MEDICAL ASPECTS OF BIOLOGICAL WARFARE



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The bacteria that cause anthrax (*green*) are being enveloped by an immune system phagocytic cell (*purple*). These bacteria live in soil and form dormant spores that can survive for decades. When spores enter humans through the respiratory or gastro-intestinal tracts or the skin, they germinate to bacilli and rapidly increase in number. Phagocytic cells of the host immune system are essential for ingesting and killing the bacteria, and this is enhanced after vaccination. This is but one example to illustrate the important interactions between pathogens and the infected host's immune system.

Photograph: Courtesy of Sarah Guilman, Camenzind G. Robinson, and Arthur M. Friedlander, US Army Medical Research Institute of Infectious Diseases, Fort Detrick, Maryland.

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Foreword

The concept of national defense has been undeniably shaped by the events of September 11, 2001. The US anthrax postal attacks immediately following 9/11 forever changed our perspective of biodefense related research. More recently, the continued threat of state-sponsored events or individual extremist groups has only compounded the severity of this facet of national security. As we focus our medical efforts to succeed at the point of injury, and to optimize the success of the operating forces, the identification and preparation for biological threats has become a synergistic force multiplier.

The US Department of Defense (DoD) continues to identify potential threats and prepare for possible biological attacks by maintaining a knowledge base and by actively developing and testing novel medical countermeasures. For example, scientists at the US Army Medical Research Institute of Infectious Diseases (Fort Detrick, MD) have developed vaccines against the causative agents of anthrax, plague, ricin intoxication, botulinum intoxication, Ebola virus, and encephalitic alphaviruses. Importantly, DoD scientists partner with other federal agencies, academic institutions, and pharmaceutical companies to test and evaluate vaccines and therapeutics against many other biological threats. There is no better example of this consortium approach then the DoD's efforts during the recent Ebola outbreak in West Africa. DoD scientists and military personnel were on the ground diagnosing samples, sequencing viral genomes, and administering supportive care. Concurrently, some of the very products tested and evaluated by the DoD were deployed during the medical emergency. If it was not for DoD intervention, this outbreak had the potential to be substantially worse and spread further across Africa and around the world. Taken together, these brief examples demonstrate exactly why *Medical Aspects of Biological Warfare* needs to be maintained as an up-to-date information source.

The first edition of *Medical Aspects of Chemical and Biological Warfare* was published in 1997. A decade later, the chemical and biological aspects of this text warranted separate volumes. Thus, in 2007, *Medical Aspects of Biological Warfare* was released as a stand-alone textbook. Because of the fast-paced nature of microbiological research, new and emerging threats, and the changing policy, the authors pursued an updated version. In this third edition of the Textbooks of Military Medicine's *Medical Aspects of Biological Warfare*, the authors have gone to great lengths to address many facets of biodefense research, preparedness, and consequence management. Individual chapters are devoted to understanding the pathogenesis and disease progression associated with bacterial and viral biothreat agents, such as *Bacillus anthracis* and Ebola virus. Additionally, intoxications by toxins such as ricin are also described in detail. These chapters highlight the current state of science for these agents and toxins: they clearly underscore the importance of pursuing basic science interests in these arenas, and the importance of maintaining a core pool of subject matter experts. Without basic science efforts, our continued understanding of these threats would suffer, and knowledge gaps would grow. Accordingly, current clinical treatment protocols and regimens are also discussed throughout the textbook and offer a bridge from the basic research to the applied clinical "real-world" applications.

This textbook also examines other less apparent biodefense-related topics. *Acinetobacter baumii* is used as an example of how a drug-resistant bacterium can impact the DoD, and further demonstrates how the institutional structure and strategic planning can be used to address such threats. Additional chapters discuss Medical Management and Consequence Management, and give current perspectives on patient care and federal and local response scenarios in the event of a biological attack. This edition also describes current laboratory biosafety and biosurety philosophies that have tremendous impacts on the execution of biodefense strategies that are constantly evolving. Finally, this version of the textbook gives a nod to the history of biodefense research while also addressing new and emerging biological threats, be they natural or engineered.

The authors, subject matter expert reviewers, and editors have produced a comprehensive and thoughtful reference source for the DoD, and I am proud of the scientists, physicians, and other professionals who contributed their time and efforts to produce the final product.

> Lieutenant General Nadja Y. West, MD The Surgeon General Commanding General, U.S. Army Medical Command

Washington, DC March 2017

Preface

In an ever-changing and complex world, medical defense against biological pathogens must be a central pillar of our national defense strategy. Although biological warfare has been a legitimate concern for centuries, our current requirements and future operations emphasize the need for a continuing holistic approach to medical biological defense against these threats. From antiquity to the present day, agents such as *Bacillus anthracis* (etiological agent of anthrax), *Francisella tularensis* (etiological agent of tularemia), *Burkholderia mallei* (etiological agent of glanders), *Yersinia pestis* (etiological agent of plague), and *Variola* (etiological agent of smallpox) have been on the forefront of biowarfare and biodefense. With increased uncertainty associated with terrorist groups, rogue nations, and "lone wolf" individuals, the threat of biological weapons is even more relevant today.

Subject matter experts who wrote and reviewed these chapters focused on the most current data available at the time to create the most comprehensive reference source available for the US Department of Defense. Revising this textbook is important, not only to highlight the current state-of-the-art application for medical countermeasures, but also to discuss myriad current and future threats. Some of these evolving issues include the ongoing ramifications of the world's largest-ever Ebola virus disease outbreak and the impact of emerging antibiotic resistance from select bacterial pathogens. Of recent note is the emerging *B cereus* biovar *anthracis* strains isolated in Africa from fatal anthrax-like infections in chimpanzees and western lowland gorillas. These strains of *B cereus* were shown to harbor plasmids highly similar to both *B anthracis* virulence plasmids and, accordingly, were included on the US Department of Health and Human Services select agent list in 2016. These are just a few of the examples that underscore the complexities of biodefense research. Although we must remain vigilant in anticipating state-sponsored or terrorist activities, new threats are evolving in the natural world that could prove equally catastrophic to our military personnel and national interests. Preparation, cooperation, and rehearsal in accordance with the latest methodologies are the key ingredients to success in these current contexts.

I am deeply grateful for the contributions of the scientists and physicians who collaborated in this endeavor. They are nationally and internationally recognized experts in their specialties, and their dedication to updating this textbook has been invaluable. I am pleased to introduce the latest edition of *Medical Aspects of Biological Warfare*.

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Fort Detrick, Maryland October 2016