Review of Literature
Origin of Human Immunodeficiency Virus

HIV is a lentivirus, and like all viruses of this type, it attacks the immune system. Lentiviruses are in turn part of a larger group of viruses known as retroviruses. The name 'lentivirus' literally means 'slow virus' because they take such a long time to produce any adverse effects in the body. They have been found in a number of different animals, including cats, sheep, horses and cattle. However, the most interesting lentivirus in terms of the investigation into the origins of HIV is the Simian immunodeficiency virus (SIV) that affects monkeys (Gao, et al., 1999).

It is now generally accepted that HIV is a descendant of a Simian immunodeficiency virus because certain strains of SIVs bear a very close resemblance to HIV-1 and HIV-2. The more virulent, pandemic strain of HIV, namely HIV-1, was until recently more difficult to place. Until 1999, the closest counterpart that had been identified was SIV cpz, found in chimpanzees. However, this virus still had certain significant differences from HIV-1. In February 1999, a group of researchers from the University of Alabama (Gao, et al., 1999) announced that they had found a type of SIV cpz that was almost identical to HIV-1. This particular strain was identified in a frozen sample taken from a captive member of the sub-group of chimpanzees known as Pan troglodytes troglodytes (P. t. troglodytes), which were once common in west-central Africa. They also concluded that all three 'groups' of HIV-1 namely Group M, N and O came from the SIV found in P. t. troglodytes, and that each group represented a separate crossover 'event' from chimps to humans (Bailes et al., 2003).
History of HIV

The first indication of new syndrome came in 1981 USA, with reports form of a sudden unexplained outbreak of two rare diseases Kaposi sarcoma and Pneumocystic jerovici in young adults who were homosexual and addicted to narcotics. The condition was termed as an acquired immune deficiency syndrome (Weiss, 1993). In 1983, Luc Mantagnier and Colleague from Pasteur institute Paris isolated the virus and named as LAV. In 1984 Robert Gallo from National Institute of Health, USA, called it as HTLV III. Elisa test was made available to detect anti HIV anti bodies (Schupbach et al., 1984).

Global epidemiology of HIV

Sub-Saharan Africa remains the more affected region. 68% of total people were infected with HIV. Within the region, Southern Africa is reported with the most HIV infections. In Asia (2007), 4.9 million people estimated to be infected with HIV, including 4, 40,000 newly infected people. Adult HIV prevalence was estimated as 1% in 2007 in the Caribbean, which remains the second most affected region in the world after sub-Saharan Africa. Some 2,30,000 people were living with HIV in 2007, and an estimated 11,000 people died of AIDS-related illnesses (UNAIDS, W.H.O., 2007) The number of people infected with HIV in Eastern Europe and Central Asia arose in 2007 to 1.6 million, with 1,50,000 new HIV infections. The estimated number of new HIV infections in Latin America in 2007 was 1, 00,000 bringing to 1.6 million the total number of people infected with HIV in this region. Overall, approximately 2.1 million people in North America and Western and Central Europe were infected with HIV in 2007. In Middle East and North Africa, an estimated 35,000 people acquired HIV in
2007, bringing to 3, 80, 000 the total number of people infected with HIV. Chatterjee has shown 5.8% of contacts of leprosy patients carry AFB in their skin (Chatterjee, 1976).

**Indian epidemiology of HIV**

HIV Fact Sheets based on HIV Sentinel Surveillance Data in India 2003-2006 released by National AIDS Control Organization (NACO) has reported a HIV prevalence of more than 15% among sexually transmitted diseases (STD) clinic attendees in 14 districts of India (Figure 1).
Overall, HIV prevalence was higher among urban than rural populations. However, some states had a slightly higher HIV prevalence among rural populations than urban populations, namely, Punjab, Tamil Nadu and Uttar Pradesh. The epidemic has stabilised or seen a drop in Tamil Nadu and other southern states with
a high HIV burden. Prevalence has fallen in some major states like Maharashtra from 0.80% in 2005 to 0.74% in 2006, in Tamil Nadu from 0.47% in 2005 to 0.39% in 2006 (Pandey et al., 2009). However, the southern states of Andhra Pradesh, Karnataka, Maharashtra and Tamil Nadu continue to have the highest HIV prevalences. Finally, despite an overall decline in prevalence, there are many pockets of high HIV transmission. 107 sentinel surveillance sites in 76 districts have HIV seropositivity greater than 1% among antenatal clinic attendees. Seventy sentinel surveillance sites in 44 districts have HIV prevalence greater than 5% in high risk groups.

The HIV epidemic in the north-eastern states of Manipur, Mizoram and Nagaland continues unabated. In 2006, HIV seropositivity among pregnant women was 1.39%, 1.36% and 0.94% in Manipur, Nagaland and Mizoram respectively. Although HIV prevalence among IDUs in Manipur has declined over the years, all four IDU sentinel surveillance sites in Manipur still have HIV prevalence of more than 10%. In addition, HIV prevalence among sex workers appears to be increasing in Nagaland and Mizoram (NACO, 2001).

Further, there has been a rise in HIV prevalence in the northern and eastern regions. Twenty six districts from Madhya Pradesh, Uttar Pradesh, West Bengal, Orissa, Rajasthan and Bihar are high prevalence districts. In West Bengal, prevalence has gone up from 0.21% in 2005, to 0.30% in 2006. In some districts of West Bengal high HIV transmission is seen among sex workers and IDUs. Among migrants at one site in Orissa, HIV prevalence was 5%. In Rajasthan, HIV prevalence has gone from 0.12% in 2005 to 0.17% in 2006. HIV prevalence continues to be higher among vulnerable groups such as IDUs in Chennai, Delhi, Mumbai and Chandigarh. (http://www.hivaidsonline.in/index.php/HIV-IN-INDIA/the-hivaidscenario-in-india.html).
In a few of India’s states, data show high HIV prevalence among female sex workers (FSW), and possibly rising HIV prevalence among people who inject drugs user (IDU) and men who have sex with men (MSM). Although HIV has spread into the wider population and, in some states, is affecting increasing numbers of women considered to be at low risk of infection, the country’s epidemic is largely a result of HIV transmission within, between and immediately beyond those most-at-risk populations.

**Epidemiological Features**

The epidemic seems to be following type 4 patterns, that epidemic spread from the highest risk group (commercial sex workers, homosexual men, and drug users) to bridge population client of sex workers, migrant population and then to general population. This shift usually occurs where prevalence of first group reaches 5%.

**Sentinel surveillance**

Based on sentinel surveillance data, HIV prevalence classified as Group I States like Maharastra, Tamilnadu, Karnataka, Andrapradesh, Manipur, and Nagaland.

II Group: States Goa, Pondicherry, and

III Group: Other states.
Table No.1: Prevalence status

<table>
<thead>
<tr>
<th>Group</th>
<th>Prevalence</th>
<th>High Risk Group</th>
<th>Antenatal mother</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>High</td>
<td>&gt; 5%</td>
<td>&gt; 1%</td>
</tr>
<tr>
<td>II</td>
<td>Moderate</td>
<td>&gt; 5%</td>
<td>&gt; 1%</td>
</tr>
<tr>
<td>III</td>
<td>Low</td>
<td>&lt; 5%</td>
<td>&lt; 1%</td>
</tr>
</tbody>
</table>

Nomenclature of HIV

A first attempt to classify HIV-1 sequences was to subdivide them into European/North American and African strains, as sequences derived from European and North American isolates formed a distinct cluster in phylogenetic trees, while strains from Africa separated into different lineages (Li et al., 1988; Myers et al., 1988). These clades were named subtypes A to F, with the prototypic “North-American/European” strains relabelled subtype B (Myers et al., 1992). Subsequently, five of these six env-based subtypes/clades (A, B, C, D and F, but not subtype E) were identified in phylogenies inferred from the gag region (Louwagie et al., 1993). In the following years four additional subtypes, G to J, were characterized based on phylogenetic comparisons of partial sequences (Janssens et al., 1994; Kostrikis et al., 1995; Leitner et al., 1995; Louwagie et al., 1995). More recently, subtype F was reported to be comprised of sub-subtypes F1, F2 and F3 based upon gag and env phylogenetic comparisons (Triques et al., 1999), but after subsequent analysis of complete genomes, sub-subtype F3 was renamed subtype K (Triques et al., 2000). [The latter subtype “K” should not be confused with partial sequences recently designated as “k” which cluster as a sister clade to subtype D (Roques et al., 1999).] Collectively all of the HIV-1 subtypes group together to form a clade which has been termed group M for “main”,

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to distinguish them from the HIV-1 group O (outlier) clade (Gurtler et al., 1994), and the recently discovered HIV-1 group N (non-M/non-O) clade (Simon et al., 1998).

The great majority of HIV-1 strains cluster consistently in phylogenetic trees. They fall into the same subtype (or group) regardless of which regions of their genomes are analyzed. However, it was recognized early on that a fraction of HIV-1 strains exhibit discordant branching orders in phylogenies inferred from different parts of their genomes (Robertson et al., 1995). This finding along with the fact that all of these viruses originated from geographic regions where the same divergent sequence subtypes co-circulated, strongly suggested that these viruses were the product of recombination events. This propensity for HIV to recombine was not unexpected, given results from previous retrovirus research (Coffin 1979; Hu and Temin 1990a; Hu and Temin 1990b) and specific HIV studies (Li et al., 1988; Sabino et al., 1994)

THE REVISED HIV NOMENCLATURE SYSTEM

Four types of categories should be used to refer to the major HIV-1 lineages: groups, subtypes, sub-subtypes and CRFs

Groups will continue to refer to the very distinctive HIV-1 lineages M, N and O. Group M includes the viruses that dominate the global epidemic and the sub-division of this group is the focus of this proposal. The groups were originally named M for main, O for outlier and N for Non-MNon-O. Sub-subtype will be used to refer to a distinctive lineage that is very closely related to a particular subtype lineage, and is not genetically distant enough to justify calling a new subtype. The previously recognized subtype, for example A, would thus be renamed sub-subtype A1 and the hypothetical newly identified lineage named sub-subtype A2. Circulating Recombinant Form (CRF) describes a recombinant lineage, which plays an important role in the HIV-1 pandemic.
The CRF members must share an identical mosaic structure, i.e., they are descended from the same recombination event(s).

**Host Factor**

*Age:* Most case occurs among the sexually active persons. In India 87.7% are in age group of 15-44 years, out of which 35% in the age group of 15-24 years.

*Sex:* In India males have higher proportion, but in Africa the sex ratio is equal.

**High Risk groups include**

It includes Male homosexual and bisexuals, heterosexual parters, (including prostitutes), intravenous drug abusers, transfusion of blood and blood products.

**Domicile:** The trend of transmission shows infection spreading from urban to rural areas.

**Structure of HIV**

Outside human cell, HIV exists as roughly spherical particles (sometimes called virions). The surface of each particle is studded with lots of little spikes. An HIV particle is around 100-150 billionths of a metre in diameter. Unlike most bacteria, HIV particles are much too small to be seen through an ordinary microscope. However they can be seen clearly with an electron microscope. HIV particles surround themselves with a coat of fatty acid material known as the viral envelope (or membrane). Projecting from this are around 72 little spikes, which are formed from the proteins gp120 and gp41. The viral envelope is a layer called the matrix, which is made from the protein p17 (Figure 2).
The proteins gp120 and gp 41 together make up the spikes that project from HIV particles, while p17 forms the matrix and p24 forms the core. The viral core (or capsid) is usually bullet-shaped and is made from the protein p24. Inside the core three enzymes required for HIV replication namely reverse transcriptase, integrase and protease are present. HIV’s genetic material is held within the core which consists of two identical strands of RNA.

HIV belongs to a special class of viruses called retroviruses. Within this class, HIV is placed in the subgroup of lentiviruses. Other lentiviruses include SIV, FIV, Visna and CAEV, which cause diseases in monkeys, cats, sheep and goats. Almost all organisms, including most viruses, store their genetic material on long strands of DNA. Retroviruses are the exception because their genes are composed of RNA (Ribonucleic Acid). RNA has a very similar structure to DNA. However, small differences between
the two molecules mean that HIV’s replication process is a bit more complicated than that of most other viruses.

**HIV and Genes**

HIV has just nine genes (compared to more than 500 genes in a bacterium, and around 20,000-25,000 in a human). Three of the HIV genes, called *gag*, *pol* and *env*, contain information needed to make structural proteins for new virus particles. The other six genes, known as *tat*, *rev*, *nef*, *vif*, *vpr* and *vpu*, code for proteins that control the ability of HIV to infect a cell, produce new copies of virus, or cause disease. At either end of each strand of RNA, sequence called the long terminal repeat, is present which to controls HIV replication.

**Replication Cycle of HIV**

*gp* 120 of the HIV binds to N terminus of the receptors CCR5 and CXCR4, on the host cell surface CD4 molecule. *gp* 120 undergoes (molecule) configurational changes which makes easy way for the penetrations of *gp* 41 (Parseval and John, 2001). After binding to CD4 molecule, virus is uncoated and the viral RNA is transcribed by enzyme reverse transcriptase (RT) into first single stranded DNA, then to double stranded DNA which is integrated into host cell chromosome (Lewinski *et al.*, 2005). The integrated DNA is then transcribed into messenger RNA (mRNA) which comes out to cytoplasm and viral proteins are synthesized using protein synthesing machinery and raw material from the host cell (Lau *et al.*, 2007). Newly synthesized progeny RNA and proteins are packaged together and are released from the infected cell by “budding” (Samuel, 2006).
Pattern of Transmission

People may be exposed to HIV during unsafe sexual activity, when a condom breaks during sex, or if they share needles for injecting drugs. HIV exposure at work is usually a one-time accident. Other HIV exposures may be due to unsafe behaviors that can occur many times. It was summarized in the following table 2 and 3.

Table 2: Exposure and Transmission Rate

<table>
<thead>
<tr>
<th>Types of Exposure</th>
<th>Percentage Global Total 2003</th>
<th>In India 2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sexual</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal</td>
<td>70-80%</td>
<td>72-85%</td>
</tr>
<tr>
<td>Anal</td>
<td>5-10%</td>
<td></td>
</tr>
<tr>
<td>Perinatal</td>
<td>5-10%</td>
<td>3.14%</td>
</tr>
<tr>
<td>Injection Drug use</td>
<td>5-10%</td>
<td>2.95%</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>3-5%</td>
<td>2.17%</td>
</tr>
<tr>
<td>Others not specific</td>
<td>1-2%</td>
<td>6.02%</td>
</tr>
</tbody>
</table>

Estimates per contact risk of HIV infection is summarized in the following table.
### Table 3: Actual risk per contact

<table>
<thead>
<tr>
<th>Activity</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Needle Sharing</td>
<td>6/1000 to 30/1000</td>
</tr>
<tr>
<td>Occupational Needle Stick</td>
<td>1/300</td>
</tr>
<tr>
<td>Receptive Anal Sex</td>
<td>8/1000 to 30/1000</td>
</tr>
<tr>
<td>Receptive Vaginal Sex</td>
<td>3/10000 to 10/10000</td>
</tr>
<tr>
<td>Receptive Oral Sex:</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

(Source: www.Cambridge.org.)

Approximate chance of infection per exposure to blood and blood products is >90% and mother to baby transmission is around 30%.

**Aetiology of HIV infection**

The causal agent of HIV infection and AIDS is a lentivirus of the retrovirus family. There are two human HIV viruses, HIV-1 and HIV-2. HIV-1 is the aetiological agent of most cases of HIV infection worldwide and HIV-2 is mainly confined to West Africa (Peeters and Sharp, 2000).

The first description of the acquired immunodeficiency syndrome was made in 1981. The HIV virus was discovered and isolated in Paris at the Pasteur Institute. The virus was obtained from cultured T lymphocytes of patients with lymphadenopathy (Gallo and Montagnier, 2003). The Besthand Myrland Centre developed a specific factor for culturing T lymphocytes, which was essential for isolating retroviruses. Gallo and colleagues further proved the HIV virus as the cause of HIV and contributed to the development of HIV testing (Gallo, 2002). Recent studies have demonstrated that the diversification of HIV-1 in West and Central Africa...
occurred long before the current AIDs pandemic. Phylogenetic analysis of viral sequences, DRC60 and ZR59 date them to near the earliest days of the twentieth century (Worobey et al., 2008).

**Pathogenesis of HIV infection**

The HIV virus is formed of a core protein enclosed in gag protein, p24 and a two RNA structure. The viral structure also contains enzymes important for its replication, RNA reverse transcriptase and HIV-specific protease. The viral envelope carries the gp120 antigen, which is important for interaction with CD4 protein in the T-cells (Volberding et al., 2003). The HIV infects the CD4 T-cell and inflicts a decline of CD4 count. The CD4 contains receptors for HIV antigen, the chemokine receptors of CCR5 and CXCR4. HIV-infected macrophages attract T-cells and bring them in contact with the HIV virus (Weber, 2001).

**Aetiological agent and pathogenesis of tuberculosis and HIV infections**

Aetiological agent of HIV and TB share some characteristic infections; immunity to both diseases is cell mediated and both have long latent periods so that disease may manifest only after several years since acquiring the infection. The aetiological agent of tuberculosis is *Mycobacterium* and the causative agent of HIV is a retro virus (Barre-Sinoussi et al., 1983 and Drobniewski et al., 2003).

**Tuberculosis aetiology**

Robert Koch discovered the Tuberculosis bacilli in 1895 and presented his finding on the aetiology of tuberculosis in a famous paper to the Physiological Society of Berlin. His description of the method of staining specimen slides, the method of culturing and inoculating of the bacilli into animals was a major advance in the understanding of TB bacteriology. The discovery enhanced further the development in finding a remedy for tuberculosis (Sakula, 1982).
*Mycobacterium tuberculosis* belongs to the genus *Mycobacterium*. The genus is classified into the *Mycobacterium tuberculosis* complex, which produces tuberculosis diseases in humans and other non-tuberculosis- Mycobacteria species or opportunistic Mycobacteria which can produce disease in immunocompromised individuals (Wayne, 1982 and Drobniewski et al., 2003). Mycobacterium complex includes *Mycobacterium tuberculosis*, *M. bovis*, *M. microti* and *M. Canetti* and *M. africanum* (Wayne 1982 and Drobniewski et al., 2003).

*M. tuberculosis* is epidemiologically the most important species because it causes tuberculosis in humans and is responsible for tuberculosis infection worldwide. *M. bovis* can also infect man, but is mainly responsible for TB disease in cattle and goats.

*M. microti* is infectious to some rodents, but occurrence of human infection is unclear. Recently discovered *M. Canetti* can also infect humans (Niemann et al., 2000a)

**Pathogenesis of tuberculosis**

*Mycobacterium tuberculosis* is transmitted by airborne nuclei droplets. The droplet is passed into the air, when a person infected with pulmonary tuberculosis coughs sneezes or speaks (Bass et al., 1990). When a healthy individual inhales the bacilli, the first implant is in the lungs at bronchiole or alveolar level. The bacilli multiply and produce the primary lesion there. Some bacilli pass into the hilar lymph nodes causing lymph node enlargement. The bacilli from the alveolar lesion, the Ghon focus and from the enlarged hilar lymph nodes can be more widely disseminated via the lymphatic system or bloodstream, leading to serious complications such as meningitis, bone, joint and renal tuberculosis (Festenstein and Grange, 1991). The host response to tuberculosis is through cell-mediated immunity, and the cells involved include macrophages and T-lymphocytes. The lymphocytes recognise TB antigens and release cytokines such as gamma interferon, which activates macrophages at the site of the
Hypersensitivity to the organism appears at 8–10 weeks and the infected individual becomes tuberculin-test positive. It is estimated that 10% of infected individuals develop clinical tuberculosis during their lifetime. Around 50% of them will develop TB during the first years of infection and the rest many years later (Bass et al., 1990).

**National TB Control Programme**

Tuberculosis has been a major health problem for developing countries including India. In the first half of the last century tuberculosis was the main focus of attention amongst all respiratory diseases. Disease surveys conducted in different parts of the country since the 1950s have reported prevalence of smear-positive pulmonary TB (PTB) of 0.6–7.6 per 1000 population (Behera, 2007), (culture-positive) TB of 1.7–9.8 and culture and/or smear-positive TB of 1.8–12.7. The incidence of smear-positive PTB has been observed in the range of 1.0–1.6/1000 and that of culture-positive PTB 1.0–2.5/1000 in the limited number of studies carried out (Behera, 2007). The present estimates differ from earlier estimates. India accounts for nearly 20% global tuberculosis burden even today (Dye et al., 1999). When reviewed in 1992, no major epidemiological impact was shown to be made (WHO, 1992). Every year there are approximately 22 lakhs new cases in the country of which approximately 10 lakhs are new smear positive highly infectious cases. Revised National TB Control Programme (RNTCP) was based on WHO recommended DOTS Strategy (Directly Observed Treatment Short Course Chemotherapy) was launched in the country in March 1997 with a soft loan from World Bank.

Previous report suggested that the estimated number of bacillary cases was 3.8 million, abacillary cases 3.9 millions, and extra-pulmonary cases to be 0.8 million with a total
burden of tuberculosis in India being about 8.5 million for 2000 (Gopi et al., 2005). The annual risk of tuberculosis infection (ARTI) had been estimated at 1-2% for most of the tuberculin surveys carried out in different areas over different time periods. During a nationwide study in 2000-2003, the average ARTI in the country was estimated at 1.5% (Behera, 2007). Against the targeted coverage of 271.21 million populations, under RNTCP more than 430 million population has already been covered under the revised strategy (Sukamal et al., 2007), the government has extended the project by two years to cover a population of 700 million by year 2004.

**Types of Tuberculosis**

Tuberculosis is divided into three clinically important categories such as, Primary TB, Secondary Reactivated TB and Disseminated TB.

Primary tuberculosis refers to the infection process which eventually eliminates the pathogen or results in a stalemate between the Mycobacteria and the immune system. With most TB infections, the immune system is able to contain, although not eliminate, the Mycobacteria within the tubercle, preventing the spread of bacteria and progression of the disease. *M. tuberculosis* can remain in this impasse of dormant infection for many years.

In Secondary or Reactivated Tuberculosis the infection can become reactivated if the Mycobacteria are able to rupture the tubercle and spread through the lungs. This reactivation typically happens to those with a weakened or suppressed immune system. In Disseminated Tuberculosis the spread of the disease within the body may result if infected macrophages moving through the blood and lymph transport the bacteria to other sites. Once infected, symptoms of disseminated TB relate to the locations infected. The antiquated term ‘consumption’ arose from the myriad of symptoms
associated with disseminated tuberculosis, when those infected seemed to slowly waste away (http://human-infections.suite101.com/article.cfm/three_types_of_tuberculosis_infection).

**EPIDEMIOLOGY OF TUBERCULOSIS IN INDIA**

It is estimated that one-third of the world population i.e. 9.2 million people have been infected with TB. Globally, TB causes approximately 2 million deaths per year which include 1/5 of adult deaths. The majority of TB cases are reported the developing countries, making TB the number one killer among adults (WHO report, 2007). Every day in India more than 20,000 people become infected with the TB bacillus and more than 5000 people develop the disease. (Bhatia et al., 2003). Every year, nearly 5 lakhs die of TB. In other word 1000 deaths occur per day that means one TB death occur every minute. Untreated TB cases spread the infection to others in the community: each infectious patient can infect 10-15 individuals in a year unless effectively treated. In India, TB kills 14 times more people than all tropical diseases combined, 21 times more than malaria, and 400 times more than leprosy. TB kills more women than all causes of maternal mortality combined (Connolly, 1996). The direct and indirect costs of TB to the country amount to Rs.12, 000 crores per year.

TB is an infectious disease caused by the bacterium *M. tuberculosis*. TB bacilli mainly affect the lungs, causing lung tuberculosis (pulmonary TB). However, in some cases, other parts of the body may also be affected, leading to extra-pulmonary TB. Extra-pulmonary TB is more common in HIV-infected TB patients. The bacterium is also called as *acid fast bacillus* (AFB) as it is resistant to decolourization by acid.

**Pulmonary tuberculosis**

Pulmonary Tuberculosis symptoms are symptoms suggestive of pulmonary TB are:

Cough for 3 weeks or more, rise of temperature in the evenings, chest pain, weight loss,
loss of appetite and haemoptysis (coughing up of blood in sputum). HIV-infected patients with milliary TB often have fever, night sweats, weight loss and anemia without specific symptoms. However, sputum smears are often positive.

**Extra-pulmonary TB**

The following general symptoms were observed such as weight loss, fever, night sweats, other symptoms depend on the organ involved. Lymph Node TB causes swelling in the neck or armpit with or without discharge. The symptoms of TB Meningitis include headache, fever, drowsiness, confusion, and neck-rigidity, where in for the Spinal TB back pain, fever and in some cases swelling of the backbone was observed. Pericardial TB symptoms were chest pain, and shortness of breath.

**LEPROSY IN INDIA**

Leprosy is a disease caused by the bacterium *Mycobacterium leprae*. It is often also referred to as Hansen's disease, after the discoverer of the bacterium. While in ancient history, the term leprosy has been used to denote a wide range of afflictions that cause boils, sores, or other skin diseases. Though the exact mode of transmission for leprosy is unknown, global use of multi drug therapy (MDT) seems. If any, effect on transmission of the disease, (Meima *et al.*, 1985) and an adequate explanation for this situation is lacking (Report of the international leprosy association technical forum, 2002) most people believe that the bacterium passes through moisture exuded from the body.

Leprosy is a chronic bacterial disease which is usually affects the areas of skin (Chatterjee, 1976), nerves in the hands and feet and in some cases the lining of the nose. It is still not very clear as to how leprosy is spread but it is obvious that it happens only with close and prolonged contact. The germ can possibly enter the body through the
nose and through some opening in the skin. The lepromatous germs can spread in the air though the nasal discharge of an untreated patient (Smith et al., 2004).

India has the largest number of known cases of leprosy and northern region incidentally happens to be endemic for the disease. WHO lists leprosy as one of the major health problems of developing countries including India, Brazil, Africa, Nepal and Bangladesh (Report of the international leprosy association technical forum, 2002). Total patient load in 1981 was four million and hence the prevalence rate (PR) was 57/10,000.

A total of 7.8 lakhs cases were detected by India in 1998 due to intensification of the programme activities which is the highest may be number of cases detected in any year. 84% of total globally detected 9.33 lakhs cases in the year 1998 were contributed by India.

**HIV – LEPROSY INTERACTION**

Early in the HIV epidemic, it was feared that the disease would undermine leprosy control, as it has occurred with tuberculosis. It was predicted that patients with leprosy and HIV coinfection would have an increased risk of lepromatous disease (Deps and Lockwood, 2008) and a faster clinical evolution, and that the leprosy would be more difficult to treat. None of these concerns have materialized and the interaction between HIV and *M. leprae* seems to be far more subtle than that between HIV and tuberculosis. The published epidemiological data are limited in quality but show neither an increased HIV prevalence among leprosy cases nor an alteration in clinical spectrum of leprosy among coinfected patients (Ustianowski et al., 2006). Some data suggest that immune-mediated reactions complicate leprosy of occurrence is a higher frequency in coinfected patients. Leprosy has now been reported as immune reconstitution disease among patients commencing highly active antiretroviral treatment (Ustianowski et al., 2006). Histopathological observations reveal a normal spectrum of appearances in biopsies of
leprosy lesions from coinfected patients, even among those with advanced immunodeficiency. These observations suggest that cell-mediated immune responses to *M. leprae* are preserved at the site of disease despite evidence that these responses are abrogated systemically, by contrast with tuberculosis, in which the host granulomatous response is impaired by HIV coinfection. Paradox may relate to differences between the activation state and rates of cell turnover within leprosy and tuberculosis granulomas that differentially affect the susceptibility of the granulomas to HIV (Ustianowski *et al.*, 2006) and HIV coinfection would have an increased risk of lepromatous disease and a faster clinical evolution, and that the leprosy would be more difficult to treat.

**IMPACT OF HIV ON LEPROSY**

Two case reports of patients with human immunodeficiency virus type 1 (HIV-1) infection along with developed leprosy are presented. Both developed type 1 leprosy reactions in the absence of antiretroviral therapy. Reactions have been described for a number of HIV-1 and *M. leprae*-coinfected patients and have been considered to be part of an immune reconstitution inflammatory syndrome (IRIS) since the reactions were usually linked to the administration of highly active antiretroviral therapy.

However, with the advent of highly active anti retroviral therapy (HAART), a new syndrome called immune reconstitution inflammatory syndrome (IRIS) has been diagnosed in previously immunosuppressed patients in association with subclinical or clinical opportunistic infections. It is characterized by the appearance or worsening of inflammatory responses related to these organisms in patients presenting with some degree of immunological recovery. Reactional states have been described recently for a small number of *M. leprae*- and HIV-coinfected patients and linked to the introduction of HAART (Couppie *et al.*, 2004, Goodless *et al.*, 1994 & Lawn, *et al.*, 2003) and as
such, they were diagnosed as IRIS. However, in the two *M. leprae* and HIV-coinfected patients reported herein, type 1 leprosy reactions occurred in the absence of any antiretroviral therapy.

**Diagnosis of leprosy**

Diagnosis of leprosy is most commonly based on the clinical signs and symptoms. In practice, most often persons with such complaints report on their own to the health centre.

**Positive skin smears** In a small proportion of cases, rod-shaped, red-stained leprosy bacilli, which are diagnostic of the disease, may be seen in the smears taken from the affected skin when examined under a microscope after appropriate staining.

**Bacteriology**

**Magnitude of the problem - Tuberculosis and HIV/AIDS**

TB is now the world’s foremost cause of death from a single infectious agent with nearly 90 million new cases and 30 million deaths annually. The economic impact of disease by way of direct and indirect costs of contact investigations, costs of TB screening and preventive therapy programs, costs of hospital and institutional infection control programs and costs to patients in lost income, is enormous. An increasing number of cases becoming to multidrug resistant to tuberculosis could escalate these costs dramatically (Smith and Moss, 1994). The common risk factors for tuberculosis includes poor social circumstances, alcoholism, diabetes mellitus, immigrant population, no previous BCG vaccination and HIV infection (Gaude, 1998).

**Impact of TB infection on the HIV epidemic**

TB is the most common serious opportunistic infection in HIV positive patients and is the manifestation of AIDS in more than 50% of cases in developing countries.
Also to be noted are the facts that TB shortens the survival of patients afflicted with HIV infection, may accelerate the progression of HIV and is the cause of death in one third of people with AIDS world wide. The higher mortality is due to the progression of AIDS rather than TB probably due to the fact that \textit{M. tuberculosis} increases viral replication. The first report of tuberculosis occurring in patients with AIDS appeared in 1983 when an illness associated with severe immunosuppression was described in a group of Haitian patients in South Florida (Hopewell, 1993).

\textbf{Indian scenario}

Very little data are available in our country about patients dually infected with HIV and tuberculosis. However, various studies reported a prevalence range from 14.6\% to 67\% in HIV infected individuals (Daley \textit{et al.}, 1992, Panda \textit{et al.}, 1996). An analysis of 8000 odd cases of AIDS reported to NACO revealed tuberculosis to be a major opportunistic infection (63\%). According to the National AIDS control organization, about 3.82-4.58 million Indians were estimated to be infected by HIV at the end of the year 2002 (NACO, 2003). Due to its large population, India ranks second after South Africa in terms of the absolute number of people living with HIV/AIDS. India has the largest number of tuberculosis (TB) cases in the world. India shoulders about 14 million cases of TB and it is estimated that about 1.8 million incident cases of TB occur in India every year of which 0.82 million are highly infectious smear positive cases. (Vaidyanathan and Singh, 2003).

\textbf{Multidrug resistant tuberculosis (MDR-TB)}

The re-emergence of multidrug resistant tuberculosis has compounded the problem of tuberculosis leading to a high rate of morbidity and mortality. Factors
contributing to recent outbreaks and continuous spread of MDR tuberculosis include the emergence of AIDS in addition to inefficient infection control procedures and laboratory delays in identification and susceptibility testing (Jacobs, 1994). In India itself the prevalence of MDR-TB has increased from zero in 1980 to 10.7% in 1995 (Cohn et al., 1997). However, the prevalence of MDR-TB with HIV infection in India, Chennai 4.42 percent was observed by Deivanayagam et al., 2002.

**Nontuberculous mycobacteria in HIV infected patients**

Nontuberculous mycobacteria (NTM) have often been identified as causing disease in HIV infected patients. However, the incidence of infection due to NTM other than *M. avium intracellulare* is low. Relatively non-virulent mycobacteria including *M. Kansasii, M. simiae, M. genavense, M. haemophilum and M. scrofulaceum* have also proved to be opportunistic pathogens in patients with AIDS (Chowgule et al., 1998).

Infection due to *M. avium intracellulare* (MAC) was relatively rare in the pre AIDS era. The most common manifestation of MAC infection was pulmonary. However, with the advent of AIDS, disseminated infection with MAC is recognized as the most common systemic bacterial infection in patients of AIDS. Disease due to MAC is geographically widespread with reports of MAC in HIV infected patients from North and South America, Europe and Australia (Garay, 1995).

*M. kansasii* is not as widespread as MAC. In the United States, it is the second most common NTM infection in patients with AIDS (Holzman, 1995). Early reports of *M. kansasii* in HIV infected individuals were focussed on the dissemination and fatality due to *M. kansasii*. Pulmonary disease is more common than extrapulmonary disease in patients of HIV coinfected with *M. kansasii* (Horsburgh et al., 1989 & Cattamanchi et al., 2008).
Other nontuberculous mycobacteria

Very few studies are available on other NTM infection in patients of AIDS. *M. haemophilum* infections have been reported, mainly causing erythematous nodular skin lesions, subcutaneous abscesses, lymphadenitis and occasional joint involvement. *M. genavense* causes infection rarely, leading to bacteraemia in patients of AIDS. *M. gordonae*, one of the least pathogenic mycobacteria, can also lead to pulmonary infection. Scattered reports are available on the occurrence of *M. scrofulaceum* and *M. celatum* infections in patients of AIDS (Horsburgh et al., 1989).

**Non-Mycobacterial bacterial infections in HIV/AIDS**

Infection due to HIV is characterised by progressive deterioration of immunologic function, which is generally measured by the CD4 lymphocyte count. As the CD4 lymphocyte count declines, HIV infected patients become susceptible to a variety of infections. This is mainly due to opportunistic pathogens. They are termed as “opportunistic” that are associated with considerable morbidity and mortality. The true incidence of non-mycobacterial bacterial infections in HIV-infected persons is difficult to discern and varies with the population surveyed. Common causative pathogens were *Salmonella enteritidis*, *Streptococcus pneumoniae*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus viridans*, and *Corynebacterium* species.

**Magnitude of problem**

Early recognition of the onset of opportunistic infection and identification of the aetiological agent(s) associated with it are essential if treatment is to succeed. The
The prime concern is to institute prompt antibiotic prophylaxis treatment while pursuing the laboratory diagnosis.

HIV infected persons, especially with advanced disease, have increased susceptibility to systemic bacterial infections, in particular with encapsulated organisms (like *Streptococcus pneumoniae* and *Haemophilus influenzae, Staphylococcus aureus*). Children with HIV infection are more susceptible to bacterial infections than infected adults (Gold, 1996). Recurrent, serious bacterial infection is included as an “indicator disease” in the case definition of AIDS in the paediatric population. Frequently recognized clinical syndromes in children with HIV infection include: pneumonia, otitis media, sinusitis, urinary tract infection, skin and soft tissue, infections, meningitis, osteomyelitis, intravenous catheter infection.

Previous studies revealed pneumococcal infection of the lung in 5% cases, *S. aureus* subcutaneous abscess in 5% and otitis media (*S.aureus*) in 3% of AIDS patients (Kumaraswamy *et al.*, 1995) while group B Salmonella septicaemia was found in 1.6 AIDS patients in a recent South Indian study (George *et al.*, 1996).

**Respiratory tract infections**

**Bacterial aetiology of pneumonia/lower respiratory tract infections (LRTI) in HIV-infected persons**

Respiratory tract infections occur more frequently HIV infected persons than in non-HIV infected persons (such as *S. pneumoniae, H. influenzae* and *Pseudomonas aeruginosa*). Such infections may be community or hospital acquired and may range from mild, self-limiting infections to those that are severe and life-threatening. Patients
with AIDS have a markedly increased risk of acquiring Legionnaires disease (PHLS Atypical Pneumonia Working Group. 2002).

**Clinical presentation**

HIV associated respiratory disease includes upper respiratory tract infections (URTI), acute or chronic sinusitis, acute or chronic bronchitis and bacterial pneumonias. Many of them also have one or more episodes of sinusitis during the course of their disease. Bacterial lower respiratory tract infections (LRTI) are manifested as cough with sputum production, variable fever, chills chest pain etc., (Farooq, 2004). Other symptoms may include headache, nausea and myalgias. Prompt and accurate diagnosis of the respiratory infection is essential. The clinical features of respiratory tract infections are the same in HIV infected individuals as in those without HIV, but their frequency and rate of complications including intra-pulmonary cavitation, abscess formation, empyema and deaths are increased. HIV infected patients with bacterial pneumonia are commonly bacteremic and may relapse after appropriate antibiotic therapy.

**Laboratory diagnosis of lower respiratory tract infection (LRTI) (Pneumonia)**

The bacterial agents that must be sought depend upon the available expertise, facilities and resources. Microscopy alone may be performed at primary/peripheral level health care setting, while culture of common pathogens may be possible at the intermediate/district health centers (Thomas, 2003). Isolation of fastidious bacterial agents should be attempted only in tertiary level hospital laboratories. Rapid, simple, non-culture methods for the detection of bacterial antigens or antibodies offer a better
alternative to culture at primary and intermediate health care facilities, provided they are reasonably sensitive, specific and economical (Venkatesh et al., 2007).

Bacterial isolates may be submitted to tertiary/referral centres for further characterization by serotyping, etc, besides, antimicrobial susceptibility testing. This is essential for designing prophylaxis by vaccination or antibiotic therapy. Tertiary health care facilities that have adequate resources and trained personnel may undertake diagnosis by the more sensitive and specific molecular methods like PCR (polymerase chain reaction) and DNA hybridization etc., primarily to evaluate other methods like microscopy and culture.

The importance of respiratory infections in HIV patients is well documented (Rosen, 1994). The true incidence of these infections is difficult to assess and varies with the population surveyed. Among the opportunistic infections associated with HIV, diseases like pneumonia of bacterial origin occur at a rate many times higher in the HIV infected patients than in the general population (Baveja, Sokhey Eds. 1999).

**Epidemiology of LRT or parenchymal respiratory infections.**

Pneumonia and influenza were the seventh leading cause of death in the United States in 2000 (24.3 deaths per 100,000 populations). Approximately, 1.8 cases of pneumonia were reported for every 100 Americans in 1996 (Kaplan et al., 1998). Pneumonia is also a very common case of nosocomial infections ranking third in occurrence behind urinary tract infections (33% of the infections acquired in the hospital) and surgical wound infections (Leth and Moller, 2005).

Respiratory opportunistic infections also evidence that noninfectious causes of chronic cough, such as asthma and smoking related lung disease are increased incidence in developing countries (Walraven et al., 2001). Sinusitis has also been reported to occur
frequently in HIV-infected people who contribute to lower respiratory tract infections (LRTI) (Zurlo et al., 1992). Among the various opportunistic infections, respiratory infections account for up to 70% of AIDS cases defining illness (Shailaja et al., 2004). Though conventionally infected by bacteria with low virulence, at the same time HIV positive patients are not spread by classical virulent ones either (Banerjee, 2005). Important opportunistic infections like Rodococcus equi or Norcardia though reported from abroad (WHO, 2001), are hardly seen from Indian patients (Banerjee, 2005). Spectrum of bacterial infection is changing, towards the tilt of infection caused by conventional pathogen (Shailaja et al., 2004).

Incidence of pyogenic bacterial lower respiratory tract infection

Wallace et al., (1997) examined trends in the incidence of specific respiratory disorders in a multicentric cohort with progressive HIV disease during a 5 years period. Individuals with a wide range of HIV disease severity and belonging to the three main transmission categories were evaluated at regular intervals and for episodic respiratory symptoms using standard diagnostic algorithms. Acute bronchitis and bacterial pneumonia were the most common respiratory diseases of cohort members (Daga et al., 2005). The respective incidences per 100 person-yrs were 13.7 for bronchitis and 5.5 for bacterial pneumonia. Similar results were found in a US case controlled study performed in an intravenous drug user cohort, in which the incidence of bacterial pneumonia per 100 person-years was 1.93 in HIV-seropositive and 0.45 in HIV-seronegative subjects (Caiaffa et al., 1994). The high incidence rates explain why, in prospective studies, pyogenic bacteria as well as Mycobacterium tuberculosis were recognized as the major cause of respiratory diseases in HIV-infected Africans (Kamanfu et al., 1993).
Risk factors for bacterial lower respiratory tract infection

The risk of bacterial pneumonia is not the same in all HIV-infected persons (Wallace, 1993). The most important risk factor for bacterial pneumonia is the degree of immunosuppression, as reflected by the CD4 T-lymphocyte count. In the previously mentioned US cohort study (Wallace et al., 1997) acute bronchitis was equally prevalent during all stages of HIV disease, whereas the risk of bacterial pneumonia was clearly related to the study CD4 count (2.3, 6.8 and 10.8 episodes per 100 person-yrs in the subgroups of cohort members with >500, 200–500 and <200 CD4 T-lymphocytes·mm\(^{-3}\)). A similar relationship between a decreased CD4 T-lymphocyte count and an increased risk of bacterial pneumonia has been found in European studies (Boschini et al., 1996). Other risks factors for bacterial pneumonia have also been identified. In the same study, tobacco was equally shown to be an independent risk factor in the subgroup of HIV-seropositive subjects with <200 CD4 lymphocytes·mm\(^{-3}\). Another risk factor is neutropenia, which may result from direct retroviral infection, the use of antiretroviral and other drug therapy, systemic opportunistic infections and autoimmune mechanisms (Moore et al., 1995). Regarding specifically nosocomial pneumonia, advanced HIV infection, (Mayaud et al., 2002) high acute physiology and chronic health evaluation III score and central nervous system diseases have been shown to be risk factors (Tumbarello et al., 2001).

Bacteria responsible for lower respiratory tract infection

The first series investigating bacterial pneumonia in patients with AIDS or AIDS-related complex have shown the predominant role of *Streptococcus pneumoniae* and, to a lesser degree, *Haemophilus influenzae*, in adults as well as children (Madhi et al.,
2000), in developed countries (Polsky et al., 1986 & Witt et al., 1987), and developing countries (Gilks et al., 1996 & Scott et al., 2000).

**Typical pyogenic bacteria**

In all series, typical pyogenic bacteria and, more particularly, *S. pneumoniae* and *H. influenzae*, were the major responsible bacteria. In US cohort study of Hirschtick et al., (1995), *S. pneumoniae* and *H. influenzae* were found in 52% and 15% of patients with confirmed pneumonia, respectively.

**Atypical pyogenic bacteria**

Atypical pyogenic bacteria may also be the causative agent, particularly in patients with advanced HIV disease. For example, *Klebsiella pneumoniae*, other members of the Enterobacteriaceae family and *Pseudomonas aeruginosa* were present in 13%, 10% and 8% of cases, respectively, of confirmed pneumonia in the US cohort study of Hirschtick et al., 1995. Similarly, *P. aeruginosa*, the *Enterobacteriaceae* family and *Staphylococcus aureus* were the cause of 25%, 9% and 10% of community-acquired pneumonia, respectively, in according to Afessa et al., (2000). These kinds of pathogen and their relative frequencies were consistent with most published reports (Tumbarello et al., 1998, Levine et al., 1990 & Schuster et al., 1994).

*S. aureus* recovered in 23% of respiratory tract cultures performed in 129 consecutive HIV-infected patients with an episode of respiratory disease. However, the presence of *S. aureus* was found to be community-acquired pneumonia in 28% of cases, of indeterminate significance in 62% and colonisation in 10%. None of the patients with pneumonia were neutropenic or on corticosteroids (Levine et al., 1990).

In HIV-infected patients, this pathogen may cause not only nosocomial pneumonia but also community-acquired pneumonia or chronic bronchitis (Shailaja et
Traditional risk factors for the development of *P.aeruginosa* infections such as neutropenia, steroids, previous antimicrobial treatment and recent hospitalisation were absent in most patients. Nevertheless, this infection occurred almost exclusively at the AIDS stage in patients with a very low level of CD4 T-lymphocytes (Schuster *et al.*, 1994 & Domingo *et al.*, 1998).

**Opportunistic bacteria**

Ultimately, if nosocomial pneumonia is considered, *P.aeruginosa*, *S.aureus* and Enterobacteriaceae were usually responsible (Tumbarello *et al.*, 2001 & Fichtenbaum *et al.*, 1994), as in HIV-seronegative patients.

Typical clinical presentation  In the vast majority of cases, the clinical presentation of HIV-infected subjects with bacterial pneumonia is similar to that of HIV-seronegative patients with community-acquired pneumonia. Onset is acute (Selwyn *et al.*, 1998) with fever, cough, purulent sputum, and dyspnoea and chest pain. Physical examination reveals abnormalities (Selwyn *et al.*, 1998), Unilateral alveolar opacities are the most frequent radiological abnormalities (Selwyn *et al.*, 1998) Laboratory evaluation usually shows a leucocytosis but leucopenia can occur. Serum lactate dehydrogenase levels are typically normal or mildly elevated (Rajpur *et al.*, 2002). Hypoxaemia may be present. In the stepwise logistical analysis of (Tumbarello *et al.*, 1998) the independent indicators of mortality were: CD4 T-cell levels <100 cells·mm$^{-3}$; arterial oxygen tension 9.3 kPa (70 mmHg); Karnofsky score <50; and neutrophil count <1,000 cells·mm$^{-3}$ (Tumbarello *et al.*, 1998).
**Course of bacterial lower respiratory tract infection**

In the majority of series of bacterial pneumonia in HIV-infected patients, the short-term mortality was the same as in HIV-seronegative subjects. Many other series with *S. pneumoniae* (Polsky *et al.*, 1986, & Frankel *et al.*, 1989), *H. influenzae* (Cordero *et al.*, 2000), and other typical pathogens (Baril *et al.*, 1998), have also shown a percentage of deaths similar to that usually observed in HIV-seronegative people. However, the bacteremia level and mortality increase with the progression of HIV disease. This is clear for pneumonia due to *P. aeruginosa* (Tumbarello *et al.*, 1998, & Schuster *et al.*, 1994) or other opportunistic bacteria (Uttamchandani *et al.*, 1994) observed exclusively at the AIDS stage. In patients cured of their acute episode of bacterial pneumonia, two late unfavourable events might occur: recurrence of LRTI and decrease in survival time (Mayaud, *et al.*, 2002).

**Effect of highly active antiretroviral therapy on incidence of bacterial pneumonia**

In a German cohort, during 1992–1996, (Brodt *et al.*, 1997) was observed a significant decrease in the number of cases of bacterial pneumonia, clearly related to the number of antiretroviral drugs administered. Similarly, in the important US cohort study of Dworkin *et al.* (Dworkin *et al.*, 2001), antiretroviral treatment was an independent factor that contributed to a two-fold decrease in the incidence of pneumococcal disease during 1990–1998. The protective effect increased with the number of antiretroviral drugs and resulting antiretroviral effectiveness.

**Pattern of Antibiotics in lower respiratory tract**

Common lower respiratory tract pathogens have become more resistant to antibiotics (Health Canada and the Canadian Infectious Disease Society, 1997). Patient
pressure and clinical uncertainty played a role in high rates of antibiotic use (Miller et al., 1999).

**Intestinal Parasitosis in HIV Patients**

Broadly classified as Protozoa, Nematode, Trematodes

1. **Protozoa**

   *Cryptosporidium parvum*
   
   *Isospora belli, Cryptosporidium hominis*
   
   *Entamoeba Histolytica*
   
   *Entamoeba coli*
   
   *Giardia lamblia*
   
   *Hymenolepis nana.*

2. **Nematode**

   1. *Ascaris lumbricoides*
   2. *Ankylostoma deodenalle*
   3. *Trichuris trichiura*

3. **Trematodes**

   : No significant percentage seen.

Cryptosporidiosis in HIV patients

**Incidence**

Incidence of Cryptosporidiosis in HIV patients with diarrhoea varies geographically from 10 to 20% in united state and Western Europe to as high as 50% in developing countries.

**Agent Factor**

*Cryptosporidium parvum* oocyst appeared as pinkish or orange spherical bodies measuring 4-6µm. In the year 1998 trends in Intestinal parasites such as *Cryptosporidium parvum* and *Isospora belli* leads to increase in morbidity and mortality.
in HIV/AIDS cases (Lindo et al., 1998). *Cryptosporidium* sp. is apicomplexan parasites that cause protracted and life threatening diarrhea in HIV infected patients (Hunter and Nichols, 2002). The life cycle of *Cryptosporidium* sp. is completed within the small intestine and colon of the host, with the developing stages associated with luminal surface of intestinal epithelial cells, where it remains intracellular but extracytoplasmic (Huang et al., 2004). The spherical thick walled, environmentally hardy oocysts (3-6 μm in diameter), shed in the fecal material of the infected host, are immediately infectious, unlike other coccidian parasites, and hence can be transmitted from person to person.

**Pathogenesis of Cryptosporidiosis**

The alterations in the intestinal structure and physiology that leads to the pathogenesis of cryptosporidiosis include rapid loss of the microvillus border, shortening and fusion of the villi and lengthening of the crypts resulting in malabsorption due to loss of membrane-bound digestive enzymes. Pro-inflammatory cytokines, especially IFNγ and TNFα, also contribute to the pathogenesis of cryptosporidiosis by increasing production of prostaglandins, neural peptides and reactive nitrogen intermediates, disruption of the epithelial barrier leading to a leaky and dysfunctional epithelium and alteration of solute transport leading to osmotic diarrhea (Tzipori and Ward, 2002).

**Immune response and Cryptosporidiosis**

Immune responses involved in mediating resistance to infection with this parasite are not well understood, but evidence obtained from immunodeficient animal models have shown that a Th1 response involving primarily TCR αβ+ CD4+ lymphocytes, IFNγ and IL-12 play a major role in the control of *C. parvum* infection (Ehigiator et al., 2007). The susceptibility of HIV/AIDS patients to this pathogen and resolution of cryptosporidiosis following immune restitution underscores the importance of CD4+ T
cells. Humoral immune response to oocyst lysates as well as to specific glycoprotein antigens, have been characterized in volunteer studies and in seroepidemiological studies (Riggs, 2002).

**Protozoan infection**

Diarrhoea is the most common gastrointestinal symptom in HIV infected patients with the incidence increasing when CD4 counts drop below 200 cells/μl (Navin et al., 1999). HIV infected patients are subject to a cumulative life time incidence of diarrhoea estimated at up to 100% in developing countries and 30 to 70% in developed countries (Call et al., 2000) with chronic diarrhoea affecting up to 76% of patients with AIDS (Misra et al., 1998). The common enteric opportunistic pathogens described are cytomegalovirus, *Cryptosporidium* sp., *Isospora belli*, *Microsporidium* sp., *Mycobacterium avium intracellulare* and more recently, *Clostridium difficile*. Many diarrhoeal episodes remain undiagnosed and this could be attributed to unidentified agents or primary HIV enteropathy. In India, *Entamoeba histolytica* and *Giardia lamblia*, along with *Cryptosporidium* sp. and *I. belli* have been reported as the most common causes of diarrhoea, however, most studies have focused only on protozoan aetiology (Attili et al., 2006, Banerjee et al., 2005 & Ajjampur et al., 2008). The other pathogens that have been reported in Indian patients with HIV related diarrhoea include *Cyclospora*, *Strongyloides stercoralis*, *Blastocystis hominis*, *Dientamoeba fragilis*, Microsporidia sp., *Campylobacter jejuni*, *Salmonella*, *Shigella* and diarrhoeagenic *E.coli* (Banerjee et al., 2005, Mukhopadhya et al., 1999, Kumarasamy et al., 1995, & Kumar et al., 2002). Risk factors associated with diarrhoeal disease due to parasites in Indian patients include previous history of diarrhoea, use of public toilets, lower education and socio-economic status, residence in slums and exposure to animals (Dwivedi et al., 2007, & Becker et al., 2007). *Cryptosporidium* is a parasite that
infects the intestines. *Cryptosporidium* is most common cause of diarrhoea in the world. Cryptosporidiosis is a substantial threat to HIV-infected individuals and in developed countries these patients have an estimated risk of infection of around 10% (Manabe *et al.*, 1998). Patients can have chronic watery diarrhoea that can last for more than 2 months and shed oocysts in stool during the entire period, resulting in severe dehydration, weight loss and malnutrition, extended hospitalizations, and mortality (Hunter and Nichols 2002, & Abubakar *et al.*, 2007). Cryptosporidiosis remains a major risk to the immunocompromised because of the lack of effective specific therapy (Abubakar *et al.*, 2007). Other symptoms are abdominal cramps, anorexia, nausea, vomiting, fatigue and low-grade fever. Cryptosporidiosis remains a major risk to the immunocompromised because of the lack of effective specific therapy. Therapeutic approaches for cryptosporidiosis in the past have included macrolide antibiotics, paramomycin, rifaximin, octreotide and immunotherapy among others. Although nitazoxanide is licensed for use in immunocompetent patients, a recent meta-analysis found it to be ineffective in HIV (Hunter and Nichols 2002, & Abubakar *et al.*, 2007). AIDS patients with cryptosporidiosis also have a significantly shorter duration of survival from the time of diagnosis (Manabe *et al.*, 1998).

Study from Thailand classified by the CD4 T-cell categories, opportunistic intestinal parasite infections showed a highest prevalence in patients with a low immune level (CD4+ < 200/μl) and diarrhoea. There was no significant predominance of non-opportunistic intestinal parasite infections at any immune level reported by (Wiwanitkit, 2001). Therefore, as shown in previous reports, opportunistic intestinal parasite infection should be suspected in any HIV-infected patient with low immunity presenting with diarrhoea. Clinical course and pattern of opportunistic infections (OIs) varies from patient to patient in different areas of India (Kumarasamy *et al.*, 2005).
Current literature (Ajjampur et al., 2008) regarding cryptosporidiosis and HIV in India is limited to a few epidemiological studies and several hospital based surveys with limited information on infecting species, host risk factors and transmission dynamics of this disease.

**Mycology**

Various mycoses form the bulk of opportunistic infections in AIDS patients and the increasing in the form of an epidemic parallel to the AIDS epidemic (Mirdha et al., 1993). Most common opportunistic fungus such as *Pneumocystis jiroveci* and candida. Human derived *Pneumocystis carinii*, an established cause of pneumonia in immunocompromised individuals is now considered as different species, *Pneumocystis jiroveci* (Frenkel 1999). The clinical spectrum caused by the organism is termed as *Pneumocystis carinii pneumonia* (PCP) or pneumocystosis. The dynamics of *P. jiroveci* took a new turn with emergence of the HIV and the AIDS in the 1980s. *P. jiroveci* infection was the first opportunistic illness to be recognized in AIDS patients and has remained as one of the most common AIDS defining illness in the western world (Walzer, 1998).

*Pneumocystis* was first observed by Chagas as a variant stage of *Trypanosoma cruzi* (Walzer, 1998). Ultrastructural studies in 1960s and 1970s and biochemical analysis were unable to conclusively place *Pneumocystis* as either fungi or protozoa. Presence of lamellar rather than vesicular mitochondria was consistent with fungi (Vavra et al., 1970).

classification based on percentage of sequence differences among selected loci, thymidylate synthase, inter-transcribed spacer region (ITS), β tubulin and arom. Highest level of divergence (15-50%), designated as class III, was among Pneumocystis from different mammalian hosts. Based on these variations, at least 59 human types have been identified so far.

**Epidemiology and transmission of P. jiroveci**

Highest transmission of Pneumocystosis is seen in HIV positive patients with CD4 count less than 200 cells/μl. Amongst non-HIV group, persons at highest risk include severely malnourished and premature infants less than three months of age. Children with primary immunodeficiency disorders, and patients with hematological and other malignancies, recipients of organ or bone marrow transplants or persons on steroid therapy (Russian *et al.*, 2001). Occasional reports are from patients without any abnormalities in immune system (Sing *et al.*, 1999).

**P. jiroveci in HIV negative patients**

In a study from Netherlands it was shown that all HIV negative patients with *P. jiroveci* had underlying disorders resulting in immunosuppression. These include hematological malignancies (49%), immunological disorders (22%), solid organ transplantations (20%) and bone marrow transplantations (9%) (Arend *et al.*, 1995). In India, various studies reported the association of *P. jiroveci* in HIV negative cases with underlying diseases, such as Hodgkin’s (Varma *et al.*, 1994) lymphoma and renal transplant patients (Sherke *et al.*, 1992).

**P. jiroveci in HIV positive patients**

Before 1989, 60-80% of HIV positive patients in developed countries were presented with *P. jiroveci* accounted for 20-25% of all AIDS related deaths (Dei-Cas, 2000 & Jones *et al.*, 1998). Now, the incidence of *P. jiroveci* has declined by 75% with prompt
diagnosis, effective prophylaxis and institution of highly active antiretroviral therapy (HAART) in AIDS patients (Dei-Cas, 2000). In USA, the incidence has declined from 9 per 100 persons year in 1991 to 5.3 per 100 persons year in 1996 as per Centre for Disease Control and Prevention (CDC) (Jones et al., 1998). In the 1980s, pneumocystosis accounted for 0-11% infectious in AIDS patients (Hughes, 1998). However, recent studies have shown an increasing trend in Africa higher percentage of AIDS patients developing pneumocystosis; 33% in Zimbabwe (1995) and 22% in Zambia in the (2002), respectively (Malin et al., 1995 & Fisk et al., 2003).

Indian studies

Pneumocystosis is fifth commonest infection in AIDS patients in India (Singh et al., 2003). In 1993 *P.jiroveci* was reported in three AIDS patients in India (Singh et al., 1993). In North Indian study, among 134 HIV positive, 12 were found to have pneumocystosis as the terminal event (Giri et al., 1995). Merchant et al., (2001) conducted study on 285 children and found pneumocystosis in 3.9% of cases. In a study from South India (Kumarasamy et al., 2003), 6% of AIDS patients had pneumocystosis. Several case reports of *P.jiroveci* infection among HIV positive individuals have been reported from India (Arora et al., 1996). In a systematic study from North India (Mirdha et al., 2000) *P.jiroveci* was found in 6.1% of HIV positive and 1.5% of HIV negative immunocompromised patients.

Transmission of *P. jiroveci*

Occurrence of *P.jiroveci* in respiratory samples from clinically normal population supports the reactivation theory. Besides host immune evasion by variation of major surface glycoprotein (MSG), species specificity of *P.jiroveci* and difficult in vitro cultivation are consistent with long term carriage or latency in the host (Gigliotti et al., 1992). Over the years, data have accumulated against reactivation theory as well. Many
studies have been unable to find *P. jiroveci* in immunocompromised host (Peters *et al.*, 1992). *P. jiroveci* genotypes in patients with recurrent *P. jiroveci* often differ from with place of infection than place of birth (Chen *et al.*, 1993). Out break of oncology and transplant unit have raised the possibility of person to person transmission (Singer *et al.*, 1975).

**Clinical aspects of pneumocystosis**

Four clinical forms of pneumocystosis have been recognized, namely asymptomatic, infantile or epidemic interstitial pneumonia, child-adult sporadic pneumonia of immunocompromised and extrapulmonary pneumocystosis. Immunocompromised hosts typically present with a triad of progressive dyspnoea of many weeks, non-productive cough or with clear sputum and low grade fever. Chest radiography usually shows diffuse interstitial or peri-hilar infiltrates but may be normal in one third of cases. Other findings such as spontaneous pneumothorax, effusions or cavity lesions can be seen in less number of cases (Opravi *et al.*, 1994). Increased serum lactate dehydrogenase (LDH) >460 IU/L has been found to be a sensitive test for this diseases (Quist *et al.*, 1995).

**Diagnosis of pneumocystosis**

It is challenging to diagnose pneumocystosis on the basis of signs and symptoms only. Curtis *et al.*, (1995) made an interesting observation that only 77% physicians included pneumocystosis in their different diagnosis, on the basis of symptoms, chest radiograph and arterial blood gas values only. Specific microbiological diagnosis, based on conventional or antibody strains or nucleic acid detection methods is therefore, imperative. Sputum induction with hypertonic saline has been found to be sensitive procedure for *P. jiroveci* recovery with a diagnostic yield of 50-90 percent (Shelhamer *et al.*, 1996). Results are much better than expectorated sputum (Elvin *et al.*, 1988).
Bronchoalveolar lavage (BAL) of two or more segments may increase the yield to 90-99 percent and is considered as a gold standard (Bjur et al., 1996). Though transbronchial lung biopsy has sensitivity of 95-100%, it carries the risk of pneumothorax. Microscopy constitutes the mainstay of diagnosis and involves visualization of trophozoites or cyst forms.

**Candidiasis**

Fungi have emerged worldwide as an increasingly frequent cause of opportunistic infections. A survey of the epidemiology of sepsis was conducted in the USA. (Martin et al., 2003) revealed that the incidence of fungal sepsis increased threefold between 1979 and 2000. In contrast, numerous studies have revealed either no increase or sometimes even a decrease in the incidence of *Candida sepsis* (Lagrou, 2007 & Pfaller and Diekema 2007). *Candida* and *Aspergillus* sp. are the most frequent causes of invasive fungal infections and are associated with high morbidity and mortality (Méan et al., 2008). The incidence of invasive candidiasis is sevenfold to 15-fold higher than that of invasive aspergillosis (Méan et al., 2008). Originally described in immunocompromised hosts, primarily cancer patients, opportunistic fungal pathogens have now been recognized as a frequent cause of infection in surgical and critically ill patients.

Candida species are the most common fungal pathogens isolated from the oral cavity. Their oral existence both as a commensal and an opportunistic pathogen has intrigued clinicians and scientists for many decades, and recent investigations have revealed many attributes of this fungus contributing to its pathogenicity. In addition, the advent of the human immunodeficiency virus infection and AIDS has resulted in a resurgence of oral Candida infections. Clinicians are witnessing not only classic forms
of the diseases but also newer clinical variants such as erythematous candidosis, rarely described hitherto (Lakshman and Samaranayake, 1994). Candidiasis is an acute or chronic, superficial or disseminated fungal infection caused by species of Candida. The disease manifests in a variety of forms. Since the pathogenic species of candida forms the commensal flora of most individuals, the diagnosis of candidiasis should be carefully established. Up to 90% of HIV-positive individuals develop candidiasis at some time during the illness (Drouet, 1989). Candida infections in AIDS are usually limited to superficial candidiasis of varying degrees of severity in the oral cavity, throat and oesophagus. Pulmonary and central nervous system candida infections have also been reported in a small number of AIDS patients. Although *C. albicans* is the most important cause (superficial form) of candidiasis in patients of AIDS, many other members of the genus have also been recognised as pathogens.

**Hematology**

A variety of hematological manifestations is seen at every stage of human immunodeficiency virus / acquired human immunodeficiency syndrome (HIV/AIDS) and often pose a great challenge in the comprehensive management. These manifestations also reflect the underlying immune status if interpreted cautiously, especially if the patients is in regular follow-up. They may cause symptoms that are life threatening and impair the quality of life of these patients (Volberding et al., 2003). The most important of them are cytopenias. Cytopenia is a common complication of infection with human immunodeficiency virus type-1 and the course of the disease more then 70% of the patient’s developed anaemia, frequently requiring transfusion (Jacobson et al., 1990). Anaemia and neutropenia are generally caused by inadequate production because of suppression of bone marrow by the HIV infection though
abnormal cytokine expression and alteration of bone marrow microenvironment (Coyle, 1997).

Some patients present with clinical features classical enough to facilitate prompt diagnosis of HIV/AIDS, while many more present with vague or ill-defined features, and this could make early diagnosis difficult (Amballi et al., 2007). On the other hand, despite the availability of various categories of diagnostic and monitoring techniques for HIV/AIDS, the cost of the techniques are still unaffordable to several people in the resource poor settings. This is therefore aims to increase the index of clinical suspicion by identifying the hematological parameters.

**Haemoglobin status**

Anemia is the late manifestation of deficiency of nutrient(s) needed for haemoglobin synthesis. Most of the anemia’s are due to inadequate supply of nutrients like iron, folic acid and vitamin B₁₂, protein, amninoacids, vitamins A,C and other vitamins of B-complex group *i.e.*, niacin and pantothenic acids are also involved in the maintenance of haemoglobin level (Lee et al., 1998). Anemia is a frequent complication of infection with the human immunodeficiency virus type-1 (HIV-1) and may have multiple causes (Doukas, 1992). The most frequent cause of anemia in HIV-infected patients is anemia of chronic disease. CD₃⁴⁺ stem cells express low levels of CD4 and CD11a, making them relatively resistant to direct infection by HIV. However, mononuclear-macrophage cells can develop productive HIV infection and the resultant release of cytokines, such as transforming growth factor-beta (TGF-β), tumor necrosis factor-alpha (TNF-α), and interleukin-1 (IL-1), contribute to the suppression of hematopoiesis (Coyle, 1997). In different study settings, the prevalence of anemia in persons with acquired immunodeficiency syndrome has been estimated at 63% to 95% (Groopman, 1990) making it more common than thrombocytopenia or leucopenia in
patients with AIDS (Jon et al., 1987). Anemia has been associated with progression to AIDS. The incidence of anemia differed by race/ethnicity, stage of disease, presence of concurrence illness, and precipitation of chemotherapeutic agents (Sullivan et al., 1998). Also, low Hb may be due to direct attack of the reticuloendothelial cells by the virus (Odunukwe et al., 2005). Lower ESR in detected tuberculosis cases might be associated HIV infection (Awodu et al., 2007).

**Red Blood cells status (RBC)**

HIV requires a cell nucleus and Golgi bodies for its replication. RBC’s do not have a nucleus or Golgi bodies and hence the virus cannot infect them. On the other hand human immune cells like macrophages, CD4+ T helper cells and dendritic cells have a cell nucleus and Golgi bodies, which are essential for the replication of HIV. That’s why HIV infects the human immune cells and not the RBC’s. HIV infection eventually destroys the immune cells, lowering their count and the cell-mediated immunity in the body, making the body more susceptible to infections (Smaglik, 2000).

**White Blood cells status (WBC)**

The range of total WBC count in this study group was not different from what is recorded from that normal population reported by Odunukwe et al (2005). This could be as a result of leucocytosis that may follow any opportunistic infection, which may have masked the leucopenia that was suppressed to have been recorded at baseline. During the course of treatment while the immunity was improving, the haemopoietetic cells were also recovering with resultant unchanging count; hence there was no significant difference between leucocyte counts at baseline.

**Absolute lymphocyte count status**

The WHO has recommended the use of absolute lymphocyte count (ALC) as a potential marker for immunosuppression where CD4+ count is unavailable. However, there are
conflicting reports on the usefulness of ALC as a surrogate marker for CD4+ counts in patients with HIV/AIDS, more so, in patients with HIV-associated tuberculosis (TB) (Jibrin et al., 2006).

**Lymphocyte**

The most common finding in HIV infection over time is actually lymphopenia. The previous studies attributed this to different phenomena over the natural history of the infection (Douek et al., 2003). Early in HIV infection, there is viral destruction of selected memory T-cell populations, followed by a combination of profound increases in overall memory T-cell turnover, damage to the thymus and other lymphoid tissues, and ultimately, physiologic limitations in peripheral T-cell renewal. If lymphocytosis is evident, there should be concern regarding concomitant HTLV-1 infection, which is often seen in certain groups in specific geographic areas (Watanabe, 1997).

**Neutropenia**

Causes of low absolute neutrophil counts in HIV patients include inhibition of granulopoiesis by the virus itself, marrow infiltration by infectious organisms or neoplasia, adverse drug effects, autoimmune neutropenia, and hypersplenism (Coyle, 1997). Treatment of neutropenia includes initiation of antibiotic therapy for fever or other overt evidence of infection; antiretroviral therapy for individuals who have untreated HIV infection; withdrawal of potential offending drugs.

**Thrombocytopenia**

An association between HIV and thrombocytopenia was first described by Morris et al., (1982). The most common cause of this complication is now known to be immune thrombocytopenic purpura (ITP), which occurs in 30% or more of patients with AIDS (Nardi et al., 2000).
Erythrocyte Sedimentation Rate status

These effects on HIV/AIDS on hematological parameters were also indicated in a previous study on the effect of anti-retroviral therapy on hematological profile of people living with HIV/AIDS (Erhabor et al., 2006) while about 95% of the patients had ESR value greater than 40 mm/hr, and lymphopenia in 24.3% agree with WHO document on clinical staging of HIV/AIDS for adults and adolescents, which ascertained both lymphopenia and CD4 deletion in HIV/AIDS (Amballi et al., 2007). The prominent elevation of ESR in all these patients is not surprising. Although the ESR is neither sensitive nor specific when used as a general screening test, it is usually elevated in the presence of infectious diseases (Smith and Samadian, 1994) chronic illness (Frank et al., 2001). One study from Japan suggested that (Yanagiasawa et al., 1996) the erythrocyte sedimentation rate and related factors that are influence ESR in 326 patients with pulmonary tuberculosis. Receiver-operator characteristic curve analysis confirmed that ESR is useful among patients with pulmonary tuberculosis. It is suggested that may be under the influence of in apparent infection decreased ESR reported at the 24th week further confirmed the clinical progress in the patients. ESR is usually increased in febrile conditions therefore on treatment with ART drugs. There was improved immune status and that may results in decrease opportunistic infections including malaria attacks with subsequent decrease in the ESR which was significantly reduce at the 24th week (Odunukwe et al., 2005).

Packed Cell Volume status

Packed Cell Volume (PCV) and total white blood count was lowered significantly in this study group reported by Awodu et al., (2007). The packed cell volume significantly increased by the 8th week of therapy.
Biochemistry

The malnutrition status and the associated micronutrient deficiency predisposes to the development of tuberculosis at the same time tuberculosis often exacerbates malnutrition. The nutritional status of pulmonary tuberculosis patients can be assessed by various parameters such as trace elements zinc, serum albumin, and Body mass index. The results of more than three decades of work zinc rapidly diminish antibody and cell-mediated responses in both humans and animals.

Nutritional status is commonly stated to be a factor that affects the acquisition and development of infection in patients in hospital (Bowell, 1992, & Kingsley, 1992). Studies shows that infection rates increase in people with abnormal nutritional factors (factors adversely affect nutritional status), which means nutrition has a role to play in the prevention of infection (Gorse et al., 1989, & Shireff, 1990). In general, the immune system works by engulfing or killing infectious agents, such as bacteria, or cells containing infectious agents, such as viruses (Linnemeyer, 1993). Minerals are needed for all process in the body, usually in small quantities. Some mineral salts required in immune function.

Zinc

Zinc is generally involved in the production of energy and in the metabolism of some components in the diet (Hambidge, 2000). It also has a part to play in several functions in the body including immunity. Zinc has a pivotal role to play in the efficiency of the immune system. In particularly, it has a role in conferring biological activity to the hormone thymulin that is produced by the thymus (Mocchegiani and Muzzioli, 2000) as zinc is required for normal thymus function. Zinc deficiency quickly leads to a reduced antibody and cell mediated response. It can greatly alter people’s immune response, leading to infection rate. However, zinc supplementation can rapidly improve function
in those with a zinc deficiency although this supplementation should not be excessive otherwise it can increase the excretion of copper from the body (Westwood, 1997).

**Nutritional status of Albumin**

The nutritional status of pulmonary tuberculosis patients can be assessed by serum albumin. The three classical plasma proteins are albumin, globulin and fibrinogen. Albumin is synthesized in liver and has a molecular weight about 68000. It has two major functions they are

a) Maintaining the colloidal osmotic tension of blood.

b) Help in transport of substance like bilurubin, thyroxine and drugs.

The concentration of serum albumin and zinc were lower in malnourished TB patients (Karyadi et al., 2000) than in well-nourished healthy controls. Malnutrition per se had a more pronounced effect on serum albumin concentration in TB patients.

The nutritional status assessed by measuring weight, height, mid-upper arm circumference, skin fold thickness and serum albumin was significantly lower in patients with active pulmonary tuberculosis compared with healthy controls. These data corroborate those found in England (Onwubalili, 1988), India (Saha and Rao, 1989) and Japan (Tsukaguchi et al., 1991). As Karyadi et al., (2000) study revealed that TB patients had significantly lower BMI, skin fold thickness and serum albumin concentration than healthy controls.

As a result serum albumin concentration in malnourished patients was lower than that it will well-nourished healthy controls. Lower values of transthyretin (previously referred to as prealbumin) and retinol-binding protein were reported in the Indian and Japanese studies. The poorer nutritional status of the patients with pulmonary tuberculosis may be anorexia (Hopewell, 1994), impaired absorption of nutrients or increased catabolism. Energy and nutritional intake tended to be lower in TB patients than in controls, but the
difference were not significant. On the other hand, patients and controls may have similar food habits and food intake because their socioeconomic background and living conditions are similar.

Thus, infectious disease such as TB may lead to impaired absorption and increased rates of metabolism (Ginzburg and Dadamukhamedov, 1990 & Ulijaszek, 1997). The disease-induced production of cytokines such as interleukin-6 and tumor necrosis factor-α may induce fever, hepatic synthesis of acute phase reactant proteins, inhibit production of serum and cause dramatic shifts in plasma concentration of certain essential micronutrients (Beisel, 1998).

TB is probably associated with more severe malnutrition than other chronic illness; in the Indian study (Saha and Rao, 1989) the nutritional status of the patients with TB was worse than that of those with leprosy. Several factors increase a person’s risk of infection, including nutritional status. Make a list of people who you think would be at increased risk of having poor nutritional status.

**HIV and Nutrition**

**Link between immune integrity and nutritional status**

Nutritional deficiency may be the common cause of secondary immunodeficiency status in humans (Chandra and Newberine, 1977). Early studies made it clear that suboptimal nutritive status associated with an inadequate diet or with disease in which nutritional status is altered could significantly impair host defense systems (Keen and Gershwin, 1990).

The human immune system is the body’s most powerful defense against HIV infection and requires appropriate nutritional to function properly. Nutritional supplementation is a crucial component for an optimal HIV treatment regimen. It also provides support in a few key areas essential for battling HIV. Vitamins and nutritional supplements
counteract the increased oxidative stress produced by the activated immune system battling HIV.

**Role of Zinc in immunity** Zinc is the generally involved in the production of energy and in the metabolism of some components of the diet (Hambidge, 2000). It also has a part to play in several functions in the body including immunity. Zinc has a pivotal role to play in the efficiency of the immune system. In particularly it has a role in conferring biological activity to the hormone thymulin that is produced by the thymus (Mocchegiani and Muzzioli, 2000). Zinc is required for normal thymus function.

Zinc deficiency quickly leads to a reduced antibody and cell mediated response. It can greatly alter people’s immune response, leading to increased infection rates (Fraker, 2000). Some zinc deficiency syndrome such as acrodermatitis enteropathica, can lead to compromised T-cell function (Hambidge, 2000). Zinc deficiency can have profound effects on practically all aspects of the immune system, including hyperplasia of lymphoid tissues, lowered lymphocyte counts, depressed humoral and cell-mediated immunity, impaired delayed type hypersensitive reactions, and decreased phagocytic function of neutrophils (Tang, 1996).

**Role Zinc in HIV and TB**

Increasing intake of risk of Zinc was also associated with an increased risk of progression to AIDS (Graham, 1991). Chandra (1991) found that this relatively large amount of zinc supplementation was associated with significant impairment of lymphocyte and polymorphonuclear leukocyte function. Zinc has been recognized as a constituent of prime important in a variety of metallo-enzyme systems and biochemical pathways essential for protein synthesis and essential in vitamin A metabolism (Smith, 1973) because it is required to mobilize vitamin A from the liver. The pivotal role of zinc in the therapy of persistent wound and ulcer was first observed by (Poriesm, 1967).
Zinc deficiency leads to affects of host defense in a variety of ways. It results in decreased phagocytosis and leads to a reduced number of circulating T cells and reduced tuberculin (purified protein derivate) reactivity (McMurray, 1990) and cell mediated delayed immune response may be impaired as evidenced by a lack of response of circulating lymphocyte to phyto-haeaggulutinin (Kaushal, 1987).

It is well known that malnutrition is a predisposing factor to decrease zinc levels, which results in reduction of thymulin activity, proliferation response of lymphocyte in the presence of mitogen and nutrophil chemotaxis (Chandra, 1991).