



One health approach prospers: antibiotic resistance remains a serious health problem

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Human, animal and environmental health are closely inter-related. The One Health approach includes the disciplines human medicine, veterinary medicine, environmental and food science, in order to ensure and further improve public health. And since humans are taking up more and more space on earth, the living environments of humans and animals are coming closer together. This makes it easier for diseases to jump from one species to another. In addition, due to climate change, infectious diseases transmitted by mosquitoes or other insects are moving further into temperate zones. Moreover, improperly produced food is another vehicle that can contribute to the spread of viral and bacterial infections.

1 Almost everything is connected

Latest with the Corona pandemic, it ultimately became clear to both authorities and scientists that only a close joint cooperation between all disciplines can help to keep health risks under control. The Corona pandemic also made it frighteningly clear how globally interconnected supply chains are. A pathogenic virus or a highly resistant bacterium can quickly reach all parts of the world on a continental flight. In this respect, the seamless monitoring of increasingly complex supply and distribution chains, including the food chain, is a key issue.

Furthermore, the use of pharmaceuticals in food production is another example of how the vital care of humans and animals are interrelated. The main entry pathways for

pharmaceuticals into the environment can be classified as follows:

- human pharmaceuticals are mainly discharged into the environment via sewage treatment plant effluents,
- veterinary pharmaceuticals mainly enter the soil via farm manure (e.g. pig and cattle slurry, chicken manure, digestate from biogas plants).

Depending on their physicochemical properties, those drugs can be translocated into groundwater or even enter (crop) plants. A further displacement of veterinary drug residues via groundwater into drinking water has not been described so far, since soil passage and also water treatment in the course of drinking water production are high barriers. Antibiotics are often added to animal feed in powder form and thus, can enter stable dusts and possibly directly expose farmers and veterinarians via inhaled stable air¹. Antibiotics were developed to combat microorganisms, so their toxicity to humans, animals, but also many soil dwellers, such as earthworms, is very low. However, a subtler effect of antibiotics in soils may affect microbial communities, which could have an impact on the soil fauna. Laboratory and field studies seem to confirm this hypothesis, although some of them used very high doses of antibiotics that are not always environmentally relevant.

2 Improper use of antibiotics

The greatest health and environmental risk posed by antibiotically active substances is considered to be the spread of antibiotic resistance in both human and veterinary medicine. Following WHO, if no action is taken, drug-resistant

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¹ Hamscher G, Bachour G (2018). Veterinary drugs in the environment: current knowledge and challenges for the future. *J Agric Food Chem* 66: 751–752.

diseases could cause 10 million deaths each year by 2050². Resistance is, first of all, a natural mechanism of microorganisms that protects them against antibiotics produced by themselves or by other microorganisms. In this respect, there has always been and still is a natural antibiotic resistance, which also represents an evolutionary selection advantage. However, it has long been known that the emergence and spread of antibiotic resistance is primarily promoted by improper use of the substances in human medicine and in animal husbandry. Improper treatment occurs, for example, when drugs are used contrary to the recommended treatment dose and duration.

If animals are treated with antibiotics, both resistant bacteria and their resistance genes can enter the immediate stable environment. Since considerable antibiotic concentrations may also be present in the manure, resistant strains are initially selected out of the (still) sensitive ones. Then, the surviving resistant strains can be introduced into the terrestrial environment via manure fertilization. The survivability of (pathogenic) microorganisms in the aquatic environment and in soil may well be several months, e.g. in case of *Salmonella*. Due to the easy exchangeability of genetic material even between different species, soil bacteria can pick up resistance genes that may be directed against many different antibiotics. If those (multi)resistant microorganisms reach humans or animals, it can lead to serious health problems when pathogenic strains are involved. The treatment of those infections is becoming increasingly difficult, because less and less effective antibiotics are available.

After more than 25 years of intensive research both in human and veterinary medicine, the issue has been comprehensively addressed scientifically and has reached the international political arena. As an issue of global importance, a declaration made by the health ministers of the seven leading industrialized nations was adopted for the first time at the G7 meeting in 2015 in Berlin. However, the Corona pandemic and also the war of aggression by Russia in the Ukraine have severely hampered the necessary joint efforts.

In the area of animal husbandry, the “Guidelines for the prudent use of antimicrobial veterinary medicines”³ have ensured a significant reduction of medicines use in Germany. They include minimum requirements for the use of antibiotics, selection criteria for the right antibiotic, advice on the correct dosage and duration of therapy, and general

recommendations for reducing the spread of antibiotic resistance. A corresponding amendment for the legal framework significantly increased the pressure on veterinarians and farmers for the implementation in practice. Similar measures could also be initiated in the field of human medicine through a new EU initiative on more environmentally sustainable medicines⁴.

3 Implementing the precautionary principle

Technical solutions for the removal of pollutants from wastewater or waste are usually very energy-intensive, associated with high investment and operating costs. In this respect, the precautionary principle must be implemented wherever possible, e.g. by:

- using medicinal products only when really necessary,
- high level of health care requires a lower level of use and,
- where waste is produced, safe disposal.

Environmental discharges from veterinary medicines can only be reduced by numerous measures at different levels. First and foremost is the responsible and economical use of pharmacologically active substances, flanked by monitoring measures. According to the current state of knowledge, technological options for the treatment of farm manure can only contribute to a very limited extent to reducing environmental inputs. The production of greener pharmaceuticals is another demanding issue, and some promising studies are available⁵. Communicating our extensive knowledge to every segment of the population, including veterinarians, farmers, elected officials, students, among others, must be a matter of course for all scientists.

4 Reducing the application of pesticides, fertilizers and antibiotics

Finally, with the European “Green Deal“, the EU Commission is pursuing the ambitious goal of creating a climate-neutral Europe by 2050. For the agricultural and food sector,

² WHO, press release 29 April (2019) New report calls for urgent action to avert antimicrobial resistance crisis. <https://www.who.int/news/item/29-04-2019-new-report-calls-for-urgent-action-to-avert-antimicrobial-resistance-crisis>. Accessed 26 July.

³ Anonymus, Bundestierärztekammer, Arbeitsgemeinschaft der leitenden Veterinärbeamten (2015). Leitlinien für den sorgfältigen Umgang mit antibakteriell wirksamen Tierarzneimitteln. https://www.dvg.net/fileadmin/Bilder/DVG/PDF/Leitlinien/15-03_Antibiotika-Leitlinien_01-2015.pdf. Accessed 26 July.

⁴ European Commission, press release 26 April (2023) European Health Union: Commission proposes pharmaceuticals reform for more accessible, affordable and innovative medicines. https://ec.europa.eu/commission/presscorner/detail/en/ip_23_1843. Accessed 26 July.

⁵ Moermond CTA, Puhlmann N, Brown AR, Stewart FO, Ryan J, Snape J, Venhuis BJ, Kümmerer K. (2021). GREENER pharmaceuticals for more sustainable healthcare. *Environ Sci Technol Lett* 9: 699–705. doi: <https://doi.org/10.1021/acs.estlett.2c00446>.

the goals are described in the Farm to Fork Strategy⁶. Overall, the production chain from field to plate must become more sustainable. At its core, this involves establishing a fair, healthy and sustainable system in the food industry in which, among other things, the use of pesticides, fertilizers and antibiotics is to be reduced and organic farming increased. Let's all work together so that the good intentions will be put into practice. Coupled with interdisciplinary scientific expertise, it will lead to a sustainable improvement of One Health.

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⁶ EU commission: https://food.ec.europa.eu/horizontal-topics/farm-fork-strategy_en Accessed 27 July 2023.

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