Antibiotics – Types and Antibiotic Therapy

Antibiotics are an indispensable part of modern medicine. Many infectious diseases are fatal without antibiotic treatment. Therefore, the empirical use of antibiotics is the basic component of many therapies. However, due to increasing resistance and incidence of long underestimated problematic bacteria, such as *Acinetobacter baumannii* complex, every medical student and practitioner should know the common antibiotics, their indications, and frequent side effects.

Basics of Antibiotic Therapy

When using antibiotics, distinctions can be made between the different approaches. This derives from the fact that the start of the use of antibiotics is often carried out prior to the final microbiological findings being available, which is approximately 48—72 hours after sampling. If the antibiotic treatment is started without knowing the exact causative pathogen, based on the expected pathogen spectrum of the injury or clinical presentation at hand, and the knowledge about sensitive and resistant pathogens, the physician can begin “generalized” treatment called empiric therapy.

In this regard, it should always be noted whether the infection was acquired nosocomially (within the hospital) or in the community, because the expected bacteria may differ
greatly. In some cases, it is necessary to start a broad-spectrum antibiotic or “omni spectra therapy”. In that case, multiple antibiotics are combined, so that every type of a certain kind of pathogen will be destroyed. For example, omni-bacterial therapy is a mix of antibiotics that would kill every or almost every kind of bacteria.

Once the causative pathogen has been confirmed, an antibiogram or resistogram may be performed. This is a graphical display of the resistance or sensitivity of a certain type of bacteria to different antibiotics. If pharmacological treatment is started and the resistogram shows that the bacterium reacts sensitively to it, it is called definitive therapy.

For cost and labor savings, antibiotic therapy in moderate to severe cases is usually begun parenterally and then to oral therapy after a few days. This concept is called sequential therapy.

Mechanisms of actions

A distinction should be made between bacteriostatic and bactericidal antibiotics. In the case of bacteriostasis, the antibiotic leads to the inhibition of bacterial multiplication. The number of bacteria regresses slowly over time due to the effects of the body’s immune system. Bactericidal antibiotics, however, kill the bacteria. For example, beta-lactam antibiotics directly destroy invading bacteria, while tetracyclines just inhibit the growth and multiplication of the pathogens.

Actions of PBPs and Transpeptidase

Penicillin-binding proteins (PBPs) mediating the removal of D-alanine from the precursor of peptidoglycan in the process of bacterial cell wall biosynthesis.

Penicillin-binding proteins or PBPs are bacterial proteins, generally enzymes, that bind to penicillin and other antibiotics of the β-lactam class. PBPs play an essential role in bacterial cell wall biosynthesis. More specifically, they contribute to the final stages of the biosynthesis of peptidoglycan, which is the major component of bacterial cell walls. Inhibition or alteration of the normal action of PBPs leads to defects in the bacterial cell wall structure, irregularities in shape, and eventual cell death.

**PBPs bind to β-lactam antibiotics because they are structurally similar to that**
of peptidoglycan’s precursor. When they bind, the β-lactam amide bond is ruptured to form a covalent bond with the serine residue at the PBPs’ active site. This is an irreversible reaction and inactivates the enzyme; thus, altering the bacteria’s cellular structure.

Susceptibility testing

As mentioned above, a resistogram is an in-vitro test of the antibiotic’s effect on a bacterial strain. The minimal inhibitory concentration indicates the lowest concentration of an antibiotic at which the multiplication of the pathogen is prevented.

The assessment is based on standardized protocols. Thus, the resultant reactions are classified as sensitive, intermediate, or resistant. The stated limits for these divisions are based on microbiological aspects, the pharmacokinetics of an antibiotic, and protein binding. Sensitive means when the minimal inhibitory concentration for a corresponding antibiotic is so low that, in case of therapy with the usual doses, therapeutic success is expected.

Mechanisms of resistance

A distinction is made between natural and acquired resistance. Some bacteria are naturally resistant to certain antibiotic classes (for example, Pseudomonas aeruginosa is resistant to penicillin) and other originally sensitive bacteria have obtained resistance through gene mutation or acquisition of R-genes.

Thus, resistant bacteria are able to inhibit, for example, the antibiotic’s penetration into the bacterial cell, change the target molecules, form enzymes that cleave antibiotics, form pumps that discharge the antibiotic out of the cell, or avoid the antibiotic’s effects by alternative metabolic pathways.
Beta-lactam Antibiotics

Beta-lactam antibiotics are named after the characteristic beta-lactam ring in their structural formula. Their effect is based on the inhibition of transpeptidase and, consequently, of peptidoglycan synthesis during bacterial cell division. Thus, they have a bactericidal effect.

The effectiveness of β-lactam antibiotics is limited by nature because they are ineffective against Chlamydia, Mycoplasma, enterococci, and Legionella. Additionally, the so-called "eagle effect" (also called paradoxical zone phenomenon) occurs: high bacterial concentrations reduce the effectiveness of antibiotics. The cause is a decreased expression of a penicillin-binding protein in the stationary phase of bacteria. Mechanisms of resistance, antagonistic effects, and penicillin precipitation also contribute to the eagle effect.

Side effects of penicillin therapy are relatively rare since the mechanism of action is based on inhibition of bacterial cell wall synthesis. That is to say, penicillins affect bacterial cells but not human cells. However, up to 10% of patients are allergic to penicillins and cross-reactively allergic to other beta-lactams.

These type 1 allergies range from light skin reactions to anaphylactic shock and are better not underestimated. In rare cases, type 3 allergies with interstitial nephritis, Stevens-Johnson syndrome, and hemolytic anemia occurs. A rare, but complicated side effect is Nicolau syndrome. This occurs in the case of accidental arterial application and causes necrosis and gangrene of the fingers and toes.
In the case of antibiotic therapy against spirochetes, such as *Treponema pallidum* or *Leptospira interrogans*, there is the risk of a Jarisch-Herxheimer reaction during the decomposition of a large number of bacteria. In this reaction, sudden fever, headache, and limb pain as well as worsening of the underlying disease pathology is caused by the release of endotoxins. Therapy consists of the inhibition of the host’s immune system through the use of cortisone.

**Penicillins**

**β-lactamase-sensitive penicillins**

**Penicillin G**

- Discovered in 1929 by Fleming
- Consists of a β-lactam ring = cyclic amide
- Fused with a substituted thiazolidine ring

Penicillin G, or benzylpenicillin, is still synthesized by fermentation of fungal cultures. Penicillin is acid-unstable and, thus, cannot be administered orally. In addition, it is labile to β-lactamases. The administration should be intravenous or intramuscular, whereby the penicillin from the intramuscular depot is released slowly and continuously. 50 % of the penicillin administered will be protein-bound in the plasma. 90 % of the elimination takes place through the kidneys, whereby it is excreted in the form of penicillic acid, which is less effective against gram-positive bacteria than penicillin but more effective against gram-negative bacteria than penicillin.

With respect to the penicillin-sensitive pathogens, penicillin G has the highest effectiveness, compared with other beta-lactam antibiotics. Indications for the use of benzylpenicillin are mainly infections with hemolytic streptococci, listeria, and bacilli.

Examples of infections treated with penicillin include erysipelas, scarlet fever, rheumatic fever, endocarditis lenta, syphilis, and leptospirosis. Non-penicillinase-producing staphylococci (account for about 20 %) are susceptible as well. Because of mixed infections and resistances, diseases such as meningitis and pneumonia are treated with broad-spectrum antibiotics despite being caused primarily by penicillin-sensitive pathogens. Notably, the penicillin resistance of gonococci has greatly increased in recent years so that penicillin is no longer recommended in the case of gonorrhea.

**Penicillin V**
Phenoxyethylpenicillin, also called penicillin V, is the acid-stable form of penicillin and, thus, can be administered orally. In the small intestine, about 60% of the administered amount of Penicillin V is absorbed. Since lactose and sucrose promote the absorption of penicillin V from the duodenum, its presentation often includes added lactose monohydrate (caution: should not be used by children with galactose metabolic disorders!).

In the skin, lungs, and kidneys, the bioavailability is high. In bones, nerve tissue, and muscles, on the other hand, it is insufficient. Consequently, it is indicated in infections of the mucous membranes and the skin. Penicillin V, analogous to penicillin G, is very effective against group A streptococci, and in the case of minor skin infections such as boils, impetigo, and erysipelas caused by staphylococci.

**Note:** Since penicillins have a bactericidal effect, they should not be coadministered with bacteriostatic antibiotics such as tetracyclines and macrolides. A synergism, however, is possible with aminoglycosides.

**The Action of Penicillins**

β-lactamase-resistant penicillins

Isoxazolylpenicillins are resistant to β-lactamases produced by staphylococci and are, therefore, also called penicillinase-solid or staphylococci penicillins. However, they are less effective against penicillin G-sensitive staphylococci. They can be administered orally
Flucloxacillin and Oxacillin

Flucloxacillin is just indicated for the treatment of diseases caused by \(\beta\)-lactamase-forming staphylococci (for example, \(S.\) \(aureus\) and \(S.\) \(epidermidis\)). It is often used for infections of the skin and mucous membranes.

Oxacillin (referred to as methicillin in the USA) is mainly used in the laboratory in order to test the resistance of \(Staphylococcus\) \(aureus\). When \(S.\) \(aureus\) is resistant, it is called oxacillin-resistant \(Staphylococcus\) \(aureus\) (ORSA or MRSA).

Likewise, some \(S.\) \(epidermidis\) strains are also resistant and called MRSA. Community-acquired MRSA has a modified penicillin-binding protein so that penicillins cannot bind to the bacteria, which makes them resistant to all \(\beta\)-lactam antibiotics. The non-community-acquired MRSA pathogens that primarily occur in hospitals are also resistant to many other classes of antibiotics, such as tetracyclines and aminoglycosides.

Aminopenicillins

Aminopenicillins are eponymous for an amino group which is attached to the penicillin benzyl group. Aminopenicillins are not \(\beta\)-lactamase-stable and only possess about one-third of the efficiency of benzylpenicillin against gram-positive bacteria.

But they are very effective against gram-negative bacteria, such as \(E.\) \(coli\) and \(Proteus\) \(mirabilis\).

Ampicillin

Even though ampicillin is acid-proof, it is mostly applied parenterally because of its low oral bioavailability. Yet, it has good tissue penetration. Ampicillin is indicated in the case of infections by hemophilia, enterococci, and listeria. Possible applications include infections of the biliary tract, respiratory tract, urinary tract, and COPD exacerbations.

**Note:** Ampicillin is often the trigger of allergic skin reactions in the form of a measles-like
exanthema, mainly in patients with chronic leukemia.

**Amoxicillin**

Amoxicillin is also acid-resistant. Compared to ampicillin, it has a considerably higher oral bioavailability and is, thus, mostly administered orally.

**Acylaminopenicillins**

Compared to ampicillin, acylaminopenicillins have an extended efficacy spectrum against gram-negative bacilli, such as enterobacteria. However, since they are not penicillinase-solid, they are ineffective against most staphylococci. Since acylaminopenicillins are not acid-stable, the application can only be performed parenterally, whereby the tissue penetration (cerebrospinal fluid excluded) is good. Excretion takes place mainly via the urine.

**Piperacillin**

![Piperacillin](image)

Piperacillin is characterized by its efficacy against *Pseudomonas aeruginosa*. Therefore, it is mainly used in combination with the β-lactamase inhibitor Tazobactam as empiric therapy in cases of sepsis, pneumonia, and abdominal infections with unknown pathogens.

**Mezlocillin**

Mezlocillin is more effective against enterococci than piperacillin and ampicillin. For this reason and due to its effectiveness against enterobacteria, it is used for infections of the urinary tract and biliary tract.

**Overview of β-lactam-antibiotics**

<table>
<thead>
<tr>
<th>β-lactam-antibiotics</th>
<th>Dosage form</th>
<th>Susceptible pathogens</th>
<th>Indication</th>
<th>Contraindication</th>
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<tr>
<td>Amoxicillin</td>
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<tr>
<td>Acylaminopenicillins</td>
<td></td>
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<td></td>
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<tr>
<td>Piperacillin</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Mezlocillin</td>
<td></td>
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</tr>
<tr>
<td><strong>Penicillin G</strong></td>
<td><strong>Parenteral</strong> (intravenous, intramuscular)</td>
<td><strong>Streptococci, Listeria, Bacilli</strong></td>
<td><strong>Erysipelas, scarlet fever, Endocarditis lenta, rheumatic fever</strong></td>
<td><strong>Allergy, gonorrhea</strong></td>
</tr>
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</tr>
<tr>
<td><strong>Penicillin V</strong></td>
<td><strong>oral</strong></td>
<td><strong>Streptococci, staphylococci</strong></td>
<td><strong>Angina tonsillaris, scarlet fever, boils, impetigo</strong></td>
<td><strong>Galactose-metabolic disorder, allergy</strong></td>
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<tr>
<td><strong>Flucloxacillin</strong></td>
<td><strong>oral, parenteral</strong></td>
<td><strong>penicillinase-producing staphylococci</strong></td>
<td><strong>Infections of the skin and mucous membrane</strong></td>
<td><strong>Allergy, infections with penicillin-susceptible pathogens</strong></td>
</tr>
<tr>
<td><strong>Ampicillin</strong></td>
<td><strong>parenteral</strong></td>
<td><strong>Haemophilus, Listeria, Enterococci</strong></td>
<td><strong>Listeriosis, biliary tract infections with enterococci</strong></td>
<td><strong>Allergy, especially in patients with chronic leukemia</strong></td>
</tr>
<tr>
<td><strong>Amoxicillin</strong></td>
<td><strong>oral</strong></td>
<td><strong>like ampicillin</strong></td>
<td><strong>like ampicillin</strong></td>
<td><strong>Allergy</strong></td>
</tr>
<tr>
<td><strong>Piperacillin</strong></td>
<td><strong>parenteral</strong></td>
<td><strong>Pseudomonas aeruginosa, enterobacteria</strong></td>
<td><strong>Sepsis, pneumonia, abdominal infections</strong></td>
<td><strong>Allergy, infections with penicillinase-producing staphylococci</strong></td>
</tr>
<tr>
<td><strong>Mezlocillin</strong></td>
<td><strong>parenteral</strong></td>
<td><strong>Enterococci, enterobacteria</strong></td>
<td><strong>Urinary and biliary tract infections</strong></td>
<td><strong>Penicillin allergy</strong></td>
</tr>
</tbody>
</table>

### β-lactamase Inhibitors

These inhibitors are competitively bound by β-lactamases, cleaved into subunits, which are in turn covalently bound to the enzymes and irreversibly inactivate them. Since both enzyme and inhibitor are destroyed, it is called a **suicide inhibition**.

In general, the effect of beta-lactam antibiotics that was annulled by beta-lactamases is restored when administered together with one of the inhibitors. Additionally, their effective range is extended to include anaerobes. Common combinations include amoxicillin and clavulanic acid (**Augmentan**), ampicillin and sulbactam (**Unazid**), as well as piperacillin and tazobactam (**Tazobac**).

### Cephalosporins

Cephalosporins are bicyclic beta-lactam antibiotics with an effect similar to penicillin, inhibiting the transpeptidase and, thus, the crosslinking of murein strands. Enterococci, *Listeria, Legionella, Campylobacter, Chlamydia*, and *Mycoplasma* are resistant to cephalosporins. Cephalosporins are categorized into generations depending on when they were discovered, synthesized, and/or manufactured.
**Note:** Cephalosporins of lower generations are effective against gram-positive bacteria. Higher generations are also effective against gram-negative bacteria, *Pseudomonas* in particular, but have a decreased effectiveness against gram-positive pathogens.

**Cefazolin: 1st-generation cephalosporin**

Cefazolin can only be administered parenterally and has good tissue penetration. Its effectiveness against *Staphylococcus aureus* must be emphasized. The main indication is **perioperative prophylaxis**. This should be done once, 30 minutes before the first skin incision. In the case of penicillin allergy, it may also be used for infections caused by staphylococci.

Allergic side effects during the use of cefazolin rarely occur.

**Cefuroxime and cefotiam: 2nd-generation cephalosporins**

Compared to cefazolin, the activity spectrum of cefuroxime and cefotiam against gram-negative bacteria is extended, which is why they are sometimes referred to as a **base cephalosporin**. These two antibiotics can only be administered parenterally as well. They are indicated in moderate organ infections with gram-positive or gram-negative pathogens.

But, they may not be used for meningitis. It should be noted that increasing numbers of enterobacteria form a so-called **extended-spectrum β-lactamase** (ESBL) so that they are resistant to these actual beta-lactamase-stable antibiotics.

**Ceftriaxone and cefotaxime: 3rd-generation cephalosporins**

These **broad-spectrum cephalosporins** are extremely effective against enterobacteria and other gram-negative bacteria, but can only be administered parenterally. Ceftriaxone is often preferred in clinical practice since it must be administered only once a day. Broad-spectrum cephalosporins are particularly effective against typical **meningitis-causing pathogens** like pneumococci, meningococci, and Haemophilus.

Other indications for empiric therapy with these antibiotics are severe infections that must be treated in the intensive care unit. Compared to 1st- and 2nd-generation cephalosporins, they are less effective against the Enterobacter species *E. cloacae, Citrobacter freundii*, streptococci, and staphylococci.

Gaps in the spectrum are closed through the combination of cephalosporins with aminoglycosides or metronidazole. It is worth mentioning that these two antibiotics are excreted via bile, so a **transient pseudocholelithiasis** can develop during the application of ceftriaxone. Therefore, its use is contraindicated for acute hepatitis and icteric newborns.

**Note:** Ceftriaxone must never be administered with calcium-containing IV solutions since calcium-ceftriaxone precipitates can occur, which can be fatal for infants.
Ceftazidime: 3rd-generation *Pseudomonas*-effective cephalosporin

Ceftazidime is a reserve antibiotic for the intravenous treatment of severe infections with suspected *P. aeruginosa* participation. Therefore, it is especially applicable in neutropenic and hospitalized patients. The gap of non-sensitivity of staphylococci and anaerobes can be closed by administering it in combination with clindamycin.

Cefepime: 4th-generation cephalosporin

Like ceftazidime, cefepime is effective against gram-negative bacteria, especially *Pseudomonas*. But in contrast to 3rd-generation cephalosporins, it is also very effective against staphylococci and streptococci. The main indications are biliary tract infections, peritonitis, nosocomial infections, and meningitis (note: ineffective against listeria).

Carbapenems

Carbapenems, like penicillins and cephalosporins, are β-lactam antibiotics. They are characterized by a broad bacterial spectrum and a high β-lactamase resistance. They must be administrated parenterally, due to low plasma protein binding. Yet, tissue distribution is good. Carbapenems are primarily metabolized through the kidneys, so that a dose adjustment will be necessary in case of renal insufficiency.

Currently, 3 carbapenems are available on the German market: imipenem, meropenem, and ertapenem. Imipenem has the best efficacy against gram-positive bacteria, while meropenem and ertapenem are more effective against gram-negative bacteria. They are absolute reserve antibiotics in case of serious life-threatening infections in the abdomen, sexual organs, bones, kidney, and respiratory system.

Ertapenem is also used as perioperative prophylaxis in colorectal surgery. This carbapenem is also applicable for the targeted treatment of multi-resistant gram-negative pathogens (ESBLs). However, *Klebsiella pneumoniae* (KPC for *Klebsiella pneumoniae* carbapenemases), *Acinetobacter baumannii* complex, and *Pseudomonas aeruginosa* can become resistant through the formation of metalloenzymes.

**Note:** Since imipenem is rapidly degraded by the endogenous enzyme dehydropeptidase I in the kidney, it is always combined with cilastatin, a dehydropeptidase inhibitor.
Vancomycin

Vancomycin is a glycoprotein that binds to the alanine terminal of the bacterial peptidoglycan. Resistant organisms have an altered terminal and, thus, a decreased affinity for vancomycin. Used for serious infections only. It does not cross the blood-brain-barrier and is used orally for luminal infections of the gastrointestinal tract.

Toxicity:

- ‘Redman syndrome’: presents as severe cutaneous flushing caused by histamine release
- Phlebitis
- Ototoxicity
- Nephrotoxicity

Bacitracin

- Used in topical treatment and decontamination syndromes.
- Used in staphylococcus colonization of the skin.
- Produces marked nephrotoxicity; thus, is not used parenterally

Daptomycin

- Cyclic lipopeptide
- Used for the treatment of vancomycin-resistant Enterococci (VRE) and vancomycin-resistant Staphylococcus aureus (VRSA)
- One should monitor creatinine kinase levels during treatment because daptomycin is myopathic.

Monobactams

The monobactam-type antibiotic called aztreonam is rarely used, even though it is a good alternative in the case of β-lactam allergy. Furthermore, it is extremely effective against gram-negative bacteria, Acinetobacter strains, anaerobes, and Stenotrophomonas maltophilia.

Fluoroquinolones

The mechanism of action of these antibiotics is based on inhibition of the bacterial DNA gyrase. Thus, the supercoiling of the DNA is abolished, so that the DNA breaks and no longer fits into the bacterial cell. Hence, the fluoroquinolones are bactericidal. Except for norfloxacin, fluoroquinolones also have a bactericidal effect in the stationary phase of bacterial growth.

Their spectrum includes gram-negative bacteria like Neisseria, Haemophilus, and Bordetella. Enterobacteria and Pseudomonas are also covered. The effect against streptococci and anaerobes, however, is not sufficient.

After oral administration, the absorption and volume of distribution is high. However, the absorption of fluoroquinolones is severely limited by a simultaneous intake of antacids or iron-containing preparations. Excretion takes place via the kidneys and feces.
Resistance to fluoroquinolones is based on point mutations in the gyrase gene and permeability disorders (reduced influx and active efflux). The development of resistance during therapy with fluoroquinolones happens relatively quickly. For this reason and the relatively-widespread use in recent years, resistant strains of *Pseudomonas aeruginosa*, staphylococci, and *E. coli* are often found.

Antibiotics of the fluoroquinolone group are contraindicated in pregnancy, children (since they damage the articular cartilage), and patients with epilepsy.

Common side effects during treatment with fluoroquinolones are gastrointestinal reactions, central nervous system reactions like dizziness, headaches, and tiredness, as well as allergic reactions.

**Bryskier Classification of Fluoroquinolones**

<table>
<thead>
<tr>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substances</td>
<td>Norfloxacin</td>
<td>Ciprofloxacin, Ofloxacin</td>
<td>Levofoxacin</td>
</tr>
<tr>
<td>Anti-microbial spectrum</td>
<td>Limited</td>
<td>Broad</td>
<td>Extended</td>
</tr>
<tr>
<td>Pathogen</td>
<td>Enterobacteria</td>
<td>Enterobacteria, <em>Haemophilus, Neisseria, S. aureus, P. aeruginosa, Mycoplasma, Chlamydia, Legionella</em> bacteria, etc.</td>
<td>Same as Group II + <em>S. pneumoniae</em> and anaerobes</td>
</tr>
<tr>
<td>Indications</td>
<td>Urinary tract infections</td>
<td>Infections of the urinary tract, gastrointestinal tract, skin, and joints, sepsis, otitis</td>
<td>Pyelonephritis, severe (nosocomial) respiratory tract, soft tissue, and systemic infections</td>
</tr>
</tbody>
</table>

**Ciprofloxacin**

Ciprofloxacin is a typical fluoroquinolone with the above-mentioned efficacy spectrum. It is not absorbed orally as well as other fluoroquinolones but achieves very high tissue levels when administered intravenously. The excretion mainly takes place via the kidneys, which is why there are restrictions on its use during renal failure.

Salmonella infections, bacterial gastroenteritis, gonorrhea, mycoplasma, and *Bartonella* infections are all indications for ciprofloxacin use. Also, it is applied for chemoprophylaxis in neutropenic patients. Furthermore, in contrast to other fluoroquinolones, it can be used in children with cystic fibrosis.

**Ofloxacin**
Ofloxacin

Of all fluoroquinolones, ofloxacin is best absorbed and has a longer half-life period. Furthermore, it is less heavily metabolized. However, there are losses in the efficacy, especially against *Pseudomonas*, *Chlamydia*, and enterococci.

**Glycopeptide Antibiotics**

Glycopeptide antibiotics like *vancomycin* inhibit the polymerization of murein strands and, thus, have a secondarily-bactericidal effect. They cover almost all gram-positive bacteria (Caution: a growing number of vancomycin-resistant enterococci = VRE) but are ineffective against gram-negative bacteria. Glycopeptide antibiotics are not resorbed orally and the absorption in the brain is very bad.

In internal organs and abscesses, on the other hand, good effective concentrations are reached. Since the excretion occurs 90% via the kidneys, toxic concentrations can be reached very quickly during renal failure, and particular care is required. It is also contraindicated in patients who are deaf.

Resistance to vancomycin is based on a change in the murein strands. Instead of the usual alanyl-alanine residue resistance, bacteria have a pentapeptide in their murein strands. The binding of vancomycin to this pentapeptide is significantly worse. Resistance genes include VanA which is plasmid-coded and causes resistance to *vancomycin and teicoplanin*. VanB and VanC, however, only encode resistance to vancomycin. As mentioned above, these resistances especially involve *Enterococcus faecium* (but less frequently *E. faecalis*) and *S. aureus*. These kinds of staphylococci are called VISA for vancomycin-intermediate *S. aureus*. 
Vancomycin is indicated for infections with staphylococci in the case of penicillin allergy, resistant corynebacteria, and enterococci. It is the medication of choice against the infection of a prosthetic or synthetic material within the body, such as prosthetic heart valves catheters, and is often combined with rifampicin or gentamicin to cover resistant staphylococci and enterococci.

For further outpatient treatment of such diseases, teicoplanin is applicable. It is a glycopeptide as well but has a longer half-life period than vancomycin. In cases of pseudomembranous colitis caused by Clostridium difficile, vancomycin can be orally administered and is nowadays often preferred rather than metronidazole.

References


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