Unit 2: Where are we heading?

Unit 1: Why should we care about infectious diseases?
Unit 2: What does it mean to have an infectious disease?
Unit 3: When does a microbe become a pathogen?
Unit 4: How do pathogens make us sick?
Unit 5: How do we get better?

In Unit 1, we learned that infectious agents such as bacteria, viruses, and parasites cause infectious diseases. Now, we are going to focus on how we identify infectious diseases. We will see that there is a significant difference between correlation and causation, and that it is sometimes very difficult to establish that a disease is caused by a pathogenic microbe.
LESSON 2.1 WORKBOOK

Infectious Disease Detectives — Typhoid Mary

Infectious diseases, and the pathogens causing them, have been with us for thousands of years. However, our ability to prove a link between a microbe and a disease dates back only to the late 1800s. At the time, this powerful new knowledge was both exciting and confusing for scientists, doctors, public health officials, and the general public. In this lesson we will see what some of the challenges were, and still are, and how they affect people.

How do you know if a disease is infectious?

Infectious diseases can be caused by all types of microbes, including viruses, bacteria, fungi, protozoa, and multicellular parasites. As diverse as these organisms are, it isn't surprising that they have equally diverse ways of infecting us. Some microbes are only infectious through the exchange of blood or other bodily fluids (HIV), while others can be transmitted by skin-to-skin contact (syphilis), and still others can be inhaled from tiny droplets in the air (tuberculosis, flu). This means that the route of “exposure” to a pathogen can differ from one microbe to another. For example, being in close contact with a cholera victim may not actually expose you to the cholera bacteria, whereas swallowing water contaminated by the feces of a cholera victim would. Conversely, being in close contact with a tuberculosis victim could definitely expose you to the tuberculosis bacterium. This certainly complicates things for researchers and doctors, who have to determine who has or has not been exposed, and to what!

As we try to uncover how a disease is transmitted, another complication is that during our daily lives we are exposed to many different microbes. Even the simple act of taking the subway may expose us to microbes...
coughed into the air, and to bacteria rubbed onto handles from poorly washed hands. In addition, our bodies harbor thousands of microbial species, and some of them can cause disease if an opportunity presents itself. **With so many potential exposures and routes of infection, how do we determine which microbe caused an infection?**

This difficulty introduces the concept of correlation versus causation. To illustrate this point, imagine an epidemic that affects all the occupants of a hotel. Let’s say, that all the sick people in the hotel watched the same TV program. Watching the program is correlated with getting the infection. But it does not mean that the TV program caused the infection. Although in this case it is obvious because a TV program could not cause an infectious disease, it might not have been so intuitively obvious if we had used the example of all the occupants eating the same breakfast. We will return to the important concepts of correlation and causation throughout this unit.

**What do we need to do in order to identify a pathogen?**

It may not be easy to find a pathogen or the source of a disease. In fact, identifying the source of an infection is often quite difficult. For example, during the years of the black plague, people knew that where there were cats, there was plague. This correlation was commonly mistaken to mean that the cats were causing the disease, when in fact the cats were hunting the rats that carried the fleas that were the true carriers of the plague bacteria. So, when people removed the cats, they inadvertently made the plague worse not better!

Identifying the source of a pathogen is particularly difficult when we have no way of actually seeing the pathogen. This was an enormous problem and the major reason pathogenic microbes were not identified before the invention of the microscope. Imagine, telling someone from before the age of microscopes that a terrible disease, such as the Black Death, was caused by something odorless, tasteless, and too small to be seen with a naked eye. Would they believe you? In addition, where there is one kind of microbe, there are often tens, hundreds, and even thousands more different types. For example, up to sixty percent of the dry weight of human faeces are bacteria and most of them are of different types. Imagine, trying to identify which type of bacteria is causing a gastrointestinal disease!

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**Workbook**

**Lesson 2.1**

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2. Correlation is ____ while causation is ____.
   a. a connection between two things; a change in one thing results in a change in another
   b. a change in one thing results in a change in another; a connection between two things
   c. the analysis of data; the result of data
   d. none of the above
LESSON READINGS

**Typhoid fever illustrates the difficulties of identifying the source of an infectious disease**

Typhoid fever is a waterborne disease caused by the bacterium *Salmonella Typhi*. Unlike *Vibrio cholerae*, which reproduces in the intestine (remember, the gut is a non-sterile organ, technically ‘outside’), *Salmonella Typhi* enters the inside of the body, and then replicates inside human cells. Annually, about 20 million people are infected with typhoid worldwide, and of those, about one in ten million die. Typhoid mainly targets children and young adults between 5 and 19 years old, and infection occurs by eating food or water that is contaminated with feces from an infected person.

The main symptoms of typhoid include a slowly progressing fever that can reach 40°C (104°F), profuse sweating, gastroenteritis, and green diarrhea with a “pea soup” smell. Less commonly, victims develop a rash of flat, rose-colored spots, and in severe cases, internal bleeding. These symptoms usually last for four weeks and if the patient survives the fever begins to resolve.

While *V. cholerae* can easily be isolated since a drop of the watery diarrhea contains hundreds of the cholera bacteria, isolating *Salmonella Typhi* is much more complicated for a number of reasons. First, unlike cholera, only a very small number of bacteria cause the infection and not many are shed into the feces. The bacteria have the ability to spread from the intestines to internal sterile organs such as blood, liver, spleen, kidneys. In addition, *Salmonella* invades host cells, making it even more difficult to detect. Since the number of bacteria in every organ is low, the bacteria first need to be grown and multiplied in the lab in order to make detection possible. To do this, patient specimens from blood, bone marrow or feces, are placed in special growth medium that the bacteria can feed off of and grow. Alternatively, antibodies (isolated from the patient's blood) against *Salmonella* flagella may be used to identify the bacteria, but this is only an option if the patient has been ill.

3. The following are symptoms of Typhoid EXCEPT
   a. slowly progressing fever that can reach 110 °F
   b. profuse sweating
   c. gastroenteritis
   d. green diarrhea with a “pea soup” smell
   e. rashes

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**DEFINITIONS OF TERMS**

**Gastroenteritis** — inflammation of the stomach and intestines usually caused by numerous viruses and bacteria.

**Cholera** — intestinal infection by the bacterium *Vibrio cholerae* characterized by watery diarrhea.

For a complete list of defined terms, see the **Glossary**.

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**Workbook**

**Lesson 2.1**
DEFINITIONS OF TERMS

Asymptomatic carrier — someone who carries a pathogen and shows no signs of a disease but can spread it to other people who can become sick.

For a complete list of defined terms, see the Glossary.

LESSON READINGS

Typhoid Mary was not sick but people she cooked for got typhoid

An asymptomatic carrier suffers no symptoms from a disease but is capable of infecting others. One of the most famous asymptomatic carriers was Mary Mallon, commonly known as 'Typhoid Mary', a young Irish cook at the turn of the twentieth century who was responsible for infecting at least 51 people with typhoid, three of whom died from the disease. It was difficult to prove that she had infected people with typhoid since she was healthy. In fact, when confronted, she denied that she was infected with typhoid and that she played a role in spreading the disease — and refused to stop working as a cook!

As a consequence, she was forcibly quarantined for decades and even died in quarantine. After her death, an autopsy was performed and Salmonella Typhi bacteria were isolated from her gall bladder.

4. Typhoid Mary was unique because
   a. she showed extreme symptoms of the disease.
   b. though she had the disease, she did not infect anyone.
   c. she had no symptoms of the disease but infected a lot of people.
   d. all of the above

Asymptomatic carrier — someone who carries a pathogen and shows no signs of a disease but can spread it to other people who can become sick.
If you can’t find a microbe, is that proof that a disease is not infectious?

Describe how observation of patterns of infection can provide evidence that a disease is infectious.

If you were Typhoid Mary, explain why you might disagree that you were the cause of spread of the disease.
<table>
<thead>
<tr>
<th>TERM</th>
<th>DEFINITION</th>
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<tr>
<td>Asymptomatic carrier</td>
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<td>When a change in one factor results in a change in another.</td>
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<tr>
<td>Syphilis</td>
<td>A sexually transmitted disease caused by a bacterium, <em>Treponema pallidium</em>.</td>
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<tr>
<td>Tuberculosis (TB)</td>
<td>A disease caused by the bacterium <em>Mycobacterium tuberculosis</em>, that affects mostly the lungs, and can be deadly, if left untreated.</td>
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