В.А. Кошечкин

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V.A. Koshechkin

Phthisiatry

Textbook

Ministry of Education and Science

Recommended by "Russian Medical Academy of Postgraduate Education" Ministry of Health of the Russian Federation as a textbook for high education students enrolled in specialty "Medicine", "Medical-preventive work" in the training direction "Phthisiatry"

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Chapter 1
A BRIEF HISTORY OF TUBERCULOSIS

Phthisiatry (from the Greek fθίσις — "Consumption, depletion" and ιατρεία — "treatment"). **Phthisiology** (from the Greek fθίσις — and 'lɒgɒs). The Greek word logos (traditionally meaning word, thought, principle, or speech) — section of clinical medicine that studies causes, patterns of distribution and mechanisms of tuberculosis development caused by Mycobacterium tuberculosis (MBT), pathological processes in the human body and methods of prevention, diagnosis and treatment. So, Phthisiology means the care, treatment, and study of tuberculosis. Phthisiatry/Phthisiology — a branch in medicine that specialize in TB, and provide specialized medical care for tuberculosis patients.

Tuberculosis (from Latin tuberculum) — is an infectious disease caused by Mycobacterium tuberculosis. Archaic names: phthisis, tuberosity, consumption, tabes, evil, grief, and etc.

1.1. THE DEVELOPMENT OF THE STUDY OF TUBERCULOSIS BEFORE THE DISCOVERY OF MYCOBACTERIUM TUBERCULOSIS BY R. KOCH

Numerous historical documents and medical investigations give evidence to the spread of tuberculosis (TB) in ancient days. This is confirmed by the data excavation of ancient documents written by people, that in the XXVII BC, traces of tuberculous lesions of the spine have been found in 4 out of the 10 skeletons of Egyptian mummies. There was an increase in mortality due to disease during periods of famine and economic crises, and significant sharp increases in the prevalence of tuberculosis as a result of numerous wars.

Hippocrates — 400–350 BC in the book "The causes and symptoms of chronic diseases" presented the description of the disease, which was later interpreted as consumption, tuberculosis — fever, sweating, fatigue and exhaustion.

Aristotle (384–322 BC) has suggested a contagion consumption, noting that in the air around the consumptive patient there is some pathogenic cause.

Since that time, he accumulated a huge amount of evidence that the main source of consumption is patient in active form of the disease with sputum particles that contaminate the air, linens, dishes, furniture, homes. Clinical-anatomical direction of the disease has change due to the long period of empirical observation and diagnosis, which contributed to a rational understanding of the pathogenesis of tuberculosis.

Girolamo Fracastoro (Fracastorius, 1478–1553) — Italian physician, who first proposed the "germ theory", believing that consumption is an infectious disease. In his book "contagious" (contagious diseases, infections), he systematically described the three main methods of transmission:

- spread by direct contact;
- spread through infectious objects (fomites), which was in contact with pathogens;
- distance infection.

Andreas Vesalius (1514–1564) was born in Brussels, the founder of scientific anatomy, and among the first to study the human body by autopsy. This method of disease studying contributed to the understanding of pathological changes in the lung, especially cavities and empyema.

Franciscus Sylvius de la Boe (1614–1672) — Dutch physician, who first linked the small, dense degenerative nodules (tubercles) found in lungs and various tissues during autopsy, on patients with signs of tuberculosis. Describing the tubercles, he noted that they are characterized by progression during the development stage, accompanied by ulceration and formation of cavities (caverns).

Richard Morton (1637–1698) — an English physician, confirmed the presence of tubercles in pulmonary tuberculosis. He believed that the disease develops in three stages: inflammation (formation of nodules / tubercles), ulceration (exulceration) and phthisis (consumption).

Benjamin Martin (1690–1782) — an English physician, in his book "New Theory of phthisis — phthisis or consumption of the lung" substantiated the theory of "contagious fluid" (contagium vivum fluidum). Hypothesized that tuberculosis could be caused by certain microscopic living organisms (virus) that penetrate the human body, and cause abnormal signs and symptoms of the disease.

Antonie van Leeuwenhoek (1632–1723) — Dutch naturalist, designer of microscopes and founder of the scientific microscope. He saw the bacteria through the microscope in 1683, and this was considered the year of birth for the science of microorganisms — Microbiology. Microscopy has extended the possibilities for the study of tuberculosis.

Bayle Gaspard Laurent (1774–1816) — French physician, who performed large numbers of autopsies of dead tuberculosis patients. This pathology-anatomical study of cadavers of tuberculosis patients in combination with a detailed analysis of patient's case histories. In the future, this was the basis for the clinical and pathological comparisons.

Rene Theophile Hyacinthe Laennec (1781–1826) — French physician, proposed the method of auscultation, which plays great importance in the development of the methods of diagnosis of tuberculosis.

Wilma Jean Anton (1827–1892) — French military doctor, began a series of experiments in 1865, 20 years before the discovery of Mycobacterium tuberculosis by Koch. Wilma demonstrated the development of disseminated tuberculosis in animals by giving rabbits, tuberculous lung tissue, blood of patients, and the pus from cavities.

Nikolay Ivanovich Pirogov (1810–1881) — Russian surgeon, a brilliant clinician and scientist, played a major role in the development and understanding of tuberculosis as a generalized disease of the organism. Pirogov described the clinical and anatomical signs of acute generalized tuberculosis, noted the possibility of the coexistence of miliary eruptions and confluent changes in the same patient. He first drew attention to the giant cells in the tubercles, later received the name "Pirogov's — Langhans cells".

1.2. THE IMPORTANCE OF THE DISCOVERY BY R. KOCH TUBERCULOSIS BACTERIA

On 24 March 1882, Robert Koch — German physician, announced the discovery of the tubercle bacillus (Koch's bacteria). He presented evidence that tuberculosis is caused by tubercle bacilli — Mycobacterium tuberculosis (MBT). The discovery by R. Koch has led to the scientific justification for the development of modern methods of diagnostics, treatment and prevention of tuberculosis as an infectious disease. The following are the most important results of research initiated by the discovery by R. Koch of M. tuberculosis.

- Shortly after the discovery of Mycobacterium tuberculosis, Russian scientist **I.I. Mechnikov** (1845–1916) — reported that other than typical Koch's bacteria, polymorphic forms are found in cultures. Polymorphism is characterized by the formation of filamentous (threadlike), granular coccoid forms. I.I. Mechnikov described the ability of MBT variability.
- German bacteriologist — **Franz Ziehl** (1857–1926) and German pathologist — **Frederick Nielsen** (1854–1898) developed a method for staining acid-fast bacilli (Mycobacterium tuberculosis, mycobacteriosis, and

leprosy), actinomycetes and other microorganisms by microscopy. This method was called Ziehl–Nielsen using the names of the discoverers.

- In 1890, **Robert Koch** discovered tuberculin. The active substance of tuberculin — tuberculoprotein allergen which causes a delayed type hypersensitivity reaction (redness and induration (papules) after an intradermal injection of tuberculin test in infected or vaccinated individuals.
- With the discovery of X-ray by German physicist **W.C. Roentgen** in 1895, radiological technology of imaging of various organs including the lungs became available. This has enabled us to compare the pathological manifestations of tuberculosis changes in various organs.
- Austrian pediatrician — **Clemens Pirke** in 1907, proposed tuberculin skin patch test (Pirke sample) to identify people infected with Mycobacterium tuberculosis. Introduced in medicine the concept of "allergy" and "prick skin test" to substantiate the specificity of the tuberculin test.
- In 1910, **Charles Mantoux** (France) and **Felix Mendel** (Germany) proposed a method of intradermal injection of tuberculin, which turned out to be a more sensitive cutaneous diagnostic. This method has been used for over 100 years and is now used as a variety of names: tuberculin test, intradermal Mantoux test, Mantoux test, Mantoux reaction and others.
- In 1919, a microbiologist **Albert Calmette** and Dr. **Camille Guerin** (both from France) created a vaccine strain of Mycobacterium tuberculosis (M. bovinus) for TB vaccination in human beings. The strain was named "bacillus Calmette–Guerin" (BCG). BCG vaccine was first vaccinated to a newborn child in 1921 and is still used for vaccination against tuberculosis.

1.3. THE HISTORY OF THE DEVELOPMENT OF THE PRINCIPLES OF TUBERCULOSIS CHEMOTHERAPY

Long before the discovery of the causative agent of tuberculosis, a variety of methods were used in the treatment of the disease. Medicine in ancient times was based on the fact that diseases were natural, and to seek treatments from natural sources. Use a variety of enriched diet, for example, milk of different animals, treatments such as bloodletting, purgation, prescribing of emetics drugs and others were recognized treatments of the time.

Empirically different chemotherapy were used: compounds of mercury, silver, copper, calcium, bismuth, iodine, antiseptics, colorants etc. In other words, the treatment of tuberculosis was nonspecific and often did not provide a cure.

Discovery of Mycobacterium tuberculosis by R. Koch has stimulated the development of specific methods of treatment using effective antibiotics and chemotherapeutic against Mycobacterium tuberculosis.

Application in the practice of treatment of tuberculosis specific anti-TB drugs

Discovery of streptomycin by **Waksman Selman** (1888–1973, Ukrainian-born American biochemist) in 1943, which has been widely used in clinical practice for the treatment of tuberculosis and leprosy since 1948, prompted other scientists to search for new antibiotics.

In 1948, **Jorgen Erik Lehmann** (1898–1989, born in Denmark) — a physician and chemist, discovered that the ingestion of amino salicylic acid (PAS) is effective in the treatment of tuberculosis.

In 1912, **Meyer et Naily** (in Prague) synthesized the organic substance of isoniazid (isonicotinylhydrazide — INH). During the period of 1941–1945 various research groups simultaneously reported effectiveness isoniazid treatment of TB.

The simultaneous combination treatment (PAS + streptomycin) is the first combination of anti-TB drugs, which increases the effectiveness of the combined treatment of tuberculosis. The combination of PAS + streptomycin was used in the treatment of tuberculosis in a few decades, but it was not effective for chronic fibro-cavernous tuberculosis.

John Crofton (Sir Crofton John Wenman, MD, 1912–2009) — Head of Department of Pulmonary Diseases and Tuberculosis at the University of Edinburgh (Scotland), has developed the so-called method of Edinburgh for the treatment of tuberculosis. The efficiency of three drugs combinations of (streptomycin + PAS + isoniazid), provides simultaneous use of it with nearly 100% cure rate and reduced the indications for surgical procedures.

A great contribution to the fight against tuberculosis has made with the development of new, effective anti-TB drugs containing rifampicin. Rifampicin — group of antibiotics that are synthesized by the bacteria Amycolatopsis mediterranei, or obtained by artificial synthesis. Rifampicins are believed to be a subclass of antibiotics ansamycins with bactericidal activity against the MBT.

Subsequently, several research groups synthesized rifampicin derivatives (such as rifabutin, rifapentine, etc.), showing high anti-TB activity.

In those years, new chemical and antibiotics with anti-TB activity were also introduced in clinical practice: pyrazinamide, ethambutol, cycloserine, ethionamide, and others.