Introduction
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WHO estimates that eight million people get tuberculosis (TB) every year, of which 95% live in the developing countries. An estimated 2 million people die from TB every year. The South-East Asia Region is home to 25% of the world’s population but carries a disproportionately high burden of TB with nearly 34% of the world’s TB cases.

There has been a great impact of human immunodeficiency virus (HIV) in the rising trend of TB. Chances are that only one of ten immuno-competent people infected with *M. tuberculosis* will become TB patients in their lifetime; but among those with HIV, one in ten per year will develop active TB. The impact of HIV infection on the TB situation, especially in the 20-35 year age group, is of deep concern.

The final factor contributing to the resurgence of TB is emergence of multi-drug resistance. Drug resistance in TB occurs as a result of mutations in the tubercle bacillus. When exposed to a single anti-TB medication, most bacilli sensitive to that drug are killed; however a few drug resistant mutants will multiply freely.

Streptomycin (1944) was introduced as the first drug for TB. Since then a rapid succession for anti-tubercular drugs appeared- para-aminosalicylic acid (1949), isoniazid (1952), pyrazinamide (1954), cycloserin (1955), ethambutol (1962) and rifampicin (1963).

The human macrophage provides preferred biotype for *Mycobacterium tuberculosis* and plays a dual role: conferring protection against the pathogen on one hand and supporting its survival on the other. Containment of bacteria in immuno-competent persons occurs through formation of granuloma at the infection foci during initial stages of infection. If the balance between host’s defense and persisting mycobacteria is tipped in favor of the pathogen, active disease occurs. Thus, two factors determine the consequence of mycobacterial infection: a) virulence of bacilli to successfully parasitize the macrophages, and b) microbicidal mechanisms expressed by host cells. The outcome of infection thus varies from latent infection with no clinical symptoms to disseminated disease.
The interplay between macrophage and mycobacteria has been studied at various stages - from entry of bacilli to the cell-mediated immunity. Several receptors are involved in the entry of mycobacterium into the macrophages; amongst which Fc-, mannose, scavenger and complement receptors are very well studied. The receptor specific entry and course of phagosome maturation are apparently interdependent. Studies have shown that entry through mannose and Fc- receptors leads to activation of macrophages leading to complete phagosome maturation and killing of intracellular bacilli. On the other hand, if the uptake is mediated by complement receptors, bacilli resist phagosome maturation beyond a certain stage and remain viable and multiply within phagosome. These studies have been done by various groups and there are differences of opinion on the outcome of the studies.

After internalization of invading organism, the macrophage gets activated and undergoes a series of events specially designed to kill the engulfed microbe. The nascent phagosome interacts with endocytic pathway and matures to phago-lysosome with capability of lytic activity. The phagosome initially interacts with mildly acidic early/sorting endosomes typically recognized by Rab5 or early endosomal antigen-1 (EEA). Then it binds to late endosomes/lysosomes and turns more acidic attaining a pH of 5.5 and gets enriched in hydrolytic enzymes. These events can be studied by using various markers like Rab7, cathepsin D and/or LAMPs (lysosome associated membrane proteins). The resulting lethal environment is specially geared to eliminate the invader and present the immune system with antigenic determinants on the surface of macrophage. The live and virulent \textit{M. tuberculosis} does not allow phagosome to mature into phago-lysosome, as studied by using various markers. The phagosome containing live virulent \textit{M. tuberculosis} retains early endosomal markers like transferrin receptors and major histocompatibility complex class-II molecules and excludes late endosomal markers like proton ATPase, mannose 6-phosphate receptor, LAMP and cathepsin-D.

The other bactericidal/bacteriostatic mechanism used by macrophages is an ‘oxidative burst’ in which NADPH oxidase generates reactive oxygen and nitrogen intermediates (ROIs/RNIs). These are highly toxic molecules and control the infectious disease due to their damaging effects on proteins. Alveolar macrophages in tuberculosis patients possess higher capacity of oxidant metabolism. Various cytokines released during...
control of infection cause induction of nitric oxide via action on inducible nitric oxide synthetase.

Early cytokine response by innate immune system has a decisive influence on host response against the infectious agents. These cytokines mobilize innate immune system to achieve rapid control as well as perform instructive role in acquired immune system. The T helper type 1 (Th1) cytokines (Interleukin-2, Lymphotoxin α and Interferon-γ) as well as the T helper type 2 (Th2) cytokines (IL-4, IL-5, IL-6, and IL-10) are predominant, respectively, in two clinical manifestations of tuberculosis-pleural effusion and milliary TB. Other cytokines which play important role in tuberculosis immuno-pathology are TNF-α and TGF-β. The well orchestrated network of cytokines and their cumulative performance decides the outcome of infection.