ECS 901 : Heterocyclic Compounds Against Resistance Infectious Diseases

What is Infection?

Infection: The invasion and multiplication of microorganisms such as bacteria, viruses, and parasites that are not normally present within the body. An infection may cause no symptoms and be subclinical, or it may cause symptoms and be clinically apparent. An infection may remain localized, or it may spread through the blood or lymphatic vessels to become systemic (bodywide). Microorganisms that live naturally in the body are not considered infections. For example, bacteria that normally live within the mouth and intestine are not infections.

Semptoms of Infections

The level of C-reactive protein (CRP), which can be measured in your blood, increases when there's inflammation in your body. Your doctor might check your C-reactive protein level for infections or for other medical conditions.

Cepsis: Sepsis is a life-threatening illness caused by your body's response to an infection. Your immune system protects you from many illnesses and infections, but it's also possible for it to go into overdrive in response to an infection. Sepsis develops when the chemicals the immune system releases into the bloodstream to fight an infection cause inflammation throughout the entire body instead. Severe cases of sepsis can lead to septic shock, which is a medical emergency. Sepsis is defined as "life-threatening organ dysfunction caused by a dysregulated host response to infection." In lay terms, sepsis is a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs.

Infectious diseases

Infectious diseases are disorders caused by organisms — such as bacteria, viruses, fungi or parasites. Many organisms live in and on our bodies. They're normally harmless or even helpful, but under certain conditions, some organisms may cause disease. Some infectious diseases can be passed from person to person. Some are transmitted by bites from insects or animals. And others are acquired by ingesting contaminated food or water or being exposed to organisms in the environment. Signs and symptoms vary depending on the organism causing

the infection, but often include fever and fatigue. Mild infections may respond to rest and home remedies, while some life-threatening infections may require hospitalization. Many infectious diseases, such as measles and chickenpox, can be prevented by vaccines. Frequent and thorough hand-washing also helps protect you from most infectious diseases

Use of Antibiotics

Antibiotics also called antibacterials, are a type of antimicrobial drug used in the treatment and prevention of bacterial infections. They may either kill or inhibit the growth of bacteria. A limited number of **antibiotics** also possess antiprotozoal activity. **Antibiotics** are not effective against viruses Depending on the range of bacterial species susceptible to these agents, antibacterials are classified as broad-spectrum, intermediate-spectrum, or narrow- spectrum.

1. **Broad spectrum antibacterials** are active against both Gram-positive and Gram-negative organisms. Examples include: tetracyclines, phenicols, fluoroquinolones, "third-generation" and "fourth-generation" cephalosporins.
2. **Narrow spectrum antibacterials** have limited activity and are primarily only useful against particular species of microorganisms. For example, glycopeptides and bacitracin are only effective against Gram-positive bacteria, whereas polymixins are usually only effective against Gram negative bacteria. Aminoglycosides and sulfonamides are only effective against aerobic organisms, while nitroimidazoles are generally only effective for anaerobes.

– **Virus**

Viruses are tiny organisms that may lead to mild to severe illnesses in humans, animals and plants. This may include flu or a cold to something more life threatening like HIV/AIDS. The virus particles are 100 times smaller than a single bacteria cell. The bacterial cell alone is more than 10 times smaller than a human cell and a human cell is 10 times smaller than the diameter of a single human hair. Viruses by themselves are not alive. They cannot grow or multiply on their own and need to enter a human or animal cell and take over the cell to help them multiply. These viruses may also infect bacterial cells. The virus particle or the virions attack the cell and take over its machinery to carry out their own life processes of multiplication and growth. An infected cell will produce viral particles instead of its usual products.

– **Bacteria**

Bacteria are microscopic single-celled organisms that thrive in diverse environments. They can live within soil, in the ocean and inside the human gut. Humans' relationship with bacteria is complex. Sometimes they lend a helping hand, by curdling milk into yogurt, or helping with our digestion. At other times they are destructive, causing diseases like pneumonia and MRSA.

Based on the relative complexity of their cells, all living organisms are broadly classified as either prokaryotes or eukaryotes. Bacteria are prokaryotes. The entire organism consists of a single cell with a simple internal structure. Unlike eukaryotic DNA, which is neatly packed into a cellular compartment called the nucleus, bacterial DNA floats free, in a twisted thread-like mass called the nucleoid. Bacterial cells also contain separate, circular pieces of DNA called plasmids. Bacteria lack membrane-bound organelles, specialized cellular structures that are designed to execute a range of cellular functions from energy production to the transport of proteins. However, both bacterial and eukaryotic cells contain ribosomes. These spherical units are where proteins are assembled from individual amino acids, using the information encoded in a strand of messenger RNA. On the outside, bacterial cells are generally surrounded by two protective coverings: an outer cell wall and an inner cell membrane. However, certain bacteria, like the mycoplasmas do not have a cell wall at all. Some bacteria may even have a third, outermost, protective layer called the capsule. Lastly, bacterial surfaces can be covered by whip-like extensions: flagella or pili. According to the authors of "Mims Medical Microbiology, 5th Ed" (Saunders, 2013), long flagella aid in motility while short pili help bacteria to attach to host surfaces.

ANTIBIOTIC RESISTANCE

Antibiotics are medicines used to prevent and treat bacterial infections. Antibiotic resistance occurs when bacteria change in response to the use of these medicines.
Bacteria, not humans or animals, become antibiotic-resistant. These bacteria may infect humans and animals, and the infections they cause are harder to treat than those caused by non-resistant bacteria. Antibiotic resistance leads to higher medical costs, prolonged hospital stays, and increased mortality.
The world urgently needs to change the way it prescribes and uses antibiotics. Even if new medicines are developed, without behaviour change, antibiotic resistance will remain a

major threat. Behaviour changes must also include actions to reduce the spread of infections through vaccination, hand washing, practising safer sex, and good food hygiene.
Antibiotic resistance is rising to dangerously high levels in all parts of the world. New resistance mechanisms are emerging and spreading globally, threatening our ability to treat common infectious diseases. A growing list of infections – such as pneumonia, tuberculosis, blood poisoning, gonorrhoea, and foodborne diseases – are becoming harder, and sometimes impossible, to treat as antibiotics become less effective. Where antibiotics can be bought for human or animal use without a prescription, the emergence and spread of resistance is made worse. Similarly, in countries without standard treatment guidelines, antibiotics are often over-prescribed by health workers and veterinarians and over-used by the public. Without urgent action, we are heading for a post-antibiotic era, in which common infections and minor injuries can once again kill. Antibiotic resistance is accelerated by the misuse and overuse of antibiotics, as well as poor infection prevention and control. Steps can be taken at all levels of society to reduce the impact and limit the spread of resistance.

To prevent and control the spread of antibiotic resistance, individuals can:

Only use antibiotics when prescribed by a certified health professional. Never demand antibiotics if your health worker says you don't need them. Always follow your health worker's advice when using antibiotics. Never share or use leftover antibiotics.

Prevent infections by regularly washing hands, preparing food hygienically, avoiding close contact with sick people, practising safer sex, and keeping vaccinations up to date.

Prepare food hygienically, following the WHO Five Keys to Safer Food (keep clean, separate raw and cooked, cook thoroughly, keep food at safe temperatures, use safe water and raw materials) and choose foods that have been produced without the use of antibiotics for growth promotion or disease prevention in healthy animals.

To prevent and control the spread of antibiotic resistance, policy makers can:

Ensure a robust national action plan to tackle antibiotic resistance is in place. Improve surveillance of antibiotic-resistant infections. Strengthen policies, programmes, and implementation of infection prevention and control measures. Regulate and promote the appropriate use and disposal of quality medicines. Make information available on the impact of antibiotic resistance.

To prevent and control the spread of antibiotic resistance, health professionals can:

Prevent infections by ensuring your hands, instruments, and environment are clean.

Only prescribe and dispense antibiotics when they are needed, according to current guidelines. Report antibiotic-resistant infections to surveillance teams. Talk to your patients about how to take antibiotics correctly, antibiotic resistance and the dangers of misuse.

To prevent and control the spread of antibiotic resistance, the health industry can:

Invest in research and development of new antibiotics, vaccines, diagnostics and other tools.

While there are some new antibiotics in development, none of them are expected to be effective against the most dangerous forms of antibiotic-resistant bacteria. Given the ease and frequency with which people now travel, antibiotic resistance is a global problem, requiring efforts from all nations and many sectors. When infections can no longer be treated by first-line antibiotics, more expensive medicines must be used. A longer duration of illness and treatment, often in hospitals, increases health care costs as well as the economic burden on families and societies. Antibiotic resistance is putting the achievements of modern medicine at risk. Organ transplantations, chemotherapy and surgeries such as caesarean sections become much more dangerous without effective antibiotics for the prevention and treatment of infections.

Description

Antibiotic resistance is the ability of bacteria to resist the effects of an antibiotic. Antibiotic resistance occurs when bacteria change in a way that reduces the effectiveness of drugs, chemicals, or other agents designed to cure or prevent infections. The bacteria survive and continue to multiply, causing more harm. ntibiotic resistance has been called one of the world's most pressing public health problems. Antibiotic resistance can cause illnesses that were once easily treatable with antibiotics to become dangerous infections, prolonging suffering for children and adults. Antibiotic-resistant bacteria can spread to family members, schoolmates, and co-workers, and may threaten your community. Antibiotic-resistant bacteria are often more difficult to kill and more expensive to treat. In some cases, the antibiotic-resistant infections can lead to serious disability or even death.

Bacterial Resistance

Some bacteria are naturally resistant to certain types of antibiotics. However, bacteria may also become resistant in two ways: 1) by a genetic mutation or 2) by acquiring resistance from

another bacterium. Mutations, rare spontaneous changes of the bacteria's genetic material, are thought to occur in about one in one million to one in ten million cells. Different genetic mutations yield different types of resistance. Some mutations enable the bacteria to produce potent chemicals (enzymes) that inactivate antibiotics, while other mutations eliminate the cell target that the antibiotic attacks. Still others close up the entry ports that allow antibiotics into the cell, and others manufacture pumping mechanisms that export the antibiotic back outside so it never reaches its target.

Bacteria can acquire antibiotic resistance genes from other bacteria in several ways. By undergoing a simple mating process called "conjugation," bacteria can transfer genetic material, including genes encoding resistance to antibiotics (found on plasmids and transposons) from one bacterium to another. Viruses are another mechanism for passing resistance traits between bacteria. The resistance traits from one bacterium are packaged into the head portion of the virus. The virus then injects the resistance traits into any new bacteria it attacks. Bacteria also have the ability to acquire naked, "free" DNA from their environment. Any bacteria that acquire resistance genes, whether by spontaneous mutation or genetic exchange with other bacteria, have the ability to resist one or more antibiotics. Because bacteria can collect multiple resistance traits over time, they can become resistant to many different families of antibiotics.

Genetically, antibiotic resistance spreads through bacteria populations both "vertically," when new generations inherit antibiotic resistance genes, and "horizontally," when bacteria share or exchange sections of genetic material with other bacteria. Horizontal gene transfer can even occur between different bacterial species. Environmentally, antibiotic resistance spreads as bacteria themselves move from place to place; bacteria can travel via airplane, water and wind. People can pass the resistant bacteria to others; for example, by coughing or contact with unwashed hands.

Bacteria, resistant to antibiotics

Antibiotic resistance is the ability of a microorganism to withstand the effects of an antibiotic. It is a specific type of drug resistance. Antibiotic resistance evolves naturally via natural selection through random mutation, but it could also be engineered by applying an evolutionary stress on a population. Once such a gene is generated, bacteria can then transfer the genetic information in a horizontal fashion (between individuals) by plasmid exchange. If

a bacterium carries several resistance genes, it is called multiresistant or, informally, a superbug. Causes Antibiotic resistance can also be introduced artificially into a microorganism through transformation protocols. This can be a useful way of implanting artificial genes into the microorganism. Antibiotic resistance is a consequence of evolution via natural selection. The antibiotic action is an environmental pressure; those bacteria which have a mutation allowing them to survive will live on to reproduce. They will then pass this trait to their offspring, which will be a fully resistant generation.

Several studies have demonstrated that patterns of antibiotic usage greatly affect the number of resistant organisms which develop. Overuse of broad-spectrum antibiotics, such as second- and third-generation cephalosporins, greatly hastens the development of methicillin resistance. Other factors contributing towards resistance include incorrect diagnosis, unnecessary prescriptions, improper use of antibiotics by patients, and the use of antibiotics as livestock food additives for growth promotion.

Researchers have recently demonstrated the bacterial protein LexA may play a key role in the acquisition of bacterial mutations. Resistant pathogens Staphylococcus aureus (colloquially known as "Staph aureus" or a Staph infection) is one of the major resistant pathogens. Found on the mucous membranes and the skin of around a third of the population, it is extremely adaptable to antibiotic pressure. It was the first bacterium in which penicillin resistance was found—in 1947, just four years after the drug started being mass-produced. Methicillin was then the antibiotic of choice, but has since been replaced by oxacillin due to significant kidney toxicity. MRSA (methicillin-resistant Staphylococcus aureus) was first detected in Britain in 1961 and is now "quite common" in hospitals. Half of all S. aureus infections in the US are resistant to penicillin, methicillin, tetracycline and erythromycin.

This left vancomycin as the only effective agent available at the time. However, strains with intermediate (4-8 ug/ml) levels of resistence, termed GISA (glycopeptide intermediate Staphylococcus aureus) or VISA (vancomycin intermediate Staphylococcus aureus), began appearing the the late 1990s. The first identified case was in Japan in 1996, and strains have since been found in hospitals in England, France and the US. The first documented strain with complete (>16ug/ml) resistence to vancomycin, termed VRSA (Vancomycin-resistant Staphylococcus aureus) appeared in the United States in 2002.

A new class of antibiotics, oxazolidinones, became available in the 1990s, and the first commercially available oxazolidinone, linezolid, is comparable to vancomycin in

effectiveness against MRSA. Linezolid-resistance in Staphylococcus aureus was reported in 2003. CA-MRSA (Community-acquired MRSA) has now emerged as an epidemic that is responsible for rapidly progressive, fatal diseases including necrotizing pneumonia, severe sepsis and necrotizing fasciitis. Methicillin-resistant Staphylococcus aureus (MRSA) is the most frequently identified antimicrobial drug-resistant pathogen in US hospitals. The epidemiology of infections caused by MRSA is rapidly changing. In the past 10 years, infections caused by this organism have emerged in the community.

Enterococcus faecium is another superbug found in hospitals. Penicillin-Resistant Enterococcus was seen in 1983, Vancomycin-Resistant Enterococcus (VRE) in 1987, and Linezolid-Resistant Enterococcus (LRE) in the late 1990s. Streptococcus pyogenes (Group A Streptococcus: GAS) infections can usually be treated with many different antibiotics. Early treatment may reduce the risk of death from invasive group A streptococcal disease. However, even the best medical care does not prevent death in every case. For those with very severe illness, supportive care in an intensive care unit may be needed. For persons with necrotizing fasciitis, surgery often is needed to remove damaged tissue. Strains of S. pyogenes resistant to macrolide antibiotics have emerged, however all strains remain uniformly sensitive to penicillin.

Resistance of Streptococcus pneumoniae to penicillin and other beta-lactams is increasing worldwide. The major mechanism of resistance involves the introduction of mutations in genes encoding penicillin-binding proteins. Selective pressure is thought to play an important role, and use of beta-lactam antibiotics has been implicated as a risk factor for infection and colonization. Streptococcus pneumoniae is responsible for pneumonia, bacteremia, otitis media, meningitis, sinusitis, peritonitis and arthritis.

What is hospital-acquired infection?

A hospital-acquired infection (HAI), also known as a nosocomial infection, is an infection that is acquired in a hospital or other health care facility. According to WHO estimates, approximately 15% of all hospitalized patients suffer from these infections. During hospitalization, patient is exposed to pathogens through different sources environment, healthcare staff, and other infected patients. Transmission of these infections should be restricted for prevention.

Hospital-acquired infection microorganisms

A nosocomial infection, also known as a hospital-acquired infection or HAI, is an infection whose development is favoured by a hospital environment, such as one acquired by a patient during a hospital visit, or one developed among hospital staff. Such infections include fungal and bacterial infections, and are aggravated by the reduced resistance of individual patients.

Known nosocomial infections include: Ventilator-associated pneumonia, Staphylococcus aureus, Methicillin resistant Staphylococcus aureus, Candida albicans, Pseudomonas aeruginosa, Acinetobacter baumannii, Stenotrophomonas maltophilia, Clostridium difficile, Tuberculosis, Urinary tract infection, Hospital-acquired pneumonia, Gastroenteritis, Vancomycin-resistant Enterococcus, Legionnaires' disease.

Methicillin-resistant Staphylococcus aureus (MRSA) is a bacterium responsible for several difficult-to-treat infections in humans. It is also called multidrug-resistant Staphylococcus aureus and oxacillin-resistant Staphylococcus aureus (ORSA). MRSA is any strain of Staphylococcus aureus that has developed resistance to beta-lactam antibiotics, which include the penicillins (methicillin, dicloxacillin, nafcillin, oxacillin, etc.) and the cephalosporins. Strains unable to resist these antibiotics are classified as methicillin-sensitive Staphylococcus aureus, or MSSA. The development of such resistance does not cause the organism to be more intrinsically virulent than strains of Staphylococcus aureus that have no antibiotic resistance, but resistance does make MRSA infection more difficult to treat with standard types of antibiotics, and thus more dangerous.

Suspectible Hosts

A nosocomial infection, also known as a hospital-acquired infection or HAI, is an infection whose development is favoured by a hospital environment, such as one acquired by a patient during a hospital visit or one developing among hospital staff. Such infections include fungal and bacterial infections. They are aggravated by the reduced resistance of individual patients. Numerous risk factors in the hospital setting predispose a patient to infection. These risk factors can broadly be divided into three areas.

- People in hospitals are usually already in a 'poor state of health', impairing their defense against bacteria. Advanced age or premature birth, along with

immunodeficiency (due to drugs, illness, or irradiation) present a general risk, while other diseases can present specific risks; for instance, chronic obstructive pulmonary disease can increase chances of respiratory tract infection.

- Invasive devices, for instance intubation tubes, catheters, surgical drains, and tracheostomy tubes all bypass the body's natural lines of defense against pathogens and provide an easy route for infection. Patients already colonized at the time of admission are instantly put at greater risk when they undergo invasive procedures.
- Patients' treatments can leave them vulnerable to infection: immunosuppression and antacid treatment undermine the body's defences, while antimicrobial therapy (removing competitive flora and only leaving resistant organisms) and recurrent blood transfusions have also been identified as risk factors.

Prevention

Hospitals have sanitation protocols regarding uniforms, equipment sterilization, washing, and other preventive measures. Thorough hand washing and/or use of alcohol rubs by all medical personnel before and after each patient contact is one of the most effective ways to combat nosocomial infections. More careful use of antimicrobial agents, such as antibiotics, is also considered vital. Despite sanitation protocol, patients cannot be entirely isolated from infectious agents. Furthermore, patients are often prescribed antibiotics and other antimicrobial drugs to help treat illness; this can increase the selection pressure for the emergence of resistant strains.

MRSA Infections

Methicillin-resistant *Staphylococcus aureus* (MRSA) is an infection caused by a type of *Staphylococcus*, or staph, bacteria that's resistant to many different antibiotics. These bacteria naturally live in the nose and on the skin and generally don't cause any harm. However, when they begin to multiply uncontrollably, a MRSA infection can occur. These infections typically occur when there's a cut or break in your skin.

MRSA is very contagious and can be spread through direct contact with an infected person. It can also be contracted by coming into contact with an object or surface that an infected person has touched. Though a MRSA infection can be serious, it may be treated effectively with antibiotics. MRSA infections are classified as either hospital-acquired (HA-MRSA) or community-acquired (CA-MRSA).

HA-MRSA: HA-MRSA is associated with infections that are contracted in medical facilities such as hospitals or nursing homes. You can get this type of MRSA infection through direct contact with an infected wound or contaminated hands. You can also become infected through contact with contaminated linens or poorly sanitized surgical instruments. HA-MRSA can cause severe problems, such as blood infections and pneumonia. CA-MRSA: CA-MRSA is associated with infections that are transmitted through close personal contact with an infected person or through direct contact with an infected wound. This type of MRSA infection may also develop as a result of poor hygiene such as infrequent or improper handwashing.

Who is at risk for developing MRSA? Risk factors vary depending on the type of MRSA infection. You're at an increased risk for HA-MRSA if you: were hospitalized within the past three months, regularly undergo hemodialysis, have a weakened immune system due to another medical condition, live in a nursing home. You're at an increased risk for CA-MRSA if you: share exercise equipment, towels, or razors with other people, participate in contact sports, work at a day care facility, live in crowded or unsanitary conditions.

Streptococcus Pyogenes

Like other potentially dangerous bacteria such as *E.coli*, *Streptococcus pyogenes* can be found in 5 per cent - 15 per cent of all humans, residing in the lungs or throat without causing any harm. *Streptococcus pyogenes* causes over 700 million infections globally every year and has a high mortality rate of 25 per cent in serious cases - once you have an infection the bacteria can cause a range of diseases ranging from sore throat and impetigo up to scarlet fever. Luckily, the bacteria is affected by penicillin so is treated easily in most cases - however several strains are building resistance to various other antibiotics.

Neisseria Gonorrhoeae

Gonorrhoea is spread through sexual contact and causes various infections in both men and women. Certain strains of the bacteria have shown resistance to antibiotics and have mutated over the course of 50 years or so, slowly adapting different resistances as doctors change their approach by using different antibiotics to counter the disease. The small hairs or 'pili' on the bacteria act like hooks that are used to move the cell and attach it to other healthy cells.

Mycobacterium Tuberculosis

Tuberculosis has been know by many names including scrofula and the White Plague and has been a huge cause of death and distraction throughout history, with evidence found in bodies estimated to be around 9,000 years old.

Acinetobacter Baumannu

Acinetobacter baumannii have become resistant to many antibiotics and like other bacteria are currently being countered most effectively through thorough hygiene in healthcare situations. The bacteria can survive in harsh conditions for long periods of time so are often difficult to deal with in weaker patients, and coupled with increasing resistance presents a tough challenge when encountered by doctors. Sometimes called *Iraqibacter*, *Acinetobacter baumannii* became very prevalent during the Iraq war amongst injured soldiers who passed through several different medical facilities.

Escherichia Coli (E.Coli)

Most *E.coli* is completely harmless and survives happily in the human digestive system. However, some strains of *E.coli*can cause serious illness and most commonly lead to severe food poisoning as well as meningitis and infections. A high level of resistance to antibiotics has been found across several strains of *E.coli* and while it is rare to find these strains causing illness, it is another concerning example of a bacteria that has the potential to cause problems if our use of antibiotics goes unchecked.

Klebsiella Pneumoniae

Klebsiella pneumoniae can cause a range of infections and has proven to be very resistance to a range of antibiotics. Primarily affecting middle-aged and older men with weakened immune systems, this bacteria can be dangerous but is mostly ‘opportunistic’ and is far less likely to affect healthy adults.

Clostridium Difficile

One of the better known ‘superbugs’ because of a consistent presence in hospitals around the world, *C.difficile* is, primarily, an easily spread type of diarrhoea that can lead to complications in the colon.

Pseudomonas Aeruginosa

Quick to mutate and adapt to counter different antibiotic treatments, *Pseudomonas aeruginosa* shows an innate ability to develop resistance to antibiotics. Described as ‘opportunistic’ because it primarily affects humans that are already critically ill, this bacteria can cause serious complications in the treatment of AIDS, cancer or cystic fibrosis patients.

While it isn't a massive threat to humanity currently, this bacteria will become an increasing threat over the next few years.

Burkholderia Cepacia

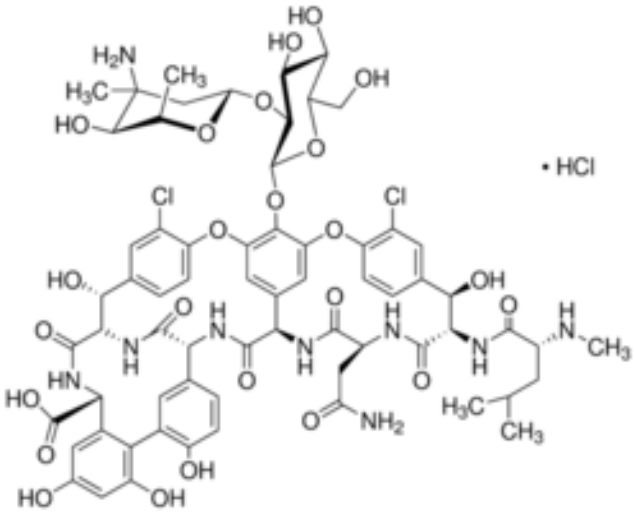
Discovered in 1949 as the bacterium that causes onions to rot, *Burkholderia cepacia* can be very dangerous to humans in the worst cases. While it mostly responds well to treatment with a combination of antibiotics, it has been shown to have high levels of resistance to several types of antibiotics and is able to survive in extreme conditions.

Staphylococcus Aureus (Mrsa)

More commonly known as MRSA (which stands for Methicillin-resistant *Staphylococcus aureus*), this 'superbug' is very easily spread through human contact and can cause a range of illnesses from skin disorders to deadly diseases like meningitis and pneumonia. Most often treated with Penicillin type antibiotics, by 1960, 80 per cent of hospital samples were antibiotic resistant.

ANTIBIOTICS USED FOR RESISTACE BACTERIA

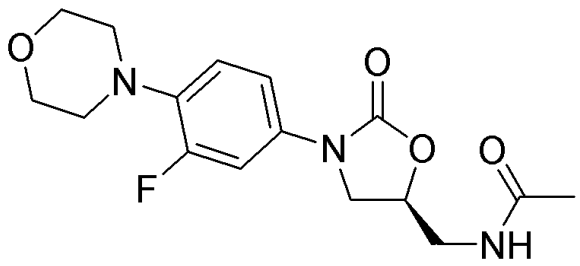
1. Vancomicin



Vancomycin is used to treat infections caused by bacteria. It belongs to the family of medicines called antibiotics. Vancomycin works by killing bacteria or preventing their growth. Vancomycin will not work for colds, flu, or other virus infections.

Vancomycin is used to treat infections in many different parts of the body. It is sometimes given with other antibiotics. Vancomycin is also used in patients with heart valve disease (e.g., rheumatic fever) or prosthetic (artificial) heart valves who are allergic to penicillin. Under certain circumstances, this medicine also may be used to prevent endocarditis (inflammation of the lining of the heart) in these patients who are having dental work done or surgery on the upper respiratory tract (for example, nose or throat). Vancomycin given by injection is used mainly for serious infections for which other medicines may not work. However, this medicine may cause some serious side effects, including damage to your hearing and kidneys. These side effects may be more likely to occur in elderly patients. You and your doctor should talk about the good this medicine will do as well as the risks associated with receiving it. This product is available in Solution and Powder for Solution forms.

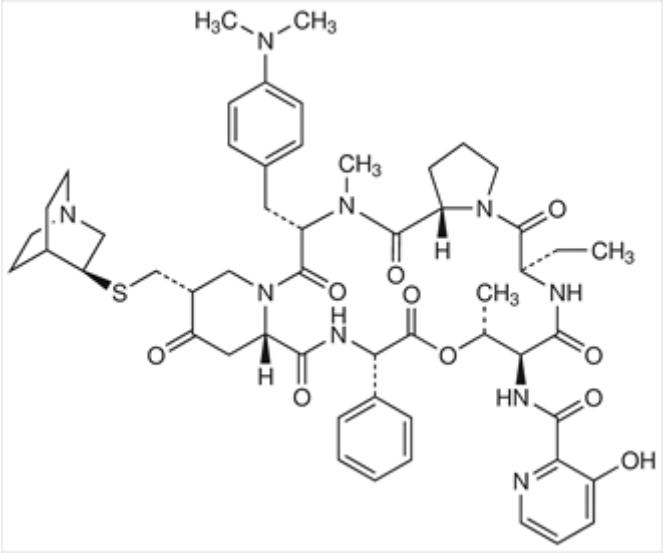
2. Linezolid



Linezolid is a synthetic antibiotic, the first of the oxazolidinone class, used for the treatment of infections caused by multi-resistant bacteria including streptococcus and methicillin-resistant Staphylococcus aureus (MRSA). The drug works by inhibiting the initiation of bacterial protein synthesis. For the treatment of bacterial infections caused by susceptible strains of vancomycin resistant *Enterococcus faecium*, *Staphylococcal aureus* (methicillin resistant and susceptible strains), *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Streptococcus agalactiae*. Linezolid is a synthetic antibacterial agent of the oxazolidinone class of antibiotics. It has in vitro activity against aerobic Gram positive bacteria, certain Gram negative bacteria and anaerobic microorganisms. It selectively inhibits bacterial protein synthesis through binding to sites on the bacterial ribosome and prevents the formation of a functional 70S-initiation complex. Specifically, linezolid binds to a site on the

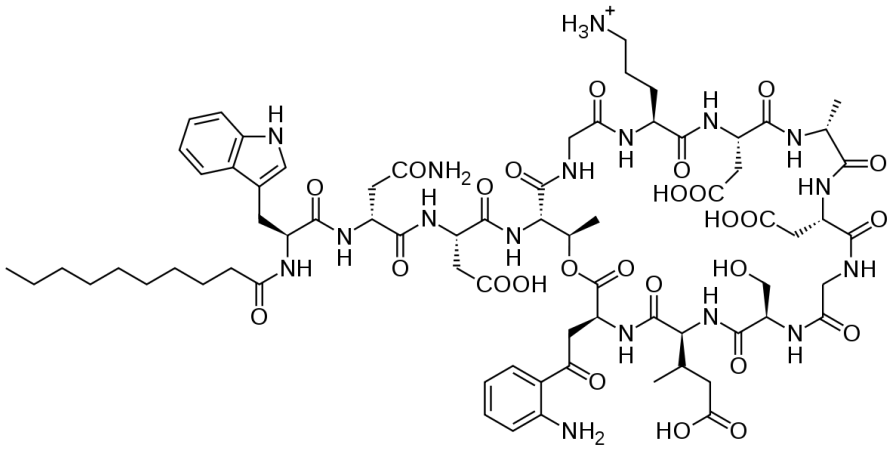
bacterial 23S ribosomal RNA of the 50S subunit and prevents the formation of a functional 70S initiation complex, which is an essential component of the bacterial translation process. The results of time-kill studies have shown linezolid to be bacteriostatic against enterococci and staphylococci. For streptococci, linezolid was found to be bactericidal for the majority of strains. Linezolid is also a reversible, nonselective inhibitor of monoamine oxidase. Therefore, linezolid has the potential for interaction with adrenergic and serotonergic agents.

3. Quinupristin/ Dalfopristin



Quinupristin and dalfopristin are intravenously administered, streptogramin antibiotics used in fixed combination to treat severe bacterial infections due to susceptible organisms including methicillin resistant Staphylococcus aureus (MRSA). The fixed combination of quinupristin and dalfopristin is associated with a low rate of serum enzyme elevations during therapy but has not been convincingly linked to instances of clinically apparent liver injury. Quinupristin, a derivative of pristamycin IA, and dalfopristin, a derivative of pristamycin IIA, are synergistic in activity and are used in a fixed dose combination in a ratio of 30:70 by weight. This combination binds and inhibits the activity of the 50S subunit of bacterial ribosomes, which yields potent bactericidal activity against many gram positive bacteria including methicillin resistant forms of Staphylococcus aureus (MRSA). Quinupristin and dalfopristin also have activity against some gram negative bacteria including Enterococcus species.

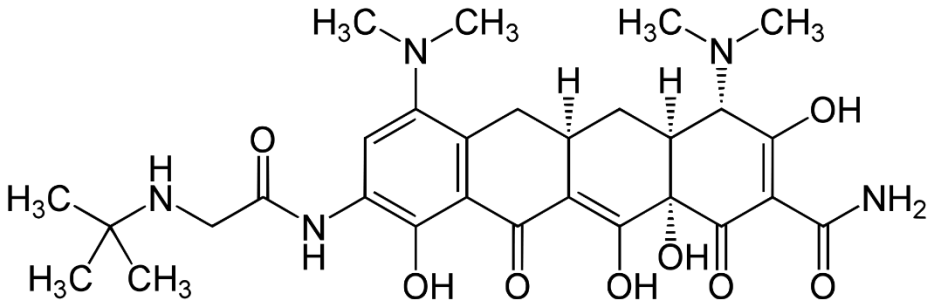
4. Daptomicin



Daptomycin is a lipopeptide antibiotic that kills susceptible gram positive bacteria by disrupting their membrane potential. It is a naturally-occurring compound found in the soil bacterium *Streptomyces roseosporus*. Antibiotics are used in the treatment of infections caused by bacteria. They work by killing bacteria or preventing their growth. Daptomycin will not work for colds, flu, or other virus infections. It was approved in September 2003 for the treatment of complicated skin and soft tissue infections. It has a safety profile similar to other agents commonly administered to treat gram-positive infections. Daptomycin is a 13 member amino acid cyclic lipopeptide antibiotic active against Gram-positive bacteria only. It has proven in vitro activity against enterococci (including glycopeptide-resistant Enterococci

(GRE)), staphylococci (including methicillin-resistant *Staphylococcus aureus*), streptococci and corynebacteria. Daptomycin is derived from the fermentation product of Streptomyces roseosporus.

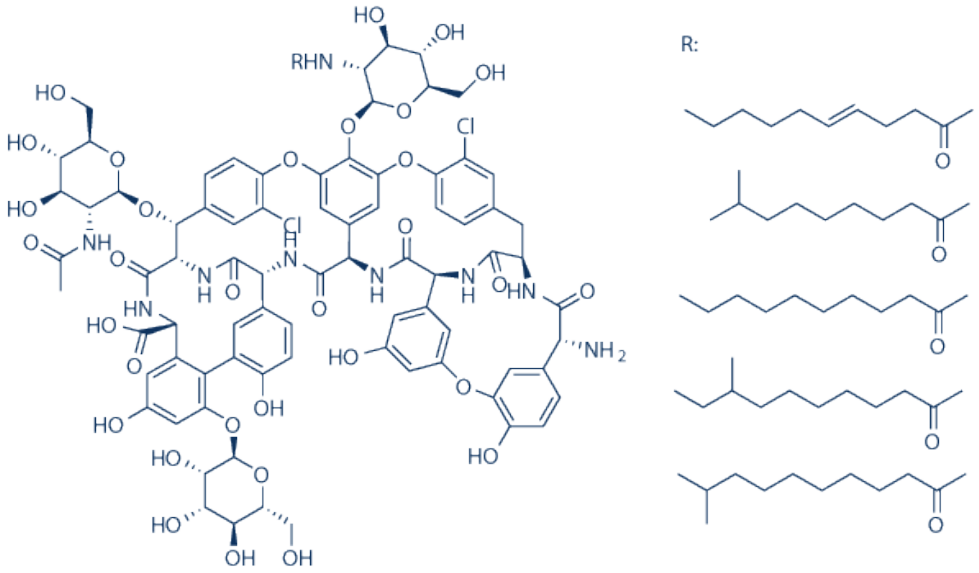
5. Tigecycline



Tigecycline is an antibiotic used to treat a number of bacterial infections. It is a glycylcycline that is administered intravenously. It was developed in response to the growing rate of antibiotic resistance in bacteria such as Staphylococcus aureus, Acinetobacter baumannii, and E. coli. Tigecycline is an injectable antibiotic used for the treatment of infections caused by susceptible bacteria. Tigecycline is similar to tetracycline antibiotics and has activity against a large number of bacteria. Tigecycline binds to bacterial ribosomes which produce the cell's proteins. The binding prevents bacterial ribosomes from producing important proteins needed for bacterial growth and multiplication. Tigecycline prevents bacteria from multiplying, but it does not kill bacteria. Tigecycline was approved by the FDA in June 2005.

6. Teicoplanin

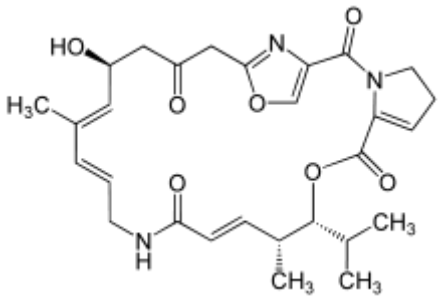
Teicoplanin is an antibiotic used in the prophylaxis and treatment of serious infections caused by Gram-positive bacteria, including methicillin-resistant Staphylococcus aureus and Enterococcus faecalis. It is a semisynthetic glycopeptide antibiotic with a spectrum of activity similar to vancomycin.



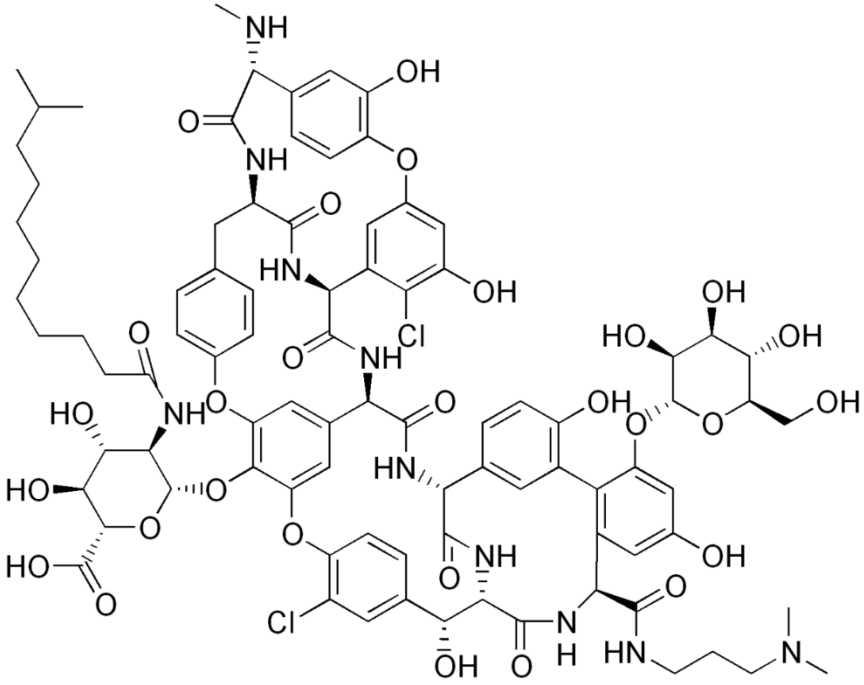
Antimicrobial Spectrum: *Staphylococcus aureus* (teicoplanin susceptible), Coagulase negative Staphylococci, *Streptococcus pneumoniae*, *Streptococcus spp.*, *Enterococcus spp.* (Teicoplanin susceptible), *C. jeikeium*, *Clostridium spp.*, *L. monocytogenes*, *Actinomyces.*

Mechanism of Action: Teicoplanin inhibits polymerization of cell wall components in susceptible bacteria

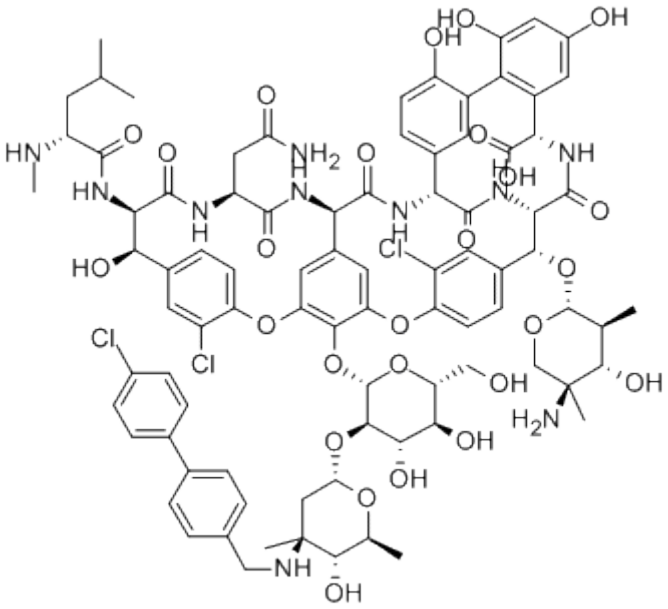
7. Pristinamicyn



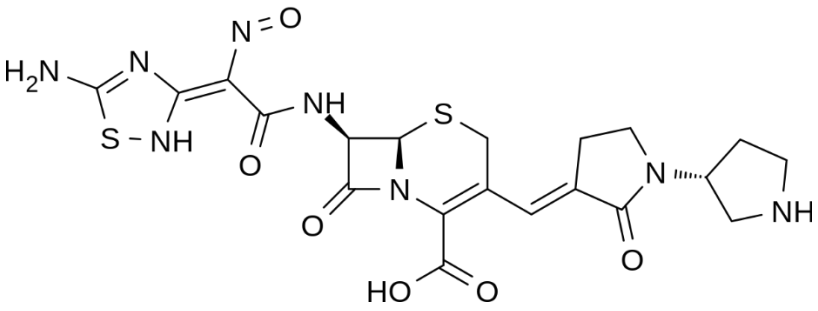
8. Dalbavancin



9. Oritavancin



10. Ceftobiprole



Ceftobiprole (Zevtera/Mabelio) is a new 5th-generation cephalosporine for the treatment of hospital-acquired pneumonia and community-acquired pneumonia (CAP). Ceftobiprole is an experimental cephalosporin antibiotic with activity against methicillin-resistant Staphylococcus aureus.