

Questions and answers about methicillin-resistant *Staphylococcus aureus* (MRSA)

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Methicillin-resistant *Staphylococcus aureus* (MRSA) are bacteria which are resistant to certain antimicrobials which can cause, among other diseases, wound infections and inflammation of the respiratory system in humans. In the past, these bacteria were mainly found in hospitals where they were transmitted via contact from person to person. In recent years, there have been increased numbers of cases of infections which people have contracted outside hospital.

MRSA have also been detected in livestock and in food which can thus become a source of infection for humans. The Federal Institute for Risk Assessment (BfR) has compiled Frequently Asked Questions about MRSA and their presence in the food supply chain.

What are MRSA?

The abbreviation “MRSA” stands for the bacterial group “methicillin-resistant *Staphylococcus aureus*”. *Staphylococcus aureus* is a widespread bacterium which colonises the skin and mucous membranes of humans and animals. According to the European Centre for Disease Prevention and Control (ECDC), about 30 % of people carry *Staphylococcus aureus* on their skin. Normally this colonisation goes unnoticed. As *S. aureus* is found on the skin, it is frequently involved in infections of the skin and mucous membranes.

The methicillin-resistant variant of *S. aureus* is resistant to beta-lactam antibiotics, i.e. to penicillins and cephalosporins. These antibiotics are no longer effective when it comes to treating an MRSA infection, i.e. they no longer kill the infectious pathogen.

What are the consequences of the methicillin resistance of *Staphylococcus aureus*?

The reason why MRSA infections pose a challenge for attending physicians is that standard antibiotics which are used against this group of pathogens are not effective. Due to the necessary switch to less well tolerated or less effective alternative therapies, MRSA infections can lead to longer hospital stays and increased death rates.

What groups of MRSA are there?

On the basis of its presence and the most important location of its transmission, MRSA are categorised into three main groups:

- MRSA that are transmitted predominantly in hospitals (hospital-acquired MRSA, haMRSA)
- MRSA that are transmitted outside the hospital setting from person to person (community-acquired MRSA, caMRSA)
- MRSA that are prevalent among livestock and mainly found in humans who are in regular contact with farm animals due to their profession (livestock-associated MRSA, laMRSA). These mainly include MRSA associated with the clonal complex (CC) 398, as well as CC9 and CC97 MRSA.

Are there different MRSA types and how do they differ with regard to their properties?

The individual MRSA types are not only differentiated with regard to their origin but also with regard to their properties, i.e. their configuration with virulence and resistance characteristics. The MRSA types that occur within livestock, which means in particular the MRSA that belong to the type CC398, carry the typical disease-causing properties described to date with

haMRSA and caMRSA only comparatively seldom. The individual MRSA types differ also clearly up to now with regard to their configuration with genes coded for resistance to antibiotics. Accordingly, resistance to the antibiotics which would be administered in human medicine in the event of a clinical infection with MRSA is rarely detected with laMRSA.

As many of these properties are located on mobile genetic elements, however, the possibility exists that an exchange will take place between bacteria, i.e. that additional characteristics will be acquired. For this reason, laMRSA types also occur in certain cases which can possibly have an advantage over other types as it is easier for them to colonise in humans, for example. It is therefore important too that MRSA are examined continuously for this occurrence and the properties that go with it.

How can a person become infected with MRSA?

Infections with MRSA most frequently occur in hospitals, especially in intensive care units. Chronic diseases, a weakened immune system, and the use of antibiotics, especially if incorrectly administered, pose a specific risk of contracting an MRSA infection. Direct contact with MRSA-carrying persons and indirect contact via shared objects such as towels and a lack of hygiene constitute the main MRSA transmission paths.

Since 2005, there have been more and more reports of MRSA being detected in persons who had contact with MRSA-positive livestock. This is mainly MRSA from the group laMRSA ("la" stands for livestock-associated MRSA). It is also being reported of late that laMRSA of this kind is being detected with persons who had no direct contact with livestock. This means that in rural regions of Germany, approx. 20-38 % of cases of the colonisation of humans with CC398 MRSA are not attributable to (in)direct contact with animals, thus indicating the possibility of other transmission paths.

What is the difference between infection and colonisation with MRSA?

A distinction must be made between infection and colonisation with MRSA. Transmission of the bacteria followed by colonisation does not lead to disease symptoms. However, the person remains a carrier. Individuals colonised with MRSA have a greater risk of contracting MRSA infections after surgical operations, for example. Consumers should discuss with their GP or local health authorities what measures need to be taken in case of MRSA colonisation.

Under all circumstances, affected individuals or individuals belonging to a risk group should state this when they are admitted to a hospital or health care centre. This will then allow doctors to take precautions to avoid an MRSA infection before any medical procedures are carried out.

How frequently do colonisations with MRSA occur in healthy individuals?

For Germany, only isolated figures are available on the frequency of MRSA colonisation in healthy individuals. From these limited tests, it can be assumed that approximately one to two percent of the population are carriers of MRSA. Higher colonisation rates are found in veterinarians and farmers who have job-related contact with domestic animals, in particular pigs. A study in Lower Saxony showed that around 25 % of persons with livestock contact were colonised with MRSA. In addition to this, screening on admission to hospitals in German regions with a high livestock density showed that roughly 20-30 % of the patients were MRSA-positive.

Can consumers notice MRSA on their skin?

No, because colonisation does not normally lead to any health impairments. MRSA behaves here like any other representative of this genus. *S. aureus* is part of the skin's normal

bacterial flora, with roughly 30 % of the population carrying this bacterium on their skin. Colonisation with MRSA can only be determined by a laboratory examination. This is normally done by taking a swab of the nasal mucosa.

To what extent is MRSA prevalent in different livestock populations?

As a coloniser, *Staphylococcus aureus* belongs to the normal skin and mucosal flora of both humans and animals. *S. aureus* has been a recognised pathogen in inflammations of the mammary gland (mastitis), particularly in cattle for some time now. In livestock, a specific MRSA type is frequently detected which is prevalent within animal populations. It was found in 2008 in more than 50 % of farms with fattening pigs and also in 20 % of veal production herds and turkey flocks in 2010. This detection rate is much lower in chicken production flocks, on the other hand (0.9 % in 2009).

The MRSA detected in livestock animals usually belong to a specific line, the so-called clonal complex (CC) 398, which is also known as laMRSA ("la" stands for livestock-associated). Colonisation of animals is usually not associated with illness. In dairy cattle, however, this MRSA-line - as is the case with other *S. aureus* - can lead to inflammation of the mammary gland.

As part of zoonosis monitoring, representative data on the prevalence of MRSA in different types of food-producing animals were collected in the years 2008 to 2012. Detailed results can be found on the Internet (in German only):

http://www.bfr.bund.de/de/a-z_index/zoonosen-4189.html

http://www.bvl.bund.de/DE/01_Lebensmittel/01_Aufgaben/02_AmtlicheLebensmittelueberwachung/06_ZoonosenMonitoring/lm_zoonosen_monitoring_node.html

Which factors influence the presence of MRSA in animal populations?

MRSA are usually transferred between animal populations when animals carrying the pathogen are bought and moved between herds/flocks. In principle, however, the presence of MRSA in animal populations is influenced by a number of factors, such as the size of the herd/flock and the use of antibiotics within the population.

This was shown clearly in a study on MRSA levels in fattening pig farms. In pure fattening populations, where all fattening pigs are bought from external sources, the bacteria were found more frequently than in farms that raised their own piglets to slaughter weight. In addition, the pathogens were more common in large animal populations than small ones. Equally, the bacteria were more prevalent in herds where antibiotics had been used.

Since when has MRSA been detected in agricultural livestock?

The first MRSA findings in animals were observed in the 1970s in mastitis isolates of *S. aureus* from cattle. Until 2005, reports on MRSA in livestock only appeared sporadically. In Germany, MRSA isolates from livestock are available since 2004. It was identified as part of a retrospective investigation into *S. aureus* which was isolated during diagnostic post mortem examinations of pigs. Older isolates were not available for that study. It is not known, therefore, whether livestock-associated MRSA (laMRSA) was already present in Germany's pig population before 2004.

The first isolates from the poultry food chain (turkey and broiler) were made available to the BfR in the year 2008 from a voluntary monitoring programme conducted at abattoirs and retail shops. Here too, the possibility of the pathogen being present in the population even earlier cannot be excluded.

Detailed reports from Belgium and Germany about MRSA in dairy cattle are available for the years 2007 and 2008. Reports on MRSA in fattening calves appeared in the Netherlands in 2008. It was possible to confirm these findings for Germany as part of the zoonosis monitoring programme 2009.

Are the same types of MRSA detected in different livestock species?

In all tested samples, types of bacteria of the clonal complex CC398 accounted for the majority. To varying extents, isolates of other clonal complexes are found as well. At present, this is most often the case with poultry where isolates of the clonal complexes CC9 (chicken) and CC5 (turkey) are found.

Are organic farms also affected by MRSA?

The number of studies conducted on the various livestock species is still limited. There are positive test results from organic pig farms. Overall, however, MRSA is found less frequently in such farms. In addition, the number of colonised animals within such facilities is usually lower than in conventional farms.

How frequently are MRSA prevalent in livestock the cause of infections in humans?

After an adaptation of the Infection Protection Law¹, it has been compulsory in Germany since July 2009 to report detected MRSA from blood cultures. In the years 2010, 2011, 2012 and 2013, 3755, 4227, 4485 and 4373 cases respectively were reported to the Robert Koch Institute (as of 17 Sep. 2014). These cases only account for a small proportion of the overall findings of MRSA, however. The proportion of these cases attributable to livestock-associated CC398 is approximately 2 % here and should be described as moderate. In regions with a high density of livestock, with a share of 10 % CC398 MRSA meanwhile accounts for a considerable proportion of the detected cases of MRSA in humans.

Can people become infected with MRSA through direct contact with livestock?

Contact with colonised animals can lead to human colonisation with MRSA. So far, this has been described most frequently after direct contact with pigs, calves and poultry. However, since there have been reports of colonisations and infections in connection with almost all types of production animals, each of these animal species is a potential source of MRSA colonisation of humans under certain circumstances.

Persons who are frequently in contact with pigs and other livestock through their profession are more frequently colonised with MRSA than the general population. A study conducted in Lower Saxony showed that about 25 % of persons who had job-related contact with farm animals were colonised with MRSA. In contrast, MRSA was found in only 1.5 % of tested persons without any occupational contact with livestock. Some of these persons colonised with MRSA had indirect contact with animals, however, or contact with such animals through household members who were exposed to them or who regularly visited agricultural facilities.

Cases of disease involving skin and wound infections or respiratory tract infections with livestock-associated MRSA have only been observed rarely compared to the high rates of colonisation of such persons. It is likely that the pathogen can be transmitted to humans both through direct contact with the animals and through inhalation of highly contaminated dust.

¹ In accordance with Art. 1 of the regulation to adapt the obligation to register to the epidemic situation in compliance with Art. 7 of the Infection Protection Law (Laboratory registration adaptation regulation – LabMeldAnpV) of 26 May 2009.

Can people become infected with MRSA during a farm visit?

As is true for all zoonotic pathogens, this is possible in principle, especially if the animals are touched or their sheds are entered. Studies from the north-west of Germany have shown that persons who visit agricultural establishments on a regular basis in order to buy eggs or milk, for example, are more frequently colonised with livestock-associated MRSA compared to the general population. However, the risk of infection or colonisation is many times lower with this group than with persons who are regularly exposed to the pathogens through their work. A study from the Netherlands has shown that in many persons who only had occasional contact with animals, the colonisation disappeared spontaneously after a short time.

Do persons who live in the vicinity of animal farms run a higher risk of colonisation with MRSA?

MRSA are contained in the shed air and are therefore also released with the exhaust air from sheds. In the surroundings of sheds, the concentration then decreases very quickly, so that MRSA can only occasionally be detected in the air in the immediate vicinity of the sheds. On the ground, these bacteria can still be detected in somewhat greater distances from the sheds. A few individual articles have been published indicating that laMRSA is more frequent in people who live in regions with high livestock densities, but the people in these regions also have more frequent direct contact with animals. Little is known as yet about the resilience of livestock-associated MRSA in the environment. More studies are needed here.

Are livestock-associated MRSA also transmitted from person to person?

In principle, MRSA can be transmitted between humans. As far as is currently known, livestock-associated MRSA is less often transmitted between humans than has been described for other MRSA (ha and caMRSA) in hospitals.

Are livestock-associated MRSA causing infections in hospitals?

According to information provided by the Robert Koch Institute in 2012, the clonal complex CC398 accounted for roughly 5 % of MRSA detected in hospitals. In most cases, the bacteria were isolated from colonised persons and only in 1.5 % of all cases in connection with an infection. In the literature, the spreading tendency within hospitals is described as lower for CC398 than for other types of MRSA. Nevertheless, this type of MRSA can in principle be found in most types of illness associated with *S. aureus*, i.e. in infected wounds and pneumonia as well as septicaemia. The percentage of laMRSA in total MRSA can be significantly higher (10 %) in regions with a high density of livestock.

How can livestock farmers reduce the prevalence of MRSA in their herds/flocks?

The presence of MRSA in animal production facilities is determined by the introduction of the bacteria into the populations and spreading of the bacteria within the population. It is to be assumed that cautious use of antibiotics can reduce the selection pressure in the direction of resistant bacteria. In addition, controlling the animals before they are put in the sheds, thorough cleaning and disinfection between fattening groups and preventing the introduction from the environment of the sheds (e.g. from neighbouring sheds) are relevant measures.

How common is MRSA in food?

Based on the current state of knowledge, raw meat of all animal species may contain MRSA, although the bacterial concentrations are often extremely low. As part of zoonosis monitoring, the federal and regional authorities have tested meat of various animal species for MRSA. The results for the period from 2009 to 2012 show that fresh meat was to some extent contaminated with MRSA. The detection rates ranged between 11.7 % and 43.4 %. Meat from calves, pigs, chicken and turkey was tested. The highest MRSA detection rate was detected in turkey meat (2009:43.4%, 2010: 32 %, 2012: 37.7 %), followed by chicken

meat (2009: 23.7%, 2011: 27.7 %).

In all tested samples, types of bacteria of the clonal complex CC398 accounted for the majority. These results are consistent with reports from the Netherlands which also described contamination of food. The detailed findings of these studies are available online on the websites of the Federal Institute for Risk Assessment and the Federal Office of Consumer Protection and Food Safety:

http://www.bfr.bund.de/de/a-z_index/zoosen-4189.html

http://www.bvl.bund.de/DE/01_Lebensmittel/01_Aufgaben/02_AmtlicheLebensmittelueberwachung/06_ZoosenMonitoring/Im_zoosen_monitoring_node.html

Can food be a source of MRSA infection?

As MRSA can occur in food, especially raw meat, in principle food may constitute a possible source of colonisation and subsequent infection of humans. As recent tests in Denmark show, there are also isolated cases of human infections where certain types of MRSA belonging to the livestock-associated clonal complex CC398 were found in humans. These MRSA in humans showed similarities and had specific common characteristics with the MRSA isolated from poultry meat. This does not necessarily mean, however, that the infection of humans actually is attributable to poultry meat as the source of infection. There are currently no epidemiological indications of any kind to suggest this.

Can people become infected with MRSA from food?

So far, there have only been few reports of cases in which an MRSA infection in humans could be attributed to food. In these few known cases, the foods had been contaminated with MRSA by infected persons. MRSA can only propagate with difficulty, if at all, in many foods, such as roasted, fried or boiled meat, but care must be taken to ensure that the food is not re-contaminated after heat treatment. Based on the current state of knowledge, raw meat of all animal species may contain MRSA, although the bacterial concentrations are often extremely low. In individual cases, for example in the thawing water of chicken meat, the bacterial count may be higher.

Provided that the rules of kitchen hygiene are observed, the risk of an infection or colonisation with MRSA via food is low.

Can consumers tell whether a food is contaminated with MRSA?

No, contamination of foods with MRSA can only be established through extensive laboratory testing.

Are organically produced foods free from MRSA?

MRSA can be detected in organically produced food as well, as animals from organic farms can also be colonised with the bacteria. The same standards of hygiene that are applied to conventionally produced meat must therefore be applied to organically produced meat too. No comparative studies on the frequency of MRSA in organically produced meat are available to date.

What can consumers do to protect themselves from MRSA found in foods and livestock?

The normal hygiene recommendations for handling food and animals apply when it comes to protection against MRSA colonisation: after contact with animals as well as before and after preparing raw meat, consumers should wash their hands thoroughly with soap and water. Furthermore, efforts should be made to avoid any direct contact between the mouth and animals or raw meat. These hygiene measures also provide protection against other

pathogens such as *Salmonella*, *Campylobacter* and verotoxin-producing *Escherichia coli* (VTEC).

The BfR has summarised further tips on how consumers can protect themselves from food-borne infections in the following leaflet (in German only):

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

Is MRSA widespread in Germany compared to other countries?

Data on MRSA infection in humans are collected and published throughout Europe in the “European Antimicrobial Resistance Surveillance System” (EARS Net) which is coordinated by the European Centre for Disease Prevention and Control (ECDC). According to this system, 15.4 % of the *Staphylococcus aureus* isolates from septicaemia in hospital patients in Germany were identified as MRSA in 2012.

Compared to other European countries, Germany is in the middle range when it comes to the prevalence of MRSA in hospitals. In Scandinavia and the Netherlands, intensive efforts have been undertaken for decades to control and monitor MRSA, and hence it is less widespread there. In the United Kingdom, intensive efforts have been made for several years to combat MRSA. As a consequence, the detection rate dropped from 30.7 % to 14 % between 2008 and 2012. A similar drop in the MRSA detection rate was observed in Germany too, however, over the same period. The proportion of methicillin-resistant *S. aureus* in all *S. aureus* is far higher in southern and eastern Europe.

In what areas does the BfR conduct research on MRSA?

Together with the federal states, the BfR studies the prevalence of MRSA in animal populations and food. In the National Reference Laboratory for coagulase positive staphylococci including *S. aureus*, the bacteria isolated in the regional laboratories are then analysed to establish in more detail their characteristics and affinities, and strains of MRSA from different sources are compared.

As part of national and international research projects, in collaboration with cooperation partners, the BfR develops methods for detecting and typing laMRSA. The BfR studies how MRSA is spread between animal populations and along the food chain. The BfR regularly updates its risk assessment on the basis of both the scientific literature and the insights gained directly. It makes this assessment available to agencies of both the federal and the state governments and also to the public.

What are public authorities doing to combat MRSA in animal populations?

Due to reports on MRSA in animals, especially production animals and animal-based foods, veterinary and food control agencies are currently conducting research at the national and international level on how prevalent methicillin-resistant *S. aureus* is in animals and foods. For example, as part of the zoonosis monitoring programme, the agencies of the federal and state governments undertook extensive studies in the period from 2009 to 2012 on the prevalence of MRSA in animal populations and foods. These annual studies provide important data on the extent of the contamination of animal populations and foods and on the properties of the MRSA types involved. The Federal Institute for Risk Assessment regularly updates its assessment of the risk for consumer health protection on the basis of emerging data and makes available this assessment to the Federal Government and veterinary agencies.

The Federal Ministry of Food and Agriculture (BMEL) and Federal Ministry of Education and

Research (BMBF) sponsor research projects on the presence and spread of livestock-associated MRSA. Additional studies are undertaken as part of EU research programmes. In these studies, universities and health research institutions closely cooperate with veterinary and food investigation centres. The BfR is directly involved in many of these projects.

What are public authorities doing to combat MRSA in hospitals?

The Hospital Hygiene Commission of the Robert Koch Institute already published recommendations in 2008 indicating that persons with exposition to livestock through their work should be tested for MRSA when admitted to hospital. The committee for biological job safety has authored an opinion on occupational contamination with MRSA.

Due to an amendment of the Infection Protection Act, it became compulsory in July 2009 to report detected MRSA from blood cultures. In the years 2010, 2011, 2012 and 2013, 3,755, 4,227, 4485 and 4,373 cases respectively were reported to the Robert Koch Institute (figures correct as of 17 Sep.2014). These cases only account for a small proportion of the overall findings of MRSA, however.

The point of contact for more information on the subject of "MRSA in Hospitals" is the Robert Koch Institute:

www.rki.de