I. OVERVIEW

The cellular world is divided into two major groups, based on whether or not the cells have a nucleus (that is, an internal membrane-enclosed region that contains the genetic material). Cells that have a well-defined nucleus are called eukaryotic, whereas cells that lack a nucleus are called prokaryotic. All bacteria are prokaryotes. In addition, bacterial DNA is not organized into the elaborate multichromosomal structures of the eukaryotes, but typically is a single double-stranded molecule of DNA. Prokaryotes and eukaryotes employ very similar metabolic pathways to achieve cell growth and maintain viability. However, prokaryotes synthesize substances and structures that are unique to bacteria, for example, peptidoglycan. A generalized prokaryotic cell is shown in Figure 6.1.

Figure 6.1
Generalized structure of a bacterial cell.
II. THE CELL ENVELOPE

The bacterial “cell envelope” is a term applied to all material external to and enclosing the cytoplasm. It consists of several chemically and functionally distinct layers, the most prominent of which are the cell wall and the cytoplasmic membrane. The cell envelope also includes the capsule or glycocalyx, if present.

A. Cytoplasmic membrane

The cell membrane is composed of phospholipid, the molecules of which form two parallel surfaces (called a lipid bilayer) such that the polar phosphate groups are on the outside of the bilayer and the nonpolar lipid chains are on the inside. The membrane acts as a permeability barrier, restricting the kind and amount of molecules that enter and leave the cell.

B. Peptidoglycan

The peptidoglycan layer determines the shape of the cell. It is composed of a cross-linked polymeric mesh (Figure 6.2.) The glycan portion is a linear polymer of alternating monosaccharide subunits:

The sequence of the peptide varies from one bacterial species to another. For example, in some species, an L-amino acid is replaced by diaminopimelic acid, which is an amino acid found only in prokaryotic structures.

The peptide chains can be cross-linked directly to each other, or via a pentaglycine bridge. The type of cross-linking bridge differs among bacterial species.

Figure 6.2
Structure of peptidoglycan, the major polymer of bacterial cell walls.
II. The Cell Envelope

N-acetylglucosamine (NAG) and N-acetylmuramic acid (NAM). This polymer is the carbohydrate “backbone” of the mesh. The “peptido” portion of the polymer is a short string of amino acids that serves to cross-link adjacent polysaccharide strands at the NAM subunits of the backbone, forming a network with high tensile strength (see Figure 6.2). [Note: The presence of D-amino acids helps render the bacterial wall resistant to host peptidases such as those in the intestine.] A discussion of cell wall synthesis is presented on p. 55.

C. Differences between gram-positive and gram-negative cell walls

The molecular details of the cell walls of gram-positive and gram-negative bacteria are shown in Figure 6.3. Additional surface layers, such as a capsule or glycocalyx, can be found outside of the cell wall in some species of gram-positive and gram-negative bacteria.

1. Gram-positive organisms: Gram-positive bacteria have thick, multilayered, peptidoglycan cell walls that are exterior to the cytoplasmic membrane. The peptidoglycan in most gram-positive species is covalently linked to teichoic acid, which is essentially a polymer of substituted glycerol units linked by phosphodiester bonds. The teichoic acids are major cell surface antigens. Teichoic acids are integrated into the peptidoglycan layers but not tethered to the cytoplasmic membrane. Lipoteichoic acids are lipid modified and integrated by this moiety into the outer leaflet of the cytoplasmic membrane.

2. Gram-negative organisms: Gram-negative bacteria have a more complex cell wall structure composed of two membranes (an outer membrane and an inner, that is, cytoplasmic, membrane). The two membranes are separated by the periplasmic space, which contains the peptidoglycan layer. The periplasmic space also contains degradative enzymes and transport proteins. In contrast to gram-positive cells, the peptidoglycan layer of gram-negative cells is thin, and the cells are consequently more susceptible to physical damage. The outer membrane is distinguished by the presence of embedded lipopolysaccharide (LPS) that is the major constituent of the outer leaflet of the outer membrane. The polysaccharide portion of LPS (O-polysaccharide) is antigenic and can, therefore, be used to identify different strains and species. The lipid portion (called lipid A) is imbedded in the membrane and is toxic to humans and animals. Because lipid A is an integral part of the membrane, it is called endotoxin, as opposed to exotoxins, which are secreted substances. Do not confuse endotoxin or exotoxins with enterotoxins, which are exotoxins that are toxic for the mucosal membrane of the intestine. “Enterotoxin” denotes the site of action, rather than its origin.

D. The external capsule and glycocalyx

Many bacteria secrete a sticky, viscous material that forms an extracellular coating around the cell. The material is usually a polysaccharide. However, in the case of pathogenic Bacillus anthracis, the capsule is composed of poly-d-glutamic acid. If the material is tightly bound to the cell and has an organized structure, it is called a cap-
sule (see Figure 6.1). If the material is loosely bound and amorphous, it is called a slime layer, or glycocalyx. The capsule or glycocalyx allow cells to adhere to surfaces, protect bacteria from antibodies and phagocytosis, and act as diffusion barriers against some antibiotics, thus contributing to the organisms’ pathogenicity. Capsules can also protect bacteria against dessication, or drying, which facilitates transmission.

E. Appendages

Many bacteria have hairlike appendages that project from the cell wall. There are of two kinds of appendages: flagella (singular, flagellum) and pili (singular, pilus).

1. Flagella: Prokaryotic flagella are long, semirigid, helical, hollow tubular structures composed of several thousand molecules of the protein flagellin. They enable bacteria to move in a directed fashion, for example, in response to a chemotactic stimulus. Flagella are anchored in the cell membranes by a basal body, which is a complex molecular machine that rotates the flagellum like the screw propeller of a ship (Figure 6.4). Cells may have one or many flagella. Flagella are highly antigenic. Bacteria that have flagella often do not form compact colonies on an agar surface, but instead swarm over the surface of the agar if it is sufficiently wet, producing a scumlike mat.

2. Pili: Pili (sometimes called fimbriae) are shorter and thinner than flagella and function as attachment structures that promote specific cell-to-cell contact (see Figure 6.1). The attachment can be between the bacterial cell and the host eukaryotic cell or between one bacterial cell and another.

F. Antigenic variation

Antigenic variation is the expression of various alternative forms of antigen on the cell surface. Most surface structures are subject to antigenic variation, including LPS, capsules, lipoteichoic acids, pili, and flagella. This variation is important for immune evasion by the pathogen. For example, in Neisseria species, antigenic variation by gene conversion (p. 101) allows the organism to produce antigenically different pilin molecules at high frequency. Variation in the surface structures between strains of the same species is detected by serology.

III. SPORES AND SPORULATION

To enhance survival during periods of environmental hostility (such as nutritional deprivation), some gram-positive rods undergo profound structural and metabolic changes. These result in the formation of a dormant cell called an endospore inside the original cell. Endospores can be released from the original cell as free spores (Figure 6.5). Spores are the most resistant life forms known. They are remarkably resistant to heat (they survive boiling), desiccation, ultraviolet light, and bactericidal chemical agents. In fact, sterilization procedures are assessed by their ability to inactivate spores.
A. Sporulation

Sporulation can be thought of as repackaging a copy of bacterial DNA into a new form that contains very little water, has no metabolic activity, does not divide, and has a restructured, highly impermeable, multilayered envelope. Spore formation begins with the invagination of the parent cell membrane, producing a double membrane that encapsulates and isolates a copy of the bacterial DNA in what will become the core of the spore. The mature spore retains the complete machinery for protein synthesis, and new spore-specific enzymes are synthesized in the core of the spore. The core also has high levels of a unique compound called calcium dipicolinate, which is thought to be important for protection of the spore DNA from environmental damage. Many enzymes of the original vegetative (nondividing) cell are degraded. When the endospore is completed, the parent cell lyses, releasing the spore.

B. Spore germination

To return to the vegetative state, spores must first be subjected to a treatment that weakens the spore coat (such as heat or extremes of pH), thus allowing germination to occur. If the activated spore is in a nutritious environment, which it senses by monitoring various key metabolites, it begins to germinate. This process involves destruction of the cortex by lytic enzymes, followed by uptake of water, and release of calcium dipicolinate from the cell.

C. Medical significance of sporulation

Some of the most notorious pathogens are spore-formers, including *B. anthracis* (anthrax, see p. 94), *Bacillus cereus* (gastroenteritis, see p. 118), *Clostridium tetani* (tetanus, see p. 155), *Clostridium botulinum* (botulism, see p. 153), *Clostridium perfringens* (gas gangrene, see p. 150), and *Clostridium difficile* (see page 157). Spores of these organisms can remain viable for many years and are generally not killed by boiling, but they can be killed by autoclaving (that is, subjecting the spores to temperatures above 120°C at elevated pressure). In the absence of an autoclave, spores can be largely eliminated by a primary boiling to activate germination and, after a short period of vegetative growth, a second boiling.

IV. GROWTH AND METABOLISM

All cells must accomplish certain metabolic tasks to grow and divide. All cells, whether bacterial or human, accomplish these metabolic tasks by similar pathways. There are, however, some important differences that set bacteria apart metabolically from eukaryotic cells, and these differences can often be exploited in the development of antibacterial therapies.

A. Characteristics of bacterial growth

If bacterial cells are suspended in a liquid nutrient medium, the increase in cell number or mass can be measured in several ways. Techniques include microscopically counting the cells in a given volume using a ruled slide, counting the number of appropriately
6. Bacterial Structure, Growth, And Metabolism

Bacterial Structure, Growth, And Metabolism

Figure 6.6
Kinetics of bacterial growth in liquid medium.

Figure 6.7
Growth of bacterial colonies on a solid, nutrient surface, for example, nutrient agar. [Note: The doubling time of bacteria is assumed to be 0.5 hr in this example]

diluted cells that are able to form colonies following transfer to a solid nutrient (agar) surface, or quantitating the turbidity—which is proportional to the cell mass—of a culture in liquid medium.

1. Stages of the bacterial growth cycle: Because bacteria reproduce by binary fission (one becomes two, two become four, become eight, etc.), the number of cells increases exponentially with time (the exponential, or log, phase of growth). Depending on the species, the minimum doubling time can be as short as 10 minutes or as long as several days. For example, for a rapidly growing species such as *Escherichia coli* in a nutritionally complete medium, a single cell can give rise to some 10 million cells in just 8 hours. Eventually, growth slows and ceases entirely (stationary phase) as nutrients are depleted, and toxic waste products accumulate. Most cells in a stationary phase are not dead, however. If they are diluted into fresh growth medium, exponential growth will resume after a lag phase. The phases of the growth cycle are illustrated in Figure 6.6.

2. Surface growth: If a single bacterial cell is placed on a solid nutrient agar surface, the progeny of this cell remain close to the site of deposition and eventually form a compact macroscopic mass of cells called a colony (Figure 6.7). For rapidly growing species, overnight incubation at 30°C to 37°C is sufficient to produce visible colonies, each containing millions of cells. The gross characteristics of colonies (for example, color, shape, adherence, smell, and surface texture) can be useful guides for identification of the species of bacterium. Some species do not form compact circular colonies because the cells are capable of movement and swarm over the agar surface, especially if the surface is moist. Other species, particularly the actinomycetes, grow as long filaments of cells (mycelial growth).

B. Energy production

A distinctive feature of bacterial metabolism is the variety of mechanisms used to generate energy from carbon sources. Depending on the biochemical mechanism used, bacterial metabolism can be categorized into three types: aerobic respiration, anaerobic respiration, and fermentation (Figure 6.8).

1. Aerobic respiration is the metabolic process in which molecular oxygen serves as the terminal electron acceptor of the electron transport chain. In this process, oxygen is reduced to water. Respiration is the energy-generating mode used by all aerobic bacteria.

2. Anaerobic respiration is the metabolic process in which inorganic compounds other than molecular oxygen serve as the terminal electron acceptors. Depending on the species, acceptors can be molecules such as nitrate or sulfate. Anaerobic respiration can be used as an alternative to aerobic respiration in some species (facultative organisms), but is obligatory in other species (some obligate
anaerobes). [Note: Other obligate anaerobes use fermentation as the main mode of energy metabolism. This is particularly true among the anaerobic bacteria of medical importance.]

3. **Fermentation** is an anaerobic process utilized by some bacterial species. It is the metabolic process by which an organic metabolic intermediate derived from a "fermentable" substrate serves as the final electron acceptor. The substrates that can be fermented and the final end products depend on the species. Regardless of the bacterium and the fermentation pathway, several unifying concepts are common to fermentation. By comparison to aerobic and anaerobic respiration, fermentation yields very little energy. The purpose of fermentation is to recycle nicotinamide adenine dinucleotide hydrogen (NADH) back to NAD. The reducing power that can be converted to energy via respiration is unrealized. The terminal electron acceptor in fermentation is pyruvate or a pyruvate derivative. Beyond these commonalities, the pathways and end products of fermentation are incredibly varied. These end products can be measured and are sometimes diagnostic for a given species. In addition, some fermentation end products can result in host toxicity and tissue damage.

C. Peptidoglycan synthesis

The bacterial peptidoglycan polymer is constructed on the surface of the cell membrane and is composed of a repeating carbohydrate backbone subunit, which is NAG–NAM (see p. 50). These backbone chains are cross-linked by short peptides (PEP) to form a rigid meshwork (Figure 6.9). Peptidoglycan biosynthesis occurs via the following series of steps.

1. **Activation of carbohydrate subunits:** As in all biologic polymerizations, NAM and NAG subunits are activated by attachment to a carrier molecule, which in this case is the nucleotide uridine diphosphate (UDP).

2. **Synthesis of the linking peptide:** A pentapeptide is added to UDP–NAM by sequential transfer of amino acids, with the two terminal alanine residues added as a dipeptide. This pentapeptide may contain some nonstandard amino acids, including, for example, diaminopimelic acid ([DAP] a metabolic precursor of lysine), and D-amino acids. The sequence of the pentapeptide is not dictated by an RNA template, but rather the specificity of the enzymes that form the peptide bonds.

3. **Transfer of the peptidoglycan unit to bactoprenol phosphate:** The NAM–PEP moiety is transferred from the UDP carrier to another carrier, bactoprenol phosphate (BPP), located on the inner surface of the cell membrane. At this point, UDP–NAG transfers NAG to NAM–PEP, completing the peptidoglycan repeat unit, NAG–NAM–PEP, which is now attached to the carrier BPP.
**Figure 6.9**
Synthesis of a bacterial cell wall.

1. Activated NAM and NAG peptidoglycan precursors.
2. Synthesis of linking pentapeptide (PEP); blocked by cycloserine.
3. NAM-PEP complex is transferred from UDP to membrane-bound BPP. Peptidoglycan repeat unit is completed by addition of NAG.
4. The repeat unit is carried by BBP to the outer surface of the membrane, where it attaches to a free end of the existing peptidoglycan. This process is blocked by vancomycin.
5. The PEP side chains are cross-linked with the release of the terminal alanine. This process is blocked by penicillin.
4. Addition of the repeat unit to the existing peptidoglycan: BPP carries the NAG–NAM–PEP repeat unit through the cell membrane to the outside surface where the peptidoglycan of the existing cell wall is located. The repeat unit is added to a free end of the existing peptidoglycan, increasing the length of the polymer by one repeat unit. Presumably, free ends are created by a limited hydrolytic loosening of the preexisting peptidoglycan.

5. Cross-linking of the pentapeptide to the peptidoglycan backbone: Although the N–terminal end of the pentapeptide is attached to the NAM moieties of the backbone, the C–terminal end is dangling free. Cross-linking is brought about by a transpeptidation reaction that bonds DAP of the peptide in one chain to the alanine (ala) at position four of the peptide in an adjacent chain, causing the release of the terminal ala. This mode of direct cross-linking is characteristic of *E. coli* and many other gram-negative species. By contrast, in gram-positive bacteria, such as *Staphylococcus aureus*, a glycine pentapeptide is usually interposed between the lysine (lys) at position three of one PEP and the ala at position four of the PEP to which the linkage is to be made (Figure 6.10).

6. Peptidoglycan biosynthesis as a target of some antibacterial agents: Because many of the reactions involved in the synthesis of peptidoglycan are unique to bacteria, cell wall synthesis is an ideal target for some highly specific antibacterial agents, particularly the β-lactam antibiotics.

   a. β-Lactam antibiotics: Penicillins and cephalosporins inhibit the enzymes that catalyze transpeptidation and carboxypeptidation reactions of cell wall assembly. These enzymes are called penicillin-binding proteins (PBPs) because they all have active sites that bind β-lactam antibiotics. No single PBP species is the target of β-lactam antibiotics. Rather, their lethal effect on bacteria is the result of inactivation of multiple species of PBPs. Most PBPs are involved in bacterial cell wall synthesis. Acquired resistance to β-lactam antibiotics may result from genetic modifications that result in production of new PBPs that have a lower affinity for β-lactam antibiotics (see p. 64).

   b. Bacitracin, cycloserine, and vancomycin: Other antibiotics that interfere with peptidoglycan synthesis include bacitracin, which inhibits the recycling of bactoprenol phosphate; cycloserine, which inhibits synthesis of the D–ala–D–ala dipeptide that provides the two terminal residues of the pentapeptide; and vancomycin, which blocks incorporation of the NAG–NAM–PEP repeat unit into the growing peptidoglycan chain (see Figure 6.9). Because vancomycin binds to the terminal D-ala-D-ala dipeptide, this antibacterial agent also prevents transpeptidation.

Figure 6.10
A. Glycine bridge in the peptidoglycan of *Staphylococcus aureus*.
B. Organization of peptidoglycan layer in gram-positive cells.
Study Questions

Choose the ONE correct answer.

6.1 A bacterial culture with a starting density of $1 \times 10^3$ cells/ml is incubated in liquid nutrient broth. If the bacteria have both a lag time and a generation time of 10 minutes, what will the cell density be at 30 minutes?

A. $1.0 \times 10^3$
B. $2.0 \times 10^3$
C. $3.0 \times 10^3$
D. $4.0 \times 10^3$
E. $6.0 \times 10^3$

Correct answer = D. After a 10-minute lag, the bacteria will double in number at 20 minutes and double again by 30 minutes.

6.2 Which of the following components are found in the cell walls of gram-positive bacteria but not gram-negative bacteria?

A. Cytoplasmic membrane
B. Lipopolysaccharide
C. Outer membrane
D. Peptidoglycan
E. Teichoic acid

Correct answer = E. Gram-positive bacteria have thick, multilayered, peptidoglycan cell walls that are exterior to the membrane. The peptidoglycan in most gram-positive species is covalently linked to teichoic acid, which is essentially a polymer of substituted glycerol units linked by phosphodiester bonds. All gram-positive species also have lipoteichoic acid in their membranes, where it is covalently linked to glycolipid. Teichoic acids are major cell surface antigens. Gram-negative bacteria have two membranes—an outer membrane and an inner (cytoplasmic) membrane. Their peptidoglycan layer is located between the two membranes in the periplasmic space. The periplasmic space also contains enzymes and various other substances. The outer membrane is distinguished by the presence of various lipopolysaccharides.

6.3 In 1998, a large botulism outbreak occurred in El Paso, Texas. The foodborne illness was shown to be caused by foil-wrapped baked potatoes that were held at room temperature for several days before their use in dips at a Greek restaurant. The dip yielded botulinum toxin type A, as did stool and, in some cases serum samples, from 18 of the 30 affected patients. Four patients required mechanical ventilation, but none died. What would be the expected outcome if the potatoes had been reheated to 100°C for 10 minutes before being served? [Hint: See pp. 153–154 for properties of *Clostridium botulinum* toxin.]

A. Heat would kill the spores of *Clostridium botulinum*.
B. Heat would promote the vegetative state.
C. Heat would inactivate the toxin in the potato dip.
D. Heat would increase the number of toxin-producing bacteria.
E. Heat would not alter the outcome.

Correct answer = C. *Clostridium botulinum* spores are commonly found on raw potatoes and generally are not killed if the potatoes are baked in foil, which holds in moisture and, thus, keeps the potatoes' surface temperature at 100°C (below the temperature required for spore killing of >120°C). During storage at room temperature in the anaerobic environment provided by the foil, spores germinate, and toxin forms. Heating at 100°C would kill most *C. botulinum* because the bacterium is in its vulnerable, vegetative state. Heat would also inactivate toxin produced during room-temperature storage. However, any remaining spores would not be killed.
Microbes That Cause Infectious Diseases

The agents of human infectious diseases belong to five major groups of organisms: bacteria, fungi, protozoa, helminths, and viruses. Bacteria belong to the prokaryote kingdom, fungi (yeasts and molds) belong to the kingdom of fungi, and protozoa are members of the kingdom of protists. Helminths (worms) are classified in the animal kingdom (Table 1–1). Protists and fungi are distinguished from animals and plants by being either unicellular or relatively simple multicellular organisms. In contrast, helminths are complex multicellular organisms. Taken together, the helminths and the protozoa are commonly called parasites. Viruses are quite distinct from other organisms—they are not cells but can replicate only within cells.

Important Features of Microbes

Many of the essential characteristics of these organisms are described in Table 1–2. One salient feature is that bacteria, fungi, protozoa, and helminths are cellular, whereas viruses are not. This distinction is based primarily on three criteria:

1) Structure. Cells have a nucleus or nucleoid (see below), which contains DNA; this is surrounded by cytoplasm, within which proteins are synthesized and energy is generated. Viruses have an inner core of genetic material (either DNA or RNA) but no cytoplasm, and so they depend on host cells to provide the machinery for protein synthesis and energy generation.

### Table 1–1 Biologic Relationships of Pathogenic Microorganisms

<table>
<thead>
<tr>
<th>Kingdom</th>
<th>Pathogenic Microorganisms</th>
<th>Type of Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal</td>
<td>Helminths (worms)</td>
<td>Eukaryotic</td>
</tr>
<tr>
<td>Protists</td>
<td>Protozoa</td>
<td>Eukaryotic</td>
</tr>
<tr>
<td>Fungi</td>
<td>Fungi (yeasts and molds)</td>
<td>Eukaryotic</td>
</tr>
<tr>
<td>Prokaryote</td>
<td>Bacteria, Viruses</td>
<td>Prokaryotic Noncellular</td>
</tr>
</tbody>
</table>
### TABLE 1–2 Comparison of Medically Important Organisms

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Viruses</th>
<th>Bacteria</th>
<th>Fungi</th>
<th>Protozoa and Helminths</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cells</strong></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Approximate diameter (μm)</strong></td>
<td>0.02–0.2</td>
<td>1–5</td>
<td>3–10 (yeasts)</td>
<td>15–25 (trophozoites)</td>
</tr>
<tr>
<td><strong>Nucleic acid</strong></td>
<td>Either DNA or RNA</td>
<td>Both DNA and RNA</td>
<td>Both DNA and RNA</td>
<td>Both DNA and RNA</td>
</tr>
<tr>
<td><strong>Type of nucleus</strong></td>
<td>None</td>
<td>Prokaryotic</td>
<td>Eukaryotic</td>
<td>Eukaryotic</td>
</tr>
<tr>
<td><strong>Ribosomes</strong></td>
<td>Absent</td>
<td>70S</td>
<td>80S</td>
<td>80S</td>
</tr>
<tr>
<td><strong>Mitochondria</strong></td>
<td>Absent</td>
<td>Present</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td><strong>Nature of outer surface</strong></td>
<td>Protein capsid</td>
<td>Rigid wall containing</td>
<td>Rigid wall containing</td>
<td>Flexible membrane</td>
</tr>
<tr>
<td></td>
<td>and lipoprotein envelope</td>
<td>peptidoglycan</td>
<td>chitin</td>
<td></td>
</tr>
<tr>
<td><strong>Motility</strong></td>
<td>None</td>
<td>Some</td>
<td>None</td>
<td>Most</td>
</tr>
<tr>
<td><strong>Method of replication</strong></td>
<td>Not binary fission</td>
<td>Binary fission</td>
<td>Budding or mitosis²</td>
<td>Mitosis²</td>
</tr>
</tbody>
</table>

1For comparison, a human red blood cell has a diameter of 7 μm.
2Yeasts divide by budding, whereas molds divide by mitosis.
3Helminth cells divide by mitosis, but the organism reproduces itself by complex, sexual life cycles.

(2) **Method of replication.** Cells replicate either by binary fission or by mitosis, during which one parent cell divides to make two progeny cells while retaining its cellular structure. Prokaryotic cells (e.g., bacteria) replicate by binary fission, whereas eukaryotic cells replicate by mitosis. In contrast, viruses disassemble, produce many copies of their nucleic acid and protein, and then reassemble into multiple progeny viruses. Furthermore, viruses must replicate within host cells because, as mentioned previously, they lack protein-synthesizing and energy-generating systems. With the exception of rickettsiae and chlamydiae, which also require living host cells for growth, bacteria can replicate extracellularly.

(3) **Nature of the nucleic acid.** Cells contain both DNA and RNA, whereas viruses contain either DNA or RNA, but not both.

### EUKARYOTES & PROKARYOTES

Cells have evolved into two fundamentally different types, **eukaryotic** and **prokaryotic**, which can be distinguished on the basis of their structure and the complexity of their organization. Fungi, protozoa, and helminths are eukaryotic, whereas bacteria are prokaryotic.

(1) The eukaryotic cell has a true **nucleus** with multiple chromosomes surrounded by a nuclear membrane and uses a mitotic apparatus to ensure equal allocation of the chromosomes to progeny cells.

(2) The **nucleoid** of a prokaryotic cell consists of a single circular molecule of loosely organized DNA, lacking a nuclear membrane and mitotic apparatus (Table 1–3).

In addition to the different types of nuclei, the two classes of cells are distinguished by several other characteristics:

(1) Eukaryotic cells contain **organelles**, such as mitochondria and lysosomes, and larger (80S) ribosomes, whereas prokaryotes contain no organelles and smaller (70S) ribosomes.

(2) Most prokaryotes have a rigid external cell wall that contains **peptidoglycan**, a polymer of amino acids and sugars, as its unique structural component. Eukaryotes, on

### TABLE 1–3 Characteristics of Prokaryotic and Eukaryotic Cells

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Prokaryotic Bacterial Cells</th>
<th>Eukaryotic Human Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA within a nuclear membrane</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Mitotic division</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>DNA associated with histones</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Chromosome number</td>
<td>One</td>
<td>More than one</td>
</tr>
<tr>
<td>Membrane-bound organelles, such as mitochondria and lysosomes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Size of ribosome</td>
<td>70S</td>
<td>80S</td>
</tr>
<tr>
<td>Cell wall containing peptidoglycan</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
PEARLS

• The agents of human infectious diseases are bacteria, fungi (yeasts and molds), protozoa, helminths (worms), and viruses.

• Bacterial cells have a prokaryotic nucleus, whereas human, fungal, protozoan, and helminth cells have a eukaryotic nucleus. Viruses are not cells and do not have a nucleus.

• All cells contain both DNA and RNA, whereas viruses contain either DNA or RNA, but not both.

• Bacterial and fungal cells are surrounded by a rigid cell wall, whereas human, protozoan, and helminth cells have a flexible cell membrane.

• The bacterial cell wall contains peptidoglycan, whereas the fungal cell wall contains chitin.

TERMINOLOGY

Bacteria, fungi, protozoa, and helminths are named according to the binomial Linnaean system that uses genus and species, but viruses are not so named. For example, regarding the name of the well-known bacteria Escherichia coli, Escherichia is the genus and coli is the species name. Similarly, the name of the yeast Candida albicans consists of Candida as the genus and albicans as the species. But viruses typically have a single name, such as poliovirus, measles virus, or rabies virus. Some viruses have names with two words, such as herpes simplex virus, but those do not represent genus and species.

SELF-ASSESSMENT QUESTIONS

1. You’re watching a television program that is discussing viruses called bacteriophages that can kill bacteria. Your roommate says, “Wow, maybe viruses can be used to kill the bacteria that infect people! You’re taking the Microbiology course now; what’s the difference between viruses and bacteria?” Which one of the following would be the most accurate statement to make?
   (A) Viruses do not have mitochondria, whereas bacteria do.
   (B) Viruses do not have a nucleolus, whereas bacteria do.
   (C) Viruses do not have ribosomes, whereas bacteria do.
   (D) Viruses replicate by binary fission, whereas bacteria replicate by mitosis.
   (E) Viruses are prokaryotic, whereas bacteria are eukaryotic.

2. Bacteria, fungi (yeasts and molds), viruses, and protozoa are important causes of human disease. Which one of the following microbes contains either DNA or RNA but not both?
   (A) Bacteria
   (B) Molds
   (C) Protozoa
   (D) Viruses
   (E) Yeasts

3. Which one of the following contains DNA that is not surrounded by a nuclear membrane?
   (A) Bacteria
   (B) Molds
   (C) Protozoa
   (D) Yeasts

ANSWERS

(1) (C)
(2) (D)
(3) (A)

PRACTICE QUESTIONS: USMLE & COURSE EXAMINATIONS

Questions on the topics discussed in this chapter can be found in the Basic Bacteriology section of Part XIII: USMLE (National Board) Practice Questions starting on page 709. Also see Part XIV: USMLE (National Board) Practice Examination starting on page 751.
SHAPE & SIZE OF BACTERIA

Bacteria are classified by shape into three basic groups: cocci, bacilli, and spirochetes (Figure 2–1). The cocci are round, the bacilli are rods, and the spirochetes are spiral-shaped. Some bacteria are variable in shape and are said to be pleomorphic (many-shaped). The shape of a bacterium is determined by its rigid cell wall. The microscopic appearance of a bacterium is one of the most important criteria used in its identification.

In addition to their characteristic shapes, the arrangement of bacteria is important. For example, certain cocci occur in pairs (diplococci), some in chains (streptococci), and others in grapelike clusters (staphylococci). These arrangements are determined by the orientation and degree of attachment of the bacteria at the time of cell division. The arrangement of rods and spirochetes is medically less important and is not described in this introductory chapter.

Bacteria range in size from about 0.2 to 5 μm (Figure 2–2). The smallest bacteria (Mycoplasma) are about the same size as the largest viruses (poxviruses) and are the smallest organisms capable of existing outside a host. The longest bacteria rods are the size of some yeasts and human red blood cells (7 μm).

STRUCTURE OF BACTERIA

The structure of a typical bacterium is illustrated in Figure 2–3, and the important features of each component are presented in Table 2–1.

Cell Wall

The cell wall is the outermost component common to all bacteria (except Mycoplasma species, which are bounded by a cell membrane, not a cell wall). Some bacteria have surface features external to the cell wall, such as a capsule,

![Cell Wall](image)

FIGURE 2–1 Bacterial morphology. A: Cocci in clusters (e.g., Staphylococcus; A-1); chains (e.g., Streptococcus; A-2); in pairs with pointed ends (e.g., Streptococcus pneumoniae; A-3); in pairs with kidney bean shape (e.g., Neisseria; A-4). B: Rods (bacilli); with square ends (e.g., Bacillus; B-1); with rounded ends (e.g., Salmonella; B-2); club-shaped (e.g., Corynebacterium; B-3); fusiform (e.g., Fusobacterium; B-4); comma-shaped (e.g., Vibrio; B-5). C: Spirochetes: relaxed coil (e.g., Borrelia; C-1); tightly coiled (e.g., Treponema; C-2).

flagella, and pili, which are less common components and are discussed next.

The cell wall is located external to the cytoplasmic membrane and is composed of peptidoglycan (see page 6). The peptidoglycan provides structural support and maintains the characteristic shape of the cell.

Cell Walls of Gram-Positive and Gram-Negative Bacteria

The structure, chemical composition, and thickness of the cell wall differ in gram-positive and gram-negative bacteria (Table 2–2, Figure 2–4A, and “Gram Stain” box).

1. The peptidoglycan layer is much thicker in gram-positive than in gram-negative bacteria. Many gram-positive bacteria also have fibers of teichoic acid that protrude outside the peptidoglycan, whereas gram-negative bacteria do not have teichoic acids.

2. In contrast, the gram-negative bacteria have a complex outer layer consisting of lipopolysaccharide, lipoprotein, and phospholipid. Lying between the outer-membrane layer and the cytoplasmic membrane in gram-negative bacteria is the periplasmic space, which is the site, in some species, of enzymes called β-lactamases that degrade penicillins and other β-lactam drugs.
The cell wall has several other important properties:

1. In gram-negative bacteria, it contains endotoxin, a lipopolysaccharide (see pages 9 and 44).
2. Its polysaccharides and proteins are antigens that are useful in laboratory identification.
3. Its porin proteins play a role in facilitating the passage of small, hydrophilic molecules into the cell. Porin proteins in the outer membrane of gram-negative bacteria act as a channel to allow the entry of essential substances such as sugars, amino acids, vitamins, and metals as well as many antimicrobial drugs such as penicillins.

**Cell Walls of Acid-Fast Bacteria**

Mycobacteria (e.g., Mycobacterium tuberculosis) have an unusual cell wall, resulting in their inability to be Gram-stained (Figure 2–4B). These bacteria are said to be **acid-fast** because they resist decolorization with acid–alcohol after being stained with carbolfuchsin. This property is related to the high concentration of lipids, called mycolic **acids**, in the cell wall of mycobacteria.

Note that Nocardia asteroides is **weakly acid-fast**. The meaning of the term “weakly” is that if the acid-fast staining process uses a weaker solution of hydrochloric acid to decolorize than that used in the stain for Mycobacteria, then *N. asteroides* will *not* decolorize. However, if the regular-strength hydrochloric acid is used, *N. asteroides* will decolorize.

In view of their importance, three components of the cell wall (i.e., peptidoglycan, lipopolysaccharide, and teichoic acid) are discussed in detail here.

### Peptidoglycan

Peptidoglycan is a complex, interwoven network that surrounds the entire cell and is composed of a single covalently linked macromolecule. It is found *only* in bacterial cell walls. It provides rigid support for the cell, is important in maintaining the characteristic shape of the cell, and allows the cell to withstand media of low osmotic pressure, such as water. A representative segment of the peptidoglycan layer is shown in Figure 2–5. The term **peptidoglycan** is derived from the peptides and the sugars (glycan) that

---

**TABLE 2–2**  Comparison of Cell Walls of Gram-Positive and Gram-Negative Bacteria

<table>
<thead>
<tr>
<th>Component</th>
<th>Gram-Positive Cells</th>
<th>Gram-Negative Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peptidoglycan</td>
<td>Thicker; multilayer</td>
<td>Thinner; single layer</td>
</tr>
<tr>
<td>Teichoic acids</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Lipopolysaccharide</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>(endotoxin)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

1. Except in *Bacillus anthracis*, in which it is a polypeptide of D-glutamic acid.
FIGURE 2–4  A: Cell walls of gram-positive and gram-negative bacteria. Note that the peptidoglycan in gram-positive bacteria is much thicker than in gram-negative bacteria. Note also that only gram-negative bacteria have an outer membrane containing endotoxin (lipopolysaccharide [LPS]) and have a periplasmic space where $\beta$-lactamases are found. Several important gram-positive bacteria, such as staphylococci and streptococci, have teichoic acids. (Reproduced with permission from Ingraham JL, Maaløe O, Neidhardt FC. Growth of the Bacterial Cell. Sinauer Associates; 1983.)

B: Cell wall of Mycobacterium tuberculosis: Note the layers of mycolic acid and arabinoglycan that are present in members of the genus Mycobacterium but not in most other genera of bacteria.

FIGURE 2–5  Peptidoglycan structure. A: Peptidoglycan is composed of a glycan chain (NAM and NAG), a tetrapeptide chain, and a cross-link (peptide interbridge). B: In the cell wall, the peptidoglycan forms a multilayered, three-dimensional structure. NAG, N-acetylglicosamine; NAM, N-acetylmuramic acid. (Reproduced with permission from Nester EW et al. Microbiology: A Human Perspective. 6th ed. Copyright 2009, McGraw-Hill.)
**GRAM STAIN**

This staining procedure, developed in 1884 by the Danish physician Christian Gram, is the most important procedure in microbiology. It separates most bacteria into two groups: the gram-positive bacteria, which stain blue, and the gram-negative bacteria, which stain red. The Gram stain involves the following four-step procedure:

1. The crystal violet dye stains all cells blue/purple.
2. The iodine solution (a mordant) is added to form a crystal violet–iodine complex; all cells continue to appear blue.
3. The organic solvent, such as acetone or ethanol, extracts the blue dye complex from the lipid-rich, thin-walled gram-negative bacteria to a greater degree than from the lipid-poor, thick-walled gram-positive bacteria. The gram-negative organisms appear colorless; the gram-positive bacteria remain blue.
4. The red dye safranin stains the decolorized gram-negative cells red/pink; the gram-positive bacteria remain blue.

The Gram stain is useful in two ways:

1. In the identification of many bacteria.
2. In influencing the choice of antibiotic because, in general, gram-positive bacteria are more susceptible to penicillin G than are gram-negative bacteria.

However, not all bacteria can be seen in the Gram stain. Table 2–3 lists the medically important bacteria that cannot be seen and describes the reason why. The alternative microscopic approach to the Gram stain is also described.

Note that it takes approximately 100,000 bacteria/mL to see 1 bacterium per microscopic field using the oil immersion (100×) lens. So the sensitivity of the Gram stain procedure is low. This explains why a patient’s blood is rarely stained immediately but rather is incubated in blood cultures overnight to allow the bacteria to multiply. One important exception to this is meningococccemia in which very high concentrations of Neisseria meningitidis can occur in the blood.

**TABLE 2–3  Medically Important Bacteria That Cannot Be Seen in the Gram Stain**

<table>
<thead>
<tr>
<th>Name</th>
<th>Reason</th>
<th>Alternative Microscopic Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mycobacteria, including <em>M. tuberculosis</em></td>
<td>Too much lipid in cell wall so dye cannot penetrate</td>
<td>Acid-fast stain</td>
</tr>
<tr>
<td>Treponema pallidum</td>
<td>Too thin to see</td>
<td>Dark-field microscopy or fluorescent antibody</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>No cell wall; very small</td>
<td>None</td>
</tr>
<tr>
<td>Legionella pneumophila</td>
<td>Poor uptake of red counterstain</td>
<td>Prolong time of counterstain</td>
</tr>
<tr>
<td>Chlamydiae, including C. trachomatis</td>
<td>Intracellular; very small</td>
<td>Inclusion bodies in cytoplasm</td>
</tr>
<tr>
<td>Rickettsiae</td>
<td>Intracellular; very small</td>
<td>Giemsa or other tissue stains</td>
</tr>
</tbody>
</table>
bacterial interior, they will survive as spherical forms, called proplasts, surrounded only by a cytoplasmic membrane.

**Lipopolysaccharide**
The lipopolysaccharide (LPS) of the outer membrane of the cell wall of gram-negative bacteria is endotoxin. It is responsible for many of the features of disease, such as fever and shock (especially hypotension), caused by these organisms (see page 44). It is called endotoxin because it is an integral part of the cell wall, in contrast to exotoxins, which are actively secreted from the bacteria. The constellation of symptoms caused by the endotoxin of one gram-negative bacterium is similar to another, but the severity of the symptoms can differ greatly. In contrast, the symptoms caused by exotoxins of different bacteria are usually quite different.

The LPS is composed of three distinct units (Figure 2–6):

1. A phospholipid called lipid A, which is responsible for the toxic effects.
2. A core polysaccharide of five sugars linked through ketodeoxyoctulonate (KDO) to lipid A.
3. An outer polysaccharide consisting of up to 25 repeating units of three to five sugars. This outer polymer is the important somatic, or O, antigen of several gram-negative bacteria that is used to identify certain organisms in the clinical laboratory. Some bacteria, notably members of the genus *Neisseria*, have an outer lipooligosaccharide (LOS) containing very few repeating units of sugars.

**Teichoic Acid**
Teichoic acids are fibers located in the outer layer of the gram-positive cell wall and extend from it. They are composed of polymers of either glycerol phosphate or ribitol phosphate. Some polymers of glycerol teichoic acid penetrate the peptidoglycan layer and are covalently linked to the lipid in the cytoplasmic membrane, in which case they are called lipoteichoic acid; others anchor to the muramic acid of the peptidoglycan.

The medical importance of teichoic acids lies in their ability to induce inflammation and septic shock when caused by certain gram-positive bacteria; that is, they activate the same pathways as does endotoxin (LPS) in gram-negative bacteria. Teichoic acids also mediate the attachment of staphylococci to mucosal cells. Gram-negative bacteria do not have teichoic acids.

**Cytoplasmic Membrane**
Just inside the peptidoglycan layer of the cell wall lies the cytoplasmic membrane, which is composed of a phospholipid bilayer similar in microscopic appearance to that in eukaryotic cells. They are chemically similar, but eukaryotic membranes contain sterols, whereas prokaryotes generally do not. The only prokaryotes that have sterols in their membranes are members of the genus *Mycoplasma*. The membrane has four important functions: (1) active transport of molecules into the cell, (2) energy generation by oxidative phosphorylation, (3) synthesis of precursors of the cell wall, and (4) secretion of enzymes and toxins.

**Cytoplasm**
The cytoplasm has two distinct areas when seen in the electron microscope:

1. An amorphous matrix that contains ribosomes, nutrient granules, metabolites, and plasmids.
2. An inner, nucleoid region composed of DNA.

**Ribosomes**
Bacterial ribosomes are the site of protein synthesis as in eukaryotic cells, but they differ from eukaryotic ribosomes in size and chemical composition. Bacterial ribosomes are 70S in size, with 50S and 30S subunits, whereas eukaryotic ribosomes are 80S in size, with 60S and 40S subunits. The differences in both the ribosomal RNAs and proteins constitute the basis of the selective action of several antibiotics that inhibit bacterial, but not human, protein synthesis (see Chapter 10).

**Granules**
The cytoplasm contains several different types of granules that serve as storage areas for nutrients and stain characteristically with certain dyes. For example, volutin is a reserve of high energy stored in the form of polymerized metaphosphate. It appears as a “metachromatic” granule since it stains red with methylene blue dye instead of blue as one would expect. Metachromatic granules are a characteristic feature of *Corynebacterium diphtheriae*, the cause of diphtheria.

**Nucleoid**
The nucleoid is the area of the cytoplasm in which DNA is located. The DNA of prokaryotes is a single, circular molecule that has a molecular weight (MW) of approximately
2 x 10^9 and contains about 2000 genes. (By contrast, human DNA has approximately 100,000 genes.) Because the nucleoid contains no nuclear membrane, no nucleolus, no mitotic spindle, and no histones, there is little resemblance to the eukaryotic nucleus. One major difference between bacterial DNA and eukaryotic DNA is that bacterial DNA has no introns, whereas eukaryotic DNA does.

**Plasmids**

Plasmids are extrachromosomal, double-stranded, circular DNA molecules that are capable of replicating independently of the bacterial chromosome. Although plasmids are usually extrachromosomal, they can be integrated into the bacterial chromosome. Plasmids occur in both gram-positive and gram-negative bacteria, and several different types of plasmids can exist in one cell:

1. **Transmissible** plasmids can be transferred from cell to cell by conjugation (see Chapter 4 for a discussion of conjugation). They are large (MW 40–100 million), since they contain about a dozen genes responsible for synthesis of the sex pilus and for the enzymes required for transfer. They are usually present in a few (1–3) copies per cell.
2. **Nontransmissible** plasmids are small (MW 3–20 million), since they do not contain the transfer genes; they are frequently present in many (10–60) copies per cell.

Plasmids carry the genes for the following functions and structures of medical importance:

1. **Antibiotic resistance**, which is mediated by a variety of enzymes, such as the beta-lactamase of *S. aureus*, *Escherichia coli*, and *Klebsiella pneumoniae*.
2. **Exotoxins**, such as the enterotoxins of *E. coli* anthrax tox in of *Bacillus anthracis*, exfoliative toxin of *S. aureus* and tetanus toxin of *Clostridium tetani*.
3. **Pili** (fimbriae), which mediate the adherence of bacteria to epithelial cells.
4. **Resistance to heavy metals**, such as mercury, the active component of some antiseptics (e.g., merthiolate and mercurychrome), and silver, which is mediated by a reductase enzyme.
5. **Resistance to ultraviolet light**, which is mediated by DNA repair enzymes.

Other plasmid-encoded products of interest are as follows:

1. **Bacteriocins** are toxic proteins produced by certain bacteria that are lethal for other bacteria. Two common mechanisms of action of bacteriocins are (i) degradation of bacterial cell membranes by producing pores in the membrane and (ii) degradation of bacterial DNA by DNAse. Examples of bacteriocins produced by medically important bacteria are colicins made by *E. coli* and pyocins made by *Pseudomonas aeruginosa*. Bacteria that produce bacteriocins have a selective advantage in the competition for food sources over those that do not. However, the medical importance of bacteriocins is that they may be useful in treating infections caused by antibiotic-resistant bacteria.
2. **Nitrogen fixation enzymes** in *Rhizobium* in the root nodules of legumes.
3. **Tumors caused by Agrobacterium** in plants.
4. **Several antibiotics** produced by *Streptomycetes*.
5. **A variety of degradative enzymes** that are produced by *Pseudomonas* and are capable of cleaning up environmental hazards such as oil spills and toxic chemical waste sites.

**Transposons**

Transposons are pieces of DNA that move readily from one site to another either within or between the DNAs of bacteria, plasmids, and bacteriophages. Because of their unusual ability to move, they are nicknamed “jumping genes.” Some transposons move by replicating their DNA and inserting the new copy into another site (replicative transposition), whereas others are excised from the site without replicating and then inserted into the new site (direct transposition). Transposons can code for drug-resistant enzymes, toxins, or a variety of metabolic enzymes and can either cause mutations in the gene into which they insert or alter the expression of nearby genes.

Transposons typically have four identifiable domains. On each end is a short DNA **sequence of inverted repeats**, which are involved in the integration of the transposon into the recipient DNA. The second domain is the gene for the transposase, which is the enzyme that mediates the excision and integration processes. The third region is the gene for the repressor that regulates the synthesis of both the transposase and the protein encoded by the fourth domain, which, in many cases, is an enzyme mediating antibiotic resistance (Figure 2–7). Note that for simplicity, the repressor gene is not shown in Figure 2–7.

Antibiotic resistance genes are transferred from one bacterium to another primarily by **conjugation** (see Chapter 4). This transfer is mediated primarily by plasmids, but some transposons, called **conjugative transposons**, are capable of transferring antibiotic resistance as well.

In contrast to plasmids or bacterial viruses, transposons are not capable of independent replication; they replicate as part of the DNA in which they are integrated. More than one transposon can be located in the DNA; for example, a plasmid can contain several transposons carrying drug-resistant

![FIGURE 2–7](image-url) Transposon genes. This transposon is carrying a drug-resistance gene. IR, inverted repeat. (Reproduced with permission from Willey JM et al. Prescott’s Principles of Microbiology. New York: McGraw-Hill, 2009.)
genes. Insertion sequences are a type of transposon that has fewer bases (800–1500 base pairs), since they do not code for their own integration enzymes. They can cause mutations at their site of integration and can be found in multiple copies at the ends of larger transposon units.

**Structures Outside the Cell Wall**

**Capsule**
The capsule is a gelatinous layer covering the entire bacterium. It is composed of polysaccharide, except in the anthrax bacillus, which has a capsule of polymerized D-glutamic acid. The sugar components of the polysaccharide vary from one species of bacteria to another and frequently determine the serologic type (serotype) within a species. For example, there are 84 different serotypes of *Streptococcus pneumoniae*, which are distinguished by the antigenic differences of the sugars in the polysaccharide capsule.

The capsule is important for four reasons:

1. It is a determinant of virulence of many bacteria since it limits the ability of phagocytes to engulf the bacteria. Negative charges on the capsular polysaccharide repel the negatively charged cell membrane of the neutrophil and prevent it from ingesting the bacteria. Variants of encapsulated bacteria that have lost the ability to produce a capsule are usually nonpathogenic.

2. Specific identification of an organism can be made by using antisera against the capsular polysaccharide. In the presence of the homologous antibody, the capsule will swell greatly. This swelling phenomenon, which is used in the clinical laboratory to identify certain organisms, is called the quellung reaction.

3. Capsular polysaccharides are used as the antigens in certain vaccines because they are capable of eliciting protective antibodies. For example, the purified capsular polysaccharides of 23 types of *S. pneumoniae* are present in the current vaccine.

4. The capsule may play a role in the adherence of bacteria to human tissues, which is an important initial step in causing infection.

**Flagella**
Flagella are long, whiplike appendages that move the bacteria toward nutrients and other attractants, a process called chemotaxis. The long filament, which acts as a propeller, is composed of many subunits of a single protein, flagellin, arranged in several intertwined chains. The energy for movement, the proton motive force, is provided by adenosine triphosphate (ATP), derived from the passage of ions across the membrane.

Flagellated bacteria have a characteristic number and location of flagella: some bacteria have one, and others have many; in some, the flagella are located at one end, and in others, they are all over the outer surface. Only certain bacteria have flagella. Many rods do, but most cocci do not and are therefore nonmotile. Spirochetes move by using a flagellumlike structure called the axial filament, which wraps around the spiral-shaped cell to produce an undulating motion.

Flagella are medically important for two reasons:

1. Some species of motile bacteria (e.g., *E. coli* and *Proteus* species) are common causes of urinary tract infections. Flagella may play a role in pathogenesis by propelling the bacteria up the urethra into the bladder.

2. Some species of bacteria (e.g., *Salmonella* species) are identified in the clinical laboratory by the use of specific antibodies against flagellar proteins.

**Pili (Fimbriae)**
Pili are hairlike filaments that extend from the cell surface. They are shorter and straighter than flagella and are composed of subunits of pilin, a protein arranged in helical strands. They are found mainly on gram-negative organisms.

Pili have two important roles:

1. They mediate the attachment of bacteria to specific receptors on the human cell surface, which is a necessary step in the initiation of infection for some organisms. Mutants of *Neisseria gonorrhoeae* that do not form pili are nonpathogens.

2. A specialized kind of pilus, the sex pilus, forms the attachment between the male (donor) and the female (recipient) bacteria during conjugation (see Chapter 4).

**Glycocalyx (Slime Layer)**
The glycocalyx is a polysaccharide coating that is secreted by many bacteria. It covers surfaces like a film and allows the bacteria to adhere firmly to various structures (e.g., skin, heart valves, prosthetic joints, and catheters). The glycocalyx is an important component of biofilms (see page 37). The medical importance of the glycocalyx is illustrated by the finding that it is the glycocalyx-producing strains of *P. aeruginosa* that cause respiratory tract infections in cystic fibrosis patients, and it is the glycocalyx-producing strains of *Staphylococcus epidermidis* and viridans streptococci that cause endocarditis. The glycocalyx also mediates adherence of certain bacteria, such as *Streptococcus mutans*, to the surface of teeth. This plays an important role in the formation of plaque, the precursor of dental caries.

**Bacterial Spores**
These highly resistant structures are formed in response to adverse conditions by two genera of medically important gram-positive rods: the genus *Bacillus*, which includes the agent of anthrax, and the genus *Clostridium*, which includes the agent of tetanus and botulism. Spore formation (sporulation) occurs when nutrients, such as sources of carbon and nitrogen, are depleted (Figure 2–8). The spore forms...
inside the cell and contains bacterial DNA, a small amount of cytoplasm, cell membrane, peptidoglycan, very little water, and most importantly, a thick, keratinlike coat that is responsible for the remarkable resistance of the spore to heat, dehydration, radiation, and chemicals. This resistance may be mediated by dipicolinic acid, a calcium ion chelator found only in spores. Once formed, the spore has no metabolic activity and can remain dormant for many years. Upon exposure to water and the appropriate nutrients, specific enzymes degrade the coat, water and nutrients enter, and germination into a potentially pathogenic bacterial cell occurs. Note that this differentiation process is not a means of reproduction since one cell produces one spore that germinates into one cell.

The medical importance of spores lies in their extraordinary resistance to heat and chemicals. As a result of their resistance to heat, sterilization cannot be achieved by boiling. Steam heating under pressure (autoclaving) at 121°C, for at least 15 minutes, is required to ensure the sterility of products for medical use. Spores are often not seen in clinical specimens recovered from patients infected by spore-forming organisms because the supply of nutrients is adequate.

Table 2–4 describes the medically important features of bacterial spores.

### TABLE 2–4  Important Features of Spores and Their Medical Implications

<table>
<thead>
<tr>
<th>Important Features of Spores</th>
<th>Medical Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Highly resistant to heating:</strong> spores are not killed by boiling (100°C), but are killed at 121°C.</td>
<td>Medical supplies must be heated to 121°C for at least 15 minutes to be sterilized.</td>
</tr>
<tr>
<td><strong>Highly resistant to many chemicals, including most disinfectants, due to the thick keratinlike coat of the spore.</strong></td>
<td>Only solutions designated as sporicidal will kill spores.</td>
</tr>
<tr>
<td>They can survive for many years, especially in the soil.</td>
<td>Wounds contaminated with soil can be infected with spores and cause diseases such as tetanus (<em>C. tetani</em>) and gas gangrene (<em>C. perfringens</em>).</td>
</tr>
<tr>
<td>They exhibit no measurable metabolic activity.</td>
<td>Antibiotics are ineffective against spores because antibiotics act by inhibiting certain metabolic pathways of bacteria. Also, spore coat is impermeable to antibiotics.</td>
</tr>
<tr>
<td>Spores form when nutrients are insufficient but then germinate to form bacteria when nutrients become available.</td>
<td>Spores are not often found at the site of infections because nutrients are not limiting. Bacteria rather than spores are usually seen in Gram-stained smears.</td>
</tr>
<tr>
<td>Spores are produced by members of only two genera of bacteria of medical importance, <em>Bacillus</em> and <em>Clostridium</em>, both of which are gram-positive rods.</td>
<td>Infections transmitted by spores are caused by species of either <em>Bacillus</em> or <em>Clostridium</em>.</td>
</tr>
</tbody>
</table>

### PEARLS

**Shape & Size**
- Bacteria have three shapes: **coci** (spheres), **bacilli** (rods), and **spirochetes** (spirals).
- Cocci are arranged in three patterns: pairs (diplococci), chains (streptococci), and clusters (staphylococci).
- The size of most bacteria ranges from 1 to 3 μm. *Mycoplasma*, the smallest bacteria (and therefore the **smallest cells**), are 0.2 μm. Some bacteria, such as *Borrelia*, are as long as 10 μm; that is, they are longer than a human red blood cell, which is 7 μm in diameter.

**Bacterial Cell Wall**
- All bacteria have a cell wall composed of **peptidoglycan** except *Mycoplasma*, which are surrounded only by a cell membrane.
- Gram-negative bacteria have a **thin** peptidoglycan covered by an outer lipid-containing membrane, whereas gram-positive bacteria have a **thick** peptidoglycan and no outer membrane. These differences explain why gram-negative bacteria lose the stain when exposed to a lipid solvent in the Gram stain process, whereas gram-positive bacteria retain the stain and remain purple.
• The outer membrane of gram-negative bacteria contains endotoxin (lipopolysaccharide, LPS), the main inducer of septic shock. Endotoxin consists of lipid A, which causes the fever and hypotension seen in septic shock, and a polysaccharide called O antigen, which is useful in laboratory identification.

• Between the inner cell membrane and the outer membrane of gram-negative bacteria lies the periplasmic space, which is the location of β-lactamases—the enzymes that degrade β-lactam antibiotics, such as penicillins and cephalosporins.

• Peptidoglycan is found only in bacterial cells. It is a network that covers the entire bacterium and gives the organism its shape. It is composed of a sugar backbone (glycan) and peptide side chains (peptido). The side chains are cross-linked by transpeptidase—the enzyme that is inhibited by penicillins and cephalosporins.

• The cell wall of mycobacteria (e.g., M. tuberculosis) has more lipid than either the gram-positive or gram-negative bacteria. As a result, the dyes used in the Gram stain do not penetrate into (do not stain) mycobacteria. The acid-fast stain does stain mycobacteria, and these bacteria are often called acid-fast bacilli (acid-fast rods).

• Lysozymes kill bacteria by cleaving the glycan backbone of peptidoglycan.

• The cytoplasmic membrane of bacteria consists of a phospholipid bilayer (without sterols) located just inside the peptidoglycan. It regulates active transport of nutrients into the cell and the secretion of toxins out of the cell.

### Bacterial DNA

• The bacterial genome consists of a single chromosome of circular DNA located in the nucleoid.

• Plasmids are extrachromosomal pieces of circular DNA that encode both exotoxins and many enzymes that cause antibiotic resistance.

• Transposons are small pieces of DNA that move frequently between chromosomal DNA and plasmid DNA. They carry antibiotic-resistant genes.

### Structures External to the Cell Wall

• Capsules are antiphagocytic; that is, they limit the ability of neutrophils to engulf the bacteria. Almost all capsules are composed of polysaccharide (polysaccharide capsule of anthrax bacillus is the only exception. Capsules are also the antigens in several vaccines, such as the pneumococcal vaccine. Antibodies against the capsule neutralize the antiphagocytic effect and allow the bacteria to be engulfed by neutrophils. Opsonization is the process by which antibodies enhance the phagocytosis of bacteria.

• Pili are filaments of protein that extend from the bacterial surface and mediate attachment of bacteria to the surface of human cells. A different kind of pili, the sex pilus, functions in conjugation (see Chapter 4).

• The glycocalyx is a polysaccharide “slime layer” secreted by certain bacteria. It attaches bacteria firmly to the surface of human cells and to the surface of catheters, prosthetic heart valves, and prosthetic hip joints.

### Bacterial Spores

• Spores are medically important because they are highly heat resistant and are not killed by many disinfectants. Boiling will not kill spores. They are formed by certain gram-positive rods, especially Bacillus and Clostridium species.

• Spores have a thick, keratin-like coat that allows them to survive for many years, especially in the soil. Spores are formed when nutrients are in short supply, but when nutrients are restored, spores germinate to form bacteria that can cause disease. Spores are metabolically inactive but contain DNA, ribosomes, and other essential components.

1. The initial step in the process of many bacterial infections is adherence of the organism to mucous membranes. The bacterial component that mediates adherence is the:

   - (A) lipid A
   - (B) nucleoid
   - (C) peptidoglycan
   - (D) pilus
   - (E) plasmid

2. In the Gram stain procedure, bacteria are exposed to 95% alcohol or to an acetone/alcohol mixture. The purpose of this step is:

   - (A) to adhere the cells to the slide
   - (B) to retain the purple dye within all the bacteria
   - (C) to disrupt the outer cell membrane so the purple dye can leave the bacteria
   - (D) to facilitate the entry of the purple dye into the gram-negative cells
   - (E) to form a complex with the iodine solution
3. In the process of studying how bacteria cause disease, it was found that a rare mutant of a pathogenic strain failed to form a capsule. Which one of the following statements is the most accurate in regard to this unencapsulated mutant strain?

(A) It was nonpathogenic primarily because it was easily phagocytized.
(B) It was nonpathogenic primarily because it could not invade tissue.
(C) It was nonpathogenic primarily because it could only grow anaerobically.
(D) It was highly pathogenic because it could secrete larger amounts of exotoxin.
(E) It was highly pathogenic because it could secrete larger amounts of endotoxin.

4. *Mycobacterium tuberculosis* stains well with the acid-fast stain, but not with the Gram stain. Which one of the following is the most likely reason for this observation?

(A) It has a large number of pil that absorb the purple dye.
(B) It has a large amount of lipid that prevents entry of the purple dye.
(C) It has a very thin cell wall that does not retain the purple dye.
(D) It is too thin to be seen in the Gram stain.
(E) It has histones that are highly negatively charged.

5. Of the following bacterial components, which one exhibits the most antigenic variation?

(A) Capsule
(B) Lipid A of endotoxin
(C) Peptidoglycan
(D) Ribosome
(E) Spore

6. β-Lactamases are an important cause of antibiotic resistance. Which one of the following is the most common site where β-lactamases are located?

(A) Attached to DNA in the nucleoid
(B) Attached to pil on the bacterial surface
(C) Free in the cytoplasm
(D) Within the capsule
(E) Within the periplasmic space

7. Which one of the following is the most accurate description of the structural differences between gram-positive bacteria and gram-negative bacteria?

(A) Gram-positive bacteria have a thick peptidoglycan layer, whereas gram-negative bacteria have a thin layer.
(B) Gram-positive bacteria have an outer lipid-rich membrane, whereas gram-negative bacteria do not.
(C) Gram-positive bacteria form a sex pilus that mediates conjugation, whereas gram-negative bacteria do not.
(D) Gram-positive bacteria have plasmids, whereas gram-negative bacteria do not.
(E) Gram-positive bacteria have capsules, whereas gram-negative bacteria do not.

8. Bacteria that cause nosocomial (hospital-acquired) infections often produce extracellular substances that allow them to stick firmly to medical devices, such as intravenous catheters. Which one of the following is the name of this extracellular substance?

(A) Axial filament
(B) Endotoxin
(C) Flagella
(D) Glycocalyx
(E) Porin

9. Lysozyme in tears is an effective mechanism for preventing bacterial conjunctivitis. Which one of the following bacterial structures does lysozyme degrade?

(A) Endotoxin
(B) Nucleoid DNA
(C) Peptidoglycan
(D) Pilus
(E) Plasmid DNA

10. Several bacteria that form spores are important human pathogens. Which one of the following is the most accurate statement about bacterial spores?

(A) They are killed by boiling for 15 minutes.
(B) They are produced primarily by gram-negative cocci.
(C) They are formed primarily when the bacterium is exposed to antibiotics.
(D) They are produced by anaerobes only in the presence of oxygen.
(E) They are metabolically inactive yet can survive for years in that inactive state.

**ANSWERS**

1. (D)  
2. (C)  
3. (A)  
4. (B)  
5. (A)  
6. (E)  
7. (A)  
8. (E)  
9. (C)  
10. (C)

**PRACTICE QUESTIONS: USMLE & COURSE EXAMINATIONS**

Questions on the topics discussed in this chapter can be found in the Basic Bacteriology section of Part XIII: USMLE (National Board) Practice Questions starting on page 709. Also see Part XIV: USMLE (National Board) Practice Examination starting on page 751.
Bacteria reproduce by binary fission, a process by which one parent cell divides to form two progeny cells. Because one cell gives rise to two progeny cells, bacteria are said to undergo exponential growth (logarithmic growth). The concept of exponential growth can be illustrated by the following relationship:

<table>
<thead>
<tr>
<th>Number of cells</th>
<th>1</th>
<th>2</th>
<th>4</th>
<th>8</th>
<th>16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exponential</td>
<td>$2^0$</td>
<td>$2^1$</td>
<td>$2^2$</td>
<td>$2^3$</td>
<td>$2^4$</td>
</tr>
</tbody>
</table>

Thus, 1 bacterium will produce 16 bacteria after 4 generations.

The doubling (generation) time of bacteria ranges from as little as 20 minutes for *Escherichia coli* to as long as 18 hours for *Mycobacterium tuberculosis*. The exponential growth and the short doubling time of some organisms result in rapid production of very large numbers of bacteria. For example, 1 *E. coli* organism will produce over 1000 progeny in about 3 hours and over 1 million in about 7 hours. The doubling time varies not only with the species, but also with the amount of nutrients, the temperature, the pH, and other environmental factors.

The growth cycle of bacteria has four major phases. If a small number of bacteria are inoculated into a liquid nutrient medium and the bacteria are counted at frequent intervals, the typical phases of a standard growth curve can be demonstrated (Figure 3–1).

(1) The first is the lag phase, during which vigorous metabolic activity occurs but cells do not divide. This can last for a few minutes up to many hours.

(2) The log (logarithmic) phase is when rapid cell division occurs. β-Lactam drugs, such as penicillin, act during this phase because the drugs are effective when cells are making peptidoglycan (i.e., when they are dividing). The log phase is also known as the exponential phase.

(3) The stationary phase occurs when nutrient depletion or toxic products cause growth to slow until the number of new cells produced balances the number of cells that die, resulting in a steady state. Cells grown in a special apparatus called a "chemostat," into which fresh nutrients are added and from which waste products are removed continuously, can remain in the log phase and do not enter the stationary phase.

(4) The final phase is the death phase, which is marked by a decline in the number of viable bacteria.

**OBLIGATE INTRACELLULAR GROWTH**

Most bacterial pathogens of humans are capable of growing on artificial media in the clinical laboratory. The term, artificial, means that the medium is composed of purified...
chemicals such as sugars, amino acids, and salts, such as sodium chloride. Often blood is added in the form of sheep's blood but that is for nutritional purposes rather than for the need of the bacteria to grow within the red blood cells.

However, certain bacterial pathogens of humans, notably *Chlamydia* and *Rickettsia* (see Chapters 25 and 26, respectively), and *Ehrlichia* and *Anaplasma* (see Chapter 26) can only grow within living cells. They are obligate intracellular parasites, meaning that it is obligatory that they grow within cells. The main reason for this is that they lack the ability to produce sufficient ATP and must use ATP produced by the host cells.

**AEROBIC & ANAEROBIC GROWTH**

For most organisms, an adequate supply of oxygen enhances metabolism and growth. The oxygen acts as the hydrogen acceptor in the final steps of energy production catalyzed by the flavoproteins and cytochromes. Because the use of oxygen generates two toxic molecules, hydrogen peroxide (H2O2) and the free radical superoxide (O2•−) bacteria require two enzymes to detoxify these molecules when oxygen is utilized. The first is superoxide dismutase, which catalyzes the reaction

\[ 2O_2•− + 2H^+ \rightarrow H_2O_2 + O_2 \]

and the second is catalase, which catalyzes the reaction

\[ 2H_2O_2 \rightarrow 2H_2O + O_2 \]

The response to oxygen is an important criterion for classifying bacteria and has great practical significance because specimens from patients must be incubated in a proper atmosphere for the bacteria to grow.

1. Some bacteria, such as *M. tuberculosis*, are obligate aerobes; that is, they require oxygen to grow because their ATP-generating system is dependent on oxygen as the hydrogen acceptor.

2. Other bacteria, such as *E. coli*, are facultative anaerobes; they utilize oxygen, if it is present, to generate energy by respiration, but they can use the fermentation pathway to synthesize ATP in the absence of sufficient oxygen.

3. The third group of bacteria consists of the obligate anaerobes, such as *Clostridium tetani*, which cannot grow in the presence of oxygen because they lack either superoxide dismutase or catalase, or both. Obligate anaerobes vary in their response to oxygen exposure; some can survive but are not able to grow, whereas others are killed rapidly.

**FERMENTATION OF SUGARS**

In the clinical laboratory, identification of several important human pathogens is based on the fermentation of certain sugars. For example, *Neisseria gonorrhoeae* and *Neisseria meningitidis* can be distinguished from each other on the basis of fermentation of either glucose or maltose (see page 131), and *E. coli* can be differentiated from *Salmonella* and *Shigella* on the basis of fermentation of lactose (see page 151).

The term fermentation refers to the breakdown of a sugar (such as glucose or maltose) to pyruvic acid and then, usually, to lactic acid. (More specifically, it is the breakdown of a monosaccharide such as glucose, maltose, or galactose. Note that lactose is a disaccharide composed of glucose and galactose and therefore must be cleaved by β-galactosidase in *E. coli* before fermentation can occur.) Fermentation is also called the glycolytic (glyco = sugar, lytic = breakdown) cycle, and this is the process by which facultative bacteria generate ATP in the absence of oxygen.

If oxygen is present, the pyruvate produced by fermentation enters the Krebs cycle (oxidation cycle, tricarboxylic acid cycle) and is metabolized to two final products, CO2 and H2O. The Krebs cycle generates much more ATP than the glycolytic cycle; therefore, facultative bacteria grow faster in the presence of oxygen. Facultative and anaerobic bacteria ferment, but aerobes, which can grow only in the presence of oxygen, do not. Aerobes, such as *Pseudomonas aeruginosa*, produce metabolites that enter the Krebs cycle by processes other than fermentation, such as the deamination of amino acids.

In fermentation tests performed in the clinical laboratory, the production of pyruvate and lactate turns the medium acid, which can be detected by a pH indicator that changes color upon changes in pH. For example, if a sugar is fermented in the presence of phenol red (an indicator), the pH becomes acidic and the medium turns yellow. If, however, the sugar is not fermented, no acid is produced and the phenol red remains red.

**IRON METABOLISM**

Iron, in the form of ferric ion, is required for the growth of bacteria because it is an essential component of cytochromes and other enzymes. The amount of iron available for pathogenic bacteria in the human body is very low because the iron is sequestered in iron-binding proteins such as transferrin. To obtain iron for their growth, bacteria produce iron-binding compounds called siderophores. Siderophores, such as enterobactin produced by *E. coli*, are secreted by the bacteria, capture iron by chelating it, then attach to specific receptors on the bacterial surface, and are actively transported into the cell where the iron becomes available for use. The fact that bacteria have such a complex and specific mechanism for obtaining iron testifies to its importance in the growth and metabolism of bacteria.
PEARLS

- Bacteria reproduce by binary fission, whereas eukaryotic cells reproduce by mitosis.
- The bacterial growth cycle consists of four phases: the lag phase, during which nutrients are incorporated; the log phase, during which rapid cell division occurs; the stationary phase, during which as many cells are dying as are being formed; and the death phase, during which most of the cells are dying because nutrients have been exhausted.
- Some bacteria can grow in the presence of oxygen (aerobes and facultatives), but others die in the presence of oxygen (anaerobes). The use of oxygen by bacteria generates toxic products such as superoxide and hydrogen peroxide. Aerobes and facultatives have enzymes, such as superoxide dismutase and catalase, that detoxify these products, but anaerobes do not and are killed in the presence of oxygen.
- The fermentation of certain sugars is the basis of the laboratory identification of some important pathogens. Fermentation of sugars, such as glucose, results in the production of ATP and pyruvic acid or lactic acid. These acids lower the pH, and this can be detected by the change in color of indicator dyes.

SELF-ASSESSMENT QUESTIONS

1. Figure 3–1 depicts a bacterial growth curve divided into phases a, b, c, and d. In which one of the phases are antibiotics such as penicillin most likely to kill bacteria?
   (A) Phase a
   (B) Phase b
   (C) Phase c
   (D) Phase d

2. Some bacteria are obligate anaerobes. Which of the following statements best explains this phenomenon?
   (A) They can produce energy both by fermentation (i.e., glycolysis) and by respiration using the Krebs cycle and cytochromes.
   (B) They cannot produce their own ATP.
   (C) They do not form spores.
   (D) They lack superoxide dismutase and catalase.
   (E) They do not have a capsule.

ANSWERS

1. (B)
2. (D)

PRACTICE QUESTIONS: USMLE & COURSE EXAMINATIONS

Questions on the topics discussed in this chapter can be found in the Basic Bacteriology section of Part XIII: USMLE (National Board) Practice Questions starting on page 709. Also see Part XIV: USMLE (National Board) Practice Examination starting on page 751.
CHAPTER

Classification of Medically Important Bacteria

CHAPTER CONTENTS

Principles of Classification
Pearls

Practice Questions: USMLE & Course Examinations

PRINCIPLES OF CLASSIFICATION

The current classification of bacteria is based primarily on morphologic and biochemical characteristics. A scheme that divides the medically important organisms by genus is shown in Table 5–1. For pedagogic purposes, this classification scheme deviates from those derived from strict taxonomic principles in two ways:

1. Only organisms that are described in this book in the section on medically important bacteria are included.
2. Because there are so many gram-negative rods, they are divided into three categories: respiratory organisms, zoonotic organisms, and enteric and related organisms.

The initial criterion used in the classification is the nature of the cell wall (i.e., is it rigid, flexible, or absent?). Bacteria with rigid, thick walls can be subdivided into free-living bacteria, which are capable of growing on laboratory medium in the absence of human or other animal cells, and non–free-living bacteria, which are obligate intracellular parasites and therefore can grow only within human or other animal cells. The free-living organisms are further subdivided according to shape and staining reaction into a variety of gram-positive and gram-negative cocci and rods with different oxygen requirements and spore-forming abilities. Bacteria with flexible, thin walls (the spirochetes) and those without cell walls (the mycoplasmas) form separate units.

Using these criteria, along with various biochemical reactions, many bacteria can be readily classified into separate genus and species. However, there have been several examples of these criteria placing bacteria into the same genus when DNA sequencing of their genome reveals they are significantly different and should be classified in a new or different genus. For example, an organism formerly known as Pseudomonas cepacia has been reclassified as Burkholderia cepacia because the base sequence of its DNA was found to be significantly different from the DNA of the members of the genus Pseudomonas.

PEARLS

- The classification of bacteria is based on various criteria, such as the nature of the cell wall, staining characteristics, ability to grow in the presence or absence of oxygen, and ability to form spores.
- The criterion currently used is the base sequence of the genome DNA. Several bacteria have been reclassified on the basis of this information.

PRACTICE QUESTIONS: USMLE & COURSE EXAMINATIONS

Questions on the topics discussed in this chapter can be found in the Basic Bacteriology section of Part XIII: USMLE (National Board) Practice Questions starting on page 709. Also see Part XIV: USMLE (National Board) Practice Examination starting on page 751.
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Genus</th>
<th>Representative Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Rigid, thick-walled cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Free-living (extracellular bacteria)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Gram-positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Cocci</td>
<td>Streptococcus</td>
<td>Pneumonia, pharyngitis, cellulitis</td>
</tr>
<tr>
<td></td>
<td>Staphylococcus</td>
<td>Abscess of skin and other organs</td>
</tr>
<tr>
<td>b. Spore-forming rods</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1) Aerobic</td>
<td>Bacillus</td>
<td>Anthrax</td>
</tr>
<tr>
<td>(2) Anaerobic</td>
<td>Clostridium</td>
<td>Tetanus, gas gangrene, botulism</td>
</tr>
<tr>
<td>c. Non–spore-forming rods</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1) Nonfilamentous</td>
<td>Corynebacterium</td>
<td>Diphtheria</td>
</tr>
<tr>
<td></td>
<td>Listeria</td>
<td>Meningitis</td>
</tr>
<tr>
<td>(2) Filamentous</td>
<td>Actinomyces</td>
<td>Actinomycosis</td>
</tr>
<tr>
<td></td>
<td>Nocardia</td>
<td>Nocardiosis</td>
</tr>
<tr>
<td>2. Gram-negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Cocci</td>
<td>Neisseria</td>
<td>Gonorrhea, meningitis</td>
</tr>
<tr>
<td>b. Rods</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1) Facultative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) Straight</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(i) Respiratory organisms</td>
<td>Haemophilus</td>
<td>Meningitis</td>
</tr>
<tr>
<td></td>
<td>Bordetella</td>
<td>Whooping cough</td>
</tr>
<tr>
<td></td>
<td>Legionella</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>(ii) Zoonotic organisms</td>
<td>Brucella</td>
<td>Brucellosis</td>
</tr>
<tr>
<td></td>
<td>Francisella</td>
<td>Tularemia</td>
</tr>
<tr>
<td></td>
<td>Pasteurella</td>
<td>Cellulitis</td>
</tr>
<tr>
<td></td>
<td>Yersinia</td>
<td>Plague</td>
</tr>
<tr>
<td>(iii) Enteric and related organisms</td>
<td>Escherichia</td>
<td>Urinary tract infection, diarrhea</td>
</tr>
<tr>
<td></td>
<td>Enterobacter</td>
<td>Urinary tract infection</td>
</tr>
<tr>
<td></td>
<td>Serratia</td>
<td>Pneumonia</td>
</tr>
<tr>
<td></td>
<td>Klebsiella</td>
<td>Pneumonia, urinary tract infection</td>
</tr>
<tr>
<td></td>
<td>Salmonella</td>
<td>Enterocolitis, typhoid fever</td>
</tr>
<tr>
<td></td>
<td>Shigella</td>
<td>Enterocolitis</td>
</tr>
<tr>
<td></td>
<td>Proteus</td>
<td>Urinary tract infection</td>
</tr>
<tr>
<td></td>
<td>Campylobacter</td>
<td>Enterocolitis</td>
</tr>
<tr>
<td></td>
<td>Helicobacter</td>
<td>Gastritis, peptic ulcer</td>
</tr>
<tr>
<td></td>
<td>Vibrio</td>
<td>Cholera</td>
</tr>
<tr>
<td>(b) Curved</td>
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<tr>
<td>(2) Aerobic</td>
<td>Pseudomonas</td>
<td>Pneumonia, urinary tract infection</td>
</tr>
<tr>
<td></td>
<td>Bacteroides</td>
<td>Peritonitis</td>
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<tr>
<td>(3) Anaerobic</td>
<td>Mycobacterium</td>
<td>Tuberculosis, leprosy</td>
</tr>
<tr>
<td></td>
<td>Rickettsia</td>
<td>Rocky Mountain spotted fever, typhus, Q fever</td>
</tr>
<tr>
<td>3. Acid-fast</td>
<td>Chlamydia</td>
<td>Urethritis, trachoma, psittacosis</td>
</tr>
<tr>
<td>B. Non–free-living (obligate intracellular parasites)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treponema</td>
<td>Syphilis</td>
</tr>
<tr>
<td></td>
<td>Borrelia</td>
<td>Lyme disease</td>
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<tr>
<td></td>
<td>Leptospira</td>
<td>Leptospirosis</td>
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<td>II. Flexible, thin-walled cells (spirochetes)</td>
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<td>Treponema</td>
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<td>Lyme disease</td>
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<td>Leptospirosis</td>
</tr>
<tr>
<td>III. Wall-less cells</td>
<td>Mycoplasma</td>
<td>Pneumonia</td>
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