

The use of antimicrobial substances in food animals

The big picture

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Abstract

The paper gives rather a broad overview on the development of the use of antibiotics and chemotherapeutics from their very beginning until today. The paper deals with scientific facts known in the medical and veterinary community, but also with speculations and "gut-feeling" demands of activist groups that criticise e.g. intensive animal production procedures as "factory farming". The discussions about the need to curb the problem of bacterial resistance and the various attempts to regulate the use of antibiotics in food animals are summarised, and the paper underlines that veterinarians carry the major responsibility for the most desirable use of antimicrobial substances, the "prudent use of antibiotics", where, when antimicrobials have to be applied, the application leads to the highest possible health effect and the lowest possible resistance in the bacteria accompanying and/or threaten humans and animals. The paper, however, also argues that meeting demand for reducing the overall amount of antibiotics used in food animals needs a different approach: instead of only asking veterinarians to refrain from an overuse (especially the routine use) of antibiotics mainly in pigs and poultry, a concerted action of the farming community together with their consulting veterinarians is necessary with the clear target to significantly increase the health of the food animal populations by optimising the herd and flock health management, which automatically will result in a measurable reduction of reliance of the food animal production on antibiotics. Concluding, the paper speculates that there will be no significant reduction in the amount of antimicrobials used in food animals, unless farmers and veterinarians find new approaches to investing money in the health of herds and flocks, i.e. paying veterinary services for maintaining the animals' health rather than for curing their diseases.

THE breakthrough in battling bacterial disease

The development of sulphonamides by Gerhard Domagk and the discovery of penicillin by Alexander Fleming have been celebrated as milestones in mankind's attempts to reduce premature death and pain and suffering due to disease. There are no hard data about the percentage of the causes of death prior to the establishment of any state health system, but it can be argued that infectious diseases have been the major death causes for thousands of years. This is definitely true for the centuries when, due to an increase of human populations moving and commingling throughout Europa and to the start of urbanisation without any coordinated sanitation, the main epidemics that killed millions of people were Plague, Cholera and Typhoid. These bacterial epidemics had an exponentially higher death toll than any viral epidemic. There are no hard data to prove or disprove, if not many a million of the many millions of deaths due to the 1918 Hongkong Flu epidemic were due to secondary bacterial infections that maybe dramatically increased the number of fatalities. There are speculations that the number of people that lost their lives in wars due to the direct effect of a weapon is manifold smaller than the number of wounded people that later died due to the bacterial infections caused by their being wounded. In other words the fact that mankind suddenly was able to cure bacterial infections and to fight life-threatening bacteria (chemotherapeutics/ antibiotics and disinfectants) was celebrated as man's victory over infectious disease.

The triumphal march, disillusionment and finally a realistic view

Whereas in the early years of the availability of sulphonamides and antibiotics, only life-threatening infections of humans were treated, but soon more and more application areas were added: less harmful infections in humans, bacterial diseases in animals, more and more non-fatal diseases in humans up to the treatment of just "annoying" infections such as common colds, growth promotion ("non-therapeutic use") in food animals, and the routine prophylactic and "metaphylactic" use in large scale food animal production units. This development of expanding the use of antimicrobial substances would have remained being welcomed and undisputed, if there were not the phenomenon of acquired bacterial resistance in bacteria species that naturally are highly sensible to certain antimicrobial substances. When the first incidences of bacterial resistance were empirically recognised, little was known about the mode of effect the antimicro-

bial substances and nothing about the molecular mechanisms that determine the inefficiency of the so far fully potent drugs. It took some decades of finger-pointing (especially between the medical and veterinary profession) and learning that there has to be a hierarchy in the use of antimicrobial substances before the development of a realistic view on how to maintain the “sharpness of this valuable tool against bacterial disease” especially for those antimicrobial groups that are of critical importance in human medicine.

The initial hope that the threat of bacterial pathogens to human health had been banned the by the use of antimicrobial substances was shattered. However, exactly this experience led, to increased research activities into the mechanisms of the development of bacterial resistance through either the acquisition of a plasmid or a single point mutation. The major step in developing a general understanding that maintaining the efficacy of whichever antimicrobial is the WAY we use them in human and veterinary medicine was that it was comprehended that ANY use of ANY antimicrobial compound leads to a selection pressure in the targeted (and the simultaneously occurring) bacterial populations towards bacteria that are less vulnerable (sensitive) and withstand the bactericidal or bacteriostatic mechanisms, and that it is necessary to develop intelligent strategies to minimise the MAGNITUDE of the selection pressure. This understanding was also supported by the relatively late realisation that bacterial populations are by far faster to adapt to antimicrobial compounds than humans are able to find or develop and produce new compounds.

Strategies to curb bacterial resistance

The most important step in guiding medical and veterinary users of antimicrobial substances as treatment of bacterial infections was the development of the concept of the “prudent use of antibiotics”, which is defined as applying antimicrobials in a way that leads to the highest possible health effect in humans or animals and to the lowest possible resistance in the bacteria that are exposed to the compound. WHO and FAO, but also many national medical and veterinary associations, chambers and international organisations such as FVE for veterinary medicine have issued guidelines on the prudent use of antibiotics. They all may differ in some details, but the following major basic principles are common for all prudent-use-guidelines:

- use only licensed antimicrobials only as much and as long as necessary and as little and as short as possible;
- select targeted antimicrobials according to the natural sensitivity of the identified bacterial species;
- use the chosen antimicrobial compound in the highest possible dosage and over the shortest possible period of time, which is yet long enough to minimise the selection of resistant bacterial strains;
- base this decision as often as possible on laboratory results on the actual sensitivity (clinical breakpoint) of the disease-causing bacterial strains;
- refrain from using broad-band antibiotics wherever possible;
- refrain from using antimicrobial groups of critical importance for human medicine in non-life-threatening bacterial infections of humans and in veterinary medicine.

These guidelines for the prudent use of antibiotics are nowadays broadly accepted in the medical and veterinary professions and they have definitively led to a higher degree of compliance with practices that are known to reduce the development of bacterial resistance (including a better supervision of the application of antibiotics in feed and water by the farmers!).

However, to which degree the magnitude of bacterial resistance in veterinary medicine has been influenced by the principles of the prudent use of antibiotics is more or less unknown, since the existing data on bacterial resistance are hardly comparable not only from country to country, but also over time. The decision of the EU to command the EFSA (based on Article 33 of the Reg. [EC] 178/2002) to carry out a standardised collection and analysis of data on zoonoses, antimicrobial resistance and food-borne outbreaks, is a major precondition for a meaningful measurement of the development of bacterial resistance specially in bacteria that cause zoonoses and food-borne diseases in humans. Unfortunately, the period of time, which EFSA needs to harmonise this data collection and to demonstrate make sound decisions on which measures which country needs to take, is longer than we need quiet down the still growing criticism with the use of antibiotics in food animals.

Measures in animal production beyond the “prudent use”

The still growing societal concerns expressed by public health authorities and organisations such as WHO, CDC and EFSA, is nowadays increasingly taken up by NGO’s targeting modern animal production systems. And their “cause” is, unfortunately, supported by an increasingly public discussion about multi-resistant Salmonella strains, MRSA in food

producing animals (laMRSA), and ESBL. Only one quote from the Global Edition of the New York Times (March 23, 2011) illustrates the general perception of the deficiencies in the use of antibiotics in general, but also in food producing animals: "...But antibiotics are frequently misused – overprescribed or incorrectly taken by patients, and recklessly fed to farm animals".

As responsible researchers used to asking for sound data-based analyses we tend to ignore statements that lack reasonable evidence (show me the data that prove that the use of ... has led to...). However, in the light of our consensus on the fact that ANY use of antimicrobial substances leads to bacterial resistance as well in the targeted bacterial strains as in all other bacteria that are exposed to the antimicrobial in question, we need to agree on the demand for reducing today's amount of antibiotics and chemotherapeutics used in general in food animals as much as possible as long as we achieve the necessary health effect in case of acute infections.

But here we need to accept that the rules for the prudent use of antibiotics are NOT able address the reliance of animal production on the routine use of antimicrobials. If bacterial disease is occurring in any animal population, it is the ethical duty of veterinarians to apply antimicrobial substances, of course following the rules of their prudent use. It has been ignored for too long that field veterinarians, although society expects them to consult farmers to optimise their husbandry systems and their management skills regarding animal health, have not the legal "power" to enforce their recommendations.

Especially in countries, where veterinarians are the only source of drugs for the farmers, it is widely believed that this fact is the major reason for a comparatively high consumption of antimicrobial substances in food animals. At first glance this seems to be supported by the relatively low amount of antibiotics (measured in mg/kg meat produced) in Norway, Sweden and Finland. However, Austria has the same low consumption, and it should not be forgotten, that the Scandinavian countries have a long tradition of animal health schemes including long-standing and successful Salmonella monitoring and reduction programmes. And, the wide range from about 50 mg/kg meat produced in Ireland and Denmark up to more than 250 mg/kg in Greece and the USA shows that there must be other factors that much more influence the quantities of antimicrobial substances that are used in food animal populations than just the way how farmers are supplied with drugs.

Not only well-proven experiences of every single veterinary practitioner, but also a growing number of scientific papers on the huge variability of the amount of antimicrobials used in food animals at the herd and flock level, tell us that the animal-health awareness of farmers and their management skills determine the health status of the herd or flock in question, which in turn, determines the necessary amount of antibiotics applied or prescribed by the veterinarian.

The results of our research projects on testing the so-called "Animal Treatment Index" and the Danish comparison of the use of antimicrobials per pig herd by measuring the Animal Daily Doses (ADD) prove that there is a need to revise the main stream attempts to force veterinarians to use less antimicrobials (which is twisting the arm of the wrong people) into first measuring the amount of antibiotics at farm level. Using a benchmarking system such the "Yellow Card Initiative", introduced last year in Denmark by the Danish Veterinary and Food Administration, will lead to concerted actions to measurably increase the health of the food animal populations, which "automatically" will lead to a reduction of routinely administered antimicrobials in food animals.