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Talking about antibiotics: the right dose at the right time

In case of a bacterial infection animals will have to be treated with antibiotics. Antibiotics that come in contact with the bacteria either kill the bacteria or reduce bacterial growth which gives the immune system of the animal enough time to remove the bacteria. To choose the right antibiotic, you need to know which type of bacteria is causing the disease and the sensitivity of that bacteria for the antibiotic. For the antibiotic to be as effective as possible, it is important that you adhere to the dose and dose intervals as given for a certain product.

What happens with an antibiotic after administration?

Some antibiotics are administered by injection and others have to be supplied with the food or drinking water. For the first type the antibiotics will go into the bloodstream departing from the site of injection, for the second type the antibiotic will enter the bloodstream after being absorbed in the intestines of the animals. Next, through transport by the bloodstream, the antibiotic is distributed throughout the body and will reach the site of infection. This can be different tissues of the body: uterus, lungs, nervous system, muscle, bones, bladder etc.

An example of this process of absorption and distribution is shown in the graph below, but it is important to realize that this graph may look different depending on the type of antibiotic: some reach a higher maximum concentration, some reach their maximum concentration quicker/slower, and some stay in the body for a longer period. This is called the **pharmacokinetics** of the product.

Why do different antibiotics have different dosing schedules?

To be effective, an antibiotic will have to come into contact with the bacteria causing the disease **and** this needs to happen at a minimal concentration. This **MIC or minimal inhibitory concentration** is the lowest concentration of an antibiotic that inhibits growth of a certain bacterial strain (blue dotted line in the graph). If the maximal concentration, C_{max}, of an antibiotic in infected tissue would be lower than the MIC of the bacteria you want to fight, or if the duration of exposure of a bacteria to an antibiotic is too short, there will be no effect at all. On the contrary, there is a possibility that resistance develops.

At which dose and with which dosing interval an antibiotic is administered depends on the specific pharmacokinetics of the antibiotic.

There are two types of antibiotics:

Concentration dependent antibiotics: having high concentrations at the site of infection will improve efficacy. For those antibiotics it is important that the concentration of the antibiotic reaches a certain level above the MIC of the bacteria. An example is gentamycin, which has to be administered once or twice a day to reach a high concentration to be as effective as possible.

Time-dependent antibiotics: the duration of exposure of a bacteria to an antibiotic will determine efficacy. For those antibiotics it is no problem that the top of the graph is not so high (as long as it is above MIC), but the concentration has to remain above the MIC for a certain period. Examples include the penicillin preparations: those types of antibiotics have to stay above MIC for a at least half the dosing interval to be as effective as possible.

Table: examples of concentration- and time dependent antibiotics.

	Concentration-dependent	Time-dependent
Goal	Maximising antimicrobial concentration	Maximising duration of exposure of a pathogen to an antimicrobial
Antibiotic	Aminoglycosides e.g. gentamicin, neomycin, streptomycin	β-lactams e.g. penicillin, amoxicillin, cephalosporin
	Fluoroquinolones e.g. marbofloxacin	Macrolides e.g. tylosin
	Metronidazole	Lincosamides e.g. clindamycin
		Glycopeptides
		Phenicols e.g. florfenicol
		Tetracyclines e.g. oxytetracycline

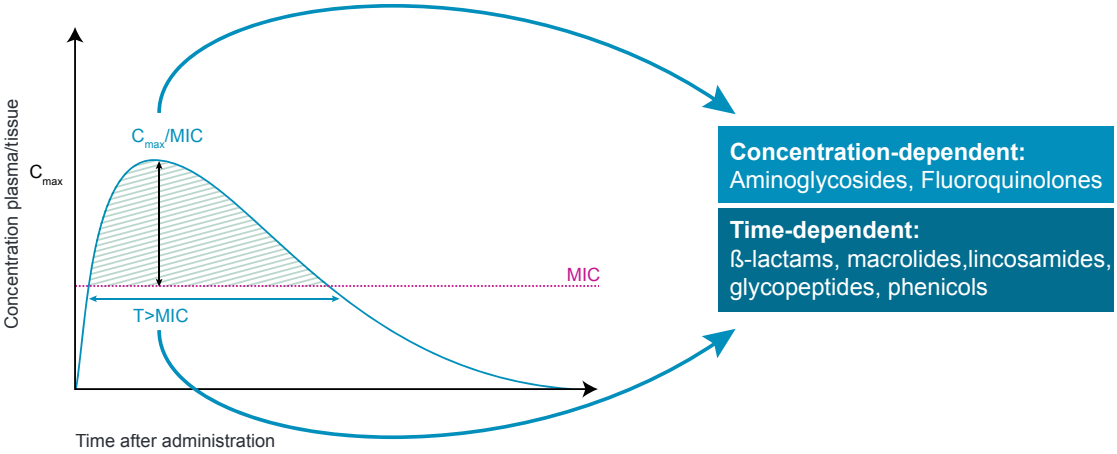

Figure: example of pharmacokinetics: concentration of an antibiotic in plasma/tissue versus time after administration.
T = time, MIC = Minimal Inhibitory Concentration, C_{max} = maximum concentration.

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