HIV\AIDS

Virology :

It is single stranded RNA Retrovirus of Lenti virus ,it is spherical bilipid membrane surround protein core which contain virus proteins ,RNA and virus enzymes like reverse transcriptase and integrase enzymes ,the virus has external spikes (glycoproteins GP) has protein core like GP 120 and GP 41.There are two types of HIV ,HIV1,and HIV2 where the later is less aggressive ,less vertical transmission and less viral production and less CD4 T-lymphocytes attrition . HIV classified into M-major ,O-outlier and N- non major non outlier .

EPIDEMIOLOGY

In 2007 the WHO estimate that there are 33.2 million people worldwide infected with HIV , 2.5 million new infection cases annually and 2.1 million death per year . The most infected area is Subsaharan Africa 22 million patients then south and south east Asia 4.2 million ,Latin America 1.7 million then Eastern Europe and Central Asia 1.5 million then North America 1.3 million then western Central Europe 730 000 patients.

VIROLOGY AND IMMUNOLOGY

The HIV virus infect CD4 T-Lymphocyte predominantly but also can infect macrophage – monocyte system like microglia cells and follicular dentritic cells in the CNS , the HIV virus when attach to mucus membrane then it transmitted to lymph nodes and then infect CD4 T-lymphocytes or langerhans cells so infection became established , HIV has stages for infection of CD4 T-lymphocytes : 1- Stage 1 Attachment, the virus attach by specific receptors to cells the stage 2 interaction of virus and cell surface through chemokines –co receptors like CXCR4 and CCR5 that lead to stage 3 FUSION between the virus membrane and cell membrane and entry of protein core of the virus to the cytoplasm of the cell . At stage 4 Reverse transcription the virus RNA transform to DNA which is similar to cell DNA by virus reverse transcriptase enzyme ,then the virus DNA integrated to enter the cell nucleus by Integrase enzyme which is stage 5 (Integration) then this virus DNA act as template for cell DNA to produce viral RNA stage 6 (transcription) this RNA is migrate outside the nucleus and processed to produce viral mRNA which translate viral peptides chain stage 7(translation) the precursors poly-proteins cleaved to form viral proteins and enzymes like reverse transcriptase and protease enzymes of the new viruses and migrate to cell surface for assembly (stage 8 cleavage and assembly) viral proteins ,RNA take bilipid layer from cell wall and viral release happened to circulation (viral release) stage 9 with lymphocyte lyses then the viruses infect

another CD4 T-lymphocytes lead to increase viral load and decrease CD4 count and that lead a level of which CD4 count became so low lead to opportunistic infection especially to organisms depend on cell mediated immunity like tuberculosis and parasites and lead to appearance of tumors in the body . The virion half life in blood 1-2 hours in the cells 1.5 days .If the virus inter the CNS monocytes it may remain inactive and dorminant for one year and it may be the source of the virus after treatment of HIV with highly active antiretrovirus therapy (HAART) .CD8 cytotoxic T-lymphocytes attack infected cells with HIV virus lead protect the body against infection .

MODE OF TRANSMISSION

The virus enter the body through mucus membrane and blood so it present in blood ,semen and saliva the routes of transmission are :

1- Blood and blood products percent of acquisition of infection 90% , in developed countries get the infection in this routes is 1|500 000 in seroconversion phase in developing countries 5-10 % .

2- Vertical transmission 15-40 % from mother to her child ,either during pregnancy ,or labour vaginal more getting chance of infection than caesarean delivery or by breast feeding .

3- Drug injection0.5- 1% either occupational like medical staff or inject able drug addiction .

4- Sexual 0.2-0.5% for single sex and non genital mucus membrane 0.1% .

NATURAL HISTORY AND CLASSIFICATION OF HIV

1- Primary infection : It is symptomatic in 70-80% of cases ,usually occur 2-6 weeks after exposure ,usually presented as fever with rash , arthralagia ,myalgia ,headache ,pharyngitis ,cervical lymphadenopathy rarly neurological presentation it similar to acute streptococcal pharyngitis, Epistein bar virus ,cytomegally virus ,toxoplasmosis and secondary syphilis .The viral load of HIV by PCR study is high and CD4 count is low 300-400 cell|mm^3 and occasionally 200 cell|mm^3 when opportunistic infection like oropharyngeal candidiasis and rarly Pneumocystic Carini (now Pneumocystic Jirovicii (PNP) later after recovery viral load decrease but not zero and CD4 increase but below normal level .Antibodies to viral proteins by immunoblot assay appear and antibodies to HIV virus anti-HIV antibody became positive usually 3-12 weeks usually 8 weeks (here it called seroconversion phase) after that the patient pass to asymptomatic phase .

2- Asymptomatic infection : The patients have no symptoms except for persistant generalized lyphadenopathy more than regions there is continued viral production 50-150 cells|mm^3 .

3- Mildly symptomatic disease : The patient has minor symptoms with decrease in CD4 count but not AIDS defining conditions these symptoms usually are oral hairy leucoplekia ,recurrent oropharyngeal candidiasis ,recurrent vaginal candidiasis , sever pelvic inflammatory disease ,Bacillary angiomatosis, cervical dysplasia ,idiopathic thrombocytopenic purpura ,weight loss, chronic diarrhea ,herpes zoaster ,peripheral neuropathy , low grade fever and night sweet and continued for 7-10 years then the patient pass to .

4- Acquired immunodeficiency syndrome (AIDS): It defined as specified opportunistic infection and tumors the CD4 count is low < 500 cells |mm^3 and viral load is high the AIDS defining conditions are :Oesophageal candidiasis ,cryptococcal meningitis ,chronic cryptosporidial diarrhea ,cerebral toxoplasmosis ,CMV retinitis or colitis, chronic mucocutaneous Herpes simplex, disseminated Mycobacterium avium intracellulare , pulmonary or extrapulmonary tuberculosis ,pneumocystis jirovecii (carini) pneumonia ,progressive multifocal leucoencephalopathy ,recurrent non typhi salmonella septicemia ,extrapulmonary coccoidioidomycosis ,invasive cervical cancer ,extrapulmonary histoplasmosis ,Kaposi ′s sarcoma, non Hodgkin ′s lymphoma ,primary cerebral lymphoma ,HIV associated wasting ,HIV associated dementia .

Examples of specific AIDS defining conditions

1- Oesophageal candidiasis : Usually involve oesophagus with oral involvement presented with dysphagia and weight loss if chronic CD4 count less than 200 cells |mm^3 treated by fluconazole or caspofungin or Amphotericin .

2- CMV retinitis or colitis : When CD4 count less than 100 cells |mm3 it cause CMV oesophagitis ,colitis or involve liver and biliary system diagnosed by endoscopy of oesophagus or colon to show shallow ulcers and hyperemia and biopsy for histopathology study shows inclusion bodies and CMV by immunofluorscence and PCR study or CMV viraemia in high titer in blood .Treated by Ganciclovir or valganciclovir .

3- Cryptosporidium and Microsporidium : Presented as chronic watery diarrhea CD4 count less than 100 cells |mm^3 ,diagnosed by stool Oocysts and by electron microscopy OGD and duodenal biopsy if stool negative treated by HAART and nitazoxanide or azithromycin and paromomycin.

MANGEMENT OF HIV

The aim of HIV treatment is to treat virus and keep it undetectable as much as possible improve CD4 count above 200 cells |mm^3 so reduce AIDS defining conditions and prevent transmission of the disease . HIV is treated by combinations of anti –HIV drugs for effective anti-virus and prevent resistance this is called highly active antiretroviral therapy (HAART) like one drug of non- nucleoside reverse transcriptase inhibitors (NNRTI) and protease inhibitors (PIs) or another regimen of drug combinations . Drugs used to treat HIV are :

1- Nucleoside reverse transcriptase inhibitors (NRTIs): The drugs in this class are Zidovudine (ZDV),Lamivudine (3TC) ,didanosine (ddI) , Stavudine (d4T) ,abacavir and emtricitabine (FTC) and lastly tenofovir is similar to NRTIs so it included in this category for HAART we use two NRTIs or one NRTIs and tenofovir the NRTIs act by prevent formation of viral RNA template at (stage 6), this group has good CNS penetration and zidovudine can be used in pregnancy . The side effects are lipoatrophy (fat accumulation in abdomen from limbs and buttock), hypersensitivity it better avoided in cardiovascular disease and tenofovir lead to renal tubule toxicity .

2- Protease inhibitors (PIs):Drugs of this group are indinavir ,ritonavir ,lopinavir, tipranavir ,atazanavir ,fosamprenavir and darunavir ,it act by inhibiting (stage 8) cleavage of polyproteins and prevent formation of viral proteins single drug of PIs is used for HAART it is side effects are central obesity , hyperlipidemia impaired glucose tolerance and coronary heart disease .

3- Non –nucleoside reverse transcriptase inhibitors (NNRTIs):There are two main NNRTIs nevirapine and efavirenz and one group is etravirine it act by inhibit reverse transcritptase inhibitor enzyme (stage 4) ,its side effects are hypersensitivity ,steven –johnson syndrome and hepatitis .

4- Entry inhibitors :Two classes are available which are enfuvirtide which inhibit fusion by binding to GP41 (stage 3)and maraviroc which inhibit attachment of the virus stage 2 by binding to CCR5 .

5- Integrase inhibitors : Raltegravir is the first drug in this group it inhibit integrase enzyme (stage 5) and has no major side effects ,the combination of drugs are raltegravir ,etravirin ,darunavir and maraviroc are used for triple class failure or resistant failure .

TREATMENT

1- NAIV EPATIENTS: The start of treatment of HIV in seroconversion ,AIDS defining conditions and CD4 count less than 200cells |ml .The patients co morbidity studied if he has hepatitis C or B drug toxicity and drug interaction .The patients will get undetectable virological load (<50 copies |ml) and increased CD4 count within 6 months usually .

2- EXPERIENCE PATIENTS : In these patients either treatment failure occur (increase viral load and decrease CD4 count in spite of treatment) ,or drug resistant here new drugs which is more effective and drug resistance must be done .

Special situations

1- Children :In this condition not all drugs are available as syrup or powder ,HAART started irrespective of the CD4 count and viral load the patient should receive pneumocystic jirovicii (carini) prophylaxis by co-trimoxazole or atovaquone or inhaled pentamidine .

2- Maternal HIV : Pregnant mother at risk of transmission of the virus from mother to child at pregnancy in 90% ,transmission occur 20% at time of pregnancy and 70% near time of the labour so prevention of the child from infection must be commence by HAART till virus less than 50 copies |ml vaginal laboure can be done with chance of infection <1% if all drug not available then zidovudine and caesarean section can be done with chance of infection <1% if nevirapine alone is used risk of fetal infection is 8% . the child should screened after laboure if negative at6 weeks and 3 months avoid breast feeding .If one parent infected with HIV and desire for child bearing external insemination done with washing the sperm or ova .

3- Post –exposure prophylaxis :In medical staff or drug abusers or in family contact within 6-8 hours boosted lopinavir ,tenofovir and emtricitabine for 4 weeks .

4- Prevention of opportunistic infection :Patient prevention against hepatitis A and B .pneumococcal vaccine ,and influenza vaccine annually .Live attenuated vaccine at low CD4 must be avoided like BCG, polio virus vaccine and yellow fever ,primary prevention against opportunistic infection when CD4 count less than 200 cells| ml and if infection occur after treatment secondary prevention at same drug but lower dose till CD4 count improve then we can stop it .

5- Prevention of HIV :Till now no vaccine against HIV . So educations about disease and its route of transmission ,prevention of mother and children infection with good antenatal screen education against needle stick transmission and post exposure prophylaxis ,screening of blood and blood products to prevent of transmission .