VIRUSES

I. GENERAL CHARACTERISTICS OF VIRUSES

I. What are Viruses?

1.

without a host cell. The textbook defines them as obligate intracellular parasites, for the same reason.

I. Components of Viruses.

1. **Peter Medawar**, a British immunologist who shared the 1960 Nobel Prize, described

components of every virus. One is a **nucleic acid** genome, either DNA or RNA (why did

2. The other component is the protein coat, called a **capsid**. Capsids are made of repeating proteins monomers, called **capsomeres**. The specific shape, number, and conformation of the capsomeres is specific to each virus.
3. A virus that contains only those two components is referred to as a **naked virus**. Some viruses contain a third component, an outer plasma membrane **envelope**. These are referred to as **enveloped viruses**. The plasma membrane was obtained from the host cell as the virus left. This membrane allows the virus to travel within the host body, disguised

spikes, allowing it target its intended victim (fortunately, these proteins allow our immune cells to

4. Viruses are considerably smaller than prokaryotic cells (make sense if they need to get inside of bacteria). This has modified our food screening and medical screening technologies, in order to ensure health and safety.
5. A **bacteriophage** is a virus that infects bacterial cells. The capsid has extensions that allow it to attach to the surface and inject its nucleic acid core into the bacterial cell.
6. The **host range** of a virus refers to the spectrum of hosts that a virus can infect. Some viruses are fairly general in being able to infect several species. Some are specific to just one species. An **emergent virus** has mutated in some way to now be able to infect a new

existed for decades or centuries (residing in non-human hosts), but have now crossed over into being able to infect human tissues. These are extra dangerous because our body has never seen them before and have that much harder of a time to combat them.

7. **Viral specificity**

specific form of host range). For example, the polio virus only attacks motor neurons in the human, ignoring almost all other tissues. The leprosy virus attacks the sensory neurons, leaving the motor neurons alone.

ب. CLASSIFICATION OF VIRUSES

I. Criteria.
1. Viruses were first classified according to the types of cells that they infected: bacterial, animal, or plant. Animal viruses were further classified according to the tissues that they infected; dermotropic, neurotropic, viscerotropic, or pneumotropic.
2. In 1966, the **International Committee on Taxonomy of Viruses** (ICTV) established a universal taxonomic scheme for categorizing viruses. They use the **nucleic acid** composition as a major tool in classification. From there, **capsid structure** and **host specificity** play a part in their classification.
3. **Tables 10.1** and **10.2** demonstrate the classification of different RNA and DNA viruses.

you to be aware of the different ways that viruses are categorized).

I. RNA Viruses.
1. Most viruses that use RNA as their nucleic acid are **single-stranded** (*ssRNA*), but there are a few that are **double-stranded** (*dsRNA*).
2. Because most eukaryotic cells do not have the enzymes to copy viral RNA strands, the RNA virus must either carry the enzymes or have the genes for those enzymes as part of their genome.
3. Many ssRNA viruses contain **positive (+) sense RNA**, meaning that during an infection

ssRNA viruses contain **negative (-) sense RNA**, meaning that their RNA must first be transcribed in the host cell to make a complementary mRNA, which can then be translated into viral proteins.
4. The **different families** of RNA viruses are distinguished from one another by their *nucleic acid content*, their *capsid shape*, and the presence or absence of an *envelope*.
5. The textbook lists several families of RNA viruses, with important characteristics and representative examples. The group that we will focus our attention is the family ***Retroviridae***, the retroviruses.
6. **Retroviruses** are enveloped viruses that contain **positive (+) sense RNA**, as well as the enzyme, **reverse transcriptase**. This enzyme will create a DNA copy of the viral RNA.

viral particles. *Human T-cell Leukemia Virus* (HTLV), which causes cancers, and *Human Immunodefiency Virus* (HIV), which causes AIDS, are members of this family.

I. DNA Viruses.
1. There is only one family of ssDNA viruses. The rest contain dsDNA. These are categorized according to their nucleic acid organization (linear or circular), capsid shape, and presence or absence of an envelope.
2. The textbook lists several groups of DNA viruses. The two groups that we will focus on are families, ***Adenoviridae*** and ***Herpesviridae***.
3. The **adenoviruses** are naked viruses with linear dsDNA. These tend to be fairly **resistant** to temperature and pH changes and cause a number of human respiratory and

dermatological diseases. The diseases tend to usually **acute**: sudden onset and short duration.

4. The **herpesviruses** are enveloped viruses with linear dsDNA. The viral dsDNA can exist as a **provirus**, demonstrating the ability of latency. This means that they can remain in host cells for long periods without expressing. Usually targeting neurons, they will become active during times of physical or emotional stress, entering a lytic cycle and spread to other cells. Table 10.3 lists a variety of herpesviruses; as you can see, there is a wide variety of diseases included within this group. Notice how many of the herpesviruses hide in the neurons of host cells; this is because neurons are the longest-living cells in the human body and the hardiest (if yo
long-lived host).

ت. VIRAL REPLICATION

I. General Characteristics of Replication.

In general, viruses go through the following five steps in their **replication cycles** to produce more virus particles:

1. **Adsorption**, the attachment of viruses to host cells.
2. **Penetration**, the entry of the virus or viral genome into host cells.
3. **Synthesis**, the formation of new nucleic acid molecules, capsid proteins, and other viral components within host cells (usually using host cell machinery).
4. **Maturation**, the assembly of new viral particles from these components.
5. **Release**, the departure of new virus particles from host cells. Release generally, but not always, kills (*lyses*) the host cells.

I. Replication of Bacteriophages.

1. **Bacteriophages** are viruses that infect bacterial cells. Whereas bacteriophages do not normally present a hazard directly to us (being eukaryotic critters), they have been useful in studying bacteria and possibly in developing treatments against certain diseases.
2. The phages have b
that the even-numbered phages are similar in structure and function, so you will

differences between T-even and T-odd phages.
3. I want you to be able to explain the replication cycle of bacteriophages. Specifically, be able to explain the purpose of the enzyme lysozyme.
4. In order to study viral replication, we need to be able to study bacterial cells that have been infected. If phages are released onto a lawn of bacteria, they will infect certain cells and cause them to change their appearance during lysis. This will result in **plaques** (see figure 10.9), which can allow us to estimate a count of viral particles in a solution as well as take samples of infected bacteria.
5. **Virulent phages** enter the *lytic cycle*, replicating and killing their host cells. **Temperate phages** may enter a dormant period of *lysogeny* for a time. If the viral genome enters the bacterial chromosome, it is referred to as a **prophage**. At some point, the viral genome will become active, a process referred to as **induction**, and enter the lytic cycle.

I. Replication of Animal Viruses.

1. I want you to focus on how the **enveloped dsDNA animal viruses** replicate (i.e. adenovirus and herpesvirus) and ignore the RNA animal viruses.
2. The **envelope** of the virus will fuse with the plasma membrane, drawing the entire virus into the host cell in a process similar to inward exocytosis. The major difference with phages is that the protein capsid comes into the cell, too. **Uncoating** is the process of the capsid dissembling, which releases the nucleic acid core into the host cell cytoplasm.
3. Synthesis and maturation are fairly similar to previous discussions. **Release** is different in that, as the virus particles leave the cell, they take a part of the plasma membrane as their envelope. Quite often, this does not kill the host cell. This actually works in the benefit of the virus, in that the host cell can continue to **shed** new viral particles over a longer period of time.

ث. CULTURING OF ANIMAL VIRUSES

I. Development of Culturing Methods.

1. Initially, it was very difficult to study animal viruses because animals are such complex organisms. There are so many effects going on in a healthy organism, much less one infected with a virus (and forget about it if the organism is also infected with something else, like a bacteria, at the same time). For this reason, virology took a long to develop.
2. **Two discoveries** greatly improved animal virus research. First, the discovery and use of **antibiotics** allowed us to control bacterial contamination of cultures of egg cells (a favorite medium for studying viral infection). Second, biologists found that **proteolytic enzymes**, particularly **trypsin**, can free animal cells from the surrounding tissues without injuring the freed cells. This allowed them to isolate certain cells and grow them separately.
3. A **monolayer** is a single layer of such cells grown in isolation (removing numerous variables during research). **Subculturing** is the process by which cells from an existing cultured are transferred to new containers with fresh nutrient media. A large number of separate subcultures can be made from a single tissue sample, thereby assuring a reasonably homogeneous set of cultures with which to study viral effects.
4. **Tissue culture** is the term used for this type of procedure, but *cell culture* would be more accurate. This technique has allowed us to isolate and characterize over 400 viruses in past fifty years.

I. Types of Cell Cultures.

1. Three basic types of cell cultures are widely used in clinical and research virology. These techniques have largely replaced animal studies in virology, but animal and embryonated eggs are still occasionally used to culture large quantities of certain viruses for study or the development of vaccines.
2. **Primary cell cultures** come directly from an animal and are not subcultured. Since normal cells will only divide so many times before expiring, the younger the culture, the better. This technique has the *advantage* of most closely simulating a viral infection in the animal, it has the *disadvantage* of usually being a mix of cell types and therefore fairly complex to study.
3. **Cell strains** are results of subculturing from a primary culture. The cells in a batch are all genetically alike, which makes analysis much easier. Another *benefit* is that these strains

are usually free of other viral contaminants which may show up occasionally in primary cell cultures. The *disadvantage* is that these divide only so many times (live only so long).

4. A **continuous cell line** is similar to a cell strain, except that these cells are derived from a cell type that has changed in such a way that it is immortal; it will divide forever. Most of these cell lines are derived from cancerous cells, such as the **HeLa cell line**. The *advantage* is that these cell lines can be used indefinitely. The *disadvantage* is that we

changes in viral infections of the organism versus infection of these cells.

5. The **cytopathic effect** (CPE) is a characteristic change in cells infected by viruses and dying. Different viruses can cause different CPEs, which allows virologists to use these histologic characters in their diagnosis of patients.

ج. VIRUSES AND TERATOGENESIS

I. Teratogenesis.

1. **Teratogenesis** is the induction of defects during embryonic development. A **teratogen** is an agent that causes such congenital defects. Several drugs, such as thalidomide, have been proven to be teratogens.
2. The earlier that a fetus is exposed to a teratogen, the more extensive the damage. If exposure occurs later in development, less damage usually occurs, because tissues have differentiated enough that each tissue reacts differently to the teratogen.

I. Viral Teratogenesis.

1. A number of viruses have been shown to be able to infect developing fetuses and cause teratogenic effects. The three most common teratogenic viruses are *cytomegalovirus* (CMV), *herpes simplex virus* (HSV) types 1 and 2, and *rubella*.
2. The **TORCH series** of blood tests are used to identify teratogenic diseases in pregnant women and newborn infants. These tests detect antibodies made against ***T***oxoplasma (a protozoan), ***o***ther disease-causing viruses (including the hepatitis B virus and the varicella, or chickenpox, virus), ***r***ubella virus, ***C***MV, and ***H***SV.

ج. VIRUS-LIKE AGENTS

I. Viroids.

1. A **viroid** is a **naked infectious RNA molecule**. This enters the host cell and causes the host cell to create copies of the RNA, allowing it to release and infect other cells.
2. Translation into proteins does not occur; just the replication of the RNA.
3. Whereas most viroid infections do not kill the host cell, they normally cause effect (usually, an impairment of growth).
4. There are a number of **plant-infecting viroids** that have been classified, there have not been any animal-infecting viroids classified yet.

I. Prions.

1. **Prions** are **infectious proteins**. In 1982, *Stanley Prusiner* proposed how such a particle could replicate and infect.
2. Most likely, prions are normal proteins that become folded incorrectly, possibly as a result of a mutation. The harmless, normal proteins cause other copies of the normal s now having several improper proteins clogging the cell (usually neurons). Eventually, this results in cell death (which, since targeting neurons, usually results in organism death).
3. The first example of a prion disease characterized was **Creutzfeldt-Jakob disease** (CJD), which results in mental retardation, loss of motor function, and eventually death.
4. **Scrapie** in sheep and **bovine spongiform encephalopathy** (BSE or **mad cow disease**) in cattle are two other examples.
5. Being tiny proteins, these are very difficult to screen. Because of the concern of infected meat reaching other herds, all of the cattle in Great Britain have been quarantined for life. This has drastically devastated the beef industry in that nation.

خ. VIRUSES AND CANCER

I. Cancer.
   1. A **cancer** is an uncontrolled, invasive growth of abnormal cells (cancer cells divide repeatedly). A **tumor** is a localized accumulation of such cells. A **benign tumor** will grow only so far and will not invade or impair neighboring tissues. A **malignant tumor** will invade and interfere with surrounding tissues. Malignant tumors and their cells can **metastasize**, or spread, to other tissues in the body.
   2. Most cancers are caused by genetic mutation or cellular damage from environmental factors (chemicals or radiation). However, some viruses have been shown to induce cancer.

I. Viruses.
   1. **F. Peyton Rous** was the first to show that a cancer could be caused by a virus. Since then, a number of DNA viruses have been shown to induce tumors in their host (approximately 15% of all cancers are believed to have a viral element).
   2. Certain viruses contain a segment of DNA called an **oncogene**. This gene contains the information for synthesizing viral particles. However, if the viral genome enters the host chromosome, a process called **neoplastic transformation**, the gene will induce the host cell to repeatedly divide (become cancerous).
   3. Some eukaryotic cells contain genes called **proto-oncogenes**. Generally, these genes are either inactive or perform some normal function. However, under the control of a viral gene (inserted into the host genome), these proto-oncogenes will induce repeated cell division (cancer).
   4. There are six viruses that are associated with human cancers (possibly more, but these have been found and characterized). *Epstein-Barr virus* (EBV) causes tumors in the jaw structures. *Human papillomavirus* (HPV) may cause benign warts or carcinoma of the uterine cervix. The *hepatitis B virus* (HBV) can lead to liver cancer.