Investigation

3.2B: Microbes

English teachers often introduce students to journalistic writing by suggesting that the author must explain to the reader "who, what, when, where, why, and how." Which of those elements would you rate the most complex or difficult to explain? *How* can sometimes prove a challenge, but most authors seem to work the hardest to figure out *why*. Human beings appear unique in the ranks of living organisms in their endless quest to puzzle over *why*. *Why* is the sky blue? *Why* does the letter Q always need a U? Why does ice float?

We apparently were born with an instinct for asking *why*. A biologist might argue that asking *why* created an **evolutionary** advantage for the human species. We have certainly begun to see that asking *why* plays a huge role in medical science. Let's follow the role of human curiosity in regard to microbes. Let's turn the clock back 500 years and consider what "*why*" questions you might then have asked. Life is very different for you 500 years ago. No one yells at you to brush your teeth. That habit did not exist. Lacking automobiles, you did not travel long distances easily. Back then you would notice that people, young and old, commonly got sick and quite commonly died from any significant illness. Doctors and nurses existed, but they believed disease came from **miasma**. Miasma? Curious people back then noticed that illness seemed associated with impurity, poor cleanliness, or foul smelling air. Thus, they concluded that foul air caused illness. They called the origin of disease miasma, an ancient Greek word meaning foul or bad air.

Pretend your teacher back then believed in homework and assigned you the task of figuring out *why* some stale bread made everyone who ate it sick, but no one who ate the fresh bread two days before got sick. How might you attack that homework assignment?

Teachers sometimes give you a choice for special homework projects. Alternatively you might have been asked to figure out *how* two people many miles apart could come down with the same set of disease symptoms, people who never met each other or shared any contact with the same miasma. How might you start to figure out that puzzle?

Amazingly 68 year-old, Girolamo **Fracastoro**, an Italian scholar assigned himself that very same homework assignment. He decided miasma made no sense at all. In 1546, he instead suggested that some sort of invisible seed must transmit illnesses. How could he prove that something invisible actually existed? What would lead him to even conjecture the existence of something solid, like a seed, with the ability to make people sick, yet the eye could not see it? Fracastoro had an unusual imagination.

Today we generally think of Louis **Pasteur** as the scientist first to understand the real origin of infectious disease. Pasteur performed experiments that linked germs to human illness, but Pasteur did that in about 1860, more than three hundred years after the period you just time traveled into. Pasteur, by then, had the benefit of Anton van Leeuwenhoek's invention. About 1670, **Leeuwenhoek** figured out how to use magnifying glasses to see tiny living things, **microorganisms**, never actually seen by anyone before. Leeuwenhoek saw germs 190 years before Pasteur linked them to disease. Leeuwenhoek made microbes visible; so why did it take 190 years to make the connection between microbes and illness? Actually other scientists did put pieces of the puzzle together much earlier; but science still seems to have moved more slowly then than we might imagine, perhaps because methods for rapidly sharing ideas and discoveries we take for granted today, did not exist then.

The years between 1860 and 1900 saw the growth of human knowledge of **germs** as a cause of disease. Robert **Koch** became a star in this area of knowledge by creating a set of rules one could use to prove a specific germ caused a specific disease by analyzing sets of specific symptoms. The rules were pretty straight forward:

Rule 1: A person with the disease must have lots of this germ, but healthy people have none.

Rule 2: You must be able to isolate the germ and grow it in a germ culture in your laboratory.

Rule 3: If you give those cultured germs to a healthy person they must get the same disease.

Rule 4: You must be able to get germs back from the person you made sick, grow them in culture, and see that they look the same as the germs you cultured back in Rule 2.

Do Koch's rules remain true for us today? They seem to make sense, but today we recognize some exceptions. Can you think of an exception?

Koch's Rule 1 failed for him fairly early after he created them because **cholera** and typhoid fever, Koch discovered, had carriers. A **carrier** we define as a person who does not have the symptoms of the disease, but can spread the disease to others. Mary Mallon's bizarre story took place in New York City in the first decade of the 20th century. Mary Mallon, known as **Typhoid Mary**, spread the deadly disease **typhoid fever** but did not have the disease herself. She was imprisoned for many years to stop her from spreading the disease and the story of her life seems impossible for us to comprehend today.

We also recognize now that some people can resist a disease that makes others sick, so Rule 3 has exceptions. We know that some people can have **immunity** to a disease that others do not; indeed we know that vaccination can create immunity to a disease.

The second half of the 19th century (1850 – 1899) saw the rapid growth of human knowledge about germs as a cause of disease, and using a **microscope** scientists could see those germs and could see them grow and divide to form increasing numbers of identical germs in a culture dish in the laboratory. These scientists understood that germs were alive, consisted of a single cell, and they used food to create energy for a biochemical process of growth similar to the functioning of cells in our own bodies.

As these scientists kept asking why, new questions arose. Near the end of the 19th century a French microbiologist invented a **membrane** with **pores** that could allow a fluid to pass through, but the pores were too small for a germ to cross. About the same time, Louis Pasteur failed to find a germ that caused **rabies;** he began to think something smaller than a germ must exist to cause that disease. Several other scientists around the world started to find diseases that were caused by something that could pass through the pores in that membrane. By 1928, the concept of a **virus,** something smaller than a germ but able to induce a disease, was widely accepted, but still no one had seen a virus. Not until 1931, with the German invention of the **electron microscope**, did humans have the ability to "see" a virus and begin to understand this simpler, smaller structure able to cause illness. In the 1970's scientists began to understand the chemistry by which viruses translate their genes into the genes of host cells that then create more viruses. We now had an understanding of how both viruses and bacteria survive and cause disease.

Bacteria, fungi and viruses, along with several less common single cell organisms, all individually too small for us to see, biologists group together in a category they call **microbes**. Microbes live all around us on the ground, in the ground, in the air, on us, and inside us. Biologists have estimated that we have more microbes on our skin than the total population of people living on this planet. We need microbes to live, but microbes do not appear to need humans. Microbes, we believe, began living on earth long, long before human life. Let's take a look at some of the similarities and differences between two principle types of microbes, bacteria and viruses.

First, biologists have found that a virus does not exhibit all the behaviors we call "life." Bacteria, on the other hand, do exhibit life, having everything necessary to live and grow with or without the help of another living host (another living organism). For example, we can stick a sterile Q-tip into an infected area on an animal or human and send that sample to a medical laboratory, where technicians can actually grow more of the bacteria in a dish containing only some simple germ friendly food. Laboratory technicians can then identify exactly which bacteria infected that wound. They cannot grow a virus in that manner. A virus needs more than just food to grow. Viruses are not considered living things because they cannot reproduce, and thus survive, without a living host (like us). Viruses reproduce by invading living cells and using the capabilities of those cells to manufacture similar viruses, until the cell dies.

When asked about your size, you might tell someone your height in feet and inches. In the world of microbes scientists measure things in **nanometers** (a billion nanometers equals one meter in length). Put another way, 25 million 400 thousand nanometers equals one inch. A typical bacterium (the singular form of the word bacteria) measures about 1,000 nanometers. If you lined up bacteria in single file you would need 25,400 to make the line one inch long, or about 645 million bacteria to cover a one-inch square area. Now if we could shrink you down to the size of a typical bacterium, and put you next to a typical virus that virus would look to you about the size of a small mouse. The unaided human eye cannot see objects less than 40,000 nanometers readily, so you certainly cannot see individual microbes. You can see a bacterium with an optical microscope, but not a virus.

Bacteria, you now recognize, have much greater complexity than viruses. Bacteria have a rigid cell wall and cytoplasm inside containing mitochondria and DNA. Viruses have only a protein coat, either RNA or DNA inside, and nothing else.

We tend to think of bacteria only as the cause of harmful infection. But in truth, most bacteria prove helpful; indeed, human beings cannot live without the help of bacteria. Only about 1% of bacteria actually cause human disease. Scientists currently believe most viruses do cause harm. However, as we look into the future of medical research, we may see viruses helping cure sickness, disease, and even genetic disorders. As you will read later in this book, finding helpful roles for viruses has already begun. We can create a virus in the laboratory that can invade cells to correct defective genes. Scientists have begun to understand that a virus can store useful traits that can help living cells adapt to changes in their environment. Some viruses in the plant world transmit the ability for plants to withstand severe drought, for example. It would appear that such viruses play the role of an outsourced set of plant skills, ready when needed to infect and assist the plant. We may in the future find that viruses play similarly useful, even necessary roles, in human life in this same fashion. The role that helpful viruses may play in our lives remains a compelling topic for medical research in the future.

Bacteria and viruses have been around for billions of years; they occur wherever life exists. They have caused an inordinate amount of sickness and death throughout the centuries. Both continue to survive due to their extraordinary ability to adapt to their changing environment. Their amazing ability to adapt and evolve results from their very rapid reproductive cycle, as compared to the much longer reproductive cycle of complex animals, including humans. Even when we think a harmful bacteria or virus has been eradicated, they seem to re-emerge, sometimes years later.

In 1928, Alexander Fleming discovered a mold that killed bacteria growing near it in a dish used to grow microbes in his laboratory. That mold produced a juice that Fleming named **Penicillin**. Penicillin, the first ever **antibiotic,** signaled an historic advance in medical treatment. Scientists went on to develop many other antibiotic medications that controlled most bacterial infections for years. Today we find that antibiotics have been overused, and bacteria have evolved antibiotic resistance so that many of our antibiotics no longer work. Indeed we now have strains of bacteria causing **super-infections** resistant to all antibiotics. We have essentially returned to the situation humans faced before Fleming discovered Penicillin. We hope that scientists can quickly develop yet newer antibiotics effective against these super-infections. So please don't ask your doctor for antibiotics every time you catch a cold. Antibiotics do not help you overcome an illness caused by a virus. We do now have anti-viral medicines available that may help if taken in the first day or two of a viral infection. Our fight against viral infections generally focuses on prevention with a **vaccine**. Once contracted, we commonly direct treatment of a viral illness to relieving the symptoms until the illness runs its course.

We say that bacteria and viruses both are **communicable**, meaning they can spread from one human to another. Methods of spreading an illness include breathing in microbes, touching contaminated objects, animal or bug bites, or eating contaminated food or water. Bacteria and viruses may cause sickness that is mild, moderate, severe, or even fatal. All you need to do to prevent getting sick is 1. Stop breathing, 2. Don't touch anything, 3. Don't eat food or drink water, and 4. Don't go outside. Good luck with that approach.

Let's introduce you to some infectious disease caused by microbes.

The common cold is an airborne, mild illness caused by a virus. The **flu**, a different airborne virus, also causes a mild to fatal **febrile** illness. Probably more people have died worldwide in the past 100 years from the flu than any other disease. More soldiers died from the 1918 flu **pandemic** during World War I, than died in combat.

Chicken pox is an airborne virus common in children, but which can also infect adults. The virus can remain dormant in the body for decades and may reappear as Shingles, a painful skin condition.

Insects, such as mosquitos, spread some very serious virus infections. Dengue Fever, Yellow Fever, West Nile, and more recently Zika virus, all are spread by mosquito bites. **Zika** is thought to cause a serious problem for pregnant women by affecting the developing fetus to produce a deformity called microcephaly. A student of one of the authors contracted encephalitis caused by the West Nile virus, and missed the entire school year. Unfortunately that student has not fully recovered and his life has been forever changed from a single mosquito bite.

Animals can spread viral diseases to humans. **Rabies** was made famous many years ago in the movie *Old Yeller*; a boy's dog contracted rabies fighting a rabid wolf while protecting his master. Old Yeller had to be put down when he started foaming at the mouth and acting crazy. Rabies can only survive in mammals, most commonly in skunks, raccoons, bats, foxes, and coyotes according to the CDC. You can't get rabies from birds, fish, or amphibians. When a person is bitten or scratched by an animal suspected of rabies, **preventive** treatment consisting of five shots given over twenty-eight days plus rabies antibodies are given. Once the signs and symptoms of rabies appear, there is no treatment; death is usually the result.

Hepatitis is a human-to-human viral infection that seeks out the liver. Several strains of hepatitis have evolved. In 2014 a new virus was discovered and named the Bourbon Virus after the county in Kansas where the infected man lived. You can look it up: Bourbon County, Kansas, USA.

Two more viruses having lethal abilities are **HIV** and **Ebola**. Both viruses are thought to have moved from the animal world of Africa to humans and then spread by human-to-human contact of bodily fluids.

Bacteria have more methods than viruses by which to spread because they can survive independently of human, mosquito or tick hosts. Ticks carry bacterium causing Lyme Disease and Rocky Mountain Spotted Fever, each common in specific areas of the United States. We can also contract bacterial diseases from food and water, even though food and water are not living carriers of infection.

How do we contract dangerous bacterial infections from our food or water? Remember microbes cover our planet. Bacteria occur naturally in the soil, and furthermore, in and on our body. When we process food without thorough cleaning, bacteria may not only survive, but also can multiply and grow. Then when we eat that food we ingest the bacteria. If that bacterium has the ability to cause illness, human beings may become ill and sometimes die.

We cannot live without water; yet contaminated water kills over a million people each year around the world. Water generally becomes contaminated in places where human and animal feces leak into the water. Organisms such as the cholera bacteria flourish in this instance. Cholera produces severe diarrhea, and massive loss of water from the colon can lead to death. The **Protozoans,** Amoebiasis and Giardiasis, single-celled organisms that biologists classify as neither a bacterium nor a virus, can also cause water-borne illness. You may have read about the rare occurrence of children getting sick and dying after swimming in warm-water lakes. Amoebas have the ability to penetrate the brain when present in water that splashes up into our noses. These children died because the organism infected their brains. **Epidemiologists** report that another protozoan causes **Malaria** and spreads by mosquitoes, killing more than 1,000 children per day around the world.

Viruses, such as **polio** and **hepatitis**, also have the ability to spread in water. In the 1950's, polio spread in public swimming pools. Thousands of children contracted the disease. Those developing the most severe symptoms suffered respiratory paralysis and required the help of an iron lung to breathe. Many polio victims suffered lifelong disabilities; boys were affected with **unilateral** muscle wasting and **paralysis** while girls were left with severe **scoliosis**. Following the development of an effective **vaccine**, polio was essentially wiped out. The success of the vaccine resulted in discontinued universal use of the polio vaccine; sadly polio has since re-emerged as a **viable** disease. Although the reason remains unclear, polio patients can experience progressive muscle weakness and atrophy, even difficulty breathing and swallowing years later, a so-called post-polio **syndrome**.

Eating contaminated food can poison our bodies, an event we call a foodborne pathogen outbreak. A foodborne outbreak occurs when two or more people get the same illness from the same food. Several types of bacteria have been proven responsible for foodborne outbreaks, but the two most prolific ones are E.Coli and Salmonella. E.Coli, short for Enterobacter Coli, has been at the root of several major food poisoning events at restaurants across our country and throughout the world. Surprisingly, E.Coli can live quite normally within our body, and yet has also made millions sick, even causing death over the years.

We have talked about the airborne spread of infections. Bacteria can invade our body when exhaled by a sick person and breathed in as we innocently walk by. **Tuberculosis** is a serious lung infection spread when infected individuals cough. This disease, often called simply TB, was at one time so difficult to treat that those infected where isolated, sometimes against their will, in special hospitals. Today we have a vaccine that can prevent TB, but experts recommend the use of this vaccine only in areas of the world with very high TB prevalence.

We can infect ourselves also directly by touching things recently touched by another infected person. Staphylococcus and Streptococcus are bacteria that spread in that way. Staphylococcus causes **abscesses** when we don't properly clean a cut or scratch, or when it infects our tonsils. Streptococcus can spread from a wound or cause "strep throat".

In summary, we have learned that microbes, whether living single cell organisms or just packets of genetic material not truly alive, surround us and can cause illness. We also know that humans require microbes to survive; we need them to digest our food and to do other tasks inside our bodies, functions still emerging today from medical research. Plants and animals that humans need for food also depend on microbes. Microbes in the roots of pea plants carry out chemical reactions that give that vegetable its nutrient value. Plants may depend on traits encoded in viruses to help them survive a drought. In the future we will probably discover humans also benefit from viral interactions. Medical scientists have begun to use laboratory-engineered viruses as a way to edit genes in plants, animals, and humans to enhance illness resistance, increase food production, restrict disease spread, and correct congenital defects. Today microbiologists estimate that the mass of the microbes within the earth's crust actually exceed the mass of living organisms on the earth's surface. We have great concerns about global warming that initially focused entirely on energy use, but now our concerns have centered on the effects on microbial population shifts that may have even more crucial impact on human life. We need to understand that humans, animals, plants, and microbes live in equilibrium and synergy with each other and those relationships contain both promise and danger. Indeed, of those four components of our world, the microbes would appear to have the least dependency on the other three. We all need to continue to ask "*why*."

[For a complete list of communicable diseases please consult the CDC, the Communicable Disease Center of our federal government at www.cdc.gov. This is an excellent place to learn about microbes and about recent epidemics of food-borne pathogens.]