FAQ

19. February 2025

ESBL- and AmpC-producing bacteria: Antibiotic-resistant bacteria and how to prevent their spread

→ Updated version of the FAQ dated January 19, 2015. The text has been revised and updated throughout.

Bacteria can become insensitive (resistant) to certain antibiotics. If these bacteria are pathogenic, the antibiotics used to treat them are ineffective. The treatment of the infection is therefore made more difficult by the resistance.

Escherichia coli (*E. coli*) and other intestinal bacteria can, for example, develop resistance to newer generations of cephalosporins - important antibiotics for the treatment of infections in humans. This resistance is caused by enzymes known as "extended-spectrum beta-lactamases" (ESBL) and "AmpC beta-lactamases" (AmpC). They render certain antibiotics ineffective.

In order to be able to form these enzymes, the bacteria need corresponding resistance genes. These genes can be inherited from one bacterial generation to the next (vertical transmission) or passed on from one bacterial cell to another (horizontal transmission). Horizontal exchange is even possible between different types of bacteria.

Bacteria that produce the corresponding enzymes have a survival advantage if they are found in an environment in which antibiotics are used. Thus, the use of antibiotics in humans and animals promotes the spread of ESBL- and/or AmpC-producing bacteria. It has been proven that bacteria with corresponding resistances are widespread in animals and in food. They can theoretically be transferred to humans. A connection between the occurrence of resistant pathogens in animals and diseases in humans is possible. However, it is not known how frequently this occurs.

What are ESBL?

ESBL stands for "extended-spectrum beta-lactamases" and refers to enzymes that also alter beta-lactam antibiotics with a broad spectrum of activity, rendering them ineffective. Bacteria that produce these enzymes become insensitive (resistant) to important active substances such as aminopenicillins (e.g. ampicillin or amoxicillin), cephalosporins (including third and fourth generation) and monobactams. This resistance can be detected in various bacterial genera, particularly in enterobacteria found in the intestine, including *Salmonella*, *Escherichia coli* and *Klebsiella*. The genes for these enzymes are often located on transmissible gene segments. These can be exchanged between bacteria of the same species or between different species (horizontal gene transfer).

What are AmpC?

AmpC beta-lactamases (AmpC) are enzymes that mediate resistance to penicillins, second and third generation cephalosporins and cephamycins. They also lead to resistance to combinations of these antibiotics and substances that are actually intended to inhibit the effect of beta-lactamases. They do not confer resistance to fourth-generation cephalosporins.

The genes for these enzymes can occur naturally in some bacterial genera as so-called "chromosomal AmpC" (e.g. in *E. coli*). However, the enzymes are only formed and efficacious to a sufficient extent under certain conditions. Important for the spread of resistance is the increasing number of AmpC genes that are localized outside the chromosome on so-called plasmids (often ring-shaped DNA molecules) and are therefore often referred to as "plasmidic AmpC" (pAmpC). These genes constantly ensure the formation of the enzyme and can be exchanged between bacteria of the same species or even between different species (horizontal gene transfer).

How do bacteria that carry ESBL and/or AmpC genes develop and how are they spread?

In order for bacteria to produce ESBL or AmpC, they must have the necessary genetic information (resistance genes). Two general principles are important for the spread of resistance genes: vertical transmission and horizontal gene transfer. In vertical transmission, the genes are passed on ("inherited") from one generation of bacteria to the next during cell division. They are therefore spread as the bacteria multiply.

Horizontal gene transfer involves the transfer of specific gene segments between different bacteria of the same species or even between different species. ESBL or AmpC resistance genes are very often located on such transmissible gene segments (e.g. on plasmids, ring-shaped DNA molecules), which makes their spread particularly fast and effective. The genes are also frequently found in non-pathogenic bacteria that naturally colonize humans and animals. Such otherwise harmless intestinal bacteria can pass on the genes for ESBL and/or AmpC to pathogenic bacteria, such as *Salmonella*.

The resistant bacteria themselves are also spread in different ways: They are often spread between livestock during animal trade, i.e. newly housed animals can bring such bacteria with them. They can then spread further in the livestock through contact between the animals. Transmission from animals to humans and vice versa as well as between humans is also possible.

Other routes of spread include hospitals, where poor hygiene usually plays a role in the spread of bacteria. In the kitchen, bacteria can be transmitted directly or indirectly via contaminated articles between different foods and ultimately to humans if hygiene is inadequate.

The use of antibiotics in animals and humans promotes the spread of ESBL- and/or AmpC-producing bacteria and their genes because resistance to certain antibiotics leads to an advantage over competing bacteria during treatment. This means that bacteria with resistance genes survive the antibiotic treatment and can continue to multiply (and their resistance genes), while bacteria without the corresponding genes are killed off. In addition, the exchange of genes between bacteria is promoted when antibiotics are used under the selection pressure that is formed, so that resistance genes may be increasingly transferred to other bacteria.

How is the presence of resistant bacteria investigated and what needs to be considered when interpreting test results?

In order to gain an overview of the spread of antibiotic resistance in livestock or food, for example, samples are taken and tested for the presence of resistant bacteria. Selective and non-selective methods are used for this purpose. Selective methods can be used to specifically detect bacteria with a certain resistance, e.g. AmpC-forming *E. coli*. Non-selective methods are used to randomly select bacteria of a certain species and test their resistance to a number of different antibiotics. The non-selective method provides a better representative overview of the resistance situation. However, it is less sensitive for detecting bacteria with a specific resistance characteristic. The choice of method therefore depends on the question being asked. The result of the investigation must also be assessed against the background of the chosen method.

It should be noted that several bacteria of the same species, e.g. *E. coli*, are present in a sample. However, since not all *E. coli* in a sample have the same resistance pattern, it is possible that a randomly selected *E. coli* in the sample is sensitive, but that a resistant *E. coli* can also be detected in the same sample using selective methods. An example: If one of 100 *E. coli* bacteria in a sample is capable of producing ESBL, this bacterium can easily be found using the selective method because the non-resistant bacteria do not grow at all during the test and only the resistant bacterium grows on the culture medium. When using the non-selective method, the chance of finding the bacterium is 1:100, because it is only detected if this bacterium is randomly selected from the culture medium, on which all non-ESBL-producing *E. coli* grow.

However, with the selective method you will never know what resistance properties the 99 other bacteria have. Therefore, both methods are justified.

How common are ESBL- and/or AmpC-producing bacteria in food?

ESBL/AmpC-producing *E. coli* has so far been examined in monitoring as a representative of all enterobacteria. They can be detected in a wide variety of foods. In targeted tests using very sensitive methods, ESBL/AmpC-forming *E. coli* can be detected particularly frequently in poultry meat (30-35% of samples), much less frequently in beef and pork (2-6% of samples) and in other animal and plant foods (2-3% of samples).

Bacteria that are detected on food originate mostly from animal husbandry and are transferred to the food during food production (e.g. during slaughter or during milking).

If, on the other hand, the food is examined using non-selective methods, ESBL/AmpC-producing *E. coli* are only rarely detected. With non-selective methods, *E. coli* are first isolated in a sample in general and the next step is to check what proportion of the *E. coli bacteria* carry the resistance genes (see also the previous question).

Detailed data on the detection of ESBL/AmpC-producing *E. coli* can be found on the data portal Zoonotify.

How common are ESBL- and/or AmpC-producing bacteria in (farm) animals?

ESBL- and/or AmpC-producing bacteria are found in all types of livestock and also in many pets (dogs, cats, etc.).

Among the non-selectively recovered *E. coli*, the highest proportion of cephalosporin-resistant *E. coli* was found in isolates from calves suffering from diarrhea. In studies on healthy animals, the proportion of cephalosporin-resistant *E. coli* in broilers was highest in 2010 at 13.5 %, but has fallen continuously since then. In contrast, the proportion of cephalosporin-resistant *E. coli* in dairy cattle and calves rose until 2018 and has only declined since then.

Investigations using selective methods to specifically search for cephalosporin-resistant bacteria have shown that such bacteria are very widespread and can be detected in the vast majority of cattle, pigs and broilers. The proportion of samples containing such bacteria in slaughter animals was between 35% and 70%, with the values fluctuating over time and showing no consistent trend. Detailed data can be found on the data portal ZooNotify.

Further information on the spread of ESBL- and/or AmpC-forming bacteria can be found in the BfR opinion "ESBL-forming bacteria in food and their transmissibility to humans".

Why is the detection of ESBL- and/or AmpC-producing bacteria in livestock and food important?

The presence of ESBL- and/or AmpC-producing bacteria in livestock and food is significant for two reasons:

On the one hand, resistant pathogenic bacteria (e.g. *Salmonella*) can reach the consumer via food (e.g. meat). If this leads to an infection that requires treatment, the antibiotics in question will not work.

Secondly, there is the possibility that resistant bacteria (even if they themselves are usually harmless) pass on their resistance genes to pathogens that can make humans ill. This is because the resistance genes are transmissible between bacteria. This way of exchanging genetic information is known as horizontal gene transfer.

Which infection pathways play a role for humans?

People can ingest bacteria through contact with other people or animals, from the environment or when eating food that is contaminated with the bacteria.

The extent to which ESBL- and/or AmpC-producing bacteria are transmitted from livestock and food to humans and contribute to the occurrence of infections with ESBL- and/or AmpC-producing bacteria in human medicine cannot be determined with certainty. The same ESBL genes are often detected in *E. coli* isolates from livestock, pets and humans, which in principle suggests a reciprocal transmission of the resistant pathogens.

However, the *E. coli* isolates from the different sources usually differ, as different *E. coli* subtypes are often found in different animal species or in humans. This in turn underlines the importance of horizontal gene transfer - the transfer of resistance genes between different bacterial species or different subtypes of a bacterial species. In so-called "source attribution" studies, in which attempts are made to trace the sources or pathways of bacteria or genes, it has been shown in the Netherlands that most ESBL/AmpC-producing *E. coli* found in humans originate from other humans rather than from animals and food. Transmission therefore occurs in hospitals and other healthcare facilities, but also in everyday life and when traveling. Transmission rarely results in illness because the bacteria are vastly part of the normal intestinal flora.

According to the study, a smaller proportion of the ESBL/AmpC-producing *E. coli* detected in humans may well come from animals and food.

How can ESBL/AmpC-producing *E. coli* be transmitted via food?

The risk of infection via food depends, among other things, on the amount of pathogens in the food. The amount of pathogen contributes to the extent to which the pathogen is transferred from the animal to the food during food production. Hygiene, e.g. during slaughter, is of paramount importance here.

Another aspect is whether the pathogen can multiply in the food. As a rule, this is hardly possible if the food is consistently refrigerated, but it is possible if the cold chain is interrupted, for example because the food is not refrigerated on the way from the supermarket to the home.

Finally, the hygiene conditions under which food is prepared are also important.

Bacteria are generally reduced or killed during cooking or frying, so that cooked food usually no longer carries (resistant) bacteria as long as it is not re-contaminated by contact with raw food or contaminated articles. Care must therefore be taken during preparation to ensure that resistant bacteria are not transferred from one food to another.

Further information on the protection against foodborne infections in private households can be found in the BfR consumer tip.

Can contact with animals also lead to infection with ESBL/AmpC-producing *E. coli*?

Bacteria can be exchanged to a considerable extent between livestock and people who handle these livestock. For example, ESBL- and/or AmpC-producing bacteria can also be transmitted from animals to employees in livestock farms via direct contact.

Bacteria can also be transmitted from animals and food to humans through direct contact at the abattoir or in food processing. Conversely, people colonized with the bacteria can also transmit bacteria to animals and food.

Direct contact with pets, such as dogs and cats, also leads to an exchange of bacteria between humans and animals.

Can humans also impurity food with resistant bacteria?

In principle, humans can also be a source of food impurities with resistant bacteria. They can transfer bacteria from one foodstuff to another without being colonized themselves, for example through poor kitchen hygiene. However, it is also possible for a person to be colonized with the bacteria themselves and transfer them to the food. This is particularly significant if the person works in communal catering facilities (retirement homes, day care centers, etc.).

How common are human infections with ESBL- and/or AmpC-producing bacteria?

The Robert Koch Institute collects data on the resistance of bacteria in humans in the database ARS (Antibiotic Resistance Surveillance, in German only). By 2018, the proportion of cefotaxime-resistant *E. coli* detected in sick people in the outpatient sector had risen to 8.2%. In the following years, it decreased and amounted to 6.9 % in 2023. In the inpatient sector, the proportion is always slightly higher. Here, the highest value was recorded in 2017 with 12.3% of the isolates examined. In 2023, it was still 9.2%.

ESBL-producing bacteria play an important role in healthcare facilities as pathogens of so-called nosocomial, i.e. hospital-acquired, infections. These are often special strains of bacteria that have adapted to the situation in the hospital. Resistance is an additional problem to their pathogenic properties. However, most bacteria that produce ESBL are harmless intestinal inhabitants ("commensals") that do not cause illness and are therefore not noticed. In Germany, asymptomatic colonization of the intestine with ESBL-E*. coli* is between 6.3 and 10.3 % in adults and 2.3 % in children.

It is not yet known how often contact or colonization with ESBL- and/or AmpC-producing bacteria leads to disease in humans. It is also not known to what extent the resistance itself influences the course of the disease. What is certain, however, is that in the event of an illness, it is more difficult to treat. Third and fourth generation cephalosporins are among the most important active substances in the treatment of bacterial infections in humans. However, ESBL-producing bacteria are resistant to this group of active substances, i.e. the substances are ineffective.

Does contact with ESBL- and/or AmpC-producing bacteria always lead to illness?

Resistance in bacteria is not in itself a disease-causing property. In most cases, humans will not notice colonization with ESBL- and/or AmpC-producing bacteria, as most of these bacteria are harmless intestinal inhabitants. However, there are also ESBL- and/or AmpC-producing bacteria that can cause illness in humans, e.g. *Salmonella, Klebsiella* or enterohaemorrhagic *Escherichia coli* (EHEC). Some of these bacteria lead to illness, particularly in risk groups such as small children, pregnant women, older people and people with weakened immune systems. If illnesses caused by these bacteria have to be treated with antibiotics, the treatment may be more difficult due to the resistance of the pathogens, either because the initial treatment with cephalosporins is not effective or because other substances have to be used if the resistance test is available, which may be less well tolerated or have other disadvantages. The disease can last longer and be more severe, requiring hospitalization and causing permanent damage to health. In the worst case, the disease can lead to death.

Can consumers recognize whether a food is contaminated with ESBL- and/or AmpC-forming bacteria?

Consumers are unable to recognize such contamination. Only targeted laboratory tests can determine whether food is contaminated with ESBL- and/or AmpC-forming bacteria. As bacterial impurities are not uncommon, care should always be taken to ensure optimum kitchen hygiene when preparing meat (see Consumer tips to protect against foodborne infections in private households).

How can the occurrence of ESBL- and/or AmpC-producing bacteria in German fattening poultry flocks be explained, although the corresponding antibiotics (3rd and 4th generation cephalosporins) are not approved for poultry in Germany?

ESBL- and/or AmpC-producing bacteria can enter poultry flocks in various ways. In principle, ESBL- and/or AmpC-producing bacteria are no different from other intestinal bacteria (e.g. *Salmonella*): On the one hand, there is the possibility that the chicks acquired the corresponding pathogens in the hatchery or that the hatching eggs were already contaminated with the bacteria. The chicks then already carry the bacteria when they enter the fattening farm. This entry into the fattening farm was frequently detected in the past, but in recent years it has been detected less frequently.

Furthermore, employees, but also animate and inanimate vectors (e.g. rodents, work equipment) could introduce the bacteria into the flocks. Bacteria from other livestock farms can also be introduced into the flocks.

Once ESBL- and/or AmpC-producing bacteria are present in the population, they are not only favored by the use of 3rd or 4th generation cephalosporins. The ESBL/AmpC genes are often present in a bacterium together with resistance genes for other antibiotic classes, so that they are also selected as free riders when these antibiotic classes are used. The use of 'simpler' beta-lactam antibiotics (e.g. aminopenicillins) also promotes the spread of ESBL/AmpC-producing bacteria. The use of cephalosporins is therefore not a necessary prerequisite for the occurrence of bacteria with resistance to these substances.

It is noteworthy that the detection rate for ESBL/AmpC-producing *E. coli* using selective methods in broilers at the time of slaughter has decreased from 52.6% in 2016 to 41.1% in 2022.

What can consumers do to protect themselves from ESBL- and/or AmpC-forming bacteria in food?

By carefully observing the rules of kitchen hygiene, consumers can largely reduce the risk of colonization or infection with ESBL- and/or AmpC-forming bacteria present on food. However, the occurrence of infections with *Salmonella* or *Campylobacter* indicates that these bacteria can also be transmitted to humans.

To protect themselves against ESBL- and/or AmpC-forming bacteria, consumers should observe the same hygiene rules that apply to other pathogens that are transmissible from animals or food to humans. These include:

- Heat food, especially fresh meat, raw eggs and raw milk, sufficiently before consumption.
- Wash raw food, such as salads, sprouts, vegetables and fruit, thoroughly with drinking water or peel fruit and vegetables before eating.
- Avoid direct or indirect contact of raw meat, raw eggs and raw milk with raw food and ready-to-eat food that will not be reheated later. It is best to first prepare food that is not to be heated.
- Strictly adhere to the relevant hygiene rules when storing and preparing food in order to keep the bacterial load as low as possible.
- Wash hands with warm water and soap after contact with animals. This also applies after contact with pets.

The BfR has published the consumer tips "https://www.bfr.bund.de/cm/364/protection-against-foodborne-infections.pdf".

What measures does the BfR recommend to prevent antibiotic resistance?

In order to prevent the development and spread of antibiotic resistance and thus also of ESBL- and/or AmpC-producing bacteria, the BfR believes that the use of antibiotics in both human and veterinary medicine should be limited to what is absolutely necessary. To this end, measures must be taken to keep humans and animals healthy and thus make antibiotic therapy unnecessary. Improved farm management, hygienic measures to prevent the entry and spread of pathogens and measures to preserve the health status through improved animal husbandry and feeding as well as vaccinations against common diseases are considered important measures for animal husbandry. In addition, it should be ensured that resistant pathogens are not introduced into the environment and thus reach the consumer via various transmission routes.

What measures have been taken to minimize the occurrence of ESBL- and/or AmpC-forming bacteria on farms?

The use of antibiotics in veterinary medicine is regulated by the European Veterinary Medicinal Products Regulation, the German Veterinary Medicinal Products Act (TAMG) and other regulations based on these laws. The total quantity of antibiotics used in animal husbandry has fallen by 70% since 2011 (from 1706 tons in 2011 to 529 tons in 2023).

In Germany, the 16th amendment to the Medicinal Products Act implemented the antibiotic minimization concept for animal husbandry. The regulations stipulate that the use of antibiotics in fattening animals must be reported to a national database. With the amendment to the Veterinary Medicinal Products Act, the range of animal populations covered has been expanded since 2023. Targeted measures are made possible on the basis of this data. Companies that use antibiotics particularly frequently must draw up action plans on how they intend to reduce this use.

In addition, the use of 3rd and 4th generation cephalosporins was made subject to conditions that increase the workload for livestock farms and their veterinarians and therefore make their use less attractive than other substances. As a result, the use of these substances declined significantly.

Finally, the use of 3rd and 4th generation cephalosporins will be counted three times in future when determining the frequency of treatment in order to take account of the particular importance of these substances. This is expected to lead to a further decline in the use of these substances.

In addition to the responsible use of antimicrobial veterinary medicinal products, what can livestock farmers do to minimize the occurrence of ESBL- and/or AmpC-producing bacteria on their farms?

The occurrence of ESBL- and/or AmpC-producing bacteria in livestock farms is determined by the introduction of the bacteria into the herds and the spread of the bacteria within the herds. It can be assumed that restrained use of antimicrobial veterinary drugs, especially cephalosporins, can reduce the selection pressure towards resistant pathogens. In addition, checking the animals before they are housed, thorough cleaning and disinfection between fattening cycles and preventing the introduction of bacteria from the environment of the stables (e.g. from neighboring stables) is helpful.

Further information on foodborne infections

BfR consumer tips: Protection against foodborne infections in private households
https://www.bfr.bund.de/cm/364/protection-against-foodborne-infections.pdf

Topic page: Assessment of microbial risks in foods
https://www.bfr.bund.de/en/assessment_of_microbial_risks_in_foods-739.html

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