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Opportunistic infections and disease implications in HIV/AIDS.

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ABSTRACT: *HIV/AIDS is the disease of prime attention in present times. Every year about 2.5 million new cases of HIV are reported with death of approximately 1.7 million people worldwide. HIV targets immune system and leaves the patient defenseless to opportunistic infections. With progression of HIV infection, there is gradual decline in CD4 T cell population, rendering patient more and more prone to opportunistic infections. Large battery of infections wreaks havoc on patients' health, ultimately causing death. Effect of cross-talk between HIV and co-infections is reciprocal in most cases. The molecular interactions complicate and worsen the situation. Even slightest interactions are expected to affect gene activity and protein expression. Timely start of antiretroviral therapy has greatly decreased the early onset of infections; however it is very difficult to treat infections in late stages. In this article, gamut of infections in cases of HIV/AIDS is reviewed along with possible implications.*

Keywords: *HIV/AIDS, opportunistic infections, CD 4 T cell count and antiretroviral therapy.*
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I. INTRODUCTION.

Acquired immuno deficiency syndrome (AIDS) is a disease of human immune system caused by human immunodeficiency virus (HIV). HIV is a slow growing retrovirus causing progressive immunodeficiency ultimately developing AIDS. Virus infects cells expressing CD4 membrane receptor molecules, such as T helper cells, macrophages, dendritic cells and microglial cells, but also requires another membrane chemokine co-receptor molecule CCR5 or CXCR4 for entry. M tropic strains use CCR5 chemokine co-receptor for entry and primarily infects macrophages, while T tropic strains use CXCR4 chemokine co-receptor extensively expressed by T helper cells. The normal range of $CD4^+$ T helper cells in healthy person is 500-1600 cells/µl of blood, which gradually depletes with progression of HIV infection rendering the patient susceptible to opportunistic infections (OIs). The advent of decline in $CD4^+$ T helper cells establishes opportunistic pathogens in the immunologically weakened host, further deteriorating patient vigor and complicating the disease. On reaching $CD4^+$ T helper cell count near 200cells/µl of blood, most patients get affected with number of OIs and the patient manifests full-blown AIDS. One can simply define AIDS as: presence of one or more OIs along with $CD4^+$ T cell count <200cells/µl of blood in HIV positive patient. The average period from initial HIV infection to full-blown AIDS is 8-10 years, but it may vary from person to person depending upon HIV strain, host genotype and nutritional factors. The natural course of HIV infection involves three stages: acute infection, asymptomatic phase and full blown AIDS. During acute phase, virus replicates tremendously resulting high viral load and increased risk of transmission. HIV takes 6-12 weeks for a person to become seropositive and this intervening period is called window period. After seroconversion, viral load starts decreasing and lowest decrease is called viral set point, which determines disease progression. A few patients may not have detectable viral load, remain asymptomatic and this phase lasts for many years depending again on infecting HIV strain, host genotype and nutritional factors. The $CD4^+$ T helper cell count drops by approximately 50-100cells/µl of blood per year. With gradual decline in $CD4^+$ T cell count, symptomatic phase with opportunistic infections manifesting thrush, weight loss and fatigue starts appearing. Once $CD4^+$ T cell count reaches below 200cells/µl, risk of OIs increases dramatically and patient is said to have progressed to AIDS. OIs attack severely compromised immune system and prove life threatening. It is very difficult to sustain with $CD4^+$ T cell count less than 50cells/µl of blood and patient generally succumbs to death. The wide spectrum OIs generally manifest as progressed stage *i.e.,* full-blown AIDS. Common OIs associated with AIDS patients are listed and described in following sections.

Opportunistic infections in HIV/AIDS.			
Viral pathogens.	**Bacterial diseases.**	**Fungal diseases.**	**Protozoan diseases.**
Epstein barr virus (EBV).	***Mycobacterium tuberculosis.* (TB)**	***Pneumocystis jiroveci* pneumonia.**	**Toxoplasmosis.**
Hepatitis B virus (HBV).	***Mycobacterium avium* complex (MAC).**	**Mucocutaneous candidiasis.**	**Cryptosporidiosis.**
Hepatitis C virus (HCV).	**Syphilis.**	**Cryptococcosis.**	**Microsporidiosis.**
Herpes simplex virus (HSV).	**Bacterial respiratory disease.**	**Histoplasmosis.**	**Malaria.**
Human herpes virus 8 (HHV-8).		**Coccidiomycosis.**	**Leishmaniasis.**
Cytomegalovirus (CMV).	**Bacterial enteric disease.**	**Aspergillosis.**	**Chagas disease.**
Varicella zoster virus (VZV).			
Human papilloma Virus (HPV)	**Bartonellosis.**	**Penicilliosis.**	**Isosporiasis**
John Cunningham (JC) Virus.			

Table: List of various opportunistic infections associated with HIV/AIDS.

II. BRIEF DESCRIPTION OF OPPORTUNISTIC INFECTIONS.

Viral pathogens.

Epstein barr virus (EBV).

Epstein Barr virus causes oral hairy leukoplakia (OHL). It is one of first OIs indicating immunodeficiency in HIV positive patients. OHL occurs as white patches with ridges and folds in mouth usually on cheeks and sides of tongue. It may look like thrush, but cannot be scrapped off. Almost all people are infected by EBV, but OHL appears in immunocompromised persons. More than 25% HIV patients develop OHL at some stage during disease course. It can occur at any $CD4^+$ T cell count below 500cells/µl of blood. It is usually not a serious complication; however sensing of food temperature becomes problematic. Antivirals are recommended observing the severity of symptoms.

Hepatitis B virus (HBV).

Hepatitis B virus, a hepadnavirus, is the main cause of chronic liver disease. It is circular partial double stranded DNA virus and one from few known non-retroviral viruses, which use reverse transcription as a part of their replication. It is transmitted generally through sexual contact, blood transfusion, and contaminated syringe needles and vertically from mother to child. It can infect even through saliva, sweat and tears with great ease. It causes chronic liver disease in 10% of HIV positive patients. Hepatitis B associated with HIV-1 is characterized by increased rates of HBV carriage, greater levels of HBV viremia, rapid decline in antibodies against Hepatitis B surface antigen, increased reactivation and faster liver disease progression to cirrhosis or liver failure. There are no reports about the effect of HBV on HIV disease progression or HBV altering the HIV response towards antiretroviral therapy. Tenofovir is promising for both HBV and HIV-1 co infections with an ART regimen. An intensive study is needed to further establish a definite molecular relationship on disease progression.

Hepatitis C virus (HCV).

Hepatitis C virus is another agent of chronic liver disease. It is a single-stranded RNA hepacivirus belonging to family flaviviridae. Transmission occurs through infected blood and HIV/HCV co-infection is

common. Co-infection occurs in almost 33% HIV positive patients and is most prevalent in drug addicts and hemophiliacs receiving contaminated blood transfusions. HIV/HCV co-infected patients have increased rate of fibrosis with higher incidence of cirrhosis and hepatocellular carcinoma. HIV/HCV co-infected people have a two-fold greater risk of progression to cirrhosis and a six-fold greater chance of developing end-stage liver disease. HCV multiply eight times faster in the presence of HIV leading to high liver and serum HCV RNA levels. HIV presence may also affect HCV heterogeneity and its transmission, but impact of HCV on HIV disease is less clear. Clinicians prefer to treat HCV first in HIV patients having $CD4^+$ T cell count above 500 cells/µl of blood. HCV treatment is less effective and not recommended in $CD4^+$ T cell count below 200cells/µl of blood.

Herpes simplex virus (HSV).

Human herpes simplex virus 1 and 2 are two candidates of herpesviridae causing ulcerative mucocutaneous disease in both immunocompetent and compromised patients. Almost 95% HIV positive patients are infected either by HSV-1 or HSV-2. HSV is an enveloped double stranded DNA neurotropic virus. Virus remains latent in nerve root ganglia and sores infection occurs periodically near mouth, lips, and genitals. HSV-1 is acquired during childhood, which causes orolabial ulcers called cold sores or oral herpes. HSV-2 is transmitted sexually and causes anogenital ulcers (genital herpes). However, oral-genital sexual practices have crossed the barrier of site restricted infection. Even HSV-1 may cause genital manifestations under distinct set of pathological conditions. Genital herpes patients are at three times greater risk of acquiring HIV. Various studies have also shown HSV-2 enhancing HIV-1 replication and disease progression.

Human herpes virus 8 (HHV-8).

Human herpes virus 8 is a double stranded DNA herpesvirus. It is responsible for Kaposi sarcoma and occurs more often among homosexuals. HHV 8 is transmitted by infected blood and saliva. Persons having HHV-8 viremia are at nine times greater risk of developing Kaposi sarcoma, where HIV Tat protein helps in transformation to Kaposi sarcoma. HHV-8 advanced stage HIV patients having $CD4^+$ T cell count <200cells/µl frequently develop Kaposi sarcoma, primary effusion lymphoma, and multicentric Castleman's disease. Current ART treatment also inhibits replicating HHV-8 in co-infected patients.

Cytomegalovirus (CMV).

Cytomegalovirus is a double stranded DNA virus of herpesvirus family. It is very common opportunistic infection in severe immunocompromised individuals causing disseminated or localized end-organ disease. Transmission occurs by touching infected blood, saliva, semen, vaginal secretions and breast milk with hands, nose and mouth. HIV patients having $CD4^+$ T cell count <50cells/µl of blood and high HIV-1 RNA load, are at higher risk for contracting CMV. Most common illness is retinitis, which if left untreated can cause blindness and spreads to other parts of body. CMV affects HIV-1 replication by transactivating HIV-1 gene expression. It can also activate latent HIV-1 infection by dysregulation of cytokines. Strong ART is the best way to maintain high $CD4^+$ T cell count to reduce the chances of CMV associated disease.

Varicella zoster virus (VZV).

Varicella Zoster Virus is a neurotropic double stranded DNA virus, a member of herpesviridae. It is also called human herpes virus type 3 (HHV-3). Its primary infection causes chickenpox. Reactivated varicella latent infection causes herpes zoster or shingles. Shingles occurs as painful skin rash with blisters often in the form of a stripe, more on tender tissues of body. Immunocompromised and aged persons are more susceptible to herpes zoster. In HIV positive patients, incidence of VZV is 15 folds more than in normal persons. Frequency of disease is highest in patients having $CD4^+$ T cell count <200cells/µl of blood. There is no clear association between VZV and HIV disease progression. Use of ART has lowered the incidence of herpes zoster; however under some circumstances ART has proved to reactivate VZV.

Human papilloma virus (HPV).

Human papilloma virus is most common sexually transmissible infection in the world. HPV infects anogenital tract causing genital warts and cervical cancer. It is double stranded DNA virus of family papillomaviridae. There are at least 13 serotypes, which are oncogenic in nature. HPV 16 and 18 are mainly responsible for cervical cancers, while HPV 6 and 11 are mainly responsible for genital warts. Incidence of genital warts is 10 folds high in HIV-1 positive patients, especially in homosexual men. Almost 77% HIV positive women have HPV infection. HIV-1 infected women have high incidence of cervical cancer. HIV tat protein may transactivate HPV long terminal region (LTR), resulting increased expression of HPV E6 and E7 oncogenes. Modulated immune system by HIV facilitates HPV multiplication and disease progression.

John Cunningham (JC) virus.

JC virus is a double stranded DNA polyomavirus, named after initials of a patient. It causes progressive multifocal leukoencephalopathy (PML), which is a disease of white matter of brain, characterized by demyelination at multiple sites. PML can occur in patients on start of ART as an immune reconstitution inflammatory syndrome. No effective therapy for JC virus is in practice.

Bacterial diseases.

***Mycobacterium tuberculosis* (TB).**

Mycobacterium tuberculosis is an acid fast bacillus responsible for highest mortality rate among people with HIV/AIDS. It is quite prevalent (33%) among patients of full blown AIDS. TB is a lung infection, but it occurs as extrapulmonory and disseminated at late stages of HIV/AIDS. TB can attack patient at any $CD4^+$ T cell count; however patients having low $CD4^+$ T cell count <200cells/µl of blood are at greater risk of contacting it. Common symptoms are fever, persistent cough, blood stained phlegm, night sweats, weight loss and fatigue. TB infection supports HIV-1 replication and dissemination through dysregulation of host cytokines, chemokines, and their receptors. TB is also responsible for activation of latent HIV-1 infection. Recent studies show that active TB patients may or may not have enhanced viral load. Multi-drug resistant (MDR) and extensively drug resistant (XDR) TB are of particular concern for people with AIDS. Most AIDS patients show MDR and XDR TB, which requires special attention to the ongoing treatment for TB. Co-infection of HIV and TB renders high mortality rate among patients in resource limited countries such as South Africa and India. It is difficult to treat MDR and XDR TB due to extreme toxicity and resistance towards drugs, even where HIV patients are on ART. It is recommended to treat patients ($CD4^+$ T cell count <200cells/µl) with antiviral and antiTB therapy concurrently to achieve substantial results.

***Mycobacterium avium* complex (MAC).**

Mycobacterium avium complex (MAC) is much more pronounced among patients of full blown AIDS and is determinant for progression of disease among terminally ill patients. It infects lungs and intestine causing disseminated disease. MAC occurs in 20-40% AIDS patients. *M. avium* and *M. intercellulare* are main constitutive members of complex. Higher viral load, presence of other pathogens such as CMV and disturbed T cell repertoire increase the susceptibility to MAC disease. MAC and HIV both infect macrophage, generating cytokine storming. MAC is also responsible for higher expression of CCR5 (principle co-receptor of HIV) further facilitating and promoting HIV infection.

Syphilis.

Syphilis is a sexually transmitted disease caused by spirochete *Treponema pallidum.* It causes genital sores among homosexuals. HIV infection interferes syphilis diagnosis, whereas presence of syphilis enhances acquisition and transmission of HIV by 3 to 5 folds. Impaired adaptive immune responses caused by HIV infection help in syphilis progression. HIV patients show early onset of new syphilis with degenerating neurological function.

Bacterial respiratory disease.

Bacterial pneumonia is a common symptom among HIV patients caused by several species of different bacteria. *Streptococcus pneumonia, Haemophilus influenzae, Pseudomonas aeruginosa* and *Staphylococcus aureus* are some of the bacteria known to cause serious to mild form of pneumonia. *Legionella pneumophila, Mycoplasma pneumoniae,* and *Chlamydia pneumonia* are other rare atypical candidates of pneumonia. Majority of HIV positive patients have shown eight times enhanced susceptibility towards bacterial pneumonia. It is very difficult to treat bacterial pneumonia in AIDS patients owing to impaired cellular functions and disturbed cytokine release. Highly active programmed death receptor 1 (PD-1) on T cell further changes the chronological events of pathogenesis on the account of functional numbness. Recurrence is also more common among HIV-1 infected patients; however a 23-valent polysaccharide pneumococcal vaccine is available for HIV patients with $CD4^+$ T cell count >200 cells/µl of blood.

Bacterial enteric disease.

Presence and recurrence of *Salmonella, Campylobacter,* and *Shigella* species are responsible for causing bacterial diarrhea, which further deteriorates the health of HIV positive patients. In resource limited countries, diarrheagenic amd enteroaggregative *Escherichia coli* is frequent cause of diarrhea among HIV infected

persons. Contaminated food and water are source of infection. Oral-anal sexual activity further increases incidence of *Shigella* and *Campylobacter.* An altered humoral immunity with HIV infection helps in acquisition of enteric bacteria. Incidence of bacterial enteric infection may be controlled to an extent by the patients undergoing ART therapy.

Bartonellosis.

Bacillary angiomatosis (BA) is a disease of skin lesions, which resembles Kaposi sarcoma, caused by *Bartonella henselae* and *Bartonella quintana* in HIV patients. This is chronic disease manifesting intermittent bacteremia and organ associated lesions. Usually BA occurs in late stages of HIV disease in patients having $CD4^+$ T cell count <50cells/µl of blood. *Bartonella quintana* is transmitted by body louse while *Bartonella henselae* transmission is cat scratch dependent, deteriorating the health of HIV positive patient aggressively. Therefore preventing cat exposure and body lice infestation are effective strategies to avoid infections.

Fungal diseases.

***Pneumocystis jirovecii* phneumonia.**

Pneumocystis phneumonia (PCP), a lung infection, caused by a fungus *Pneumocystis jirovecii*, transmistted by air, is a major killer of HIV patients. Immunocompromised patients having $CD4^+$ T cell count <200cells/µl of blood such as AIDS patients are 4.9 times more prone to develop PCP. Presence of other OIs also increases the susceptibility to it. Use of ART has considerably decreased the incidence of PCP among HIV patients. HIV positive smoker develop PCP three times more than HIV non smokers, therefore HIV patients are advised to quit smoking. Antibiotic treatment with TMP-SMX and pentamidine is effective in HIV patients against PCP.

Mucocutaneous Candidiasis.

Candidiasis is caused by yeasts *Candida* species, which are normal residents of human body. In HIV infection, mucocutaneous candidiasis occurs in three forms: oropharyngeal, esophageal and vulvovaginal disease. There are many species of *Candida* such as *C. albicans, C. glabrata, C. parapsilosis, C. tropicalis, C. krusei* etc. responsible for candidiasis; however *C. albicans* is significantly important due to its intense association with AIDS. It is more prominent among patients having $CD4^+$ T cell count <200cells/µl of blood. Oropharyngeal candidiasis (Thrush) is the first indicator of immunosuppression in most HIV patients occurring in almost 90% HIV patients during course of HIV infection. High levels of HIV-1RNA in plasma increases susceptibility to candidiasis. Relationship between HIV and vulvovaginal disease is unclear as vulvovaginal candidiasis is also frequent in normal women. Introduction of combinational ART has significantly declined the prevalence of candidiasis in HIV patients.

Cryptococcosis.

Cryptococcosis, a fungal meningitis, transmitted through respiratory route, is caused by members of the *Cryptococcus neoformans* species complex and almost 5-8 % HIV positive patients experience the disease during course of AIDS. Cryptococcosis is observed mostly in advanced stage HIV patients having $CD4^+$ T cell count <50cells/µl of blood. Pathogen is resistant to ingestion and killing due to impaired cell mediated immunity. With intake of ART regimen and proper antifungal drugs, incidence of cryptococcosis can be controlled to an extent.

Histoplasmosis.

Histoplasmosis is caused by dimorphic soil inhabiting fungus *Histoplasma capsulatum* and almost 2 to 5% HIV positive patients develop histoplasmosis. Patients get infection by fresh inhalation of microconidia or reactivation of latent infection. Defective functional properties of macrophage and lower CD4 count help in the establishment of infection. Almost 95% cases of histoplasmosis show disseminated histoplasmosis where $CD4^+$ T cell count are <150cells/µl of blood. ART has proved quite successful among HIV positive patients resolving incidence of histoplasmosis.

Coccidioidomycosis.

It is caused by air borne spores of soil inhabiting fungi *Coccidioides immitis* and *C. posadasii.* Coccidioidomycosis is quite prevalent among HIV patients with $CD4^+$ T cell count <250cells/µl of blood. Loss of immunological functions by lymphocytes in HIV positive patients further accelerate coccidiomycosis. It is manifested by local or diffused pneumonia, meningitis, lymph nodes and liver abnormalities. HIV patients are

advised to avoid exposure to disturbed soil contact. Patients on ART treatment show decline in incidence to coccidiomycosis.

Aspergillosis.

Aspergillosis is a fungal disease caused by *Aspergillus fumingatus* and other species such as *A. niger, A. flavus* and *A. terreus*. It is associated with late stage HIV positive patient. HIV infected people having $CD4^+$ T cell count <100cells/µl of blood are more prone for aspergillosis. It manifests as respiratory tract disease and CNS meningoencephalitis among AIDS patients. ART therapy helps in controlling aspegillosis to a limited extent.

Penicilliosis.

Penicilliosis is caused by dimorphic fungus *Penicilliosis marneffei,* which is endemic in certain parts of world. It manifests as systemic disease with skin lesions, fever, weight loss, lymph nodes, bone marrow and hepatic involvement. Recently, 50 cases of indigenous penicilliosis have been reported from newly found endemic region in Manipur (India). Almost 6-8% HIV patients show penicilliosis, where $CD4^+$ T cell count are <100cells/µl of blood. Rate of mortality is very high near to 20% even after treatment. ART treatment and specific antibiotic therapy are helpful in controlling penicilliosis.

Protozoan diseases.

Toxoplasmosis.

Toxoplasma encephalitis (TE) is caused by an obligate intracellular ubiquitous protozoan parasite *Toxoplasma gondii* and is very important CNS opportunistic infection in AIDS patients. Infection occurs exclusively due to reactivation of asymptomatic latent tissue cysts. Immunocompromised patients, particularly AIDS patients having $CD4^+$ T cell count <100cells/µl of blood can have reactivation from asymptomatic latent infection. However, most vulnerable patients are those having $CD4^+$ T cell count <50cells/µl of blood. It is transmitted through contaminated vegetables, undercooked meat and contact with cat feces. Abnormal cytokine profile and impaired cytotoxic T cell functionality are responsible for easy susceptibility among HIV patients. Effective treatment of TE with drugs pyrimethamine, sulfadiazine and TMP-SMX, is available for HIV patients. ART treatment lowers the incidence of Toxoplasmosis.

Cryptosporidiosis.

Cryptosporidiosis is a disease caused by protozoan parasites infecting large bowel and extraintestinal mucosa causing diarrheal illness among immunocompromised patients. There are three species causing cryptosporidiosis: *Cryptosporidiosis hominis, C. parvum* and *C. meleagridis.* Out of which, *C. parvum* has been commonly reported from HIV positive patients. HIV patients having $CD4^+$ T cell count <100 cells/µl of blood are at greater risk. HIV-1 tat is shown to enhance *C. parvum* induced apoptosis of infected cells. Preventive measures, such as awareness among HIV patients about routes of infection and general hygiene (e.g. washing hands properly) can reduce the risk to considerable extent. Usually disease resolves within 14 days in HIV patients having $CD4^+$ T cells count >200 cells/µl of blood.

Microsporidiosis.

Microsporidiosis is caused by number of obligate intracellular microsporidia, such as species of *Vittaforma*, *Nosema*, *Enterocytozoon*, *Encephalitozoon*, and *Pleistophora*. It manifests as gastrointestinal infection relating diarrhea. It may also occur as encephalitis, myositis, sinusitis and disseminated infection. Disease generally occurs in patients having $CD4^+$ T cell count <100cells/µl of blood. ART therapy has proved quite successful in controlling the disease.

Malaria.

Malaria is one of the most prevalent infections affecting 300-500 million people worldwide. *Plasmodium falciparum, P. vivax, P. ovale, P. malariae,* and *P. knowlesi* cause malaria in different geographical regions. Sub Saharan Africa is highly infected with *P. falciparum,* therefore HIV positive patients experience falciparum malaria during lengthy stage of AIDS. Slightest interaction between malaria and HIV infections is expected to significantly affect the disease output; however relationship seems subtle. HIV impairs acquired immunity to malaria and increases frequency of parasitemia and clinical malaria with greater risk of severity. Rates of increased malaria among persons with HIV are not as great as observed with classic OIs like TB and PCP. *P. falciparum* is shown to stimulate HIV-1 replication through enhanced CCR5 co-receptor expression on macrophage and thus increasing viral loads among patients. Therefore, it helps in vertical transmission of HIV.

Unscreened blood transfusions associated with malaria can indirectly increase HIV transmission in Africa. These studies suggest increased HIV-1 disease progression and transmission. However, true and detailed relationship between HIV and malaria remains to be determined.

Leishmaniasis.

It is endemic in 88 countries globally, infecting more than 12 million people with an incidence of 2 million new cases annually. In HIV patients, leishmania has been found to occur in 28 countries mainly Spain, Italy, France, Portugal and India. Leishmaniasis is caused by obligate intracellular protozoan *Leushmania spp.*, which replicate within intracellular vacuoles of macrophages. It is transmitted by sandflies and may also transmit through drug addicts. Visceral leishmaniasis with short incubation period usually occurs in HIV positive patients having low $CD4^+$ T cell count <100cells/µl. Visceral leishmaniais is a serious complication. Leishmaniasis may involve spleen and liver, affecting associated enzyme discharge and function.

Chagas disease.

Chagas disease is caused by flagellated protozoan *Trypanosoma cruzi.* It is anthropozoonosis transmitted to humans and mammals by blood sucking insects called kissing bugs. Bug feces on skin have parasites, which enroute in the system during blood sucking. Transmission may also occur through blood transfusions, organ transplant and through placenta. Reactivation of chronic latent infection is high due to immunosuppression in HIV-1 patients. Disease can cause serious heart and gastrointestinal illness, but CNS involvement is very high in HIV patients. Studies have indicated that *Trypanosoma cruzi* inhibits replication of HIV infection across placenta.

Isosporiais.

It is caused by a protozoan *Isospora belli,* which is quite prevalent in tropical and subtropical countries. It can infect immunocompetent, as well as immunocompromised persons, but AIDS patients are at higher risk. Transmission occurs with ingestion of oocysts in contaminated food and water. Oral-anal sex may also transmit this infection. Disease involves small intestine and manifests as non-bloody profuse and prolonged diarrhea. With use of ART, incidence of isosporiasis has decreased; however $CD4^+$ T cell count <50cells/µl of blood helps for own disease setting.

III. CONCLUSION.

There are a lot of viral, bacterial, fungal and protozoan pathogens associated with AIDS, changing symptomatology and pathology of disease. HIV prepares ground for successful invasion by OIs, that are etiological killers of patients. OIs are very difficult to treat in HIV patients in the absence of normal functioning immune system. However, with the introduction of combinational Antiretroviral Therapy (ART), the incidence of OIs has declined substantially, but cannot be eliminated. HIV and OIs interact synergistically, resulting overall increased disease progression and viral load. The molecular interactions between OIs and their impact on HIV pathogenicity is not fully understood and is still under active research.

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APPENDIX.

[1]. **Thrush**: Yeast infection of mouth and throat characterized by white patches mainly caused by Candida albicans.
[2]. **Cirrhosis**: Chronic liver degenerative disease in which normal liver tissue is replaced by fibrous scar tissue leading to progressive loss of liver function.
[3]. **Fibrosis**: Proliferation of fibrous connective tissue resulting in formation of scar tissue as a reparative process.
[4]. **Hepatocellular carcinoma**: A dangerous cancer of liver cells (hepatocytes), mostly occurs in hepatitis patients.
[5]. **Hemophiliacs**: Persons suffering from hemophilia. Hemophilia is a genetic disorder in which blood fails to clot resulting in excessive bleeding due to deficiency or abnormality in clotting factors.
[6]. **Kaposi sarcoma**: A multicentric, malignant neoplastic vascular proliferation presenting bluish-red nodules on skin, subcutaneous tissue and may be widespread involving viscera. It occurs in immunocompromised like AIDS patients and human herpes virus 8 is responsible for it.
[7]. **Primary effusion lymphoma**: It is a B cell lymphoma associated with human herpes virus 8 causing lymphomatous effusions in body cavities without the presence of a solid tumor.
[8]. **Multicentric Castleman's disease**: A rare, progressive and serious disorder of lymphoid tissue with massive non-cancerous growth of lymph nodes at multiple sites throughout the body. It is associated with human herpes virus 8.
[9]. **Retinitis**: Inflammation of retina.
[10]. **Immune reconstitution inflammatory syndrome**: In some cases when HIV patients starts ART, paradoxical reactions results in worsening of clinical conditions due to restoration of immune system. This syndrome is characterized by overwhelming inflammatory response.
[11]. **Meningitis**: Inflammation and swelling of membranes covering brain and spinal cord.
[12]. **Encephalitis**: Inflammation and swelling of brain.
[13]. **Myositis**: Disease in which muscles and skin become inflamed and damaged resulting in muscles weakness.
[14]. **Sinusitis**: It is the inflammation of hallow areas within bones of skull (sinuses) around nose usually due to infections in these spaces.