



EDITORIAL

Tuberculosis: an ancient disease that remains a medical, social, economical and ethical issue

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Keywords

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At the end of the eighteenth century, following the middle-class and industrial revolution, important urbanization phenomena arose – dragging with them social and sanitary issues [1].

In this evolving historical scenario, tuberculosis spread quickly by taking advantage from rapid urbanization leading to metropolitan overcrowding combined with poor quality of hygienic conditions. Thus, tuberculosis became the first cause of death in Europe.

At the end of the eighteenth century one citizen out of four was dying of tuberculosis in London and comparable percentages were recorded in big cities of Northern America.

The causes of the disease were not yet clarified: the so called “*scientific visions*” supported the theory of a congenital disease, already argued by Hippocrates, opposed to the idea of an infectious and transmissible illness, already speculated by Aristotle [2-4].

Over the centuries, several attempts to demonstrate that “*phthisis*” was spread through unknown microorganisms can be found.

Girolamo Fracastoro (1476-1553) was the first to blame an invisible microorganism as a causative agent of tuberculosis. Nevertheless, he did not understand that the transmission could occur by air. His theory was resumed by Benjamin Marten in 1720. He speculated that tuberculosis was due to “*animacula*”, microscopic living beings able to survive in a new body, as a previous theorized by Anton van Leuwenhoek (1632-1723).

In this age the first theories about tuberculosis arose from a careful observation of clinical and anatomic phenomena.

Moreover, a change in the diagnostic approach to the disease was happening. In fact, by the end of the eighteenth century tuberculosis was still diagnosed by thoracic chest percussion introduced by J. Leopold Auenbrugger (1722-1809).

The advent of auscultation, thanks to the invention of the stethoscope in 1818 by René Laennec, significantly improved the diagnostic path of tuberculosis. Unfortunately, the same Laennec – died at the age of 45 due

to tuberculosis, presumably as a consequence of close contact with contagious patients [5].

Approximately fifty years later, in 1865, Jean Antoine Villemin finally proved the infectiousness of the disease by combing the clinical observations with laboratory experimentation on guinea pigs [6, 7].

The path traced by Villemin was completed on the 24th of March 1882, when Robert Koch revealed the discovery of “*the bacillus responsible of the disease*” [8].

All debates were suddenly over: tuberculosis is an infectious and contagious disease.

In addition, Koch’s discovery further improved the diagnosis of tuberculosis through the microscopic identification of the bacillus. The discovery was not well received by all the scientific environment: Rudolf Ludwig Karl Virchow (1821-1902), who is considered the father of social and hygiene medicine, was still claiming the multifactorial genesis of the illness.

In fact, he realized that the infection with the bacillus was not enough to get sick, but multiple causes contributed to the development of an active disease.

Moreover, he understood that the presence of what we call today the “clinical and social determinants” (immunological status, poverty, malnutrition, lack of hygiene, individual behaviors) were strictly related to the development of tuberculosis. In other words, he realized the systemic complexity of the disease. A few years later, in 1895, Wilhelm Roentgen, with the X-ray discover, finally managed to see the damages generated by the disease [9].

Nowadays, chest X-ray and bacteriological examination of the expectorate are still the diagnostic tools that we use to support and confirm the clinical suspicion of tuberculosis. Those confirm the pivotal role of the discovery made by Koch and Roentgen in the fight against tuberculosis.

The new awareness of contagiousness, arisen from Koch’s discovery, implied the need for patient’s isolation. As a consequence, sanatoriums were then born [10]. The recognition of the social determinants that foster the disease obliged to provide assistance and preventive in-

terventions for the sick and families. Consequently, dispensary networks and hospitals for preventive care were established.

In the history of vaccine and vaccination we remember that in 1895 Edoardo Maragliano could announce to the scientific community, at the Second Congress of the French Society of Internal Medicine, the existence of a tubercular antitoxin in infected animals (dogs, asses, and horses), and the consequent use of animal serum as therapeutic agent, by immunizing various animals with two different liquid cultures of *M. tuberculosis*, one of which obtained from a heated to 100° C, filtered and concentrated culture, the other from a filtered and evaporated culture by vacuum at 30° C [11, 12].

After demonstrating the prophylactic and the protective effect in guinea pigs, serum was administered to patients: in 1896, Maragliano published data about 412 patients affected by tuberculosis and treated with serum, reporting a complete recovery in 16%, significant improvement in 40%, no change in 37% and death in 11%. Maragliano also claimed that better results of serum therapy were obtained in patients with circumscribed lesions with good nutritional conditions than patients with diffuse illness [12-14].

In 1896, Maragliano proposed a vaccination practice against *Mycobacterium tuberculosis*: after the administration of dead strains in a cohort of children by subcutaneous grafting, an increase in the antibody titer was found in sera of these children. Nevertheless his discovery was ignored by the scientific community, above all because of the large use in the western world of Calmette and Guérin (BCG)'s vaccine, made of live strains, from 1928 [12, 15].

We can therefore say that many efforts have been made to fight and win the challenge against this dangerous disease and now more than ever a clear and decisive joint commitment is needed.

The strong social and economic impact that the disease still carries today entails forced governments to sensitize inhabitants and raise public awareness about prevention and treatment.

The great campaign against tuberculosis came to light. The same industrial revolution that played a huge part in spreading the disease through urbanization facilitated, at the same time, a slow economic and social growth that resulted in better living and sanitation.

Tuberculosis related mortality reverted its trend and began to decrease in the early twentieth century. The discovery of effective treatments after the II World War allowed the cure of the sick and, at the same time, prevented the transmission.

Progressively, the health and social emergency of the "white plague" seemed to be over.

The institutions adapted quickly and sanatoriums were closed such as dispensaries which were redirected to other functions. Control programs were then targeted according to the new epidemiological situation. Today, for people living in high income countries, tuberculosis is an ancient disease, a memory of the past, a memory of time of poverty. Sadly, the current perception of the

disease is incorrect. Nothing has changed all over the planet: those "socio-economical determinants", intuited by Virchow, still exist today.

Starvation, wars, poverty affect million of people, and tuberculosis remains a global health emergency with one and a half million death and nine million new patients every year, even if new diagnostic tools and effective therapies are available [16]. Since the early eighties the detrimental intersection between tuberculosis and HIV infection posed new diagnostic, therapeutic and management challenges. The two diseases since the HIV advent appeared clearly to be connected by the same underlying "socio-economical determinants".

Every effort to end these diseases should be collaborative as advocated by the WHO to break the barriers related to the TB/HIV double stigma [17].

Vaccines are important in the prevention and control of tuberculosis, but the only now available preventive vaccine against TB, bacilli Calmette-Guérin (BCG), is not effective for prevention of pulmonary TB. For this reason, it is very important to develop new vaccines for TB prevention and control in adults [18].

Around 14 TB vaccine candidates are in this moment in clinical evaluation, they can be classified into two groups including preventive pre- and post-exposure vaccines: subunit vaccines, and whole-cell vaccines [19].

Once again, the problem of tuberculosis is not only a medical challenge, but a social, economical and ethical issue that needs to be ended.

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Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

GB and MM conceived the study, GB, MM, NR drafted the manuscript, GB, AG and VG revised the manuscript. GB, MM, AG performed a search of the literature. All authors critically revised the manuscript. All authors have read and approved the latest version of the manuscript.

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