Antimicrobial Resistance in Livestock and Food - Its Significance for Human Medicine and Options for Action in Risk Management

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Bacteria which are resistant to antimicrobial substances (antibiotics) are widespread. These bacteria are selected by the use of antibiotics. In the presence of antibiotics, they have advantages over their competitors without resistance properties and can multiply faster and more strongly. This is true in livestock as well as people. It becomes a problem when the bacteria in question are pathogenic.

The Federal Institute for Risk Assessment (*Bundesinstitut für Risikobewertung*, BfR) has evaluated the significance of these resistances in livestock and in food for human consumption. The BfR concludes that the assessment of the contribution made by antimicrobial resistance in livestock that may be transmitted to humans through food to the extent of antimicrobial resistance in human medicine varies according to the bacteria and type of resistance.

In the case of multi-resistant *Staphylococcus aureus* (MRSA) bacteria, the strains originating from animals (livestock-associated MRSA) are currently of minor importance for infections in humans with the exception of people who have frequent contact with livestock (farmers, veterinarians, farm workers. The latter can be carriers of livestock-associated MRSA. These people should be tested to determine whether they are carriers of MRSA prior to treatment with antibiotics, surgery or admission to a clinic,

The situation is assessed differently when it comes to ESBL/AmpC-producing strains of bacteria. These resistances severely impair treatment with 3rd and 4th generation cephalosporins, which are used to combat a variety of bacterial infections. The resistant strains of bacteria such as *Escherichia coli*, *Klebsiella* and *Citrobacter* are a cause of concern because the resistance genes are located in mobile genetic elements. They can be easily transferred and recombined among these and other pathogenic bacteria. This transfer is increased with antibiotic treatment. Since these bacteria occur both in humans and in animals, such resistances are equally problematic in the treatment of livestock and the treatment of humans. Preventive measures to counter their prevalence should be taken on livestock farms as well as in human medicine.

Initial analyses quantifying the significance of livestock as a reservoir for ESBL-producing *E. coli* in Germany show that the most common ESBL genes occur in isolates of humans as well as various animal species. This substantiates previous findings that animals play a role as a source of such bacteria or resistance genes. In addition to direct transfer of the bacteria, the fact that resistance genes can be transferred to other bacteria is of particular importance here.

For this reason, only a joint preventive control strategy of veterinary and human medicine (one health approach) against the spread of resistant pathogens can be successful.

Bacteria that are resistant to antimicrobial substances including multi-resistant strains are widespread and are selected by the use of antibiotics. However, a large number of factors with complex interrelations contribute to the spread of these pathogens. The relationship between livestock farming and consumer health protection with respect to antimicrobial resistance needs to be analysed in view of this complexity.

There are considerable problems with antimicrobial resistance, both in human and veterinary medicine. However, these problems only partially share the same origin. Moreover, the extent of this common resistance problem and the transmission paths between the animal and human population differ depending on the bacteria in question.

Methicillin-resistant *Staphylococcus aureus* (MRSA)

For example, methicillin-resistant *Staphylococcus aureus* (MRSA) from livestock (la-MRSA) plays a minor role as a pathogen causing difficult-to-treat infections in humans compared to MRSA types from humans (community- and hospital-acquired MRSA). In total, la-MRSA account for less than 5% of all detected and typified MRSA in humans. They are mostly detected in people who are exposed to livestock in their working life, such as farmers and veterinarians. Conversely, this means that 95% of detected MRSA in humans originates from the field of human medicine. As la-MRSA are mostly sensitive to other therapeutically significant classes of antimicrobials, it is usually possible to treat these infections.

To date, there has been little evidence of **MRSA** being transmitted to people through food. The risk of MRSA being transmitted to people through food is currently assessed as low. Risks could arise from direct contact of injured skin with the pathogen or manual transfer to wounds at other body sites. Adherence to kitchen hygiene rules is important here. In principle, MRSA CC398 (la-MRSA) can be detected in most illness types associated with *S. aureus*, i.e. from wound infections to pneumonia and septicaemia. In regions with a high livestock density, the proportion of la-MRSA among all MRSA in humans may be significantly higher than in regions with a low livestock density.

ESBL/AmpC-producing strains of bacteria

The resistance problem through ESBL/AmpC-producing bacteria shared by human and veterinary medicine is more significant problem than with MRSA. 3rd and 4th generation cephalosporins are important in the treatment of a large number of infections. For this reason, this resistance greatly restricts treatment options in the event of an infection. The mobility of the underlying resistance mechanisms represents an additional challenge. Intestinal bacteria such as *Escherichia coli, Klebsiella* and *Citrobacter*, which occur frequently in both humans and animals, can transfer their resistance properties to one another. This means that different properties can be combined and dangerous pathogens can result from these recombinations which could be problematic in both humans and animals in the event of an infection requiring treatment.

Consumers can be exposed to these pathogens through food, but also through direct contact with animals. Human-to-human transmission in hospitals and in the general population also plays a significant role in the spread of ESBL-producing bacteria.

People can be colonised, for instance, through the consumption of food contaminated with **ESBL**-producing bacteria. The significance of this transmission path is difficult to assess. The risk of colonisation and infection of people via food depends among others on the quantity of these bacteria in the food. The question of whether the pathogen can multiply in the food contributes to the pathogen quantity. Kitchen hygiene during food preparations is an additional factor.

Initial analyses attempting to quantify the significance of livestock as a reservoir for ESBL-producing *E. coli* to humans in Germany show that the most common ESBL genes occur in isolates of both humans and animals. However, the proportions of these genes in ESBL-

producing *E.coli* isolates of animals and humans differ substantially. This substantiates previous findings that animals play a role as a source of such bacteria or resistance genes. At the same time, these studies elucidated that the same resistance genes occur in all observed groups of livestock, i.e. that not only poultry plays a role as a reservoir. Currently, the vast majority of colonisations of humans with ESBL-producing *E. coli* cannot be directly explained by exposure to livestock farming or food-producing animals. In addition to direct transmission of bacteria, there is also the possibility that these bacteria merely act as a vehicle from animals to humans. The resistance genes are then transferred to other bacteria in the human body. In this case, it is often difficult to trace the transmission path because the bacteria causing the infection and the resistance gene have different sources.

Recommendation for consumers on preparing meat

For protection again MRSA and ESBL-producing bacteria, consumers should adhere to the same hygiene rules that apply to other pathogens that can be transferred to humans from animals or from food. These rules include the following:

- After contact with animals, wash your hands with warm water and soap. This also applies to contact with household pets.
- Wash your hands thoroughly with soap and water before and after preparing raw meat.
- Where possible, avoid touching animals and raw meat with your mouth.
- Make sure that food, particularly meat and eggs, is fully cooked before consumption.
- Wash uncooked fruit and vegetables, such as lettuce and sprouts, thoroughly with drinking water before consumption and peel fruit and vegetables.
- Prevent raw meat or eggs from coming into direct or indirect contact with prepared food that will not be heated up again. Adhere strictly to the relevant hygiene rules for storing and preparing food in order to keep the bacterial count as low as possible.

You can protect yourself and others from infections by observing hygiene rules in order to prevent the transmission of bacteria to other food and by cooking poultry thoroughly before consumption.

The BfR has provided additional tips in the leaflet “Protection against food infections in private households”:

http://www.bfr.bund.de/cm/350/verbrauchertipps_schutz_vor_lebensmittelinfektionen_im_privathaushalt.pdf

Action required in livestock farming

From the veterinary point of view, the following action is required in livestock farming:

1. The selection pressure in the direction of resistant bacteria should be reduced. Methods for this include:

- Improving animal health, for example by means of zootechnical measures, optimised feeding, hygiene and management, and targeted evidence-based treatment of infectious diseases actually requiring treatment are necessary.

- Systematic recording of the use of antibiotics in livestock farming, which was introduced with the 16th amendment of the German Drug Act (AMG), results in an important measure for the success of the reduction strategies.

- One important component of any reduction strategy is the systematic evaluation of this data in order to detect the main problem areas and address them in a targeted manner.

2. The transmission of resistant bacteria from animals to people and from the health system to livestock should be reduced through a variety of measures:

   - In the area of food production, the spread of bacteria along the chain to the consumer should be avoided. This requires further improvements in slaughterhouse hygiene.

   - Consumers should carefully select food and ensure adequate kitchen hygiene in order to prevent infection with existing bacteria.

   - More efficient technology for minimising emissions containing bacteria from livestock farming should be developed.

   - Because of intensive contact with animals, veterinarians and farmers constitute potential sources for the entry of resistant pathogens into the healthcare system. For this reason, the Hospital Hygiene Commission at the Robert Koch Institute has issued the following recommendation since 2008: persons belonging to these groups should be subjected to routine screening for MRSA before admission to a hospital or senior citizens' home.

The challenges posed by the development of antimicrobial resistance are complex and need to be tackled jointly by veterinary and human medicine (one health approach). Best practice examples should be developed and communicated. Interdisciplinary research projects in which the BfR is involved (e.g. MedVetStaph, RESET) contribute to further important findings for understanding the common resistance problem.