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A journey Across Time with an Ancient Disease : Tuberculosis

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Tuberculosis (TB) is known as an ancient disease and often described as a disease older than history. The tubercle bacilli or the causative organism of tuberculosis named *Mycobacterium tuberculosis* existed 15000 to 20000 years ago (1-3). It has been found in relics from the ancient Egypt, China, and India. Many famous people had TB. Among these famous persons were the authors Robert Louis Stevenson, Emily Bronte, and Edgar Allen Poe, the musicians Nicolo Paganini and Frederic Chopin (*Mycobacterium tuberculosis* was demonstrated by Robert Koch in 1882). In 1884, Edward Livingston Trudeau started the first sanatorium in the United States (1-3). In this place, patients with infection were isolated from society, treated with rest and had a good nutrition. Koch was awarded the Nobel Prize in 1905. In 1908, the French scientists Albert Calmette and Camille Guerin grew Koch's bacillus in several mediums to decrease its virulence and increase the capacity to produce immunity (4, 5). This led to a famous vaccine called BCG. BCG was introduced in 1921. The efficacy of vaccine varies from 0 to 80% with consistently low effects in tropical areas such as India and Africa (4). Factors such as unsuitable treatment, storage of vaccine and inadequate strains of BCG have been attributed to the failure of the vaccine (4, 5). Today, after the development of advanced screening, diagnostic tools and treatment methods for TB, one third of the world's population has been infected with the organism and about 95% of infected people are living in developing countries. With emergence of HIV infection in the world, a dramatic revitalization of tuberculosis with more than eight million new cases each year and more than three million death have been reported (3, 6-8). Antibiotic was used against tuberculosis for the first time in 1944 after the discovery of streptomycin (STM). Using this agent alone led to antibiotic resistance, which is still a major problem in the world. Better results observed with the development of PAS (para-aminosalicyclic acid) (3). Thereafter, more effective drugs such as INH (isoniazid) came in 1950's and treatment with rifampicin followed. During the last 50 years, scientific progress in the treatment of patients with tuberculosis has been developed. Currently, there are nearly 20 agents with activity against mycobacterium (3, 8). WHO recommended at least four drugs for the treatment of patients with TB to avoid the development of further resistance. Multidrug-resistant TB (MDR-TB) is defined by resistance to the two most commonly used drugs in the current four-drug regimen, (Isoniazid and Rifampin). Treatment for MDR-TB is commonly administered with at least five drugs, for two years or longer and with daily injections for six months (3, 8, 9). Many second-line drugs are toxic and have severe side effects. Extensively drug-resistant TB (XDR-TB), also known as extremely drug-resistant TB, is emerging as an even more serious problem. XDR-TB is defined as TB which is resistant to any fluoroquinolone, and at least one of three injectable second-line drugs (capreomycin, kanamycin, and amikacin), in addition to isoniazid and rifampin. This makes XDR-TB treatment extremely complicated. In a 2006 XDR-TB outbreak in South Africa, 52 of 53 people infected died within months (3, 9). It is estimated that 70% of XDR-TB patients die within a month of diagnosis. The most recent drug-resistance surveillance data issued by the WHO estimates that an average of roughly 5% of MDR-TB cases are XDR-TB (9). Estimating the incidence of XDR-TB is extremely difficult, because most laboratories have no equipment to diagnose it. In Iran, the rate of MDR is reported between 5% and 7% and about 5-6% of MDR-TB were XDR-TB (10-13). Totally drug-resistant tuberculosis (TDR-TB) is a term for tuberculosis strains that are resistant to a wider range of drugs than strains classified as extensively drug-resistant tuberculosis. TDR-TB has been identified in three countries; India, Iran, and Italy (12-14). TDR-TB is relatively poorly documented, and many countries do not test patients' samples against a broad enough range of drugs to show this kind of resistance. There is an aim to eradicate TB as a public health problem by 2050 by the World Health Organization. Therefore, there is a need to improve TB data collection at all care units and health facilities. There is also a requirement to develop specific and more sensitive diagnostic tests

to identify drug-resistant TB strains. Scientists need to identify suitable biomarkers of the disease and genomic studies to achieve a rapid diagnosis and observe the risk factors for TB and the routes for prevention. It is time for researchers and scientists to work together to eradicate this ancient pandemic.

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