OVERVIEW

Rationale: This lesson introduces viruses by demonstrating how important differences between the relative sizes of bacteria and viruses contribute to their modes of action. The lesson then extends the previous focus on bacterial structures by showing how viral structures also play important roles in infectivity and disease. However, because students are less likely to have basic familiarity with viruses, the lesson is organized as a lecture, rather than as an interactive activity.

Do Now: Students are not likely to be familiar with the units that measure microbe sizes, but they are important because the identification of an infectious agent partly depends on its size, as we will see later. Therefore you will use analogies to illustrate the sizes difference between bacteria and to familiarize students with the units of measurement used to measure microorganisms.

Lecture and Virus Structure Worksheet: Students are encouraged to extrapolate from their knowledge of bacterial structures to hypothesize how viral structures function. Video clips are used to provide real-time illustrations. Investigating the relationship between viral structure and function provides students with the tools with which to hypothesize how viral structures function in disease.

Wrap Up: Recap the important structures to ensure that all students understand all the structures.

Homework: Through the Venn diagram worksheet, students will consolidate their understanding of how bacterial and viral structures contribute to disease by compiling a “compare and contrast” worksheet.

The Lesson Plan

What is an infectious agent?
II. What viruses do to make us sick.

1. Do Now (5 min):
Discuss analogies for bacterial vs. viral size, being critical of students’ accuracy.

2. Lecture and Worksheet (35 min):
In the lecture (20 minutes), explain that viruses, like bacterial infections, use specific structures to help them infect their host cells. The virus structure worksheet (15 minutes) then allows the students to consolidate the information you have given them in the lecture.

3. Wrap Up (5 min):
Reinforce the importance of knowing how viral structures contribute to function and recap the functions of the structures critical to disease.

4. Homework:
Complete the Venn diagram worksheet and use it to study for the quiz on day 6. Also complete the virus structure worksheet if it is not finished during class time.
Lesson 1.4

1. **DO NOW**

Important points:

Before beginning the discussion/activity ask the students whether they understand the difference between a eukaryote and a prokaryote (as discussed in the background).

- Let the students know that you will be using the word prokaryote and bacteria interchangeably from now on.

   

- Roughly, a bacteria is a thousand times smaller than a red blood cell, and a virus is a thousand times smaller than a bacteria. Hence a virus is a million times smaller than a red blood cell.

The link on the slide allows you to zoom in on cells and viruses. You must be connected to the internet to use the link.

2. **Lecture**

Slide One: The size of microbes

Important points:

The goal here is to familiarize students with the actual units of measurement of bacteria and viruses, since they are unlikely to have encountered such small sizes before.

- Emphasize the importance of the micron as the central unit in these measurements and make sure that students can convert readily between microns and millimeters and between microns and nanometers.

- Most bacteria are of the order of 1 micron in diameter. This means that you would need 10,000,000 bacteria in each ml of water to turn it cloudy. What are the implications of this? - that water might be contaminated with pathogenic bacteria and still appear clear. Explain how this hampered efforts to understand the role of contaminated drinking water in the spread of cholera.

- Viruses are the smallest microbes. They can vary in volume by several hundred fold. Only the largest ones such as smallpox virus are visible with the light microscope, and then only barely. These largest viruses fall within the lower size range of prokaryotes.
Lecture

Ask the students whether they can think of an analogy linking the size of a bacteria and virus with a red blood cell.

- A legitimate analogy would be that if a virus was the size of your nose, then a red blood cell would be the size of the Empire State Building.
- In this analogy one of your fingers would span the entire continental United States, and an average person would be size of six or seven planet Earths.

Slide Two: The structure of viruses

The rest of this lesson focuses on viral structures.

The structure of viruses from the inside out

- The genome – where the genes are located.
- The capsid – a protein coat that covers the genome.
- The envelope – a protein coat that covers the capsid.

Important points:

- The functions of the structures should be discussed in the context of viral attachment, entry, and exit.
- Replication and host damage will be the focus of Unit 4.4.

Slide Three: The structure of viruses, cont.

To simplify the discussion of viral structure, it has been broken into three main parts:

1. Viral genome
2. Protein coat (capsid)
3. The envelope

Important Points

- It is important to emphasize that all viruses have a genome and a capsid, however only some have an envelope.
- Those with an envelope are called enveloped viruses while those without an envelope are called naked viruses. The figure can be used to explain these points.
Lecture

Slide Four: The genome

The Genome
- Is inside the capsid.
- Can be DNA or RNA.
- Codes for viral proteins.

Important points:
- Viral genomes code for viral proteins. They are much smaller than either bacterial or eukaryotic genomes because the virus uses many of the host cell proteins to replicate. Viral proteins have unique structures that the immune system can recognize as foreign.
- Viral genomes can be either DNA or RNA.

Review with the students the central dogma of gene transcription.
Be prepared to spend considerable time on mastering this material.
- DNA replicates in the nucleus when the cell is dividing.
- DNA makes RNA in the nucleus.
- RNA makes protein in the cytoplasm.

Make sure these questions are answered:

Where will a virus whose genome is made of DNA have to go to replicate the DNA?
- To the nucleus.

Will it be able to use host machinery to replicate in the nucleus?
- Yes, because the host replicates DNA in the nucleus.

Then where will the DNA go to make protein?
- Into the cytoplasm.

Will it be able to use host machinery to make protein in the cytoplasm?
- Yes, because the host makes protein in the cytoplasm.

If the genome of a virus is made of RNA, where will that virus replicate its RNA?
- Not in the cytoplasm, because RNA isn’t made from RNA in cells, it is made from DNA.

So what will the virus have to do?
- It will have to make DNA from its RNA first.

Will it be able to use host machinery (proteins)?
- No, because host cells don’t make DNA from RNA, it will have to bring its own machinery with it.
Lecture

Once it has made the DNA and replicated it, what will it do?
- It will make RNA from the DNA to replicate its genome.

What else will it do?
- It will make protein from the RNA for its capsid and envelope.

It is important to review this process here so the students have a clear idea of how viruses function.

Slide Five: The capsid

Important Points:
- Both enveloped and naked viruses have capsids that encapsulate the genome of the virus.
  - The capsid is composed of virally encoded proteins, it does not contain lipids.
  - The capsid carries some viral proteins, which are not found in the host and are required for viral replication.

Ask the students whether they can think of one of the proteins that the capsid may contain if the virus is an RNA virus.
- It would contain the enzyme that makes the viral RNA into DNA inside the host cell nucleus.

Slide Six: The envelope

Important Points:
- Enveloped viruses have an envelope while naked viruses do not.
- The envelope is made of viral proteins plus host cell membrane. This means that enveloped viruses have membranes that resemble the host cell.
Ask the students:

Do you think the presence of an envelope affects how well the immune system will recognize the virus?

- Yes, the presence of the host cell membrane camouflages the enveloped virus from the immune system. In contrast, naked viruses lack this camouflage.

Slide Seven: Virus life cycle

The next few slides show how the genome, capsid and envelope of the virus are used in the viral life cycle.

For this introductory part of the curriculum the viral life cycle has been simplified to focus on attachment, entry, and exit. This will leave viral replication for Unit 4.4.

A major focus of this lesson is the notion that, like bacterial structures, each viral structure performs its own unique, and key, function.

Slide Eight: Attachment

Important Points:

- Both naked and enveloped viruses need to attach to their host cells before they can enter the cell.
- To do this they have receptors on their surface that act like ‘keys’ to interact with receptors on the host cell surface that act like ‘locks’.

Example: The slide shows HIV. HIV’s ‘key’ is the receptor protein gp120. Gp120 interacts with a ‘lock’ on the host cell surface called CD4. Cells of the immune system like T cells and macrophages have the CD4 ‘lock’. So, HIV can only infect cells with this kind of lock.
Other viruses have different keys that bind to different locks.

Example: For example, H1N1 uses a receptor key called hemagglutinin (the H in H1N1). H1 binds to sialic acid sugars on epithelial cells in the respiratory tract. Different variants of H1N1 have different ‘H’ keys that attach to different kinds of sialic acid sugars. The different sialic acid sugars are on different cells in the respiratory tract. This enables different variants of H1N1 to infect different sites in the respiratory tract. For example the H1N1 that caused the Spanish flu of 1918 was able to infect the epithelial cells in the lower lungs, which is believed to be one of the reasons that this strain of flu was so deadly. That is why people were nervous about the 2009 H1N1. If it had been able to infect the lower lung too, it would have been much more deadly. However, it infected only the upper respiratory tract.

Slide Nine: How naked viruses enter host cells

Important Points:

- Some naked viruses release enzymes that punch holes in the host cell membrane.
  - The virus then injects its genome and other viral proteins into the host cell cytoplasm.
  - The genome will then enter the host cell nucleus and use its machinery to replicate.
- Some naked viruses are endocytosed by the host cell.
  - Endocytosis is a normal cellular process by which small particles are engulfed by host cell membrane and internalized. It differs from phagocytosis, which is used to internalize large particles like bacteria.
  - After being endocytosed the virus needs to punch its way out of the endosome so that it gets into the cytoplasm, using enzymes as described above. Then it too can enter the nucleus.

It is important that the students understand the difference between being in the cytoplasm and being inside the cell in the endosome.
2. Lecture

Slide Ten: How enveloped viruses enter host cells

**Important Points:**

- Because some of the viral envelope is composed of host cell membranes, some viruses can fuse their envelope with the host cell membrane.
  - This happens because both viral envelope and host cell membrane are mostly lipid. Think of it like two oil droplets in water fusing together.
  - The virus can then spill its capsid and genome into the cytoplasm.
- Other enveloped viruses are endocytosed by the host cell.
  - After being endocytosed the enveloped virus needs to get its genome into the cytoplasm like the naked virus did. It will fuse with the endosome, since the endosome is composed of lipid membrane too.
  - Once it is in the cytoplasm, it too can enter the nucleus.

Slide Eleven: How naked viruses exit host cells

**Important Points:**

- Naked viruses replicate and make new virus particles in the host cell cytoplasm.
- The cytoplasm fills with virus until it can't sustain it any more. Then the membrane bursts and the virus particles are released.
- This process is called **cell lysis**.

**Ask the students what will happen to the cell after it has lysed.**

- The cell will die. Infection with a naked virus always causes **cell death**.
- The cell debris will attract an **immune response**.
Lecture

Slide Twelve: How enveloped viruses exit host cells

**Important Points:**

- Enveloped viruses leave the cell in five distinct stages.
  1. Envelope proteins collect in areas of the host cell membrane.
  2. The capsid proteins are made in the cytoplasm and gather up the genome within them.
  3. They travel to the membrane where they attach to the inside of membrane in the region, where the envelope proteins have accumulated.
  4. The capsid buds off of the host cell gathering the envelope proteins with it as it goes.
  5. The envelope protein seals up to form a new virus particle.

- Whether or not the process of budding off causes the host cell to die depends on how fast the virus is replicating. If it is replicating slowly it may not cause cell death.

Slide Thirteen: Video and worksheet

**Important Points:**

- The goal of this activity is to reinforce for the students that a virus must infect a host cell in order to replicate and survive.
- This is in contrast with bacteria, that are usually free living – bacteria that infect host cells, such as Chlamydia, do so because the cells provide key nutrients, not because they need their replication machinery.

**Have the students watch this short and highly engaging video (about 4 minutes) on how the flu infects cells of the respiratory tract.**

The NPR video (5 min) can be found at the links below:

**Have the students complete the worksheet in small groups.**

This can be found in the materials folder for this lesson. It may be completed as homework if time is limited.
4. Wrap Up

Important points:

Ask the students:

What problem would an enveloped virus encounter as it buds out of the host cell? How could it solve that problem?

- Stimulate student discussion in the context of receptor keys specifically designed to bind to a lock on the host cell that it is trying to leave from.

How does the virus manage to leave? Why doesn’t it keep re-infecting the same cell?

- The goal is for students to realize that the same ‘lock and key’ receptors that allowed the virus to get into the cell in the first place could prevent the budding virus from leaving the cell.
- You want students to suggest that the budding virus might have to inactivate the host cell receptor before it can leave.
  - This point is explained in the next slide.

Important points:

In the case of Influenza virus like H1N1, one of the surface proteins is an enzyme neuraminidase (the N in H1N1). The enzyme can chew up sialic acid sugars on the host cell membrane that act as ‘locks’. This prevents the receptor ‘lock’ interacting with the hemaglutinin ‘key’ on the virus envelope. This means that the new viruses don’t re-infect the same cell. This is important because infecting a cell weakens it if it does not kill it. So a second round of infection would not be as effective in producing new virus as infecting new host cells.

Walk the students through the diagram, then ask them:

Why does influenza go to the trouble of having neuraminidase?

- To enter cells influenza must bind to a host receptor. The same entry receptors may then prevent budding off, so one way to solve this problem is for the virus to express a factor that cleaves the receptor. In influenza this factor is neuraminidase.
What do you think would happen if the virus lost the neuraminidase?

- If it weren’t able to inactivate the host cell receptor the virus would be unable to detach and look for other hosts to infect.
- If the virus were unable to infect another host and continue replicating, it would eventually die out.

An overall message is the complexity involved in trying to infect a host. At every step along the way the host is trying to prevent infection, while the infectious virus is trying to maximize its chances.

**Homework**

Have the students complete the Venn Diagram worksheet.

- This homework asks students to list the structural elements specific to bacteria and viruses, and those that they share. It also asks the students to indicate which of these elements are important and how each kind of microbe causes disease.
- The homework will provide the students with the opportunity to consolidate their understanding of the key structural and functional differences between microbe bacteria and viruses. These differences are important foundations for future concepts in this module.

Also have the students complete the virus structure worksheet if it is not finished in class.