SEFARI

Leading ideas on Antimicrobial Resistance

LEADING IDEAS ON ANTIMICROBIAL RESISTANCE

The Scottish Environment, Food and Agriculture Research Institutes (SEFARI) is a collective of six research institutes, Biomathematics and Statistics Scotland, James Hutton Institute, Moredun Research Institute, Rowett Institute, Royal Botanic Garden Edinburgh, Scotland's Rural College each with their own global capability, expertise and reputation.

Through collaborative multi- and interdisciplinary research, SEFARI are responsible, with Higher Education Institute partners, for delivering the Scottish Government (Rural and Environment Science and Analytical Services, RESAS) funded Strategic Research Portfolio on environment, agriculture, land, food, and rural communities (2016-2021). The Portfolio includes the Strategic Research Programme (SRP), Centres of Expertise, Innovation Partnerships and Underpinning Capacity funding of national research resources within SEFARI. SEFARI Gateway, the knowledge exchange and impact hub for SEFARI, works to enhance stakeholder access to SEFARI's research knowledge and expertise.

Antimicrobial resistance (AMR) is a global, immediate and ongoing concern to human health. Approaches to address this challenge involve reducing and optimising antimicrobial usage and improving our understanding of how AMR can occur, may be amplified and might be transferred from other sources such as the natural environment and animals.

This leaflet focuses upon SEFARI research on understanding the patterns, challenges and solutions to AMR, particularly from a rural and agricultural perspective across Scotland.

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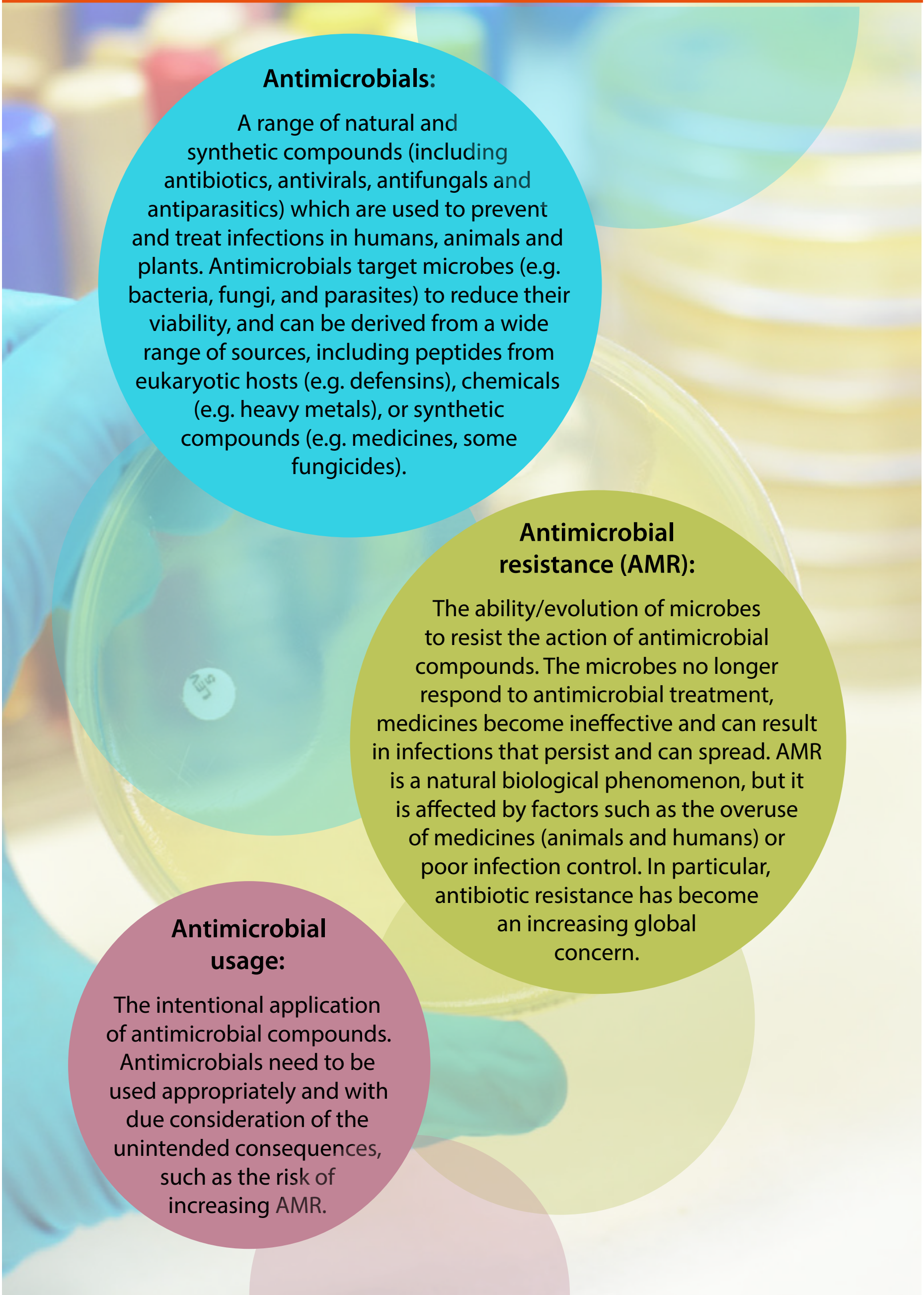
Glossary



Antimicrobials:

A range of natural and synthetic compounds (including antibiotics, antivirals, antifungals and antiparasitics) which are used to prevent and treat infections in humans, animals and plants. Antimicrobials target microbes (e.g. bacteria, fungi, and parasites) to reduce their viability, and can be derived from a wide range of sources, including peptides from eukaryotic hosts (e.g. defensins), chemicals (e.g. heavy metals), or synthetic compounds (e.g. medicines, some fungicides).

Antimicrobial resistance (AMR):

The ability/evolution of microbes to resist the action of antimicrobial compounds. The microbes no longer respond to antimicrobial treatment, medicines become ineffective and can result in infections that persist and can spread. AMR is a natural biological phenomenon, but it is affected by factors such as the overuse of medicines (animals and humans) or poor infection control. In particular, antibiotic resistance has become an increasing global concern.

Antimicrobial usage:

The intentional application of antimicrobial compounds. Antimicrobials need to be used appropriately and with due consideration of the unintended consequences, such as the risk of increasing AMR.

The antimicrobial resistance (AMR) 'ecosystem'

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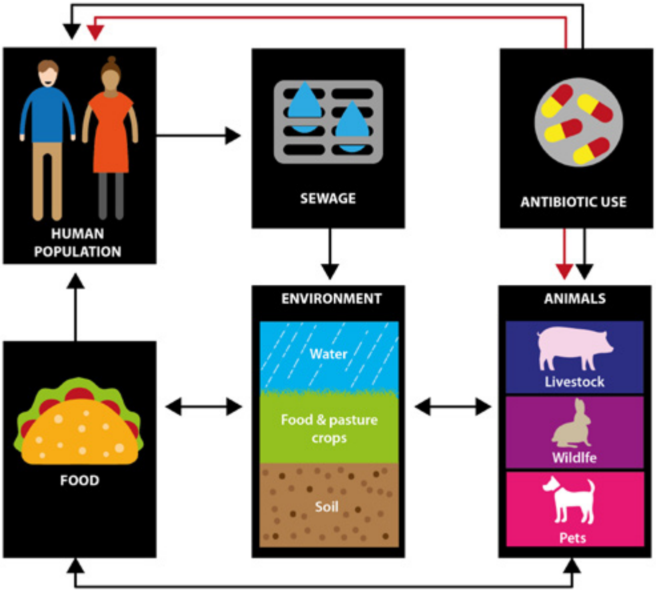

Figure outlining transmission pathways showing the potential flow of antimicrobial resistance. Through the food chain and via environmental sources (black arrows). Into the human population and animals (red arrows)

AMR is often only considered a problem associated with the overuse of antimicrobials in human medicine. However, AMR can also be generated in agriculture by the over-use of antimicrobials in veterinary medicine, resulting in the emergence of resistant microbes that can then be transferred to humans directly, via the food chain or via the environment.

Consequently, it is important to our future health to understand the occurrence of and selection for antimicrobial resistance in agriculture, and the transmission of resistant organisms to humans, which puts AMR firmly into the 'One Health' agenda. 'One Health' is a concept where multiple sectors work together to achieve better outcomes for animals, humans and the environment.

Across SEFARI, our work includes research on antimicrobial resistance within rural agricultural and environmental settings. We investigate a wide range of topics from antimicrobial usage to the surveillance of microbes and development of resistance and spans a range of agricultural environments. This enables us to better understand the sources where antimicrobial resistance is found and how it can be transferred between farmed animals, wildlife, soil, water and into our food chain.

Antimicrobial resistance (AMR) in the environment

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Antimicrobial resistance is naturally present in the environment, but additional resistant microbes can enter soils, water and plants via livestock faeces and human sewage. Furthermore, antimicrobial residue treatments can enter the environment, affecting the levels of AMR present. It is important we understand how AMR microbes move through the environment and where they can be found, as they can infect/re-infect livestock or be transferred to us via the food chain, water supplies or through direct contact with the environment.

SEFARI institutes have generated archives of microbial DNA from the environment which has been collected from all over Scotland. These resources have enabled detailed surveillance of more than 300 AMR genes in soils and waters, helping us to understand their national distribution.

In particular, we found:

- There is a high degree of antibiotic resistance in soil.
- There was a difference in the distribution; while some antibiotic resistance was rarely detected (e.g. carbapenems - used only in human medicine in the UK), other antibiotic resistance was more commonly detected (e.g. tetracyclines – most widely used in veterinary medicine).
- Resistance to the antibiotic vancomycin (a 'drug of last resort') was commonly found in soils.

Our research is seeking to provide evidence of the main predictors of AMR in soils, the probability of the transfer of AMR into water from soils, and hence guide policy on how we can reduce the risk of transferring resistance into the human population.

Tracking antimicrobial resistance (AMR) through the food chain

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SEFARI researchers are tracking the presence of AMR genes in the food chain. One of the priority public health pathogens in Scotland is *Campylobacter jejuni*, a bacterium which is most commonly associated with poultry such as chicken, which is the main cause of foodborne gastroenteritis. By improving our understanding of how AMR occurs in this pathogen, and whether resistant strains are different in food products, we are seeking to predict and improve public health.

Our research:

- Is undertaking the surveillance of AMR genes in meat and poultry products.
- Found two antibiotic resistance genes conferring tetracycline resistance were particularly prevalent in *Campylobacter* isolates from both animal and human sources.
- Showed that tetracycline resistance genes found in *Campylobacter* were identical to those present in some human gut bacteria.
- Identified that the type of resistance varied depending on the source of *Campylobacter*, which indicates different routes by which the resistance had been acquired.

The work raises important questions about how resistance occurs and why there are differences between human and animal samples. There may be different evolutionary pressures at work and our ongoing research aims to understand how resistance genes are transferred between individual bacteria. A better understanding will help to inform strategies to prevent the spread of AMR.

Detection of antimicrobial resistance (AMR) in wildlife

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Wildlife species can carry resistant bacteria as well as pathogens that cause foodborne disease. For example, seal pups that live in a Scottish estuary that is bordered by a city and towns, have been shown to carry the foodborne pathogen *Campylobacter jejuni,* and evidence suggests that the seals acquired the pathogen from sewage and wastewater contamination.

To investigate whether these seal populations also carry resistant bacteria we have:

- Developed methods to monitor microbial contamination of seal populations.
- Surveyed the presence of 80 AMR genes in seals.
- Specifically analysed AMR genes in *Campylobacter jejuni* isolated from seals.

Conventional scientific methods can take several days to correctly identify pathogens and any AMR, so SEFARI researchers are exploring new ways for rapid detection. Work has focused on the development of a surveillance tool by adapting existing methods that are currently used for the identification of pathogens in hospitals. It is hoped we can generate unique 'fingerprints' that are specific to different pathogens and will indicate their susceptibility to antibiotics. By shortening turnaround times by 2-3 days, this tool could also offer advantages in diagnostic laboratories.

Antibiotic use in livestock production

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AMR is commonly associated with livestock production as a result of antibiotic use to support animal health. However, and similar to human medicine, veterinary practice is seeking to reduce the unnecessary prescribing of antibiotics with the overall aim of reducing the selection for and evolution of AMR.

We need to measure AMR in livestock to better understand where the greatest risks of possible transfer to humans could occur and measure antibiotic use on farms to help guide strategies, set targets and assess their impact. SEFARI scientists are working to help understand how AMR and antibiotic usage can be best measured by using mathematical modelling approaches.

Robust statistical analysis of pharmaceutical sales data from beef and dairy farms shows that usage is already below the current target defined to reduce antibiotic applications. However, comparison of surveillance approaches with large-scale collections of bacteria from farmed animal sources has shown that the definition of antibiotic resistance is complex, and it is important to take into account several variables:

- The sample that was first taken.
- How representative any bacteria obtained are in the samples.
- Whether or not detection of a resistance gene translates into resistance to that antibiotic.
- How the level of resistance relates to the amount of antibiotic that is supplied in veterinary practice.

Therefore, any approach to reduce AMR needs to be appropriately defined, measured and considered.

Transfer of antimicrobial resistance (AMR) into livestock

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AMR can be transferred to farmed animals from sources, such as bulky fertilisers termed sludge pellets - these are applied as dried pellets spread onto the grass. This type of research is important because the use of sludge pellets in such as manner contributes towards the circular economy, making use of sewage waste. However, there is a potential risk of transferring AMR to the animals from the pellets.

Obtaining evidence of whether AMR transmission can occur via this route is inherently challenging because of the background level of AMR that exists naturally in soils and in farmed animals. SEFARI scientists have carried out surveillance on a sheep farm that has used sludge pellets as a form of pasture fertiliser. We looked for the presence of a wide range of AMR genes in soil and sheep faecal samples and found:

- There was a degree of naturally occurring AMR evident in the sheep and in the soil samples, which supports findings from the national soil survey.
- Both sludge pellets and sheep faeces contained a relatively high number of AMR genes, but the types of resistance were different between the groups. The lowest levels were detected in the soil.
- There was no evidence for the direct transfer of AMR from sludge pellet applications to soil samples in the pasturelands.

One of the main findings from this pilot study was the difference in AMR between sludge pellets, soil and sheep, indicating that AMR genes could be transferred via fundamentally different biological mechanisms. In addition, so far no significant difference between sludge pellet treated pasture and non-treated pasture samples was observed. However, the study of multiple sludge pellets applications is still needed to analyse the long-term risk.