BACTERIAL INFECTIONS AND TREATMENT WITH ANTIBIOTICS IN SNAKES, A RECENT VISION. PART 3

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INTRODUCTION

In practice it seems more important to know which antibiotic should be administered for adequate treatment of the infection instead of knowing which bacteria are the agents of the disease. The bacteriological examination and sensitivity test will take some days, therefore most snake owners will start treatment in the blind when the infection has started, even just using an antibiotic they have in stock.
The bacterial flora of poikilotherm animals, consists mostly of gram negative rods, indicating that many of the antibiotics using for human medicine do not work against these micro-organisms. That is the antibiotics which act against gram positive micro-organisms, e.g. the classic penicillins, the penicilinase resistent penicillins, the macrolides like erythromycine, tylosine, the peptolipids, the lincocines like lyncomycine, clindamycine, fusidineacid, vancomycine and metronidazole, are worthless antibiotics in the treatment of the most common bacterial infections (pneumonia, gastro-enteritis, sepsis), at best they can

be used in local infections caused by gram positive micro-organisms. Remarkable however, is the mentioning in the literature in the case of bacterial infections in snake the use of antibiotics which are either toxic or inadequate for treatment. E.g. in a wellknown and well read book on snakes, in case of enteritis (Salmonellosis) paromomycine and neomycine are advised (Trutnau, 1981). Paromomycine is very toxic so it should not be used. Neomycine is a good gut antisepticum and is effective against Salmonella spp., but since it is practically not absorbed from the gut, it will not influence the extra-intestinal salmonella infections. Furthermore, in case of minimal absorbtion (3% of the dose) it will act nephrotoxic and cause a neuromuscular blockage. Chloramphenical, kanamycine and streptomycine are often prescribed in all kind of infections (Isenbugel and Frank, 1985; Ippen et al., 1985; Cooper and Jackson, 1981). They are hardly effective against Pseudomonas spp. The same is the case with spectinomycine, which is often combined with licomycine in veterinary practice. Because of the Pseudomonas problems, certain researchers have started to use the aminoglycosides such as gentamycine and tobramycine in herpetological medication. These antibiotics are fairly effective against Pseudomonas spp and in combination with one of the penicillins a remarkable synergisme is brought about, in which even the highly resistant Speudomonas spp are inhibited. A big disadvantage of the aminoglycosides is that they are highly nefrotoxic, and may only be used in low dosages: 2.5 mg per kg bodyweight per 72 hours (Bush et al., 1976). Such dosages are

very inconvenient in small animals and may easily lead to an overdose with death through intoxication or nephrosis. Because of this we started to test the more recently developed antibiotics against potential pathogenic micro-organisms in snake. Antibiotics, which are less toxic and above all have a good action against even the most resistant bacteria: cotrimoxazole, the anti-pseudomonas-penicillins, the cephalocporines of the third generation, the monobactams and the fluoroquinolones. The anti-pseudomonas-penicillins and the fluoroquinolones may prove to be of great importance in herpetological medication.

SUSCEPTIBILITY TESTS.

In order to test the in vitro susceptibility of bacteria for a certain antibiotic we use standard tests, the diffusion-method. In table 8 the in vitro susceptibility of the main pathogenic bacteria in Ophidia for the tested antibiotics are summarized. Ampicilline, a well known antibiotic, has a good action against Salmonella spp, but is of course ineffective against Pseudomonas spp, Serratia marcescens and Aeromonas hydrophila. Aeromonas produces beta-lactamase, an enzyme that opens the beta-lactan ring of penicillins (ampicilne) and of cephalosporines, hydrolize and inactivate them. For this reason using ampicilline in case of mouthrot is useless! Piperacillin works well against Pseudomonas aeruginosa (all tested bacteria were susceptible) but proves to be inactive against Pseudomonas maltophilia. It seems to be resistant

against the betalactamases of Aeromonas spp. (100% susceptibility). Pseudomonas maltophilia is also resistant to the third generation cephalosporines. Two tested populations of Pseudomonas aeruginosa were both susceptible to cefsulodine, a third generation cephalosporine, with a small anti-bacteriological spectrum, but with a bactericide action against Pseudomonas aeruginasa, although in human bacteriology resistent bacterial populations have been formed (personal investigations).
Aztreonam, the first of a new group of antibiotics (the monobactams) only moderately acts against Pseudomonas and Serratia marcencens. The aminoglycosides, except kanamycine, act well against Pseudomonas aeruginaosa and maltophilia. Remarkable is the fact that in snake bacterial populations have developed resistence against gentamycine and tobramycine. It is known that aminoglycosides induce resistence fairly fast. For this reason these antibiotics are combined with penicillin in human medicin.
All tested Salmonella spp were susceptible to chloramphenicol, which also acts well against Aeromonas hudrophila. Pseudomonas maltophilia is moderately susceptible, whereas Pseudomonas aeruginosa and Serratia marcescens are resistent.
The tetracyclines are active against Salmonella spp., but less useful against Aeromonas.
Colistine only has a moderate action against the tested populations: only 14% of the Salmonella's were susceptible, Aeromonas did not do better. The susceptibility of Pseudomonas spp. varied.
Cotrimoxazole acts very well against Pseudomonas maltophilia and Aeromonas hydrophi-

la. It is inactive against Pseudomonas aeruginosa. The 2 tested populations of Serratia marcescens were susceptible in vitro, but from human medicin it is known that treatment with cotrimoxazole in Serratia-septicaemia does not improve the clinical condition of the patient.
Ofloxacine, one of the newest fluoroquinolones proves to have a very wide anti-bacterial action and is a bactericide for all the tested populations.

TREATMENT OF THE MOST FREQUENT OCCURRING INFECTIONS.

Pneumonia caused by Pseudomonas aeruginosa.

Pseudomonas aeruginosa may well be considered as one of the most important causative agents in respiratory disease, especially in type II diseases (Ross and Marzec, 1984; personal investigations). In type II pneumonia the patient is seriously ill: apathy, impaired, heavy respiration, signs of decay, purulent mucus in the mouth. Without adequate treatment death follows swiftly.
The aminoglycosides were almost the only possible chemotherapeutic treatment for these infections (Ross and Marzec, 1984). But, as they are nephrotoxic we think that the use of Piperacilline is a much better alternative in treatment. It is active against Pseudomonas and reaches the lungs in high concentrations (Valenti et al. 1981). It has not many side effects. However it cannot be administered orally but

has to be given by injection (intramuscular or intracoeliacal). Per day per kg bodyweight a dose of 150-200 mg has to be given for 10 days at least. Although treatment of most of the pneumonia with piperacilline was succesful, we established during treatment a shift of flora towards Pseudomonas maltophilia, these bacteria are not susceptible for piperacillin. Clinically a swift improvement of the situation at first, where all the symptoms disappear, but without a complete cure of the animal. The animal still has much mucus and looks apathetic. From oropharyngeal probes a pure culture of Pseudomonas maltophilia could be isolated. The animal is probably suffering from a Pseudomonas maltophilia infection. Treatment with piperacilline combined with cotrimoxazole orally 35 mg/kg of bodyweight per day for 10 days cures the animal. These complications will not occur when ofloxacine is used, because this antibiotics acts against Pseudomonas aeruginosa as well as Pseudomonas maltophilia. Ofloxacine has a wide spectrum and is not nephrotoxic. A big advantage is that it can be administered orally, being almost completely absorbed. The dosage per day in reptiles is 7 mg/kg of bodyweight for 14 days. For little snakes of course reaching such a low dosage is difficult. One big disadvantage is that ofloxacine cannot be given to young, growing animals because of the negative action on bone development.

Gastro-enteritis and septicaemia caused by Salmonelle spp.

Although in vitro Salmonella are very sus-

ceptible to most of the tested antibiotics, in vitro treatment is not always succesful and treated snakes may remain carrier of the bacteria expelling them via their faeces. These symptomless carrier snakes do not need treatment. But in case of gastro-enteritis possibly combined with septicaemia, treatment with an adequate antibiotic is necessary. Chloramphenicol still is a good choice in treatment of Salmonella induced septicaemia. It is almost completely absorbed and can be given orally, 50-75 mg/kg of bodyweight per day. Stomach disorders occur less frequently than with other antibiotics, due to the good absorption and of its minor action against anaerobic bacteria of the gut. An injectable solution of chloramphenicol also exists, it has to be administered deep intramuscularly and causes pain, therefore it is often combined with lidocaine, an analgetic.
The fluoroquinolones also act very well against Salmonella induced gastro-enteritis or septicaemia. Because of their little action against the anaerobic bacteria (Verbist 1987) they do not disturb the flora of the gut. We were able to establish that orally administered ofloxacine (7mg/kg) for 15 days fully eliminated the Salmonella bacteria.

Mouthrot (stomatitis ulcerosa) caused by Aeromonas hydrophila.

Mouthrot may well be one of the most frequently occuring infections in snake. The clinical symptoms are well known by snake keepers. A necrotic infection of oropharyngeal tissues, with gray-white to yellow-

white coloured mucus. Followed by cheese-like matter around the teeth and on the palatum. Teeth may be lost and even the tongue may be affected. Because of the edema of the tissues infected snakes may not be able to shut their mouth completely, the tissues may bleed easily when touched. In an early stage the disease may be cured by the use of antiseptics like isobetadine in water, sprayed with force on the affected area 2-3 times a day. But when the sisease has become worse and underlying tissues have been affected local treatment will not be effective enough. The use of antibiotics is needed.
In case of Aeromonas infections cotrimoxazole is the first choice antibiotic. Treat with 35 mg/kg for 14 days at least or longer until the symptoms have gone. All the necrotic and loose tissue has to be removed and infected tissues sprayed with e.g. isobetadine in water. The drinking water should be supplied with HCl (6 ml HCl 1 N per litre of water).

Mouthrot caused by Pseudomonas aeruginosa and/or Serratia marcescens.

Mouthrot can also be caused by Pseudomonas aeruginosa and/or Serratia marcescens or in some cases by a mixture of gram negative bacteria. In these cases antibiotics with a wide antibacterial spectrum have to be used. The fluoroquinolones are the first choice in these cases. Ofloxacine or Ciprofloxacine 7 mg/kg bodyweight for 15 days. In smaller snakes the alternative might be Piperacilline (150-200 mg/kg) possibly combined with cotrimoxazole (35 mg/kg orally) for 14 days.

Infections caused by a combination of gram negative rod shaped bacteria.

Pseudomonas aeruginosa belongs to this group of bacteria. It causes cloacitis, panophthalmitis, oropharyngeal cellulitis. For these sort of infections the fluoro-quinolones and Piperacillin are the first choice antibiotics.

SEPSIS.

Sepsis frequently occur in snakes, but culturing bacteria from the blood is hardly possible in snake because of the non sterile conditions of blood sampling. Clinical signs of septicaemia in snake are seriously apathetic animals with many haemorrhages in the lining of the mouth and in the skin. Oropharyngeal samples often reveal a pure culture. The isolated bacteria may be the causative agent for the sepsis. Pseudomonas aeruginosa, Pseudomonas maltophilia, Salmonella spp. and Aeromonas hydrophila are the most frequent occuring micro-organisms in sepsis. Untreated sepsis will swiftly lead to death, and as bacteriological diagnosis may take a couple of days, we advise starting treatment with antibiotics immediately. Treatment with ofloxacine or piperacillin combined with cotrimoxazole is suggested.

CONCLUSIONS.

The recently developed antibiotics prove to be very useful in treatment of bacterial infections in snake and in the future they may replace the more 'classic' chemotherapeutics. Many of those are not useful at all because of the special bacterial flora of coldblooded animals. The anti-pseudomonas-penicillins, the monobactams, the third generation cephalosprines and the fluoroquinolones are used in human medicine mostly in hospital surroundings, because of the occurrence of highly resistent potentially pathogen bacterial populations, amongst which are Pseudomonas aeruginosa, Pseudomonas maltophilia and Serratia marcescens. Accidentally, these bacteria are very often the agents of disease in snakes and other coldblooded animals. Unfortunately, Aztreonam proves to have little action against Pseudomonas spp. The third generation cephalosporines are very active against Pseudomonas aeruginosa, but it seems superfluous at the moment to use these in herpetological treatment. Piperacillin, the anti-pseudomonas-penicillin and the fluoroquinolones give new perspectives in the treatment of various infections in reptiles. The big advantage of the fluoroquinolones is the fact that they can be administerd orally. On top of this resistence against these antibiotics only develops by selection of mutants and not by transfer of plasmides. These mutant are not very stable in nature if antibiotics are used selectively (Verbist, 1987). Because of their low toxicity (only in high dosages to young experimental animals were there disorders of the growth disk), good

tissue penetrating ability and wide bactericide action they can be used in almost all bacterial infections against reptiles.

Tabel 8: In vitro susceptibility of the most important pathogenic bacteria to antobiotics. In backets: the number of tested populations. Underlined: the % of sucseptible populations.

S = sucseptible. R = resistent.

	Salmonella spp.	Pseudomonas aeruginosa	Pseudomonas maltophilia	Aeromonas hydrophila	Serratia marcescens
Ampicilline	(13) 100	(7) 0	(7) 0	(6) 0	(2) 0
Piperacilline	(9) 100	(13) 100	(7) 0	(4) 100	(3) 100
Cefotaxime	(10) 100	(2) 0	(6) 0	(4) 100	(3) 100
Cefsulodine	(-) -	(2) 100	(-) -	(-) -	(-) -
Ceftazidime	(1) S	(3) 100	(4) 0	(1) S	(2) 100
Aztreonam	(12) 100	(2) 50	(2) 50	(1) S	(2) 50
Kanamycine	(14) 100	(5) 0	(6) 33	(3) 67	(2) 100
Neomycine	(11) 100	(2) 100	(2) 50	(2) 100	(1) S
Gentamycine	(6) 100	(11) 82	(5) 100	(4) 100	(2) 100
Tobramycine	(6) 100	(9) 89	(2) 100	(5) 100	(3) 100
Amikacin	(4) 100	(3) 100	(1) S	(1) S	(2) 100
Chloramphenico	(14) 100	(8) 0	(5) 60	(2) 100	(2) 0
Tetracycline	(14) 100	(3) 0	(4) 50	(3) 75	(2) 0
Colistine	(14) 14	(7) 57	(6) 67	(4) 25	(2) 0
Cotrimoxazole	(11) 90	(7) 0	(7) 100	(5) 100	(2) S!
Nitrofuranes	(7) 100	(3) 0	(1) R	(1) S	(1) R
Ofloxacine	(10) 100	(3) 100	(3) 100	(1) S	(2) 100

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