BioMath

Pass It On!
Disease Competition

Student Edition

COMAP

DIMACS

Pass It On! Disease Competition

Overview

Members of a **population** display many variations. They may be visible traits or internal differences in genetic make up. These variations may result in either "success" or "failure" of the individuals. The concept of natural selection is developed in that those organisms with more successful traits reproduce at a greater rate than those with less successful traits. Some research uses the concept of infectious disease-causing organisms to model this concept. The ability to increase their rate of transmission from one host to another increases these organisms' chance of being successful in an evolutionary sense; therefore, various methods of transmission are important to discuss. Mathematical analysis of these different methods of transmission provides insight into their possible evolutionary success rates and perhaps even that of the organisms that utilize these methods. This analysis illustrates connections between reproductive success and evolutionary success.

Unit Goals and Objectives

Goal: Explore the connections between the mathematical and biological sciences.
Objectives:
- Experience the excitement of modern biology from both the biological and mathematical point of view.
- Develop a deeper understanding of evolution through the study of probability and disease transmission.

Goal: Understand how mathematical modeling simulates the theoretical behavior of a proposed system.
Objectives:
- Use the proper terminology when describing basic probability.
- Calculate the probability of an event, knowing the number of successful and unsuccessful outcomes.
- Calculate the probability of an event not occurring, given the probability that it will occur.
- Calculate the expected number of successful events, given multiple chances of the event occurring.
- Explain the difference between the calculated expected value and the observed result of a series of random events.

Goal: Explore the concepts and connections of disease competition and evolution.
Objectives:
- Understand that different modes of transmission for diseases exist.
- Relate the reproductive success of disease-causing organisms to evolutionary success.
- Evaluate the success of different evolutionary strategies that a disease may adopt over time.

Lesson 0   Evolution and Infectious Disease Background

Evolution

Members of a population display differences, or **variations**, in traits. Some, like hair color, height, length of fingers, are obvious; others, like blood type, are not. These variations may arise from new combinations of **genes** when organisms reproduce sexually or from mutations. The variation will result in either "success" or "failure" of the individuals. In the evolutionary sense, success means the individual having a certain trait survives and reproduces. Failure means he or she either doesn't survive or doesn't reproduce.

When something in the environment, such as competition or **predation**, results in one variation having greater success than another variation, this is called **selective pressure**. Those with successful traits have more offspring than those with unsuccessful traits. It is expected then that over time a population with a lot of variation will have more and more individuals with successful traits and fewer and fewer individuals with less successful traits. This process is called **adaptation**. What is successful though depends on the environment. If the environment changes, so may the success rate of that trait.

The process of **evolution** can be thought of as when selective pressure acts upon variations producing populations in which most individuals are "well adapted" to their environment. These individuals possess traits that allow them to survive and reproduce under the selective pressures present in their natural environment.

Infectious Diseases

Infectious diseases can be thought of as organisms that cause adverse or unfavorable reactions in their host organisms. The **host** is the organism in which they live, such as an animal or plant. These organisms get into new host organisms by some kind of host-to- host contact. These diseases can be a type of fungus, virus, bacteria, protist, or **macroparasitic** (like insects). When an uninfected individual comes into contact with the infectious agent, the individual is said to be **exposed** to the disease. If, as a result of that exposure, the disease infects a **susceptible** individual (an individual capable of becoming infected with the disease), then we say the disease has been **transmitted**. There are many ways in which a disease can be transmitted from host to host.

- **Droplet**: The host coughs or sneezes on a susceptible individual.
- **Airborne aerosolized**: The host releases infectious **microorganisms** into the air, where they can remain for long periods of time before settling on/in a susceptible individual.
- **Direct physical contact**: The host passes **infection** by touching a susceptible individual; this can include direct sexual contact.
- **Indirect contact**: The host contacts and contaminates an inanimate surface, which is then contacted by a susceptible individual.
- **Fecal-oral**: Food or water sources are contaminated by contact with host feces and are then consumed by a susceptible individual.

- **Vector-borne**: The infection is carried by insects or other animals from a host to a susceptible individual without the insect or other animal itself being made sick; this transmission is usually accomplished via biting/feeding of the vector on the host.
- **Other** (less common) modes of transmission.

This invasion of a new individual – by one of these modes of transmission - resulting in the disease having a new host relies on a susceptible individual being exposed to the disease.

Not only do infectious diseases have different causes and different modes of transmission, they also have different effects in the body of the host. Diseases can cause **symptoms** in the host, and this is called being "**symptomatic**." If the infected host does not show symptoms, it is called "**asymptomatic**." The same disease can cause symptoms in some hosts but still not cause any symptoms in others. Frequently, people studying the disease will measure the rates of symptomatic disease rather than the overall rate of disease occurrence. This is because it is difficult to diagnose diseases that cause no symptoms. The easiest of these effects (and frequently the easiest to measure) is mortality risk — how likely the disease is to kill the host. In some cases treatments, such as taking an antibiotic, can affect mortality risks associated with particular diseases. This unit does not discuss the effects of treatment, but it can be interesting to consider the implications.

Lesson 1   Modeling Disease

Assumptions in Disease Modeling

For the purposes of this unit, we assume that only one disease can infect a host at a time. Another assumption is that during the time frame being considered, neither the host nor the disease populations will evolve. Finally, we also assume that people who have been vaccinated will be completely immune to the disease in question. This ensures that the characteristics of the diseases will be constant over time. These assumptions are not necessarily true, but they assist in simplifying our analysis. It is interesting to think through the implications of relaxing these assumptions to the evolutionary success of the host-disease interactions.

The introduction of this unit raises many questions. One of these questions is, "*What is the best evolutionary strategy for a disease to adopt over time*?" In order to answer this and similar questions, it is important to determine the factors that have an impact on whether or not a disease survives to reproduce. The search for these factors begins by examining some specific diseases.

Questions For Discussion

1. How are transmission and infection related?

2. How are transmission and infection different?

When trying to build a model to explain a phenomenon, it helps to spend time getting familiar with the background. It is not a generally approved method to go out and contract some diseases in order to study what happens next. Examining several representative diseases will help identify the factors that need to be studied more closely.

## *ACTIVITY 1-1* — Some Infectious Diseases
Objective: Learn about three infectious diseases and identify their key factors.
Materials:
         DC-H1: Some Infectious Diseases Activity Worksheet

Case 1: Tuberculosis
Tuberculosis is the common name for *Tubercle Bacillus* (TB). It is a deadly bacterial infectious disease that most often affects the lungs. Over one-third of the world's population has the bacterium in their bodies, but only 10% of untreated infections lead to active disease. Symptoms of TB found in the lungs include prolonged coughing, chest pain, and coughing up blood, and can continue for years or even decades. TB can be accompanied by fever, chill, appetite and weight loss, paleness, and fatigue.
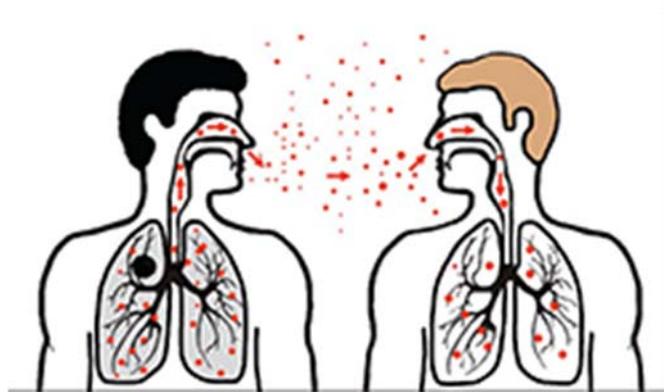
TB is spread by aerosol droplets sent into the air when people with the active disease cough, sneeze, speak, or spit. Transmission can only occur from people with active TB disease, and depends on the amount of bacteria in the droplet, length of time of exposure, ventilation available, and the specific **strain** of TB. It is estimated that approximately 22% of people without **immunity** in close contact with an infected person will catch the disease. Antibiotics can combat the symptoms of the active disease, as well as prevent inactive or latent TB from becoming active.[1][2]

1. What are the symptoms of TB?

2. How do the symptoms of TB help expose other people to the disease?

3. If a medicine that didn't cure the disease but stopped the coughing completely was available, would that prevent any new infections?

4. Since so many people have TB, do you expect it to be highly **contagious**?

Case 2: Measles

Measles is caused by a virus of the genus *Morbillivirus*. Symptoms include a fever (lasting at least three days), coughing, runny nose, sneezing, and red eyes. The fever can reach up to 105°F (40.6º C). Several days after the onset of fever, a rash begins on the head. The rash spreads to most of the body, often causing itching. In extreme cases, the virus can cause fluid buildup in the lungs and swelling of the brain. The virus was identified in 1954, and vaccines protecting against new infection began to be available in 1963. Schools now require that students have the MMR (measles, mumps, and rubella) vaccine before entering.

MEASLES SYMPTOMS TYPICALLY INCLUDE

- High fever (may spike to more than 104° F)
- Cough
- Runny nose
- Red, watery eyes
- Rash breaks out 3-5 days after symptoms begin

http://www.cdc.gov/measles/images/measles-symptoms-include.jpg
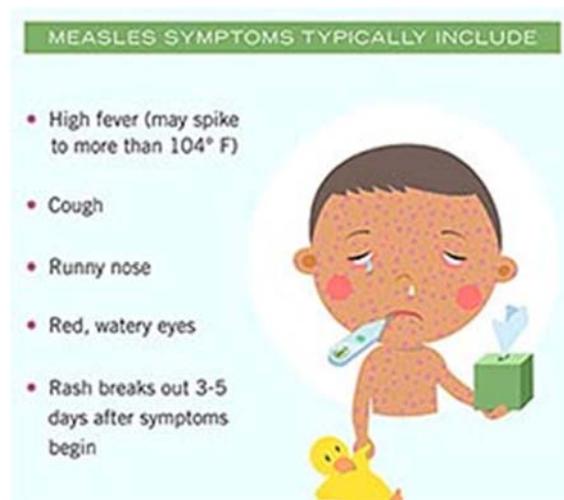
Someone infected with measles can spread the virus by either providing direct contact with the fluids from his or her nose and mouth, or by exhaling viruses in droplets from sneezes, coughs, and breathing. Measles is highly contagious, and it is estimated that 90% of people without immunity who share a house with an infected person will catch it. The **incubation period** (the period between infection and the appearance of signs of a disease) usually lasts from 4–12 days, before symptoms develop. Once symptoms appear, infected people remain contagious until 3–5 days after the characteristic rash appears. It is rare to get the disease a second time.

As recently as 2001, there were approximately 770,000 deaths worldwide from the disease. Despite being "under control" in the United States, it still receives high priority from organizations like the Centers for Disease Control. Since it is so infectious, if an **outbreak** occurred among a highly susceptible population, the resources for taking care of infected people would be quickly overextended. The availability of effective **vaccines** minimizes the impact of an outbreak of the disease.[3][4]

5. What are the symptoms of measles?

6. How do the symptoms of measles help expose other people to the virus?

7. How do the symptoms of measles limit the exposure of other people to the virus?

8. If a medication that eliminated the rash and fever but did not relieve other symptoms or cure the disease was available, would you recommend treating all infected patients with it?

Case 3: Ebola virus

Named after a river in the Democratic Republic of the Congo, where it was first discovered, Ebola is a member of the group of RNA viruses called *Filoviridae*. Scientists believe animals native to the African continent act as natural hosts, and that people are infected when they come in contact with an infected animal. Once in the human population, it is spread by direct contact with the blood or secretions of an infected person. It may also be spread by indirect contact with objects, like needles, that have been contaminated with infected secretions. The transmission rate is approximately 27%.

http://sdc.gov.jm/assets/Ebola-Virus-Graphic.jpg
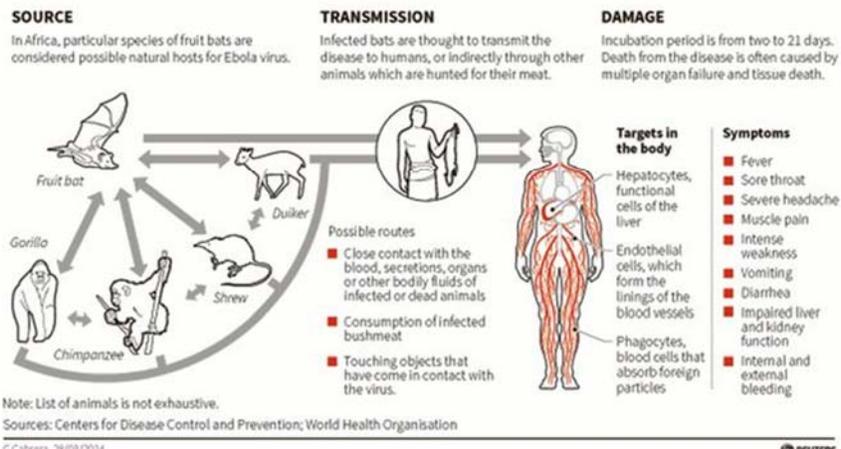
Once infected, the host body develops Ebola hemorrhagic fever (Ebola HF). There is a 2−21-day delay before the first appearance of symptoms but once symptoms appear, it quickly progresses to extreme illness. Symptoms include headache, fever, sore throat, joint and muscle aches, and weakness. These are followed by stomach pain, diarrhea, and vomiting. Red eyes, hiccups, rashes, and internal and external bleeding have been found in some patients. The person is capable of transmitting the disease for approximately 5 days starting shortly before symptoms begin to appear. Estimates from different outbreaks in humans place the **mortality rate** for infection between 50% and 90%. Death occurs, on average, ten days after onset of symptoms.
[5][6]

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9. What are the symptoms of Ebola HF?

10. How do the symptoms of Ebola HF help expose other people to the virus?

11. How do the symptoms of Ebola HF limit the exposure of other people to the virus?

12. If Ebola HF were to become aerosolized, would the outbreaks still be limited to sub-Saharan Africa?

The paragraphs above introduced you to three types of infectious diseases. They may seem very different from each other, but on a very simple level, they are just trying to survive. As someone who is trying to model the behavior of these diseases, you need to identify their key factors and then determine how to relate those factors mathematically.

Practice

1. Identify five possible factors that may have an impact on whether a disease survives or not over a long period of time.

2. The Centers for Disease Control and Prevention (CDC) in their Surveillance Resource Center (http://www.cdc.gov/surveillancepractice/data.html) provide databases of information on a variety of infectious diseases, like the ones presented in Activity 1-1.[7] Choose two diseases from the database and write short descriptions of their biology to include their causes, distribution, symptoms in the host and control methods. Be sure to include how the diseases are transmitted, whether or not the diseases are fatal to the host, and how the diseases' symptoms both help and/or hinder their spread in a population.

Lesson 2   Coughing In Biology class

Exposure

It is flu season again. The Centers for Disease Control have indicated that Influenza A is reported in various regions of the country. Until now, it hasn't been a problem at your school — at least not until one of your classmates attended a family wedding last weekend in another part of the country and was exposed to the flu virus. In spite of his symptoms, his parents made him go to school on Monday because he had missed class the previous Friday. This infected classmate will be referred to as "J. Source." Assume that his first cough in class is the beginning of an outbreak, since one of the ways the flu virus spreads is through coughing, and that this flu is highly contagious.

There are 27 students in the Period 1 Biology class. A seating chart of that class is provided in Table 2.1. All students were present on Monday.

	Row 1	Row 2	Row 3	Row 4	Row 5
Seat 1	empty	No Vacc	Vacc	No Vacc	No Vacc
Seat 2	No Vacc	No Vacc	No Vacc	empty	Vacc
Seat 3	No Vacc	**J. Source**	No Vacc	No Vacc	No Vacc
Seat 4	No Vacc	No Vacc	No Vacc	No Vacc	Vacc
Seat 5	Vacc	No Vacc	No Vacc	No Vacc	No Vacc
Seat 6	No Vacc	empty	Vacc	No Vacc	No Vacc
Seat 7	empty	empty	empty	empty	empty

Table 2.1: Seating Chart for Period 1 Biology

Students who have received the flu vaccination shot are indicated by the "Vacc" designation. Empty desks have been indicated as well. The origin of the disease in the classroom, J. Source, has the desk in Row 2, Seat 3.

Probability Review

In many situations, key features of diseases do not behave in such a way that they always take place. When an event is not certain, modelers try to describe the event in terms of how likely it is to take place. For these situations often use the mathematics of **probability**. The probability represents the chance of something occurring. This means assigning a fractional value between 0 and 1, inclusive, to an event according to this definition:

P(event of interest) = Number of times the event of interest occurred
                                        Total number of events

If an event is certain, the probability of the event is 1. If the event is impossible, the probability of the event is 0. Uncertain events have probabilities between 0 and 1. We will explore what this uncertainty means for the problem of modeling the evolution of infectious diseases.

As a review, to find the probability of a die rolling a 3, count the number of ways it can occur successfully (1) and divide by the total number of possible outcomes (6) for a probability of 1/6. Note that "divide" doesn't mean that the process of division must performed. Simply write the two numbers as a ratio and reduce the new fraction to lowest terms. Alternately, this probability can be expressed as the decimal 0.167 or converted to the percentage 16.7%. All three forms mean the same thing and can be used interchangeably.

This lesson will use the notation P(event) to represent the probability of an event. So in this example, the probability of rolling a 3 on a 6-sided die is represented as: P(3) = 1/6. Whatever combination of words, letters, or numbers that is convenient can be used to represent the event. Using symbols that have meaning is preferable since it makes it easier for others to understand what is represented.

At this point it is important to note that the probability of an event occurring plus the probability of an event not occurring equals 1: P(e) + P(not e) =1. So, the probability of an event will not occur is always 1 minus the probability that the event will occur: P(not e) = 1 - P(e). In the previous example, the chance that a 3 will not be rolled is: P(not 3) = 1 – 1/6 = 5/6. This leads to and so it follows that

Question for Discussion

1. Based on the information provided in Table 2.1, determine the probability for each of the following situations on the Monday that J. Source returns to school. Assume all students are present for class.

      a. P(a randomly chosen desk in the Biology classroom that day contains a student)

      b. P(a randomly chosen student attending class that day has had the flu vaccination and is therefore no longer susceptible)

      c. P(a randomly chosen row of desks contains more than one empty desk that day)

      d. P(a randomly chosen student attending class that day is infected with the influenza virus)

ACTIVITY 2-1 **Catching the Flu**
Objective: Analyze exposure and infection by the various methods of disease transmission.
Materials:
      DC-H2: Catching the Flu Activity Worksheet

Part I
The flu has at least two methods of transmission: droplet or aerosolized particle (which is a droplet small enough to be suspended indefinitely in air). For droplet transmission, the source will be the infected person and only people within a small space around the source are exposed to the disease. With aerosolized transmission, the infected person contaminates all of the air in the classroom.

1. For a simplistic model, assume that the flu is primarily transmitted by aerosolized particles and the classroom is clearly one big air supply. The diagram below highlights the exposure of students in the Biology classroom when transmission is by aerosolized particles. Each student shaded represents a student that was exposed.

	Row 1	Row 2	Row 3	Row 4	Row 5
Seat 1	empty	No Vacc	Vacc	No Vacc	No Vacc
Seat 2	No Vacc	No Vacc	No Vacc	empty	Vacc
Seat 3	No Vacc	**J. Source**	No Vacc	No Vacc	No Vacc
Seat 4	No Vacc	No Vacc	No Vacc	No Vacc	Vacc
Seat 5	Vacc	No Vacc	No Vacc	No Vacc	No Vacc
Seat 6	No Vacc	empty	Vacc	No Vacc	No Vacc
Seat 7	empty	empty	empty	empty	empty

Table 2.2: Exposed Students, Period 1 Biology

   a. Under these conditions, what is the probability that a student from the Period 1 Biology class list, picked at random, was exposed to the flu virus on Monday?

   b. Under these conditions, what is the probability that a student attending Period 1 Biology that day, picked at random, is susceptible to (at risk of becoming infected by) the flu virus?

   c. Under these conditions, what is the probability that a healthy student from the Period 1 Biology class list, picked at random, was exposed to the flu virus on Monday?

   d. Under these conditions, what is the probability that a susceptible student attending Period 1 Biology on Monday has been exposed to the flu virus?

2. For a more realistic model, assume that the flu is spread through droplet transmission.

   a. Assume that the virus can be projected one desk around the source in all directions. This means that the virus could be projected to the students in front and behind the infected student, to the right and left of the infected student, and diagonally to the four students at the corners of the infected student. Identify the seats within the exposure area and determine the probability that a susceptible student attending Period 1 Biology that day was exposed to the flu virus?

   b. Assume that the virus can be projected two desks around the source in all directions. This means that any student accessible by a path of two desks is susceptible. Identify the seats within the exposure area and determine the probability that a susceptible student attending Period 1 Biology that day was exposed to the flu virus?

Part II

On Tuesday, although no one who was present on Monday is absent, two more students are sick. These students are represented by the symbol ☹ in the table below. We assume that the students caught the flu from J. Source as he is the only infected person.

	Row 1	Row 2	Row 3	Row 4	Row 5
Seat 1	empty	No Vacc	Vacc	No Vacc	No Vacc
Seat 2	No Vacc	No Vacc	No Vacc	empty	Vacc
Seat 3	No Vacc	**J. Source**	☹	No Vacc	No Vacc
Seat 4	☹	No Vacc	No Vacc	No Vacc	Vacc
Seat 5	Vacc	No Vacc	No Vacc	No Vacc	No Vacc
Seat 6	No Vacc	empty	Vacc	No Vacc	No Vacc
Seat 7	empty	empty	empty	empty	empty

Table 2.3: Class Attendance for Period 1 Biology on Tuesday

3. What is the probability of a student picked at random, who was in the class healthy on Monday, is sick on Tuesday?

4. For the following, assume the transmission is aerosolized (spread into the air across the classroom).

   a. What percentage of the class present on Monday could not contract the flu from J. Source?

   b. What percentage of the susceptible students in the class on Monday contracted the flu?

   c. Of the students exposed on Monday, what percentage contracted the flu?

5. For the following, assume droplet transmission with a range of one desk.

   a. What percentage of the class present on Monday could not contract the flu from J. Source?

   b. What percentage of the susceptible students in the class on Monday contracted the flu?

   c. Of the students exposed on Monday, what percentage contracted the flu?

6. For the following, assume droplet transmission with a range of two desks.

   a. What percentage of the class present on Monday could not contract the flu from J. Source?

   b. What percentage of the susceptible students in the class on Monday contracted the flu?

   c. Of the students exposed on Monday, what percentage contracted the flu?

Lesson 3   Exposure and Transmission

Some of the probabilities, percentages and values calculated in Lesson 2 have little or nothing to do with the spread of disease. Can you see why? What is the difference between what a probability tells us, what a percentage tells us, and what a value tells us? This lesson looks at mechanisms of exposure and the probability of transmission from that exposure.

Assumptions
For purposes of our study of the first two days, we assume that this Biology class is representative of the entire population under consideration. In other words, 1 of every 27 people initially has the flu and 5 of every 27 have been vaccinated. Additionally, during the course of our initial investigation, we assume these students are only in contact with each other in the arrangement shown in the diagram in Lesson 2. In other words, they never leave this room or their desk position. Although this is an extreme simplification, it illustrates the concepts under study.

Rates of Transmission and Infection

In Monday's Biology class, assuming aerosolized transmission, J. Source infected two of the 21 susceptible students in the class. In simplest terms, the probability of a susceptible student in this Biology class becoming infected is 2/21 or 0.095. This represents the **rate of transmission**. If the rate of transmission is constant for a particular disease, then it is exactly the rate that susceptible individuals will become infected – the **rate of infection**. In this case, this is 0.095, or 9.5%. The rate of infection is used to predict the number of new cases per unit of time.

The **rate of incidence** in a population is the ratio of the number of new infections in a given time period to the number of uninfected at the start of that time period.

ACTIVITY 3-1 Transmitting the Disease
Objective: Investigate various impacts of transmission modes
Materials:
     DC-H3: Transmitting the Disease Activity Worksheet

Part I – Aerosol Transmission
1. Using the first period Biology classroom as our total population and aerosol transmission:
        a. What is the rate of infection of the disease after one day?

        b. Assuming that the Biology classroom represents the total population, what is the rate of incidence of the disease after one day?

2. Imagine now that our Biology students are released from their classroom and J. Source goes to Math class. This Math class is not in itself representative of the world. There are 31 students in Math class; 30 of them healthy and no one is vaccinated. Using information from item 1, and aerosol transmission determine the following:

        a. How many students will be exposed and how many students will be susceptible?

b. Assuming the same infection rate determined from Biology class, how many students do you expect to be infected after one day?

c. What rate of incidence should we apply to second period Math class to predict the number of new cases?

d. Using the rate of incidence, how many students from the Math class would you predict to become infected in one day?

e. Why does using the rate of infection and the rate of incidence result in two different predictions?

Part II - Droplet Transmission With a One-Desk Range

3. Using the first period Biology classroom as our total population and droplet transmission with a one-desk range:
   a. In Monday's Biology class, assuming droplet transmission with a one-desk range, what was the rate of transmission, in both fraction and decimal form?

   b. Assuming that the Biology classroom represents the total population, what is the rate of incidence of the disease with one-desk range droplet transmission?

4. Now again imagine J. Source in Math class. This Math class is not in itself representative of the world. There are 31 students in Math class; 30 of them healthy and no one is vaccinated. J. Source sits in the corner and so only three other students are within a one-desk range. Use droplet transmission with a one-desk range.
   a. In Math class, how many students will be exposed and many students will be susceptible?

   b. Assuming the same infection rate for droplet transmission as found in Biology class, how many students do you expect to be infected in Math class?

   c. What rate of incidence should we apply to second period Math class given droplet transmission to predict the number of new cases?

   d. Using the rate of incidence, how many students from the Math class would you predict to become infected in one day?

   e. Why does using the rate of infection and the rate of incidence result in two different predictions?

Conditional Probability

Let's take a side trip to visit some **conditional probabilities**. A conditional probability is the probability that one event will occur, given that one or more other events have already occurred. It is often denoted P(E/F) meaning the probability that event E occurs given that event F has already occurred.

You want to determine a random individual's risk of infection. There are two necessary conditions to become infected: susceptibility and exposure.

The probabilities involved include:
      1) The probability of being susceptible (uninfected and unvaccinated)
      2) The probability of being exposed
      3) The probability of a susceptible and exposed individual becoming infected

Think of this as computing the probability of each necessary condition happening independently. Two events are **independent** if they do not affect each other. For example, the event of a person being susceptible (i.e. not vaccinated and not infected) is independent of the event of a person being exposed. To compute the probabilities of multiple independent events happening at the same time, multiply their probabilities together. If A and B are independent:
      $P(A \text{ and } B) = P(A) \times P(B)$.

Two events are **dependent** if one depends upon the other. For example, the event of a person becoming infected is dependent upon the event of a person being susceptible and upon the event of a person being exposed. If A and B are dependent:
      $P(A \text{ and } B) = P(A) \times P(B|A)$.

In the Biology class, assuming aerosolized transmission, the probability of a random student becoming infected given being exposed and susceptible is the product of 21/26 (the probability of being susceptible: uninfected and unvaccinated) and 26/26 (the probability of being exposed due to aerosol transmission) and 2/21 (the probability of infection given an individual is susceptible and exposed). This means that the probability of a random student in the class contracting the disease and becoming infected is:

P(susceptible and exposed and infected) =
P(susceptible and exposed) × P(infection|susceptible and exposed) =
P(susceptible) × P(exposed) × P(infection|susceptible and exposed) =

$$\frac{21}{26} \times \frac{26}{26} \times \frac{2}{21} = 0.807 \times 1.0 \times 0.095 = 0.077 = 7.7\%$$

Note that multiplying this answer by the uninfected class population, (26*.077=2.002) predicts that two students will be infected. This matches what occurred in the Biology class on Tuesday.

Does the same thing hold true for Math class?

To compute the risk of infection assuming aerosolized transmission in Math class, use the same method used for Biology class. Assume aerosolized transmission in the Math class, with 31 students, one infected student and no vaccinated students. The average risk of infection for a student is the product of 30/30 (the probability of being susceptible) and 30/30 (the probability of being exposed due to aerosol transmission) and 2/21 (the probability of infection given an individual is susceptible and exposed). This means that the probability of a random student in the class becoming infected is:

$$\frac{30}{30} \times \frac{30}{30} \times \frac{2}{21} = 1.0 \times 1.0 \times 0.095 = 0.095 = 9.5\%$$

Note that multiplying this answer by the uninfected class population ($30 \times 0.095 = 2.85$) predicts that three students will be infected.

Now consider the method of droplet transmission, with a range of one desk in Biology class. To compute the risk of infection assuming a one-desk droplet transmission in Biology class, use the same method of calculating a conditional probability. The average risk of infection for a student is the product of 21/26 (the probability of being susceptible) and 8/21 (the probability of being exposed due to range-one droplet transmission) and 2/8 (the probability of infection given an individual is susceptible and exposed). This means that the probability of a random student in the class becoming infected is:

$$\frac{21}{26} \times \frac{8}{21} \times \frac{2}{8} = 0.808 \times 0.381 \times 0.025 = 0.077 = 7.7\%$$

Note that multiplying this answer by the uninfected class population ($26*.077=2.002$) predicts that two students will be infected. This matches what occurred in the Biology class on Tuesday because this is essentially how we determined the rate of incidence.

To compute the risk of infection assuming a one-desk range droplet transmission in Math class, where there are three students exposed to the disease by J. Source, we can again use the same method of calculating a conditional probability. The average risk of infection for a student is the product of 30/30 (the probability of being susceptible) and 3/30 (the probability of being exposed due to one-desk range droplet transmission) and 2/8 (the probability of infection given a person is susceptible and exposed). This means that the probability of a random student in the class becoming infected is:

$$\frac{30}{30} \times \frac{3}{30} \times \frac{2}{8} = 1.0 \times 0.1 \times 0.25 = 0.025 = 2.5\%$$

Note that multiplying this answer by the uninfected class population ($30*.025=0.75$) predicts that one student in Math class will become infected with a one-desk range droplet transmission.

Lesson 4   Keeping the Disease Alive

In the previous lessons, we've looked at the transmission of disease. If an infected person does not transmit the disease to another, the disease remains only with the initial infected person. This infected person, or host, could either die or recover and, if the host has not infected another person, the disease dies also.

Virulence and Duration

When epidemiologists study a disease, one of the important characteristics of the disease is its **virulence**. Virulence is the relative ability of the infectious organism to cause rapid and severe disease once the individual has been infected. An individual infected with a disease is called the host. For many diseases, once the host dies, the disease can no longer be transmitted. On the other hand, the host can recover and stop transmitting the disease. Either of these outcomes limits the duration of the exposure that the host can cause. For the purpose of this lesson, assume that the host, once infected, is capable of exposing others to the disease until the study of the population is done. This length of time of infectivity is called the **duration**.

Although diseases reproduce inside the host body, if there is no successful transmission of disease to a new host, then that host acts as a dead end for the disease. As soon as the host dies (whether from the disease or not), the disease will die with it. The same will happen if the host recovers without first transmitting the disease to a new host. So, when talking about successful reproduction for an infectious disease, think in terms of successful transmission to new hosts. The ability to transmit infection (in other words, the disease's **reproductive success**) is one of the most important traits being selected for in the evolution of an infectious disease. Naturally, this reproductive success is influenced by a lot of things, including method of exposure, probability of transmission, behavior of the sick host, duration of infection, and the mortality risk to the host as a result of the disease.

What if a disease requires direct contact between infected hosts and susceptible individuals for successful transmission but makes the infected hosts so sick that they can't move around? This will then limit the number of people exposed to those hosts. Imagine if J. Source was so sick he had stayed at home because of his illness rather than coming to school. This will limit the reproductive success of the disease.

If the probability of transmission from exposure is low, the disease will still only have limited spread even if a susceptible population is exposed to the disease. So a disease has to rely on both the frequency of contact between infected and susceptible individuals and the probability of successful transmission resulting from that contact in order to achieve successful reproduction. Having thought through all these considerations regarding infectious diseases in host populations, it is now possible to consider the ways in which particular modes of exposure and rates of transmission affect reproductive success for a disease.

More on Transmission and Infection

Using the aerosolized transmission method, recall from the previous lesson that after one day, J. Source had infected two people in his Biology class (☹1 and ☹2). Each of these represents a reproductive success for the disease and can be thought of as a new generation of the disease, with J. Source's disease as its parent. These new hosts can now be a source of exposure to other susceptible individuals.

	Row 1	Row 2	Row 3	Row 4	Row 5
Seat 1	empty	No Vacc	Vacc	No Vacc	No Vacc
Seat 2	No Vacc	No Vacc	No Vacc	empty	Vacc
Seat 3	No Vacc	**J. Source**	☹1	No Vacc	No Vacc
Seat 4	☹2	No Vacc	No Vacc	No Vacc	Vacc
Seat 5	Vacc	No Vacc	No Vacc	No Vacc	No Vacc
Seat 6	No Vacc	empty	Vacc	No Vacc	No Vacc
Seat 7	empty	empty	empty	empty	empty

Table 4.1: Period 1 Biology on Day 2

Questions For Discussion

1. For the sake of simplicity, assume that with aerosolized transmission, the number of hosts causing a susceptible individual to be exposed does not matter. Once aerosolized, disease is already in the air and additional hosts will not increase the probability of transmission.

 a. In Biology class, on the second day, how many people will be exposed due to aerosol transmission? Explain.

 b. How many students are expected to contract the disease? Hint: Remember that the rate of infection is constant. In this case, 2/21 or 0.095.

2. Assume that the Biology class is representative of the entire population. Using the rate of infection predict the number of students who will become infected each day. Assume no students recover.

 a. On the third day?

 b. Fourth?

 c. Fifth?

 d. Sixth?

3. Why does the number of susceptible students drop on each consecutive day?

Who Infected Whom?

By going through the same process with a disease with range-one droplet transmission, it will become obvious that the disease could spread differently depending upon who contracts the disease. First observe the calculations for a simple example.

	Row 1	Row 2	Row 3	Row 4	Row 5
Seat 1	empty	No Vacc	Vacc	No Vacc	No Vacc
Seat 2	No Vacc	No Vacc	No Vacc	empty	Vacc
Seat 3	No Vacc	**J. Source**	☹1	No Vacc	No Vacc
Seat 4	☹2	No Vacc	No Vacc	No Vacc	Vacc
Seat 5	Vacc	No Vacc	No Vacc	No Vacc	No Vacc
Seat 6	No Vacc	empty	Vacc	No Vacc	No Vacc
Seat 7	empty	empty	empty	empty	empty

Table 4.2: Period 1 Biology on Day 2

The fact that two students in Biology class became ill on the second day led to the calculation of a transmission rate of 2/8 because 2 of the 8 exposed students became ill. The number of expected new infections on the third day will be determined by the number of contacts between infected and susceptible individuals.

J. Source will be in contact with six susceptible students, ☹1 will also be in contact with six susceptible students, and ☹2 will be in contact with three susceptible students. But, some of these students are the same students! This makes determining the expected infections a bit more difficult. We'll look at an easier case first.

Let's assume that each separate contact has its own separate probability of infecting the person and that no exposed students are the same. Making this simplification, we add together all of the individual probabilities of infecting each susceptible exposed student. J. Source exposes six students, and each student has a 2/8 chance of catching the disease. ☹1 exposes a different six people, and ☹2 an additional three different people. This is shown mathematically as:

$$6 \times \frac{2}{8} + 6 \times \frac{2}{8} + 3 \times \frac{2}{8} = \frac{30}{8} = 3.75$$

In our actual situation, 3.75 is a 'worst-case' expectation for our Biology class because this calculation assumes each person that the sick students infected is different. In reality, two different infected students could try to infect the same susceptible student. If the susceptible student catches the infection from the first contact, then they are no longer susceptible when they meet the second infected person, dropping the number of susceptible students the second infected student can meet.

Since this worst-case scenario is the most conservative, we could use it to prepare for the worst possible outcome. On day 3 then, we expect four additional students infected. The number of

potential contacts on day 4 depends on which actual students were infected on day 3 (i.e. where the newly infected student were seated). Because the outcome of this depends on random selection of newly infected hosts, there are many different possibilities.

Questions For Discussion

4. Why do we say that the 3.75 students infected is a worst-case outcome?

5. What issues arise with this range-one droplet transmission and determining a more accurate number of expected infections?

6. How might you get a better estimate of the number of additional students infected?

Simulating Disease Outbreaks

Using a computer simulator makes the process a bit more manageable in that we can add randomness to our estimate process. Your teacher will supply you with the computer program and instructions on how to run the scenarios in Activity 4-1 through the simulator using a population size of 30.

ACTIVITY 4-1   **Spread of Disease Simulation**
Objective: Analyze the spread of disease using computer-assisted simulation.
Materials:
        DC-H4: Spread of Disease Simulation Activity Worksheet

The simulator begins with Day 0 to show what the scenario was before the disease was introduced. Begin recording data with Day 1. Run the scenarios to see how large or small a difference it actually makes.

1. Use the following table to record the results of your simulation with a population of 30, a range-two droplet transmission rate of 65% and duration of five days.

Population Size		Mechanism	Transmission Rate		Duration of Infectivity		
30		Range-two Droplet	65%		Five days		
Day	1	2	3	4	5	6	7	8	9	10
No. infected										
No. susceptible										

> a. Roughly sketch a graph for the number of infected and the number of susceptible people over 30 days.

> b. How many susceptible people remain at the end of 30 days?

c. What was the maximum number of people infected at one time?

d. At the end of 30 days has the disease died out?

2. Use the following table to record the results of your simulation with a population of 30, an aerosolized transmission rate of 5% and duration of five days.

Population Size		Mechanism	Transmission Rate				Duration of Infectivity		
30		Aerosolized	5%				Five days		
Day	1	2	3	4	5	6	7	8	9	10
No. infected										
No. susceptible										

a. Roughly sketch a graph for the number of infected and the number of susceptible people over 30 days.

b. How many susceptible people remain at the end of 30 days?

c. What was the maximum number of people infected at one time?

d. At the end of 30 days has the disease died out?

3. Use the following table to record the results of your simulation with a population of 30, a range-one droplet transmission rate of 5% and duration of three days.

Population Size		Mechanism	Transmission Rate				Duration of Infectivity		
30		Range-one Droplet	5%				Three days		
Day	1	2	3	4	5	6	7	8	9	10
No. infected										
No. susceptible										

a. Roughly sketch a graph for the number of infected and the number of susceptible over 30 days.

b. How many susceptible people remain at the end of 30 days?

c. What was the maximum number of people infected at one time?

d. At the end of 30 days has the disease died out?

Biological fitness is the ability of an organism to persist, to live and reproduce, over time. You have probably heard of "survival of the fittest." For diseases, this same concept applies.

Organisms that can reproduce and leave more offspring for the next generation have a higher fitness level than those that die out.

Questions For Discussion

7. If the disease has extremely low transmissibility, would a shorter or longer duration lead to its greater biological fitness? Why?

8. If the disease has a short duration, is there a danger of it dying out quickly? Why?

9. If the disease has a short duration, a greater transmissibility will increase its reproductive success, but what effect will that have on its biological fitness?

ACTIVITY 4-2 **Reproductive Success and Biological Fitness**
Objective: Investigate the impact of changing transmission method and rate, duration and population size of disease survival.
Materials:
> DC-H5: Reproductive Success and Biological Fitness Activity Worksheet

1. Use your simulation program to design a disease that will survive the longest and infect the greatest number of people over 30 days (leaving the least number of susceptible people). Set the population for 144 people. Record the transmission method, transmission rate, and the duration of infectivity. Then record the number of days the disease survived and the total number of people infected.

Transmission method	
Transmission rate	
Duration of infectivity	
No. of days the disease survived	
Total no. of people infected	

2. This unit has, to this point, modeled a population size of 30. Obviously, populations of many different sizes exist. Would an increase in the population size to 225 have a significant effect on the biological or reproduction success of the disease? Write a hypothesis.

3. Run simulations to support or refute your hypothesis from item 2. To test your hypothesis, run the following scenarios with population 30 and population 225. For each scenario, record the percentage of the population that was infected at the end and the percentage of the population that remains susceptible at the end of the simulation. Record any other observations that may be important in evaluating your hypothesis.

> a. Range-one Droplet   Transmission rate: 8%   Duration: 5 days
> Recorded observations:

  b. Range-two Droplet   Transmission rate: 3%   Duration: 5 days
  Recorded observations:

  c. Aerosol   Transmission rate: 5%   Duration: 5 days
  Recorded observations:

4. Review your observations and compare with your hypothesis. What are your conclusions?

Questions For Discussion

10. Review the three case studies presented in the background material.

  a. What best describes the transmission of tuberculosis? Circle the best answers.

Method of transmission	Aerosol		Contact
Transmission rate		Medium	Low
Duration of infectivity		Medium	Short

  b. What best describes the transmission of measles? Circle the best answers.

Method of transmission		Droplet	Contact
Transmission rate		Medium	Low
Duration of infectivity	Long		Short

  c. What best describes the transmission of Ebola? Circle the best answers.

Method of transmission	Aerosol	Droplet	
Transmission rate	High		Low
Duration of infectivity		Medium	Short

11. Hepatitis C virus (HCV) infection is the most common chronic blood borne infection in the United States, but has a low transmission rate. How is this possible?

Glossary

Adaptation – the process by which populations of individuals (on average) come to possess traits that allow them to survive and reproduce successfully under the constraints of selective pressure in an environment.

Airborne aerosolized – a type of transmission whereby the host releases infectious microorganisms into the air, where they can remain for long periods of time before settling on/in a susceptible individual.

Asymptomatic – when a host does not experience or exhibit symptoms of disease, despite having been infected by a pathogen.

Centers for Disease Control and Prevention (CDC) – an agency of the United States Department of Health and Human Services. It works to protect public health and the safety of people. The CDC is responsible for developing and applying disease prevention and control, especially in infectious diseases.

Competition – a type of organism interaction that can be either between members of the same species or members of different species. The relationship occurs when resources such as food, water, and space are in limiting supply.

Conditional probability – the probability that one event will occur, contingent on the occurrence of another event.

Contagious – capable of being transmitted by infection. Relates to diseases that are capable of spreading by contact with disease-causing organisms from another infected organism.

Dependent events – two events in which the outcome or occurrence of the first affects the outcome or occurrence of the second.

Direct contact – a type of transmission whereby the host passes infection by touching a susceptible individual; this can include direct sexual contact.

Droplet (transmission) – a type of transmission whereby the host coughs or sneezes releasing droplets onto an exposed organism.

Duration (of infectivity) – the length of time of an average infection in a host, during which time that host can serve as a source of exposure to uninfected individuals.

Epidemic – an infectious disease that occurs suddenly in numbers clearly in excess of normal expectancy.

Evolution – the process changes in the gene pool of a population of living organisms over time. Evolution cannot take place without genetic variation.

Exposure (to disease) – when an uninfected organism comes into contact with a pathogen.

Fecal-Oral – a type of transmission whereby food or water sources are contaminated by contact with host feces and are then consumed by a susceptible individual.

Gene – a specific location of a segment of DNA that is necessary for the production of a protein.

Host – an organism that is infected with a parasitic or disease-causing organism.

Immunity – the state in which an organism can resist a disease.

Incidence – the frequency a disease appears in a population.

Incubation period – the time from the moment of exposure to the development of the symptoms of a particular infectious disease.

Independent events – two events in which the outcome or occurrence of the first has no affect on the outcome or occurrence of the second.

Indirect contact – a type of transmission whereby the host contacts and contaminates an inanimate surface, which is then contacted by a susceptible individual

Infected – a host who has an infection.

Infection – invasion by and multiplication of disease-causing organisms in a host, which may result in the host experiencing the disease.

Infectious diseases – diseases resulting from the presence and activity of a disease-causing organism and resulting in adverse reactions in host organisms.

Macroparasitic – parasites that are large enough to be seen with the naked eye, in contrast to microparasites. They grow in the host but multiply by producing infective stages that are released from the host, allowing the parasite to spread to other hosts. These generally include such parasites as ticks, mites, nematodes, and flatworms, and can be either external or internal.

Microorganisms –microscopic organisms; those that can cause disease, including bacteria, algae, fungi, and protozoa. Viruses are often included in this group even though they are not classified as living organisms.

Mode of transmission – ways in which a susceptible individual can be successfully infected by disease from a host source.

Mortality rate – the death rate, given as the ratio of the total number of deaths to the total population.

Outbreak – The occurrence of a large number of cases of a disease in a short period of time.

Population - a group of individuals of the same species living in the same area at the same time. It is the smallest biological unit that can evolve.

Predation - a type of organism interaction in which one species feeds on another species.

Probability – a mathematical estimation of how likely it is that an event will occur.

Rate of incidence – the rate of new infections in the uninfected population, regardless of whether or not the population is susceptible or is even actually exposed to the disease. The numerator is the number of new infections occurring in a defined period; the denominator is the population at risk of experiencing the event during this period.

Rate of infection – the rate susceptible individuals exposed to a disease contract the disease.

Rate of transmission – the rate of infection of susceptible individuals, given exposure to a disease. If this is constant, this is the rate of infection.

Reproductive success (of a disease) – the successful transmission of infection to a new host.

Selective pressure – external pressure applied to a process such as change in the genetic makeup of a population, thereby favoring one genetic variant, yielding it greater success over another variant.

Strain – a group of organisms within a species that differs in trivial ways from similar groups. For example, *Escherichia coli* is a bacterium that is common and generally harmless, but *E. coli* strain O157:H7 is a pathogen that results in gastrointestinal illness.

Susceptible – capable of becoming infected with a disease.

Symptom – any subjective evidence of disease or of a patient's condition, such as a fever, chills, nausea, or rash.

Symptomatic – when a host experiences or exhibits symptoms of disease due to infection by a pathogen.

Transmission – the transfer of a disease from one individual to another.

Vaccination – the process of applying a vaccine.

Vaccine – a preventative medicine consisting of a suspension of weakened or killed microorganisms (bacteria or viruses), which protects otherwise susceptible individuals from becoming infected from exposure to a pathogen.

Variation – characteristics in an organism that result from altered states of genes.

Vector – any agent (person or animal or microorganism) that carries and transmits a disease; "mosquitos are vectors of malaria and yellow fever"; "fleas are vectors of the plague"; "aphids are transmitters of plant diseases."

Vector-borne – a type of transmission whereby the infection is carried by insects or other animals from a host to a susceptible individual without the insect or other animal itself being made sick; this transmission is usually accomplished via biting/feeding of the vector on the host.

Virulence – The degree or ability of a disease-causing organism to cause disease.

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