Basic Microbiology and Immunology
(MICRO 402)

Lecture Notes
for
Third Year Pharmacy Students

Edition 2015
Preface

About This Book:
This book includes lecture notes for the General Microbiology and Immunology course (Micro402) offered to third year students at the Faculty of Pharmacy, Cairo University. Students are encouraged to read the appropriate chapters ahead of the lectures to get prepared for better understanding.

Organization:
The book is divided into three major parts or modules, covering three different areas of concentration. **Part I** deals with the principles and foundations of microbiology: its history, origins, and the basic concepts of microbial classification, identification, structure, nutrition, and metabolism. **Part II** focuses on microbial genetics, with emphasis on the basics of molecular biology, microbial genetics, and microbial genomics and metagenomics. **Part III** represents a comprehensive overview of basic and applied immunology.

What do Pharmacy Students Need to Know about Microbiology and Immunology?
Microbiology, the study of microscopic living organisms, or the biology of microbes, is becoming one of the cutting edge sciences as we enter the XXI" century. In the current general pharmacy program offered by Cairo University, undergraduate students have to study six microbiology-related courses. Why is microbiology important to pharmacy students, and what is the importance of this general course, in particular?

- This course is almost the only biology course, offered in the general program, that offers thorough explanation of the major biological concepts of diversity, natural selection, adaptation, mutation, rapid evolution, etc.
- The course is essential for understanding medical microbiology, and the information presented are pivotal to understanding the mode of action of antibiotics and chemotherapeutic agents, which are at the core of pharmaceutical microbiology.
- The course is a good introduction to the following courses of biotechnology and pharmaceutical microbiology as well.
- Understanding the basics of molecular biology, microbial genetics, and recombinant DNA technology is indispensable for nowadays pharmacists. This course presents a thorough explanation of molecular biology and genetics from a microbiological perspective.
- The study of basic and applied immunology and immunological products is essential for pharmacists who administer vaccines and those who work in vaccine development or quality control.
- This is one of the few courses covering recent advances in genomics, notably bacterial and viral genomics.
Acknowledgements and Credits

Many tables and parts of the text are taken from Todar’s Online Textbook of Bacteriology (http://www.textbookofbacteriology.net), with full permission from the textbook’s author. In addition, these notes have used material from the following textbooks:

- Alcamo’s Fundamentals of Microbiology, 7th edition
- Brock’s Biology of Microorganisms, 9th edition
- Bauman Microbiology, 2nd edition
- Hugo and Russel, Pharmaceutical Microbiology, 4th edition
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Chapter I: The Development of Microbiology

Microbiology is the science of minute organisms, invisible to the naked eye, named 'microbes' or 'microorganisms'. It is a relatively recent science just over 150 years old. However, long before the discovery of microorganisms, certain processes caused by microbial activities were known to man. Primitive biological processes were discovered by accident and were incorporated into daily life. Humans have made use of microbes for centuries without knowing what they were or what they did. Thus, in ancient times at the beginning of civilization, man employed the processes of fermentations for souring of milk, making of bread, and for producing alcoholic beverages and vinegar. These processes could not be explained, and the mystery remained until the latter part of the 19th century when Louis Pasteur introduced his germ theory in 1876 and identified a number of microbes and their functions.

Before that period, much has been written about the nature of disease and the spontaneous generation of living things. Thus, the peoples of Asia had certain ideas on the contagiousness of some disease and they isolated those suffering from leprosy, and Avicenna (980-1037) thought that all infectious diseases were cause by minute living creatures invisible to the naked eye and transmitted through air and water. However, these were only speculations lacking experimental or observational evidences.

The first person to see and describe microbes was Antony van Leeuwenhoek (1632-1732), a Dutch cloth merchant living in the town of Delft, Holland. He learned grinding tiny lenses of high magnifications (up to 300x) and became interested in things he could see through the lenses he produced. He made simple microscopes, and it was in 1677 that he first saw 'animalcules', as he called the microorganisms' while examining a drop of rain water. Thus a new world was discovered, and the new science now called 'microbiology' was born.
Since no other person succeeded in using single lenses as effectively as Leuwenhoek, the compound microscope was perfected to follow up this discovery. When he died in 1723, his field of science went in a dormant stage for almost 150 years and was forced to wait for Louis Pasteur (1822-1895), Robert Koch (1843-1910), and other distinguished microbiologists of the golden age of microbiology (1850-1950).

Although the emergence of experimental microbiology was slow, the development of reliable methods was very much stimulated by the prolonged and intense controversy over the “theory of spontaneous generation of life,” which faced the microbiologists. Thus, from the time of Aristotle (384-422 BC) till the middle of the 19th century, it was widely believed that animals and other living beings could be generated de novo from non-living matter. For animals and other visible organisms, this idea was disproven in the 17th century when 'Redi' demonstrated that maggots no longer appeared in decomposing meat if it was protected from deposition of eggs by flies. However, the idea of spontaneous generation existed for the new world of microbes. John Needham (1713-1781), a Roman priest, was one of the early investigators supporting the theory of spontaneous generation. He boiled meat broth or vegetable infusions in corked flasks and found that the infusions were putrefied upon standing.

However, the first strong laboratory evidence that life does not arise spontaneously de novo was demonstrated by Lazzaro Spallanzani (1729-1799) who repeated the experiments of Needham and arrived at the opposite conclusion. He criticized Needham for using cork (a porous material) which allowed the entrance of microorganisms from air into his boiled infusions, especially during cooling when negative pressure developed within containers and contaminated air was sucked into the vessels. When Spallanzani boiled the infusions and then sealed the openings of his vessels in a flame, none of them revealed spoilage. However, others claimed that the absence of decomposition in these sealed vessels was due to the limited supply of air rather than to the exclusion of air-borne contaminants. The answer to this objection was made by A. Schroeder and Van Dusch (1853-1854) when they suggested the use of the cotton plug, which is still widely used today. These plugs mechanically remove air-borne microorganisms but allow the entrance of bacteria-free air required by so many microorganisms.
An interesting and economically significant application of Spallanzani’s discovery was made in 1810 by Nicholas Appert (1750-1841), when the French government (Napoleon I) offered a prize to the first person who could perfect a useful technique for the preservation of food. Appert developed the art of preserving food by canning (boiling in airtight containers).

Nevertheless, the controversy continued because skeptics criticized the use of cotton plugs by claiming that air is devitalized as it passes through these plugs. Moreover, some investigators were unable to reproduce the stability of certain sterilized organic infusions; unfortunately because they used infusions of hay (we know today such material is largely contaminated by the spores of Bacillus subtilis which are so difficult to kill by mere boiling).

The history of bacteriology is closely connected with the names of Louis Pasteur and Robert Koch because of their ingenious work. Pasteur led concreted attacks in support of Spallanzani’s discovery because he was convinced that microbes were the cause of fermentations. He showed that boiled medium could remain clear in an unsealed ‘swan neck’ flask open to the air through an S-shaped capillary tube. Since bacteria cannot move, Pasteur reasoned that it would be impossible for contamination of his medium to occur unless he tilted the flasks and allowed some of the sterile liquid to come in contact with the tip of the capillary tube containing contaminated dust particles. Fortunately enough, Pasteur used sugar, yeast extract, and water for his medium, which is relatively easy medium to sterilize.

The most important experimental step in finishing this controversy was taken when John Tyndall compared various kinds of extracts. He found that after he had brought a bale of hay into his laboratory he could no longer repeat his earlier success in achieving sterility by boiling; but he could repeat in a separate room. He finally concluded that the hay has contaminated his laboratory with a kind of living organism that could survive boiling for hours. In the same year (1877), Ferdinand Cohn demonstrated the resistant forms as small refractile endospores of the hay bacillus (Bacillus subtilis).

Microbiology then developed largely through interest in three different groups of microbes responsible for: fermentations, cycling of organic matter in nature and for diseases of man and animals. These developments gave rise to industrial,
agricultural and medical microbiology, respectively. The studies of fermentations came earliest and contributed too much for the development of biochemistry. It was fortunate for microbiology that not all investigators during the golden era of fundamental discoveries devoted their energies to exactly the same problems. Thus, with the development of microbiology attempts were made to apply this science to the practical problems being faced at that time.

- The name of the great French scientist chemist and microbiologist, **Louis Pasteur** (1822-1895) is linked with the most important discoveries in the field of microbiology and thus deserved to be the 'Father of Microbiology'. As a professor at the University of Lille, in the heart of the wine industry in France, he has been asked by Napoleon I to study a serious wine problem that was threatening the wine industry in France and no one seemed able to correct. He stressed that spoilage of wine could be directly attributed to the action of certain microbes that produced undesirable end products and ‘diseased’ the wines. By selectively heating the fresh grape juice after it was bottled, he prevented such spoilage. This heating has been given the name **pasteurization**. He concluded that fermentations were due to living organisms and that different kinds of microbes were associated with different kinds of fermentations. When Pasteur subsequently turned his attention to disease, he suggested that infection was due to organisms. Thus, in 1865, Pasteur discovered a protozoan that was threatening to ruin the European **silkworm industry** and by excluding the diseased worms, he could maintain a healthy stock.

- In addition, the investigations of Pasteur on the causative agents on **chicken cholera**, **anthrax**, and **rabies** formed the bases for the use of protective vaccines. Moreover, the works of Pasteur drew the attention of many scientists to the study of important problems and encouraged this new science (microbiology) to flourish. Thus, the English surgeon **Joseph Lister** introduced into surgery the principle of **antiseptics** (disinfection of wounds with chemical agents) to combat supportive processes in wounds.

- Of great importance in the progress of microbiology were also the discoveries made by the German scientist **Robert Koch** (1843-1910). He and his students introduced solid nutrient media (potatoes, gelatin, coagulated serum, meat-peptone agar), the isolation of pure culture technique, staining of microorganisms
with aniline dyes, the oil immersion system, and microphotography into laboratory techniques. Koch established the aetiology of anthrax, discovered the causative agents of tuberculosis and cholera, and obtained tuberculin from tubercle bacilli. Koch also formulated his famous **Koch's postulates** to prove the causative agents of disease. Thus, before an organism could be said to be the cause of a specific disease, the agent must fulfill the following postulates:

1. The suspected organism must be found in every case of the disease.
2. The organisms must be isolated in pure culture from every case of the disease.
3. The pure culture must be capable of reproducing the original disease in its typical clinical form when introduced into susceptible animals.
4. The same organism must be re-isolated from the injected test animal.

These postulates were proposed before the discovery of viruses and other strict parasites, which cannot grow on inanimate media, and subsequently Koch's postulate cannot be fulfilled for every disease.

- In addition to the above-mentioned discoveries of Koch, he developed a large school of microbiology and among his students were Friedrich Loeffler, Emil Behring, G. Gaffky, and many others. **Loeffler** discovered the causative organism of **diphtheria** and advanced the hypothesis that diphtheria organisms, though localized in the throat, made a poison that escaped from the cells and diffused to other parts of the body causing death. **Behring** was the first to introduce **antitoxic sera** to cure diseases. He used antidiphtheritic serum to cure diphtheria in 1891 and from this date the production of antitoxic sera for several diseases was developed.

- Immunity studies have had their origin in 1796 with the pioneer work of the English physician **Edward Jenner** (1749-1823). He learned from his patients in farm country that milkmaids who contracted cowpox were resistant to the dreadful smallpox, and, he postulated that there must be a relation between the two diseases. In his famous experiment in 1796, Jenner scratched a farm boy with a needle bearing fluid from a sore of a milkmaid who had cowpox. When the boy later exposed to smallpox, he resisted the disease. Jenner introduced the word **vaccine** (which means cow in Latin) and the technique of vaccination against smallpox by rubbing the cowpox vaccine into scarified skin of humans. The
cowpox and smallpox viruses are so similar that vaccination with the cowpox virus stimulates the immune system to react against if it is exposed to smallpox. However, relatively little was done with this revolutionary discovery until about 1880 when Pasteur discovered a useful vaccine for chicken cholera and applied the word ‘vaccination’ in the honors of Jenner’s studies. Pasteur then introduced the protective vaccines against rabies and anthrax.

- These research efforts were paralleled with the early work on genetics by Gregor Mendel in mid 1800s and the beginning of the industrialization of the fermentation processes (the practical side of biotechnology). Breweries and distilleries became big industries and baker’s yeast was produced in specialized factories. During this period microbes have become the basis of great industries. It began with the production of industrial chemicals and antibiotics by fermentation under the pressure of World War I and World War II, respectively. Thus, in 1914, H. Weizman introduced the manufacture of acetone (as essential ingredient of explosives) by fermentation in the U.K.; and U.S.A. contributed its facilities for large-scale production (rows of 50,000 gallon tank fermenters, the largest in the history). Although Alexander Fleming published his famous discovery of penicillin in 1929, he abandoned his research due to the instability of penicillin. In 1938, Florey and Chain (Oxford University) purified small quantities of penicillin and demonstrated its therapeutic value for humans and animals but it remained difficult and expensive to produce the drug in any quantity. The problems of large scale production of penicillin were resolved under the pressure of World War II, namely, the pressing need to produce this drug for treating battle casualties.

- Today, fermentation is carried out in huge vessels, 150 cubic meters or more, using highly developed computer control of temperature, pH, aeration, and stirring to give the optimum conditions for production. Careful selection of production strains of microbes and improved methods of extraction and purification have increased yields many times over the last 70 years or so. These traditional techniques are used to produce yeast, alcohol, antibiotics, enzymes, vaccines and drugs of many kinds (e.g. steroid biotransformations) as well as basic materials for the food and other industries as dextrans, organic acids (e.g. citric acid, glutamic acid lactic acid), vitamins, and many kinds of amino acids.
A new era of microbiology began with the development of and advances in recombinant DNA technology in 1973. The technology permitted human genes to be cut and inserted into microorganisms thus enabling them to manufacture the gene products far more efficiently than traditional methods of extraction from animal or human tissues. These techniques used to rearrange the genetic code to produce an organism with new desirable characteristics such as the ability to produce certain substance are often referred to as genetic engineering. The ‘genetic’ is concerned with gene or part of DNA that code for the desired characteristic and ‘engineering’ refers to cutting out that part of the DNA from one organism and joining or grafting it into the DNA of another organism (cutting and splicing).

It was so spectacular that these processes are described nowadays as ‘modern or new biotechnology’ to distinguish them from all the previous conventional ones. Recombinant DNA technology is reshaping medicine and the pharmaceutical industry; it was used to produce many therapeutic products such as insulin for human use in 1982 followed by human growth hormone, interferon, blood clotting factors and many other products. It also allowed the development of more effective and safer vaccines (compared to those produced by traditional methods) which use genetically engineered surface antigens rather than whole viruses. Great potentials lie in gene therapy, which consists of the insertion of genetic material into cells to prevent, control or cure disease. It includes repairing or replacing defective genes and making tumors more susceptible to other kinds of treatment. Recombinant DNA technology also offers forensic, agricultural and environmental applications and raises important safety and ethical questions.

Finally, another new era and a new golden age of microbiology has started near the end of the 20th century and the start of the current millennium. A genomic revolution is being driven by the advances in DNA sequencing, and new technologies have emerged, such as metagenomics, or the study of microbial life in different environments by directly sequencing DNA. Today, the Human Microbiome Project, the Earth Microbiome Project, and other genomic-based projects are changing the way we understand microbes, our planet, and even ourselves. Details on these technologies are presented at the end of Part II of this book.
Chapter 2: Classification and Identification of Microorganisms

I. Classification of Microorganisms

A. Nomenclature

All organisms have a double name usually from Latin or Greek stems. The name consists of two parts, the first part is the genus name to which the microorganism belongs and the second part is the species name which is usually a descriptive adjective that further describes the genus name. This system of nomenclature is called the binomial system (binomial = “two names”), it was first suggested by Carolus Linnaeus and it gives scientists throughout the world a universal system of naming microorganisms to avoid any confusion. When the name is written, the first letter in the genus name is capitalized while the remainder of the genus name and the species name is written in lowercase letters. Both names have to be italicized or underlined when printed.

Examples:

• *Escherichia coli* or *Escherichia coli* refers to a species of bacteria that inhabit the intestines. The genus name is after Theodor Escherich (the scientist who discovered it) while the species name refers to where the bacteria is located (the colon).

• *Staphylococcus aureus* or *Staphylococcus aureus* refers to a species of bacteria that forms grape like clusters of spherical cells. The genus name is after the words (*staphyle*=grape and *coccus*=sphere) while the species name (*aureus* = golden yellow) refers to the color of the colonies these bacteria form when they grow on solid media.

Scientists usually abbreviate the binomial names by writing only the first letter of the genus name together with the full species name. This abbreviation should also be italicized or underlined. Thus, *Escherichia coli* becomes *E. coli* or *E. coli* and *Staphylococcus aureus* becomes *S. aureus* or *S. aureus*. 
B. Classification Systems

B.1. The three-kingdom classification

In 1866 the German scientist Ernst H. Haeckel proposed a new system to separate microorganisms and distinguish them from the plant and animal kingdoms which were the only two divisions known at that time. Haeckel grouped all microorganisms including bacteria, protozoa, algae and fungi in a new third kingdom known as Protista. At that time there was a plethora (excess) of newly identified microorganisms as a result of both Pasteur and Koch work and the new kingdom Protista came to include all the newly discovered microorganisms that share plant and animal characteristics but were not plants or animals.

B.2. The five-kingdom classification

In the 20th century, advances in cell biology led scientists to question the two- or three- kingdom classification. In 1969 Robert H. Whittaker proposed a system that classified all living organisms into five kingdoms.

- Kingdom Monera (bacteria).
- Kingdom Protista (unicellular algae and protozoa).
- Kingdom Fungi (mushrooms, mold and yeast).
- Kingdom Plantae (multicellular plants).
- Kingdom Animalia (multicellular animals).

Consequently, microorganisms comprised three out of the five kingdoms of Whittaker classification (Monera, Protista and Fungi).

B.3. Two types of cellular organizations, Prokaryotes and Eukaryotes

In the 1940’s and 1950’s the electron microscope was being developed and was able to magnify objects and cells thousands of times more than a typical light microscope. With the electron microscope, bacteria were seen as being cellular like other microbes, plant and animals. However, their cells were organized in a fundamentally different way from other organisms. Plant and Animal cells had a cell nucleus that houses the genetic material in the form of chromosomes and this structure is physically separated from other cellular structures by a membrane envelop. This type of cellular organization is called eukaryotic (having true nucleus) (eu=true; karyon=kernel, nucleus). Microscopic observation of protista and fungi also revealed that their cells had a eukaryotic organization (true nucleus). Bacteria on the other hand lack the presence of a true nucleus as the genetic material in the form of the bacterial chromosome is not surrounded by a membrane. Bacteria is therefore classified as prokaryotes meaning it has a primitive cellular organization as (pro=primitive). Eukaryotic cells, including eukaryotic microbes, have a variety of structurally discrete compartments called organelles (endoplasmic reticulum, golgi apparatus, lysosomes and mitochondria). These organelles are absent from prokaryotic cells. Therefore and based on the Whittaker five-kingdom classification only one kingdom (Monera) is prokaryotic while the four other kindgdoms (Protista, Fungi, Plantae, and Animalia) are eukaryotic.
B.4. The three-domain system classification

In the 1970’s and with the advent of new techniques in molecular biology and biochemistry Carl Woese proposed the three-domain system or suprkingdoms for classification of living organisms.

- Domain Archaea
- Domain Eubacteria
- Domain Eukarya

The Archaea included a group of bacteria that were formally known as archaebacteria (archae=old) and were known for their ability to live under harsh environmental conditions that were dominant in early stages of life. The Eubacteria (true bacteria) included all other types of bacteria (Similar to kingdom Monera but without the archaebacteria). The separation between these two types of bacteria as distinct domains was based on the differences in the composition of their cell walls, lipid composition of their membranes, the sequence of their ribosomal RNA (the RNA component of the ribosome), and their sensitivity to different antibiotics. These differences were only discovered after the advances in molecular biology techniques at that time and were confirmed with more studies that were done in the 1990’s when it became feasible to know the complete sequence of DNA of many bacterial species. The third and last domain: domain Eukarya comprised the four remaining kingdoms of Whittaker (Protista, Fungi, Plantae and Animalia). Consequently, the first two domains (Archaea and Eubacteria) are Prokaryotes while the last domain (Eukarya) is Eukaryotic.

Bacterial taxonomy on the molecular level

Because of the important position that bacteria occupy in microbiology and because bacterial taxonomy has been through complex systems, there exists a guide which includes the official listings of all recognized bacteria. This guide is known as **Bergey's manual of systematic bacteriology** or simply **Bergey's manual**. The system of classification and identification was devised by David Hendricks Bergey in the 1920’s. The manual has been updated in several editions and is a complete guide for the identification and classification of bacteria and now has information about each organism on the molecular level.
Whittaker five-kingdom classification

Woese three-domain classification
Main differences between Prokaryotic and Eukaryotic cell structures

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<th>Character</th>
<th>Prokaryotes</th>
<th>Eukaryotes</th>
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<tbody>
<tr>
<td>Nucleus</td>
<td>No nuclear envelop</td>
<td>True nucleus, with nuclear membrane</td>
</tr>
<tr>
<td>DNA structure</td>
<td>Single, circular chromosome</td>
<td>Multiple linear chromosomes in the nucleus</td>
</tr>
<tr>
<td>Membranes</td>
<td>Cell membrane only</td>
<td>Cell and organelle membranes</td>
</tr>
<tr>
<td>Organelles</td>
<td>absent</td>
<td>Present (Endoplasmic reticulum ‘ER’, mitochondria, golgi bodies, lysosomes) some have chloroplasts</td>
</tr>
<tr>
<td>Ribosome</td>
<td>70S (smaller than eukaryotic ribosome), free in the cell</td>
<td>80S (larger than prokaryotic ribosome) free or bound to ER</td>
</tr>
<tr>
<td>Cytoskeleton</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Cell wall</td>
<td>Present, formed of peptidoglycan</td>
<td>Present in fungi, algae and plants formed of chitin (fungi) or cellulose</td>
</tr>
<tr>
<td>Flagella</td>
<td>Rotating movement</td>
<td>Whipping movement</td>
</tr>
<tr>
<td>Cilia</td>
<td>absent</td>
<td>Sometimes present</td>
</tr>
<tr>
<td>Cell division</td>
<td>Binary fission</td>
<td>Mitosis and meiosis</td>
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<tr>
<td>Reproduction</td>
<td>Asexual</td>
<td>Sexual and Asexual</td>
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<td>Examples</td>
<td>Archaea, Eubacteria</td>
<td>Fungi, Protista, Plants, Animals</td>
</tr>
</tbody>
</table>

*Note: Bacteria and archaeabacteria are prokaryotes. All other organisms are eukaryotes.

*Diagram: A Prokaryotic cell does not have internal organelles surrounded by a membrane. Most of a prokaryote's metabolic functions take place in the cytoplasm.

*Diagram: This eukaryotic cell from an animal has distinct membrane-bound organelles that allow different parts of the cell to perform different functions.
C. Various groups of microorganisms

Fungi

- Fungi are eukaryotic microorganisms; their cells wall contains the polysaccharide “chitin” which distinguishes them from plant cells.
- Fungi do not carry out photosynthesis, but absorb and use preformed organic matter from the environment as their nutritional source. This is another difference that fungi have from plant cells that carry out photosynthesis. They grow best in warm, moist places.
- Fungi are divided into two main groups: the unicellular fungi (yeast) and multicellular fungi (molds), again both types of cells are eukaryotic.
  - Yeasts are unicellular organisms larger than bacteria. They play an important role in industry particularly in fermentation and production of bread.
  - Molds are multicellular organisms. Their body consists of a fluffy mass of filaments called hyphae (sing., hypha). The hyphae form dense network called mycelia (sing., mycelium).
  - The hyphae can have cross walls or septa (sing., septum) that divide the cytoplasm within the hypha into separate cells, such fungi are described as septate. The septa are incomplete as there are pores within the septa to allow the contents of the cell cytoplasm to mix with the adjacent ones freely. Other types of fungi do not have these septa and are (non septate).
- Among The important fungi to humans are those that produce antibiotics such as the fungus Penicillium, a mold that produces penicillin.
- Some types of fungi play an important role in decomposing organic matter, few species do not wait for an organism to die and consequently cause disease to humans and also to plants.
- Among the diseases caused to humans by fungi are candidiasis, which is a skin infection caused by Candida albicans, and dermatophytosis which is a fungal infection of the hair, skin and nails caused by certain species of the genus Trichophyton, Microsporum or Epidermophyton.
Algae

- Algae are **eukaryotic** organisms that carry out photosynthesis but are different from plants.
- Two types of unicellular algae, the **diatoms** and **dinoflagellates**, play an important role in marine life as they both make up the phytoplankton which is a major food source for marine and aquatic animals.
- Both types of algae carry out photosynthesis and trap the sun’s energy to manufacture carbohydrates, which are passed to other aquatic organisms in the food chain.
- The cell wall of diatoms is impregnated with silicon dioxide, which is a glass-like substance. When they die these glassy remains accumulate on the seafloor as **diatomaceous earth**, which is extracted and used in filtering devices and as mild abrasives in toothpastes.
- The cells wall of dinoflagellates is encased in hard cellulose shells.

Protozoa

- Protozoa are **eukaryotic** single-celled microorganisms. Most of them lack cell walls, move freely, and ingest food particles.
- Digested food particles enter the food vacuoles, which are then joined by lysosomes where digestive enzymes digest the food. Nutrients are absorbed from the food vacuole, and any waste is eliminated.
- Many protozoa decompose dead organisms and recycle nutrients.
- Some species are **important links in the food chain** as they help other organisms break down complex molecules into simple ones that can be utilized. For example: some protozoa live in the intestine of grass-feeding animals and help break down cellulose.
- Protozoa have a different assortment of shapes, sizes and structural components, but they are classified according to their movement mechanisms into four groups (amoebas, flagellates, ciliates, and sporozoa).
  - Amoebas move by pseudopods (false feet), example: *Entamoeba histolytica* which causes diarrhea.
  - Flagellates move by a whip like flagella, example: *Euglena* which lives in fresh water ponds and can carry out photosynthesis.
  - Ciliates move by hair like structures (cilia) that protrude from all around the body, example: *Paramecium*.
  - Sporozoa: No pseudopods, flagella, or cilia, examples: *Plasmodium* which causes malaria and *Toxoplasma* which causes toxoplasmosis.
Bacteria

- Bacteria are among the most abundant organisms on earth ($\sim 10^{10}$ cells)
- The term 'bacteria' is a plural form of the Latin word *bacterium* meaning “staff” or “rod”.
- There may be more than 10 million species of bacteria.
- Bacteria are single-celled and they are divided into two main domains: the *Archaea* and *Eubacteria*. Both groups are more metabolically diverse than any other microbes.
- Bacteria come in three different shapes: bacillus (rod shaped), coccus (spherical) and spirillum (spiral).
- Most bacteria absorb their food from the environment but some of them (*Cyanobacteria*) can carry out photosynthesis.
- Bacteria more than any other organism have adapted to the diverse environments on earth. They inhibit air, soil and water and they exist with large numbers on the surfaces of all plants and animals.
- Bacteria can be isolated from arctic ice, thermal hot springs, animal tissues and even outer space.
- Certain types of bacteria can withstand the powerful activity of digestive enzymes the crushing pressure of deep oceans and the acidity found in volcanic ash. Others can withstand boiling water, extremely dry conditions and some can survive in oxygen-free environment.
- Bacteria have so completely colonized every part of the earth that the mass of bacterial cells is estimated to outweigh the mass of all plants and animals combined.
- The vast majority of bacteria play a positive role in nature; they break down remains of dead organisms and recycle the carbon, digest sewage into simple chemicals, extract nitrogen from air and make it available for plants for protein production and produce foods for human consumption like cheese and yogurts and products for industrial technology. It is safe to say that life as we know it would be impossible without bacteria.
- Some bacteria (disease causing bacteria or *pathogenic* bacteria) are harmful as certain species multiply within the human body where they disrupt tissues or produce toxins that result in human disease (*Typhoid, Plague, Tuberculosis* and *Cholera* just to name a few). Other bacteria infect animal herds and plant crops.
- The diseases bacteria cause will be handled in the Medical Microbiology course next semester.
Special types of bacteria

Rickettsiae

- First described by Howard Taylor Ricketts in 1909.
- Very tiny nonmotile organisms can be barely seen with the light microscope.
- Must be grown on living tissues such as fertilized eggs.
- They are transmitted among humans by arthropods like ticks and lice. They cause a number of important diseases like Typhus fever and Rocky Mountain spotted fever.

Chlamydiae

- Very tiny organisms - half the size of rickettsiae.
- Cannot be seen with the light microscope and must be grown in living cells.
- They can cause pneumonia (chlamydial pneumonia) and Chlamydial urethritis (sexually transmitted disease).

Mycoplasma

- The smallest of all types of bacteria.
- Can be cultivated on artificial media in the laboratory.
- Prokaryotic but lacks the presence of a true cell wall which is present in all other bacteria.
- Certain species of mycoplasma can cause pneumonia.

Cyanobacteria

- Cyanobacteria were once known as blue green algae but are now grouped among bacteria due to the structural and biochemical similarities to typical bacteria.
- Cyanobacteria still have a major difference from typical bacteria which is their ability to carry our photosynthesis similar to unicellular algae; this character makes them unique among prokaryotes.
- Cyanobacteria possess light trapping pigments that function in photosynthesis. The pigments are usually blue or green but some are yellow, black or even red.
- The periodic redness of the Red Sea (hence the name) is due to the presence of cyanobacteria whose members contain large amounts of red pigments.
Non-cellular microscopic life forms

Viruses

- Viruses are the most abundant life forms on this planet (~ $10^{31}$ viral particles)
- Viruses are structurally simpler than other microbes because they are not made of cells.
- Viruses are smaller than the tiniest bacteria and can only be seen by electron microscope.
- They are neither prokaryotes nor eukaryotes.
- They have a core of nucleic acids (DNA or RNA) surrounded by a protein coat or shell (capsid).
- As independent entities they do not grow or show any metabolic activity. They only replicate when they are inside a living cell.
- When a virus penetrates a host cell its genetic material is released inside the cell.
- The virus utilizes the cell enzymes and structures and replicates itself hundreds of times thus, destroying the cell.
- Newly formed viruses attack neighboring cells and repeat the cycle where the virus particles replicate inside the host cells leading to their destruction and forming more virus particles until the whole tissue is destroyed.
- Viruses cause many diseases in humans among them are (AIDS, SARS, Bird flu).
- Certain types of viruses attack bacteria they are known as bacteriophages or simply phages.
Prions

- Prions are considered to be infectious protein structures. They are composed solely of proteins and contain no nucleic acids.
- They cause mad cow disease or **bovine spongiform encephalopathy (BSE)** in cows (bovine). They cause scrapie in sheep and goats which is a similar neurological degenerative disease.
- They cause **Creutzfeldt-Jacob disease** in humans which is also a neurological degenerative disease.
- All these diseases belong to a rare group of diseases called **transmissible spongiform encephalopathy (TSEs)** as they can be transmitted among animals of the same species as well as other animals in different species and to humans.
- Some theories hypothesize that infection is due to the presence of two types of prion protein the normal PrP<sup>c</sup> and the abnormal PrP<sup>Sc</sup> which has a defective shape.
- The normal prion protein is present in normal brain cells while the abnormal one is present in the infected cells and is believed to be the causative agent of the disease.
- With PrP<sup>c</sup> (abnormal shape) proteins cannot organize well in the cell membrane and the cell eventually dies.
- The defective protein binds to normal ones causing them to change their shape and become defective and so on that is how the disease spreads without the need of DNA or any genetic materials.
- Infection occurs after eating products contaminated with the defective protein PrP<sup>Sc</sup> as it can cross the blood brain barrier and reaches the brain where it can remain dormant for up to 10 years. Once active, the disease runs its course in less than one year.
- It is still not clear how the abnormal protein (PrP<sup>Sc</sup>) causes the clinical symptoms of the disease or the deadly pathogenesis that result.
<table>
<thead>
<tr>
<th>Microorganisms</th>
<th>Classification</th>
<th>Distinguishing character</th>
</tr>
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<tbody>
<tr>
<td>Bacteria</td>
<td>Prokaryotic</td>
<td>Extremely abundant, microscopic. Many play positive role in nature, some cause diseases. Special types such as rickettsiae and chlamydiae multiply only in host cells, mycoplasma do not have a cell wall and cyanobacteria can carry out photosynthesis</td>
</tr>
<tr>
<td>Fungi</td>
<td>Eukaryotic</td>
<td>Unicellular (yeast) or multicellular (molds) which are filamentous. Unique cell wall (Chitin), not photosynthetic</td>
</tr>
<tr>
<td>Protozoa</td>
<td>Eukaryotic</td>
<td>Animal-like, classified by type of motion, no cell wall not photosynthetic</td>
</tr>
<tr>
<td>Unicellular Algae</td>
<td>Eukaryotic</td>
<td>Plant-like, photosynthetic, usually marine forms include diatoms and dinoflagellates</td>
</tr>
<tr>
<td>Viruses</td>
<td>Acellular</td>
<td>Ultramicroscopic, non-cellular inert particles formed of DNA or RNA, enclosed in protein capsule, cannot replicate except in living cells.</td>
</tr>
</tbody>
</table>
II. Identification of Microorganisms

A. Size, shape and arrangement of bacterial cells

Most bacteria range from 0.2-2 µm in diameter and from 2-8 µm in length.

**Bacteria can have three basic shapes:**

- Bacillus (pl., bacilli): rod shaped.
- Coccus (pl., cocci): spherical.
- Spirals.

**Rod shaped bacteria (Bacilli)**

- Bacilli have a cylindrical shape.
- The cylindrical cell may be as long as 20 µm or as short as 0.5 µm.
- Some bacilli are slender such as those of *Salmonella typhi* that cause typhoid fever, others such as those of *Bacillus anthracis* (which causes anthrax) are rectangular with square ends and others as those of *Corynebacterium diphtheriae* (which causes diphtheria) are club shaped.
- Most rods are singly arranged, but sometimes the bacilli form long chains called streptobacilli as (*strepto*=chain).

**Spherical shaped bacteria (cocci)**

- Spherical bacteria tend to be small usually 0.5 to 1 µm in diameter.
- They are usually rounded but sometimes they may be oval, elongated or indented on one side.
- Many bacterial species that are cocci stay together after cellular division resulting in a cellular arrangement characteristic of the organism.
- The cocci that remain in pairs after division are called diplococci examples are *Nisseria gonorrhea* (the causative agent of gonorrhea) and *N. meningitis* (the causative organism of meningitis).
- Cocci that remain in chains are called streptococci as *Streptococcus pyogenes*, which causes throat infections, and *S. lactis*, which is harmless and is used in manufacture of yogurt.
- When four cocci form a square, the arrangement is known as tetrad.
- A cube like packet of eight cocci is known as “Sarcina” as *Micrococcus luteus*, a common inhabitant of the skin.
- Other cocci may divide irregularly and forma a cluster of grape-like cluster of cells known as “Staphylococcus”. Example is *Staphylococcus aureus* the causative bacterium for certain type of food poisoning and skin infections.
**Spirals and other shapes**

- The third most common shape is the spiral.
- The spiral can be of three different shapes (vibrios, spirilla, and spirochetes).
- Curved rods that resemble commas are known as **vibrios**. An example is *Vibrio cholerae*, the causative agent of cholera.
- Spiral bacteria with a helical shape, a thick rigid cell wall and flagella that assist in movement are known as **spirilla** (sing., spirillum).
- Spiral bacteria with thin flexible cell wall and no real flagella are known as **spirochetes**. Movement of spirochetes occurs by contraction of an axial filament that runs through the length of the cell. An example is the bacterium *Treponema pallidum* the causative agent of syphilis.

**Other shapes**

In addition to the usual bacilli, cocci and spiral shaped bacteria, some types of bacteria have branching filaments such as (*Nocardia*), others may have square, star, or irregular shapes.

![Different shapes of bacteria](image-url)
B. Bacteria form colonies on solid culture media

Bacterial cells divide very rapidly (E.coli divides every 20 minutes). A single cell can produce millions of cells if the conditions are favorable. This collection of identical cells arising from the division of one single cell is called a clone. If these cells are grown on a solid medium (nutrient agar plates), the cells grow close to each other and the large number of cells produced becomes visible in the form of a colony.

Bacterial colonies have distinct shapes, sizes and morphological characters that help in the identification of bacteria.