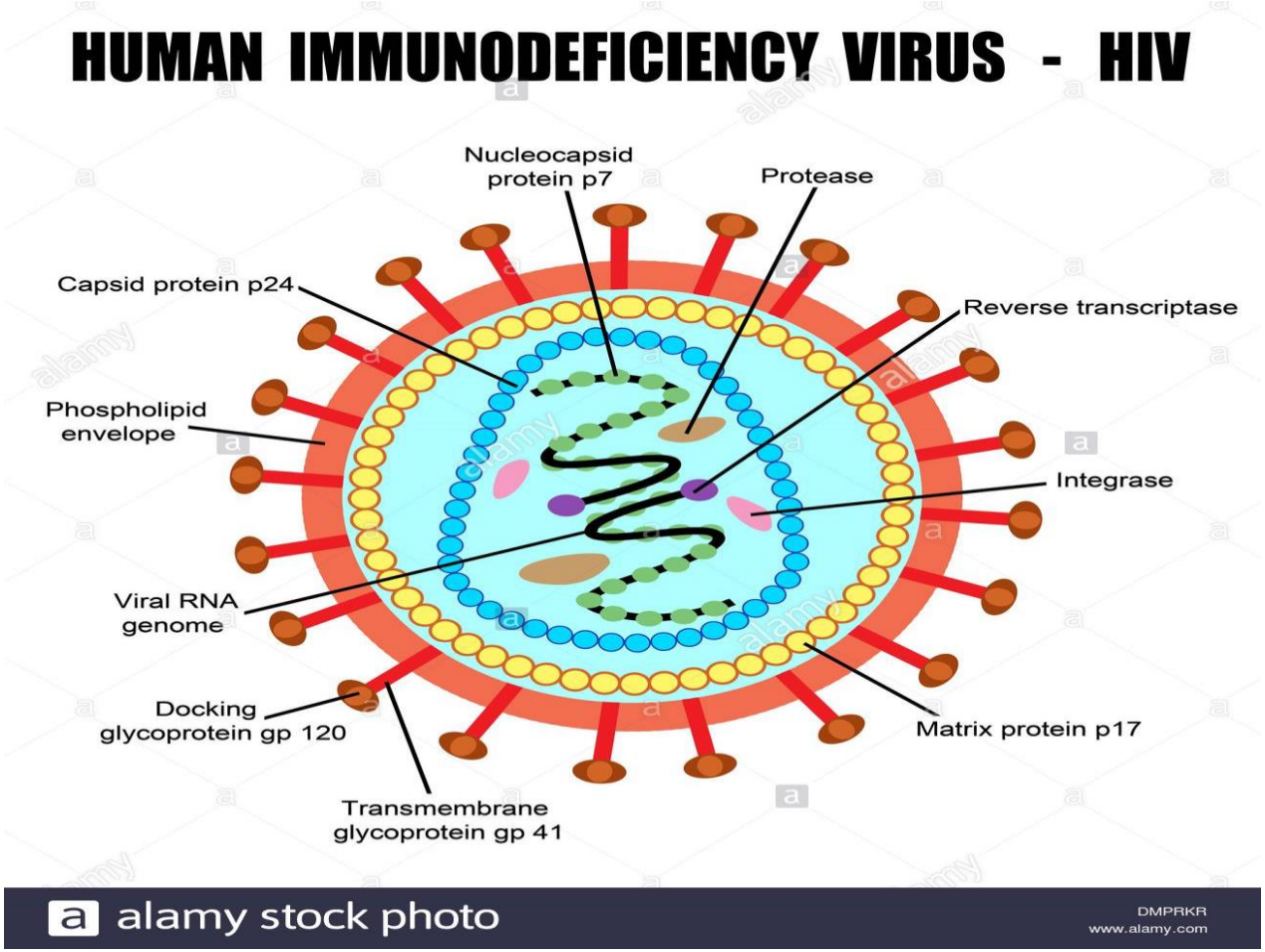
HUMAN IMMUNODEFICIENCY VIRUS/ ACQUIRED IMMUNODEFIENCY SYNDROME (HIV/AIDS)

VERONICA WACU

Introduction

- HIV is a retrovirus which is responsible for the Acquired Immune Deficiency Syndrome (AIDS)
- Through microscope it appears as icosahedral structure containing reverse transcriptase.

Structure of HIV virus



Life cycle

- The HIV life cycle begins with the high affinity binding of the GP 120 proteins to the CD4 molecules on the T-lymphocytes (also called the T-helper cells)
- Fusion with the host cells membrane occurs via the GP 41 molecules and the HIV genomic RNA is uncoated and internalized
- The reverse transcriptase enzyme then catalyzes the reverse transcription of the RNA to double stranded DNA.

Cont. Life cycle

- The DNA migrates to the nucleus where it is integrated into the host chromosomes through an enzyme called integrase
- Activation of the host cells leads to transcription of integrated proviral DNA into either genomic RNA or messenger RNA,
- The messenger RNA is used for translating protein synthesis, processing and assembly

Cont. Life cycle

- The viral core is formed by the assembling of HIV protein enzymes and genomic RNA at the plasma membrane of the cells
- On 1st exposure there is 2-4 weeks period of intense viral replication before onset of an immune response and clinical illness
- Acute illness lasts 1-2 weeks this is however rarely diagnosed

Cont. Life cycle

- Clinical manifestations resolve as antibodies to virus become detectable in patients serum
- Patients then enter a stage of asymptomatic infection lasting from months to years.

Transmission

- Sexual contact (homosexual, heterosexual)
- Parenteral

➢ Transfusion of infected blood or blood products

➢ Exposure of infected blood or body fluids through contaminated sharps- IDU through needle sharing or in needle stick accidents

➢ Donated organ

Cont. Transmission

- Traditional procedures
- Perinatal
- Transplacental
- During labour/delivery
- Breast-feeding
- HIV is not transmitted through casual contact, surface contact of from insect bites

Clinical manifestations

- The clinical manifestation ranges from an acute syndrome associated with primary infection to advanced disease
- Clinical findings in HIV syndrome

1. General (usually seen in acute retroviral infection 2-4 weeks)

- Fever
- Pharyngitis

Cont. Clinical manifestations

- Lymphadenopathy
- Arthralgia/myalgia
- Lethargy
- Amnesia
- Nausea, vomiting and diarrhoea

Cont. Clinical manifestations

2. Neuropathic manifestations

- Meningitis- viral meningitis
- Encephalitis
- Peripheral neuropathy
- Myopathy
- Retinitis
- Primary CNS lymphoma
- Toxoplasmosis

Cont. Clinical manifestations

- CMV
- Mycobacteria

Cont. Clinical manifestations

3. Dermatological manifestations

- Erythematous maculopapular rash
- Mucocutaneous ulcerations
- Bacterial, viral, fungal infections
- Kaposis sarcoma

Cont. Clinical manifestations

4. Gastrointestinal disease

- Diarrhoea- giardia, cryptosporidium, TB, candida, microsporidia
- Painful oropharyngeal ulcers- candida, Kaposis sarcoma
- Hepatitis- HBV, HCV, CMV, drug toxicity
- Intestinal tumours- Kaposis sarcoma, Lymphoma (Non-hodgkin lymphoma)

Cont. Clinical manifestations

5. Renal manifestations

- HIV associated nephropathy

6. Pulmonary diseases

- Infections
  - Viral
  - Bacterial- PTB, Mycobacterium avium Intracellulare infection
  - Fungal- Cryptococcus, Histoplasma, Norcadia
  - Parasite- pneumocystis jirovecii (Fungal)
- Tumours- Kaposis sarcoma of the lungs

Cont. Clinical manifestations

7. Hematological manifestations

- Pancytopenia or isolated cell lines depression in the bone marrow e.g. anemia, leucopenia, thrombocytopenia

Laboratory investigations

- **Detection of HIV antibodies**
- Enzyme linked immunosorbent Assay (ELISA)
- Western blot
- Determine test I & II
- **Detection of antigens**
- DNA PCR (Polymerase Chain reaction)
- RNA PCR
- Reverse transcriptase PCR

Cont. Laboratory investigations

- Viral culture
- **Other tests (monitoring)**

- CD4/CD8 count and ratio
- Viral load
- Resistance testing
- **Other tests**
- Hemoglobin

Cont. Laboratory investigations

Assess

Hemoglobin

- Anemia before AZT
- Bone marrow suppression during ARV

White blood cell count and differentials

- High WBC may signify infection
- Low WBC may indicate disease progression or bone marrow suppression

Cont. Laboratory investigations

Serum alanine or aspartate aminotransferases

- Assess possible hepatitis co-infection
- Monitor liver toxicity from ARVs

Serum creatinine +/- blood urea nitrogen

- Baseline renal function
- Possible renal toxicity

Serum glucose

- Hyperglycemia and diabetes in PI based regimen

Cont. Laboratory investigations

Pregnancy test

- To R/O pregnancy and avoid drugs contraindicated in early pregnancy such as Efavirenz

Serum bilirubin

- Elevation associated with NNRTIs toxicity and PIs (Indinavir, Atazanavir)

Serum amylase

- Pancreatitis (DDI, D4T)

Cont. Laboratory investigations

Lipids (cholesterol, triglycerides)

- Elevation in PI based regimen, D4T

Others

- RPR,VDRL,TPHA (confirmatory)

➢ Screening for syphilis

- CXR in symptomatic patients

➢ Evaluation for possible active TB

Cont. Laboratory investigations

- Pap smear/VIA VILLI

➢ Screening for cervical cancer

❖ WHO stage IV disease in HIV infected women

❖ Annual screening recommended in HIV positive women

WHO clinical staging

Stage 1

- Asymptomatic
- Persistent generalized lymphadenopathy
- Acute retroviral infection syndrome

Performance scale

- Asymptomatic normal activity

Cont. WHO clinical staging

Stage 2 (mildly symptomatic stage)

- unexplained weight loss of less than 10 percent of total body weight
- Recurrent respiratory infections (such as sinusitis, bronchitis, otitis media, and pharyngitis)
- Dermatological conditions including herpes zoster flares, angular cheilitis, recurrent oral ulcerations, papular pruritic eruptions,

Cont. WHO clinical staging

seborrhoeic dermatitis, and fungal nail infections

Performance scale

- symptomatic with normal activity

Cont. WHO clinical staging

Stage 3 (moderately symptomatic stage)

- Weight loss of greater than 10 percent of total body weight
- Prolonged (more than 1 month) unexplained diarrhea, unexplained fever
- Pulmonary tuberculosis
- Severe systemic bacterial infections including pneumonia, pyelonephritis, empyema, pyomyositis, meningitis, bone and joint infections, and bacteremia.

Cont. WHO clinical staging

- Mucocutaneous conditions, including recurrent oral candidiasis, oral hairy leukoplakia, and acute necrotizing ulcerative stomatitis, gingivitis, or periodontitis.

Performance scale

- Bed ridden but for below 50% of the day during the past 1/12

Cont. WHO clinical staging

Stage 4 (the severely symptomatic stage)

- HIV wasting syndrome,
- Pneumocystis pneumonia (PCP)
- Recurrent severe or radiological bacterial pneumonia
- Extrapulmonary tuberculosis
- HIV encephalopathy
- CNS toxoplasmosis

Cont. WHO clinical staging

- Chronic (more than 1 month) or orolabial herpes simplex infection
- Esophageal candidiasis
- Kaposi’s sarcoma
- Cytomegaloviral (CMV) infections (CMV retinitis or infection of organs other than the liver, spleen or lymph nodes)
- Extrapulmonary cryptococcosis

Cont. WHO clinical staging

- Disseminated endemic mycoses (e.g., coccidiomycosis, penicilliosis, histoplasmosis)
- Cryptosporidiosis
- Isosporiasis
- Disseminated non-tuberculous mycobacteria infection,
- Tracheal, bronchial or pulmonary candida infection,

Cont. WHO clinical staging

- Visceral herpes simplex infection
- Acquired HIV-associated rectal fistula
- Cerebral or B cell non-Hodgkin lymphoma,
- Progressive multifocal leukoencephalopathy (PML)
- HIV-associated cardiomyopathy or nephropathy

Treatment

- Gold standard of HIV therapy is HAART (Highly Active Anti-retroviral Therapy)
- HAART is a combination of 3 or more ARVS in the treatment of HIV infection

Classes of ARTs

- Nucleoside or nucleotide reverse transcriptase inhibitors (NRTIs)
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
- Protease inhibitors (PIs)
- Integrase inhibitors (IIs)
- Fusion inhibitors (FIs)
- Chemokine receptor antagonists (CRAs)

Cont. Classes of ARTs

- Entry inhibitors (CD4-directed post-attachment inhibitors)
- Pharmacokinetic enhancers (boosting agents)

➢ Initial therapy should be started with a combination of 3 ARTs, including a backbone of 2 NRTIs plus an NNRTI, *or* 2 NRTIs plus a protease inhibitor.

Cont. Classes of ARTs

1. Nucleoside or nucleotide reverse transcriptase inhibitors (NRTIs)

- They act by incorporating themselves in to the DNA of the virus thereby stopping the building process. The resulting DNA is therefore incomplete or defective.
- They include;

Cont. Classes of ARTs

Abacavir (ABC)

Formulation

- Oral solution 20mg/ml
- Tablet 300mg
- **Dosing** 300mg BID of 600mg OD
- Dosing modification-renal and hepatic impairment

Cont. Classes of ARTs

Side-effects

- Headache, malaise/fatigue, nausea and vomiting, hypersensitivity reaction, diarrhea musculoskeletal pain, hypertriglyceridemia, hepatic: AST increased, depression, fever/chills, viral respiratory infections, Ear/nose/throat infections, rash, anxiety, thrombocytopenia, Anaphylactoid reaction, pulmonary hypertension, erythema multiforme

Cont. Classes of ARTs

Redistribution/accumulation of body fat, Stevens-Johnson syndrome, toxic epidermal necrolysis, pancreatitis, GGT increased, hepatic steatosis, hepatomegaly, hepatotoxicity, lactic acidosis, MI

Cont. Classes of ARTs

Didanosine (DDI)

Formulations

capsule, extended release

- 125mg
- 200mg
- 250mg
- 400mg
- Dosing; 25 to <60 kg: 250 mg PO OD
- ≥60 kg: 400 mg PO OD

Cont. Classes of ARTs

Side effects

- Diarrhea, peripheral neuropathy, increased amylase, abdominal pain, increased LFT, increased uric acid, pancreatitis (patients >65 years have higher frequency of pancreatitis than younger patients), pruritus, rash

Cont. Classes of ARTs

Lamuvidine (3TC)

Tablet formulations

- 100mg
- 150mg
- 300mg
- Dosing; ≥25 kg: 150 mg PO BID, OR 300 mg PO OD

Cont. Classes of ARTs

Side-effects

- Cough, diarrhea, fatigue and malaise, fever, headache, musculoskeletal pain, nausea, neuropathy, pancreatitis, peripheral neuropathy, vomiting, abdominal pain, anorexia and/or decreased appetite, arthralgia, chills, depression, dizziness, dyspepsia, insomnia, myalgia, rash, thrombocytopenia, creatine phosphokinase increased

Cont. Classes of ARTs

- Body fat redistribution, elevated amylase, neutropenia, hepatitis B exacerbation

Cont. Classes of ARTs

Stavudine (D4T)

Formulation

Capsule

- 15mg
- 20mg
- 30mg
- 40mg
- Dosing >60 kg: As adults; 40 mg PO BID

Cont. Classes of ARTs

Side-effects

- Headache, chills/fever, malaise, insomnia, anxiety, depression, rash, nausea and vomiting, diarrhea, pancreatitis, abdominal pain, peripheral neuropathy, neutropenia, thrombocytopenia, increased hepatic transaminases, increased bilirubin, myalgia, back pain, weakness

Cont. Classes of ARTs

Zidovudine (AZT)

Formulation

Capsule

- 100mg

Tablet

- 300mg

Dosing 300mg BID

Cont. Classes of ARTs

Side- effects

- Anemia, anorexia, diarrhea, fever, Granulocytopenia, headache, leukopenia, nausea, rash, vomiting, weakness, malaise, dizziness, insomnia, somnolence, hyperpigmentation of nails (bluish-brown), dyspepsia, changes in platelet count, paresthesia

Cont. Classes of ARTs

Tenofovir (TDF)

Tablet

- 150mg
- 200mg
- 250mg

Cont. Classes of ARTs

Side-effects

- Asthenia , diarrhea, nausea, anorexia, depression, myalgia, peripheral neuropathy, dyspepsia, rash, headache, vomiting, flatulence, abdominal pain, neutropenia, increased transaminases

Cont. Classes of ARTs

- Emtricitabine

Cont. Classes of ARTs

2. Non- nucleoside Reverse Transcriptase Inhibitors (NNRTI)

- They bind on to the reverse transcriptase enzyme thereby preventing conversion of RNA to DNA

Cont. Classes of ARTs

Efavirenz (EFV)

capsule

- 50mg
- 200mg

Tablet

- 600mg
- Dosing ≥40 kg: 600 mg PO OD

Cont. Classes of ARTs

Side- effects

- Total cholesterol increased, diarrhea, HDL increased, dizziness , rash, fever, depression , insomnia, cough, vomiting , anxiety, nausea, neutropenia, pruritus, impaired concentration, transaminases increased, somnolence, abnormal dreams, amylase increased, hyperglycemia, dyspepsia, abdominal pain, anorexia, hallucinations

Cont. Classes of ARTs

Nevirapine (NVP)

Formulations

Oral suspension

- 10mg/mL

Tablet, immediate-release

- 200mg
- Dosing; 200 mg PO BID

Cont. Classes of ARTs

Side- Effects

- Diarrhea , Rash , Headache , Neutropenia, Fever, Ulcerative stomatitis, Increased LFTs , Abdominal pain, Paresthesia, Nausea, Anemia, Peripheral neuropathy, Myalgia, Potentially fatal hepatotoxicity (fulminant hepatitis, Cholestatic hepatitis, hepatic failure, hepatic necrosis), Stevens-Johnson syndrome, Toxic epidermal necrolysis, Rhabdomyolysis

Cont. Classes of ARTs

- Rilpivirine
- Etravirine

Cont. Classes of ARTs

3. Protease inhibitors

- They prevent HIV virus from being successfully assembled and released from the infected cell
- Saquinavir (SQV)
- Indinavir (IDV)
- Nelfinavir (NPV)
- Ritonavir (RTV)
- Atazanavir (ATV)

Cont. Classes of ARTs

- Ampenavir
- Lopinavir (LPV/r)
- Darunavir (DRV)
- Fosamprenavir (f- APV)
- Tipranavir (TPV)

Cont. Classes of ARTs

4. Integrase inhibitors

- Prevent HIV integrase is responsible for the transport and attachment of proviral DNA to host-cell chromosomes, allowing transcription of viral proteins.

E.g.

- Raltegravir (RAL)
- Dolutegravir (DTG)

Cont. Classes of ARTs

5. Fusion inhibitors

- These agents disrupt HIV binding and hence fusion with host cells.

E.g.

- Enfuvirtide

Cont. Classes of ARTs

6. Chemokine Receptor Antagonists

- Two chemokine receptors, CXCR4 and CCR5, are necessary for the virus to enter the cell.
- The drugs inhibit the entry of human immunodeficiency virus (HIV) into the host cells.

E.g.

- Maraviroc

Initial evaluation and follow-up for PLHIV

Initial clinical evaluation

- Counselling, assessing for ART readiness and providing/linking to psychosocial support
- Complete medical history
- Thorough physical examination
- Appropriate lab investigations

Cont. Initial evaluation and follow-up for PLHIV

CD4 monitoring recommendations;

- Normal value ranges from 500-1400 cells/ml of blood
- With ART the median increase in CD4 count is 100-150 cells per year
- Baseline investigation for all PLHIV
- Any patient with suspected treatment failure
- Any patient on fluconazole maintenance therapy or on Dapsone as prophylaxis to determine when prophylaxis can be discontinued

Cont. Initial evaluation and follow-up for PLHIV

Viral load monitoring

- For PCR positive HEI(HIV exposed infants) at baseline at the time of ART initiation
- Age 0-24 years old; every 6 months
- Age 25 years and above at month 6, 12 and then annually

Cont. Initial evaluation and follow-up for PLHIV

- Pregnant or breastfeeding at confirmation of pregnancy (if already on ART) or 3/12 after ART initiation (if ART is initiated during pregnancy/breastfeeding) and then every 6/12 until complete cessation of breastfeeding
- Before any drug substitution (If no VL results available from the prior 6/12)
- 3/12 after any regimen modification (including single drug substitution)

Standard package of care for PLHIV

8 components

1. ART therapy

- All PLHIV are eligible for ART
- Initiated as soon as the patient is ready to start preferably within 2 weeks from time of HIV diagnosis * (except for patients with cryptococcal meningitis or TB meningitis)

Cont. Standard package of care for PLHIV

2. **Positive health, dignity and prevention, GBV/IPV (intimate partner violence) and health education and counselling;**

- Counseled and supported for disclosure of HIV status partner/ family testing and engagement
- Condom use
- Family planning
- STI screening and treatment

Cont. Standard package of care for PLHIV

- Adherence services
- Screen for IPV
- HIV education and counselling

Cont. Standard package of care for PLHIV

3. Screening for and prevention of specific opportunistic infections;

- Lifelong CTX (Cotrimoxazole) unless they have allergy to sulfa drugs
- CTX prevents toxoplasmosis, PCP, CAP, Staph. Aureus, Non-typhi salmonella, other gram negative GI organisms, malaria, Isospora

Cont. Standard package of care for PLHIV

- Dapsone used as a substitute for CTX. Recommended for patients in WHO stage 4 and/or absolute CD4 count < or equal to 200cells/mm^3 (or CD4% < or equal 25% for children who are < or equal to 5 years old)

Cont. Standard package of care for PLHIV

and should be discontinued once a patient achieves viral suppression and a sustained CD4 count of > 200cells/mm^3 (or CD4 % > 25% for children < or equal to 5 years old) for at least 6/12

- All PLHIV screened for TB at every visit and assessed for Isoniazid preventive therapy (IPT) if negative for TB
- All PLHIV baseline CD4 count < or equal to 200cells/mm^3 should be screened for cryptococcal infection using serum cryptococcal antigen test

Cont. Standard package of care for PLHIV

4. Reproductive health services;

- All PLHIV screened for STIs at every clinic visit
- Assess all women for pregnancy of reproductive age
- All HIV positive women 18-65 years screened for cervical cancer

Cont. Standard package of care for PLHIV

5. Screening for and management of NCDs (Non-communicable Diseases)

- HTN, DM, dyslipidemia and renal disease
- Lifestyle modification for prevention and management

Cont. Standard package of care for PLHIV

6. Mental Health screening and management

- Screen for depression before initiation ART and screen for annually thereafter and PRN where there is clinical suspicion
- Screen for alcohol and drug use

Cont. Standard package of care for PLHIV

7. Nutritional services

- Nutritional assessment, counselling and support

8. Prevention of other infections

- Vaccinations as recommended by the National vaccines and immunization programme

ART therapy

- Goal of ART is suppression of viral replication to reduce patients viral load to undetectable levels
- All individuals with confirmed HIV infection are eligible for ART irrespective of CD4 count/%, WHO clinical staging, age, pregnancy or breastfeeding status, co-infection status, risk group, or any other criteria, provided that the individual is willing and ready to take ART and adhere to follow-up recommendations.

Cont. ART therapy

1st line

>15 years of age or > 35kgs body weight

- TDF (or ABC)+ 3TC+ DTG (or TDF+ 3TC+ EFV for women and adolescents girls of childbearing potential)
- AZT+3TC+DTG (or EFV)
- DTG (or ABC or AZT)+3TC+ATV/r(or LPV/r

➢ LPV/r- Lopinavir/ritonavir

Cont. ART therapy

- Treatment failure suspected when a patient has a high viral load > or equal 1000 copies/ml after at least 6/12 of using ART.
- It is confirmed when VL > or equal to 1000 copies/ml after assessing for and addressing poor adherence or other reasons for high viral load and then repeating VL after at least 3/12 of excellent adherence to allow for viral suppression

Cont. ART therapy

2nd line

- AZT+3TC+ATV/r3
- TDF+3TC+ATV/r3
- DRT-based 2nd line

➢ DRT-Drug resistance testing)

Cont. ART therapy

3rd line

- DTG+3TC+DRV/r
- DTG+AZT+3TC+DRV/r
- DTG+TDF+3TC+DRV/r
- DTG+TDF (or AZT)+3TC
- ETV+3TC+DRV/r

➢ DRV/r-Darunavir/ritonavir

Cont. ART therapy

ARVS for post-exposure prophylaxis (PEP)

- Offered <72 hours after high risk exposure
- TDF+3TC+DTG (or TDF+3Tc+ATV/r for women and adolescents girls of child bearing age)

Cont. ART therapy

Oral pre-exposure prophylaxis (PrEP)

- HIV negative individuals at ongoing risk of HIV infection including the sero-negative partner in a discordant relationship)
- TDF (300mg)+FTC (200mg) once daily

➢ FTC-Emtricitabine

- Test HIV every 3/12

OPPORTUNISTIC INFECTIONS

Common opportunistic infections

- Tuberculosis
- Bacterial infections
  - Pneumonia
  - Gram negative sepsis
- Pneumocystis pneumonia-PCP (now pneumocystis jirovecii)
- Cryptococcal meningitis
- Toxoplasmosis

Cont. Common opportunistic infections

- Candidiasis
- Infective diarrhoea
- Herpes zoster
- Infective dermatoses

HIV related malignancies

- Primary CNS lymphoma
- Ca cervix
- Other lymphomas
- Kaposis sarcoma

Cont. Common opportunistic infections

Other conditions

- HIV wasting syndrome
- Non-infective dermatoses
- HIV nephropathy
- HIV cardiomyopathy

Tuberculosis

- Major opportunistic infection in Kenya
- Occurs;
  - Reactivation of latent infection
  - Newly acquired infection
- HIV is the single most important risk factor for TB
- HIV increases the risk of TB progression
- HIV increases the rate of TB progression
- TB may speed the progression of HIV disease
- ART reduces the incidence of TB in PLHIV

Cont. Tuberculosis

Clinical presentation of TB in HIV patients;

- Depend with the immune status of patient
- In early HIV disease, presentation tends to be typical pulmonary TB (Cough for > 2weeks, fever, night sweat, chest pain, weight loss, signs (wasting, crepitations, consolidation, effusion etc.)
- As the immune status deteriorates extrapulmonary TB (pleural effusion, lymphadenopathy, pericardial disease, Miliary TB, TB meningitis, peritoneal and spinal TB)

Cont. Tuberculosis

Extrapulmonary TB clinical manifestation

- Fever, weight loss and lethargy
- Focal lymphadenopathy, Septic arthritis, signs of meningitis, pericarditis, peritonitis, hepatosplenomegally

Cont. Tuberculosis

Diagnosis of pulmonary TB

- Sputum examination
- In HIV, sputum negative results does not exclude TB. Only 50 % sensitive
- Chest radiograph
- No typical TB x-ray. It can create almost any abnormality or even none. Cavities, pericardial effusion, apical disease, pleural effusion
- DDX-pneumonia, PCP, KS, abscess

Cont. Tuberculosis

Diagnosis of extrapulmonary TB

- CXR often normal and sputum if available is negative
- If the lymph nodes are enlarged-aspirate
- If meningism present-lumbar puncture
- If septic arthritis or abscess-aspirate
- Do ZN stain or gene Xpert on the samples

Cont. Tuberculosis

Tuberculosis treatment

- All forms of TB except TB meningitis and osteo-articular TB

❖2RHZE/4 RH

- TB meningitis and osteo-articular TB

❖2 RHZE/10RH

Cont. Tuberculosis

- If patient not on ART, start anti-TBs first then ART 2 weeks after starting anti-TBS
- PIs and NVP interact with Rifampicin
- Immune reconstitution syndrome-paradoxical worsening of symptoms due to immune recovery. Presents with fever, lymphadenopathy, worsening CXR, CNS symptoms, pleural effusion. DDX TB treatment failure, lymphoma

Cont. Tuberculosis

TB prevention using Isoniazid prophylaxis

- For HIV positive patients that screen negative for TB, given INH prophylaxis dose of 10mg/kg/day (Max 300mg OD) for 6 months, once.
- Benefits last up to 2.5 years.

Pneumocystis carinii pneumonia (PCP)

Clinical presentation

- Shortness of breath/respiratory distress
- Cough- usually dry
- Fever

Signs

- Tachypnoea
- Tachycardia
- Cyanosis
- Oxygen saturation< 90%
- Lung auscultation is normal

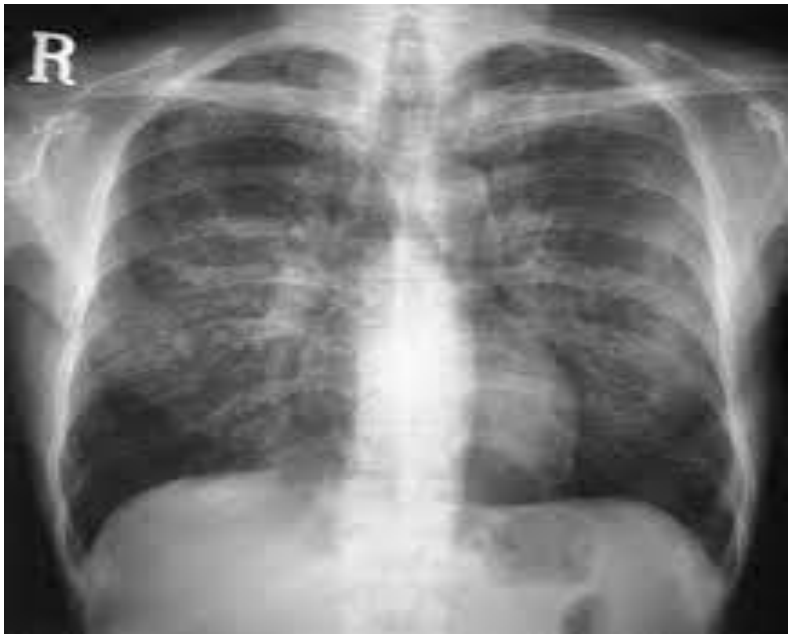
Cont. PCP

Diagnosis

- High index of suspicion
- CRX- bilateral, diffuse interstitial shadowing/opacities. It can be relatively normal even with severe respiratory distress
- Induced sputum and bronchoalveolar lavage

➢ Can give a definitive diagnosis

Cont. PCP



Cont. PCP

Management

- Severe disease

- High dose CTX for 21 days
- 120mg/kg per day in 3-4 doses
- If allergic to or intolerant of CTX
- Clindamycin at 900mg IV 8 hourly plus Primaquine 30mg orally/day. Clindamycin may also be given orally at a dose of 600mg 6 hourly

Cont. PCP

- For mild to moderate disease
- Trimethoprim 15mg/kg/day + Dapsone 100mg/day PO for 21 days
- CTX: 1 to 5 ratio (trimethoprim: Sulfamethoxazole)
- Prednisolone for severe respiratory distress or those with cyanosis
- Dose 40mg BD for 5 days, then 40mg OD for 5 days, then 20mg OD for 11 days then stop

Cont. PCP

Supportive therapy

- Oxygen therapy
- IV fluids
- Nutrition
- Monitor blood

➢ CTX toxicity

➢ Multiple organ dysfunction in severely ill

- Secondary prophylaxis needed after treatment is complete

Cont. PCP

PCP prophylaxis

- CTX 960mg OD
- For those allergic to CTX give Dapsone 100mg OD
- It is effective against PCP and Toxoplasmosis. Discontinued following immune reconstitution

Cryptococcal meningitis

- Caused by cryptococcal neoformans

Clinical presentation

Symptoms

- Headache- severe
- Fever- often absent in early disease
- Neck stiffness

Cont. Cryptococcal meningitis

Signs

- Abnormal gait
- Cranial nerve palsies
- Papilledema
- Confusion
- Convulsions
- Coma

Cont. Cryptococcal meningitis

Diagnosis

- High index of suspicion
- LP- most useful

➢ Raised intracranial pressure

➢ Usually mild lymphocytosis

➢ Indian ink stain- positive in 60-80% cases

➢ Negative Indian ink does not exclude cryptococcal meningitis

Cont. Cryptococcal meningitis

- Cryptococcal antigen (CRAG)
- Highly sensitive and specific (>95%)- expensive
- Useful in differentiating CM from TB meningitis due to similar presentation and CSF cell/biochemistry

Cont. Cryptococcal meningitis

Management

For severe/advanced disease

- Amphotericin B 0.7-1mg/kg daily for 2 weeks/until clinically stable
- Followed by
- Fluconazole 400mg daily for 8-10 weeks

Cont. Cryptococcal meningitis

- **If diagnosed early/amphotericin B is unavailable**

➢ Fluconazole alone 400-800mg daily for 10-12 weeks

➢ Treatment failure and mortality higher

➢ Use higher dose if patient is on Rifampicin i.e. 1600mg

Cont. Cryptococcal meningitis

During treatment with Amphotericin B;

- Check potassium and creatinine every 48 hours
- Give IVF before and after administration of amphotericin B

Cont. Cryptococcal meningitis

Supportive treatment

- If raised ICP indicated by severe headache, visual disturbance, perform repeated LP and drain CSF e.g. 30mls/day
- ➢ Reduces mortality
- ➢ Reduced blindness
- ➢ Help with pain, and consciousness level
- No evidence of benefit from steroids, they are beneficial in TB meningitis

Cont. Cryptococcal meningitis

Maintenance therapy (secondary prophylaxis)

- Fluconazole 200mg OD
- If on ART continue until CM therapy completed AND CD4 raised > or equal to 200cells/ml for more than 6 months
- Relapse rate with prophylaxis and immune reconstitution due to ART
- Primary prophylaxis not recommended

Toxoplasmosis

- Caused by Toxoplasma gondii (a protozoa whose definitive host is the cat)
- Humans are infected by ingesting of T. gondii in food contaminated with cat faeces or undercooked meat
- Vertical transmission occurs- with serious consequences if it occurs in the 1st trimester
- Asymptomatic in >90% of immunocompetent adults and children

Cont. Toxoplasmosis

- Commonly a result of reactivation of latent diseases in patients with AIDS and those on chemotherapy for lymphoproliferative disorders
- CD4< 100cells/mms^3
- Commonly encephalitis

Cont. Toxoplasmosis

Clinical presentation

Symptoms

- Can be acute or progressive
- Headache- can be severe- no meningism
- Neurological deficits
- Fever-only in 50% at presentation
- Confusion-Sometimes present as subtle personality change
- Convulsions

Cont. Toxoplasmosis

Signs

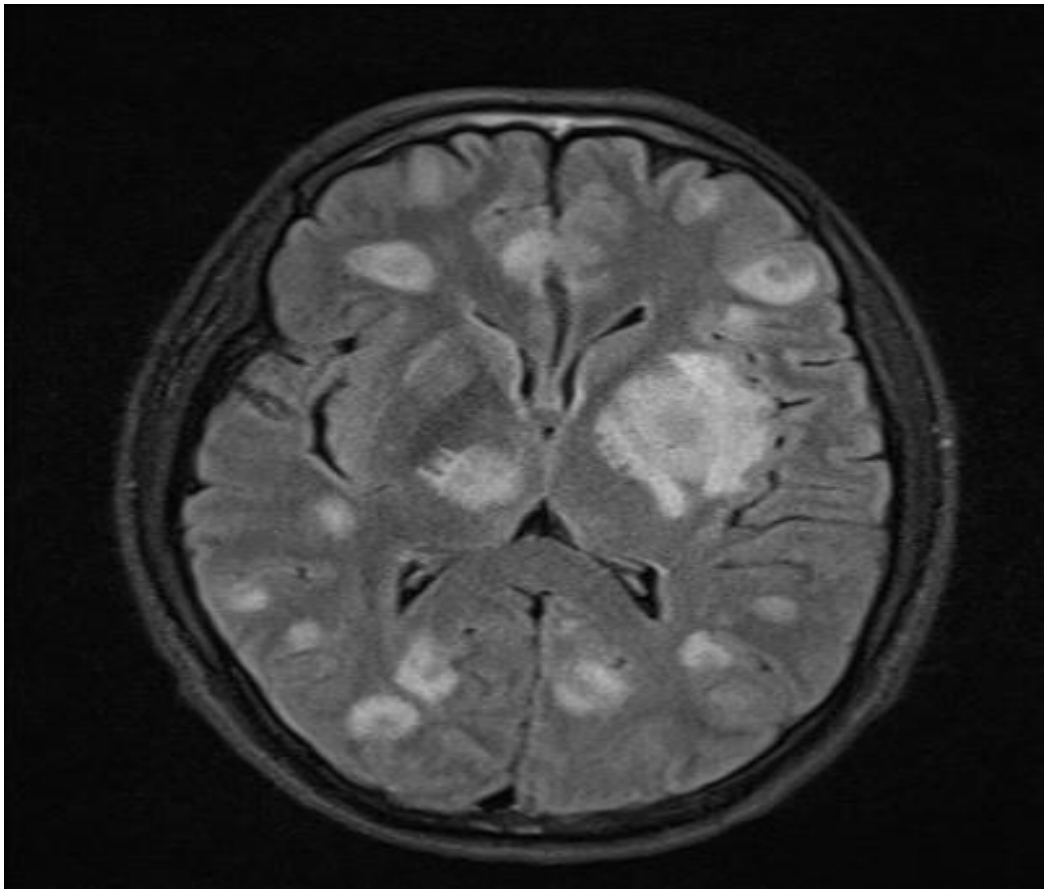
- Focal neurological deficits
- Progressive paralysis
- Blindness
- Cerebellar signs, incontinence
- Fever

Cont. Toxoplasmosis

Diagnosis

- Typically CD4 count <100
- Brain CT scan ideal if available >2 ring enhancing lesions
- High index of clinical suspicion needed
- Any HIV positive patient with headache, confusion and signs of SOL with a relatively normal CSF has toxoplasmosis until proven otherwise

Cont. Toxoplasmosis



Cont. Toxoplasmosis

- DDX- Tuberculoma, bacterial abscess, CVA, primary CNS lymphoma
- A response to empirical treatment is virtually diagnostic usually within 2 week

Cont. Toxoplasmosis

Management

- Pyrimethamine 200mg loading dose followed by 50mg daily

Plus

- Sulphadiazine 1g-1.5g OD

Plus

- Folinic acid 20mg daily for 6-8 weeks

Cont. Toxoplasmosis

OR

- CTX for 4- 6 weeks

➢ 25mg/kg daily of sulphamethoxazole or 5mg/kg TMP in 2 divided doses

Maintenance therapy

- Pyrimethamine 50mg+ Sulphadiazine1g + Folinic acid 20mg OD until CD4 count is >200 for more than 6 months (clindamycin 300mg OD can replace Sulphadiazine

Cont. Toxoplasmosis

Prevention of toxoplasmosis

- Basic food hygiene
- Eating well cooked meat

Primary prophylaxis

- CTX 960mg OD

Secondary prophylaxis

- Same as the maintenance therapy

Bacterial pneumonia

Clinical presentation

- Acute productive cough
- Fever
- Chest pain
- Breathlessness
- CXR-consolidation

Bacterial pneumonia

Management

- Amoxicillin
- 0r
- Erythromycin
- Or
- Cephalosporins

➢ CTX if effective prevention for bacterial pneumonia

Candidiasis

Vaginal

- Not strictly an OI unless chronic (>1month) or unresponsive to treatment

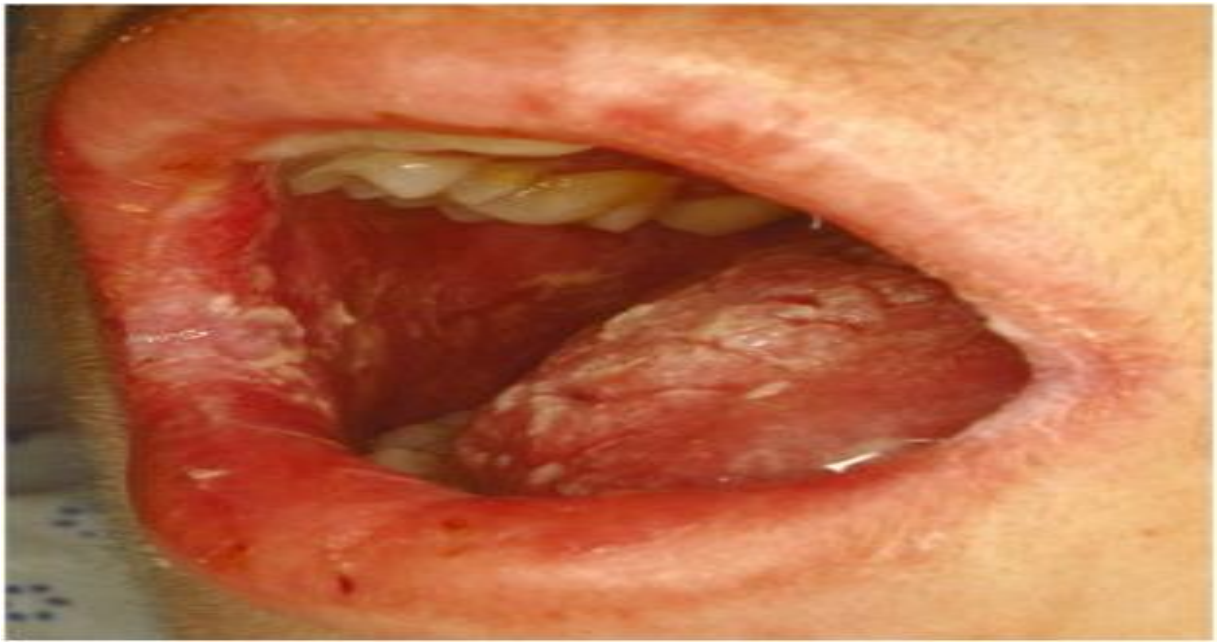
Oropharyngeal

- Very common
- WHO stage III defining- CD4 usually < 300

Esophageal

- Significant cause of mortality and morbidity
- WHO stage IV defining –CD4 usually <100

Cont. Candidiasis



Cont. Candidiasis

Figure 1: Gastrointestinal upper endoscopy: several white patches

Cont. Candidiasis

Vaginal candidiasis

- Clotrimazole vaginal pessary
- 200mg daily for 3 days or 500mg stat

Alternative

- Fluconazole 150mg stat

Recurrent (>4 episodes per year)

- Clotrimazole pessary 500mg weekly
- Fluconazole 100mg weekly

Cont. Candidiasis

Oro-pharyngeal candidiasis

- White pseudomembranous plaques, atrophic/erythematous, angular cheilitis

Treatment

- Nystatin drops or tablets500,000 IU QID
- Miconazole oral gel 60mg QID
- Miconazole buccal tablet OD for 7 days

If unresponsive

- Fluconazole 100mg OD for 7 days

Cont. Candidiasis

Esophageal candidiasis

- Causes odynophagia
- Results in inadequate oral intake- dehydration, malnutrition, wasting

Treatment

- Fluconazole 200mg stat, then 100mg daily for 14 days
- Ketoconazole 200mg daily for 14 days
- Maintenance therapy required unless immune reconstitution occurs.

Infective diarrhoea

Acute diarrhoea (>3 loose motions/day X < 2 weeks

- Stool cultures where possible
- If acutely unwell and pyrexia with blood in stool
- Consider a quinolone (ciprofloxacin 500mg BID for 10-14 days)
- Remember drugs as a cause of diarrhoea including antibiotics

Cont. Infective diarrhoea

Chronic /recurrent diarrhoea (>1 month)

- Copious amount of waterly diarrhoea associated with abdominal pain+/- fever
- Symptoms intermittent CD4 < 200
- Often associated with wasting, malabsorption
- Cause usually not identified in practice; rule out acute infections where possible
- CTX reduces incidence of diarrhoea in PLHIV
- Lab- stool for modified AAFB- microsporidia

Cont. Infective diarrhoea

Management

- Oral rehydration therapy
- IV fluids- if severe dehydration

Antimicrobials

- If possible, treat according to stool analysis
- Stool analysis often not helpful
- Empirical treatment justified in chronic debilitating diarrhoea
- Symptomatic treatment a relief to patients

Cont. Infective diarrhoea

Empirical management of chronic diarrhoea

- Trial of CTX- 2 tabs BID for 5 days (not in patients already on CTX prophylaxis

If no improvement

- Trial of metronidazole- 400mg TDS for 7 days plus anthelmintic e.g. Albendazole 400mg BID for 14 days

Cont. Infective diarrhoea

If no improvement

- Symptomatic management and prepare for ART
- Eg loperamide, dietary advice etc.
- ART effective in eliminating chronic diarrhoea

Skin conditions

1. Herpes zoster

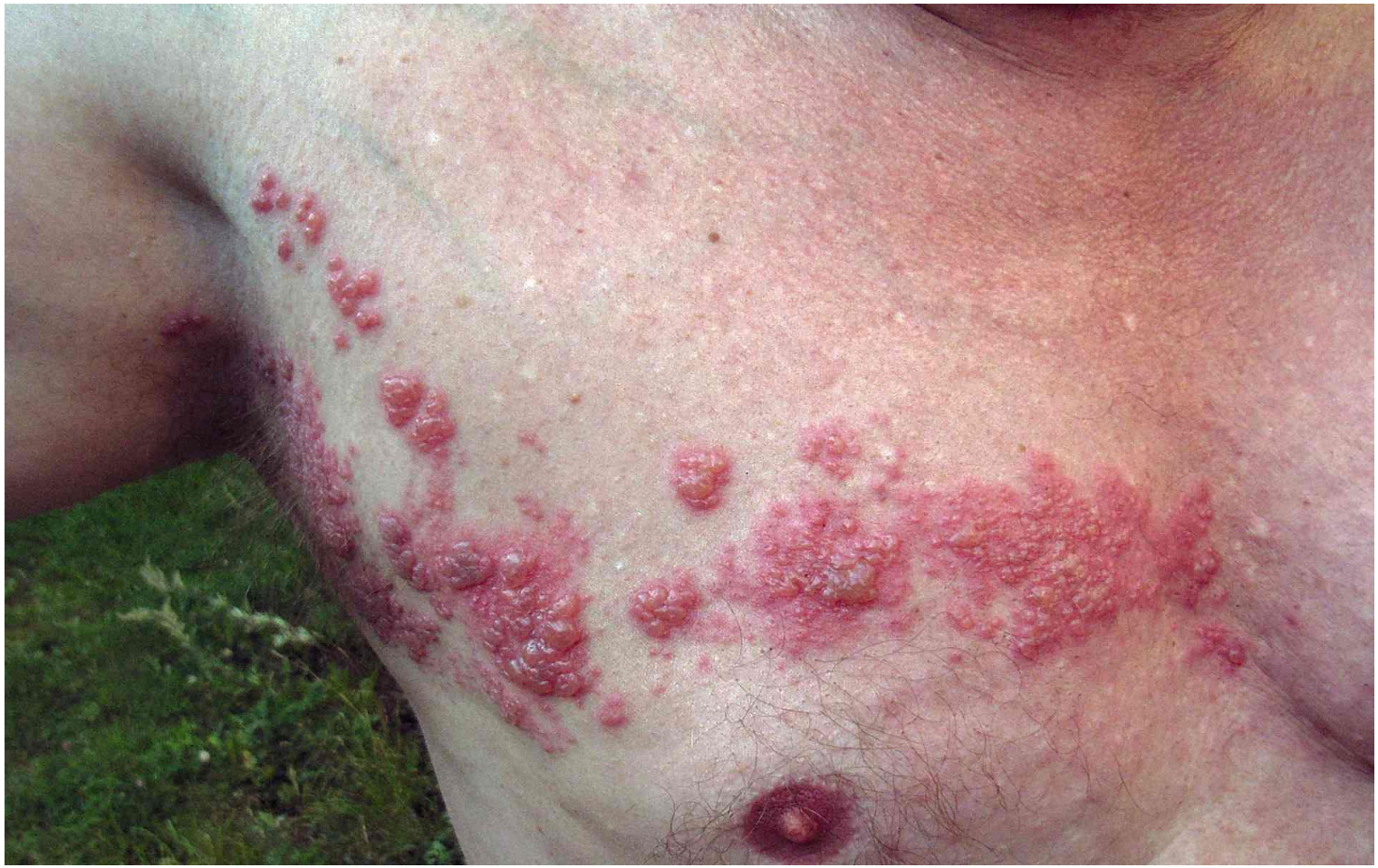
- Reactivation of previous varicella (chicken pox)
- Very common
- Can occur early in HIV disease
- Multi- dermatomal, recurrent
- Causes acute, severe pain
- Risk of debilitating post herpetic neuralgia (PHN) more common in older patients
- Disfiguring keloid formation
- Diagnosis clinical

Cont. Skin conditions

Ophthalmic herpes zoster

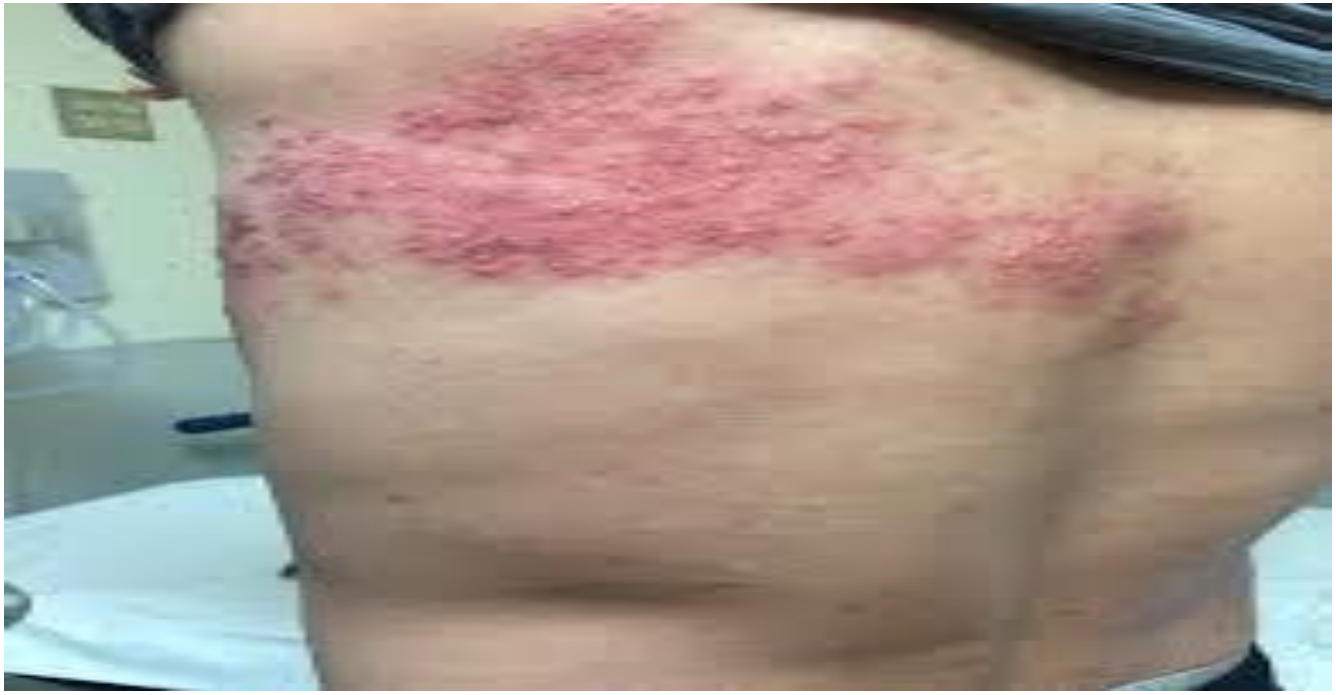
- Risk of permanent visual impairment
- Need to treat early and aggressively using IV Acyclovir

Cont. Skin conditions



Cont. Skin conditions

Cont. Skin conditions



Cont. Skin conditions

Cont. Skin conditions

Herpes zoster management

- Analgesic- for acute pain
  - ➢ Paracetamol plus and NSAID (+/-opiate)
- Apply calamine lotion regularly
  - ➢ Reduces itch and secondary infection

If present with new lesions

- Give acyclovir (the sooner the better)
  - ➢ Reduces acute pain, duration of lesions, number of new lesions and systemic complaints
  - ➢ Acyclovir does not alter the rate of PHN

Cont. Skin conditions

- Acyclovir 800mg 5 times a day for 7-10 days
- If visceral/ extensive or disseminated or ophthalmic where possible give IV acyclovir 10mg/kg TID

Cont. Skin conditions

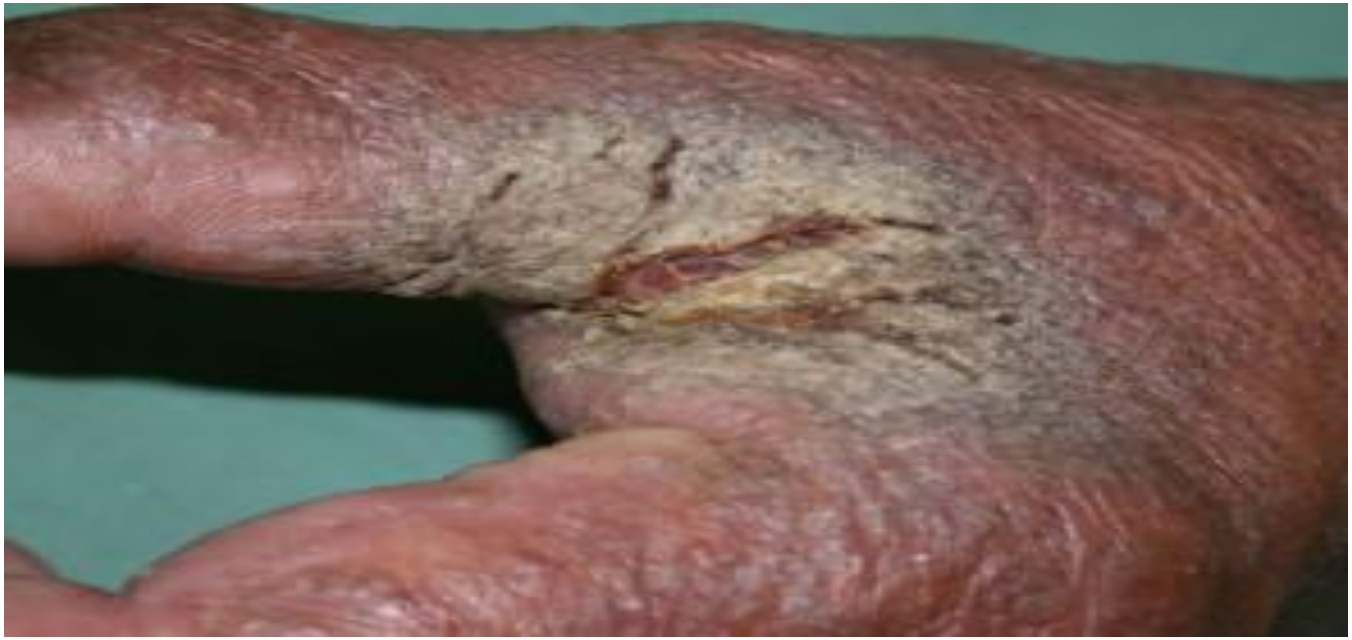
2. Scabies

- Sarcoptes scabiei
- Very common- under diagnosed and undertreated
- Papular intensely itchy rash

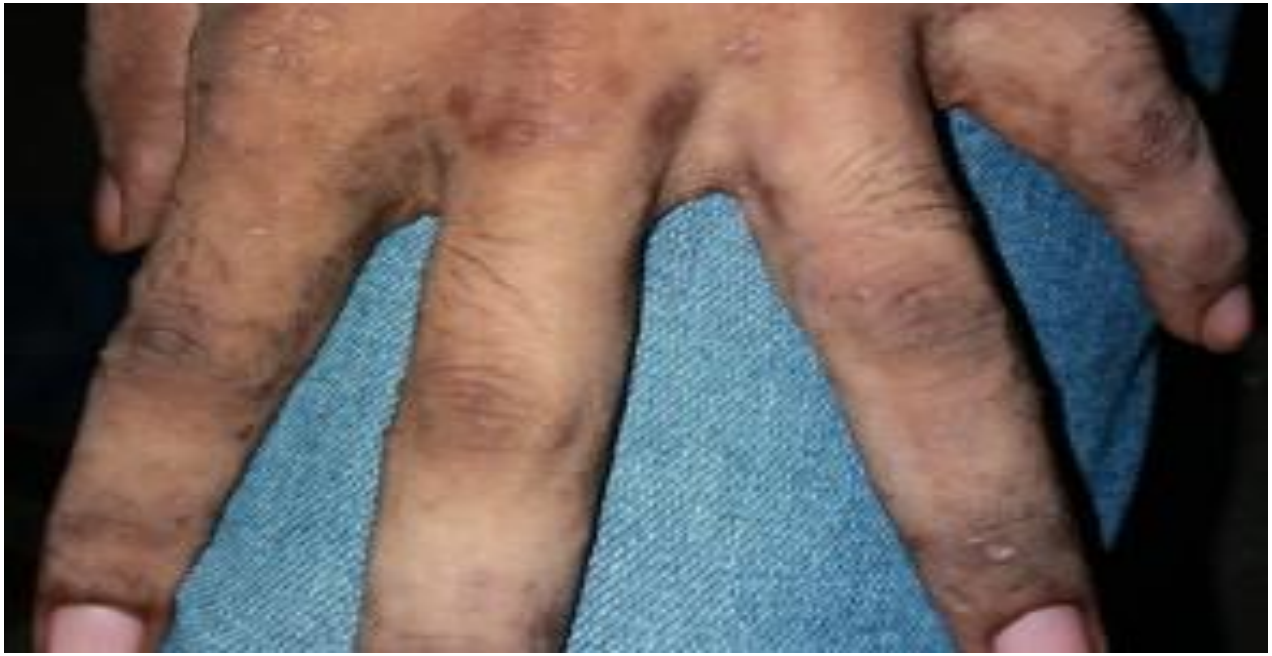
Treatment

- 5% permethrin cream
- 25 % benzyl benzoate lotion at night for 3 nights
- 10 % sulfur ointment
- 1 % lindane lotion

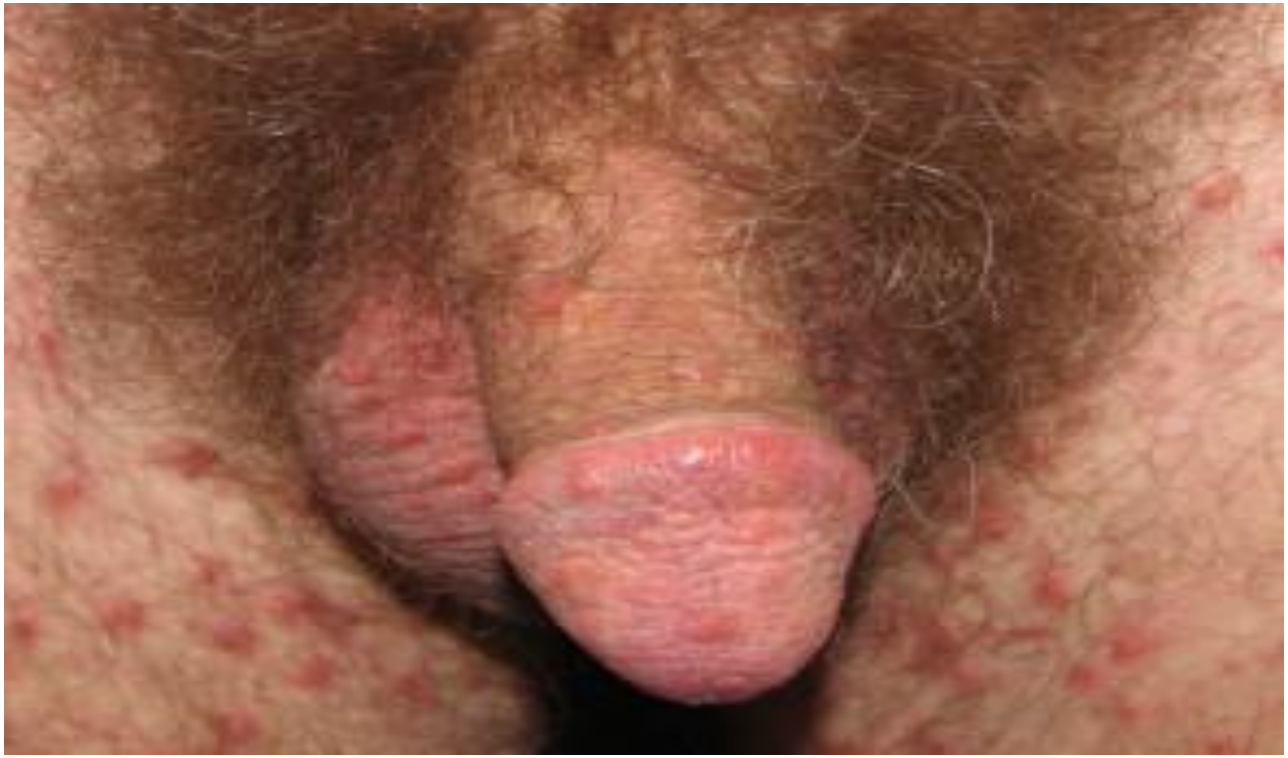
Cont. Skin conditions



Cont. Skin conditions



Cont. Skin conditions



Cont. Skin conditions

3. Seborrhoeic dermatitis

- Pityrosporum yeast
- Erythematous plaques with scales at the edge of scalp around the nose and ears

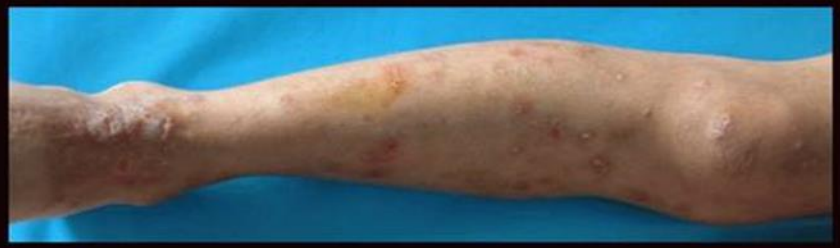
Treatment

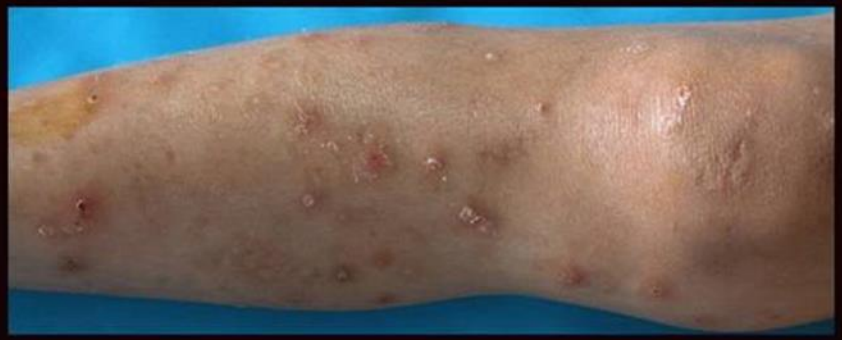
- 2.5% hydrocortisone cream with anti-fungal cream + tar based/ antifungal shampoons

Cont. Skin conditions

4. Papular Pruritic Eruptions (PPE)

- Purigo Nodularis
- Cause unknown
- Occurs with CD4 count <200
- Severe itching, with hyperpigmented, hyperkeratotic, excoriated papules and nodules
- Associated thickening of skin (lichenification) and scarring





Pruritic papular eruption

Picture Credit: Dr Sirisanthana

www.aids-images.ch

Cont. Skin conditions

Management of PPE

- Chlohexidine/Cetrimide ointment
- Antihistamines
- ART

HIV related malignancies

- Kaposis sarcoma
- Lymphomas
- HPV associated carcinoma (cervical, anal and penis)

Cont. HIV related malignancies

1. Kaposis sarcoma

- Firm dark nodule, papules, patches that are not symptomatic

➢ Skin

➢ Oropharyngeal

➢ Multisystem (GI, lungs)

- WHO stage IV defining disease

Cont. HIV related malignancies

Clinical diagnosis; biopsy if uncertain

- Prognosis depends on extent of disease and CD4 count
- ART associated with;

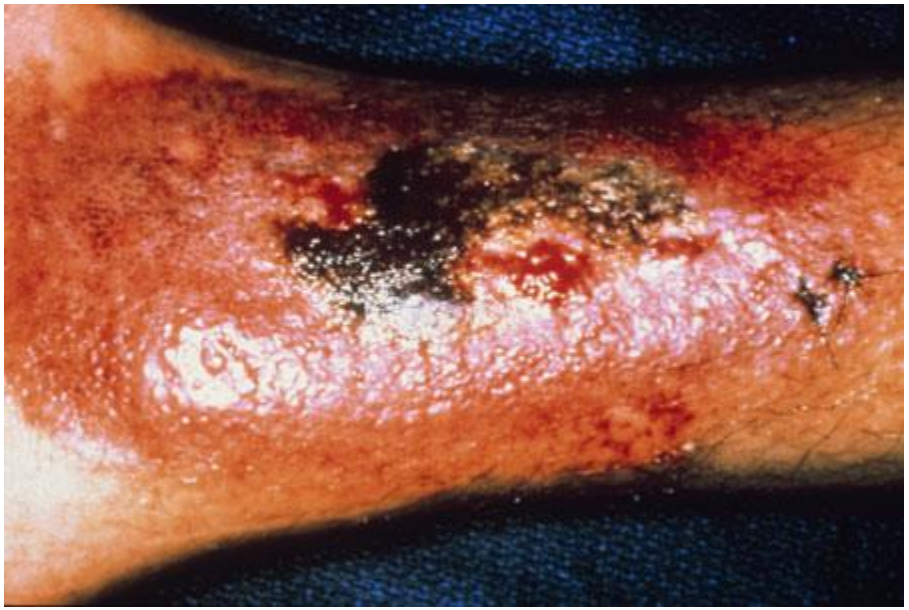
➢ Reduced incidence of KS

➢ Regression of lesions

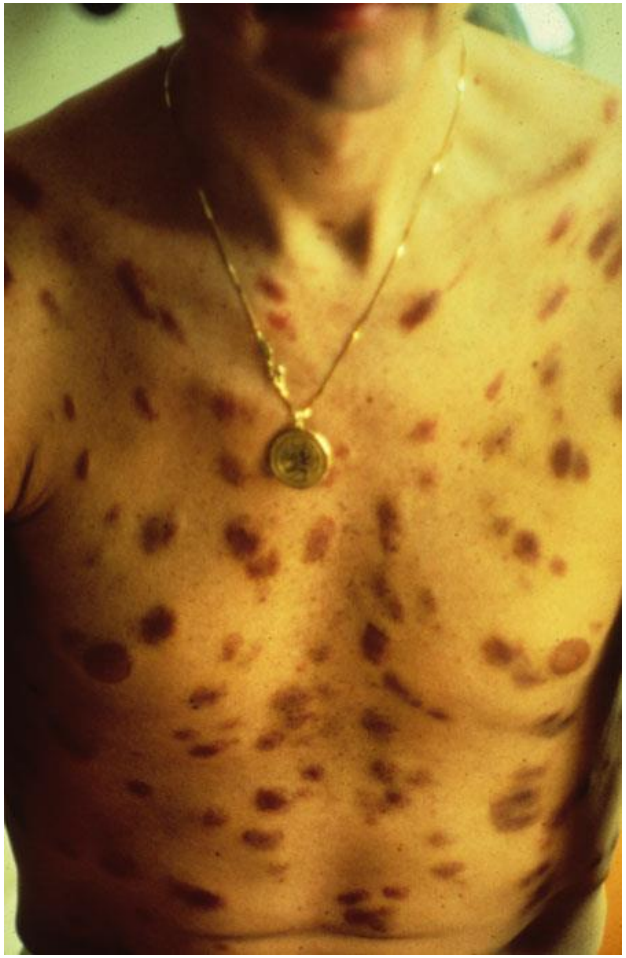
➢ Prolonged survival

- Incurable condition; treatment aims to reduce symptoms and prevent progression

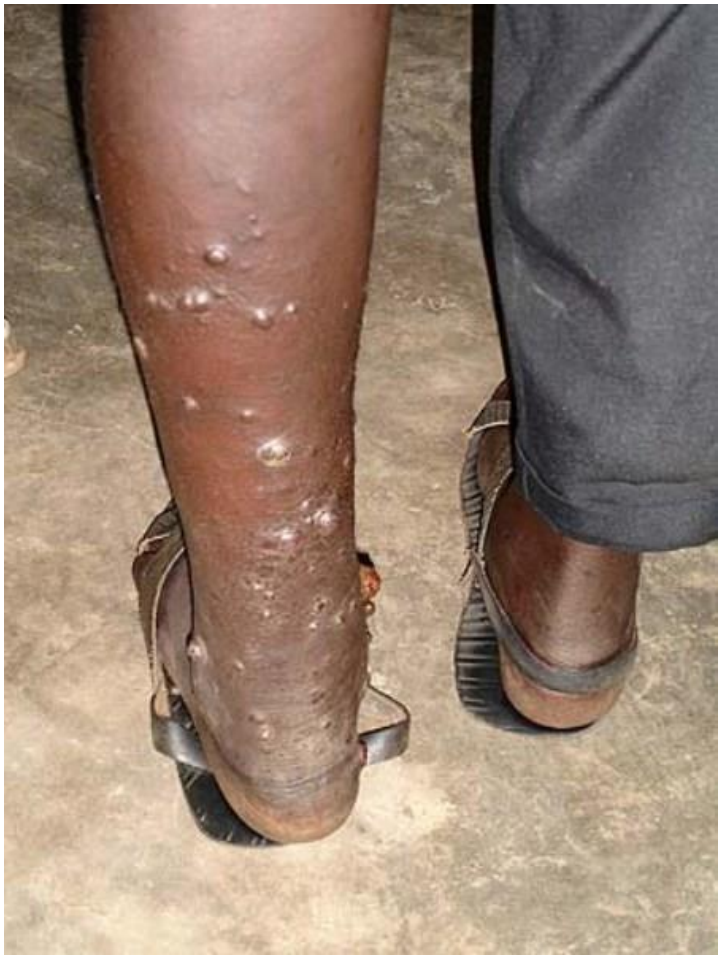
Cont. HIV related malignancies



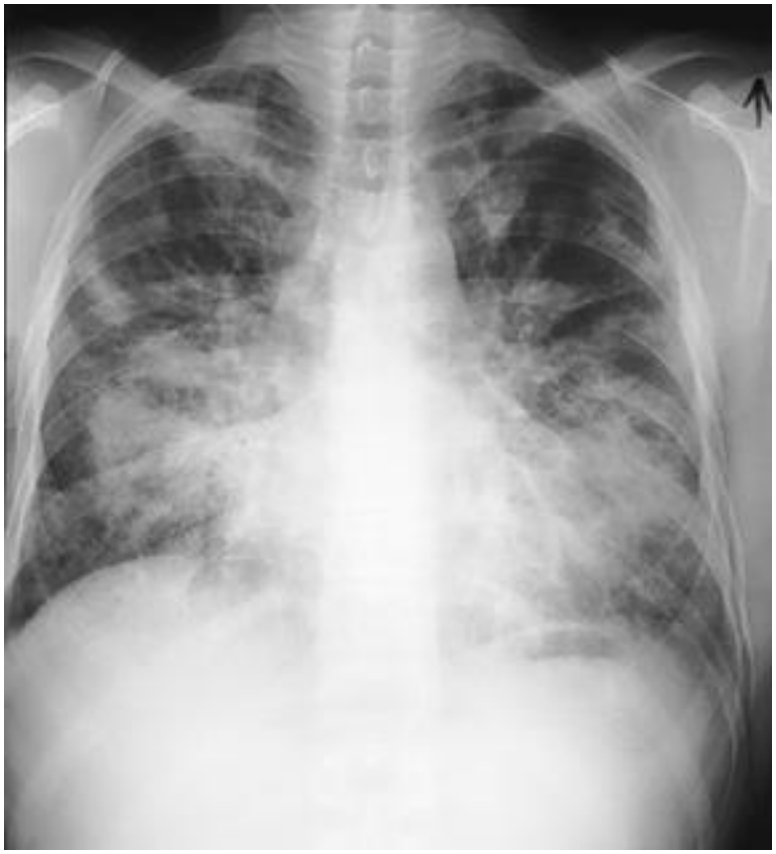
Cont. HIV related malignancies



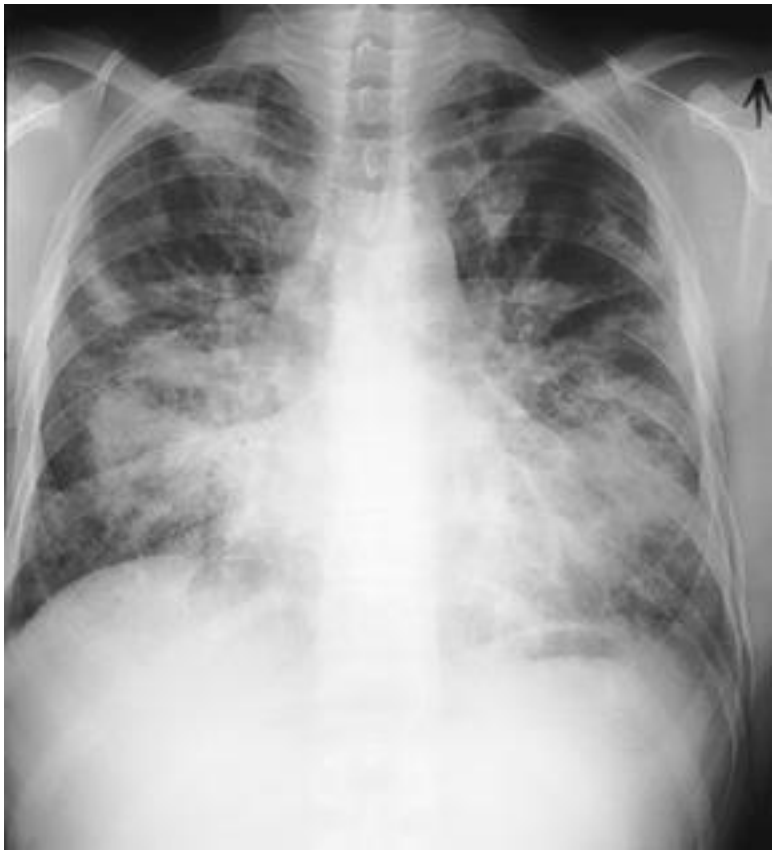
Cont. HIV related malignancies



Cont. HIV related malignancies



Cont. HIV related malignancies



Cont. HIV related malignancies

Management

- Disease limited to skin, relatively few lesions, no systemic symptoms
- Radiotherapy
- Intra-lesional vincristine

Systemic treatment for extensive disease, systemic involvement

- Combination of chemotherapy, vincristine +Bleomycin
- Vincristine alone

Cont. HIV related malignancies

Lymphoma

2. Primary CNS lymphoma

- EBV associated
- Much more frequent and commonest lymphoma in HIV infected
- Incidence somewhat reduced by effective ART
- Usually CD4 low (<50)
- CNS symptoms without fever

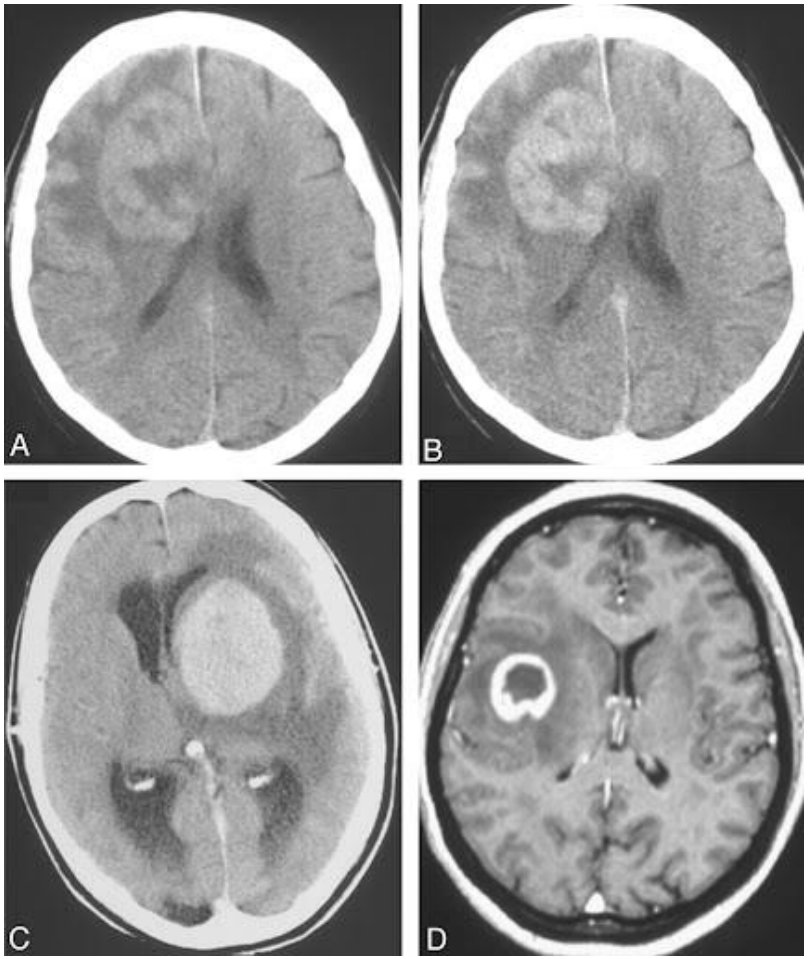
Cont. HIV related malignancies

- Diagnosis: CT scan, failure to respond to empiric toxoplasmosis treatment

Treatment- refer (Radiotherapy, steroids, chemotherapy)

- Poor outcome
- Effective ART prolongs survival

Cont. HIV related malignancies



Cont. HIV related malignancies

3. Non- Hodgkin's lymphoma

- More frequent in HIV infected
- Caused by EBV in the presence of immunosuppression (CD4 <100)
- More likely to present with systemic symptoms (fever, hepatitis, effusions, GI)
- Biopsy required for diagnosis
- Treatment: refer (combination of radiotherapy and steroids)

Cont. HIV related malignancies

4. Cervical cancer

- AIDs defining disease
- Presence of HIV infection allows permissive replication of human papilloma virus (HPV)

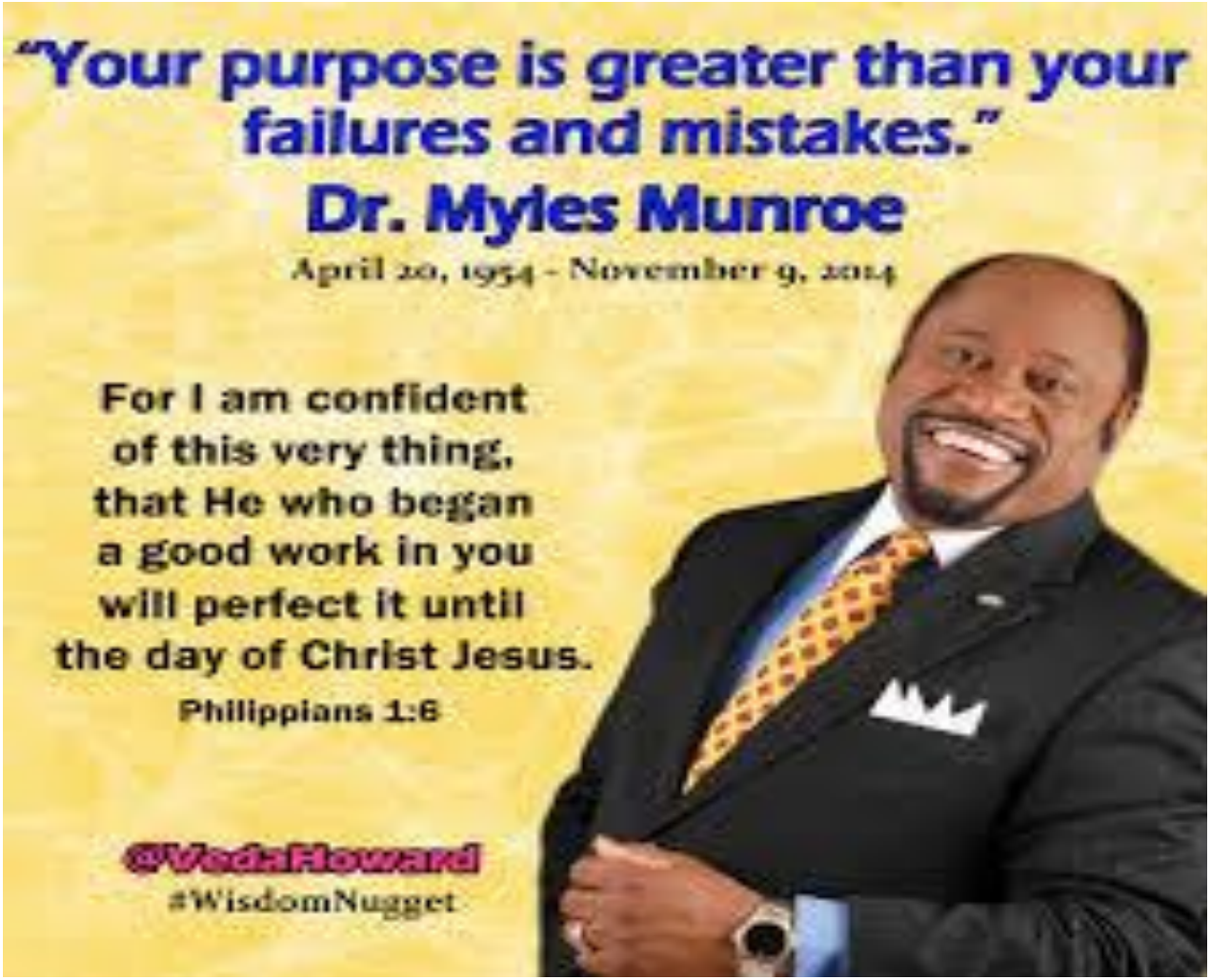
Diagnosis

- VIA (acetic acid) VILLI (Lugols iodine)
- Pap smear
- HIV positive women should be screened at enrollment then annually

THE END

?


THANK YOU!


"Your purpose is greater than your failures and mistakes."
Dr. Myles Munroe
April 20, 1954 - November 9, 2014
For I am confident of this very thing, that He who began a good work in you will perfect it until the day of Christ Jesus.
Philippians 1:6
@VedaHoward
#WisdomNugget