



Microbes, just like the ones you observed in Activity 36, “Looking for Signs of Micro-Life,” were discovered in the late 1600s. But the idea that such tiny organisms could cause disease did not develop until the 1860s, less than 150 years ago. Why did it take so long to figure this out?



How did the germ theory of disease develop?

MATERIALS



For each group of four students
miscellaneous props



For each student

- 1 Student Sheet 37.2, “Timeline of the Germ Theory of Disease”**

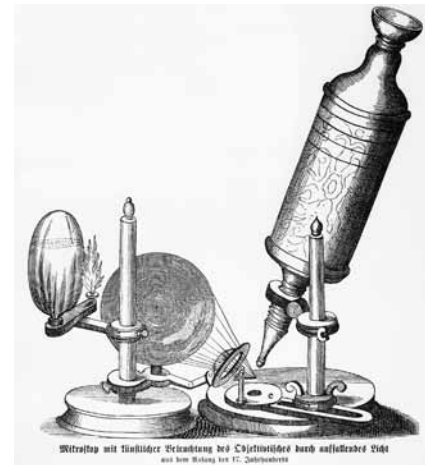
PROCEDURE

1. Your group will be assigned one of the sections under “Cast of Characters.”
2. With your group, read the section carefully and identify the important contribution(s) to science made by your character(s). Record these in your science notebook.
3. Develop a skit to present these important points to your class. You can make your skit historical (for example, show how your scientist made the discovery) or modern (for example, create an ad to sell Hooke’s book). Be sure to create a role for each person in your group.
4. Collect any props or additional materials you require.
5. Present your skit to the class.
6. As you watch the various skits, complete the timeline on Student Sheet 37.2, “Timeline of the Germ Theory of Disease.”

CAST OF CHARACTERS

Robert Hooke (1635–1703)

The late 17th century was a period of great scientific discovery. While many people offered theories without experimentation or evidence, English scientist Robert Hooke believed that good science resulted from making observations on what you could see. In his twenties, he wrote a book of his observations and drawings of the natural world called *Micrographia*, meaning “tiny drawings.” It was first published in 1665. In this one book, he presented his ideas about the life cycle of mosquitoes, the origin of craters on the moon, and fossils. But Hooke is most remembered for including drawings of what he saw through a microscope.

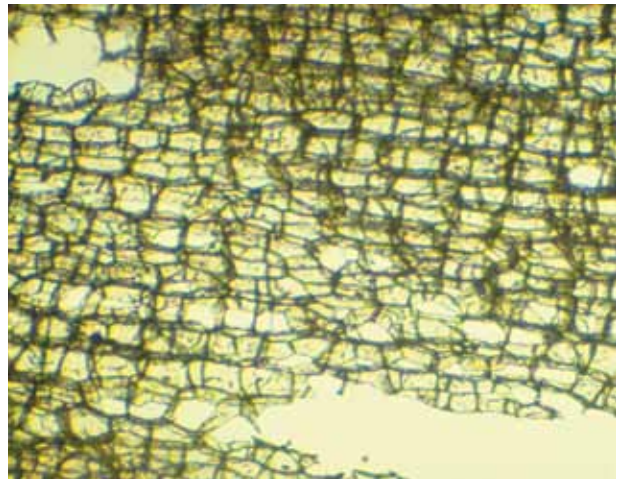


HOOKE'S MICROSCOPE

Hooke developed his own version of the compound microscope (above), and it was one of the best available at the time. Today, his most famous drawing from *Micrographia* is a drawing of cork—the same kind of cork that is used in corkboards and bottle stoppers. Since cork is made from the bark of the cork oak tree, it is essentially dead plant tissue. Using his microscope, Hooke looked at very thin slices of cork. He noticed what looked like little rooms (below right). Because of this, he called these shapes **cells**, another word for *rooms*. With this simple observation, Hooke introduced an idea that would become the basis of new fields in biology—but not for almost 200 years!



Cork tree



Cork cells



LEEUVENHOEK'S
MICROSCOPE

The small hole in the board contained the magnifying lens. The material to be observed was placed on the point in front of the lens.

Anton van Leeuwenhoek (1632–1723)

Anton van Leeuwenhoek (LAY-vun-hook) was a cloth salesman in Holland and an amateur scientist. He knew how to make very simple microscopes. (Today they would be considered magnifying glasses.) But he did not become interested in studying the microscopic world until he read Hooke's *Micrographia* (see the section on Robert Hooke), which was a very popular book at the time.

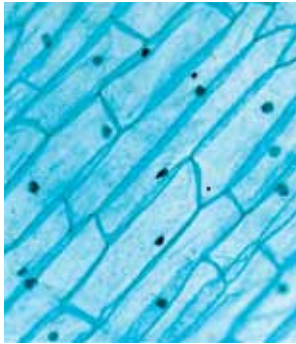
Leeuwenhoek's skill at building microscopes (like the one shown at left) enabled him to magnify objects over 200 times. This, combined with his curiosity, led to observations almost identical to those that you made in Activity 36, "Looking for Signs of Micro-Life." In 1673, Leeuwenhoek described what he saw in a drop of water: ". . . wretched beasties. They stop, they stand still . . . and then turn themselves round . . . they [are] no bigger than a fine grain of sand." By examining scrapings from his teeth, he found additional evidence of these "many very little living animalcules, very prettily a-moving." Leeuwenhoek was one of the first people to observe and record microbes. He continued his observations until the end of his life.

How Leeuwenhoek Described Spirogyra

Look at the picture of the green alga *Spirogyra* shown to the right. Since Leeuwenhoek was not a good artist, he wrote very precise descriptions of his observations. (In addition, he hired someone to make drawings to go with his descriptions.) On September 7, 1674, he described *Spirogyra*, which can be found on lakes: "Passing just lately over this lake . . . and examining this water next day, I found floating . . . some green streaks, spirally wound serpent-wise. The whole circumference of each of these streaks was about the thickness of a hair of one's head . . . all consisted of very small green globules joined together: and there were very many small green globules as well."

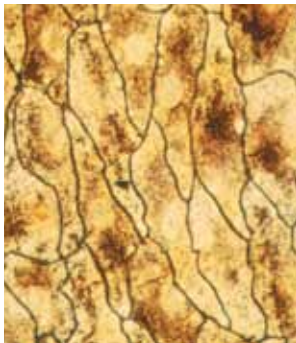


How do Leeuwenhoek's descriptions of micro-life compare with your own?



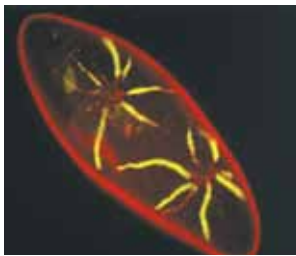
PLANT CELLS

Plants are made up of cells, like the plant cells shown in the photo above.



ANIMAL CELLS

Animals are made up of cells, like the skin cells shown in the photo above.



A MICROBIAL CELL

Many microbes are made up of just one cell, like the microbe shown in the photo above.

Matthias Jakob Schleiden (1804–1881)

Theodor Schwann (1810–1882)

Karl Theodor Ernst von Siebold (1804–1885)

Over the next 150 years, scientists continued to use the microscope to study living organisms such as plants, insects, and microbes. But by the early 1800s, most botanists—scientists who study plants—were not using microscopes. They were busy naming and describing entire plants. German biologist Matthias Schleiden (SHLY-dun) was an exception. Although he was trained as a lawyer, he left the law to become a professor of botany. Schleiden preferred to use a microscope to study plants. (Look at Plant Cells, in the margin column, to see what Schleiden may have seen.) Based on his study, he suggested in 1838 that all plants are made of cells. This was a completely new idea: just as a house could be made up entirely of bricks, plants were made up entirely of cells!

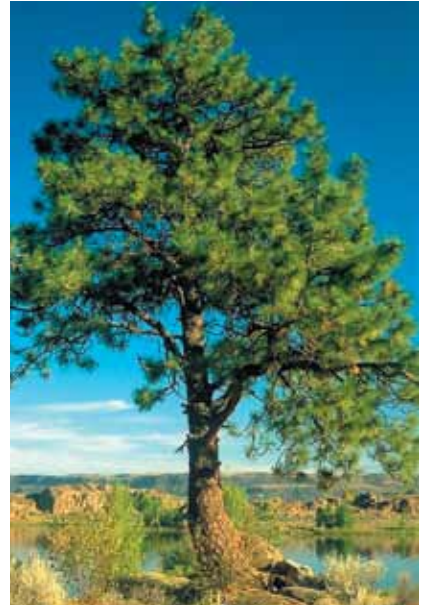
Schleiden knew another German biology professor, Theodor Schwann, who spent his time studying animals. Schwann was particularly interested in the digestive system. In 1839, one year after Schleiden proposed his theory, Schwann suggested that animals, and not just plants, were made up of cells. You can see animal cells in the margin column photo. Because of their ideas, Schleiden and Schwann are credited with developing the **cell theory**: that all living organisms are made up of cells.

Other scientists began to build on Schleiden’s and Schwann’s ideas. In 1845, Karl Theodor Ernst von Siebold (SEE-bold) suggested that microbes were also made up of cells—or more specifically, one cell (see the Microbial Cell photo in the margin column). In fact, Siebold believed that organisms made up of many cells, like animals, were built out of single-celled microbes! While Siebold was wrong about this idea, he was right in stating that microbes were living creatures made up of the same material as animals and plants.

Rudolf Carl Virchow (1821–1902)

Why is Schleiden’s and Schwann’s cell theory important for understanding infectious disease? Their work influenced Rudolf Carl Virchow (VIR-koh), a Polish doctor. He had been treating and studying ill patients for many years. He is famous for saying, in the 1850s, “all cells arise from cells,” meaning that cells reproduce to create new cells. He was right. When you see a new plant or a baby animal, you see a **multicellular** (many-celled) creature. All living organisms begin as a single cell. Most microbes are made up of *only* a single cell, as Siebold believed (see the section on Schleiden, Schwann, and Siebold). The cells of some living organisms, like people, continue to divide and grow. An adult human being is made up of about 10 trillion cells!

Activity 37 • The History of the Germ Theory of Disease



Did you know that each of these organisms is multicellular? Each is made up of millions of cells. You could collect evidence of this with a microscope.



Virchow applied his ideas to disease. He knew that all cells grow from other cells. He thought that all diseases are caused by cells that do not work properly. He believed that diseased cells come from other usually healthy cells of the sick person. Virchow's ideas about disease were not completely correct, although they are correct for some diseases. His ideas were based on his work with leukemia (loo-KEE-mee-uh), which is a cancer of the blood. Cancer and other hereditary diseases are diseases of the cell. They *are* caused by cells that do not work properly. Infectious diseases are different, as scientists after Virchow discovered.

Ignaz Philipp Semmelweiss (1818–1865)

At the same time that Schleiden, Schwann, and Siebold were developing their ideas on cells, a Hungarian doctor working in Austria was trying to prevent young women from dying. It was the 1840s and pregnant women often died of a disease called childbed fever. Dr. Semmelweiss (sem-ul-VICE) noticed that many pregnant women were examined by doctors who had just completed an autopsy. He also observed another doctor die of childbed fever after he cut himself on the scalpel he was using to perform an autopsy. Semmelweiss concluded that childbed fever must be infectious and could be spread from something found in the dead bodies. He believed that doctors were carrying the disease from patient to patient.



Today, childbed fever is called puerperal infection. It is caused by several different microbes, including Streptococcus (similar to the microbes shown above).

Semmelweiss decided to try washing his hands between patients. As a result, fewer of his patients died. In two years, he reduced the death rate among his patients from 12% to 1%. He encouraged other doctors to use a strong chemical solution to wash their hands between patients. But because Semmelweiss could not explain why hand washing worked, many doctors refused to change their ways.

Semmelweiss tried hard to get hospitals to change their policies, but many people resisted his ideas. He eventually suffered a mental breakdown and died soon after. Within 10 years of his death, the development of the germ theory of disease would explain what he could not—that hand washing reduces the risk of infectious disease by removing germs like the ones shown at left.

Louis Pasteur (1822–1895)

Louis Pasteur (pass-TUR), a French chemist, began studying microbes in 1864. He was working on an important business in France: the fermentation of wine and vinegar. He noticed that certain microbes could cause food and drink to spoil. Pasteur discovered that different microbes cause different kinds of spoiling, but heat can kill many of these microbes. Today, because of his work, milk is heated to 71°C for 15 seconds to kill the microbe that causes tuberculosis. Using heat to kill microbes is now known as pasteurization in Pasteur’s honor. Look at the milk carton shown at right. The word “pasteurized” on milk sold in stores tells you that the milk is safe to drink.



PASTEURIZED MILK

Pasteurization kills microbes that may be present in milk.

In 1865, Pasteur was asked to help the silk industry of France, which was having problems with silk production. Silk is produced from threads spun by a worm known as the silkworm. Pasteur observed a microbe that was infecting the silkworms and the leaves they ate. When he recommended that the worms and their food be destroyed, the silk industry was saved.

Pasteur knew that some diseases were infectious. He suggested that microbes, which he referred to as “germs,” could cause infectious diseases and were easily spread by people. This idea is the basis of the **germ theory of disease**.

Robert Koch (1843–1910)

Slowly, the role of microbes in causing infectious diseases began to be accepted. But there was still more work to do. Which microbe caused which disease? In 1876, Robert Koch (KOKE), a German doctor, identified the microbe that caused anthrax (AN-thraks), an infectious disease that was killing cattle. He later went on to identify the microbes that caused tuberculosis and cholera. Amazingly, he did all of his work in the four-room apartment that he shared with his wife.



The substance inside this dish is known as agar. Many kinds of microbes can grow on agar, which provides food for the microbes.

Koch developed a way to prove that a specific microbe caused a particular disease. In the case of anthrax, he injected healthy mice with blood taken from farm animals that had died of anthrax. He injected another group of healthy mice with blood taken from healthy farm animals. All of the mice injected with the blood from the infected animals died of anthrax. None of the other group of mice developed anthrax. He then showed that he could isolate anthrax microbes only from the mice that were injected with blood from infected animals. He did not find anthrax microbes in the healthy mice. In this way, Koch was able to provide scientific evidence that the anthrax microbe caused anthrax. The figure shown below summarizes his experiment.

Koch also created new ways to grow cultures of uncontaminated microbes. In particular, he developed agar (AH-gur), a gelatin-like substance which is used to grow microbe cultures. Agar is still used today, as you will find out in Activity 47, “Reducing Risk.”

KOCH'S EXPERIMENT

Healthy mice



Inject with blood from cow with anthrax



Mice die: Anthrax microbes can be isolated from blood of infected mice

Healthy mice



Inject with healthy cow blood



Mice live: No anthrax microbes in blood of healthy mice

Florence Nightingale (1820–1910)

Joseph Lister (1827–1912)

William Stewart Halsted (1852–1922)



Florence Nightingale

Ideas such as those of Pasteur and Koch were very important in the field of medicine. Florence Nightingale, an English nurse, published her ideas on disease in 1860. At the time, the idea that cleanliness was important in preventing disease was not a common one. She was one of the first to recognize the value of cleanliness and recommended it as a part of good nursing. Her efforts improved sanitary practices in military hospitals and led to fewer soldiers dying from infections due to contaminated battle injuries.

Scottish surgeon Joseph Lister had been concerned at the high death rates of patients following surgery. Surgery would be completed successfully, but about 45% of patients would die of infections afterward. When Lister heard about Pasteur’s germ theory of disease, he came up with the idea of killing germs with chemicals. In 1867, he began using an antiseptic to clean surgical instruments. He also sprayed the air, and required hand washing and clean aprons. As a result, the death rate of patients following surgery dropped to 15%.

American surgeon William Halsted took these ideas one step further. Instead of just trying to kill the microbes once they were there, why not try to prevent them from being spread in the first place? In 1890, Halsted became one of the first surgeons to use rubber gloves during surgery. The gloves could be sterilized with heat and chemicals that were too hard on human hands. This helped reduce the presence of even more microbes and improve patient health.

By 1931, the germ theory of disease had become so accepted that ads for a disposable tissue read: “A new era in handkerchief hygiene! Use once and discard—avoiding self-infection from germ-filled handkerchiefs.”



Joseph Lister supervises as antiseptic is sprayed before surgery

The Theory of Spontaneous Generation

Virchow stated that cells reproduce to create new cells. However, many scientists did not accept Virchow's ideas. They believed in spontaneous generation—the idea that living things grow from non-living things. For example, someone who believed in spontaneous generation might think that plants grow from soil. If you wanted to grow a plant, you would need only soil (no seeds or plant cuttings). After some time, a plant would spontaneously grow out of the soil. It took the experiments of many people to disprove the idea of spontaneous generation.



Maggots are now known to be a juvenile stage of flies.

In 1668, an Italian doctor named Francesco Redi set out to show that maggots grew from eggs laid by flies. Because maggots were often found in rotting meat, many people believed that they just appeared spontaneously. To test his hypothesis, he set up several flasks containing meat. Some of the flasks were open to the air, some were sealed completely, and some were covered with gauze. As he expected, maggots appeared only in the open flasks in which the flies could reach the meat and lay their eggs.

In 1767, Italian priest Lazzaro Spallanzani conducted experiments to disprove spontaneous generation. He tightly sealed some bottles that contained liquid and then boiled them for more than 30 minutes. Nothing grew in the bottles. But because he had removed the air from the bottles using a vacuum, many scientists believed that Spallanzani proved only that spontaneous generation did not occur without air.

It was not until 100 years later, in 1859, that French chemist Louis Pasteur conducted a now-famous experiment that convinced most

people. The French Academy of Sciences had sponsored a contest for the best experiment to either prove or disprove spontaneous generation. Pasteur's winning experiment was a variation of the method used by Spallanzani. He put a mixture of yeast, sugar, and water in several glass flasks. He then heated the necks of the flasks to bend them into

the shape of an "S" (see "Pasteur's Experiment," below). Air could enter the flasks, but airborne microbes could not. Because of gravity, they would land somewhere along the neck of the flasks. Finally, he boiled the flasks to kill any microbes that might already exist in the mixtures. As Pasteur had expected, no microbes grew in the flasks. When Pasteur broke the neck of a flask and exposed it directly to air, microbes grew. Pasteur provided convincing evidence against the idea that living organisms come from non-living things.



PASTEUR'S EXPERIMENT

ANALYSIS



1. Why is the germ theory of disease important in understanding infectious diseases?



2. How important was the development of the microscope in discovering the cause of infectious diseases?

3. **Reflection:** Imagine that each of the scientists in this activity wanted to hire an assistant. With which scientist would you most like to work? Why?



EXTENSION

Robert Hooke was an amazing scientist. His scientific ideas in the areas of physics, paleontology, biology, and chemistry are still relevant today. Why don't we know more about Hooke today? Some people believe it could be because the influential Sir Isaac Newton was his enemy. Find out more about Robert Hooke and the other scientists in this activity. Begin by checking out links on the *Issues and Life Science* page of the SEPUP website.