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Exploring Antibiotics
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Welcome to this presentation entitled Exploring Antibiotics. The intent of this session is to provide an overview of how antibiotics work against bacteria, as well as some basic guidance for choosing antibiotics based on what type of infection you are wanting to address.

Antibiotics are a type of chemotherapy used to treat infections by killing bacteria which are living cellular organisms. Antibiotics are effective against bacteria but not against viruses. Antibiotics are one of the most significant medical advances in the 20th century. But as resistance to them continues to develop we are in danger of losing antibiotics as an effective method for treating infections.

Before talking more about how antibiotics work and what factors are taken into account when selecting an antibiotic to treat a specific infection it is helpful to understand some basics about bacteria. Bacteria are single cell organisms with different sizes and shapes. This helps in identification when viewing with a microscope. Common shapes are round which are referred to as cocci and rods which are referred to as bacilli, chains or spirals. They also differ in how they react to Gram Stain; some being positive or taking on a purple color and others being negative and turning red in color.

Although shape and Gram Stain are the most common descriptors other characteristics that help with differentiation between bacteria include size, growth weights and growth patterns. Bacteria can also be classified by their need for oxygen to grow. Aerobic bacteria need oxygen and anaerobic bacterias survive without oxygen. Each of these factors and classifications can be used to characterize bacteria and can be used to select antibiotics that would be most likely to treat an infection.

As mentioned in the previous slide bacteria can be either Gram Negative or Gram Positive. On this slide are two types of bacteria stained with Gram Stain. On the left the purple color organisms are called Gram Stain Positive because the bacteria take up a crystal violet stain which gives it a purple color. On the right side you see a pink or red looking group of organisms. Those are considered Gram Stain Negative.

So which types of bacteria do we commonly see in healthcare? A lot of the organisms that we see in healthcare setting that are noticeably Gram Positive in staining are cocci or the round shape bacteria. Some common examples of Gram Positive cocci that we see treated in long term care residents and healthcare in general are staphylococci, streptococci and enterococci.
One of the common Gram Positive rods that we encounter is called *clostridium difficile*, also, referred to as C.*diff*. It infects the gastrointestinal tract. It is an anaerobic bacteria meaning that it doesn't like to grow in the presence of oxygen, making the GI tract a perfect place.

The Gram negative bacteria that we frequently encounter in healthcare are bacilli or rod shaped. The common organisms that fall into this group of Gram Negative rods are E. coli, Klebsiella, Proteus and Pseudomonas. You may recognize these as common culprits causing urinary tract infections.

Now let's switch some to some of the terminology we use to describe or classify antibiotics. Like bacteria, antibiotics can be described in various ways. Antibiotics are grouped into different classes based on their chemical structure. You will likely recognize these classes as penicillins, cephalosporins, fluoroquinolones, Aminoglycosides, Monobactams, Carbapenems, Macrolides and others. They can also be described by the spectrum of their activities. Narrow spectrum antibiotics are drugs that target very specific bacteria while broad spectrum agents can kill across the diversity of organisms. It may seem that always using the broadest spectrum antibiotic possible is best, however, this is not true. The goal is to choose the antibiotic that acts on the bacteria involved in the infection in order to minimize the development of resistance and to avoid killing the many types of good or helpful bacteria we have in our bodies.

It's important to keep in mind that antibiotics do not take the place of the body's immune system. Antibiotics work best when they can work in conjunction with the immune system. There are many times the body's immune system can clear the infection without the help of antibiotics. However sometimes the body's immune system is unable to activate itself quickly enough to outpace the reproductive rate of invading bacteria. Other times the bacteria are producing toxins so quickly they will cause permanent damage before the immune system can fully eliminate the bacteria. In these cases the immune system needs help from something that can kill the offending bacteria directly. Antibiotics that kill bacteria are called bactericidal. However, not all antibiotics kill bacteria. Some prevent or slow the growth. These antibiotics are called bacteriostatic because they prevent the growth of bacteria by keeping them in the stationary phase of the growth rather than killing them immediately. This will eventually lead to bacterial death. It also gives time for the body's immune system to pitch in and help.

How do antibiotics work? Similar to other chemotherapeutic agents they basically get in the way of their targets. In this case the bacteria's ability to reproduce or stay intact. They make the bacteria more vulnerable to the body's immune system. They can do this by a variety of mechanisms. Antibiotics can block protein formation within the bacteria. Examples include macrolides, tetracyclines, aminoglycosides; they can inhibit some wall formation, examples include; beta lactams, vancomycin, bacitracin. They can interfere with DNA formation; examples include Quinolones, or Rifampin. And they can prevent folic acid synthesis, an example is the Sulfonamides, one of the first groups of antibacterial agents that was developed.

The most obvious way antibiotics are used is to treat a known infection an infection that has been diagnosed by clinical exam and typically with additional testing. This is the most common way antibiotics are utilized. However, you will see antibiotics used for prophylactic treatment and as empiric therapy. Prophylactic treatment is when antibiotics are used to prevent an infection. Commonly this is done with surgical procedures or when a person is receiving other treatments that will impact their immune system. Sometimes, especially in situations where a person is critically ill antibiotics will be

started empirically, meaning we do not know if there's an infection causing illness or we have tests and cultures pending but feel the risk of waiting is too great. Both prophylactic and empiric therapy should be uncommon in the long term and post-acute care settings.

Choosing antibiotics correctly requires use of a variety of tools. These include direct examination, meaning the lab prepares or stains a specimen obtained from the person to allow for identification of the infecting organism under the microscope. Cultures where the lab isolates and grows the microorganism in the lab. And sensitivities, these are done once a microorganism is cultured in order to determine that antibiotics will work. And finally, antibiograms. This is a summary of antibiotic's susceptibility in resistance for a specific setting such as a hospital or a nursing home. This tells the clinician ordering the antibiotic if a specific type of bacteria is common in that facility and if it's commonly sensitive or resistant to certain antibiotics. Antibiograms can be helpful in the fight against antibiotic resistance.

Next, let's match some of the common classes of antibiotics with the types of bacteria they treat. Let's start with Beta Lactams. These include Penicillin, as well as the Cephalosporins. In Penicillin there have been changes made over time to the basic structure of Penicillin to extend the activity of some of these drugs. For example, Methicillin is specifically active against staphylococcus. Beta lactams, like piperacillin, have a much broader coverage. It includes both Gram Positive and Gram Negative organisms.

For several of these drugs we can actually combine them with another agent to help them overcome some of the common bacterial resistance that can emerge. A bacteria may be resistant to Amoxicillin by itself but when you add Clavulanate and make Augmentin, that molecule now allows the drug to be active. Cephalosporins are cousins to Penicillin and there are several generations of these. The first generation drugs can have more Gram Positive activity and examples of that are Cephalexin and Cefazolin but when you get into third and fourth generations Cephalosporins, like Ceftriaxone and Ceftazidime you tend to have more Gram Negative activity. And Ceftazidime, in particular, is known to be effective against Pseudomonas unlike Ceftriaxone. So it is important to recognize that even within a class you can see different spectrums of coverage.

Another class of antibiotics are the Carbapenems. These are among some of the broadest spectrum agents that we have. They're powerful drugs. As you can see on the slide there are a number of different bacteria that are affected and killed by Carbapenems. You may hear Carbapenems being referred to as big guns or broad spectrum agents because many of them are only available in IV formulation and they tend to be more costly as well.

This slide highlights some of the other common antibiotics that you encounter that treat Gram Positive bacteria, however some may not be as common in long term care and some are only available for intravenous use. For the treatment of infections due to Gram Positive bacteria there are drugs such as Vancomycin and Daptomycin. Each of these are used to treat MRSA and often enterococci. Remember with Vancomycin, although there is a oral form the Vancomycin isn't absorbed from the GI tract into the

blood or tissues so it's only used to treat infections that can happen locally in the intestines like C.difficile. The IV form is the version you need to treat infections like MRSA to get good levels in the blood stream.

This slide shows some of the other agents you will see that are aimed at treating infections due to Gram Negative bacteria. These include the Fluoroquinolones. Ciprofloxacin which is commonly used for urinary tract infections; levofloxacin and moxifloxacin may also be seen as treatments for UTI but because of their broader spectrum of activity you also see them used for respiratory infections as they cover streptococcus pneumoniae and other respiratory bacteria.

The Fluoroquinolones come in oral and IV forms and like all newer, more broad spectrum antibiotics, should only be used if a more narrow spectrum antibiotic would not adequately address the infection. Aminoglycosides are also excellent drugs for Gram Negative infections. However, they are only available in intravenous form and we tend to be more cautious about using them because they're known to have serious toxicities if levels are not appropriately monitored. Common toxicities include kidney toxicity as well as damage to the inner ear and vestibular nerve damage which can happen with long exposure to Aminoglycosides.

This slide shows some of the miscellaneous antibiotics that are commonly used in the long term care setting. Trimethoprim, Sulfamethoxazole, or Bactrim, is used a lot for treatment of urinary tract infections. However, it is important to monitor kidney function because there can be an impact on creatinine clearing with the use of Bactrim. Sometimes people think of it as a narrow spectrum agent but it is actually a pretty broad activity against both Gram Negative and Gram Positive bacteria.
A drug that we often see for respiratory infections is Azithromycin, commonly referred to as a Z-Pack. It is considered narrow spectrum and typically reserved for sinus and respiratory infections.
Metronidazole, or Flagyl, is primarily used for the treatment of C.difficile infections. It is a drug that's focused on anaerobic bacteria, those bacteria that don't like or need to have oxygen around in order to grow. The oral form of Metronidazole can lead to nausea and GI upset making it harder to be tolerated for older people.

This slide lists some of the key takeaway messages from this presentation. Antibiotics are a powerful treatment against infections due to bacteria. They are not effective against viral infections. Choosing antibiotics wisely requires taking into account a number of factors regarding the targeted bacteria and the individual being treated. Antibiotics are not a substitute for the immune system. They work most effectively in conjunction with the immune system to stop bacteria from reproducing and clear them from the body before they cause damage.

There are a number of tools that should be used to guide antibiotic selection and to help make sure we are using antibiotics wisely in order to most effectively treat infection as well as decrease the rate of development of resistance.

Thank you for listening to the presentation on exploring antibiotics.