This is the beginning of the second 45 minute lesson module. We will talk more about bacteria, learn about the discovery of antibiotics, how antibiotic resistance developed and how to fight antibiotic resistance in the future.
Text:
As you will learn, antibiotic resistance is a global problem!
We will talk about why antibiotics were developed, how antibiotics work against bacteria, how bacteria become resistant, and strategies for overcoming antibiotic resistance in the future.
What is an antibiotic?

Key points:
Antibiotics are chemicals that kill bacteria or stop them from growing. There are different types of antibiotics, each designed to work on specific types of bacteria. Only a healthcare provider can prescribe the right antibiotic for your bacterial infection. It is important to use the right drug for your bug!

Instructor’s note:
Ask the students if they have ever taken an antibiotic. Ask them about their experience: did they visit the doctor? Did they take all of the medicine? Did the medicine make them feel better?
We are going to begin with the timeline of antibiotics and the development of resistance.
Text:
Antibiotic Timeline:
Bacteria have been around for a long, long time. They were among the first forms of life on this planet. By the time dinosaurs appeared, bacteria had already been here for millions of years. Antibiotics have also been around since prehistoric time, since they were produced by some bacteria and other microbes to defend themselves against aggressive bacteria. Humans discovered penicillin in the 1920s and this began a search for others as well. By the 1940s, antibiotics began to be used to cure bacterial infections. Before antibiotics, people often died from bacterial infections. This timeline puts the evolution of antibiotics into perspective; within just a few years of their introduction into use by doctors - bacteria were becoming resistant to these important, life-saving medicines.

Key points:
Bacteria have been around for millions of years, surviving the ice age and the dinosaurs.
In the 1940s, antibiotics were mass produced and first used by humans to treat infections in people.
Before antibiotics were discovered and made available for physicians to prescribe, there was no effective treatment for bacterial infections. People often died from these infections. In 1924, President Calvin Coolidge’s 16-year old son, who had the best treatment available, died from an infected blister on his foot.
Bacteria have continued to develop new resistance, outsmarting our antibiotics. If we don’t use antibiotics properly, they may not work in the future. Today, microbiologists and researchers are discovering strains of bacteria that are resistant to multiple types of antibiotics. We even have some pathogenic bacteria that do not appear to respond to any of the antibiotics currently available.
The first antibiotics were naturally occurring by-products of soil microbes such as fungi and bacteria. They evolved as weapons to fight with other microbes to preserve their own space to live and grow in the soil. Chemists developed the first mass-produced antibiotics in the 1940s. Almost as soon as physicians began prescribing antibiotics in the 1940s, mutant bacteria that were resistant to the antibiotics were selected as the susceptible bacteria were killed off.

Key Knowledge About Antibiotics

- The first antibiotics were made from by-products of soil microbes (fungi and bacteria)
- These microbes were competing with other microbes for space to live and grow in the soil
- Chemists developed the first mass-produced antibiotics in the 1940s
- These antibiotics did not maintain their effectiveness very long because some bacteria mutated and thus became resistant and could survive and proliferate
As resistance began to increase, chemists made new, more sophisticated antibiotics. Within a short period of time, even the more sophisticated antibiotics lost their original effectiveness against bacteria as they continued to mutate and become resistant. Today, some newer antibiotics are specifically designed to prevent the proliferation of bacteria and to kill them. Unfortunately, bacteria continue to be able to mutate and survive our newest antibiotics that have been developed.
A new antibiotic is most effective when it is first released for human use. Shortly after it becomes broadly used, it will select resistant bacteria. Today, some bacteria have developed multidrug resistance, and, in some cases, bacteria are resistant to all available antibiotics. Over time, even fewer antibiotics will be effective, unless newer ones can be developed to replace them. The development of new antibiotics has slowed, primarily due to the cost of development and the lower financial incentive, since the income from an antibiotic taken for 10 days is less than from other drugs that are prescribed for lifetime use.  

Key Concepts to Remember About Antibiotics

- A newly developed antibiotic is most effective when it is first released for human treatment.
- Today some bacteria have developed multidrug resistance, and, in some cases, bacteria are resistant to all available antibiotics.
- Over time, even fewer antibiotics will be effective, unless newer ones can be developed to replace them.
- The development of new antibiotics has slowed, primarily due to the cost of development and lower financial incentive, since the income from an antibiotic taken for 10 days is less than from other drugs that are prescribed for lifetime use.

Text:

• A new antibiotic is most effective against bacteria as soon as it is approved for human use by the Food and Drug Administration (FDA). Shortly after it becomes broadly used, it will select resistant bacteria.
• Today, some bacteria have developed multidrug resistance, and, in some cases, bacteria are resistant to all available antibiotics.
• Over time, even fewer of our current antibiotics will be effective, unless newer ones are developed to replace the antibiotics that are no longer working well.
• Research and development of new antibiotics has slowed down. It takes up to ten years to get FDA approval for a new drug and it can cost over $1 billion to develop and test it.
• There is less financial incentive to develop an antibiotic, which is usually taken for a limited period of time, as opposed to a drug for high blood pressure that would be taken for life by a larger group of people.
There are many different types of antibiotics available for human use. Antibiotics fall into several classes or types. Several types of antibiotics may be effective against several types of bacteria. Bacterial resistance mechanisms may cause resistance to some types but not to others. Sometimes new types of antibiotics are developed to have activity against some bacteria that are resistant to other types of antibiotics.
The best way to determine the correct antibiotic for a pathogenic bacterium is first to see your care provider. The care provider will:

• Take your history and do a physical exam to determine the site of infection and the likely cause (virus vs. bacteria)
• Specimens collected for lab testing are examined for the growth of bacteria, which are then identified and tested for susceptibility to a range of different antibiotics
• For certain infections (like ear infections), the clinician may treat based on the bacteria that are likely to cause the infection without testing
• There are also other considerations, such as allergies, toxicities of various antibiotics, and other conditions of the patient.
Antibiotics are chemicals that kill bacteria or stop them from growing. There are various types of antibiotics, each with activity against specific types of bacteria.

Before prescribing any medication, your care provider or a laboratory may take a sample of tissue, blood or other fluid from your body and test it for the presence of bacteria. Agar plates are sometimes used for these tests. Agar plates contain nutrient-rich food for bacteria, which helps the bacteria grow very quickly. Once the results come back to the care provider, your care provider will choose the antibiotic most likely to kill the bacterial infection.

Instructor’s note: This slide shows an Agar Plate. The white spots are filter papers containing different types of antibiotics. The antibiotics diffuse out into the agar and prevent the growth of the bacteria that are susceptible to them. When the bacteria grow even in the presence of an antibiotic, that shows that the bacteria are resistant to it.
Narrow- and Broad-Spectrum Antibiotics

- Narrow-spectrum antibiotics are targeted to a limited group of bacterial species.
- Broad-spectrum antibiotics are effective against a wide range of bacterial species.
- A narrow-spectrum antibiotic should be used to target the specific bacterial infection, preserving the colonizing bacteria and avoiding selection of resistance in these bacteria that might later cause infection.
- A broad-spectrum antibiotic is used when you do not know the infecting bacterium and its susceptibility pattern, or when the bacteria are known to be resistant to narrow-spectrum drugs and you don’t have any other choice.

Text:
Narrow-spectrum antibiotics are targeted for a limited group of bacterial species. Broad-spectrum antibiotics are effective against a wide range of bacterial species. A narrow-spectrum antibiotic should be used, whenever possible, to target the specific bacterial infection. This preserves the colonizing bacteria in your body and avoids selection of resistance in these bacteria that might later cause an infection. A lab test will show the sensitivity (or susceptibility) of the bacteria to specific antibiotics. This is the most effective way to treat the bacterial infection and prevent the development of resistance.
Sometimes a laboratory sensitivity test cannot be done. In that case, a broad-spectrum antibiotic is often used. This may or may not be the most effective antibiotic for the specific bacteria causing the infection.
How Antibiotics Work

If you think of bacteria as a lock, then an antibiotic is like a key.
Antibiotics are designed to disrupt a specific function of the bacteria, making them no longer able to grow and replicate by one of four ways:

1. Interfering with DNA or RNA replication
2. Disrupting the production of the bacterial cell wall
3. Preventing the production of proteins and smaller molecules that are necessary for growth and replication
4. Dissolving the cell membrane, causing leakage of cytoplasmic contents
Critical bacterial cell functions are targets of antibiotic action.

A bacterium is depicted surrounded by a cell wall. Within the cell (or cytoplasmic) membrane is the cytoplasm, showing the DNA, from which messenger RNA is transcribed. The mRNA is then read (or translated) by the ribosomes and corresponding proteins are synthesized. Thus, various targets, DNA replication, transcription into mRNA and translation at the ribosomes are targets that are interfered with by various antibiotics, as are also the integrity of the cytoplasmic membrane and the synthesis of the cell wall.
There are two types of bacterial resistance:
1. Intrinsic resistance – existed before antibiotics were introduced, a natural characteristic of the bacterial species
2. Acquired resistance –
   • random mutations in bacterial genes resulting in new resistance, or
   • acquisition by a sensitive bacterium of existing resistance genes from an already resistant bacterium
Resistance can develop when:

1. There are mutations in the bacterium's genes that make it less susceptible to some antibiotics
2. The DNA from resistant bacteria can be transferred to susceptible bacteria. (Hereagain, in this context, “susceptible” mean the same as “sensitive”).
3. Selective pressure causes proliferation of resistant cells, which are preserved and able to multiply, while the susceptible cells are killed.
If you think of bacteria as a lock and antibiotics as a key – four things can happen:

Text:
1. The antibiotic key is the right key and unlock the bacteria and kills them
2. The antibiotic key becomes damaged so it cannot open the bacterial lock
3. The bacterial lock can alter itself (mutate) so the key (antibiotic) no longer can open the lock
4. The bacterial keyhole can become blocked so the antibiotic can not enter
Bacteria are clever! Bacteria become resistant to antibiotics by mutations in their bacterial genes preventing susceptibility to current antibiotics. Such bacterial gene mutations include:

- Changing the bacterial membranes, so they are less permeable, thereby reducing the entry of antibiotics into the cell
- Producing enzymes that inactivate the antibiotic
- Pumping the antibiotic out of the cell before it gets a chance to work
- Altering the target site where the drug usually binds to the bacteria, so it can’t bind anymore
Transfer of genetic material can occur between bacteria in one person to another. This can be done by:
- Exchanging DNA between bacteria of the same, or sometimes even different, species.
• Bacteria have evolved numerous mechanisms to evade antimicrobial drugs.
• Chromosomal mutations are an important source of resistance to some antibiotics.
• Acquisition of resistance genes or gene clusters, via conjugation, transposition, or transformation, accounts for considerable antimicrobial resistance among bacterial pathogens.
• Multidrug resistance can occur when numerous individual mutant genes are present (especially in tuberculosis) and/or by the transfer of multiple resistant genes as a unit on DNA elements, such as plasmids or transposons.
III. Selective Pressure

The presence of an antibiotic exerts selective pressure because resistant bacteria continue to grow while susceptible (or sensitive) bacteria are eliminated.

Text: Selective pressure means that the presence of an antibiotic selects the growth of an organism to become resistant by mutation or acquiring new DNA.
Even in the absence of an antibiotic, small numbers of sensitive cells of bacteria are always evolving by mutation to resistant cells. In addition, bacteria that are already resistant can be acquired in small numbers from the environment, usually from other people who have resistant bacteria, but also from other objects and even soil. Every time you take an antibiotic, even when there is a good reason and the antibiotic is appropriate, you subject the bacteria to this selection process.

As you can see in this slide, the result is that resistant bacteria proliferate and become dominant. When a person develops resistant bacteria, other antibiotics that have disadvantages (such as toxicity, less convenient administration, or greater cost) may be required. Some resistant bacterial infections become resistant to multiple classes of antibiotics and in extreme cases cannot be treated at all.
Once resistant strains of bacteria are present in a population, continuing exposure to antimicrobial drugs favors their survival.

Reducing antimicrobial selection pressure is one key to preventing antimicrobial resistance and preserving the utility of available antibiotics for as long as possible.
Other Factors Contributing to Selective Pressure:

1. Patient non-compliance (taking only for a few days or skipping doses)
2. Inadequate dosing (not high enough dose, or doses spaced too far apart)
3. Misuse of antibiotics
   - Overuse (prescribing when not needed)
   - Inappropriate use (patient taking antibiotics prescribed for a different infection)
   - Unnecessary use of broad-spectrum antibiotic (exposing patient to a drug that can affect colonizing bacteria elsewhere in the body)

The use of any antibiotic contributes to the possibility of its loss of effectiveness because of selection of existing resistant bacteria.
Important Things to Remember About Antibiotics

• Antibiotics kill bacteria, not viruses.
• Taking an antibiotic unnecessarily for colds and flu can select bacteria in the body that are resistant to the antibiotic.
• Never save or share your antibiotics.
• Take your antibiotics as prescribed by your care provider.
Why Should We Be Concerned About Antibiotic Resistance?

- Antibiotic resistance is a serious global problem
- Resistant infections are difficult to treat: the bacteria may be resistant to multiple types of antibiotics
- Resistance limits the range of effective antibiotics, sometimes leaving only antibiotics that are expensive, inconvenient to use, or even dangerous (toxic)

Text Notes:
In many developing countries, the use of antibiotics does not require a medical provider’s prescription, and antibiotics can be freely purchased in pharmacies. Therefore, such excessive use of antibiotics combined with poor hygiene leads to more frequent selection and spread of resistance. Also contributing is the ease of international travel leading to the dissemination of resistant strains to other regions of the world.
Why Should We Be Concerned About Antibiotic Resistance? (cont.)

- It takes 10 years to develop a new antibiotic and over $1B to fund the development
- Newer antibiotics may have more side-effects or may be more expensive and/or less effective than drugs previously developed but now compromised by resistance
- Antibiotics are generally less profitable to drug manufacturers, so there are fewer financial incentives to develop new antibiotics
Additional Environmental Concerns

• Antibiotics have been used to treat meat animals and poultry to prevent infections rather than to treat them, and to promote faster growth; this excessive antibiotic usage can lead to selection of antibiotic-resistant bacteria which can get into humans, either from close contact or consumption of infected meat or dairy products.

• Improper disposal of old or unused antibiotics can pollute the water supply, exposing the general public to low levels of antibiotics which can select for resistance in colonizing bacteria.

Text:
Federal legislation is pending to establish parameters about appropriate use of antibiotics in animal husbandry. Many people do not know how to properly dispose of old or unused antibiotics or other medication. Contact your pharmacy to see if they have a policy of accepting unused medication or if they can direct you to a proper disposal location.
Key points:
**Prevention is the best medicine** -- take care of your body! Eat healthy foods, hydrate yourself with water, exercise regularly and get plenty of rest to keep your immune system strong and functioning. Keep your hands clean! Washing them with soap and warm water for at least 30 seconds if the best way to get bacteria and viruses off your hands. If you need to cough or sneeze, use a tissue or cough into your sleeve. Only your care provider can determine whether you have a viral or bacterial infection and what treatment you need. Never take an antibiotic for a viral infection!
What Else Can You Do?

• If you are prescribed antibiotics, take all of the medication as prescribed by your care provider
• Do not stop taking an antibiotic before the end of the treatment course just because you start to feel better; residual bacteria may multiply, causing recurrence of symptoms that may require retreatment increasing the likelihood of selecting resistant cells
• Never share or save antibiotics
• **Spread the word, not the resistance**

**Text:**

*Remember – spread the word, not the resistance!*
Remember....... 

• Every time someone takes an antibiotic, resistant bacteria may be selected and then multiply 
• Resistant bacteria may then spread to others, compromising the effectiveness of treatment for future infections 
• Share what you have learned with your friends and family members
Another way you can make a difference is to share what you have learned about bacteria, appropriate antibiotic use, how resistance develops and how to prevent it. Share this information with your families, friends and other people in your community. Think twice about asking your care provider for an antibiotic. You can also consider how you can make a difference in the professional world when you graduate. There are many kinds of jobs in multiple fields that can help prevent antibiotic resistance including research, microbiology, animal husbandry, medicine, and health care administration to name a few. YOU CAN MAKE A DIFFERENCE!