CHAPTER 1

Introduction and History of Tuberculosis

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INTRODUCTION

Tuberculosis is undoubtedly an ancient disease. Indeed, man may have been affected by it ever since he evolved as a species on this planet. Evidence of the existence of tuberculosis has been found in the bones of pre-historic man, excavated in Germany. These remains date back to about 8000 B.C. Typical tuberculous changes have been found in the spines of the skeletons of ancient Egyptians dating from about 2500 to 1000 B.C. The typical skeletal abnormalities of tuberculosis, including characteristic Pott's deformities, have been found in Egyptian mummies and are clearly depicted in early Egyptian art. Among the early descriptions of Egyptian tuberculosis was that of A.J.E. Cave, published in 1939 in the British Journal of Tuberculosis. More recently, *M. tuberculosis* DNA has been amplified from tissues of Egyptian mummies leaving no doubt as to the cause of the early skeletal disease. Tuberculosis is clearly noted in the Biblical books of Deuteronomy and Leviticus, however, using the ancient Hebrew word schachepheth.

Description of what could be tuberculosis has also been noted in the ancient Hindu and Chinese writings. Tuberculosis was well known in classical Greece, where it was called phthisis. Hippocrates (460–377 B.C.) recognised and understood the clinical presentation of tuberculosis. "Phthisis makes its attacks chiefly between the age of eighteen and thirty-five," he wrote in his aphorisms, clearly recognising the predilection of young adults for active tuberculosis. "Consumption was the most considerable of the diseases which then prevailed, and the only one which proved fatal to many persons," he wrote in Book I, of the Epidemics. The theory that tuberculosis is an infectious disease was conceived by Aristotle more than 2000 years before the discovery of tubercle bacillus. This followed his discovery that persons who had been in close contact with consumptives often developed the same illness. Subsequent generations of physicians from Galen confirmed this astute observation, but little progress was made towards a scientific explanation until the 16th century. During the Dark Ages (400–1400) all the knowledge of tuberculosis was lost. The touching of a king's feet for the cure of tuberculosis was popular in England. The Arabian Physician, Rhazes (850–923) and Avicenna (980–1037) looked for causes for human ailments. Though they believed in the incurability of tuberculosis, they did not despair. In the 16th century, Frascatorius, anticipating the germ theory of disease, postulated that phthisis and other maladies were caused by small particles, the contagium vivum, which could be carried in the air from person to person. Not everyone, however, believed that tuberculosis was a communicable disease, and there was strong support for the alternative theory, that heredity was the main causative factor. The issue was finally settled by Villemin who demonstrated in a series of classical experiments that tuberculosis is caused by a specific agent and that it can be transmitted from man to animals by inoculation of infected material (1865). All that remained to complete the picture was to find the causative agent. Robert Koch applied himself to this task and in 1882, the elusive microbe was identified.[1] Laennec (1781–1826), laid the foundation for our knowledge of the aetiology of tuberculosis. In 1819, he invented the Stethoscope and described auscultation. Laennec and Bayle described the tubercles and added new knowledge.

Rudolph Virchow, the founder of cellular pathology, described the development of caseation in tuberculous tissue and believed susceptibility to the disease is inherited and not the disease itself. In 1890, Koch produced tuberculin and described Koch's phenomenon. X-rays, discovered in 1895 by Roentgen, were put to clinical use by 1904. The findings of Radiology and Bacteriology helped in developing further knowledge of the disease and correlation between them. Von Pirquet, described in 1907 his cutaneous

reaction and introduced the term allergy to explain the altered reaction. Calmette and Guerin produced attenuated Bovine Bacillus after sub-culturing about two hundred and thirty times from 1908 till 1921. Figure 1.1 shows images of famous scientists who contributed to understanding of tuberculosis in early era.

HISTORY OF TB IN INDIA

TB has existed in India for several thousand years; it is an ancient disease. In Indian literature, there are passages from around 1500 BCE in which consumption is mentioned, and the disease is attributed to excessive fatigue, worries, hunger, pregnancy and chest wounds. From around 500 BCE, there are a number of Sanskrit manuscripts that mentioned existence of the disease—texts from which the Ayurveda system of general Indian medical practice is derived. In at least one of these there is a group of diseases referred to as *Sosha*.[2]

These are diseases with a prominent feature of wasting , and there are other symptoms such as "cough and blood-spitting". It is also said that the moon god, the king of the Brahmanas was the first to become a victim of this disease, which is as a result also known as *Rajayakshma*, or king's disease. A subsequent important compendium on Indian medicine is the *Rogaviniscaya*, usually referred to as the *Madhavanidana*, and one of a number of commentaries on it is the *Madhukosa*. Neither the date of the *Madhavanidana* or the Madhukosa is absolutely clear but both are likely to have been written around 800–1000 CE.

The Madhukosa describes the disease referred to in a number of different texts as yaksman, consumption or rajayaksman (kingly consumption) and it also refers to how it has been identified by many as being what is in the twenty first century called tuberculosis. However, the Madhukosa also says that the texts are clear that the ancient disease had a much wider range than TB, and covers a number of conditions between physical exhaustion through to cachexia or physical wasting. At the beginning of the nineteenth century, it was generally thought that there was hardly any TB occurring in India. But then in 1829, W.E.E. Conwell said that, *"It is a generally received error that pulmonary disease in India is rare and readily cured"*.

Conwell, a respected surgeon had also been able to observe the occurrence of TB more widely. By the middle of the nineteenth century, TB was thought to be common in some districts particularly among the English troops, and in some areas such as in the district of Madras, it was thought to be common "among natives as well". It was also believed that TB in India was of "an extremely pernicious type". In 1881, it was still believed that TB or "Phthisis" as it was often called, was more prevalent in India among European soldiers and their families, than among the native troops. This led some people to consider whether Europeans suffering from confirmed Phthisis would be better off going to India for a prolonged period. However, when this was considered in greater detail, it was believed that any advantage from the improved climate would be offset by other disadvantages. Towards the end of the nineteenth century, there were an increasing number of Christian Missionaries in India. A sanatorium for "consumptive girls" was opened at Tilaunia, between Ajmer and Phalera, by the American Methodist Episcopal Church in 1907. It was particularly meant for girls from the boarding schools and orphanages in Northern India that were connected with the mission. Cases of advanced consumption were said to be welcomed, and then segregated, rather than being turned away as they were from some other sanatoria.

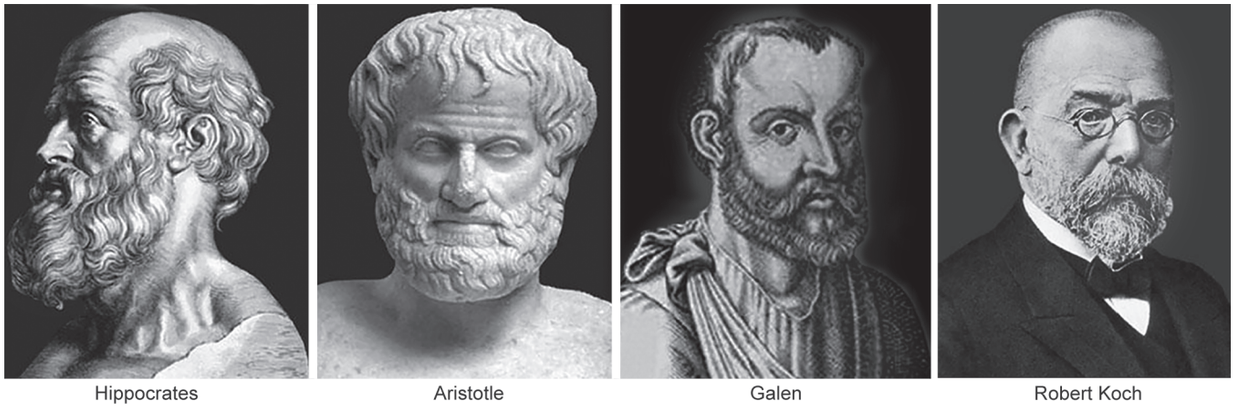

Fig. 1.1: Famous personalities who contributed in understanding tuberculosis in the early era

A second smaller sanatorium, also established under mission auspices was started at Almora in 1908. The first sanatorium under Indian management was opened in 1909 at Dharmpur near Kasauli, and the first government run sanatorium was the King Edward VII sanatorium started at Bhowali near Nainital which opened in 1912. A variety of other institutions were set up around this time for the open air treatment of TB but in general, only those people who could pay for their stay were admitted, and by around 1920, there were less than 500 beds available in all these institutions. A number of special wards were also set up in civil hospitals, but they could do little more than provide segregation and open air "treatment". The numbers that could be accommodated though was tiny compared with the need. Dispensaries were also established in some places for outpatient treatment, and from some of these nursing aid was provided. In some instances, tuberculin injections were provided, but overall the major benefit of the dispensaries was their educational value.

TB in the 1930s

From the reports collected from medical officers and others throughout India, it was estimated by Major General Sir John Megaw that in 1933 (at the time he was the Director General of the Indian Medical Service), there were probably two million cases of TB in India. He said that:

"Tuberculosis is evidently very widespread throughout the villages of India, but is especially serious in Bengal, Madras, Punjab, Bihar and Orissa. Pulmonary tuberculosis seems to be much more common than extrapulmonary except in the United Provinces and Bombay".

The Tuberculosis Association of India

In 1937, the wife of the Governor General, the Marchioness of Linlithgow, issued a public appeal "in the name of the King Emperor" for an anti-tuberculosis fund, and nearly a crore of rupees was collected. Five % of this money was retained and the balance distributed to the Provinces and States. The Tuberculosis Association of India was formed in February 1939 using mainly the retained money. The King George V Thanksgiving Anti-tuberculosis Fund was merged into the funds of the Tuberculosis Association of India. In May 1939, Dr Frimodt Moller became the Association's first Medical Commissioner. During the time that he held office three major measures were carried out by the Association. These were the establishment of the TB clinic in New Delhi, the creation of the Lady Linlithgow Sanatorium at Kasauli, and the formation of a scheme for organising home treatment as an essential part of India's anti-TB campaign.

EARLY TREATMENT REGIMENS

In 1881, the year before Robert Koch's discovery of tubercle bacillus, Professor Jaccoud of Paris published: "The curability and treatment of pulmonary phthisis". The treatment consisted of "hygienic measures" and prophylactic treatment. In addition, several drugs were advised including salts of iron, cod-liver oil, preparations of arsenic and antimony, quinine salts, salicylates and counter irritants applied to the chest, as well as inhalations of carbolic acid, iodine, creosote and turpentine.

Sanatorium Treatment

In Germany, Brehmer is credited for being the first to use it in 1859 at Gorbersodorf. However, there had been earlier references to it, for instance, by Bodington in England in 1840. Trudeau established one at Saranec lake in the USA in 1885. However, the common usage of them spread slowly and it was not until the first decade of the 20th century that Sanatoria sprung up in large numbers in countries that could afford such huge expenditure. The vast majority of the world, however, could not afford the same.

Collapse Therapy

In 1882, the year of Koch's discovery, Carlo Forlanani of Milan published a paper, in which he speculated the feasibility and efficiency of collapsing the lung by introducing air into the pleural space. This concept was not new, since there had been earlier attempts, but nevertheless, he is rightfully honoured as the originator of artificial pneumothorax treatment. As with many other treatments, this too spread slowly. There were other procedures such as pneumoperitoneum, phrenic crush, and thoracoplasty. There were pioneers in many countries, but this did not become a widely used procedure until the 1920s reaching its zenith just before chemotherapy made it obsolete.

Surgery

Surgeons also had been searching for different surgical ways to treat tuberculosis. The earlier attempts of removing the affected portion of the lung, in the 1880s had been unsuccessful and resection was given up as too dangerous a procedure.

Tuberculin Therapy

Advised by Robert Koch himself after his discovery in 1882, which was soon given up.

Gold Therapy

Another curious episode in the early treatment of tuberculosis was the gold decade. It began in 1925. its popularity spread rapidly, but after a few years it faded.

Modern Chemotherapy

It had its beginning with the discovery of streptomycin by Walksman, a German in 1944. Soon, other drugs were discovered PAS (1948) and INH (1952) followed by rifampicin and pyrazinamide and other reserve drugs. Standard chemotherapy with SM, INH and PAS became right choice for treatment of tuberculosis after the 1950s. Studies conducted in TRC, Madras (India) and other countries in 1956 have shown that domiciliary treatment with chemotherapy is as good, as sanatorium treatment with chemotherapy, which subsequently became the mainstay of treatment, especially in the developing world.

The Madras Study—Efficacy of Home Treatment

The initial impetus for the establishment of this centre was to explore the possibility of treating tuberculosis patients at their residence. This was done by a meticulously planned and executed randomised controlled trial which later became famous as the Madras study. This landmark study established certain ground truths regarding treatment of tuberculosis. The conclusions of this study were:

i. Tuberculosis can be effectively treated at home with no need for the patient to be admitted to a sanatorium.
ii. The key to successful chemotherapy is regularity of drug intake.
iii. Nutritious diet does not play a role in the treatment.
iv. Contacts of the patient at home do not have a greater risk of developing the infection.
v. Most of the patients become non-infective within 2 months of regular treatment.

These findings revolutionised the approach to the treatment of tuberculosis and laid the foundation for the National Tuberculosis Control Programme in India, and in other developing countries. There are several advantages of domiciliary treatment, which include substantial reduction in capital expenditure, reduction in cost of treatment per patient and feasibility of the organisation of mass chemotherapy programmes. Bed strength in a sanatorium was no longer a key factor involved in successful treatment. Patients in rural areas far from sanatoria could also be treated at no extra cost since the treatment given on an outpatient basis for one year is less than 10 % of the cost of maintaining a bed in a sanatorium for the same period.

Supervised: Intermittent chemotherapy is found to be successful from studies conducted in TRC, Madras (India) and other countries in 1962.

Short Course Chemotherapy (SCC)

With the discovery of rifamipicin in the 1970s and rediscovery of pyrazinamide, shortening the duration of treatment became a possibility and a reality; and now it is the mainstay for treatment.

Control of Tuberculosis in the World and India

With the birth of WHO in 1948, a global approach to tackle the problem of tuberculosis was made. The BCG vaccination was given top priority and was taken up in collaboration with UNICEF and International Tuberculosis Campaign (ITC). Simplified technology has been developed against tuberculosis for prevention, case finding and chemotherapy which was affirmed in WHO's 8th report, and subsequently in its 9th report (1974) and reaffirmed in 1982 in the World Health Assembly of WHO and IUAT. Ironically 40 to 50 years after introduction of chemotherapy of TB, in 1993 WHO declared tuberculosis as a global emergency with upsurge of tuberculosis in the developed world and increased prevalence and incidence of tuberculosis in the developing world which coincides with HIV pandemic. Directly Observed Treatment-Short course (DOTS), which was tested since 1993 is used all over the world to improve compliance as ambulatory treatment failed and resulted in increase of MDR and another reason being HIV pandemic. In India, mass BCG campaign was started in 1951 with the help of ITC. The National Tuberculosis Programme evolved in 1962 and was based on the work done by NTI, Bengaluru and TRC, Chennai (India) and other relevant studies. DOTS is being introduced in RNTCP of India since 1993. Figure 1.2 shows famous institutes in India for tuberculosis.

RNTCP—National Tuberculosis Elimination Program (NTEP), National Strategic Plan (NSP)

RNTCP Renamed

At the start of 2020, the central government has renamed the RNTCP to the National Tuberculosis Elimination Program (NTEP). In a letter to all the State Chief Secretaries of states and Union Territories, the commitment is emphasized of the Union government achieving the sustainable development goal of ending TB by 2025, five years ahead of the global targets.

Missionary Building, Almora, India

The Avalon, National TB Institute, Bengaluru

National Institute for TB, Chennai

Fig. 1.2: Famous institutes of tuberculosis in India

The RNTCP in India

The large-scale implementation of the Indian government's Revised National TB Control Program (RNTCP) (sometimes known as RNTCP I) was started in 1997. The RNTCP was then expanded across India until the entire nation was covered by the RNTCP in March 2006. At this time, the RNTCP also became known as RNTCP II.

RNTCP II was designed to consolidate the gains achieved in RNTCP I, and to initiate services to address TB/HIV, MDR-TB and to extend RNTCP to the private sector.

RNTCP uses the WHO recommended DOTS strategy and reaches over a billion people in 632 districts/reporting units. The RNTCP is responsible for carrying out the Government of India five-year TB National Strategic Plans.

With the RNTCP, both diagnosis and treatment of TB are free. There is also, at least in theory, no waiting period for patients seeking treatment and TB drugs.

The initial objectives of the RNTCP in India were:

- To achieve and maintain a TB treatment success rate of at least 85% among new sputum positive (NSP) patients.
- To achieve and maintain detection of at least 70% of the estimated new sputum positive people in the community.

New sputum positive patients are those people who have never received TB treatment before, or who have taken TB drugs for less than a month. They have also had a positive result to a sputum test, which diagnoses them as having TB.[3,4]

There is more information about the current provision of TB treatment in India and the testing and diagnosis of TB in India.

National Strategic Plan (NSP) 2012–2017

There have been a number of five-year National Strategic Plans (NSP) since the start of the RNTCP. The NSP 2012–2017 had the aim of achieving universal access to quality diagnosis and treatment. Before this there was a little treatment available through the RNTCP for the treatment of drug resistant TB.

Complete geographical coverage for diagnostic and treatment services for multi-drug resistant TB was achieved in 2013. A total of 93,000 people with MDR-TB were diagnosed and had been given treatment for drug resistant TB by 2015. Also, the National AIDS Control Organisation (NACO) had collaborated with the RNTCP and had made the HIV-TB collaboration effective. Most TB patients registered by the RNTCP were receiving HIV screening and 90% of HIV positive TB patients were receiving antiretroviral treatment.[3]

The Central TB Division developed a case based and web-based system called "Nikshay". This helped with the reporting of all TB cases. It was scaled up nationally.

The Joint TB Monitoring Mission (JMM)

Meanwhile, the Joint TB Monitoring Mission (JMM) of the RNTCP had brought together a number of national and international experts and organisations in 2014. They were to generally review the progress, challenges, plans and efforts of the RNTCP to control TB. The implementation of the NSP 2012–2017 was one of the areas looked at carefully.

Recommendations Made by the JMM Report

The report gave extensive recommendations for each part of the report, and these included:

- A significant increase in government funding for TB control. RNTCP will need 1500 crores/year to achieve the targets of the NSP and achieve the goals of the END TB strategy.
- All patients should receive care based on the "Standards for TB Care in India".
- The Ministry of Health should ensure that private sector TB patients receive early TB detection, appropriate treatment, sustained adherence support and a reduction of their out of pocket expenses.
- There is a need for a high level sustained national campaign on TB: "TB Free India/TB Mukt Bharat".

Launch of the NSP 2017–2025

In 2017 it was announced that the national goal was now the elimination of TB in India by 2025. At the same time the launch took place of the next 5-year plan, the NSP 2017–2025.

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