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“If the number of victims which a disease claims is the measure of its significance, then all diseases, particularly the most dreaded infectious diseases such as bubonic plague, Asiatic cholera etc, must rank far behind tuberculosis”

Robert Koch 1882.¹

The year 2005, marked the one hundredth anniversary of Robert Koch’s Nobel Prize for his research on tuberculosis. In his acceptance speech, Koch said “…if we look back on what has happened in recent years in the fight against tuberculosis ……we cannot help but gain the impression that quite an important beginning has been made.”²

Yes, an important beginning had indeed been made. Yet one hundred years later, the WHO has reaffirmed its designation of tuberculosis as a “Global Emergency.” Tuberculosis remains a worldwide scourge. This ancient adversary continues to challenge all aspects of medical care, from prevention to diagnosis and therapy particularly in developing countries.²

Tuberculosis detected as far back as 10,000 B.C. still remains a major public health problem worldwide. It is one of the oldest recorded human afflictions that have plagued humans throughout recorded and archaeological history. It ravaged mankind for centuries. Though, the disease was known since ancient times, the organism causing tuberculosis was described only a century ago by ‘Robert Koch’ on 24th March 1882. Robert Koch’s discovery of the tubercle bacillus “Mycobacterium tuberculosis” in 1882 was a major event in the history of medicine, a turning point in our understanding and conquest of that deadly disease.¹,²
*Mycobacterium tuberculosis* is a formidable pathogen. It has patiently waited and endured the era of anti-tuberculosis chemotherapy. The ancient foe has stuck back with a vengeance. If concerted efforts at containing this ‘Global Emergency’ are not effectively implemented, the prospect of returning to the era of untreatable seems to be a dreadful reality.\(^1\)

*Mycobacterium tuberculosis* infects one third of the world’s population. India bears 28.4% of the entire world’s tuberculosis burden. Every second an Indian over twenty years of age is infected with *M. tuberculosis*. There are 14 million estimated tuberculosis cases in India. Of these 3.5 million are sputum positive which means that they spread the disease to at least 10 to 15 people they come in contact with. Every year 2.2 million people contract tuberculosis but only half of them seek medical help. One Indian dies of TB every minute and over a thousand die of TB every day. Thus, about five lakh people die of TB in India every year by a disease that is eminently curable.\(^1,2\)

It is ironic that India with a population lesser than China has double the number of tuberculosis patients. Tuberculosis is a disease that gets no publicity. The sheer lack of glamourlessness of TB in a mediacentric society has celebrities shaking hands with AIDS patients, has managed to push it out from its priority position in our public health agenda.\(^1\)

Significant treatment was restricted to the conventional methods until 1942. However, the convincing treatment was established in early 1944, when the ‘Streptomycin’ and ‘Patricia’ was discovered. With amazing speed after the introduction of streptomycin, para-amino salicylic acid (PAS), isoniazid and pyrazinamide were introduced into the clinical practice. With the development of effective surgery and therapeutic drugs, the
pulmonary TB was almost eliminated. TB had been transformed from a relentlessly progressive, often fatal illness to an infection which responded to appropriate drugs.\textsuperscript{3,4}

Throughout the 20\textsuperscript{th} century, the number of cases and the death rate has declined dramatically in the U.S.A. and Europe. However, since 1985, this decline halted and a progressive rise has been seen with total increase of about 9\% per year. This can be due to the initiation of the partnership of TB with HIV which can be evident by the fact that the first reported case of HIV was detected by 1984. In March 1993, the WHO took an unprecedented step and declared tuberculosis as a \textquotedblleft Global Emergency\textquotedblright.\textsuperscript{2-4}

Today, tuberculosis has returned with a new face and the global scourge of Multi-drug resistant TB (MDR-TB) and the recalcitrant nature of persistent infections pose additional challenges to treatment with currently available anti-TB drugs. The situation is exacerbated by the emergence of extensively drug resistant tuberculosis (XDR-TB). Patients with XDR-TB are virtually untreatable and carry rapid and extremely high fatality rate.\textsuperscript{5}

Human Immunodeficiency Virus (HIV) infection has further complicated the disease burden as it dramatically increases the risk of developing active tuberculosis. Infection with HIV results in progressive immunodeficiency and renders the infected person increasingly vulnerable to a wide range of pathogens. In many parts of the world, tuberculosis is the most common opportunistic infection in HIV-infected persons. The immune defects produced by HIV, influence the natural history of tuberculosis infection. Thus the HIV pandemic has altered both the epidemiology of tuberculosis and the measures for approaches to its control.\textsuperscript{6}
In 2004, it was estimated that 4.3% of all new and previously treated tuberculosis cases worldwide were multi-drug resistant. A WHO study has slammed India as one of the ‘hot zones’ for the deadly MDR-TB along with Russia, Latvia, Estonia, the Dominican Republic Argentina and the Ivory Coast. Combined with a sister disease HIV, tuberculosis is a formidable evil which could reduce to sickness any health budget and economy.⁶

Rapid and accurate diagnosis of infectious cause is a cornerstone of global tuberculosis control strategies. Remarkable progress has been made in upgrading the speed and quality of Mycobacteriological diagnostic methods. Diagnosis of Mycobacterium species ranges from Ziehl–Neelsen smear technique to molecular diagnostic methods. However it is essential to evaluate these methodologies clinically, before bringing them into routine laboratory diagnosis.⁷

Sputum smear microscopy is the most efficient way of identifying sources of tuberculosis infection. It is also used to monitor the progress of infectious patients during treatment including confirmation of cure. It also has several operational advantages even over culture like the results are available sooner, correlation with infectiousness and identify both patients at high risk of death from tuberculosis if untreated and patients who require more drugs in the initial treatment regimen because of greater bacterial load.⁸

For our country, the smear microscopy is likely to remain for the foreseeable future, the only cost-effective tool for diagnosing patients with infectious tuberculosis and monitoring the progress of treatment under the Revised National Tuberculosis Control Programme (RNTCP), Government of India has ensured good quality sputum microscopy in all aspects in the entire RNTCP implemented area of the country.⁹
The sensitivity of direct smear examination can be increased by the concentration method. This is also a useful method for sputum samples which can be liquefied by using sodium hydroxide or N-acetyl-L-cysteine (NALC-NAOH) in combination or using other mucolytic agents.8,9

Culture techniques are more sensitive than microscopy and may detect as few as 10-100 organisms per ml of specimen. Culture can identify the Mycobacterium species on the basis of biochemical and other properties. It is also useful to perform the drug susceptibility testing of the Mycobacterium species isolated. Lowenstein-Jensen medium, a solid egg based medium containing glycerol is widely used for the isolation of M. tuberculosi. The agar based medium like Middle brook 7H10, 7H11 and liquid media such as Kirchner’s or Middle brook 7H9 are also used for conventional culture. The major constraint is its slow growth which necessitates a mean incubation period of at least four weeks. The cultures inoculated are examined up to eight weeks for growth.9,10

During the last two decades, several rapid manual and automated techniques for detection of early growth (5-14 days as compared to 4-8 weeks with conventional methods) have been described which can help in obtaining the culture and sensitivity reports relatively early. Prominent among such methods are BACTEC MGIT 960, MB/Bact Alert, Mycobacterial growth indicator tube (MGIT) and Septi-chek AFB system.11

Advances in knowledge about genetic structure of tubercle bacillus helped develop gene probes and gene amplification methods for identification and detection of tubercle bacillus from culture or directly in clinical specimens and molecular detection of drug resistance. While the gene probes can help in rapid identification of
isolates, gene amplification methods developed for diagnosis of tuberculosis are demonstrable highly sensitive specially in culture negative specimens from different paucibacillary forms of disease. With these molecular methods, drug resistant mutants for drugs like Rifampicin can be detected with reasonable certainly within hours. These gene probes, gene amplification methods and in situ approaches offer unparallel capability to enhance the diagnosis of tuberculosis in near future. 9, 11

Even though there are so many different types of diagnostic tests based on different principles, in general, diagnostic capabilities depend upon the technical expertise involved, geographical region like high endemicity, hot zones etc, type of laboratory involved and so many other factors. It is very important to evaluate the correlation of different diagnostic tests with caution from different geographical regions. 11

The ultimate move to eradicate tuberculosis is the proper diagnosis along with prompt treatment. While the incidence of TB has been rapidly rising, the large outbreak of drug resistant TB contributes more to this pandemic. The size of the recent MDR-TB and the rapidity with which it has propagated has been so alarming that WHO had to declare it as the 3rd emergency. (Resurgence of TB being the 1st and its association with HIV being the 2nd). 12, 13

Moreover, chronic excretors of drug resistant bacilli pose a serious public health problem as they may infect and spread drug resistant TB in the society. To add further, previously treated patients are much more likely to have resistant TB bacilli, and therefore, treatment failure, relapse cases and defaulters should be meticulously investigated for drug resistance. The issue of drug resistance will perhaps be more important for formulating their re-treatment regimens. Hence it is very important to
evaluate the “Primary Drug Resistance” and “Acquired Drug Resistance”, pattern of individual first line anti-TB drugs and evaluate the Multi-Drug Resistance.\textsuperscript{12, 13}

Thus, considering all the facts mentioned above, it has been decided to undertake studies on the bacteriological aspects of Tuberculosis such as characterization of Mycobacteria isolated from the patients of pulmonary tuberculosis, comparison of conventional diagnostic techniques, prevalence of primary and acquired anti-tuberculosis drug resistance and HIV-TB co-infection.