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BIOLOGICAL WEAPONS

Recognizing, Understanding, and Responding to the Threat

KRISTY YOUNG JOHNSON
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BIOLOGICAL WEAPONS

Recognizing, Understanding, and Responding to the Threat

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We dedicate this book to first responders everywhere.
May they never face any of the agents discussed herein.

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PREFACE

In September of 2001, I was teaching undergraduate Microbiology at The Citadel, the Military College of Charleston, South Carolina. Students, faculty, and staff were horrified by the terrorist attacks of September 11th, and the anthrax attacks that began that October raised numerous questions in my class, many of which I could not answer. As I delved into the subject of anthrax and bioterrorism in general, I realized that the subject of bioterrorism is only mentioned tangentially, if at all, in most undergraduate programs. I spent the last portion of that fall semester, 2001, focusing on bioterrorism in my Microbiology class, but we could only cover the tip of the iceberg in such a short time.

As I gathered more and more information on various agents of biological warfare, I began to design an entirely new course on the subject. This course was first offered at The Citadel in the spring of 2007 as an elective course for students of any academic major. We used reference books for several years until I embarked on a journey to write a textbook tailored specifically for the course. This book is designed for anyone seeking knowledge on the topic; one does not have to be a medical professional or even a science major to understand the discussions and terminology in each chapter. Chapters 1 and 2 provide a basic overview of bacteria, toxins, viruses, and the human immune system; while this information will be a review for some readers, it will provide sufficient background for those unfamiliar with the subject matter. Some chapters are noticeably longer than others, largely because our experience with certain agents has been comparatively extensive, but the entire book can be completed in one semester. The Reality Checks scattered throughout the chapters are often difficult to answer because they force the reader to consider how society would react to bioterrorism. The Chapter Review Questions provide a quick way to test your understanding of the material, and the Unit Reviews help tie it all together. Chapter 18 does not focus on a particular agent of bioterrorism; rather, it is a discussion of the policies and procedures that must be considered in preparation for dealing with

potential future acts of biological terrorism. Documents that were too cumbersome to be included within the chapters of the book are instead located in the appendices or in the online supplements. It is my sincere hope that the material presented here will increase the general knowledge of biological warfare agents and the dangers they represent. The more aware we are of the threat, the more prepared our society will be to respond to an act of biological terrorism.

KRISTY YOUNG JOHNSON, PH.D.

ACKNOWLEDGMENTS

First and foremost, thanks go to the students at The Citadel. Their endless questions led to the development of this book, and they were its original intended audience. Veteran students such as Wes Powers have also added insight and personal experience to classroom discussions, furthering our understanding of this subject as no book can. Thanks also go to our colleagues at The Citadel for patience, support, and a sense of humor during the writing process. And, last but certainly not least, many thanks are due to Michael Leventhal and Bob Esposito at Wiley for initially recognizing the merit of this book.

ABOUT THE COMPANION WEBSITE

This book is accompanied by a companion website:
http://www.wiley.com/go/Johnson/BiologicalWeapons

The website includes:

- Powerpoint Slides
- Reading Recommendations and Project Ideas
- Test Bank
- FBI's entire report on the Amerithrax case in PDF form

INTRODUCTION

A war is raging. The combatants include every life form on the planet, and the casualties far outnumber those from all human wars combined. Many of the deadliest weapons in this conflict evolved in some of the smallest life forms. While our ancestors fought for survival against these weapons of nature, they also began to harness the same weapons for use against each other. Modern technology and advances in the fields of microbiology and genetics have made possible the modification or even combination of weapons to create new ways to sicken or kill with increasing efficiency. With the dawn of a new age of biological warfare, many battles of the future will be won not on a battlefield but in a laboratory, and their outcome could very well mean the extinction of the human race.

THE THREAT

Biological weapons are a very real threat to the societies around the world. Some agents are available for legal purchase on the Internet with the proper credentials, and it is extremely likely that an international black market exists for the deadliest of these agents. Protocols for weaponizing some agents can also be found on the Internet, and most of the required materials are available at any large hardware store. In many cases, an inch-long canister may hold enough weaponized agent to kill thousands and can easily be disguised as a keychain that would be largely ignored at an airport security checkpoint. For highly contagious agents, the most effective weapon may be a single inoculated martyr. An individual in the early stages of disease could initiate

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a pandemic simply by riding the subway in New York City or spending a few hours inside any major airport. Within weeks, civilian hospitals would be overwhelmed with patients, and the death toll would be horrific. Understanding how biological weapons work allows us not only to respond appropriately to terrorist attacks but also, hopefully, to prevent them.

WHERE DID BIOLOGICAL WEAPONS ORIGINATE?

Evolution by natural selection allows features that increase the likelihood of surviving and reproducing to become more common within a population. Because life involves competition for limited resources, some of those features may repel, harm, or even kill fellow competitors. Many microbes secrete chemicals that kill other microbes, and some of these chemicals also happen to be harmful to humans. Viruses, while dependent on a living host for their continued existence, can be fatal to hosts of other species. Furthermore, viruses are often highly contagious, spreading rapidly through a densely populated area, leaving behind a grisly trail of sickness and death.

Even before the existence of microbes was discovered, people knew that some diseases were highly contagious. By noting that infection could result from contact not only with an infected person but also with that person's belongings, humans developed the first crude, yet effective, methods of biological warfare. There are numerous historical accounts of decomposing bodies being thrown into wells to contaminate water supplies. In the 14th century, the Tatar army launched one of the earliest documented bioterrorist attacks on the city of Caffa, catapulting corpses of plague victims over the walls of the city (discussed in Chapter 5). There are even strongly supported allegations that the British Army purposely distributed blankets laden with smallpox to Native Americans in the 18th century (discussed in Chapter 12).

WHY MIGHT TERRORISTS FAVOR BIOWEAPONS?

In August of 1945, the world witnessed the unimaginable destruction caused by the atomic bomb. While the effects were horrendous, they were confined to a specific geographical area. Unlike atomic or chemical weapons, many biological weapons possess the threat of contagion, often spreading from person to person long before symptoms become obvious. In a modern world with thousands of intercontinental travelers crossing oceans each day, such weapons could cause a worldwide pandemic within weeks of release.

The atomic bombs dropped on Hiroshima and Nagasaki took years of specialized research and enormous funding to build. Modern technology has allowed us to read the genetic details of many microbial species, and the instructions for growing and manipulating these species are well-documented and available on the Internet. The equipment necessary for the development of biological weapons need not be very sophisticated and is often attainable for a few hundred American dollars. The manufacture of some biological weapons does not even require an actual research laboratory and can be accomplished in an individual's kitchen or garage. Most alarming, many of these protocols now make it possible to manipulate organisms to create

new, "hybrid" microbes that simultaneously produce symptoms of multiple existing agents. For example, it has been reported that the smallpox and Ebola viruses, two of the deadliest biological weapons on the planet, have already been combined to create a weapon no human would be likely to survive (discussed in Chapter 12).

Furthermore, even the less deadly weapons have the potential to wreak havoc on society. With appropriate supportive care, victims of botulism will usually make a complete recovery, but they may experience months of full or partial paralysis during which they require intensive inpatient care (discussed in Chapter 9). A bioterrorist attack using botulinum toxin would incapacitate victims for months, engendering extreme fear in society and easily crippling the affected health-care system.

WHY STUDY BIOLOGICAL WEAPONS?

Because the best defense is a good offense, it is imperative that society be aware of the dangers of biological weapons. Biological terrorism is not limited to a battlefield; all civilians are potential targets. When two bombs exploded at the Boston Marathon in 2013, three people were killed, hundreds were injured, and thousands were terrified. Imagine the outcome if, instead of leaving pressure cookers loaded with explosives, the terrorists had carried small handheld devices the size of a tennis ball, silently releasing a fine mist containing a biological weapon as they walked along the sidewalk. No one would have detected any danger, so there would have been no reason to evacuate the scene. The marathon would have ended uneventfully, and the terrorists could have quietly left the area. Instead of three dead and hundreds injured, tens of thousands could have been infected, many of whom would have boarded planes and returned home before developing symptoms, but perhaps not before becoming contagious. If symptoms did not appear for a few days, the weapon would have spread around the world before anyone even knew of its existence. By the time medical professionals identified the agent and determined the point of exposure for the earliest cases, the terrorists could easily have essentially disappeared.

UNIT I

AGENTS, IMMUNITY, AND AGENCIES

The chapters in this unit provide a basic overview of bacteria, toxins, and viruses as well as a general discussion of some key components of the human immune system. These chapters are designed to give readers background information essential to understanding the clinical symptoms caused by the agents in subsequent chapters. Chapter 3 focuses on vital national and worldwide agencies that study and monitor all known and suspected agents of biological terrorism.

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BACTERIA, TOXINS, AND VIRUSES

A staggering variety of microbes and chemicals found in the environment pose serious health threats to humans, but some can be manipulated to be even more dangerous. Certain types of bacteria, toxins, and viruses have been identified as potential weapons of bioterrorism. While each agent has its own unique characteristics, it is worthwhile to consider some traits common to each group.

1.1 BACTERIA

Bacteria are too small to be seen without a microscope, yet they comprise more of the total biomass of Earth than all plants and animals combined. Different species are adapted to different conditions, and bacteria can be found in virtually every environment on the planet. Many species have established mutually beneficial, **symbiotic** relationships with humans; our bodies provide a home and nutrition for the bacteria, and the bacteria provide some type of benefit to our health. The human digestive system is particularly dependent on the multitude of bacteria occupying the intestines. In fact, the population of bacteria living in and on the human body outnumbers human body cells by 10 to 1. The presence of symbiotic bacteria also confers protection against other bacterial species that are actually **pathogenic** to humans, causing various symptoms of disease or, in many cases, death. Some of these pathogens, however, are undaunted by symbiotic bacteria and will cause disease in virtually everyone they encounter.

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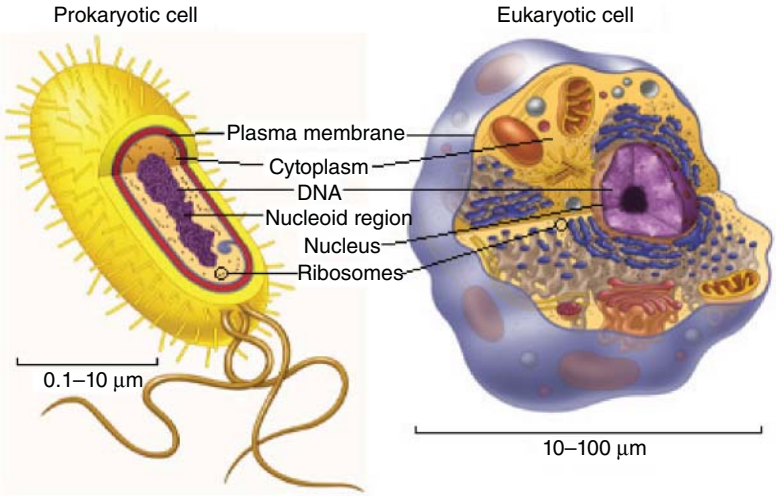

Figure 1.1 Prokaryotic and eukaryotic cells share many features, but eukaryotic cells are typically larger and have their DNA enclosed in a nucleus Source: Wikipedia, https://biology12-lum.wikispaces.com/Recombinant+DNA, Used under CC BY-SA 3.0, http://creativecommons.org/licenses/by-sa/3.0/

Organisms such as plants and animals consist of many cells and have numerous intracellular structures called **organelles** that perform specific cellular functions; some of these organelles are enclosed in membranes within the internal environment of the cell. Such organisms are considered **eukaryotic**. Bacteria, however, exist as individual cells that also have organelles, but none of their organelles are membrane-bound; these organisms are considered **prokaryotic** (Fig. 1.1).

The genetic material of bacteria is composed of **deoxyribonucleic acid** (DNA), the same molecule that carries hereditary information in all living cells. While eukaryotic DNA is organized into linear, thread-like **chromosomes** (imagine miniscule strands of spaghetti) encased in a membrane to form the nucleus (Fig. 1.2), bacterial chromosomes have a circular formation (as microscopic SpaghettiOs™) and are not bound by a membrane. Most bacterial cells have one large, circular chromosome, and many also have smaller, circular strands of DNA called **plasmids** (Fig. 1.3). Bacteria frequently exchange copies of plasmids, easily generating diversity within a bacterial population descended from the same bacterial cell.

Without microscopes, bacterial species can often be differentiated based on the appearance of their **colonies**, macroscopic clusters of cells growing on a solid surface. However, many species produce colonies with similar appearances and must be distinguished by other means. Often, extensive laboratory tests are required to identify bacterial species conclusively, but the first step in identification is to characterize the shape of the individual cells. Most bacterial cells can be categorized as rod-shaped (**bacillus**), spherical (**coccus**), corkscrew-shaped (**spirillum**), or comma-shaped (**vibrio**) (Fig. 1.4). Some bacterial species do not fit neatly into one of these cell-shape categories; for example, those that are more round than bacilli but more elongated than cocci are referred to as **coccobacilli**.

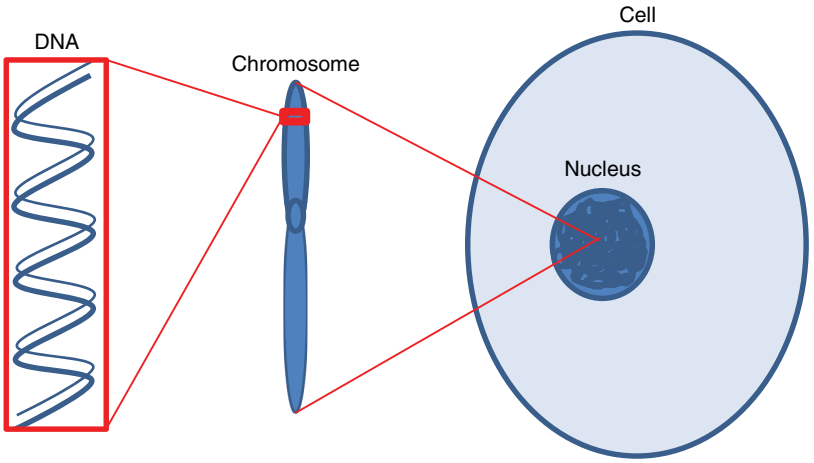

Figure 1.2 Long strands of DNA are folded into chromosomes and located in the nucleus of eukaryotic cells

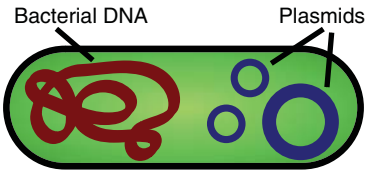

Figure 1.3 Prokaryotic DNA is not enclosed in a nucleus. Small molecules of DNA called plasmids are often present Source: Wikipedia, https://commons.wikimedia.org/wiki/File:Plasmid_(english).svg. Used under CC BY-SA 2.5, https://creativecommons.org/licenses/by-sa/2.5/deed.en

Another step in the initial identification of bacterial species is based on their appearance after certain staining procedures. While all living cells have a flexible **cell membrane** that envelops their internal components, bacteria have an additional **cell wall** composed of **peptidoglycan** (a complex of protein and sugar molecules) on the outer surface of their cell membrane (Fig. 1.5). A staining procedure known as the **Gram stain** distinguishes bacteria with thick cell walls (**Gram positive**) from those with thin cell walls (**Gram negative**). After staining, Gram positive bacteria appear purple (seen here as dark gray), while Gram negative bacteria appear pink (seen here as light gray) (Fig. 1.6). In many cases, the bacterial cell wall renders the bacteria impervious to medications, making some bacterial infections extremely difficult to treat.

Reality Check:

What are some tests scientists could use to identify biological agents rapidly in the field?

Some bacteria that are pathogenic to humans also infect other species. For instance, the bacterium that causes plague in humans also infects rodents and fleas.

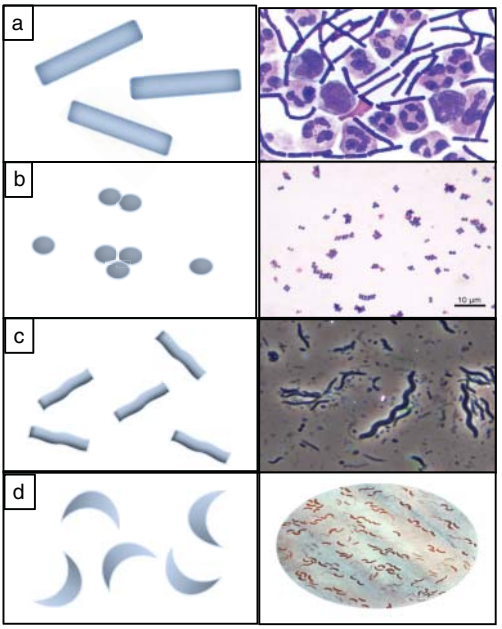

Figure 1.4 (a) Rod-shaped *Bacillus anthracis* cells among large, round neutrophils. (b) Spherical *Staphylococcus aureus* cells. (c) Spiral-shaped Spirillum volutans cells. (d) Comma-shaped Vibrio

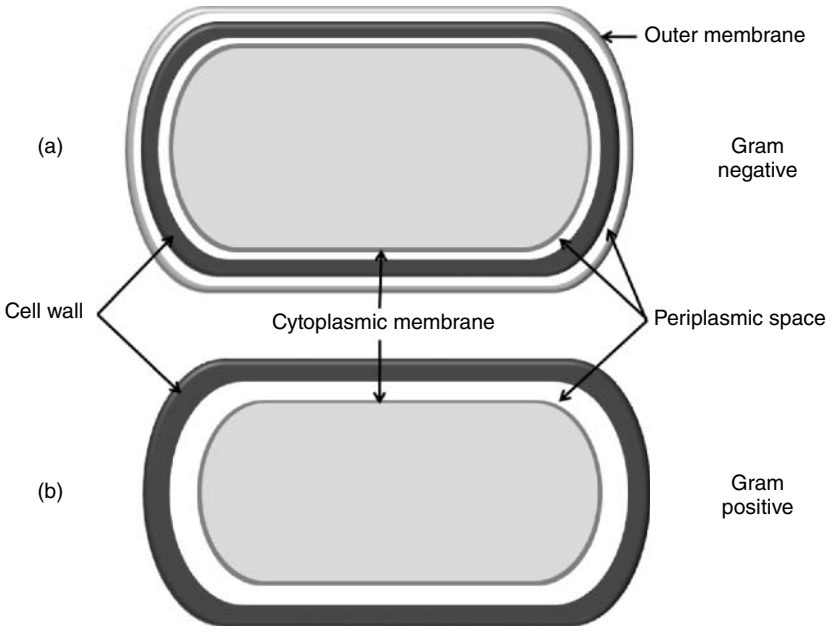

Figure 1.5 Some prokaryotic cells have a thin peptidoglycan layer (a), while others have a thick peptidoglycan layer (b) Source: http://www.intechopen.com/books/viscoelasticity-from-theory-to-biological-applications/viscoelasticity-in-biological-systems-a-special-focus-on-microbes, Used under CC BY 3.0, http://creativecommons.org/licenses/by/3.0/

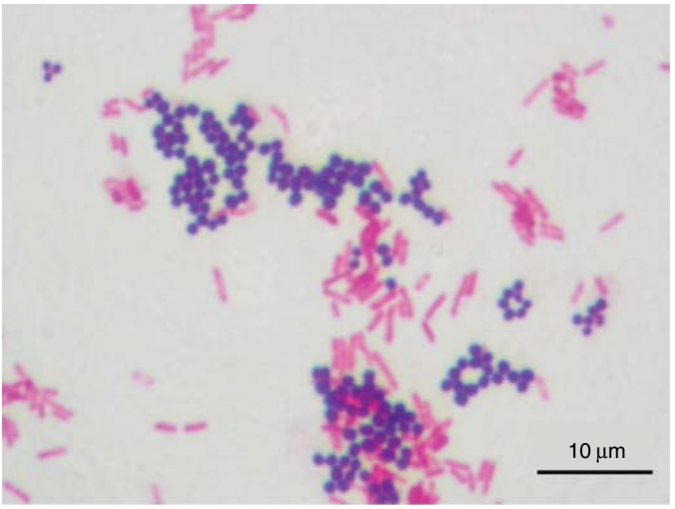

Figure 1.6 Gram positive cocci appear dark gray, while Gram negative bacilli appear light gray Source: Wikipedia, https://commons.wikimedia.org/wiki/File:Gram_stain_01.jpg, Used under CC BY-SA 3.0, https://creativecommons.org/licenses/by-sa/3.0/

A species that commonly carries but is not killed by a pathogen is known as a **reservoir host**. While infection with the bacterium that causes plague produces nonfatal sickness in rodents, the same bacteria do not cause those symptoms in fleas. Thus, fleas ingest the bacteria while feeding on an infected rodent. If the rodent dies, the fleas often turn to humans as a source of food, transmitting plague bacteria with every bite. Any species that is involved in transmitting a pathogen to humans is considered a **vector**. Vectors can be employed by bioterrorists as a means of spreading a biological weapon across borders, particularly if the vector is a flying insect such as a mosquito that could easily bypass security checkpoints.

Some bacteria can live and multiply only in the presence of oxygen; these are known as **aerobes**. Others grow best in the absence of oxygen; these bacteria are called **anaerobes**. Aerobes are most commonly found in open environments, while active anaerobes are found in closed environments such as sealed jars and cans. Because of their different environmental requirements, these categories of bacteria pose different threats. Aerobes can be dispersed in open-air environments, while anaerobes can be covertly distributed in canned food or other sealed containers.

While there are specific environmental conditions that are ideal for each species of bacteria, most are able to tolerate a range of conditions, if only for minutes or hours. This hardiness allows bacteria to be transmitted via **fomites**, inanimate objects that can become contaminated when touched by an infected individual. Some frequently encountered fomites include monetary currency (especially paper bills), elevator buttons, door handles, and even restaurant menus. Because infection often results from touching the mouth, nose, or eyes after making contact with a fomite, frequent hand-washing is one of the best defenses against everything from bacteria to viruses (Fig. 1.7). Similar to vectors, fomites can also be used to spread biological weapons, and an object as innocent as the contaminated surface of a

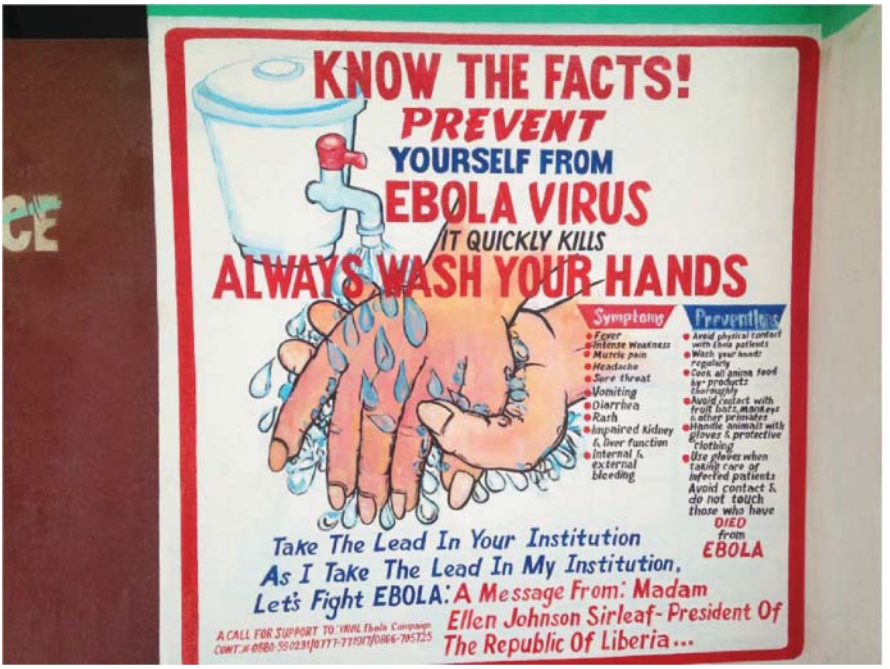

Figure 1.7 The CDC recommends frequent hand-washing to prevent Ebola

sticky ketchup bottle in a restaurant can instantly become a deadly weapon. In some cases, live aerobic bacteria can be **aerosolized**, traveling on air currents for great distances, possibly miles, before being inhaled by unsuspecting victims. Most living bacteria have a low tolerance to ultraviolet radiation and would be most effective if released at night, indoors, or in an underground structure such as a subway. Chapter 6 includes a discussion of the harrowing results of government-sponsored testing of the release of a bacterial agent in a New York City subway.

While they are generally considered simple organisms, bacteria possess some bizarre qualities not found in eukaryotic organisms. Some bacterial species possess the astounding ability to survive extended periods of harsh environmental conditions in a state of suspended animation by forming structures known as **endospores**. Each bacterial cell forms a single endospore that consists mainly of its genetic material encased in several protective layers of protein (Fig. 1.8). Endospores are most often generated in response to nutrient depletion and are able to "awaken" and become actively growing bacteria when nutrients are again present. Bacteria growing in a laboratory environment can be induced to form endospores simply by not replenishing their nutrient supply. Because endospore formation can be completed in a matter of hours, these bacteria can survive even rapidly changing environments. While this ability to survive a period of dormancy is impressive, it is even more amazing to consider the conditions tolerated by the endospores themselves. Endospores may be thoroughly desiccated, soaked in bleach, boiled for over an hour, exposed to extreme levels of ultraviolet radiation, or frozen for centuries, yet remain capable of reactivation as soon as they encounter a favorable environment. This freakish

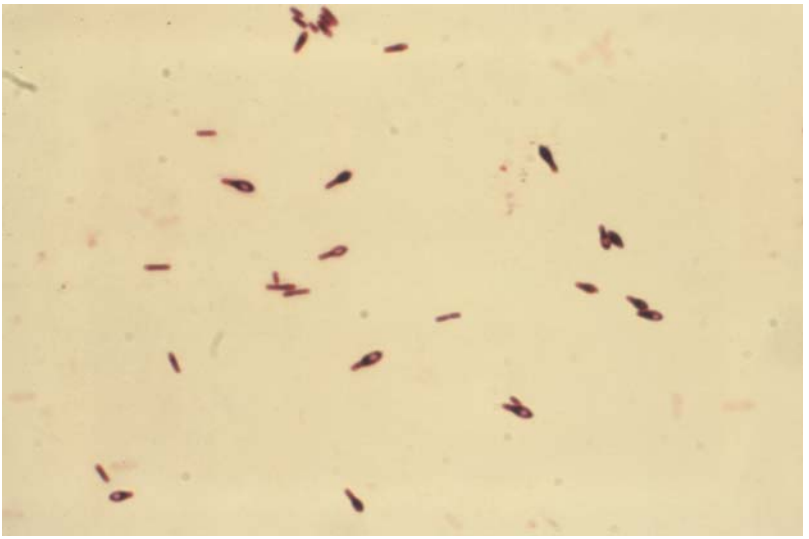

Figure 1.8 Endospores forming in *Clostridium botulinum* cells appear as clear areas

behavior makes these bacterial species particularly well-suited for weaponization because endospores are easier to concentrate, transport, and disseminate than living cells. A single gram of the notorious white powder sent through the US postal system in 2001 (discussed in Chapter 4) contained over 1 trillion anthrax endospores, each able to transform into a live anthrax bacterium once inside a human host. The powder could be stored in airtight containers for decades without losing potency and was so fine that it literally wafted into the air like smoke when the envelopes were opened. A weapon of this nature could be manufactured and then placed into long-term storage or transported around the world, remaining as deadly as the day it was made.

Reality Check:

Why would endospores be easier to transport than live bacteria?

Fortunately for modern society, most pathogenic bacteria can be killed with **antibiotics**. Early antibiotics were produced naturally by microbes and were essentially biological weapons employed in the war between microbes competing for resources. In 1928, a Scottish scientist named **Alexander Fleming** (Fig. 1.9) accidentally contaminated a bacterial culture in the laboratory with a fungus. Within days, he noticed that a substance produced by the fungus actually killed the bacteria; that substance is now known as penicillin. In the decades following Fleming's discovery, many other natural and synthetically modified antibiotics have been discovered, making possible the successful treatment of previously untreatable infections. Antibiotics work by various methods, but most target the synthesis of prokaryotic proteins and do not interfere with similar processes in eukaryotic cells. The most common deleterious effect of antibiotic treatment is the depletion of populations of symbiotic bacteria within the human digestive tract.

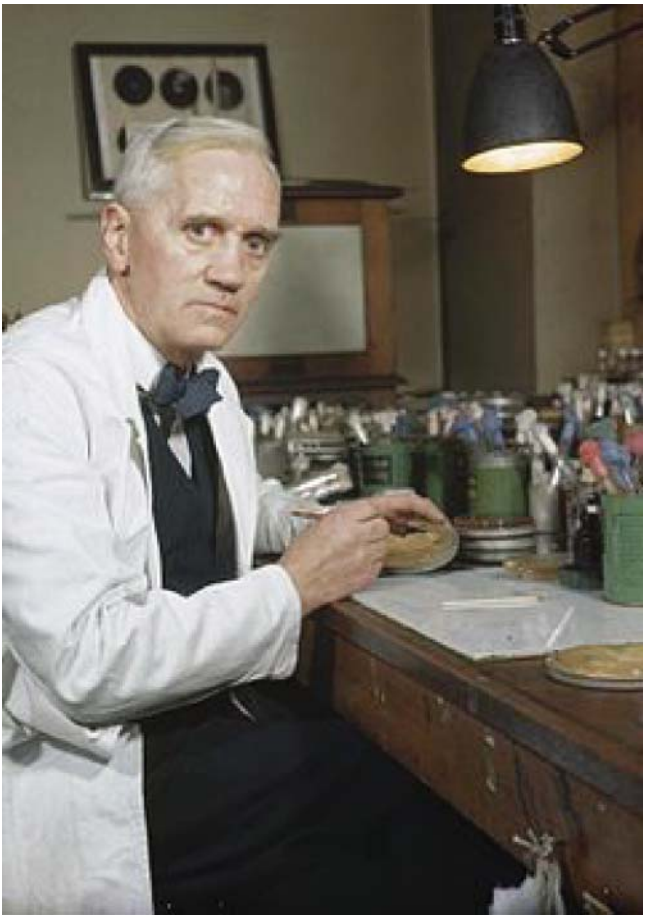

Figure 1.9 Sir Alexander Fleming was best known for his discovery of penicillin

Unfortunately, with extensive use of antibiotics has come the development of **antibiotic resistance**. Because bacterial cells of the same species may possess different plasmids, making some genetically different from others, individual cells may be resistant, or able to withstand longer exposure, to a particular antibiotic. If an entire course of antibiotic treatment is not completed, the resistant bacterial cells can survive and reproduce, causing a rebounding infection that is largely impervious to the original antibiotic. Widespread use of penicillin over many decades eventually generated such an abundance of penicillin-resistant bacteria that alternative versions of penicillin are now much more commonly prescribed. In effect, using antibiotics leads to the natural selection of antibiotic-resistant bacteria; thus, antibiotic treatment should be reserved for serious infections only (Fig. 1.10). Inevitably, a widely prescribed antibiotic will become less effective as more and more populations of resistant bacteria develop.

Bacteria considered potential biological weapons discussed in this book include *Bacillus anthracis* (anthrax), *Yersinia pestis* (plague), *Francisella tularensis* (tularemia), and *Vibrio cholerae* (cholera).