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Health and the Invisible World

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Introduction

Have you ever wondered why all the schools suddenly have posters about washing your hands and hand sanitizer in every room? Ever wondered why we suddenly have motion activated paper towels everywhere? Seen the signs for MRSA and how to avoid it? Looked at headlines about flesh eating bacteria and wondered why we suddenly have these weird monsters that sound like they are from outer space?

These questions can all be answered at the nanometer scale, and they involve what we are doing to ourselves with our modern technology and medical care. If we were more knowledgeable and careful about how we take our medications, we would have less of these frightening, difficult-to-combat invaders. We are in a battle against both bacteria and viruses. Bacteria are developing strategies to evade our antibiotics, so scientists have to change them and find new ones. Viruses are even more insidious, invading our cells and turning our own genetic machinery against us. Can we slow these terrifying microbes down? Yes, we can do it by taking medications as prescribed and avoiding unnecessary use.

Justification

I teach health, which is an extremely practical subject. Standards include sex education, emotional health, communication, dealing with stress, dealing with peer pressure, drugs and many other topics, many of high interest to adolescents. I talk to my students about the differences between viral and bacterial infections when we study sexually transmitted and other communicable diseases. I have been concerned for years that they do not understand that diseases caused by viruses and bacteria are different and are treated differently by medicines. One of my concerns is that prescription drugs of all kinds are misused, not only recreationally, but also through a basic lack of understanding of how and why to take them as prescribed. Having worked for many years in both research and clinical laboratories, I correct friends and relatives when they say there is no difference between bacteria and viruses or offer prescription antibiotics they didn't use as directed to friends for their undiagnosed sore throat. As drug resistant bacteria become more of a problem, I would like to combat this, starting with a unit in my health class.

Oceana High School

Oceana High School, where I am a health and mathematics teacher, is a small school, less than seven hundred students, in a small district of five high schools, including one continuation school. As the name implies, we have views of the ocean that realtors drool over. We are just south of San Francisco, CA. The school is up on a hill overlooking the Pacific coast. Our population of students is very diverse. We have approximately 45% Filipino, 35% Caucasian, 10% Latino, 5% African American and the remaining 5% is a mix of Pacific Islander, Asian, Native American and others. About 50% of our students are on free or reduced lunch. There is a culture of racial mixing at the school and it is rare to see students segregate themselves by race. There is an acceptance of diversity due to the make up of the population, the work by the teachers, and the proximity to San Francisco. We have a humanities emphasis and all students must take four years of humanities to graduate.

One of the California health standards for high school is to "describe the use and abuse of prescription and non-prescription medicines...." This unit will address that standard and others as students learn about the use of medications for viral and bacterial infections. They will be able to understand why antibiotics are not useful against viruses. They will be able to differentiate between bacteria and viruses as a function of size and biological function. They will also become aware of the challenge of studying viruses and of treating viral disease. The very simplicity of the viral structure impedes medical progress in treatment.

Background

Size

The nanoscale size of viruses is not comprehensible to most of us. We have a very small range of comprehension as to size. We find the size of the largest living animals on earth, blue whales, very difficult to understand. When we consider planets, stars, galaxies, the universe, the scale becomes incomprehensible. On the other end, it is difficult for us to imagine anything that we cannot see. Gnats are about the limit of our comfortable range. Generally, people do not differentiate between the size of a eukaryotic cell and a virus, despite the fact that the scales involved are vastly different. As a result of their great difference in size, an infected cell can release millions of viral particles after the virus reproduces.

We will do various size activities at this point. It is important for the students to differentiate between microscopic and submicroscopic sizes. The emphasis in these activities will be on powers of ten. We will work mainly visually on this.

Cell membranes

A key concept in nanotechnology is self-assembly. Because of their very small size, nanoparticles are very difficult to manipulate physically. Scientists working on the nanoscale have learned to use nature's methods to work with small particles. Many molecules self-assemble: they naturally move to form a structure, based on polarity or hydrogen bonds, for instance. A common example of self-assembly is a bilayer lipid membrane, like the ones surrounding all cells and like the ones scientists use to build liposomes and micelles, structures

common in nanotechnology.

Cells are in an aqueous (water-based) solution and contain a different aqueous solution inside. So, both the inside and outside of a membrane are solutions with water. The molecules that make up the membrane are dual in nature. One side is hydrophilic, attracted to water. This can be one of several molecules that are polar. Like water, the electrons are not uniformly distributed, but rather have a slight positive charge on one side and a slight negative charge on the other. When another polar molecule is near water molecules, the molecules line up so that the positive charges are near as many negative charges as possible and vice versa. The molecules that make up the bilayer also have a hydrophobic part, not attracted to water. This is the long chain of the fatty acid of the molecule. These are non-polar molecules and tend to avoid polar molecules such as water. If you put membrane lipid molecules into water, they will spontaneously arrange into a layer on top of the water, with the polar part in the water and the lipid part in the air due to the natural hydrophilic and hydrophobic properties of the molecules. In membranes that have aqueous solutions on both sides, the molecules form a bilayer. The hydrophobic portions face each other on the inside and the hydrophilic portions face outward in both directions toward the water. The membrane is fluid and the molecules move around, but maintain their orientation because of the hydrophilic and hydrophobic forces acting on the membrane molecules. The membrane is permeable to lipids, but not many polar molecules, so cells have evolved to include various molecules embedded in the membranes which let specific types of molecules through (see figure 1 below).

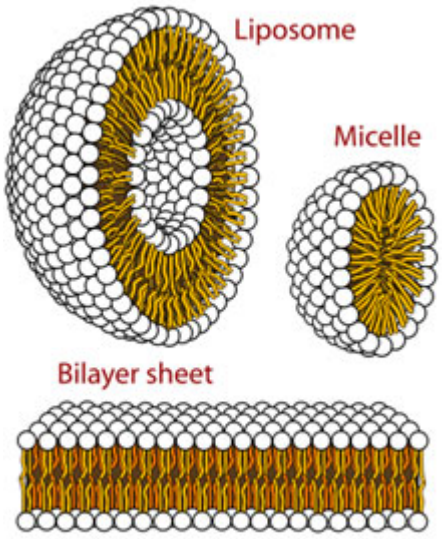

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Figure 1

We will work on the concept of self-assembly with a kinetic activity. We will study soap bubbles as a great example of self assembly. This will be especially helpful in understanding the cell membrane since both are based on polarity of water. They will see a hydrophilic and hydrophobic assembly in action.

Bacteria

In general, bacterial cells are much smaller (about two micrometers) than eukaryotic cells (about ten micrometers). Eukaryotic cells are the cells we are most familiar with, such as human cells. Prokaryotic, for

instance, bacterial, cells are much simpler, without many of the various components of the more advanced eukaryotic cells. There are two key differences in bacterial cells that are relevant to this unit. First, bacteria generally have a cell wall, which eukaryotic cells do not. The cell wall is outside of the cell membrane, which all cells have. Because the cell wall is made of materials unique to it, antibiotics can disrupt the bacterial cell wall without affecting eukaryotic cells. The second key difference is the inclusion of plasmids in the cytoplasm of bacterial cells. Plasmids are small circular strands of DNA that are normally independent of the chromosomal material. They are found in the cytoplasm of the bacterial cell. They generally carry several genes. There can be up to nine plasmids in a bacterial cell. They are, in fact, nanomaterial inside the cell. Plasmids can be passed between individual bacteria of some species, which results in the rapid spread of a gene, for instance, antibiotic resistance between individual bacteria that are not daughter cells. They can also replicate when the rest of the bacterial genome replicates, so can be passed on to both daughter cells.

DNA

Generally, DNA is found in the nucleus of the cell. It is a double strand of nucleic acids. There are four base pairs, thymine and adenosine, guanine and cytosine. Because of the pair formations, one strand of DNA is considered the positive and one is considered the negative. DNA can partially unravel to be copied. Messenger RNA (mRNA) will make a "negative" copy of the "positive" side of DNA. mRNA then goes into the cytoplasm and attaches to ribosomal RNA (rRNA), which provides a surface for the interactions of the mRNA and transfer RNA (tRNA). The mRNA then bonds with tRNA, each of which carries one of the twenty amino acids in humans. A codon of three nucleic acids in tRNA codes for each amino acid. As the tRNA brings each amino acid and attaches it to the next amino acid, they bond and the tRNA drops off. Because of the specificity of the strand of mRNA and the tRNA, a specific protein is built from each strand. There are many regulators involved in the system, but that is the basis. DNA codes the RNA, which makes the protein, which does the actual work in the cell. The nucleic acids that are relevant to this unit which are external to the nucleus are mRNA, rRNA and tRNA. In prokaryotes, there are also plasmids made of DNA, as previously mentioned, which can also code for proteins. As previously mentioned, plasmids can be transferred from one bacteria to another. If the plasmid codes for a protein that can confer resistance to an antibiotic, this can have major consequences as it can be shared with previously susceptible pathogenic bacteria.

DNA transfer

There are three ways for bacteria to transfer DNA to each other. The first is transformation. A bacterial cell is lysed and releases free DNA. Another bacterium takes up fragments of the free DNA and recombination of the DNA takes place. The second method is transduction. Bacteriophages, which are viruses that infect bacteria, integrate viral DNA into the bacterial DNA to make new viral components. When the viral DNA is cut from the bacterial DNA to form virions within the cell, sometimes bacterial DNA comes with it. When the bacteriophage infects the next cell, the bacterial DNA from the first can combine within the new bacterium. Finally, conjugation is the third method used by bacteria to share DNA. Two bacteria close to each other physically can share both chromosomal DNA and plasmid DNA. In E. coli, this is shared via a small structure one of the bacteria makes called a sex pilus. It is a rod that extends from the donor to the recipient bacterium. Portions of the chromosomal DNA are transferred and can combine with the DNA of the recipient. Plasmids can also be transferred. They generally replicate with the genetic material of the cell and are passed to daughter cells as well as transferred through conjugation. Some carry genes coding for antibiotic resistance proteins, which enable the bacterium to resist chemical antibiotics. Because of the ability of bacteria to pass this resistance to daughter cells and to other cells, antibiotic resistance is growing.

Specific examples

Streptococcus pyogenes is a common cause of disease in children and young adults. Most adolescents have heard of strep throat and know that they need to go to the doctor. S. pyogenes is a gram positive coccus susceptible to penicillin, which is the drug of choice. Penicillin is classified as a beta-lactam. Beta-lactams inhibit cell wall synthesis. Since human cells have no cell wall, *S. pyogenes* can be killed by the antibiotic with relatively little toxicity. It is extremely important to treat strep throat, not because of the disease itself, but because of the possible sequelae. Because of the cross reactions of anti-streptococcal antibody, the patient can develop rheumatic fever, which affects the heart, or glomerulonephritis, which affects the kidney. It is extremely important for the patient to complete the entire course of antibiotic treatment. If they take penicillin only until they feel better in two or three days, they will destroy the easily susceptible bacteria. The more resistant strains will be left to reproduce and continue the infection. The patient will have depopulated most of his or her "beneficial" bacteria and the infection will be more difficult to cure the next time. The interrupted course of antibiotics can also affect other areas of the body and other bacteria, leaving the patient without normal flora and open to pathogens that are more resistant to penicillin than the normal flora.

Virus

Viruses are in the nanometer size range, most being less than 100 nanometers. Bacteria are larger, typically 1 micrometer, and can be seen with a light microscope. Often they are stained, to be seen more clearly, but sometimes they can be visualized without staining using special optics, such as in phase contrast microscopy. Bacterial colonies are easily visible by eye when grown on agar. Viruses, however, are not visible with a light microscope, not even the largest of them. They can be seen only with electron microscopes. Bacteriophages, which are viruses that attack bacteria, can be visualized macroscopically by looking for holes in colonies, where the viruses have destroyed bacteria. Colonies of viruses are not visible.

Viral particles are not considered living entities. They are intracellular parasites. Most viruses consist of a protein coat and either RNA or DNA. The protein coat can be regular or irregular. It is often icosahedral, consisting of twenty flat sides. Some viruses have an envelope on the outside. Some have proteins on their surface to aide in identification of their host cell. Their only biological function is to invade a host cell and reproduce using the host organelles, hence the current theory that they are non-living. The DNA from the virus integrates into the DNA of the invaded cell and takes over its function. In the case of RNA viruses, a viral enzyme, reverse transcriptase, transcribes a DNA strand to integrate into the host chromosome.

Viruses are far too small to have even the fairly simple cell structure of a bacterium. The protein coat is a self-assembling structure that many of the manufactured particles in the nanotechnology field are based on. Many viral coats are icosahedral. Twenty identical proteins self-assemble into the coat. It becomes a regular polygon with identical faces and angles. There are some additions to different types of virus. Some cover the protein coat with the cell membrane of the host as they leave the cell. Viruses are very specific parasites and target only one type of cell. There are often discrete proteins imbedded in the protein coat, which react with proteins on the host cell's surface.

Because of their incredibly small size, and their dependence on host biochemical mechanisms to propagate, they cannot be destroyed by conventional means. There are antibacterials that target various cellular functions and necessary proteins of bacteria. There are antiparasitics that target Eukaryotic parasites. Because viruses do not have unique biochemical functions outside of the host cell to target, they are much more difficult to destroy without destroying the host cell. They become integrated into the DNA of the living host cell. DNA is necessary to make proteins, through a complex process of translation and transcription,

briefly described above. When the cell cannot replace necessary proteins, it will die fairly soon.

Viruses have much in common with human-made nanoparticles and, in fact, some of the basis for the nanotechnology uses information gained by studying viruses. Virus protein coats are self-assembling, just as many of the nanoparticles, such as buckyballs, are. They are specific for certain cells, which is much of the basis of nanotechnology, at least in the medical field. Much of the emphasis now in nanotechnology is to deliver drugs. The delivery site of the drug depends on the disease being targeted. Cancer drugs target the specific cancer cells present in the patient, for instance. By studying how viruses attain their specificity, scientists can mimic them and add proteins that bind with surface proteins on the cancer cells. That would save patients from some of the terrible side effects of the anti-cancer drugs. Doctors could use a much stronger dose delivered directly to the cancer cells, instead of throughout the body. Then the virus enters the cell and either integrates viral DNA directly into the chromosome or, in the case of retroviruses, makes a DNA copy of the RNA genome and integrates it into the chromosome. It also activates its own genes and deactivates the host cell genes.

Practical applications

Currently human insulin can be made within bacteria by introduction of a special plasmid containing the insulin gene. According to the pamphlet available at nih.gov, the gene for the human insulin was inserted into a non-disease producing E. coli. The bacteria produces the insulin, which is harvested and given to the patient. E. coli is a natural bacterium that we all have and the non disease producing type actually blocks out pathogens in our guts. Our bodies do not make antibodies against this insulin. The old insulin was usually made in pigs, since they are close to humans physiologically. This sometimes caused an immune reaction since the pig insulin is slightly different from human insulin. Actually inserting the human gene for insulin solves this problem. The insulin still has to be given to the patient. Imagine if we could insert a gene for insulin directly into the patient's pancreatic cells. That would cure at least one type of diabetes and the patient would no longer have to take insulin or deal with the side effects of diabetes.

HIV

The unit will concentrate on HIV. It is a well-known virus, and is a focus of the California health standards for high school. It is an RNA virus, which is believed to have arisen fairly recently. Hypotheses on its origins have not been verified, but there is one that it mutated from SIV (simian immunodeficiency virus) when humans in West Africa were infected by chimpanzees. Knowledge of the virus came to the attention of the pubic in the 1970's and 1980's. Doctors were suddenly seeing otherwise healthy young men with unusual infections and cancers. Many competing hypotheses arose after it was finally recognized as a new disease agent. It was seen as targeting homosexual men at first and was thought to be a reaction to an inhalant used recreationally by many homosexual men. Some religious groups thought it was a punishment from God. There were hypotheses by many, especially the United States Army, that it was spread by casual contact. At one point, the accepted hypothesis was that mosquitoes carried it, much like they carry malaria. Eventually, it was realized that the disease is spread through blood and body fluids and does not target homosexuals, but is a risk for any sexually active individual or for anyone in contact with blood or body fluids. In the mid 80's, HIV was isolated in three different labs and identified as a retrovirus. Two labs were in the United States, including Jay Levy's lab at University of California San Francisco, where I worked as a staff research associate in the late 1980's. It is classified as a lentivirus and has an icosahedral protein coat. It infects human lymphocytes mainly, specifically the helper T-cells. HIV attaches to a specific protein on the T-cell known as CD-4. This particular protein is named for the antibody that is used to differentiate helper T-cells from other kinds of T-cells. Since

these are the cells that target viruses, it has made treatment of HIV positive patients especially difficult.

Immune system

The immune system in humans is an incredibly complex organ system, which functions throughout the body to protect us from diseases. Knowledge about the immune system has grown rapidly since the identification of HIV. Lymphocytes, one of the five types of white blood cell, play a central role in immune response.

Lymphocytes are divided into two types, based on the type of immune responses they are most important in and on their surface markers. Surface markers are usually proteins that are incorporated into the membrane of the cell. They are important to scientists to distinguish between types of cells. They are often involved in the unique functions of the cells as well. Scientists have developed antibodies to surface markers on lymphocytes to distinguish types. Antibody mediated response is mainly done by the B-lymphocytes. Each carries a specific antibody on its surface and can bind a specific antigen, generally a protein. In general antibody antigen actions can be represented like an old-fashioned lock and key. Each antibody can react with one antigen and vice versa. If a B-cell finds its corresponding antigen, it can transform to a plasma cell and begin producing many antibodies. T-cells have different surface antigens and hence different functions.

T-cells

T-cells are involved in cell-mediated responses: they "assist" the B-cells, they produce cytokines (chemicals produced by cells which activate other cells), and they are the main defense by the body against cancers and against viral and parasitic attack. They can live up to eighty years. T-lymphocytes have been characterized by the antigens on their surfaces. The type heavily involved in HIV infection is called a T-helper cell or CD4 cell, using the terminology of the antibody used to characterize the cell. HIV particles attach to the T-helper cell. The virion, including the core that contains RNA and enzymes enter the cytoplasm, leaving the membrane cover outside of the cell. Reverse transcriptase, an enzyme unique to retroviruses, then makes a DNA copy of the viral RNA, which can insert into the nuclear DNA of the T-cell. The DNA can be quiescent in the cell for years. At some point it will subvert the protein-making capability of the cell. At that point, all of the mRNA and tRNA in the cell will be involved in making protein coats and viral enzymes, in support of production of more virus particles. The DNA in the nucleus will be directing the mRNA and making viral RNA. Each protein coat will self assemble and will be large enough to include some viral enzymes and the viral RNA. In the end, a typical infected cell will contain a million assembled virions, which will burst the cell.

At the point where there are less than two hundred T-helper cells per cubic centimeter left in the blood of the HIV positive patient, he or she is considered an AIDS patient. At that point, there are too few T-helper cells to fight off infections and cancers. AIDS patients have infections that are normally seen only in immunocompromised patients, which helped doctors realize that a new disease was emerging in the 1970's and 1980's. Some of the common presentations of AIDS patients are infections with Cryptococcus and Candida (yeasts), Toxoplasma (a parasite), various viral diseases (CMV, herpes, papiloma virus), Kaposi's sarcoma and lymphomas (cancers) and mycobacteria (bacteria usually causing a cell mediated response in disease such as tuberculosis and leprosy).

Medications

A bacterial infection such as strep throat, caused by Streptococcus, can be cured relatively easily by penicillin, destroying all of the bacteria causing the disease. This is not true of viral infections. The antivirals in use today are only a treatment: none are cures. A common cold, caused by rhinovirus, can only be endured with some

relief of symptoms by medication. There are approximately forty antivirals in use, about twenty of which are specifically anti-HIV. The first class of anti-HIV therapies was the reverse transcriptase inhibitors. As was previously mentioned, reverse transcriptase is an enzyme found only in retroviruses, those that carry RNA as their sole nucleic acid. There have been hopes of a cure by targeting reverse transcriptase, but none of the treatments so far have eliminated the virus totally in an infection. AZT is the oldest of the medications used to treat HIV. It inhibits reverse transcriptase activity and HIV replication, but does not affect viral DNA integrated into the chromosome of the T-cell. AZT is also quite toxic to humans. The same problems have been found in other reverse transcriptase inhibitors: they reduce HIV replication but are toxic to various organs in the human body. Protease inhibitors are the second classification of HIV inhibitors. Protease is a viral enzyme that is necessary to viral reproduction, forming protein units for the viral particles. Protease inhibitors do not eliminate infection by HIV, but do inhibit reproduction. They also can be quite toxic to humans.

Currently the trend is to do combination therapies, using several different drugs, inhibiting the virus and minimizing the toxicity to the patient. Last year, an HIV positive patient came to health class with a rolling suitcase full of his medications and an explanation of his medication schedule. It was an extremely eye-opening experience for my health students. Still, with the set of antivirals now available, patients infected with HIV can expect to live much longer and stay healthy much longer than was possible in the 1980's or even the 1990's.

Importance of correct use of antibiotics

Since the middle of the twentieth century, there has been a constant race between humans and bacteria. Humans develop new antibiotics to kill bacteria and bacteria develop resistance. Multiple drug resistant bacteria have become more of a problem with modern times. As we take more medications, we select for more resistant bacteria. When penicillin was first identified as useful against disease, it was hailed as a miracle cure. As it came into common use, some diseases that had been curable became incurable. As our knowledge increased, scientists realized that the bacteria were fighting back. As we take antibiotics, we actually select for resistant genes. Some bacteria are naturally more resistant to antibiotics than others. They can carry various genes that interfere with the actions of antibiotics. These are naturally occurring, just as antibiotics like penicillin are naturally occurring protections by fungus against bacteria. As we take more antibiotics, the more susceptible bacteria are destroyed and do not reproduce. If we take antibiotics as instructed, generally even the most resistant bacteria are destroyed, either by the dosage or by a combination of antibiotics with different actions. However, bacteria that are resistant can sometimes survive and, with exchange of plasmids, can sometimes survive even combination therapy. If most other bacteria in the ecosystem are destroyed, the resistant bacteria can multiply rapidly without competition for resources. Then, the disease can no longer be treated with the formerly effective antibiotics. Adding to this in a probably very significant, but not yet measurable way is our current system of raising animals for food. They are also given antibiotics, but continuously if they are being raised in feedlots because of the rapid spread of disease from animal to animal. How does this affect humans who eat the beef or chicken? We are not yet sure, but it probably contributes to the problem of antibiotic resistance in human bacteria.

Antibiotic resistance is an extremely visible problem is in hospitals. The rise in *Pseudomonas aeruginosa* infections is a huge problem in every hospital. Generally, *P.aeruginosa* infections are nosocomial, meaning that they are acquired within the hospital. They are rapidly spreading bacteria and will overgrow other types of bacterial colonies quickly. This causes a problem in microbiology laboratories, as it is difficult to obtain a pure culture of the bacteria being cultured when P. aeruginosa is present. It invades as a secondary infection in wounds and also causes post surgery infections. *P. aeruginosa* has become resistant to most antibiotics due

to exchange of plasmids and overuse of antibiotics and must be treated aggressively with multiple antibiotics.

Another example is methicillin resistant Staphylococcus aureus. All over the dormitory at Yale, as at universities everywhere, I am seeing signs to be careful of methicillin resistant *Staphylococcus aureus*. This bacterium causes necrosis of tissue and can be deadly. It has recently become huge news because of the methicillin resistance and has been responsible (along with H1N1 virus) for schools putting hand sanitizers and automatic paper towel dispensers everywhere, even in a time of major budget crisis, when many schools cannot afford the most basic supplies. Methicillin is a beta lactam antibiotic that is the preferred treatment for *S. aureus. S. aureus* is a common cause of nosocomial infections. It is very invasive and has acquired antibiotic resistance, especially those bacteria found in a hospital. It has also become a problem in the community now. It can cause rapidly spreading necrosis of tissue and can be fatal if not treated quickly and appropriately.

One thing we can do to combat the rapid rise of multiple resistant bacteria is to understand and take medications properly. Many patients do not take their prescription medications as directed. Many share their prescription medications with others. If we understand why bacteria and viruses are different and why antibiotics are prescribed for one group and not the other, there will be a decrease in misuse of medications. Specifically, this unit is designed to decrease the use of antibiotics without a diagnosis of bacterial infection. Many people actually have a viral infection, take antibiotics, do not get better, and so stop the antibiotics. Or, conversely, they have a bacterial infection, feel better in two days and stop the medication. They are actually selecting for resistant bacteria by doing this. All of the nonresistant bacteria are killed quickly. Because of the interrupted dose, the resistant bacteria are free to grow. When the bacterial infection reemerges with mostly resistant bacteria, it will be very difficult to treat and may require exotic and expensive antibiotics or treatment with multiple antibiotics at once. If the person with the viral infection has a secondary bacterial infection, the same problem arises. They have killed most of the bacteria through misuse of an antibiotic and have selected for antibiotic resistant bacteria. Again, the secondary infection will be difficult to cure.

This unit, health and the invisible world, will address several of the California health standards for high school. It will involve learning about HIV and the dangers in contracting the disease. This is an important part of our unit on sexually transmitted disease. Students need to know that it is an incurable disease and why. We also learn about use and misuse of prescription drugs. As bacteria seem to be winning the war, this becomes more important. As pharm parties become more popular among younger adolescents, this may give them another reason to avoid this dangerous practice. Pharm parties are gatherings of young people, usually college or high school age. Everyone brings prescription drugs, their own or stolen from relatives usually. They throw them in a bowl and pull out pills and take them, with no knowledge of what they are or what they do. Possibly it will also make the students think twice about participating in pharm partiesand the dangers in taking prescription drugs with no idea what they are or what they are for. It also covers general information about communicable disease. Students will also be able to understand the some of the challenges involved in nanotechnology, especially the dangers of the original nanotech device, the virus.

Strategies

This unit will take two weeks of class time. My health students are mainly high school freshmen. I always have some sophomores, juniors and seniors as well, since there are some students who transfer in without prior health credits or delay taking health for various reasons. Almost all of the special day class students and resource students take health with me, so I often have a high percentage of students with learning disabilities. I generally find that students learn much better when they are actively involved in what they are learning. Because Oceana was founded on the principles of the Coalition of Essential Schools, we are very activity oriented. One of the principles is depth over breadth, so we try to explore concepts as deeply as we can. Another is teacher as coach. The student is in charge of his or her own learning with guidance from the teacher.

Because nanotechnology is such a size related concept and because I need the students to clearly understand size differences between bacteria and viruses, we will start with size concepts. First we will begin with a powerpoint or keynote presentation about size differences. I will have a comparison chart with meter compared to micrometer and nanometer. We will do some simple activities associated with this slide presentation, such as figuring out if you start with a decimeter long strip of paper and cut it in half each time, how many times would you have to cut it to get to the nanometer scale? Then we would see how many cuts they could actually make. We will also do some estimating, starting with simple ones and working up to how many 20 nm virus particles would fit into a 10 micron cell? Students would have to be in groups for this since they are on variable levels in math.

The next major topic will be self assembly. We will start with blowing bubbles outside. Students will be assigned to small groups with assigned roles. Students will be asked to closely observe the bubbles and come back into the class and record observations about the bubbles. They will then go on to brainstorm ideas about why the bubbles do what they do. Then we will do a powerpoint or keynote presentation on self assembly, with explanations of bubble formation and expansion to cell membrane formation.

Students will be given handouts about various baterial and viral diseases. Each group will make a poster about their particular organism with facts about the disease and characteristics of the organism. Groups will do brief presentations on their particular topic. Groups with a virus will make a model of the virus with tag board that assembles into icosahedral shapes. Groups with a bacteria will draw a picture of a rod or coccus. I also want to do a shape sorting activity to show the specificity of the infecting organism. Students will be required to take notes and grade each group as they present.

We will introduce the topic of antibiotic resistance and selecting for resistant bacteria. I want them to take a bag of mixed beans of two different colors and envision them as susceptible and resistant bacteria. We will then "kill" all the bacteria in the bag. Starting over, we will stop our antibiotics early and only "kill" the white beans, but leave all the red beans.

We will finish with a brainstorm about the information from the week. We will come up with strategies to inform others about bacteria and viruses and to teach them about proper use of prescribed medication. The brainstorm will also give us all a chance to clear up misconceptions and extend the lesson if necessary.

Lesson plans and activities

We are on a block schedule, so have one hundred minute periods every other day. Therefore, two weeks of lessons will occur over five days, rather than ten days.

Day 1

Introduction of topic, concept of size

The opening activity will be a quick write. Quick writes are a short writing done by the students, generally at the beginning of class. I use them as a transition, review or introduction. Students write for a set amount of time, I usually do five to ten minutes. I am usually looking for prior knowledge or for how well they understood a concept or giving them a chance to give me their opinions privately. Students will write a minimum of four full sentences on the topic of "Why do we have hand sanitizers in every room in the school?" As soon as they are finished writing, they will do a pair-share. I will put them into groups of two, they will quickly discuss what they wrote and each student will report on what his or her partner said.

Next, I will introduce the idea of communicable disease, a short lecture, with time for questions. If there is time, I will also have them read a short section in our health book and will randomly pick students to answer questions on the reading.

I will then show a power point about size. It will include a meter chart with sizes from kilometers to nanometers. We will put a category of plant or animal at some levels, such as redwood tree at about one hundred meters, a giraffe at three meters, and a fly at one centimeter. We will include a calculation on halving numbers, how many times would it take to go from 100 km to 100 m, from 100 m to 100 cm, from 100 cm to 100 nm.

We will take strips of paper, cut at 100 cm, and scissors and see how many times we can cut them in half. What size are the last cuts? How many cuts would it take to reach 100 nm?

To extend the concept, we will do some guesses about various things. How many soccer balls would fit in the earth, how many 100 nm particles would fit in a soccer ball? I will model the math and give a treat to the person with the closest guess. The final part of this activity will be calculating how many 20 nm virus particles will fit into a 10 micrometer cell.

We will end the day with a debrief. What did they learn? How different in size are objects on the earth, including bacteria and viruses? I may do a round robin with a chance to comment on sticky notes and put them on chart paper around the room, or just do a class discussion if we do not have enough time.

Materials needed: powerpoint with meter chart, size comparisons, pictures, last slide halving numbers; strips of paper 100 cm long, scissors

Day 2

Self-assembly

I will start with soap bubbles. Each group of four, which I will assign, will be given wands and a bucket of soap

to make bubbles with. They are to note the shapes, sizes, colors and properties of the bubble and theorize on why the bubbles have those properties. Each group will then report to the class on their observations and theories.

I will then show another powerpoint on self-assembly, with soap bubbles and incorporating figure 1 above to explain in simplified terms what hydrophobic and hydrophilic mean in practical terms. I will also include an introduction to self-assembling nano particles and viruses.

We will do an activity on self-assembly at this point. I have a picture of an icosahedron that looks like it will never form a shape. I will copy it onto tag board and have the students make their own viral protein coat. We will also put a length of string inside to represent DNA.

We will preview day 3 by assigning groups and giving a handout on their disease to each group. I have several handouts on various diseases, what causes them, the symptoms, cure if there is any, as well as prevention. I have classes of thirty-four students, so will do eight groups of four to five, each with a communicable disease. I will give some viral, including flu and HIV. I may include one fungal disease, since they are quite common. I will include both sexually transmitted infections and non-STI's. They will be given some time to strategize their presentations.

Days 3 - 4

Disease presentations

Groups will be allowed to choose their format for presentations. They may do posters, they may do a skit or, if I have the computers available, they may do a powerpoint presentation. They will be given time in class to work on their chosen form of presentation. They will receive a rubric that includes what information must be given accurately in the presentation, length of time, participation, clarity of presentation, etc. Students forming the audience will complete a note taking form, also for a grade, that includes a place to write information, an evaluation of the group presenting and an evaluation of their own group, including what work was done by each person. These are also for a grade. If students choose to do powerpoint, they may have to research pictures and/or diagrams either in the computer lab or on their own time and bring the results in a flash drive.

Materials needed: handouts on various diseases, be sure to mix viral and bacterial, include 2 to 3 STI's, including HIV, rubric for group presentation (I generally grade the rubric during the presentaton), note taking worksheet for each student

Day 5

We will start with a quick write-up on presentations. What did they learn that was new? What surprised them? I will have them discuss their quick writes in groups of four and have each group report to the class.

I will hand out a bag with a mix of red and white beans for nine groups of three to four students. Buried inside each one is a piece of paper with further instructions. Three groups take nothing and just count their beans. Three groups take their antibiotics incorrectly and take out all the white beans, but leave and count the red beans. Three groups take their antibiotics correctly and take out all the beans. Each group will be asked to speculate on what the beans represent and why the antibiotic took out some and not others. The disease presentations should give them enough background to explain.

Each group will do a calculation on how many of each bean there will be in ten hours if the population doubles every thirty minutes. Since three of the groups will have zero beans, they can calculate the number of white beans for the three groups with mixed beans. Then, they will calculate how many bacteria there will be if there is a limited amount of resources. I will have them do a proportion of white beans to red beans to show that the groups with no antibiotic will have few white beans relative to the red beans, the groups who took their antibiotic incorrectly will have all white beans, and the groups that took their antibiotics correctly will have none. The groups will then discuss what if the white beans carry a resistance to the antibiotic. What happened to the group that took theirs incorrectly? Why is this not a good idea? We will end this activity with a class discussion on implications of taking medications incorrectly.

The final activity will be a round robin. There will be chart paper around the room and students will be given markers. Some of the headings will be bacteria, viruses, antibiotics, etc and students can make a note of something they learned. One of them will have a heading of what can we do to prevent the spread of antibiotic resistance. We will end with a class discussion on the charts and see if students are interested in doing a community activity to spread the word to others on how important it is to take medications correctly.

Works Cited

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Bonner, John Tyler. *Why Size Matters: From Bacteria to Blue Whales*. Princeton: Princeton University Press, 2006. This book is a general introduction to the idea of size and how it is very different on the nanoscale vs. the macroscale.

Bryant/Franis. *Eukaryotic Cell Cycle: vol 59 SEB Symposium (Experimental Biology Reviews)*. 1 ed. Washington, DC: Taylor & Francis, 2008. This book gives me more information on cell reproduction and DNA replication.

Enquist, L. W., S. J. Flint, and V. R. Racaniello. *Principles of Virology: Molecular Biology*. Washington D.C.: Asm Press, 2008. This book gives me insights into general virology, structure and reproduction.

Falvo;Taylor;Broadwell, Jones;. *Nanoscale Science*. Arlington: NSTA Press, 2007. This book is useful in giving me ideas for classroom activities.

Forbes, Betty A., Daniel F. Sahm, and Alice S. Weissfeld. *Bailey & Scott's Diagnostic Microbiology (Diagnostic Microbiology (Bailey & Scott's))*. 12 ed. St Louis, Missouri: Mosby, 2007. This book is helpful about virology, plasmids, antibiotic action, transmission of resistance to antibiotics and other laboratory related topics.

Krajcik, Joseph, Shawn Stevens, and LeeAnn Sutherland. *The Big Ideas of Nanoscale Science and Engineering: A Guidebook for Secondary Teachers (PB241X)*. Danvers, Ma: National Science Teachers Association, 2009. This book is useful in presenting the nanoscale background that I need.

Levy, Jay A.. *HIV and the Pathogenesis of AIDS*. 3 ed. Washington D.C.: Asm Press, 2007. This book has specific information about HIV and how it infects cells, as well as anti viral medications.

Pelesko, John A.. *Self Assembly: The Science of Things That Put Themselves Together*. 1 ed. Boca Raton: Chapman & Hall/Crc, 2007.

This book also has useful information on activities I can do in class.

Apendix 1

California Department of Education Health Education Content Standards, March 2008

3.2.G

Identify local resources concerning reproductive and sexual health, including all FDA-approved contraceptives, HIV/STD testing and medical care. We are touching on this standard as we focus on HIV during the student presentation.

5.4.G

Evaluate the risks and consequences associated with sexual activities, including HIV, other STD's, and pregnancy. We are addressing this standard as we talk about HIV and the fact that it is incurable.

1.5.A

Describe the use and abuse of prescription and nonprescription medicines and illegal substances. This is the key standard I am addressing with this unit.

1.4.P

Identify types of pathogens that cause disease. Our disease presentations and differentiating between bacteria and viruses address this standard.

1.5.P

Investigate the causes and symptoms of communicable and non-communicable diseases. Again, we address this in our disease presentations.

1.10.P

Explain how public health policies and government regulation influence health promotion and disease prevention. This will be looked at when we talk about the government strongly suggesting that schools install hand sanitizers.

3.2.P

Access valid information about common disease and biological function. The entire unit addresses this as we study common diseases and the roles of bacteria, viruses, and our bodies in disease.