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MEDICAL MICROBIOLOGY

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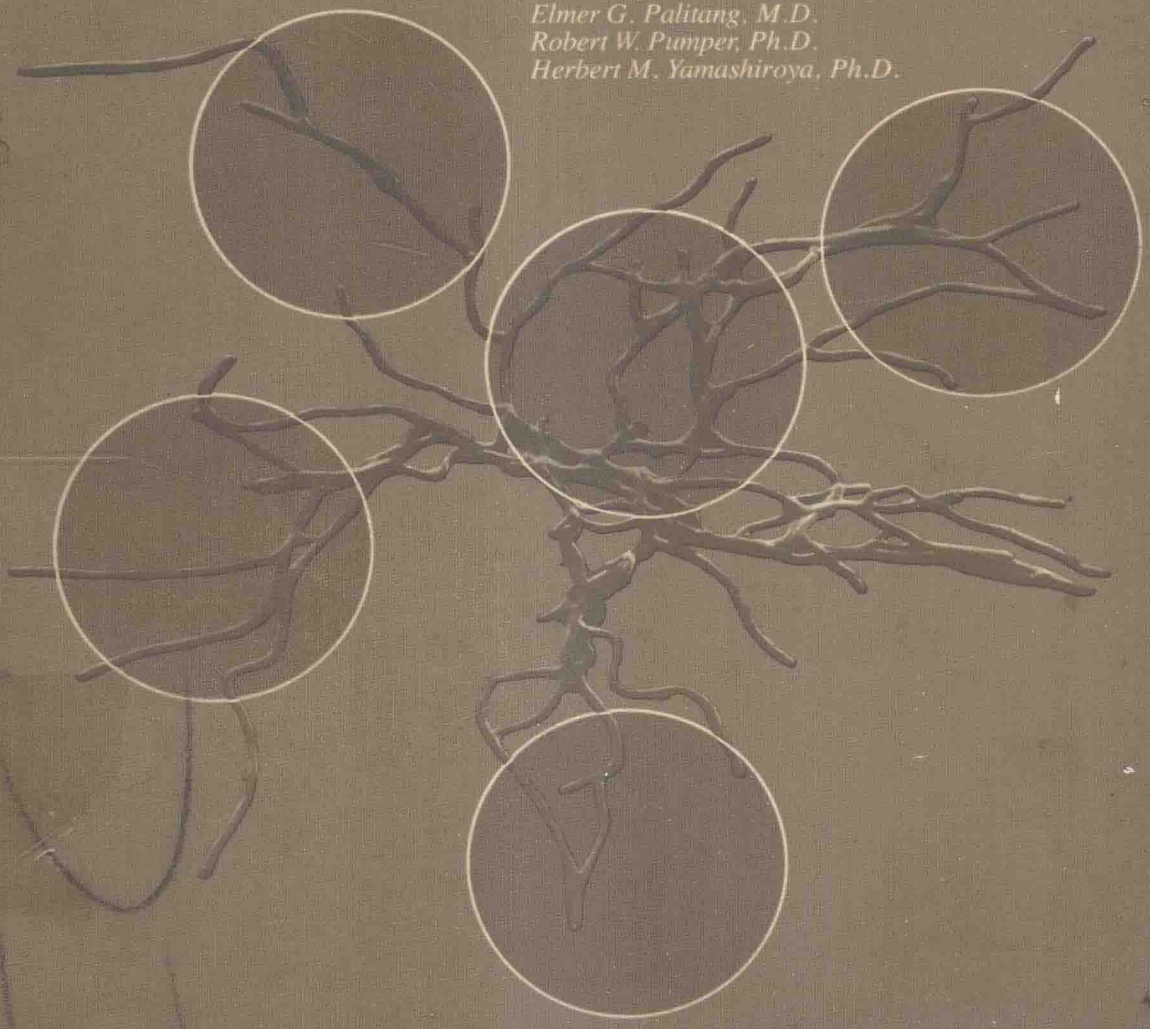

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PREFACE

Medical Microbiology was written primarily for use by medical students, but it is also valuable to those advanced students who seek more information about infectious disease. It was designed with two purposes in mind: to be used as a teaching text and to combine in one volume the concepts of basic microbiology and the clinical and diagnostic approaches to infectious disease.

Often we, as teachers, assume that because a student has taken one course in a particular subject his level of comprehension is equivalent to that of someone who has majored in that academic area, i.e., the professor. Realizing the invalidity of such an assumption, yet trying to avoid insulting some advanced readers, we have explained terms and concepts that may be unfamiliar to most students. We believe this approach is crucial to teaching.

Each chapter is as concise, comprehensive, and up-to-date as we could make it. In order to expand on current topics that are in the forefront of medical microbiology, such as venereal disease, antibiotic resistance, nongonococcal urethritis, and legionnaires disease, less coverage has been given to many topics that once demanded extensive discussions. *Medical Microbiology* does not provide detailed lessons on molecular biology. Rather, only those aspects of molecular biology that have greatly influenced our understanding of the infectious disease process have been discussed at length.

Part I is a general introduction to bacteriology and genetics as they pertain to the infectious disease process. A unique chapter devoted to the methods employed in the clinical microbiology laboratory prepares the student for discussions of laboratory diagnosis that appear later in the book and gives him an appreciation of the problems associated with identification of infectious disease agents.

Chapter 10, Sterilization and Disinfection, offers important, thorough instruction in aseptic technique, the physical and chemical methods used to attain this state, and organisms that present special problems. Extensive discussion of most major chemotherapeutic agents rounds out Part II. Attention is paid to the toxic properties of the drugs, the major groups of microorganisms affected by them, problems that might be associated with drug administration, and microbial drug resistance.

Contemporary understanding of the clinical implications of the immune response suggests that the phenomena of immunology (Part III) pervade all aspects of basic science and clinical medicine. Without an overabundance of experimental data or theoretical musings, we have stated the major principles of immunology, thought to operate at organismic, cellular, and molecular levels. This approach allows students with no previous experience in the study of immunology to assimilate the clinically relevant facts without becoming entangled in experimental protocol.

To help the reader understand advanced bacteriology (Part IV), we first explore the mechanisms of host defense against infections and the microbial factors that permit infection in the host, offering vital, new information on microbial adherence and nutrition. Characteristics of the major groups of bacteria are then examined, and close attention is paid to the newly discovered legionnaires disease.

The study of virology (Part V) is introduced by a chapter on the structure, composition, and classification of viruses, stages involved in viral infection of the cell, transcription processes of the RNA viruses, and the effects of physical and chemical agents on viruses. In addition to the relevant molecular biology, this section includes discussion of epidemiology, viral vaccines, and much recent information on hepatitis viruses. Of particular note in the virology section are the electron micrographs of the major virus agents as well as many photographs of clinical manifestations of infection.

The field of medical mycology (Part VI) has expanded in recent years due to increased travel abroad and the more frequent occurrence of opportunistic fungal infections in the hospital. We have kept abreast of the changes to provide broader coverage of this growing field than is of-

fered in other microbiology textbooks. This section is organized into discussions of the systemic, subcutaneous, superficial, and opportunistic mycoses; these are useful distinctions for both the clinician and the student of microbiology.

Parasitology (Part VII), a discipline that has received inadequate attention in the past, has been generously explored in this volume. There is a need for current information in this field and, with the expanding political and social importance of the Third World, a knowledge of parasitology will be of increasing value to clinicians in the coming years. We have provided specific information regarding the recognition of signs and symptoms of parasitic disease, diagnostic techniques, and current treatment. A chapter on medical entomology, uncommon to most microbiology textbooks, concludes this section.

Finally, our Selected Topic is one we believe to be especially important to medical students and other health professionals: Chapter 48 examines the epidemiology of hospital-associated infections, including hospital and patient factors that contribute to diseases. With more widespread use of immunosuppressive drug therapy in clinical medicine, the frequency of these infections has increased and will continue to do so. The treatment and prevention of these infections is explored with particular reference to the problems associated with overuse of antibiotics.

We would like to thank all those who kindly supplied many original photographs, tables, and line drawings. We would especially like to thank Mary Ann Komorowski, who drew most of the elegant illustrations for this book, and Mrs. Kathleen Lee and Mrs. Beverly Boyd, who spent many hours typing the manuscript. Finally, we express our appreciation to the staff of Little, Brown and Company (especially Curtis Vouwie, Robert Davis, and Lois Hall) for their cooperation in the production of this book and their patience with one of its irascible authors (R.F.B.).

R. F. B.
J. J. M.

CONTENTS

I General Microbiology

1 HISTORY AND SCOPE OF MICROBIOLOGY

Outside of wars, man's most formidable enemy has been the microbe. History books are filled with accounts of the devastating effects of diseases such as plague, cholera, and dysentery, to name a few. Yet it took until the latter part of the nineteenth century to establish the relationships that exist between some microorganisms and the disease process. Much of the credit for the discovery of these relationships must be given to Louis Pasteur and Robert Koch. Their work placed microbiology on a firm scientific foundation. The acceptance of microbiology as a science, however, began with the observation of microorganisms by Anton van Leeuwenhoek (1632–1723). Leeuwenhoek's hobby was lens grinding and microscope production. With his primitive microscopes (Fig. 1-1) he observed pond water, pepper infusions, and scrapings from teeth. The finding of "little animalcules" from these specimens was probably the first description of microorganisms (Fig. 1-2). Unfortunately Leeuwenhoek's discoveries were not fully appreciated in terms of their possible implications in infectious disease, and 200 years passed before this relationship was demonstrated.

THE THEORY OF SPONTANEOUS GENERATION

At one time it was accepted in many scientific communities that certain forms of life could arise spontaneously from inanimate organic matter. The presence of maggots on meat that had been exposed to the air for several days was accepted as a prime example of the theory of spontaneous generation. In the seventeenth century a chemist named van Helmont reported that mice could be produced if soiled linen plus cheese were placed in a container. Most such claims were quickly challenged and disproved. However, the "animalcules" discovered by Leeuwenhoek around 1676 were so small that they were believed by many scientists to arise from chemical reactions in decaying organic matter, and this theory was not refuted until late in the nineteenth century. Experiments devised by Spallanzani (1729–1799), Schulze (1815–1873), and Schwann (1810–1882) showed that if organic matter were heated to a high enough temperature and protected from air (which they thought contained microorganisms) no further microorganisms would appear. Numerous investigators were not convinced and suggested that spontaneous generation in those experiments was prevented by the absence of air or oxygen. In 1854 Schroeder and von Dusch heated a flask of broth and instead of heating the air that passed over the broth they filtered the air by passing it through cotton. This procedure removed microorganisms that were present and prevented growth. Yet the doubters persisted, and only the experiments of Louis Pasteur destroyed the last remnants of the spontaneous generation theory. Pasteur prepared flasks in which the neck of each was drawn out to a fine point. The broth in each flask containing yeast and sugar was boiled to destroy any living microorganism. With the necks resealed, the flasks were then placed in various geographic locations—on the streets of Paris, for example, as well as on mountaintops. When the necks of the flasks were broken, air rushed in, carrying bacteria into the medium. The flasks opened in the streets of Paris revealed maximum growth, as measured by turbidity, while little or no growth was observed in the flasks exposed to mountain air.

From the experiments of Pasteur, Koch, and others in the mid 1800s microbiology began to develop into a respected science. As microscopy, staining, and isolation and cultivation techniques improved, more microbial agents were identified. These discoveries drew other investigators into the field of microbiology, thereby ensuring its development, recognition, and importance in medical science as well as other areas.

THE GERM THEORY OF DISEASE

Man's initial attempts at explaining the cause of infectious disease were often influenced by religious beliefs or folklore. Nevertheless, many valid concepts were put forth that stimulated interest and prompted investigation into the cause

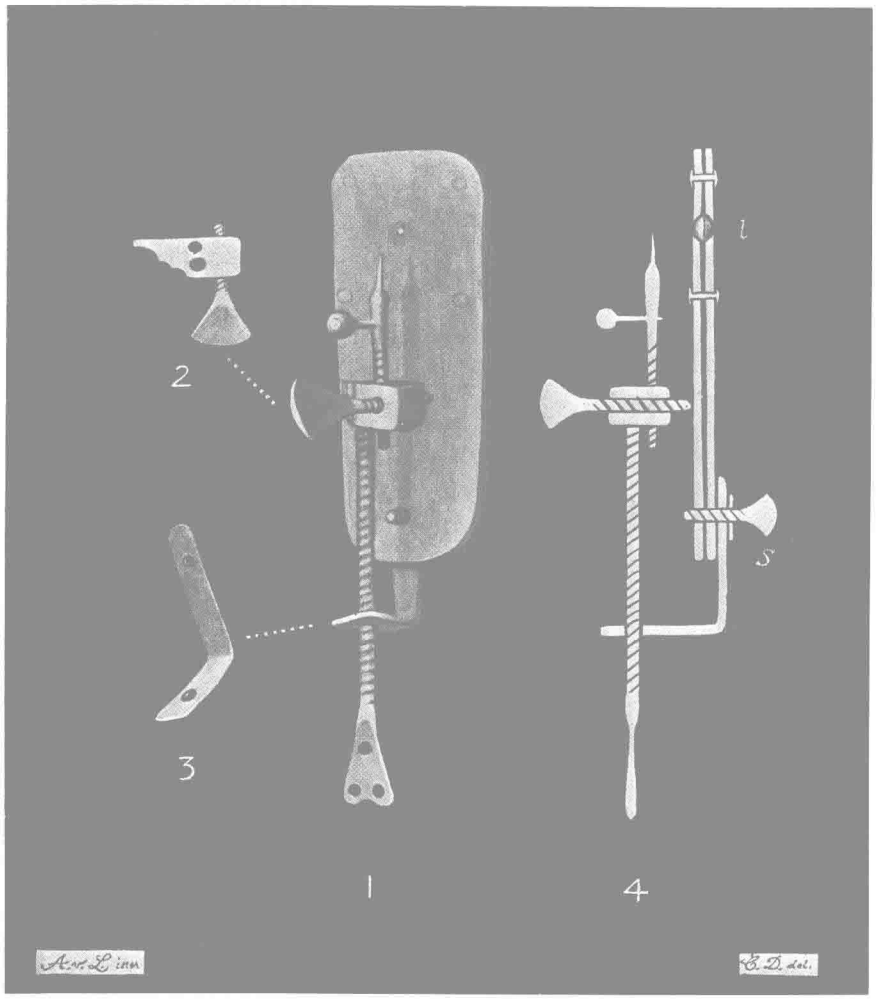

Fig. 1-1. Leeuwenhoek's "microscope." Number *1* represents a view of the entire instrument; *4* is a longitudinal section; *l* is a minute convex lens mounted between two plates of metal, usually brass; *2* is the screw for adjusting the distance of the object from the lens; *3* is the angle piece controlled by thumbscrews and providing lateral motion to the object being observed. (From C. Dobell, *Antony van Leeuwenhoek and His "Little Animals."* New York: Harcourt, Brace and Company, 1932. Used with permission of Harcourt Brace Jovanovich.)

of infectious disease. As early as 100 B.C. the Roman scholar Varro implied that disease was caused by invisible agents in the air that were passed through the mouth and nose. This concept reached alternating peaks and valleys of acceptance for hundreds of years. Then in 1762 Anton von Plenciz of Vienna stated that the invisible agents were specific; i.e., one agent was the cause of one kind of disease. Not until the nineteenth century, however, would investigators be capable of conclusively establishing the germ theory of disease.

In 1842 the Hungarian physician Ignaz Philipp Semmelweis, working in a maternity hospital in Vienna, believed that infectious agents were being transmitted from the hands of physicians to pregnant women during examination, resulting in

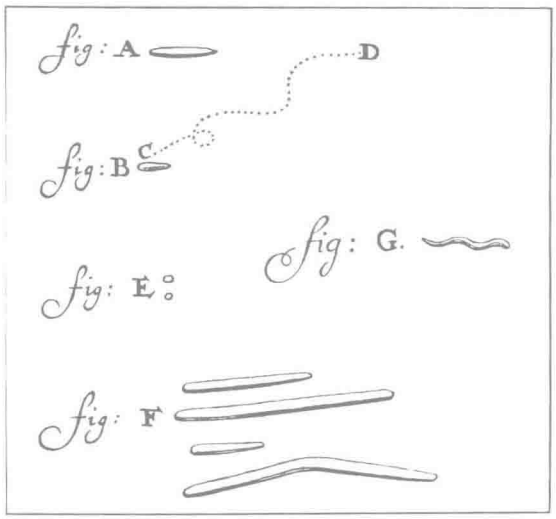

Fig. 1-2. Leeuwenhoek's figures of bacteria from the human mouth. A. A motile bacillus. B. A motile *Selenomonas sputigena* (C and D represent the path of its motion). E. A coccus. F. A fusiform bacillus. G. A spirochete. (From C. Dobell, *Antony van Leeuwenhoek and His "Little Animals."* New York: Harcourt, Brace and Company, 1932. Used with permission of Harcourt Brace Jovanovich.)

fatal blood poisonings. He insisted that attending physicians wash their hands in a solution of chloride of lime before puerperal examination. At the same time in the United States Oliver Wendell Holmes noted that women whose children were born in hospitals were more likely to develop childbed fever than those who had their babies at home. Although both men spoke out for the necessity of what we now call aseptic technique, their ideas were severely criticized by their coworkers, who steadfastly maintained that they were not "unclean."

Further support for the germ theory of disease would be forthcoming from England. In 1867 the respected physician Joseph Lister realized the significance of Pasteur's work with fermentation and putrefaction and suggested that wound sepsis could be prevented if the wound was treated with chemical agents (disinfectants) and kept covered by antiseptic dressings. This work was later published in *The Lancet* in 1867.

In 1874 the Norwegian Armauer Hansen was the first to describe an organism that he believed to be the cause of leprosy. Because of his often imprecise techniques, many scientists doubted the authenticity of his findings.

Earlier, in 1850, Davaine had noted the appearance of rod-shaped microorganisms in the blood of sheep and cattle that had died of the disease anthrax. Armed with these observations, Robert Koch set out to demonstrate the relationship between a microbial agent and infectious disease. In a series of papers he proposed that this relationship could be established if the following conditions were adhered to:

1. Demonstrate the presence of the microorganism in all cases of the disease and its absence in healthy individuals.
2. Isolate the suspected microorganisms in pure culture.
3. Reproduce the disease in susceptible animals.
4. Reisolate the suspected pathogen from the infected animals.

Koch was able to show that the blood of anthrax victims, when injected into healthy animals, could cause anthrax. Many detractors of Koch's experiments reasoned that something in the blood other than the so-called bacilli was responsible for this dread disease. Their contention was that, in disease, changes take place in the host because of poor nutrition that results in the formation of pathological products, the pathological products in this instance being microorganisms. Louis Pasteur, who is considered the father of microbiology, dispelled the theory put forth by Koch's critics by growing the anthrax bacillus outside the animal host. He later inoculated a pure culture of the bacilli into healthy animals and produced the disease in them. Koch's postulates are still valid except in the case of "carriers" of infectious microorganisms that show no symptoms of the disease and in the case of viruses that do not replicate outside the animal host.

CONTROL OF INFECTIOUS DISEASE

IMMUNITY

Present understandings of the mechanisms of immunity actually originated with the work of Metchnikoff about 1885. He introduced a thorn under the skin of a starfish and noticed the collection of mobile cells around the site of insult. He also injected microorganisms into marine invertebrates and observed their engulfment by phagocytic cells. Later experiments by Metchnikoff revealed that the leukocytes of an artificially immunized rabbit engulfed microorganisms more rapidly than did those of a nonimmune animal. On the basis of his experiments Metchnikoff proposed the "cellular" or phagocytic theory of immunity. Bacteriologists at that time

believed, however, that chemical substances in the blood (humoral theory) were responsible for the destruction of microorganisms during infection and that phagocytes merely cleaned up the debris.

Although our knowledge of the mechanisms of immunity were no more than theories in the late nineteenth century, some of the practical aspects of immunity were already known. For centuries smallpox had ravaged populations, causing death in over 30 percent of those infected and scarring survivors. In 1717 a method for smallpox immunization was devised by the wife of a British ambassador to Turkey. A mild form of the disease was induced by drawing a thread, previously soaked in fluid from a pox pustule, through a small incision in the arm. Later Edward Jenner (1749–1823) noted that milkmaids suffering from cowpox, a mild form of pox, were protected from the more virulent smallpox. Jenner introduced fluid from a cowpox pustule into the arm of a healthy boy. Later the same boy was challenged with the fluid from a smallpox victim, and no severe reactions occurred. Jenner's work received considerable attention from Louis Pasteur. Pasteur observed that cultures of an organism that caused chicken cholera lost their virulence when left standing in the laboratory. When the old culture was injected into healthy animals, no disease symptoms appeared but an immunity to fresh virulent strains had been induced. Pasteur coined the term *vaccination* (*vacca*, a Latin term meaning "cow") in honor of Jenner's original work with cowpox. Pasteur later developed immunization techniques for anthrax and rabies.

In 1890 Emil Behring and S. Kitasato, working in Koch's laboratory, published the first of their findings on antitoxic immunity. They had discovered that the culture filtrate (the bacterial toxin) of the organism causing diphtheria was the active immunizing principle as well as the major virulence factor. The same conclusion was arrived at when the culture filtrate of the organism causing tetanus was used. They also showed that the serum from immunized animals (for example, animals immunized against tetanus) protected healthy animals from challenges with lethal doses of toxin. This work soon led to the production of an antitoxin for diphtheria and to fame and monetary rewards for Behring.

CHEMOTHERAPY

Chemotherapy is not a recent aspect of medical science, though its scientific basis is most often associated with the early years of the twentieth century. Malaria had for centuries been treated with the bark of the cinchona tree. Syphilis had been treated with various heavy metals such as antimony, mercury, and bismuth, treatments that predominated until the discovery and use of penicillin in the early 1940s.

Paul Ehrlich (1854–1915), working with aniline dyes, noted their selectivity for certain types of cells. He believed that certain chemicals could selectively destroy microorganisms without harming host tissue. His observations ultimately led to the discovery and use of an arsenical called *606* (salvarsan). Later one of Ehrlich's pupils, Gerhard Domagk (1895–1964), discovered the importance of sulfonamide in the treatment of certain infectious diseases. In 1935 the first sulfonamide derivative, Prontosil rubrum, was used for human treatment. In 1929 Alexander Fleming in England discovered that a compound produced by a mold called *Penicillium* was toxic to bacterial cells, specifically the staphylococci, but not to human tissue. This compound, which we now call penicillin, was difficult to purify because of its apparent instability. Several years elapsed before its usefulness was appreciated. Purification was accomplished by Florey and Chain in England and reported in *The Lancet* in 1940. Large-scale production of penicillin began in the United States, and in 1943 there were sufficient supplies for the armed forces in World War II, resulting in the saving of innumerable lives.

Research into the chemical characteristics of penicillin led to the purification and formation of pure crystals of the penicillin nucleus in 1959. This development was of particular importance because it allowed chemists to produce synthetic modifications of the penicillin molecule. Today many penicillin derivatives are widely used in the treatment of infectious disease.

From early experiments on the number and kind of microorganisms found in the soil Selman Waksman became interested in a little-known genus called *Actinomyces* and a related genus called *Streptomyces*. He noted that in a soil community certain species inhibited the growth of some soil microorganisms while not affecting others. In 1939 René Dubos successfully isolated an antibacterial substance called *tyrothricin* from soil bacteria. Although the antibiotic was not clinically acceptable for use, its discovery stimulated Waksman to search for other antibiotics. In 1943, after years of trial and error, he succeeded in isolating an antibiotic, called *streptomycin*, from the soil bacterium *Streptomyces griseus*.

Streptomycin was soon found to be useful in inhibiting the growth of microorganisms resistant to penicillin—the bacillus responsible for tuberculosis, for example. In addition, streptomycin was especially effective against gram-negative bacteria. Waksman's success led others into the field of chemotherapy. The discovery of such antibiotics as the cephalosporins, chloramphenicol, and the tetracyclines in the 1950s has saved countless lives.

VIROLOGY

The immunization practices and discoveries of Jenner and Pasteur were discussed earlier. Jenner knew nothing about bacteria or viruses, and scientists in the Pasteur era, including Pasteur himself, believed that the infectious agent for rabies was a bacterial species for which the proper isolation medium had not been devised. Of course we now know that the infectious agents of smallpox and rabies are viruses and that they cannot be cultivated on ordinary laboratory media.

In the early 1890s Iwanowsky began research on the tobacco mosaic virus. He demonstrated that fluid from the diseased plants, when filtered to remove bacteria, was still infectious. Most of the scientific community remained unimpressed with Iwanowsky's work. In 1898 Beijernick performed experiments similar to those of Iwanowsky and showed that, although the infectious agent would not grow aerobically or anaerobically in laboratory culture, it could replicate in host tissue. The filtered infectious agents were called *viruses*. The first filterable agent known to bring about infection in animals was the virus that causes foot-and-mouth disease. It was discovered by Loeffler and Frosch in 1898. In 1915 Twort showed that bacteria could also become infected by viruses. In 1935 Wendell Stanley crystallized the first virus. His technique would be used later to crystallize other viruses. Such studies actually paved the way for the era of molecular biology in the early 1950s and the 1960s, which was aided by the development of the electron microscope and the ability to manipulate bacterial viruses genetically.

In 1951 Max Theiler used chick embryo tissue for the passage and eventual attenuation of the virus causing yellow fever. Later investigations led to the use of different tissue cell cultures for the large-scale production of several viruses. This research ultimately led to techniques for vaccine production against polio and measles as well as many other viral diseases.

SCOPE

Microbiology deals with the study of microorganisms and viruses. It requires an understanding of the structure, physiology, metabolism, classification, and genetics of microorganisms. In addition, the student of microbiology must have an insight into the relationship of microorganisms to man and his environment.

Even though all infectious agents have one thing in common—i.e., being small—there is a tremendous diversity in their individual members. Microorganisms can be divided into representative groups based upon differences in biological properties. These groups include the bacteria, yeasts and molds, protozoa, and viruses. The explosion of microbiological information in the past 20 years has been so great that it has resulted in the creation of specialties within each of the representative groups of microorganisms. For example, the bacteriologist may develop special skills in various aspects of bacteriology such as bacterial physiology, bacterial genetics, or bacterial cytology. The microbiologist may specialize in the study of microorganisms as they appear in certain environments; there are now divisions of applied microbiology such as space microbiology, soil microbiology, and food microbiology.

At one time medical microbiologists dealt only with the detrimental effects of microorganisms on man and animals. Knowledge of the structure, physiology, and genetics of microorganisms has expanded so greatly in the past few decades that the modern microbiologist is now exploring the role of microorganisms in the "normal" host as well as studying how pathogenic microorganisms affect the diseased host. Because various medical procedures and treatments require the use of antibiotics and other drugs, man's normal flora has become altered. In consequence the so-called nonpathogens present in the normal host have become pathogenic and cause disease—a dramatic illustration that the ecological balance in the normal host is maintained on a precarious level. A relationship that might be considered normal at one time could quickly become abnormal. The medical microbiologist must therefore understand the interactions between microorganisms and host as well as the influence that one microorganism has upon another. Once these relationships are grasped, control of all infectious disease becomes more nearly possible.

Medical microbiologists must be jacks-of-all-trades and should have a basic knowledge of the chemical and physical properties of all patho-

genic microbial agents—bacteria, viruses, yeasts, molds, and animal parasites. Their primary responsibility is the understanding of the etiology (causation), pathogenicity (disease manifestation), laboratory diagnosis, and treatment of infectious agents, but they may also be required to determine the epidemiology of disease and to develop measures for the control and prevention of infections in the community. The fact that many major pestilences (smallpox, diphtheria, plague) no longer decimate populations as they once did is testimony to the advances made in epidemiology, control, and prevention of infectious disease. Man's resistance to disease, his immunity to infection, has been known for years. This area of study is referred to as *immunology* and deals specifically with the relationship of antigens or foreign substances to antibody production in the host. Because of its connection to disease, immunology is also considered an important part of the medical microbiologist's background. The development of new concepts in molecular biology and cellular immunity has not only expanded knowledge of the immune process but provided the microbiologist with new laboratory diagnostic tools. Thus the medical microbiologist can now identify and classify microorganisms using immunological techniques.

In its early history, microbiology as a science was concerned with the identification and control of microorganisms. With major advances in microscopy and biochemical techniques from 1940 to the present, the microorganism has become a useful model for studying biological properties particularly in the areas of genetics and metabolism. The studies were aided by the fact that microorganisms divide very rapidly and are easily cultivated and maintained in the laboratory, properties not common to higher forms of life. It soon became apparent that many of the metabolic processes occurring in microbial systems were similar if not identical to those of cells in higher systems, including man. In 1944 Avery, MacLeod, and McCarty discovered that isolated DNA (cell free) was capable of transforming certain intact bacterial cells. This was one of several experiments proving that DNA was the hereditary material of the cell. The discovery of the structure of DNA by Watson and Crick in 1953 and results obtained from various experiments in microbial genetics provided the basic clues to genetic mechanisms not only in bacteria but in higher forms of life as well. The analysis of the chemical makeup of biological material and its relationship to genetic information is the foundation of the science of molecular biology. With the aid of microorganisms as experimental "guinea pigs" a broader understanding of all life processes is being developed.

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2 CHARACTERISTICS OF THE MICROBIAL WORLD

MICROBIAL DIVISIONS

The descriptive term *microorganism* means small organism. But how small is small? We generally assume that a microorganism is one-celled and can be observed only with the microscope. It is true that organisms such as bacteria and viruses can be observed only with the microscope. Others, however, are macroscopic and include members of the fungi, algae, and animal parasites. Microscopic unicellular organisms were at one time classified as either plant or animal depending upon various characteristics normally associated with those two groups. As our knowledge of microorganisms expanded, it became clear that their separation into two kingdoms was not an adequate means of classification. Many microorganisms have qualities distinct from those of either plant or animal while others possess characteristics that are common to both groups. A third kingdom was eventually proposed, called the *Protista,* to include the organisms that do not have extensive tissue development—one-celled microscopic forms such as bacteria as well as multicellular macroscopic forms such as algae. The Protista was subdivided into two groups: the lower protists (bacteria and blue-green algae) and the higher protists (algae, fungi, and protozoa). The major distinction between the higher and lower protists was that the lower protists did not possess a nuclear membrane. The term *prokaryotic* has been applied to cells that lack a nuclear membrane, while *eukaryotic* describes those that have a nuclear membrane. Other distinctions separating eukaryotic and prokaryotic cells are listed in Table 2-1. In 1974 *Bergey's Manual of Determinative Bacteriology,* the bacteriologist's classification handbook, proposed that the bacteria and blue-green algae be placed in the kingdom Procaryotae, with two divisions: the Cyanophyceae, or blue-green algae, and the Bacteria.

Although organisms have been conveniently divided into eukaryotes and prokaryotes (see Table 2-1 for a comparison of these groups), a third class has been proposed by Carl Woese and George Fox. Members of this group resemble bacteria but have genetic and metabolic differences that make them candidates for a new class. These unique organisms are the methanogens or methane-producing bacteria found in the intestinal tract of man and animals as well as in water sediments. They utilize the gases hydrogen and carbon dioxide and convert them to methane gas. The evidence suggesting their separate line of descent runs as follows: Their cell walls do not contain muramic acid, a component of bacterial cell walls; methane formation requires unique coenzymes that so far have not been found in other organisms; and the manner in which carbon dioxide is fixed during the formation of cell material has not been elucidated. Furthermore, methanogens have RNA sequences that suggest they are not related to prokaryotes. Woese and Fox propose that the methanogens, which could have survived in the primeval environment, may have shared a common ancestor with prokaryotes and eukaryotes and simply branched off independently from the two major divisions.

CHARACTERISTICS OF THE MAJOR GROUPS OF MICROORGANISMS

Algae, fungi, parasites, and the viruses will not be discussed at any great length in this chapter. The bacteria are given closer attention because most of this book deals with them. Details on structure, morphology, classification, etc., of the viruses, fungi, and parasites are presented in separate chapters devoted only to those groups. Table 2-2 compares the size of microorganisms pathogenic (disease producing) to man.

THE EUKARYOTES

The Algae

For the most part algae are photosynthetic microorganisms found in most bodies of water. Some are microscopic (diatoms) while others reach a length of 60 meters (kelp). Most algae are related to eukaryotic plant forms; i.e., they contain cellulose in the cell wall and have a defined

Table 2-1. Characteristics Distinguishing Eukaryotic from Prokaryotic Cells

Characteristic	Eukaryotic	Prokaryotic
Organisms included in the group	Man, animals, plants, algae, fungi, and protozoa	Bacteria and blue-green algae
Nuclear membrane	Present	Absent
Chromosomes	More than one	One
Mitochondria	Present	Absent
Chloroplasts	Present only in some	Absent
Cytoplasmic streaming	Present	Absent
Mitotic division	Present	Absent
Endoplasmic reticulum	Present	Absent
Golgi apparatus	Present	Absent
Proteins associated with chromosome(s)	Present	Absent
Sedimentation coefficient of ribosomes	80S	70S
Initiating amino acid in protein synthesis	Methionine	N-formylmethionine

Table 2-2. Size Comparison of the Various Types of Microorganisms Pathogenic to Man

	Size		
Group	Smallest	Largest	Average
Bacteria			
Cocci	0.4 μm	1.2 μm	0.8 μm
Bacilli	0.25 μm	12.0 μm	4–6 μm
Spirochetes	5.0 μm	30 μm	8–10 μm
Viruses	0.020 μm	0.3 μm	0.080 μm
Parasites			
Protozoa	5 μm	100 μm	15 μm
Nematodes	0.125 mm	3–10 m	10 mm
Fungi*	1–2 μm	300 μm	10–15 μm

*Many of the fungi infectious to man exist as spherical yeast forms in tissue rather than the branched filamentous types. The figures for the fungi represent only the yeast forms.

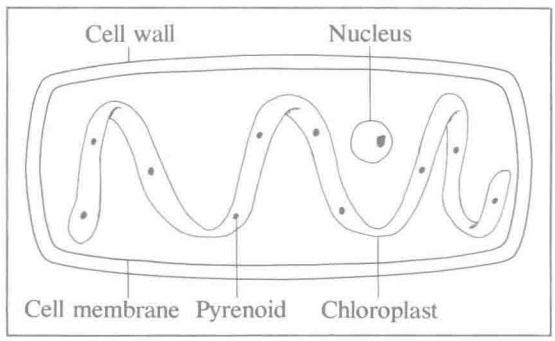

Fig. 2-1. Structure of a vegetative algal cell.

nucleus and a photosynthetic apparatus for the synthesis of starch (Fig. 2-1). The blue-green algae, however, are primitive forms of microorganisms that can be found in a variety of environments extending from volcanic mountaintops to fresh or marine water. The algae are not pathogenic to man.

The Fungi

The study of fungi is called *mycology*. The fungi differ morphologically and physiologically from the bacteria. The differences are described in Table 2-3. The fungi are eukaryotic cells and have a cell wall and cell membrane. They have been conveniently divided into two descriptive but not taxonomic groups: the molds and the yeasts. *Mold* refers to a filamentous multicellular type of fungus while *yeast* refers to a unicellular spherical type. The filamentous form is made up of a vegetative structure called a *hypha*. A mass of hyphal units is called a *mycelium* (Fig. 2-2). Practically all fungi produce reproductive units called *spores;* some sexually, others asexually. Many species, particularly the yeasts, can reproduce by a process called *budding*.

The habitat of the fungi is diverse; however, most are found as saprophytes in the soil. Some are important as agents of disease in man, plants, and animals. Of the more than 80,000 species of