CHAPTER II

REVIEW

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The world came to know for the first time about a new disease when the American scientists had published articles in the prestigious medical Journal The New England Journal of Medicine on 10th December, 1981. The diseases were reported in Los Angeles and subsequently in New-York and California in previously healthy male homosexuals who suffered from Pneumocystis Carinii Pneumonia (PCP) and Kaposi’s Sarcoma (KS) with clinical and laboratory evidence of immune system dysfunction (Centre for Disease Control, 1981a, 1981b; Gottlieb, et al, 1981; Ansary, et al, 1989). Among a large number of homosexuals who are also called Gayman, opportunistic infections caused by microorganisms that rarely give rise diseases in persons with normal immune defence mechanism were also reported (National Academy of Science, 1986a). AIDS is a long, often painful and fatal disease that develops in people up to a decade or more after they have been infected by the Human-Immuno-deficiency Virus (HIV). AIDS is the late, stage of HIV infection. It has got no cure, no effective treatment, no vaccine for its prevention till date. The only vaccine available against AIDS to day is education. AIDS stands for Acquired Immuno Deficiency Syndrome .HIV stands for Human Immuno deficiency Virus, the virus that causes AIDS. Since HIV is the causative organism for AIDS, sometime it is called AIDS virus. The virus was isolated in 1983 by Dr.Luc Montagnier and his team at the Pasteur Institute of Paris. HIV has a diameter of 100nm
(1nm=1 million of a millimeter) and 230 million virions can fit in just one fullstop. Body fluids which are associated with HIV transmissions are: blood, semen, vaginal fluid, breast milk and other body fluids containing blood. There are additional body fluids that may transmit the virus that health care workers may come into contact with: Cerebrospinal fluid surrounding the brain and the spinal cord, synovial fluid surrounding bone joints, amniotic fluid surrounding a foetus.

By early 1982, the disease was known by a variety of names and acronyms. Some called it Gay plaque. Others called it GRID, for the gay-related immune deficiency. When the disease was detected in groups other than gays such as intravenous drug users, blood transfusion patients and haemophiliacs (Centre for Disease Control, 1982), the staff members at the Centre for Disease Control (CDC) refused to call it GRID because they were aware that the disease was not restricted to homosexuals only. To solve the problem of nomenclature, the experts met under the aegis of CDC in 1982 and came out with a resolution to name the disease AIDS, an acronym for Acquired Immunodeficiency Syndrome (Shilts, 1987). Among the heterosexual individuals, the first AIDS cases were recognized from Central Africa and Haiti in 1983 (ASTPHLD, 1994). In India, the first AIDS case was detected in 1987 (NACO's Newsletter, 1992).

2.1 ORIGIN OF HIV

Almost immediately after first case of AIDS was reported in 1981, researchers at the CDC began tracking the disease backward in time to discover its origin. They ultimately determined that the first cases of AIDS in the United States of America probably occurred in 1977 (Bigger, et al., 1988). Several reports of cases resembling AIDS both
clinically and immunologically have appeared in the literature (Katner and Pankey, 1987; Huminer, et al. 1987).

Another report rather convincing is that the first case of AIDS in united States may be dated back to the 1960s. This was known when a 15 year old boy who had anal sex was found to have been infected with HIV (Garry, et al. 1988). So, it is believed that HIV or a genetically related virus may have entered several communities before the current epidemic. However, the actual origin still remains undecided. But different school of thoughts have given different opinions regarding its origin.

One school of thought believed that HIV were existing for decades, nestled in remote regions of Africa and limited to small, relatively isolated population (National Academy of Sciences, 1989). The social mores of those populations may not have been conducive to the rapid spread of the disease, and the few cases that did develop could likely have escaped detection against the backdrop of multiple life threatening infections that are common in Africa.

An alternative theory suggests that the original source of the AIDS virus was an animal. The African green monkey has been singled out as a prime suspect with the hypothesis that somehow the virus mutated and entered human population when monkeys bite hunters in their attempt to capture them for food (National Academy of Science, 1986 b).

Several hypotheses have also been postulated to explain the possible route of transmission from monkey to human. One such hypothesis is that certain practices might have favoured transmission of SIV to humans, which through genetic mutation lead to
emergence of HIV-I and HIV-II in humans. One such practice is the sexual customs and culture of the Idjai; who reside on an island in Lake Kivu between Rwanda and Zaire. “To stimulate a man or a woman and induce in them intense sexual activity; male monkey blood (for a man) or female monkey blood (for a woman) was directly inoculated in the pubic areas and also in the thighs and back”.

Several commentators have also pointed out that African Green Monkey were imported from Zaire to Haiti and kept as pets in male houses for prostitution (Altman, 1987). This finding might serve to corroborate with the hypotheses that “HIV infection might have existed and remained stable in central Africa for a long period of time”. Recent evidence of HIV-I infection among the Sangha Pygmy group in the isolated ecosystem of the central African republic as reported by Gonzalez (1987) further support the hypothesis.

Scientists have different theories about the origin of HIV, but none have been proven. The earliest known case of HIV was from a blood sample collected in 1959 from a man in Kinshasha, Democratic Republic of Congo. (how he became infected is not known). Genetic analysis of this blood sample suggests that HIV-1 may have stemmed from a singled virus in the late 1940s or early 1950s. The origin of HIV remains a matter of speculation. (Singh 2004)

Another hypothesis reflects that AIDS and HIV might have made their ways in North America from Africa via Haiti. More specifically, from the early 1960s through mid-1970s, there were considerable migration from Zaire to Haiti, and many of these immigrants are believed to have settled in the United States (DeVita, et al. 1985). Haiti
was also known for its vacation spot for gay Americans who brought the disease home with them and infected the mainland population (Altman, 1987).

A large number majority of Haitians also practiced the Voodoo cult, a religion with a pantheon of Gods. Spirit possession of “hounkans” or Voodoo priests is an element of oodoo cult, where the spirits of the Gods are invoked by the blood sacrifice of bulls, goats, pigs, pigeons and most commonly chickens. The priest and his assistants ingest a portion of the blood sacrifice. In performing the curing ceremonies, the blood from the sacrificed animal may be rubbed on or into a patient’s afflicted part. These cultural practices provide frequent opportunities for exposure of a person to animal blood that may contain a precursor of HIV (Singh, 2004).

In another quarter, there was a belief that AIDS virus was created by Pentagon Experiment which was carried out at Forte Detrick, Maryland in 1987 by Soviet scientists in an attempt to launch biological warfare. Dr. Francis Cress Welsing opined that AIDS was an instrument of genocide likely introduced into blacks and other undesirable groups for the purpose of a systematic depopulation agenda (Welsing, 1987). In conclusion, nobody is definite about the origin of HIV or AIDS.

In India, about 84.53% of HIV infections are through sexual transmission-both heterosexual and homosexual, 3.36 is through sharing of needles and syringes among the injecting drug users, another 3.27% through blood transfusion and 2.14% through prenatal. The factors which make India vulnerable to HIV/AIDS are:

a. Prevalence of commercial sex and casual sex with non-regular sex partners
b. Large migrant population particularly male population—approximately 180 million people migrated per year. There is inter-state migration and also migration from rural to urban areas.
c. Traditional beliefs and practices.
d. Poverty - 35% of the population are below poverty line
e. Low literacy - particularly very low female literacy - 65% literate males: 75.8%, Females: 54.2%,
f. High prevalence of STDs in some states
g. The prevalence of STDS on the national average is 4.2%, Andhra Pradesh -6.7%,
   Gujarat - 7.2%, Madhya Pradesh - 8.2%, Uttar Pradesh - 8.0%, Maharashtra - 4.4%,
h. High prevalence of sexual practices outside marriage-national average: 5.6%, Andhra Pradesh - 13.3%, Gujarat - 9.1%, Goa - 8.2%, Madhya Pradesh - 9.2%, Maharashtra - 11.8%
i. High social stigma for every issue related to sex and sexuality

The epidemic pattern shows great variance across the country. The worst affected states are-

a. Tamil Nadu - 24,667
b. Maharashtra + Mumbai MC - 12,237
c. Andhra Pradesh - 4339
d. Karnataka - 1849
e. Manipur - 1238
f. Nagaland - 370
In the beginning, the HIV positive cases were reported only from people with high risk behaviours like commercial sex workers, injecting drug users, STDs patients. Now the epidemic is no longer confined to these high risk groups. During that time, it was known as “Concentrated epidemic: From the findings of the nation wide sentinel surveillance, it is now understood that the HIV seroprevalence rate among pregnant women attending antenatal clinics are increasing slowly and steadily. Pregnant women are a surrogate representative of the general population. If the HIV seroprevalence rate among pregnant women is 1%, it means that the HIV seroprevalence rate in the adult general population is 1%. The HIV seroprevalence rate among injecting drug users in Manipur was more than 80% in 1997 and more than 44% of the female spouses of IDUs were HIV infected. The HIV seroprevalence rate among pregnant women was more than 1%. Similar situations have been observed in the other stat of Maharastra, Tamil Nadu, Andhra Pradesh, Karnataka and Nagaland where the HIV seroprevalence rate among the high risk population groups is more than 5% and the prevalence among pregnant women is more than 1%. These findings showed that the HIV infection is spreading from the high risk to the general population.

The most common opportunistic infection in India is Tuberculosis, Candidiasis, Cryptococcosis, Cryptosporodiasis, PCP, Kaposi’s Sarcoma, Herpes Simplex, Herpes Zoster, Toxoplasmosis, CMV infection etc (Singh, 2004).

2.1.1 Diagnosis of HIV/AIDS

It is important to distinguished between being infected with HIV and having AIDS. People infected with HIV may take 7-10 years to develop AIDS. During this period, HIV
infected individuals may suffer from a variety of disorders and develop signs which are suggestive of being infected by HIV/AIDS. Since sophisticated blood test may not be available in many developing countries, WHO has laid down clinical criteria for the provisional diagnosis of AIDS.

The presence of at least two major signs and one minor sign can be an indication for AIDS provided other causes of depleted immunity are ruled out.

A. Major Signs

(a) Weight loss >10% of the body weight.

(b) Fever for more than one month, intermittent or continuous.

(c) Chronic diarrhoea for more than one month.

B. Minor Signs

(a) Persistent cough for more than one month

(b) Generalized dermatitis.

(c) Recurrent herpes Zoster.

(d) Oro-pharyngeal candidiasis.

(e) Chronic progressive and disseminated herpes simplex infection

(f) Generalized lymphadenopathy.

All suspected cases of HIV/AIDS should be referred to the Voluntary Counselling and testing centres (VCTCs) for confirmation of diagnosis (Training Manual, 2002).

2.1.2 Natural History of HIV disease

In the study of natural history of HIV infection elsewhere in the world, it has been confirmed that infected individuals passed through a phase in the beginning during which
no signs and symptoms of any associated diseases were detected. This phase of the HIV infection disease is called asymptomatic condition. It is an established fact that there is a spectrum of disease from the point of infection with asymptomatic condition to the development of AIDS with clinical manifestations varying from individual to individual and from community to community taking different courses of Natural History or Clinical Events. While a clear definition exists for AIDS, the intermediate manifestations of HIV infection are poorly classified. Now, we know a little about the natural history of HIV disease. Therefore, study on natural history of HIV infection spectrum is highly needed for better intervention and therapeutic management of AIDS disease.

In fact, in a broader sense, the natural history does not just begin with its biological infection and end with the death of the ailed person. To extend, the problem behaviours for HIV transmission may be considered as the beginning of natural history of HIV disease and the emotional and economic trauma left after the expiry of the patients may also be considered as part and partial of the natural course of HIV disease (AIDS). Before he dies, there is always a chance for transferring HIV and associated illness to the other members in the community through physical contacts with exchange of body fluid conditioned by cultural system or sub-culture. There is always variation among different risk groups as well as in different communities. (Libman and Witzburz, 1993).

**Primary Infection:** Within the individual, HIV infection into the body takes place through mucous membrane or by parental injection. It is uncertain that cells of which kind in the blood or lymphatic tissue is the first to actually become infected. It has been assumed that CD4 + T-cells or monocytes were the initial targets. But, dendrite cells have been demonstrated to be efficient transporters or presenters of HIV to the CD4+T cells
(Fauci and Lane, 1994). Still others specified that for infection to occur the virus needs to get into the target host cells and it does so by attaching itself either to the CD4 receptor on the surface of T4 cell or to Fusin (CXCR) co-receptor. Following the entry into the target host cells, symptoms of the acute HIV syndrome were reported to the patients that last for several weeks. It is highly likely that during this period, most patients develop some degree of viremia which contributes to virus dissemination even though they remain asymptomatic or do not recall experiencing symptoms. To be particular, the clinical features associated with initial phase of infection variably starts from 2 to 4 weeks after infection although it may prolonged sometimes to 36 weeks. It was described originally as mononucleosis (Flu) like illness but now recognized as a distinct clinical entity (Shiv Lal Sengupta, 1993). It is manifested by fever, lymphadenopathy, skin rashes, headache encephalitis and aseptic meningitis, joint pain and muscle pain, at times thrombocytopenia. By this time, the antibodies start appearing in blood and the blood results to positive for HIV antibody. The CD4 + cell count at this stage is not affected much. The diagnosis of primary HIV infection is made by demonstrating HIV antibody seroconversion (Libman and Wizburg, 1993). This episode of initial infection is called Primary Infection. It is these early events which likely play a major role in the subsequent course of infection in that the degree of initial virus replication and seeding organ such as lymph nodes establishes the magnitude of virus burden which the immune system will be required to contain and which will expose susceptible cells to infection.

Clinical Latency Period: A combination of the development of an HIV specific immune response (both humoral and cell mediated) and the efficient trapping of virions in the Follicular dendritic cells (FDC) of the Lymph node germinal centre leads to the
curtailment of viremia, disappearance of symptoms, and the beginning of the so-called Clinical Latency. This lasts for a variable period with a median duration of approximately 10 years (Fauci and Lane, 1994). In adults duration may be longer (Bacchett and Moss, 1989). It is so far reported in India to be 3-5 years. During this period, patients usually recover from illness of primary infection except in few cases.

Secondary Infection and the AIDS: After a variable period of time (i.e. about 10 years or so), the CD4 + cell count falls below a critical level say less than 200 cells per microliter of blood and the patients become highly susceptible to opportunistic diseases. The patients show constitutional signs and symptoms or may develop Secondary Infection which is primarily caused by opportunistic organisms including PCP, CMV and Common bacterial as well as mycobacterial pathogens. The secondary infections are the leading cause of morbidity and mortality in patients with HIV infections. Approximately 80 percent of AIDS patients died as a direct result of secondary infection (Fauci and Lane, 1994). The clinical spectrum of diseases caused by secondary infection is constantly changing as patients live longer and as new and better approaches to treatment and prophylaxis are developed. Recent data have shown that vast majority of death in patients with HIV disease occurred when the CD4 cell count falls below 50/mm³. The common causes of death in America, Africa and other European countries include bacterial infection, PCP, Kaposi’s Sarcoma, wasting syndrome, and lymphoma (Stein, et al. 1992). Early survival data comes from a large cohort study of 5,833 AIDS patients diagnosed before 1986 in New York City (Rothenburg, et al. 1987). One year survival was reported to be approximately 50 percent, and 2-year survival was 30 percent. Women, blacks, and IDUs are shown having shorter survival than men, whites and
homosexuals respectively. However, differences in survival rate may have the results of delayed access to medical care or delayed diagnosis (Libman and Witzburg, 1993).

So far, a clinical manifestation of medical importance has been reported in the construction of natural history of AIDS. The author has so far not come across any study/literature on physical anthropological parameters associated to these clinical events excepting the body weight and arm circumference till the time of designing this study. Among other anthropological variables which may me incorporated to the establishment of natural history of HIV disease, arm circumference yield a relatively reliable estimation of the body mass, the reduction of which is one of the striking mechanism by which the body adjust to inadequate energy intakes. In a similar way, the skin with its adipose tissues beneath it, function as reservoir of fat, a high energy yielding metabolites. The skin with its fat content is highly adaptive and sensitive in the sense that any diseased condition whether of environmental origin or nutritional, may bring drastic changes which can be detected through simple measurement of the skinfold at selected sites such as triceps and biceps, etc. When the food absorption or intake has problem with the opportunistic infection of the GI system after the episode of HIV infection, the stored metabolites (fat) in the muscle and adipose tissues are utilized. If the repletion does not take place quickly it may lead to shrinking of the tissues resulting cachexia or wasting syndrome as often called slim disease in African situation.

In developing countries where AIDS has added to the already existing burden of under nutrition, both among adults and children, very few initiative on need assessment of nutritional status of HIV infected individuals have been taken up (ICMR,1991).

Persons with AIDS often suffer from protein energy malnutrition (Raiten and
Fisher, 1991; Haffeman, et al. 1993). Nutritional intervention through correction of deficiencies and maintenance of good nutritional status are important at all stages of HIV infection spectrum to prevent and/or delay from further deterioration of immunity and progression of the HIV related diseases. Loss of body weight, decreased skinfold thickness, body cell mass depletion, hypoalbuminemia, decreased iron binding capacity of haemoglobin molecules, etc. among persons with HIV disease are commonly reported and associated nutritional problems.

Several methods are now available to assess the nutritional status of which mention may be made of nutritional anthropometry, clinical observations and bio-chemical test, etc. Of all these techniques, bio-chemical test which involved invasive procedures and costly laboratory investigations are hardly feasible although it has been suggested to be more accurate for community based researches. In the field, nutritional anthropometry and clinical examination methods are the most commonly employed techniques as these are required with less time and minimum expenditure. On other hand, unless the measured values are computed into accepted indices and the clinical findings are grouped to explain the various grades of nutritional status, simple measurements and clinical features does not reveal much about malnutrition (Jelliffe, 1966).

2.1.3 Prevention of HIV

Prevention is indisputably the most important objective as no curative drug is universally effective and no affordable prevention vaccine is likely to be neither available in, nor accessible to developing countries in the foreseeable future. Health education and
behaviour modification is the prime focus of action for interrupting transmission. It is therefore important to have an information and education programme for all men and women, including adolescents, especially aimed at those who are at greater risk of HIV infection. It is also important to have facilities for detection and treatment of other sexually transmitted infections and to encourage an environment that promotes free and frank dissemination of information without stigmatization and discrimination against suspected/known cases of HIV/AIDS (Training Manual, 2002). Risky practices like re-use of injection equipment and syringe pulling i.e. the use of left over drugs in particular, were frequently described and observed. Needle and syringe distribution programmes were in place but carrying needles and syringes and particularly drugs could result in being arrested and fined. Fear of rejection and of loss of intimacy made disclosure difficult and was perceived as a major obstacle for condom use among recently diagnosed HIV infected individuals. HIV positive injecting drug users continue to practice HIV risk behaviours. The anti-drug law and the police crack-down policy appeared as critical factors hampering ongoing prevention efforts with needle and syringe distribution programmes in VietNam (Thanh et. Al. 2009).

2.1.4 Trends of Research on HIV and AIDS

Francoise Barrefinoussi working in Montaigner’s Laboratory was the first to peep the others to the post. Working with the lymph node of a patient with early AIDS, she was clearly able to demonstrate the presence of a new virus which was the most likely cause of this dreaded disease-AIDS. Subsequently, the special efforts made by Montaigner’s
and later by Robert Gallo’s groups made it possible to grow the virus in the laboratory in bulk amounts. In 1983, Montaigner and his colleagues, in the Institute of Pasteur (Paris) had confirmed the causative agent and the name Lymphadenopathy Associated Virus (LAV) was given to it. Almost simultaneously in 1984, Robert Gallo and colleagues in USA isolated a retrovirus. They termed it *Human T-cell Lymphotrophic Virus type-III* (HTLV). These two isolates have subsequently been found to be identical, and are now recognized to be the cause of AIDS (Farthing et al, 1987). However, there was a dispute between the two research Institutes to claim to be the first discoverer of AIDS virus. But in 1987, both scientists were given credit for the first discoverer of AIDS virus. But in 1987, both scientists were given credit for the discovery and in 1991, Gallo dropped his claim to have discovered the virus. In meantime, the virus was renamed as Human Immuno deficiency Virus (HIV) by an international team of virologists (Connor and Kingman, 1989). Thus, the causative agent for AIDS was finally discovered to be HIV (National Academy of Sciences, 1986 b)

Today, the molecular structure of HIV and its responses to treatment was unlike that of two decades ago. Much had been advanced in the molecular and genetic variability of HIV. It has been classified into HIV type-1 and 2 (Biberfeld, et al. 1987).

Researches on HIV and AIDS has been undergoing extensively with reference to risky human behaviours in different parts of the globe with implications of public health services. AIDS has been understood not simply as a bio-medical problem but as a complicated psychosocial development too (Kapur and Mukhopadhyay, 1995) requiring multidisciplinary approaches to prevent it from further ramification. Detection of the virus (HIV) in different risk behaviour groups, isolation of the viral component for
further investigation at the genetic level to understand the strain of the virus and the mechanism of the disease, study on the progressive clinical manifestation with molecular changes in the cellular immunity, study on therapeutic intervention of the associated opportunistic infections, changes in the nutritional status in different stages of the HIV infection etc are the priority areas for researches from the angle of bio-medical sciences.

In India, many investigators have studied geographical distribution of HIV among the so-called risky behaviour groups. Many attempts were also made to characterize them with respect to their HIV status. No study independent of the Government has been attempted to explain these data, regional trend of infection and clinical pattern of associated illness (Jain, N. et al. 1994)

Both HIV-I and HIV-II infection were detected in India too (Rubsamen-Waigmann, et al. 1992). Epidemiological study has shown that HIV transmission in India is primarily among heterosexuals fitting the description of pattern-III HIV transmission with alarmingly high prevalence among female sex workers and those men who recently had sexual contact with sex workers (Rodrigues, et al. 1995). However, the pattern has become more complex as the number of infected persons has increased other than the heterosexual type.

Researches on molecular structure of HIV and its variants have been attempted elsewhere in the world for identification of candidate vaccine preparation. Dr Jones Salk, the discoverer of the Polio Vaccine, reported at the eight International Conference in Amsterdam in July, 1992 that “the space of AIDS vaccine will be limited. The vaccines currently under investigation consist of genetically engineered parts of the virus, mainly
from the outer coat. These would be administered by infection and it is known whether this systematically administered HIV immunogens will induce mucosal immunity. There are 4 main types of vaccines currently being considered.-

(a) Sub-unit peptide
(b) Vector Vaccines
(c) Whole killed virus
(d) Live attenuated Virus

All candidate vaccines must go through a series of rigorous tests to make sure that they are safe and effective for humans. After initial laboratory research; there are three main stages of testing-

(a) Preclinical trial
(b) Phase I/II clinical trial
(c) Phase-III clinical trial.

Despite the promise of a number of candidate vaccines, a vaccine may accelerate rather than slow down the disease. Because of this; the vaccine-induced protection vs disease will require trials for many years of duration. Even with a highly efficient preventive vaccine and the best vaccination policy; the number of people with AIDS will continue to grow because of having a base population of millions of people having infected already. HIV prevalence will also continue to increase. Vaccinating all adults will be impossible in the short term given the limited resources. Targeting people at high risk are a possible strategy; but this may increase stigmatization and discrimination. “An AIDS vaccine will be powerful” said June Osborn of the US National Commission on AIDS; but “it would not replace the need for education and counselling” (Singh, 2004).
According to the Director General of the Indian Council of Medical Research (ICMR), the Indian AIDS vaccine is entering phase-I human trials in mid-2004. The efficacy and safety of the vaccine will be tested in a small group of human volunteers during the phase-I. The vaccine is likely to offer 50% protection against the virus. This is not bad considering that most of the vaccines offer only 60% to 70% protection. The vaccine planned for production in India is for the HIV subtype C, which account for 90% of all infections in India. Vaccines for subtype B and E are being produced in western countries and in Thailand.

The first clinical trial of HIV vaccine started in 1986. Since then more than 25 experimental preventive vaccines have been evaluated. Much of the vaccine research is funded by National Institute of Health (NIH), USA, Walter Reed Army Institute of Research in Washington, D.C, and pharmaceutical companies like Chiron, Oasteur Merieux Connaught, and the International AIDS Vaccine Initiative (IAVI).

2.2 TUBERCULOSIS:

Tuberculosis (TB) is an airborne, infectious disease caused by bacteria which primarily affect the lungs. Tuberculosis (TB) has affected mankind for over 5000 years and the disease continues to be a major cause of morbidity and mortality. Although the bacilli has been discovered over a century back in 1882 by Robert Koch, and drugs available for more than 70 years, nearly a third of the world’s population is infected with TB bacilli, i.e. have latent TB, of these 10% have a life time risk of developing to active disease. Poor living conditions, debility and malnutrition predisposes population to disease.
(WHO, 2008). While both preventable and curable, TB remains one of the world's major causes of illness and death, and in 1993, the World Health Organization (WHO) declared TB to be a global health emergency: One-third of the world's population, or two billion people, carry the TB bacteria, more than 9 million of whom become sick each year with "active" TB which can be spread to others. "Latent TB" disease does not spread.

TB disproportionately affects people in resource-poor settings, particularly those in Asia and Africa. More than 90% of new TB cases and deaths occur in developing countries, posing significant challenges to the livelihoods of individuals and developing economies as TB primarily affects people during their most productive years. DOTS, "directly observed treatment, short-course", is the internationally recommended strategy to control TB. DOTS aims to decrease TB-related morbidity, prevent TB deaths, and decrease TB transmission, and there are some promising signs that such efforts are beginning to pay off. TB incidence, prevalence, and mortality rates appear to have declined in recent years while case detection and treatment rates have increased (while the number of people living with TB has increased, it is largely due to population growth). Still, many challenges remain. Poor health systems, limited laboratory capacity for case detection, treatment barriers and complications (unreliable drug supply, patients not completing treatment, or prescribing errors), the relationship between TB and HIV, and the emergence of drug-resistant TB pose serious threats to global TB control. TB is found in every country in the world, but the majority of TB cases are concentrated in developing countries, particularly those in Asia and Africa.
2.2.1 TB Burden in India

TB is one of the known oldest diseases in the world. The causative organism, Mycobacterium Tuberculosis was known for more than 100 years. Transmission of TB is through airborne. The source of infection is a person with TB of the lung who is coughing or sneezing and in whose sputum the offending germ i.e Mycobacterium Tuberculosis is present (Sputum positive). When the person coughs or sneezes, he spreads Mycobacterium tuberculosis into the air in the form of tiny droplets. When a healthy person who comes nearby happens to inhale these tiny droplets, he may contract TB. Most primary infections heal with or without calcification of the primary complex but it may spread through blood or lymphatic system to other parts of the lung or other organs of the body. Effective drugs are available for more than 50 years. Still TB kills more persons than any other infectious diseases.

India is the highest TB burden country globally, accounting for one fifth of the global incidence and 2/3rd of the cases in south East Asia. Nearly 40% of the Indian population is infected with the TB bacillus. Each year, 1.9 million new cases of TB occur in the country, of which about 0.8 million are infectious new smear positive pulmonary TB cases. The estimate of TB incidence in India is based on findings of the nationwide annual risk of TB infection (ARTI) study conducted in 2000-03. The national ARTI was estimated at 1.5% i.e. 75 new smear positive pulmonary TB cases are expected per 100,000 populations annually. The prevalence of TB has been estimated at 3.8 million bacillary cases for the year 2000, by the expert group of Govt. of India (Gopi et al, 2005). By any measure the burden of TB in India is staggering. More than 80% of the burden of tuberculosis is due to premature death, as measured in terms of disability-adjusted life
years (DALYs) lost. Every day, more than 5,000 people develop TB disease, and nearly 1,000 people die of TB, i.e. 2 deaths every 3 minutes. As per WHO estimates in 2006, nearly 322,000 persons in India died of tuberculosis (mortality rate 28 per 100,000 persons), which was estimated at over 500,000 annually at the beginning of the revised national TB control programme (WHO, 2006). In 1995, there were about 9 million new cases of TB with 3 million deaths in the world. HIV epidemic increases the burden of TB. Today, more than two billion people are infected with TB in the world of which 95% are in developing countries. 98% of all TB death and 25% of all avoidable deaths due to TB are happening in the developing countries. Out of these deaths, 75% are in the economically productive age group (15-50 years). More than 42 million people in the world are infected with HIV, of which around 5-6 million are co-infected with both HIV and TB. 70% of the HIV/TB dual infections are in Sub Saharan Africa, 20% are in Asia. The incidence of TB in some countries has doubled during the last ten years. HIV is most powerful factor known to increase progression of TB infection to diseases. In 1993 the World Health Organization (WHO) declared a “global emergency” and called countries to adopt DOTS as a TB control strategy. Each day approximately 2000 people die due to TB in South East Asia. Each year, nearly 3 million cases and 750,000 deaths due to TB are estimated to occur in the region. Five countries namely- India, Bangladesh, Indonesia, Myanmar and Thailand account for 95% of the total TB cases in the region. Each year, TB kills at least 250,000 people in the region. The South East Asia region accounts for 38% of the world’s burden with 3 million new TB cases and nearly three quarters of a million deaths every year. The incidence is highest in the 20-45 years age group; thus seriously affecting the economic development. The economic lost due to TB is estimated
to be 4 billion US dollar every year. TB carriers who are infected with HIV are 30-50 times more likely to develop active TB than those without HIV. The presence of TB may result in more rapid progression of HIV to AIDS.

The main reasons for the increasing global TB burden are the following:

(a) Poverty and the widening gap between the rich and the poor in various populations.
(b) Inadequate health coverage and poor access to health care
(c) Neglect or inadequate case detection, diagnosis and cure
(d) Changing demography-increasing population, migration, overcrowding etc
(e) HIV epidemic
(f) TB is more common in poor and malnourished people, but spread without regard for socio-economic status
(g) Access to treatment is more difficult for the poor
(h) Lack of political leadership and commitment.

Direct costs of TB in India are estimated to be around $300 million, not including economic cost of deaths. The above estimated include loose of 100 million work days. Direct expenditure incurred by the patient themselves for treatment comes more than $100 million annually. More than 300,000 children leave school as a result of parents’ TB. More than 1,00,000 women are rejected by families on account of TB (Singh, 2004). Revised National Tuberculosis Control Programme (RNTCP Phase II-2006-2011) is a step towards achieving the TB-related UN Millennium Development Goals. The programme has developed a ‘Strategic Vision for TB Control for the Country up to 2015’, under which it aims to achieve and maintain a cure rate of at least 85% in new
sputum positive pulmonary TB patients, and detection of at least 70% of such cases (TB India, 2009).

2.2.2 TB in Manipur

Revised National Tuberculosis Control Programme covered 26 lakh population in Manipur and out of 1064 lakh new smear positive cases reported in 2007, 82.6% was cured, 3.1% failure and 9.5% was defaulted and among 1893 lakh new smear negative, 86.2% completed the treatment, 2.8% died, 0.1% failure and 10.7% defaulted. District wise performance of RNTCP in Manipur reveals that Imphal West has the highest population covered (5 lakh) while Chandel and Tamenglong district has the least coverage of 1 lakh each.

2.2.3 Signs and Symptoms of TB

The typical signs and symptoms of TB are as follows-

(a) Cough for more than three weeks with or without low grade fever sweats

(b) Loose of appetite.

(c) Loss of weight

(d) Chest pain

(e) Haemoptysis (blood in sputum)

Diagnosis of Pulmonary TB depends on three specimens of spectrum.

(a) Sputum specimen on the first visit
(b) Early morning collection of sputum by the patients on the next day

(c) Spot specimen on second visit.

There are some important points for diagnosis-

(a) Tuberculin skin test

(b) Past history of TB treatment

(c) Assess risk factor-incomplete previous treatment, close contact

(d) Anti retroviral treatment

(e) History of pregnancy for female patients

(f) Investigations

(g) Sputum smear examination, culture if possible

(h) X-ray

Early and prompt initiation of effective treatment increases the probability that a patient with HIV who develops TB will be cured of this disease. TB treatment also quickly renders the patient non-infectious to others and minimizes the risk to death. Patients' with TB and unknown HIV status should be counselled and offered HIV testing. HIV infected patients undergoing TB treatment should be evaluated for antiretroviral therapy. Some patients of TB with HIV are candidates for concurrent administration of anti tubercular and anti retroviral drug therapies. Health care providers for TB programme and AIDS programme must strive to promote co-ordination in the treatment of TB+HIV patients.

Treatment regimen comprises of two phases-

(a) Intensive phase

(b) Continuation phase
The intensive phase includes daily supervised treatment with four drugs for two months—Isioniazide, Rifampicin, Pyrazinamide and Ethambutol.

Ethambutol and streptomycin can be interchanged where either one of the two drugs is not available. The continuation phase means daily supervised treatment with Isoniazide and Rifampicin for four months.

2.2.4 Diagnosis of Pulmonary Tuberculosis

Clinical features: In this aspect there seems very less difference between HIV positive and HIV negative patients. However, among HIV-infected patients, cough is reported less frequently, probably because there is cavitations, inflammation and endobronchial irritation as a result of decrease in cell-mediated immunity. Similarly, haemoptysis, which results from caseous necrosis of the bronchial arteries, is less common in HIV-infected patients.

Sputum Microscopy: It is the cornerstone to diagnosis of TB even in high HIV-prevalence areas. Patients suspected of having TB should have three sputum specimens examined for AFB. HIV-infected, smear positive patients tend to excrete significantly fewer organisms per ml of sputum than HIV-negative patients, which can lead to AFB being missed if the appropriate number of sputum samples as well as high power fields is not examined by microscopy.

Chest X-ray: Needed for persons suspected of having TB who are smear-negative and who do not respond to 10-14 days of antibiotics. No radiographic pattern is diagnostic of
TB, although the classical hallmarks of the disease are cavitations, apical distribution, pulmonary fibrosis, shrinkage and calcification. HIV infected persons with a relatively well preserved immune function will show these typical features. However, as immune suppression worsens, chest X-rays more often show typical findings such as pulmonary infiltrates affecting the lower lobes, intrathoracic lymphadenopathy and sometimes a normal chest radiograph.

2.2.5 AIDS and TB

The emergence and spread of HIV and drug-resistant tuberculosis further threaten to complicate the tuberculosis situation in the country. India, the third highest HIV burdened country, had an estimated 2.31 million (0.36% of adult population in the country) people living with HIV/AIDS (PLHAs) in 2006, emphasizing the enormous challenge ahead (NACO, 2008). All States and Union Territories of the country have reported HIV/AIDS cases. However, the HIV epidemic pattern shows great variance across the country. The worst affected states are Andhra Pradesh, Karnataka, Maharashtra, Manipur, Nagaland and Tamil Nadu. These six states have reported more than 75% of all the AIDS cases in India and are classified as High Prevalence States. Three other states namely Goa, Gujarat and Pondicherry, have been classified as Moderate HIV prevalence states. Even within then high prevalence states, there are districts which have ante-natal HIV levels below 1%. Tuberculosis is one of the earliest opportunistic diseases to develop amongst persons infected with HIV. HIV infection is the most powerful risk factor for the progression of TB infection to TB disease, of those infected with TB bacilli. An HIV
positive person also infected with TB bacilli has 50-60% life time risk of developing TB disease, as compared to an HIV negative person who has a 10% life-time risk of developing TB disease (WHO, 2004) In India, the TB epidemic in the country is predominantly driven by the non-HIV positive TB cases. It is estimated that nearly 5% of the TB patients are HIV infected. The periodic HIV survey in TB patients, which was carried out in 4 districts in 2005-06, was scaled up to 15 districts in 2006-07. The 2007 survey represents the most detailed evaluation to date of HIV epidemiology among TB patients in India. The survey demonstrated that the prevalence of HIV among TB patients varied substantially across the geographic regions between 1% and 13.8% across the 15 surveyed districts. TB and HIV are frequently referred to as co- or dual-epidemics due to their high rate of co-infection. The HIV epidemic has been largely responsible for the resurgence of TB starting in the 1980s, as HIV weakens the immune system, increasing the likelihood that an individual will become infected and develops active TB. Additionally, TB is harder to diagnose and progresses more rapidly in someone with HIV. As a result, TB is a leading cause of death among people with HIV, especially in developing countries. An estimated 1.4 million of the 9.3 million new TB cases were also HIV positive in 2007. 79% of co-infections were in Africa, the region hardest hit by HIV. South Africa alone accounted for 31% of the total number of HIV-positive TB cases in the Africa region. Of the 1.8 million people who died from TB in 2007, an estimated 4,56,000 were HIV positive (WHO, 2005). The diagnosis of TB in HIV infected patients may be difficult due to lack of typical symptoms or paucity of findings in the chest x-ray. The starting point for diagnosis with unusual clinical and radiological findings is a positive tuberculin test. All patients with positive tuberculin test should be evaluated to
rule out active TB. If the person is not infected with HIV, the lifetime risk of developing TB is about 10%. But if the person is infected with HIV, the lifetime risk of developing TB is between 50% to 60%. (Singh, 2004). Pulmonary tuberculosis is the most common manifestation of tuberculosis in adults infected with HIV. Tuberculosis can occur at any point in the course of progression of HIV infection. The clinical pattern of tuberculosis correlates with the patient's immune status. If TB occurs in the early stages of HIV infection when immunity is only partially immuno-compromised, the features are more typical of tuberculosis, commonly with upper lobe cavitations, and the disease resembles that seen in pre-HIV era. As immune deficiency advances, HIV-infected patients present with atypical pulmonary disease resembling primary tuberculosis or extra pulmonary and disseminated disease, commonly with hilar adenopathy and lower lobe infection. It is important to note that HIV-infected patients with pulmonary TB may have a normal chest X-ray. Mycobacterium TB infection develops when the CD4 count falls below 400/ml as compared to other infections which develop when the CD4 counts falls much below 250/ml. Thus it means that one of the earlier infections to occur in an HIV positive is Mycobacterium Tuberculosis. It may therefore happen that TB is diagnosed much earlier than the HIV infection in such patients.

2.2.6 Treatment of TB in HIV-infected patients

In general, anti-TB treatment is the same for HIV-infected and HIV-negative TB patients, with the exception of the use of thiacetazone. Thiacetazone causes severe cutaneous reactions. Exfoliative Dermatitis or Steven Johnson’s syndrome may occur and
can be fatal. Stev Johnson's Syndrome is a special type of hypersensitivity reaction. It is characterized by generalized bullous eruption, sometimes haemorrhagic involving skin and mucous membranes. In HIV positive patients, cutaneous reaction with Thiacetazone occurs more frequently and is more severe. Ethambutol should therefore be used instead in patients known or suspected of having HIV infection. Adequate sterilization and safe disposal of syringes and needles should be ensured whenever streptomycin is administered.

Response to treatment: Patients who complete treatment show the same clinical, radiographic and microbiological response to short-course treatment irrespective of whether they are HIV positive or negative. The only exception was that on an average, weight gain was less in HIV-positive than in HIV-negative patients.

Case fatality: HIV-infected patients have a much higher mortality during and after anti-TB treatment compared with HIV-negative patients. Approximately 30% of HIV-infected, smear positive TB patients die within 12 months of starting treatment, and about 25% of those who complete treatment will die during the next 12 months. This is partly due to TB itself, but largely due to other HIV-related problems like septicaemia, diarrhoea, pneumonia, anaemia, Kaposi's sarcoma, cryptoccal meningitis. HIV-infected smear-negative pulmonary TB patients may have a worse prognosis than HIV-positive patients with smear-positive Pulmonary TB. Delays in the diagnosis of TB have been associated with worse outcomes, so initiation of treatment as soon as TB is suspected is very important. Case fatality is lower in HIV-infected TB patients treated with short-course treatment than with the standard 12-month treatment regimens which do not include rifampicin. This is partly because short-course treatment is more effective, but
may also be related to the fact that rifampicin has broad spectrum antibacterial activity. This may decrease deaths due to HIV-related bacterial infections during anti-TB treatment.

2.2.7 Drug Resistance

Outbreaks of multi-drug resistant TB have been reported in patients with HIV infection. HIV itself does not cause multi-drug resistant TB, but it fuels the spread of this dangerous condition by increasing susceptibility to infection and accelerating the progression from infection to disease.

Treatment with DOTS for HIV-infected TB patients not only improves their quality of life but also has been shown to prolong their life span by an average of two years. DOTS can prevent emergence of MDR-TB and also will reverse the trend of MDR-TB. Drug-resistant TB has emerged as a major challenge facing TB-control efforts. The number of drug-resistant TB cases has risen in recent years, and resistant cases have been identified across the world. There are two forms of drug-resistant TB: multidrug-resistant TB (MDR-TB), which fails to respond to standard first line drugs, and extensively drug resistant TB (XDR-TB), which fails to respond to both first and second line drugs. MDR-TB and XDR-TB result from inconsistent or partial treatment, incorrect prescribing, and/or shortages or interruptions in the drug supply chain. In 2007, there were an estimated 5,11,000 cases of MDR-TB, the highest to date. By the end of 2008, XDR-TB had been reported in 55 countries and territories. In an outbreak in South Africa, 52 out of 53 people infected with XDR-TB died within an average of 3 weeks of being
diagnosed. The highest numbers of MDR-TB were found in India, China and the Russian Federation. In some areas of the former Soviet Union, more than 15% of new cases were MDR-TB. Treatment of MDR-TB can take much longer and be up to 100 times more expensive than standard TB treatment. Currently, XDR-TB is virtually untreatable (WHO, 2008). The emergence of resistance to drugs used to treat TB, and particularly MDR-TB, has become a significant public health problem in a number of countries and an obstacle to effective TB control. Several small surveys conducted across the country have shown the prevalence rates of MDR-TB in the country at around 3% among new cases, and 12% among retreatment cases. A large scale population based survey in the states of Gujarat and Maharashtra has also indicated similar resistance levels (new-3% and retreatment- 12-17%). Available information suggests that the proportion of MDR-TB is relatively low in India. However, this translates into a large absolute number of cases, with an estimated annual incidence of 1,10,000 cases of MDR-TB. XDR-TB has been reported in India by isolated studies with non-representative and highly selected clinical samples. The magnitude of the problem remains to be determined due to the absence of laboratories capable of conducting quality assured second line Drug Susceptibility Testing (DST). However, what is frightening is the potential threat of XDR-TB in India, with unregulated availability and injudicious use of the second line drugs along with non-existence of systems to ensure standardized regimens and treatment adherence for MDR-TB outside the national programme. The problem of MDR and XDR-TB in India and across the world raises the possibility that the current TB epidemic of mostly drug susceptible TB will be replaced with a form of TB with severely restricted treatment options. If this happens it would jeopardize the progress made in recent years to
control TB globally as well as in India and would also put at risk the plans to progress towards a world where TB ceases to be a public health problem (Tuberculosis Research Centre, 2003).

2.2.8 Recurrence

When TB recurs after previous cure, there are 2 possibilities:

(a) True relapse-reactivation of persisters not killed by an anti-TB drugs
(b) Re-infection due to re-exposure to another source of infection.

The proportions of recurrences due to these 2 possibilities are not known.

2.2.9 Relapse

The relapse rate of TB is low in HIV-infected TB patients who complete a fully rifampicin containing short-course treatment regimen. The use of non-rifampicin containing regimens and treatment interruptions due to drug reactions are associated with an increased risk of relapse of TB. Extending the duration of treatment regimen from 6 to 12 months in HIV-infected TB patients further reduces the frequency of relapse. However, this difference is marginal and, given the expense, toxicity and difficulty of longer duration, most programmes treat HIV-infected patients for 6 or at the most 9 months. The relapse rate is higher if they are treated with the standard treatment regimen or a short-course treatment regimen which uses ethambutol and INH during the continuation phase. Similarly relapse is more in self administered treatment as compared
to directly observed treatment (Training Manual, 2002). Retrospective study conducted by Nahid P et al. (2007) reported that, duration of mean treatment was significantly longer for HIV infected patients, 10.2 vs 8.4 months (p<0.001). Relapse rates were higher in HIV infected individuals, 9.3 per 100 person-years versus 1.0 (p<0.001). Increase relapse rates were also seen in HIV infected individuals who were treated with a standard 6-month rifamycin based regimen compared to those who were treated for longer (HR 4.33; P=0.02) and those who received intermittent versus daily therapy (HR 4.12; P=0.04). Highly active anti-retroviral therapy was associated with faster culture negativity and improved survival. The author concluded that “standard 6-month therapy may be insufficient to prevent relapse in patients with HIV”. This study challenges current recommendations regarding the preferred length of TB treatment in patients co-infected with HIV. Concerning the final outcome of TB treatment, it should be stressed that the failure rate in HIV seropositive patients was much greater than in HIV negative cohorts, in spite of the use of newer and more effective antiretroviral drugs which were available at the time this research was conducted. Actually, there is no consensus about the role of co-infection with HIV as a risk factor associated with an unfavourable treatment outcome. Studies found no significant difference in cure rates between TB patients with and without HIV infection. On the other hand, in another series co-infection with HIV was a risk factor associated with an unfavourable treatment outcome and the mortality rate for TB patients with HIV infection was twice as high as for HIV seronegative patients. On the other hand, the mortality rate for HIV seronegative patients with tuberculosis is twice as great as for those without HIV. Illness severity is the major cause of treatment failure among co-infected patients. However, lack of compliance to a
treatment regime also plays an important role. The simultaneous use of multiple drugs and the common side effects partly explains why patients fail to comply with the treatment. Considering all these causes of treatment failure, emphasis should be placed on development of new strategies. (Isabela et al. 2004.

2.3 SIDE EFFECTS OF ANTI-TB DRUGS IN TB/HIV PATIENTS

Adverse drug reactions are more common in HIV-positive than in HIV-negative TB patients. Risk of drug reaction increases with increased immuno-compromised. Most reactions occur in the first 2 months of treatment.

(a) Skin reaction is the commonest reaction. Fever often precedes and accompanies the rash. Mucous membrane involvement is common. The usual drug responsible is thiacetazone. Streptomycin and rifampicin are sometimes to blame. Severe skin reactions, which may be fatal, include exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis.

(b) Other reactions: The commonest reactions necessitating change in treatment include GI disturbances and hepatitis. There may be an increased risk of rifampicin associated shock and thrombocytopenia.
2.3.1 Anti Tuberculosis therapy and Antiretroviral therapy

Till date no cure is available for HIV/AIDS. Only the opportunistic infections in HIV positive patients are effective in slowing down the action of the virus and prolonging life. These drugs are the -

(a) Protease inhibitors- Ritonavir, Indinavir, Saquinavir, Nelfinavir.

(b) Nucleoside reverse transcriptase inhibitors – Zidovudine, Didanosine, Zalcitabine, Stavudine, Lamivudine and Abacavir can be safely co-administered with antituberculosis drugs.

(c) Non-nucleoside reverse transcriptase inhibitors- Nevirapine, Delavirdine, Thiober

Nucleoside reverse transcriptase inhibitors like Zidovudine, Didanosine, Zalcitabine, Stavudine, Lamivudine and Abacavir can be safely co-administered with antituberculosis drugs. Co-administration of Rifampicin with any of the protease inhibitors or non-nucleoside reverse transcriptase inhibitor is contraindicated. Protease inhibitors and non-nucleoside reverse transcriptase inhibitor may inhibit or induce cytochrome P-450 isoenzymes and thus these drugs may alter the serum concentration of rifampicins. Rifamycins induce cytochrome P-450 and may substantially decrease blood levels of the antiretroviral drugs resulting in the potential development of resistance. Rifabutin is a less potent Cytochrome-450 inducer than rifampicin and thus can be used concurrently with the NNRTIs (eg nevirapine, efavirenz) or with certain protease inhibitors (eg indinavir, nelfinavir). Rifabutin is at present not available in India. Isoniazide, Ethambutol, Pyrazinamide and Streptomycin can be concurrently used with protease inhibitors or non-nucleoside reverse transcriptase inhibitors. If protease inhibitor or non-nucleoside reverse transcriptase inhibitor is to be stated after giving Rifampicin, then at
least two weeks should elapse after the last dose of Rifampicin. This time gap is necessary for reduction of the enzymes inducing activity of Rifampicin prior to commencing of antiretroviral drugs (Training Manual, 2002). Studies conducted by Fiske et al.2009 reported that excess alcohol use represents a significant challenge in tuberculosis control. Whether alcohol use enhances transmission of Mycobacterium tuberculosis is not known. Cases with excess alcohol use were more likely to have pulmonary tuberculosis compared with cases without excess alcohol use (92.5% Vs 72.2%, P<0.0001). Among pulmonary cases, excess alcohol use was associated with cavities on chest radiograph (36.8% Vs 28.2%, P<0.0001) and positive acid-fast sputum smears (65.9% Vs 45.8%, P<0.0001). In a comparative study conducted by Sidhu et al.1975, among one hundred and fifty TB patients from the Tuberculosis and Chest Disease, Department Medical College, Patiala, and normal population of the same ages from Patiala district, the TB patients and the normal individuals do not differ significantly in height, lower extremity length, bicristal breadth and humerus bicondylar diameter. However, the values of weight, sitting height, biacromial diameter, chest circumference and femur bicondylar diameter are significantly less among the patients.

2.3.2 Factors associated with TB treatment failures

Treatment failures may be due to

(a) Large mycobacterium load
(b) Non-adherence with drug regimen
(c) Inappropriately low medication doses
(d) Impaired absorption of drugs

That is why regular review of the progress of treatment is very important on each visit. If the patients develop hepatitis manifested by anorexia, nausea, vomiting, abnormal pain and jaundice, anti-TB medication should be immediately stopped and the patient should immediately consult the treating physician.

2.3.3 Impact of TB on HIV and HIV on TB

The impact of TB on HIV are-

(a) Shortens survival of the patient
(b) Accelerates progression of HIV infection
(c) Cause of death in one-third of HIV cases worldwide
(d) TB can occur at any point in the course of progression of HIV infection.

If person is not infected with HIV, the life time risk of developing TB is about 10%. But if the person is infected with HIV, the life time risk of developing TB is between 50% to 60%. Impact of HIV on TB are-

(a) Increased number of TB cases
(b) Reactivation of TB
(c) Susceptibility to new TB infections.
(d) Most common serious opportunistic infection in HIV positives is the first manifestation of AIDS in >50% cases in developing countries. HIV fuels the spread of MDR TB.
In India, about 50-60% of HIV positive patients will develop TB in their lifetime (Singh.2004).

2.3.4 Socio-economic impact

Besides the disease burden, TB also causes an enormous socioeconomic burden to India. TB primarily affects people in their most productive years with important socioeconomic consequences for the household when an individual falls sick with TB. The disease is even more common among the poorest and marginalized sections of the community. Almost 70% of TB patients are aged between the ages of 15 and 54 years. While two thirds of the cases are male, TB takes a disproportionately larger toll among young females, with more than 50% of female cases occurring before 34 years of age. In addition there is a devastating social cost – more than 3,00,000 children are forced to leave school because their parents have TB, and more than 1,00,000 women with TB are rejected by their families. Studies suggest that on an average, 3 to 4 months of work time is lost as a result of TB, resulting in an average potential loss of 20-30% of the annual household income. This leads to increased debt burden, particularly for the poor and marginalized sections of the population (Ramachandran et al. 1999).