

Unit 1 Cram Sheet

Lesson 1.1: The Mystery Infection

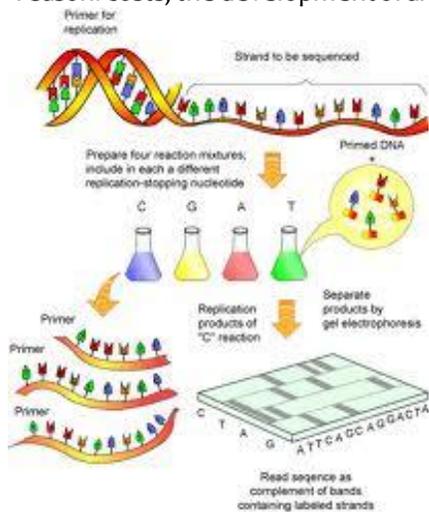
In Unit 1, we were first introduced to the meaning of “medical intervention.” Remember that a medical intervention is anything that is used to treat, prevent, cure, or relieve the symptoms of human suffering whether it is caused by a disease, accident, or something as simple as hygiene. Officially, a medical intervention is a measure to improve health or alter the course of an illness and can be used to prevent, diagnose, and treat disease. Medical interventions can be broken down into categories and grouped together. Some of the categories include: genetics, pharmacology, diagnostics, surgery, immunology, medical devices, or rehabilitation. There are many other categories used to group medical interventions, mostly for the purposes of comparing remedies used for patients.

Once we learned about medical interventions, you were introduced to the Smith family for the first time. Remember Sue? She, her roommates, and several other friends came down with a mysterious illness, and we then focused on the methods that were used to discover what was causing the symptoms, come up with a diagnosis, perform tests to confirm the diagnosis, and treatments for the disease. This is a routine often used in healthcare settings: someone comes to a healthcare provider complaining of something wrong, and the healthcare professional must figure out the problem and the best course of action to get the patient back to a healthy (or more healthy) state. In Sue’s case, an outbreak was suspected, so it was also our job to determine whether or not the disease had spread, and how to manage it if it had.

To figure out what was wrong with Sue and her friends, we completed the first step of a medical investigation: linking symptoms together and tying them to suspected disease-causing agents. It may be helpful to go back to activity 1.1.2 and to examine the symptoms that all patients shared. Client issues that can be measured and recorded are typically referred to as signs – temperature, heart rate, blood pressure, rash, swollen glands, etc. – while problems the patient reports are considered symptoms – tiredness, sore throat, nausea, etc. These signs and symptoms are the ultimate clues that are used to find out what is making patients sick so that the all-important job of making patients better can be performed. The symptoms we discovered could all be caused by several different pathogens, so steps had to be taken to determine WHICH infectious agent was making Sue and her friends sick.

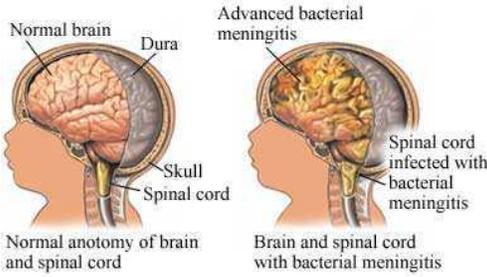
We also had to figure out the root cause of the infection. In the case of a disease outbreak, finding “Patient 0,” the first person infected at a site, can help medical professionals to determine what the disease was, how it spread, and who was likely exposed so that they, too, can get help.

OK – so, we had sick people. We thought we knew what was wrong with them: bacterial meningitis. What has to be the next step? Yep – we need to begin trying to confirm this diagnosis. You don’t want to give treatment to people who aren’t sick for all kinds of reasons: costs, the development of antibiotic resistance, making a misdiagnosis and having your patient get sicker, etc. – so it is important to know FOR SURE what is responsible for any disease, and especially an outbreak. We used two separate procedures to determine if our patients actually had meningitis, with the first being an application of bioinformatics (Bioinformatics, the collection, classification, storage, and analysis of biochemical and biological information using computers, can be used to identify disease pathogens) through the use of a program called BLAST. Essentially, this is a form of DNA sequencing – scanning the DNA of something to figure out what the heck it is. The first step was isolating the disease-causing agent. In the case of meningitis, a disease that causes bacteria to build up in the meninges of the brain and in the spinal fluid, a sample of cerebrospinal fluid (CSF) is taken by doing a spinal tap. The CSF is then processed to separate human components from disease-causing agents. For bacterial infections, this is done through “plating” the CSF, which will allow any bacteria growing in the CSF – where there should be NO bacteria EVER – to grow outside the human body. If bacteria grow, that’s your first sign that something is really, really wrong. Once bacteria are grown, they are lysed (blown up) and their DNA is isolated. This DNA is amplified, then run through a machine that completes DNA sequencing. The machine “reads” the DNA of whatever goes through it and produces something people can see – a long string of the letters A T C and G. This sequence can then be



input into BLAST, where the DNA sequences of millions of genes and whole organisms are stored. BLAST compares the DNA sequences input into it to its large database. It then tells whoever asks the identity of the agent the DNA belonged to. In this case, the procedure was able to reveal that several people did, indeed, have bacterial meningitis. Others, however, did not, and we learned that some of Sue’s other friends had the diseases infectious mononucleosis, Strep throat, and influenza. It may be helpful for you to look up the effects of all four of these diseases, as they will not be discussed here.

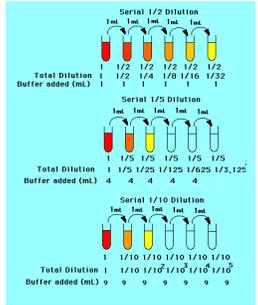
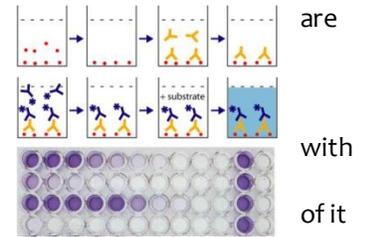
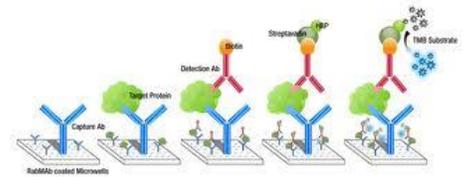
Because meningitis is such a serious disease, we also did a second test that helped us confirm whether our clients were sick with it (or not). This test also revealed HOW sick the patients were. Sounding familiar? Hopefully, the ELISA test is in your mind right about now. ELISA stands for Enzyme-linked Immunosorbent Assay. This is a test that takes advantage of some of the body's natural immune



responses to identify the presence of illness. Understanding this test requires you to know the difference between an antigen and an antibody. An antigen is really a type of protein found on the outside of every living cell (and virus!). Antigens are surface markers that cells use to identify each other. It's how your body knows that your body cells are truly yours, and they are how your body identifies cells and viruses that aren't yours. Antigens on the outside of a bacteria are very different than the antigens on your own cells. Because of this, your body's immune system cells (white blood cells) are able to identify them and mount a defense against them, hopefully killing those pathogens before they can make you sick or kill you. If a pathogen is able to get through your non-specific defenses (skin, mucous, urine, etc.) designed to keep things OUT of your body,

then more specific defenses are activated. One of these defenses is antibodies. These are produced by a type of leukocyte called a B lymphocyte. The job of antibodies is to attach to foreign antigens. By attaching, those foreign antigens are neutralized. That attachment also signals other types of leukocytes (T lymphocytes) to come in and destroy whatever the antibody is attached to. So, antibodies attach to antigens. That is the principle behind an ELISA.

The ELISA test is based a very simple concept: color changes mean a positive result, with stronger colors meaning more of whatever you're testing for is present. It is found in pregnancy tests, rapid strep test, and drug tests as well as being used to test for antigens from all kinds of infectious agents including bacteria, viruses, and worms. The ELISA test begins with a pre-treated tray full of small wells. These wells are pre-coated with antibodies for the pathogen being studied (in this case meningitis). The serum of patients is then added to these wells. If the serum (CSF for meningitis) contains the bacteria *Neisseria meningitidis*, the antigens on the outside of those cells will be bound to the antibodies in the wells, trapping the antigens on the wells using antigen-antibody interactions. So, now the antigens are trapped, but that doesn't show us anything. The ELISA test relies on a visible color change, and nothing is visible yet. To make this test something with visible results, MORE antibodies are added. First, something called a primary antibody is added. The role of this is to latch on to the antigen, forming a platform on which a secondary antigen with an enzyme attached can be added. This is the next step – adding the second antigen which is linked to an enzyme. Finally, a substrate is added that the enzyme responds to. The enzyme acts on the substrate and causes a color change. IF a color change occurs, it means that the antigen (the infection) is present. This is a qualitative result, meaning it is something that is simply observed (hot/cold, soft/hard, clear/blue). Qualitative results are not measurable. The intensity of the color can be used to find out the degree of infection, with the darker color meaning a greater infection. This is actually measurable (quantitative) if you have



created a serial dilution to compare it to. A serial dilution is something that is created and used to compare the results of an ELISA to. It involves beginning a known concentration of antigen (say 100 ng/mL) and diluting it (watering it down). It involves placing that 100 ng/mL sample in a well, transferring part to a new well with a set amount of water. If you use equal parts water and antigen, 100 becomes 50. In the next well, it's repeated to reduce the amount of antigen to 25, then 12.5, then 6.25, and so on. When the antibodies and substrate are added to this a series of colors, from darker to lighter, is created. These samples have KNOWN amounts of antigen. Patient samples can be compared to this to determine how much of the infectious agent is in the body, which is often extremely useful in determining how aggressive to be with treatment. It can help doctors to determine how much antibiotic to give, how long

care will be needed, and how it is that permanent damage will result. In our scenario with Sue, this test revealed which patients actually had meningitis, and who had the greatest concentrations of the antigen. Knowing that makes it possible to make a reasonable assumption about who got the disease first – whoever had the most antigen was probably the first person infected.

Lesson 1.2: Antibiotic Treatment

Now that we know for sure that Sue has meningitis, and we know which of her friends have the same infection, what's next? If you're thinking we need to treat the infection, you're right! Bacterial infections are treated with antibiotics.

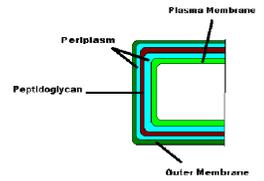
We know that antibiotics kill bacteria, but why? Understanding that requires knowing what bacteria are and how they work. A couple years back, we discussed how most bacteria are either gram positive or gram negative. Gram positive bacteria have a very thick cell wall made mostly of peptidoglycan, while gram negative bacteria have a much thinner cell wall. Sometimes, this influences how they respond to antibiotics.

Bacteria are classified into two main groups, Gram positive bacteria and Gram negative bacteria, distinguished by the structure of their cell walls.

Gram Negative Bacteria

- The cell wall contains multiple layers, including a thin layer of *peptidoglycan*.
- The outside layer is called the outer membrane, which is made of a lipid bilayer whose outside is composed of lipopolysaccharides called *endotoxins*.
- The outer membrane serves as a barrier to the passage of most molecules and contains specialized proteins, called *porins*, which allow certain molecules to pass through the membrane.
- The region between the plasma membrane and the outer membrane is called the *periplasm* and is filled with a gel-like fluid and proteins involved in a variety of cellular activities.
- The Gram-stained cell is reddish-pink.

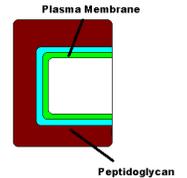
Gram Negative Bacteria



Gram Positive Bacteria

- The cell wall contains a thick layer of peptidoglycan and teichoic acids. There is approximately twenty times more peptidoglycan than the Gram negative bacteria.
- There is no outer membrane present.
- There are no porins present.
- The Gram-stained cell is purple.

Gram Positive Bacteria



Below, the chart lists some of the major components of bacterial cells and their functions.

Cellular Part:	Description:
Nucleoid	Gel-like region within the cytoplasm containing the single, circular, double-stranded DNA molecule. This chromosomal DNA is <i>supercoiled</i> , meaning tightly packed into a twisted form. The DNA contains all of the genetic information necessary for normal functioning of the cell.
Plasmids	Circular double-stranded DNA molecules. They are typically 0.1% to 10% of the size of the chromosomal DNA and only carry a few to several hundred genes. A single bacterial cell can carry multiple plasmids. Normal functioning of a bacterial cell is not dependent on the genetic information contained in a plasmid, but the DNA often codes for proteins that are advantageous to the cell. For example, plasmids might contain the information coding for the proteins that enable the cell to destroy or be immune to certain antibiotics. Plasmids can be transferred from one bacterial cell to another bacterial cell.
Ribosomes	Structures involved in protein synthesis. They facilitate the joining of amino acids.
Cell Wall	Rigid barrier that surrounds the cell, keeping the contents from bursting out. <i>Peptidoglycan</i> provides the rigidity for the cell wall.
Plasma Membrane (also called the cytoplasmic membrane)	Semipermeable membrane that surrounds the cytoplasm of the cell. This phospholipid bilayer is embedded with proteins that act as a barrier between the cytoplasm and the outside environment.
Capsule	A distinct and gelatinous layer, called <i>glycocalyx</i> , enveloping the cell. This layer enables the bacterial cell to adhere to specific surfaces and sometimes protects bacterial cells from human immune systems.
Flagella	Protein appendages that are anchored in the membrane and protrude out from the surface. The flagella spin like propellers, moving the bacterial cell forward.
Pili	Filamentous appendages which are similar in structure to flagella, but function in a different manner. Some pili enable the bacterial cell to attach to a specific surface (these pili are called <i>fimbriae</i>). Other pili are involved in <i>conjugation</i> , a mechanism of DNA transfer from one bacterial cell to another (these pili are called <i>sex pilus</i>).
Endotoxins	Lipopolysaccharide molecules that make-up the outer leaflet of the outer membrane of Gram negative bacteria. Endotoxins are different from <i>exotoxins</i> , which are proteins synthesized by both Gram negative and Gram positive bacteria and function as potent toxins.

So – we have bacteria parts, but what does that have to do with getting rid of an infection? What does that have to do with how infections are treated with antibiotics? Great questions! Antibiotics work by disrupting the pathways that bacteria use to survive. This may mean stopping the bacteria from reproducing, inhibiting protein synthesis, or disrupting the cell wall. Different antibiotics work in different ways – which is good because not all antibiotics work on all bacteria.

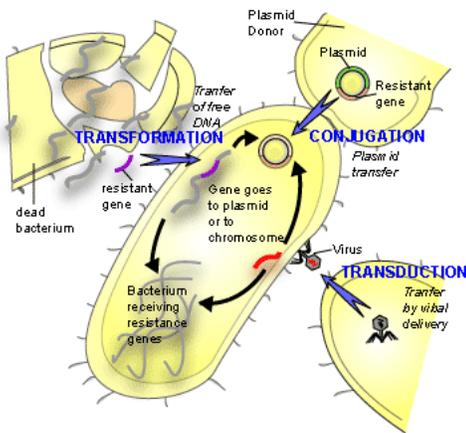
Mechanisms of Action of Antibiotics

A number of bacterial processes, including the synthesis of bacterial cell walls, proteins, metabolic pathways, and the integrity of the cytoplasmic membrane, are the targets of most antibacterial drugs. The following table outlines the mode of action for some of the main classes of antibiotics:

Antibacterial Medication:	Mode of Action:
β -Lactam Antibiotics	Irreversibly inhibit enzymes involved in the final steps of cell wall synthesis. The enzymes inhibited by these drugs mediate the formation of the peptide bridges between adjacent strands of peptidoglycan. These drugs vary in their spectrum of activity; some are more active against Gram positive bacteria; whereas, others are more active against Gram negative bacteria.
Tetracyclines	Reversibly bind to the 30S ribosomal subunit, blocking the attachment of tRNA to the ribosome and preventing the continuation of protein synthesis. They are effective against certain Gram positive and Gram negative bacteria.
Fluoroquinolones	Inhibit one or more of a group of enzymes called <i>topoisomerases</i> , which maintain the supercoiling of the chromosomal DNA within the bacterial cells. The inhibition of these enzymes prevents essential cell processes. The fluoroquinolones are active against a wide variety of bacteria, including both Gram positive and Gram negative bacteria.
Sulfonamides	Inhibit the growth of many Gram positive and Gram negative bacteria. They are structurally similar to paraminobenzoic acid (PABA), a substrate in the pathway for folic acid biosynthesis. Because of this similarity, the enzyme that normally binds with PABA preferentially binds with the sulfonamide drugs, resulting in its competitive inhibition. Human cells are not affected by these drugs because they lack this enzyme.

A good resource on antibiotic mechanism of action is the Howard Hughes tutorial found at: http://www.hhmi.org/biointeractive/Antibiotics_Attack/pw_1.html

At this point, we know that antibiotics work to stop bacterial infections from spreading. So, then, why not give them for everything? Why not take them all the time to prevent bacterial infections. The truth is, healthcare professionals used to do this regularly. It was standard practice to take antibiotics any time a patient even suspected an infection. Antibiotics were prescribed for everything, and doctors only delved further into a disease if the antibiotics didn't seem to help. This practice has ended in modern times because we have learned that bacteria are capable of evolving and becoming immune to antibiotics. They are able to become antibiotic resistant. Often, this begins with one bacterium that develops a mutation. This mutation may give it a stronger cell wall that can resist B-lactam antibiotics. It may mutate the way proteins are produced, so that tetracyclines don't work. No matter, the mutations that randomly develop cause the bacteria to evolve into something that an antibiotic doesn't work on. That bacteria then grows and divides, and suddenly there are even MORE bacteria with the same mutation. These divide, and lead to an infection with an antibiotic-resistant



strain of bacteria that is more difficult to kill, requiring better and stronger – and possibly completely new – bacteria. As if that isn't bad enough, there's another concern: bacteria are able to share the plasmids that contain antibiotic-resistant genes. There are three methods that are commonly used: transduction, transformation, and conjugation. Conjugation (bacteria sex) is the most common method. Here, two bacteria – which do not even have to belong to the same species – link their pili, forming a bridge between the two bacteria. A plasmid can be exchanged over this bridge, allowing a bacteria with antibiotic resistance to give the gene for that resistance to another (previously susceptible) bacteria. Plasmids carrying antibiotic-resistant genes can also simply be scavenged from a dead bacterial cell through the process of transformation. Additionally, resistance can be “delivered” to bacteria using some sort of vector through the process of transduction.

When bacteria gain antibiotic-resistance, treating them becomes a whole lot more complicated. There's no predicting when this will happen. There's no predicting how it will spread. We simply know that it does. We also know that not every infection will respond to an antibiotic in the same way, and there is no way to know whether the population of pathogenic bacteria you are treating will be controlled more or less quickly by the antibiotic than expected. Also, bacterial populations vary and the presence and number of antibiotic resistant bacteria will depend on the genetic variability in the population.

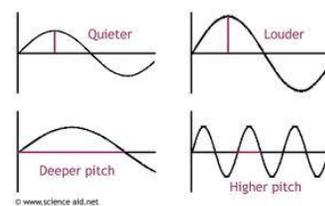
Because of antibiotic resistance, there is growing concern for the ways that we use antibiotics today. As stated earlier, it is less common for healthcare providers to give antibiotics as a preventative measure. It is less common for people to take them unnecessarily as we become more educated. However, they're used excessively elsewhere – for example, when raising livestock. Antibiotics are added to chicken and cow feed to prevent the animals from getting sick before sale. These antibiotics can stay in the meat and be passed to us – as can resistant bacteria in the meat. America is one of the few countries where this practice is used, and it is certainly likely to contribute to the development of antibiotic resistant strains of bacteria. Overprescription and overuse of antibiotics NOW is probably going to cause extremely scary problems in the future.

Lesson 1.3: Aftermath – Hearing Loss

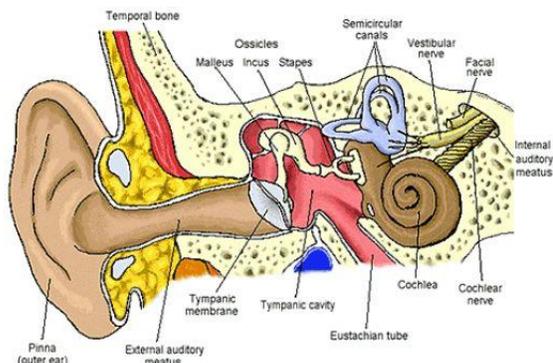
Well – let's get beyond the antibiotic scare, and back to poor Sue Smith's story. Sue had meningitis, got it diagnosed, and got it treated. Her life was saved, but not before the bacteria caused some permanent damage. Sue has hearing loss, which was diagnosed

by an audiologist. Hearing loss affects millions of people in the United States. Hearing loss can drastically impact a person's ability to communicate. Therefore, a lot of time and money has been invested into research to develop interventions to treat hearing loss. Although the degree of hearing loss varies from individual to individual, there are only three types of hearing loss: sensorineural hearing loss, conductive hearing loss, and mixed hearing loss. Hearing loss has many causes and in many cases can even be prevented.

Before we talk about the three types of hearing loss, you need to know the parts of the ear and their functions as well as some basic information about sound. We will begin with sound. You may recall that sound cannot travel through a vacuum. It must travel through something – air, water, or even bone. There are a few major aspects of sound: intensity (loudness) which is measured in decibels, This has a profound effect on hearing, as listening to loud sounds for prolonged periods can have a permanent impact of hearing – and not in a good way. Two other aspects of sound are frequency and amplitude. These two terms deal with the waves that sound produces. Frequency is the number of sound waves that cross a point in a certain amount of times. Sounds with the highest frequency produce more waves to pass a point, and sound higher in pitch. (Think of nails on chalkboard compared to thunder – the nails produce packed waves and the thunder produces very wide waves.) Pitch is the way we perceive frequency. (Nails vs. thunder – very different sounds) Amplitude deals with how high the waves are, which is what we perceive as loudness.

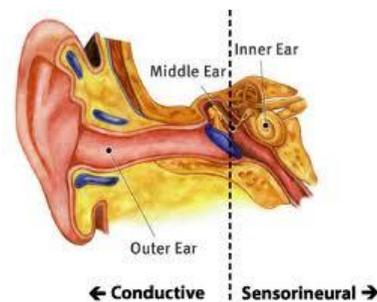


So, pitch is caused by how close together waves are (frequency) while intensity is determined by how tall the waves are (amplitude). This influences hearing in a couple ways. The human ears are designed to detect sounds in a set range of pitches and frequencies. Detecting this sound involves the ear. Sound is collected in the outer shell of the ear, called the pinna. This sound travels in air through the auditory canal until it reaches the tympanic membrane (the eardrum). Sound causes the tympanic membrane to vibrate. When the tympanic membrane vibrates and converts sound to mechanical waves, causing the ossicles (earbones) to vibrate. The malleus vibrates, causing the incus to vibrate, causing the stapes to vibrate. The stapes hits the oval window as it vibrates, pushing on the fluid inside the cochlea to vibrate in the form of a fluid wave. This vibration travels through the cochlea, stimulating the sensory hair cells, which are incredibly sensitive. Their stimulation results in a signal passing to the cochlear nerve, which sends a signal to the brain so sounds can be interpreted.

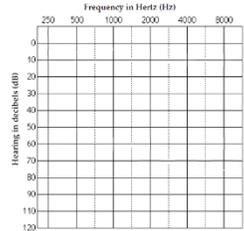
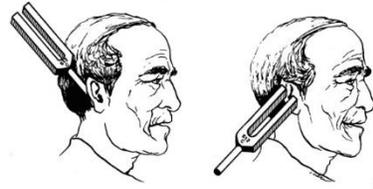


While the primary job of the ear is hearing, it also plays a role in balance. This involves the vestibule of the ear, which houses the semicircular canals. This is a set of three tubes that give you the ability to sense up, down, and sideways. Body position shifts fluids around in this area, allowing you to sense your position in space when the signals produced by the nerves in the canal send signals via the vestibular nerve to the brain. Also in the ear is the eustacian tube, which is there to maintain pressure within the inside and outside of the ear. If pressure is different, sound doesn't travel right!

At this point we've discussed sound and the parts of the ear. These both play a role in the different types of hearing loss mentioned earlier: sensorineural hearing loss, conductive hearing loss, and mixed hearing loss. Conductive hearing loss is caused by damage to the wave-carrying portions of the ear: the pinna, the auditory canal, the tympanic membrane, or the ossicles. This type of hearing loss usually involves a reduction in sound level or the ability to hear faint sounds. This type of hearing loss can often be corrected medically or surgically. It can be caused by a loss of the outer ear, damage to the tympanic membrane, or damage to the ossicles. With sensorineural hearing loss, there is damage to the cochlea (inner ear) or the auditory nerve. In many cases, it cannot be corrected. It can be caused by repeated exposure to loud noises, an extremely loud noise one time, or aging of the cochlea. Mixed hearing loss is a combination of both. In all cases, patients (like Sue) might benefit from a hearing aid. Hearing aids amplify sounds, making them louder to the person with a device in their ear and allowing them to hear better. Another option – for sensorineural hearing loss, anyway – is a cochlear implant. This is a small device inserted surgically in two phases, with a wire placed in the cochlea to do the job of hair cells and direct sound waves from the fluid in the cochlea to the auditory nerve, and with an external implant (on the head) to pick up sounds from around the patient. Because this procedure is very expensive, may result in complete hearing loss, and is offensive to the deaf community as an infringement on their lifestyle, it remains somewhat controversial.



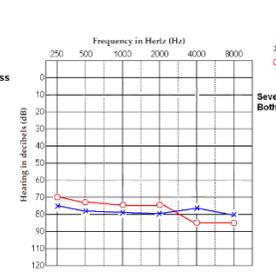
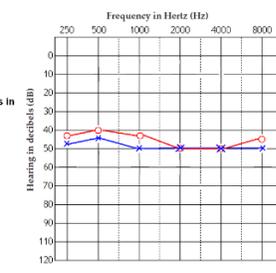
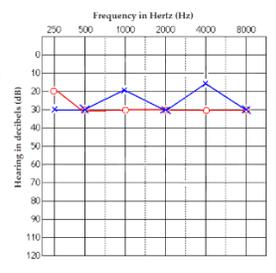
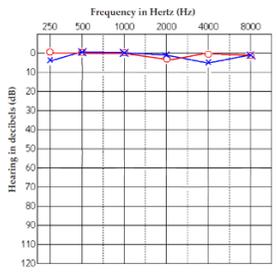
Earlier, it was stated that Sue suffered from hearing loss as a result of her meningitis. How is this tested for? There are actually several types of tests that can be performed. The Rinne test involves using a timer and a tuning fork to determine the difference between conductive and sensorineural hearing. Sensorineural hearing is tested by placing the handle of a tuning fork that has been hit on a table and is humming against the mastoid process on the skull and listening until the sound goes away while timing the length of time the patient can hear. When the sound is no longer heard, with no delay, the tuning fork is flipped and the pronged end is placed in front of the ear, with the patient listening again. Air conduction (conductive hearing) is checked in this way, with the tester then noting the time elapsed. If hearing is normal, the air conduction will be heard twice as long as bone conduction. If there is conductive hearing loss, bone conduction is heard longer or as long as air conduction. A speech in noise test can be done for some types of sensorineural hearing loss. This involves listening to speech with a background static of varying types and determining how well the patient is able to detect actual speech under those circumstances. If there is sensorineural hearing loss, hearing the speech will be incredibly difficult or not possible. Finally, there are audiograms, which detect both sensorineural and conductive hearing loss. Audiograms are made during a pure tone test. This involves using an audiometer to measure hearing sensitivity. The test will begin by playing a series of beeps or tones at a distinct frequency. Every time the subject hears the beep, they raise a finger or push a button or raise their hand. The tone will continue to get softer and softer until it can no longer be heard – determining the threshold for the patient for a certain frequency. The test is then repeated at other frequencies between 250 and 8000 Hz. An audiogram records thresholds, which can be used to detect where hearing loss exists at different frequencies. The thresholds are recorded on a graph, called an *audiogram*, with the frequencies on the x-axis and the hearing thresholds in decibels on the y-axis. The thresholds for the right ear are represented with a red circle and the thresholds for the left ear are represented with a blue 'X.' The following diagram is an example of a blank audiogram.



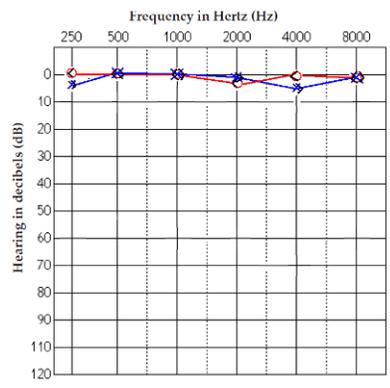
The Xs and Os are connected with lines to help keep track of the hearing levels across the different pitches. Hearing levels are often described in a progression of loss: normal hearing, mild hearing loss, moderate hearing loss, moderately severe hearing loss, severe hearing loss, and profound hearing loss. The following chart shows the ranges for each type of hearing level.

Normal Hearing	0-20 dB
Mild Hearing Loss	21-40 dB
Moderate Hearing Loss	41-55 dB
Moderate to Severe Hearing Loss	56-70 dB
Severe Hearing Loss	71-90 dB
Profound Hearing Loss	>90 dB

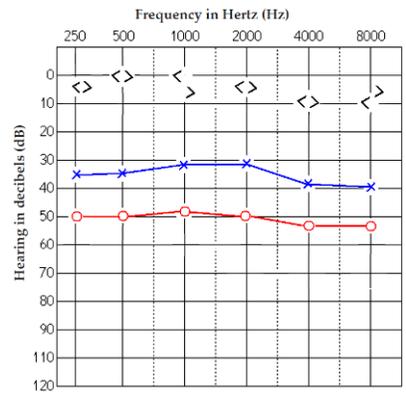
The figures below show example audiograms for different levels of sensorineural hearing loss in both ears.



Conductive hearing loss can also be represented in an audiogram. The air conduction levels are represented as Xs and Os and the bone conduction levels are represented as < and >. Because conductive hearing loss is due to problems with the middle ear, hearing levels are better with bone conduction than with air conduction. Conductive hearing loss is therefore represented when bone conduction is at least 10 decibels better than air conduction, after it has been determined with a version of the Rinne test. Below are two examples of audiograms. The audiogram on the left shows no hearing loss and the audiogram on the right shows conductive hearing loss.



X Left Ear
 O Right Ear
 < Bone Conduction Right Ear
 > Bone Conduction Left Ear

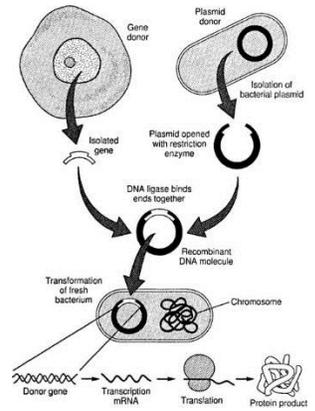


X Left Ear
 O Right Ear
 < Bone Conduction Right Ear
 > Bone Conduction Left Ear

Lesson 1.4: Vaccination

Are your ears ringing yet? Eyes blurring? Vision fading in and out? Drooling? Relax – we’re almost done.

We’ve spent a great deal of time discussing infections, how they are diagnosed and confirmed, how they are treated, and some of the serious consequences that they can have. The last thing that we need to look at is how it is possible to prevent getting an infectious disease in the first place. How is that possible? How do we keep ourselves from getting sick? No – the answer is not “live in a bubble”. Rather, the trick is to convince our bodies that we’ve *already* had the infection that we’re trying to prevent getting. This is done through a process referred to as vaccination. A vaccination is an injection of dead, weakened, or modified pathogens into the body. Their presence in the body activates the immune system, which responds to the substances within the vaccine the same way it responds to any other infection: by activating lymphocytes, producing antibodies, and then remembering that disease for a very long time so you don’t get it again. Antigens in the material contained in the vaccine cause the body to produce antibodies. A specialized type of lymphocyte referred to as a memory cell will remain long after the “infection” is cleared out, and will be able to rapidly produce antibodies when you are exposed to the true infection, thus keeping you from ever getting sick. Vaccinations have been used to reduce the incidence of several types of disease. It has eliminated smallpox and polio, in this country and many others; it keeps us from getting the flu; it is even used to protect us from certain types of cancer, such as HPV. As insane as it sounds, there are 6 methods used to create vaccines, and we will discuss each of them here. We will begin with the “similar-pathogen” vaccine, which is used to make a vaccination for polio. Here, you find a virus similar to the one you want to protect against (as cowpox is similar to smallpox), isolate the virus, and inject it “live” into the person being inoculated. Smallpox and cowpox are similar enough that protection against one provides protection against the other – they are similar pathogens! Another option is an attenuated virus, as is used to protect against the measles virus. This is also a live vaccine. It involves altering the virus enough that it is weakened in the human body. In the case of measles, the virus is adapted to grow in cold environments. The human body is warm enough that cold-loving viruses don’t do well, so the body has time to make antibodies before an infection sets in. After antibodies are present in the body, you are protected from the normal measles as well as the weakened version. A killed vaccine is what we use to protect against polio. Here – you guessed it – the virus is killed with heat, radiation, or some other means, then injected dead into your body. The dead virus produces a weak response in the body – not enough for true immunity to set in, which is why boosters are often required. Which shots have you had that required boosters? A Toxoid vaccine is created for pathogens like tetanus. Here, the goal is to expose the body to the toxins a pathogen produces, rather than to the pathogen itself. Tetanus is caused by toxins produced by the bacteria *Clostridium tetani*. Toxins are extracted from the pathogenic organism (the bacteria in this case) and are neutralized so the body isn’t harmed by them. Neutralization can involve chemicals like formaldehyde or aluminum salts. After neutralization, you are injected with the toxin, and the body produces a response. Like with dead viruses, boosters are also required. A subunit vaccine is made for hepatitis B. A subunit vaccine consists of nothing more than a portion of a pathogen - a chunk. A specific “chunk” of virus is chosen for vaccination, and the body recognizes that “chunk” on a pathogen when it encounters it. FINALLY, there is a vaccine called a Naked-DNA vaccine, which is currently being developed to use in an HIV vaccine. Here, a single gene (which will produce a protein) is selected for vaccination. This gene is amplified and placed into a vector of double-stranded DNA. This DNA is injected into a bacteria, the bacteria grow and are lysed, and the DNA is extracted for injection into the human.



The last thing we need to go over is how recombinant DNA technology is being used to create vaccinations. This is briefly discussed above in the naked DNA vaccination for HIV described above. We just need to add a few more details. Recombinant DNA technology involves modifying DNA by adding or removing genes, placing this modified DNA into an organism, and letting that organism replicate. It begins by selection of a gene of interest. This gene is removed from the organism it belongs to by isolating its DNA, then using restriction enzymes to “cut out” that particular section of DNA, which is then amplified (copies are made). The genes are then ligated into double-stranded DNA. Remember that to ligate it is to seal it in, as though it had been glued in place and is now a permanent part of the DNA. This DNA, often double-stranded, circular, and referred to as a plasmid, is pretty useless outside of a living cell. To get beyond that, the DNA is put into a cell using a chemical or electrical shock that makes the bacteria porous enough for the plasmid to enter. Heat shock is then used to seal the cell up again, with the plasmid inside. Once that plasmid is inside a bacterium, the bacteria produces more of that plasmid, incorporating that DNA and making copies of it before the cell divides. Soon, colonies of this modified bacteria live, containing the recombinant DNA we wanted. This DNA can be extracted from the bacteria after they have been killed, and used for the purpose of vaccination, with the DNA injected into the person who needs the vaccine.

Everything we have discussed: studying symptoms of disease, detecting disease, making diagnoses, administering treatments, studying the after-effects, and finding ways to prevent diseases from happening all together, are the jobs of an epidemiologist. Epidemiology is the study of disease, and epidemiologists are dedicated medical professionals at the heart of the public health field, monitor the health of populations and search for patterns in disease. They may assist in outbreak investigations or they may examine lifestyle factors and their relationship to chronic illnesses such as heart disease, diabetes, and cancer. Whether in the field, in a lab, or in an office, epidemiologists play a crucial role in maintaining human health.

Please, take the time to review this material in your binder. No matter how much I type here, there’s no way I can put into a few pages everything that goes into your binder. Also be sure to review the unit 1 vocabulary.