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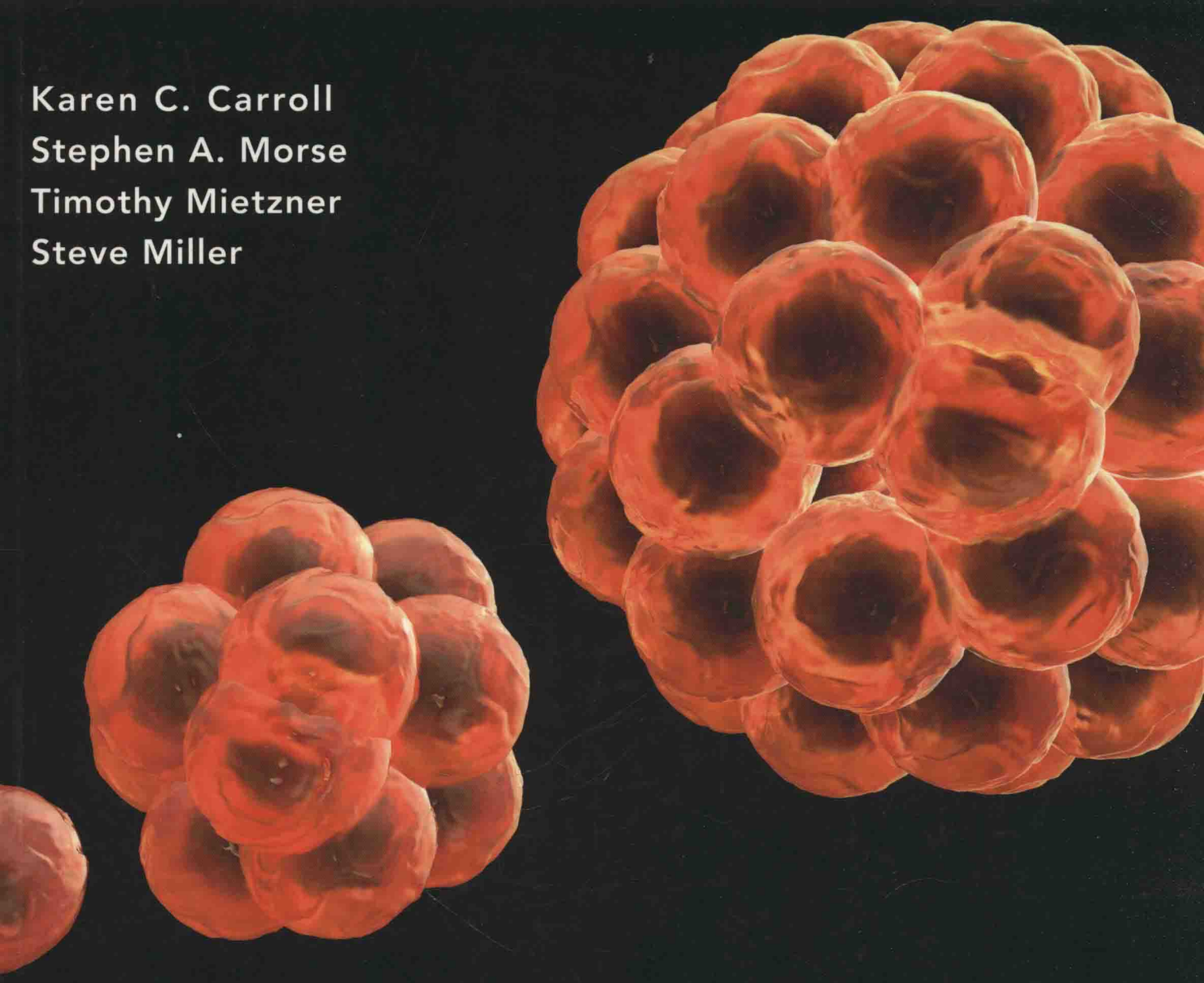

Jawetz, Melnick & Adelberg's

MEDICAL MICROBIOLOGY

27th Edition

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Jawetz, Melnick, & Adelberg's Medical Microbiology

Twenty-Seventh Edition

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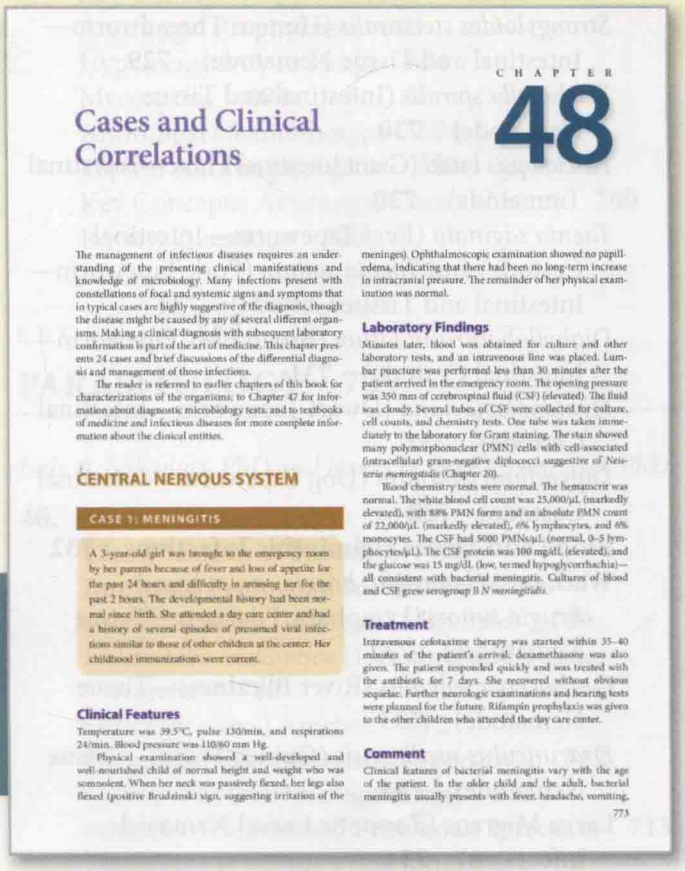
Understand the clinically relevant aspects of microbiology with *Jawetz, Melnick, & Adelberg's Medical Microbiology, Twenty-Seventh Edition*

- Delivers a concise, up-to-date overview of the roles microorganisms play in human health and illness
- Links fundamental principles with the diagnosis and treatment of microbial infections
- Reflects the tremendous expansion of medical knowledge afforded by molecular mechanisms, advances in our understanding of microbial pathogenesis, and the discovery of novel pathogens
- Includes brief descriptions of each organism, along with vital perspectives on pathogenesis, diagnostic laboratory tests, clinical findings, treatment, and epidemiology
- Features an entire chapter of case studies that focuses on differential diagnosis and management of microbial infections
- Introduces you to basic clinical microbiology through the fields of bacteriology, virology, mycology, and parasitology
- Revised and updated immunology chapter

Cases and Clinical Correlations show readers how to apply the material to real-world situations



CHAPTER 48

Cases and Clinical Correlations

The management of infectious diseases requires an understanding of the presenting clinical manifestations and knowledge of microbiology. Many infections present with constellations of focal and systemic signs and symptoms that in typical cases are highly suggestive of the diagnosis, though the disease might be caused by any of several different organisms. Making a clinical diagnosis with subsequent laboratory confirmation is part of the art of medicine. This chapter presents 24 cases and brief discussions of the differential diagnosis and management of those infections.

The reader is referred to earlier chapters of this book for characterizations of the organisms; to Chapter 47 for information about diagnostic microbiology tests; and to textbooks of medicine and infectious diseases for more complete information about the clinical entities.

CENTRAL NERVOUS SYSTEM

CASE 1: MENINGITIS

A 3-year-old girl was brought to the emergency room by her parents because of fever and loss of appetite for the past 24 hours and difficulty in arousing her for the past 2 hours. The developmental history had been normal since birth. She attended a day care center and had a history of several episodes of presumed viral infections similar to those of other children at the center. Her childhood immunizations were current.

Clinical Features

Temperature was 39.5°C, pulse 130/min, and respirations 24/min. Blood pressure was 110/60 mm Hg.

Physical examination showed a well-developed and well-nourished child of normal height and weight who was somnolent. When her neck was passively flexed, her legs also flexed (positive Brudzinski sign, suggesting irritation of the meninges). Ophthalmoscopic examination showed no papilledema, indicating that there had been no long-term increase in intracranial pressure. The remainder of her physical examination was normal.

Laboratory Findings

Minutes later, blood was obtained for culture and other laboratory tests, and an intravenous line was placed. Lumbar puncture was performed less than 30 minutes after the patient arrived in the emergency room. The opening pressure was 350 mm of cerebrospinal fluid (CSF) (elevated). The fluid was cloudy. Several tubes of CSF were collected for culture, cell counts, and chemistry tests. One tube was taken immediately to the laboratory for Gram staining. The stain showed many polymorphonuclear (PMN) cells with cell-associated (intracellular) gram-negative diplococci suggestive of *Neisseria meningitidis* (Chapter 20).

Blood chemistry tests were normal. The hematocrit was normal. The white blood cell count was 25,000/μL (markedly elevated), with 88% PMN forms and an absolute PMN count of 22,000/μL (markedly elevated), 6% lymphocytes, and 6% monocytes. The CSF had 5000 PMNs/μL (normal, 0–5 lymphocytes/μL). The CSF protein was 100 mg/dL (elevated), and the glucose was 15 mg/dL (low, termed hypoglycorrhachia)—all consistent with bacterial meningitis. Cultures of blood and CSF grew serogroup B *N meningitidis*.

Treatment

Intravenous cefotaxime therapy was started within 35–40 minutes of the patient's arrival; dexamethasone was also given. The patient responded quickly and was treated with the antibiotic for 7 days. She recovered without obvious sequelae. Further neurologic examinations and hearing tests were planned for the future. Rifampin prophylaxis was given to the other children who attended the day care center.

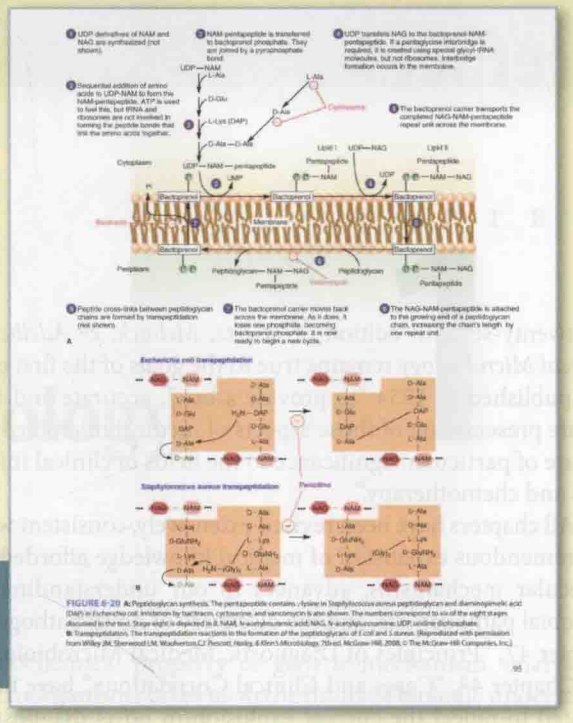
Comment

Clinical features of bacterial meningitis vary with the age of the patient. In the older child and the adult, bacterial meningitis usually presents with fever, headache, vomiting,

773

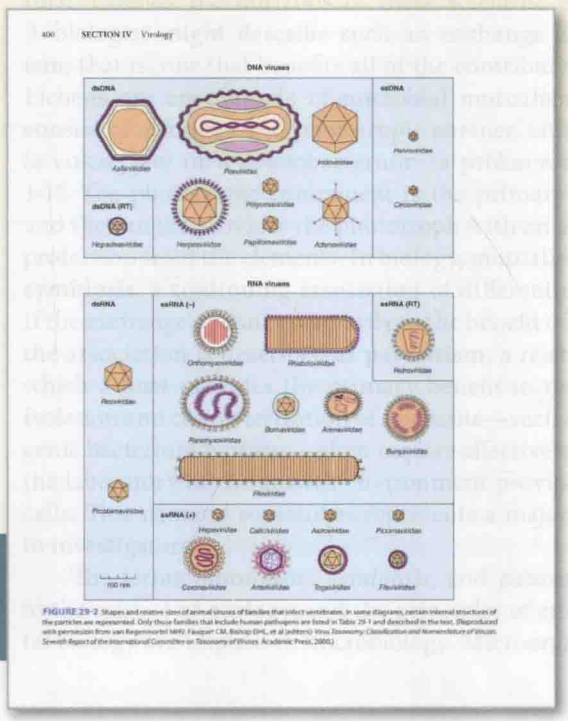
Here's why *Jawetz, Melnick, & Adelberg's Medical Microbiology* is essential for USMLE review:

- 650+ USMLE-style review questions
- 300+ informative tables and illustrations
- 23 case studies to sharpen your differential diagnosis and management skills
- An easy-to-access list of medically important microorganisms
- Coverage that reflects the latest techniques in laboratory and diagnostic technologies
- Full-color images and micrographs
- Chapter-ending summaries
- Chapter concept checks



Diagrams that crystallize what is stated in the text

Full-color images bring the subject matter to life



Complete coverage of essentials such as *Virology*

Preface

The twenty-seventh edition of *Jawetz, Melnick, & Adelberg's Medical Microbiology* remains true to the goals of the first edition published in 1954 "to provide a brief, accurate and up-to-date presentation of those aspects of medical microbiology that are of particular significance to the fields of clinical infections and chemotherapy."

All chapters have been revised extensively, consistent with the tremendous expansion of medical knowledge afforded by molecular mechanisms, advances in our understanding of microbial pathogenesis, and the discovery of novel pathogens. Chapter 47, "Principles of Diagnostic Medical Microbiology," and Chapter 48, "Cases and Clinical Correlations," have been updated to reflect the current explosion in novel diagnostics over the last several years as well as new therapies in the treatment of infectious diseases.

New to this edition are Steve Miller, MD, PhD, and Jeffery Hobden, PhD. Dr. Miller is the Medical Director of the University of California, San Francisco Clinical Microbiology Laboratory and Health Science Associate Professor of Clinical Laboratory Medicine, UCSF, and he brings extensive expertise in virology. Dr. Hobden is an Associate Professor in the Department of Microbiology, Immunology, & Parasitology, Louisiana State University Health Sciences Center, New Orleans, Louisiana, and his interest is in bacterial pathogens, especially *Pseudomonas aeruginosa*. We welcome their participation.

The authors hope that the changes to this edition will be helpful to the student of microbiology.

Contents

SECTION I FUNDAMENTALS OF MICROBIOLOGY

CHAPTER 1

The Science of Microbiology

INTRODUCTION

Microbiology is the study of microorganisms, a large and diverse group of microscopic organisms that exist as single cells or cell clusters; it also includes viruses, which are microscopic but not cellular. Microorganisms have a tremendous impact on all life and the physical and chemical makeup of our planet. They are responsible for cycling the chemical elements essential for life, including carbon, nitrogen, sulfur, hydrogen, and oxygen; more photosynthesis is carried out by microorganisms than by green plants. Furthermore, there are 100 million times as many bacteria in the oceans (13×10^{28}) as there are stars in the known universe. The rate of viral infections in the oceans is about 1×10^{23} infections per second, and these infections remove 20–40% of all bacterial cells each day. It has been estimated that 5×10^{30} microbial cells exist on earth; excluding cellulose, these cells constitute about 90% of the biomass of the entire biosphere. Humans also have an intimate relationship with microorganisms; more than 90% of the cells in our bodies are microbes. The bacteria present in the average human gut weigh about 1 kg, and a human adult will excrete his or her own weight in fecal bacteria each year. The number of genes contained within this gut flora outnumber that contained within our genome 150-fold, and even in our own genome, 8% of the DNA is derived from remnants of viral genomes.

BIOLOGIC PRINCIPLES ILLUSTRATED BY MICROBIOLOGY

Nowhere is **biologic diversity** demonstrated more dramatically than by microorganisms, creatures that are not directly visible to the unaided eye. In form and function, be it biochemical property or genetic mechanism, analysis of microorganisms takes us to the limits of biologic understanding. Thus, the need for **originality**—one test of the merit of a scientific **hypothesis**—can be fully met in microbiology. A useful hypothesis should provide a basis for **generalization**, and microbial diversity provides an arena in which this challenge is ever present.

Prediction, the practical outgrowth of science, is a product created by a blend of technique and theory. **Biochemistry**, **molecular biology**, and **genetics** provide the tools required for analysis of microorganisms. **Microbiology**, in turn, extends the horizons of these scientific disciplines. A biologist might describe such an exchange as **mutualism**, that is, one that benefits all of the contributing parties. Lichens are an example of microbial mutualism. Lichens consist of a fungus and phototropic partner, either an alga (a eukaryote) or a cyanobacterium (a prokaryote) (Figure 1-1). The phototropic component is the primary producer, and the fungus provides the phototroph with an anchor and protection from the elements. In biology, mutualism is called **symbiosis**, a continuing association of different organisms. If the exchange operates primarily to the benefit of one party, the association is described as **parasitism**, a relationship in which a **host** provides the primary benefit to the parasite. Isolation and characterization of a parasite—such as a pathogenic bacterium or virus—often require effective mimicry in the laboratory of the growth environment provided by host cells. This demand sometimes represents a major challenge to investigators.

The terms *mutualism*, *symbiosis*, and *parasitism* relate to the science of **ecology**, and the principles of environmental biology are implicit in microbiology. Microorganisms are

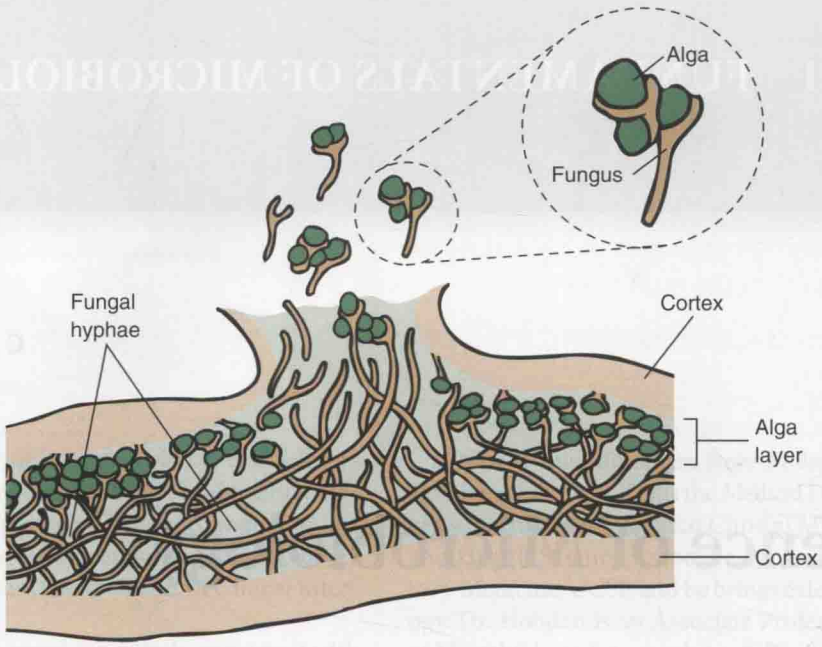


FIGURE 1-1 Diagram of a lichen, consisting of cells of a phototroph, either an alga or a cyanobacterium, entwined within the hyphae of the fungal partner. (Reproduced with permission from Nester EW, Anderson DG, Roberts CE, Nester MT (editors): *Microbiology: A Human Perspective*, 6th ed. McGraw-Hill, 2009, p. 293.)

the products of **evolution**, the biologic consequence of **natural selection** operating on a vast array of genetically diverse organisms. It is useful to keep the complexity of natural history in mind before generalizing about microorganisms, the most heterogeneous subset of all living creatures.

A major biologic division separates the eukaryotes, organisms containing a membrane-bound nucleus, from prokaryotes, organisms in which DNA is not physically separated from the cytoplasm. As described in this chapter and in Chapter 2, further major distinctions can be made between eukaryotes and prokaryotes. Eukaryotes, for example, are distinguished by their relatively large size and by the presence of specialized membrane-bound organelles such as mitochondria.

As described more fully later in this chapter, eukaryotic microorganisms—or, phylogenetically speaking, the Eukarya—are unified by their distinct cell structure and phylogenetic history. Among the groups of eukaryotic microorganisms are the **algae**, the **protozoa**, the **fungi**, and the **slime molds**.

VIRUSES

The unique properties of viruses set them apart from living creatures. Viruses lack many of the attributes of cells, including the ability to replicate. Only when it infects a cell does a virus acquire the key attribute of a living system—reproduction. Viruses are known to infect all cells, including microbial cells. Recently, viruses called **virophages** have been discovered that infect other viruses. Host–virus interactions tend to be highly specific, and the biologic range of viruses mirrors the diversity of potential host cells. Further diversity of viruses is exhibited by their broad array of strategies for replication and survival.

Viral particles are generally small (eg, adenovirus is 90 nm) and consist of a nucleic acid molecule, either DNA or RNA, enclosed in a protein coat, or capsid (sometimes itself enclosed by an envelope of lipids, proteins, and carbohydrates). Proteins—frequently glycoproteins—in the capsid determine the specificity of interaction of a virus with its host cell. The capsid protects the nucleic acid and facilitates attachment and penetration of the host cell by the virus. Inside the cell, viral nucleic acid redirects the host's enzymatic machinery to functions associated with replication of the virus. In some cases, genetic information from the virus can be incorporated as DNA into a host chromosome. In other instances, the viral genetic information can serve as a basis for cellular manufacture and release of copies of the virus. This process calls for replication of the viral nucleic acid and production of specific viral proteins. **Maturation** consists of assembling newly synthesized nucleic acid and protein subunits into mature viral particles, which are then liberated into the extracellular environment. Some very small viruses require the assistance of another virus in the host cell for their duplication. The delta agent, also known as hepatitis D virus, is too small to code for even a single capsid protein and needs help from hepatitis B virus for transmission. Viruses are known to infect a wide variety of plant and animal hosts as well as protists, fungi, and bacteria. However,

most viruses are able to infect specific types of cells of only one host species.

Some viruses are large and complex. For example, Mimivirus, a DNA virus infecting *Acanthamoeba*, a free-living soil ameba, has a diameter of 400–500 nm and a genome that encodes 979 proteins, including the first four aminoacyl tRNA synthetases ever found outside of cellular organisms and enzymes for polysaccharide biosynthesis. An even larger marine virus has recently been discovered (Megavirus); its genome (1,259,197-bp) encodes 1120 putative proteins and is larger than that of some bacteria (see Table 7-1). Because of their large size, these viruses resemble bacteria when observed in stained preparations by light microscopy; however, they do not undergo cell division or contain ribosomes.

A number of transmissible plant diseases are caused by **viroids**—small, single-stranded, covalently closed circular RNA molecules existing as highly base-paired rodlike structures. They range in size from 246 to 375 nucleotides in length. The extracellular form of the viroid is naked RNA—there is no capsid of any kind. The RNA molecule contains no protein-encoding genes, and the viroid is therefore totally dependent on host functions for its replication. Viroid RNA is replicated by the DNA-dependent RNA polymerase of the plant host; preemption of this enzyme may contribute to viroid pathogenicity.

The RNAs of viroids have been shown to contain inverted repeated base sequences at their 3′ and 5′ ends, a characteristic of transposable elements (see Chapter 7) and retroviruses. Thus, it is likely that they have evolved from transposable elements or retroviruses by the deletion of internal sequences.

The general properties of animal viruses pathogenic for humans are described in Chapter 29. Bacterial viruses are described in Chapter 7.

PRIONS

A number of remarkable discoveries in the past three decades have led to the molecular and genetic characterization of the transmissible agent causing **scrapie**, a degenerative central nervous system disease of sheep. Studies have identified a scrapie-specific protein in preparations from scrapie-infected brains of sheep that is capable of reproducing the symptoms of scrapie in previously uninfected sheep (Figure 1-2). Attempts to identify additional components, such as nucleic acid, have been unsuccessful. To distinguish this agent from viruses and viroids, the term **prion** was introduced to emphasize its proteinaceous and infectious nature. The cellular form of the prion protein (PrP^c) is encoded by the host's chromosomal DNA. PrP^c is a sialoglycoprotein with a molecular mass of 33,000–35,000 Da and a high content of α-helical secondary structure that is sensitive to proteases and soluble in detergent. PrP^c is expressed on the surface of neurons via

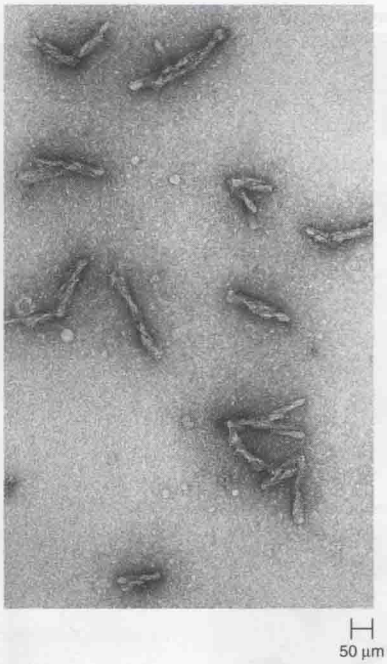


FIGURE 1-2 Prion. Prions isolated from the brain of a scrapie-infected hamster. This neurodegenerative disease is caused by a prion. (Reproduced with permission from Stanley B. Prusiner.)

a glycosylphosphatidyl inositol anchor in both infected and uninfected brains. A conformational change occurs in the prion protein, changing it from its normal or cellular form PrP^c to the disease-causing conformation, PrP^{Sc} (Figure 1-3). When PrP^{Sc} is present in an individual (owing to spontaneous conformational conversion or to infection), it is capable of recruiting PrP^c and converting it to the disease form. Thus, prions replicate using the PrP^c substrate that is present in the host.

There are additional prion diseases of importance (Table 1-1 and see Chapter 42). Kuru, Creutzfeldt-Jakob disease (CJD), Gerstmann-Sträussler-Scheinker disease, and fatal familial insomnia affect humans. Bovine spongiform encephalopathy, which is thought to result from the ingestion of feeds and bone meal prepared from rendered sheep offal, has been responsible for the deaths of more than 184,000 cattle in Great Britain since its discovery in 1985. A new variant of CJD (vCJD) has been associated with human ingestion of prion-infected beef in the United Kingdom and France. A common feature of all of these diseases is the conversion of a host-encoded sialoglycoprotein to a protease-resistant form as a consequence of infection.

Human prion diseases are unique in that they manifest as sporadic, genetic, and infectious diseases. The study of prion biology is an important emerging area of biomedical investigation, and much remains to be learned.

The distinguishing features of the nonliving members of the microbial world are given in Table 1-2.

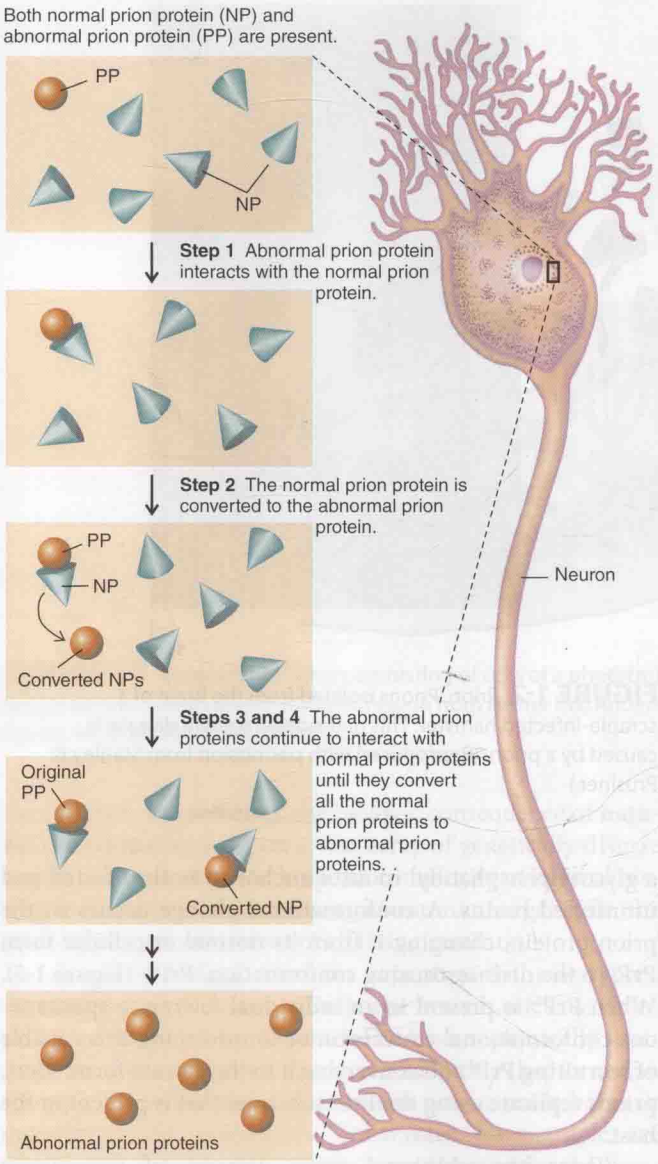


FIGURE 1-3 Proposed mechanism by which prions replicate. The normal and abnormal prion proteins differ in their tertiary structure. (Reproduced with permission from Nester EW, Anderson DG, Roberts CE, Nester MT (editors): *Microbiology: A Human Perspective*, 6th ed. McGraw-Hill, 2009, p. 342.)

PROKARYOTES

The primary distinguishing characteristics of the prokaryotes are their relatively small size, usually on the order of 1 μm in diameter, and the absence of a nuclear membrane. The DNA of almost all bacteria is a circle with a length of about 1 mm; this is the prokaryotic chromosome. Most prokaryotes have only a single chromosome. The chromosomal DNA must be folded more than 1000-fold just to fit within the prokaryotic cell membrane. Substantial evidence suggests that the folding may be orderly and may bring specified regions of the DNA into proximity. The specialized region of the cell containing DNA is termed the **nucleoid** and can be visualized by electron microscopy as well as by light microscopy after treatment of the cell to make the nucleoid visible. Thus, it would be a mistake to conclude that subcellular differentiation, clearly demarcated by membranes in eukaryotes, is lacking in prokaryotes. Indeed, some prokaryotes form membrane-bound subcellular structures with specialized function such as the chromatophores of photosynthetic bacteria (see Chapter 2).

Prokaryotic Diversity

The small size of the prokaryotic chromosome limits the amount of genetic information it can contain. Recent data based on genome sequencing indicate that the number of genes within a prokaryote may vary from 468 in *Mycoplasma genitalium* to 7825 in *Streptomyces coelicolor*, and many of these genes must be dedicated to essential functions such as energy generation, macromolecular synthesis, and cellular replication. Any one prokaryote carries relatively few genes that allow physiologic accommodation of the organism to its environment. The range of potential prokaryotic environments is unimaginably broad, and it follows that the prokaryotic group encompasses a heterogeneous range of specialists, each adapted to a rather narrowly circumscribed niche.

The range of prokaryotic niches is illustrated by consideration of strategies used for generation of metabolic energy. Light from the sun is the chief source of energy for life. Some prokaryotes such as the purple bacteria convert light energy to metabolic energy in the absence of oxygen production. Other prokaryotes, exemplified by the blue-green bacteria (**Cyanobacteria**), produce oxygen that can provide energy through respiration in the absence of light. **Aerobic organisms** depend on respiration with oxygen for their energy. Some **anaerobic organisms** can use electron acceptors other than oxygen in respiration. Many anaerobes carry out **fermentations** in which energy is derived by metabolic rearrangement of chemical growth substrates. The tremendous chemical range of potential growth substrates for aerobic or anaerobic growth is mirrored in the diversity of prokaryotes that have adapted to their utilization.

Prokaryotic Communities

A useful survival strategy for specialists is to enter into **consortia**, arrangements in which the physiologic characteristics of different organisms contribute to survival of the group as a whole. If the organisms within a physically interconnected community are directly derived from a single cell, the community is a **clone** that may contain up to 10^8 cells. The biology of such a community differs substantially from that of a single cell. For example, the high cell number virtually ensures the presence within the clone of at least one cell carrying a variant of any gene on the chromosome. Thus, genetic variability—the wellspring of the evolutionary process called natural selection—is ensured within a clone.