoroquinolones (only **ciprofloxacin** and levofloxacin)<br>• Aminoglycosides<br>• Colistin<br>• Ceftolozane/tazobactam and Ceftazidime/avibactam (new agents). |

# L43: Use of Antibiotic

## ◄ Antimicrobial agents as prophylaxis:

- **Presurgical Antimicrobial Prophylaxis:** to reduce the incidence of postoperative surgical site infections.
  - A single dose of cephalosporin (such as cefazolin) administered within 1 hour before the initial incision is appropriate for most surgical procedures.
- **Prevent Transmission of Communicable Pathogens to Susceptible Contacts:**
  - Ciprofloxacin or Rifampicin for close contacts of a patient with N.meningitidis
- **Antimicrobial Prophylaxis Before Dental Procedures:** Prosthetic valves, Rheumatic heart, Unrepaired congenital heart disease, Previous infective endocarditis → to prevent endocarditis

## ◄ Positive culture in the absence of disease

- **Colonization occurs frequently in:** older women with indwelling urinary catheter, mechanically ventilated patients (endotracheal tubes), or chronic wounds.
- **No need to treat colonization** except in special cases ( e.g. UTI +ve culture, if patient is pregnant or symptomatic or going for a procedure → treat)

## ◄ Antimicrobial decision making

When most culture results are available, one of the following five decisions should be made:

- **Stop antibiotic treatment**
- **Step down to an oral alternative**: For uncomplicated infections
- **Switch treatment**: because of an unanticipated site of infection (e.g. infective endocarditis requiring prolonged intravenous antibiotic treatment) or unanticipated resistance (such as urosepsis and bacteraemia caused by an **ESBL-producing E. coli requiring treatment with an intravenous carbapenem**).
- **Continue with intravenous treatment**: The patient has a more complicated infections
- **Discharge on outpatient parenteral antibiotic treatment**: