Cover images: Coding M. tuberculosis infected by fluorescent reporter phage φ DRM9, courtesy of Paras Jain and Torin Weisbrod, Albert Einstein College of Medicine, Bronx, NY.
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It is the height of irony that the man who discovered the smallpox vaccine, Edward Jenner, lost both his wife and son to tuberculosis (TB). By the time smallpox was essentially eradicated, it is estimated that over 300 million people had died from this disease over the preceding century. Its eventual prevention—by a simple vaccine—clearly illustrates the power of scientific discovery and how its application can affect human health. Hundreds of millions of people have been spared death and suffering from infectious diseases because of the development of vaccines and chemotherapeutic agents in the last 100 years. Millions of lives have been saved with the use of the TB vaccine, BCG, and the development of chemotherapeutic regimens for TB. Depressingly, despite these effective interventions, TB remains one of the most challenging problems of global health, with over 9 million new cases and 1.6 million deaths each year. This crisis has been further compounded by the emergence of the HIV epidemic, as this explosive and deadly combination has dramatically increased the global spread of TB, including increasing numbers of cases of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB.

Historically, mycobacterial disease has long been at the forefront of scientific discovery for infectious diseases. The leprosy bacillus, Mycobacterium leprae, the first bacterium to be associated with human disease, was initially visualized by Gerhard Armauer Hansen in 1873. Earlier, Jean Antoine Villemin was the first person to realize that lung tubercles were infectious and not cancerous. By the 1880s, Robert Koch, aware of both of these discoveries, not only observed the tubercle bacilli in tubercles, but developed a growth medium of heated serum to cultivate the tubercule bacillus outside of humans. He went on to repeat the transfer experiment of Villemin and transferred the disease of TB to numerous animal species, establishing the experimental paradigm (“the postulates”) of how to prove that an infectious agent is a cause of a disease. Koch’s findings led Albert Calmette and Camille Guérin to follow Jenner’s approach of developing an attenuated pathogen for use as a vaccine, using the bovine tubercle bacillus to develop the bacille Calmette-Guérin (BCG) vaccine that bears their names and is still used to this day.

It is noteworthy that Paul Ehrlich was sitting in the lecture hall when Robert Koch presented his work in 1882; he later went on to help Koch improve his staining techniques. By observing the selective staining of various cell types, including human cells and different bacteria, Ehrlich also developed the idea of chemotherapy—“magic bullets” that could kill microbial pathogens. He tried for years to develop a chemical that could kill the tubercule bacillus, with little success, though at the same time was far more successful in developing a treatment for syphilis. In the 1930s, his protégé Gerhard Domagk discovered the first sulfonamide to treat bacterial infections such as streptococcus, and as this fledging field expanded, para-aminosalicylic acid and isoniazid were discovered to be active against the TB bacillus. Parallel studies by Salaman Waksman and Albert Schatz in the 1950s led to the discovery of streptomycin, the first bactericidal drug for the tubercle bacilli.

Despite these many historical advances, the TB bacillus—Mycobacterium tuberculosis—has proven to be a formidable adversary against numerous interventions. Nevertheless, despite the arduous challenges of
working with this dangerous pathogen, the field continues to persevere, and our continued success in the pursuit of knowledge would, we suspect, be applauded by Koch, Ehrlich, Calmette, and many others, as we strive to find and apply more effective cures for this dreadful disease. In this spirit, this textbook is a collection of state-of-the-art research aimed at understanding the TB bacillus, the way it infects its host, the mechanisms by which it persists in the face of host immunity, and current intervention and therapeutic methods. The contributors of this book believe that such continued and dedicated research efforts will eventually lead to better vaccines, better chemotherapies, and ultimately the eradication of TB—Edward Jenner’s revenge.

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