

When antimicrobials don't work - one of the biggest threats to health

According to figures from the EU, antimicrobial resistance kills 25,000 Europeans annually. The WHO considers antimicrobial resistance to be one of the biggest threats to human health, and the National Food Institute has made Denmark a global pioneer in the battle against resistant bacteria.

Repeated use of penicillin and other types of antimicrobials can cause these substances to lose their effect because the bacteria develop resistance to the substances. This can make it more difficult - and impossible at worst - to treat bacterial infections in humans and animals. When bacteria become resistant, even a trivial infection can be fatal.

"In the 1990s, cows and pigs were brimming with antimicrobials. They were added to the feed in order to promote growth. Large amounts of antimicrobials made the bacteria resistant and this spread to humans via the food chain," Professor and Head of Research Group Frank Møller Aarestrup says.

The problem was not identified until 1994. Ever since, the National Food Institute has researched antimicrobial resistance and participated in the global monitoring of the ways in which resistance spreads. Bacteria can quickly spread to the entire world, e.g. when we travel or eat imported meat.

The research is crucial in order to advise national and international authorities and other stakeholders on how to minimize

antimicrobial resistance nationally and globally. The monitoring efforts - e.g. via the national VetStat - ensures that the amount of medicine given to Danish animals is controlled.

In 2000, Denmark was the first country in the world to ban the use of growth promoters in animal feed, and in 2006, the ban was implemented across the EU.

Other countries pay great attention to the research conducted in Denmark, and the National Food Institute has been appointed both as an EU reference laboratory for antimicrobial resistance and as a WHO and FAO collaborative centre for antimicrobial resistance.

In order to monitor the occurrence of antimicrobial resistance in Denmark, a national monitoring programme was established: DANMAP, which monitors the consumption of antimicrobials and the presence of antimicrobial resistance among bacteria in animals, people, and foods in Denmark. The programme, which has existed for more than 20 years, was the first of its kind in the world and is often highlighted overseas as a good example.

Whole genome sequencing and vast amounts of data are used at the National Food Institute to develop systems for the global surveillance of pathogenic microorganisms and antimicrobial resistance.

Human DNA. Philippe Plailly, Science Photo Library, Scanpix



The National Food Institute develops detection methods that can be used to determine the cause of foodborne disease outbreaks both in Denmark and abroad.

📷 Lollo Bionda salad. Colourbox

Data ensure better surveillance

Since the National Food Institute took steps back in the 2000s to create a global overview of antimicrobial resistance in Salmonella bacteria, the way in which research is conducted has developed significantly. Previously, information arrived from all over the world in the form of Excel sheets, faxes, photocopies, and even handwritten pages in languages almost as diverse as the abundance of Salmonella bacteria.

“Today we use the large quantities of available data in our research in an intelligent way in order to create an overview, and we look at many other threats than just Salmonella. We use a brand new technique - whole genome sequencing - which can identify disease-causing microorganisms’ entire DNA profile in one go,” Frank Møller Aarestrup says.

This new approach offers the researchers a head start when trying to discover outbreaks of diseases among animals and

people, and the huge amounts of data are collected and analysed in collaboration with DTU Computerome.

Whole genome sequencing and the use of data make it possible to increase monitoring and reduce the consequences and costs when recurring epidemics and food outbreaks threaten the health of humans and animals.

Besides putting pressure on the healthcare system and the barns with domestic animals, the epidemics also put pressure on consumers’ trust in foods.

“The sooner we are able to detect an outbreak of for example Salmonella, Ebola, or the flu, the sooner we can make an effort to stop it, make the authorities intervene, and return to normal conditions,” Frank Møller Aarestrup says.

The National Food Institute is running a large EU project, COMPARE, which is working to develop a global platform that makes it possible to quickly and efficiently identify and analyse disease-causing microorganisms that may cause outbreaks of diseases worldwide.

Sewage reveals resistance

Researchers at the Institute have also examined the sources that create a basis for outbreaks of diseases and cause bacteria to develop resistance. In an international study headed by the National Food Institute, sewage from 74 cities and 60 countries has been analysed in order to create an overview of the amount and type of resistant bacteria that healthy people carry. The results have shown that it is not only an excessive use of antimicrobials that creates resistance.

“Sewage analyses can very accurately show the types of bacteria that are prevalent in an area. Sewage also serves as a great source for the analyses since consent from each individual is not needed because sewage cannot be linked to individuals. Another interesting aspect is that it is not very costly to analyse sewage,

so it is definitely possible to create a surveillance programme - also in developing countries,” Frank Møller Aarestrup says.

Denmark has the sixth lowest occurrence of resistance

All the DNA material in the sewage samples has been mapped out, and the results show that North America, Western Europe, Australia, and New Zealand have the lowest levels of resistance, while Asia, Africa, and South America have the highest levels.

Using data from the World Bank, the researchers have predicted the levels of resistance in 259 countries/territories and drawn a map of the occurrence of resistance in healthy populations. Denmark reports the sixth lowest occurrence of resistance. The Netherlands, New Zealand, and Sweden have the lowest levels of resistance, whereas the highest levels were found in Tanzania, Vietnam, and Nigeria.

“The results of the sewage analysis show that sanitary conditions are crucial in the development of resistant bacteria along with the population’s general state of health,” Frank Møller Aarestrup says and adds: “So a good place to start the fight against resistant bacteria is to make an effort to improve the sanitary conditions and to reduce the spread of rubbish. In some places, this would actually be more efficient than to limit the use of antimicrobials.”

A step closer to global surveillance

When new resistance genes are identified in the future, the researchers will be able to reuse publicly available raw data from whole genome sequencing in order to quickly identify how these resistance genes have emerged and spread.

The researchers want to use the experiences from the projects to meet the overall ambition to develop a global surveillance system that can continuously survey the occurrence and spread of disease-causing microorganisms and antimicrobial resistance.

Whole genome sequencing detects disease outbreaks faster

Until a few years ago, it could take several weeks for doctors and veterinarians to identify which disease-causing microorganism is causing a disease, and how the disease has spread.

Today, techniques for whole genome sequencing can quickly and relatively cheaply map the entire DNA profile of disease-causing microorganisms in one go. By mapping the genetic material of bacteria, it is also possible to determine their kinship and other factors such as virulence and antimicrobial resistance. This provides an understanding of how bacteria are related and have developed over time.

Whole genome sequencing has revolutionized the work of investigating disease outbreaks because technology makes it possible to more quickly and precisely identify the source of the outbreak. The consequences of and the costs related to the outbreak are thus reduced. Whole genome sequencing can also provide knowledge about antimicrobial-resistant genes in bacteria by monitoring resistant clones in people and the environment.

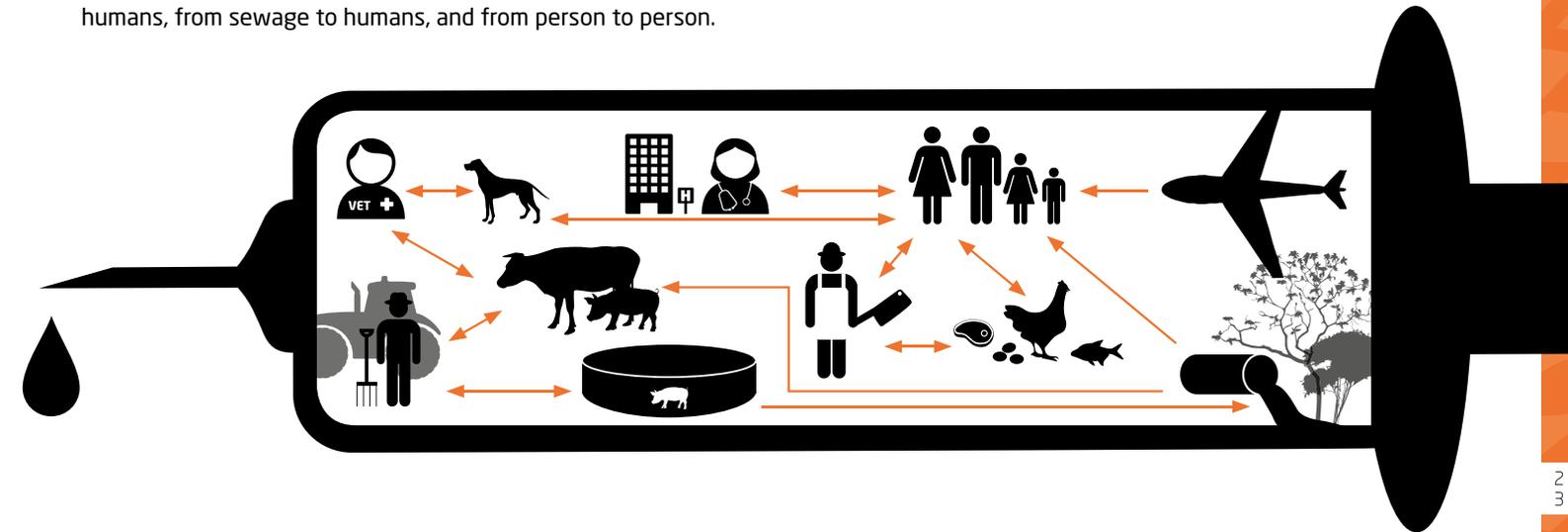
The National Food Institute conducts research in whole genome sequencing techniques. The Institute’s research sets the international standard for the identification, monitoring, and study of the global spread of disease-promoting microorganisms and antimicrobial-resistant bacteria. The Institute also makes an effort to promote the use of the technology internationally.

“The ambition is to develop a surveillance system that makes it possible to exchange and interpret data on disease-causing microorganisms in ‘real time’. In that way, it would be possible to use the global surveillance data, for example to tackle diseases when they are at risk of spreading beyond a country’s borders and turn into pandemics such as Ebola, measles, polio or cholera.”

Frank Møller Aarestrup
Professor and Head of Research Group

Many ways to spread resistant bacteria

The use of antimicrobials for animals and humans causes the bacteria to develop resistance, which can be spread via many routes - from animal to animal, from animals to humans, from food to humans, from sewage to humans, and from person to person.



DANMAP - the Danish monitoring system

Researchers, authorities, and industry in Denmark have long been aware that decision-makers need to be equipped with solid data in order to make knowledge-based decisions on how to handle problems related to antimicrobial resistance.

In 1995, this realization led to the establishment of the DANMAP programme, which is operated by the National Food Institute and Statens Serum Institut (the Danish national institute for surveillance and preparedness of human infectious diseases). In this programme, the researchers monitor the use of antimicrobials in humans and animals in Denmark and the occurrence of antimicrobial resistance in bacteria in animals, humans, and foods.

Since 1995, DANMAP data have, among other things, led to a ban on the use of antimicrobial growth promoters in the last part of the 1990s. DANMAP’s continuous focus on the use of antimicrobials in domestic animals was also instrumental in the implementation of the ‘yellow card’ initiative, which was developed by the Danish Veterinary and Food Administration for livestock with a high consumption of antimicrobials.

The farming sector has also actively used data from DANMAP. The farming sector has voluntarily minimized the use of cephalosporins in domestic animals - antimicrobials that are critically important in the treatment of humans.