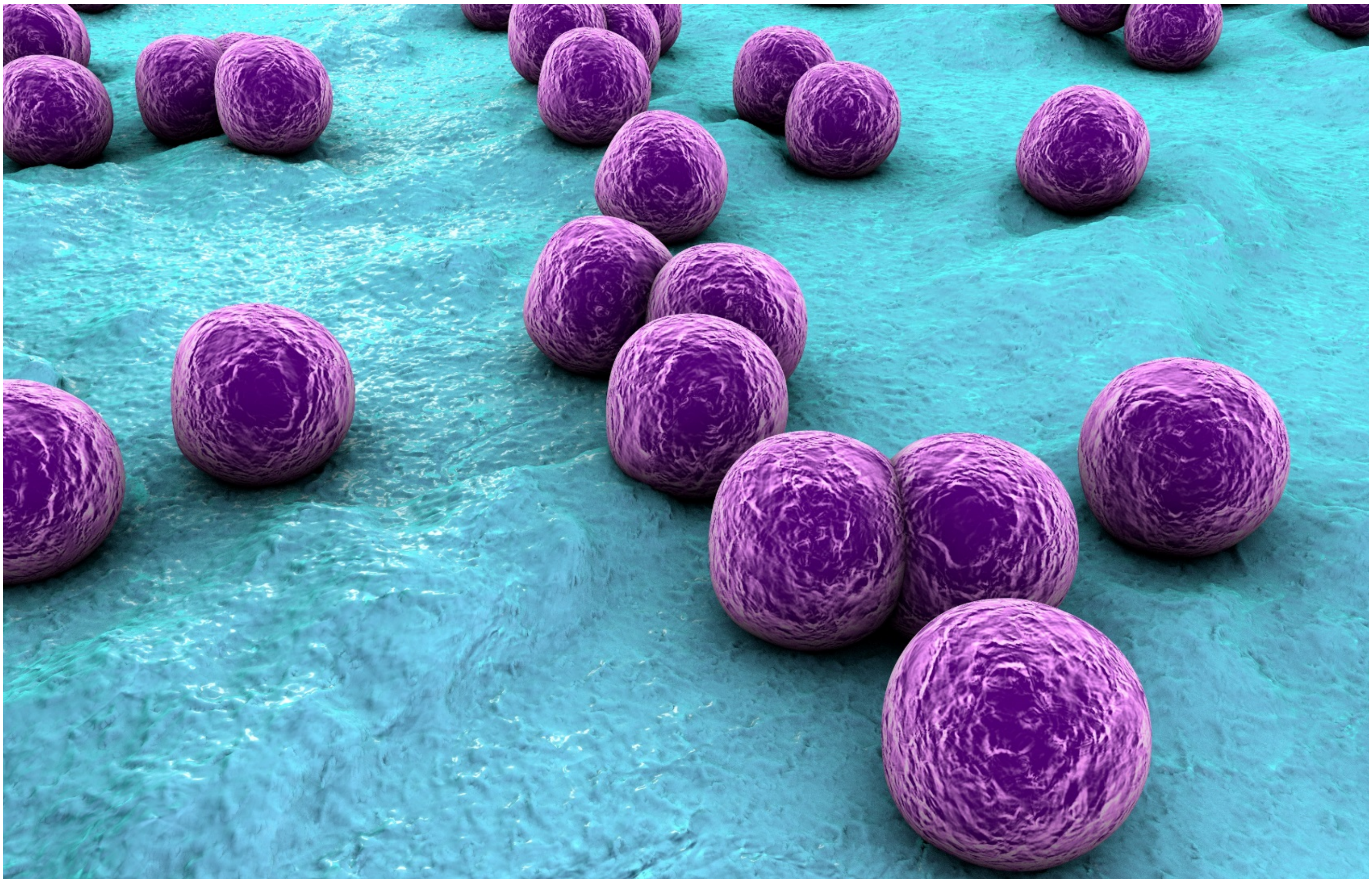

Antimicrobial resistance

Impact on the food industry

Dr Peter Wareing

A Leatherhead Food Research white paper

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Antimicrobial resistance

In this white paper, Dr Peter Wareing discusses antimicrobial resistance, why we should pay attention to this serious issue and how the food industry can help to reduce its impact.

What is antimicrobial resistance?

There are many definitions of antimicrobial resistance (AMR); one of the simplest is by the Chief Scientific Advisor of the Food Standards Agency (FSA) who said AMR was:

"the ability of a microbe to withstand the effects of antimicrobials to which it would normally be susceptible."

What are antimicrobials?

Antimicrobials are substances that stop the growth of, or kill, microbes. These include:

- Antibiotics
- Antifungals
- Antivirals
- Antiparasitics
- Antiseptics
- Disinfectants
- Sterilants
- Preservatives
- Heat, pH, and reduced water activity could also be considered as antimicrobials

Although antibiotics are the antimicrobials that first come to mind when AMR is discussed, resistance to all of the above-mentioned antimicrobial treatments has also been reported; this will be discussed in more detail later in this paper.

Why is it a problem for the food industry?

The European Food Safety Authority (EFSA) considers AMR to be "a growing threat that is responsible for 25,000 deaths in the EU every year".

The global impact of AMR is predicted to cost US $100 trillion by 2050[1], with a projected global mortality rate of 10 million. This will be higher than deaths caused by diarrhoeal disease, cancer and diabetes.

AMR bacteria have been found in the food chain since 2000, and ever increasing numbers of bacteria are becoming resistant to antimicrobials, in particular antibiotics. This has led to a growing number of reports of patients dying from hospital-acquired infections, where the bacterial pathogen is resistant to one or more antibiotics (multi-drug resistance), for example, Methicillin-resistant *Staphylococcus aureus* (MRSA).

How does it occur?

Several causative factors have been suggested:

[1] Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations (2014) Review on Antimicrobial Resistance: Tackling drug-resistant infections globally.

- Over or incorrect use of antimicrobials, both in human treatment and also in farm animals
- Random mutation
- Release of antimicrobials into the environment
- Other selection pressures (heat, low pH/acid, low water activity)

It is worth bearing in mind that AMR is a recent manifestation of the age-old ability of bacteria to respond to environmental pressures or changes. Bacteria adapt to their environment – and always have – in order to survive. Antibiotics can be viewed merely as the latest selection pressure to which bacteria have been subjected.

The mechanisms of resistance are broadly the same for any environmental pressure, of which antimicrobials are an example.

Where does it occur?

AMR microorganisms have been found in the environment (soil and water), agricultural commodities (for example, livestock, poultry, fish, shellfish, cereals, fruit and vegetables) and also in food manufacturing, food service, the home and in hospitals.

Ultimately, scientists are most worried about its occurrence in the healthcare environment and in people who are unwell but being cared for at home, because of its potential for life-threatening illness.

How does AMR enter the food chain?

AMR organisms can be spread by the usual contamination routes, such as:

- Contamination of meat at slaughter by faecal material
- Contamination of water used for growing plants, fish and shellfish with human or animal faeces
- Environmental contamination of food
- Cross-contamination of food by food handlers or contaminated equipment

These routes can continue to humans via poor hygiene or the ingestion of contaminated food.

What's the extent of AMR?

AMR is reported more often from animals or meat products than from plants, and multi-resistant strains are becoming increasingly important.

For example, FSA surveys between 2014-2015[2] for *Campylobacter* isolated from chickens have shown that 70.7% are resistant to one or more of the antimicrobials tested, a quarter (24.7%) are sensitive to all antimicrobials tested, and 4.6% are resistant to three or more – see Figure 1.

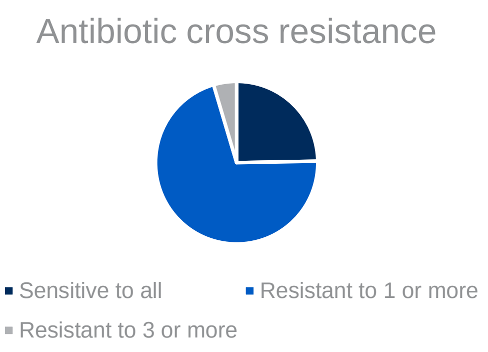

Figure 1

To combat this, the British Poultry Council (BPC) introduced the Antibiotic Stewardship

[2] Food Standards Agency (2016) Chief Scientific Advisor's Science Report. Issue 4: Antimicrobial resistance in the food supply chain.

Scheme, and the poultry industry has committed to reducing antibiotic use. Consequently there has been a 44% decrease in use between 2012 and 2015. In conjunction with this, improvements in hygiene have led to a downward trend in contamination[1] – see Figure 2.

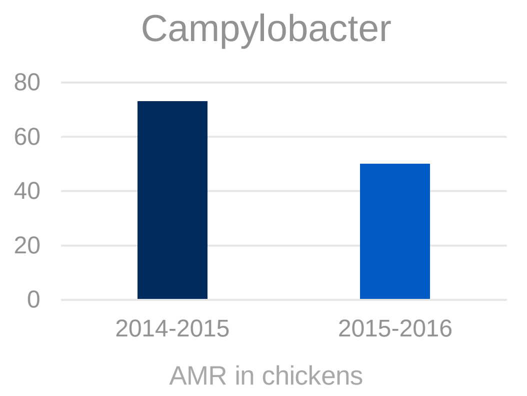

Figure 2

Globally, the World Health Organisation (WHO) has reviewed the incidence of AMR and produced a list of 'at risk' microorganisms. In this context, 'critical' bacteria are multi-drug resistant, posing a significant threat in hospitals, nursing homes and patients requiring higher levels of care. The infections they cause are often fatal. Bacteria in the 'high' and 'medium' lists in Table 1 have become increasingly resistant to key

Critical	High	Medium
Pseudomonas aeruginosa	*Enterococcus faecium*	*Shigella*
Enterobacteriaceae	*Staphylococcus aureus*	
	Campylobacter	
	Salmonella	

Table 1

antibiotics, and cause more common diseases, for example, *Salmonella* food poisoning.

It is important to determine the relationship between the level of AMR in the hospital environment, versus the level in the environment, or in foodborne disease cases and that found within the home, to understand the extent of its spread.

Resistance and cross-resistance

Research on Shiga-Toxin (STEC) *Escherichia coli* has examined the effects of other antimicrobial interventions (apart from antibiotics) on the development of cross-resistance, for example: oxidative, osmotic and acidic stresses, and also cross resistance between biocides and antibiotics.

In addition, small adaptive heat treatments can induce an increased heat resistance in *E. coli* and other bacteria, so that it is more tolerant than expected. This means heat treatments are less effective at killing these organisms.

It is important to note, however, the extent of resistance to some of these factors is limited. If a high enough temperature is used, then bacteria will still be killed, due to the effects of heat on cellular components

These small increases in tolerance of bacteria to, for example, heat or pH are more relevant if a food product is controlled with a series of small, sub-lethal hurdles, rather than single factors, which are applied more aggressively to control bacterial growth or survival.

When bacteria adhere to a surface, for example utensils, equipment, walls and floors, they can produce a biofilm. When bacteria are enclosed in a biofilm, they can be many times more resistant to antimicrobial treatments than when they are in their free-floating form.

Implications for industry

For the meat industry, where AMR is having the greatest effect, governments may have to restrict the use of certain antibiotics in farming, particularly if they are associated with AMR in humans.

For example, the US has now banned the use of antibiotics as growth promoters, a practice which formerly led to their widespread use in agriculture.

In addition to the BPC initiative noted above, other agricultural groups are driving the movement towards a reduction in use, e.g. The Red Tractor Scheme, and Responsible Use of Medicines in Agriculture (RUMA).

At the processor level, it is ever more important to ensure that basic hygiene measures are in place, for example Good Hygienic Practices (GHP), in order to minimise the likelihood of cross-contamination. The FSA's 'Four C's', (cooking, chilling, cleaning and cross-contamination) although intended for small-scale caterers, are equally applicable to food processors.

As noted above, cross-resistance between different types of antimicrobials can occur. Many bacteria have genes that cause a wide-ranging response when presented with an environmental challenge. For example, incorrect use of some cleaning chemicals has led to antibiotic resistance in some pathogenic bacteria, as well as resistance to the biocide. Switching between different types of biocides can help to reduce this risk.

It is important to examine the applicability of other, non-chemical treatments, and accurate and effective use of heating cycles to ensure that bacteria do not survive any processes.

All suppliers should be approved, and preferably subject to supply chain audits before approval. As part of the approval process, their antimicrobial governance policies should be reviewed.

Knowledge gaps

At a recent FSA AMR review meeting, it was acknowledged that data on AMR microorganisms in or on crops was relatively unknown. In addition, the contribution of food to AMR is also largely unquantified, as were the effects of food handlers, both within processing and catering environments.

Other factors which require quantification are the extent of AMR in imported foods vs UK foods, and the movement of resistant microbes and genes throughout the supply chain.

Instances of AMR genes transferring from non-pathogens to pathogens have occurred. However this has not yet been properly quantified, neither have the non-pathogens that are of most concern been appropriately identified.

Analysis of regional hotspots is required, to understand areas where a more precautionary approach to supply should be taken, and to understand the reasons for these hotspots.

Controlling its spread

Controlling the spread of AMR can be achieved by collecting data on its extent, both in the UK and globally, as well as reducing the use of treatments to reduce selection pressure. For example, DEFRA has been working to reduce the use of antibiotics in livestock and fish to a mean of 50 mg/kg by 2018 compared with 2014. Additional measures include: training to ensure the responsible use of treatments; the introduction of certification schemes; improvements to sanitary conditions in food preparation; and possibly introducing vaccinations.

The European Food Safety Authority (EFSA) has launched an action plan to tackle antimicrobial resistance. The plan is built around three pillars:

- Make Europe a best practice region
- Boost research, development and innovation
- Shape the global agenda

EFSA notes that it has contributed to making Europe a best practice region by:

- Reviewing measures in the EU to reduce or replace the use of antimicrobials in animals
- Assessing the association between antimicrobial use and development of resistance
- Providing a snapshot of resistance levels in bacteria found in animals, food and humans for each country

Following a request from the European Commission, the European Food Safety Authority (EFSA) has also published a scientific opinion on how to assess progress on the reduction of antimicrobial resistance and antimicrobial consumption using a set of indicators established by EFSA, the European Medicines Agency and the European Centre for Disease Prevention and Control.

Novel antimicrobial treatments

Any novel treatments must be food-safe and have no deleterious side effects for humans or animals.

Bacteriophages are viruses that are programmed to attack bacteria, and are usually very specific to particular species. These could be used as pre-treatments to reduce the pathogen loading on livestock, for example, or even used in processing plants to reduce the background contamination levels.

Essential oils, for example rosemary, oregano, and basil, are noted to have antimicrobial properties; rosemary extracts have been used as antimicrobial treatments in the food industry, on finished products.

Certain ingredients are known to have antimicrobial properties. Chitosan is produced by chemically modifying chitin, which is a polysaccharide derived from glucose. Chitin is a primary component of cell walls in crustaceans, including shellfish. It has antimicrobial properties against some pathogenic Gram-negative bacteria, for example, *E. coli*, *Vibrio cholera* and *Shigella dysenteriae*.

Antimicrobial peptides are usually produced by one microbial species against another species, and again, can be target-specific. Isolation and use of these as AMR treatments could prove effective.

Outlook

AMR is not just about resistance to antibiotics, though this remains a key concern. It has wider implications than just affecting the healthcare industry, with animal health concerns also an issue. The immediate food safety risk low, but there is a risk to the sustainability of food systems in the long term.

The outlook for the future is therefore very serious. Hygienic practices are essential, but they must be properly applied to be effective, and not contribute to the problem. Bacteria are naturally programmed to resist change, in order to be able to survive adverse events. If antimicrobial use is limited, the selection pressure on bacteria is reduced and this should result in the frequency and extent of AMR declining. In the short to medium term, alternative therapies must be developed, so that they can start to have an effect.

How Leatherhead can help

At Leatherhead Food Research, we have accredited microbiology and food safety labs and personnel that can undertake studies on microbiological contamination and growth in products. We are also able to undertake challenge tests to determine the potential microbial risk within a product and conduct risk assessments on your supply chains and processes in order to highlight the potential places and processes where contamination and growth could occur, whilst offering solutions. We can also undertake HACCP and other reviews, as part of a consultative approach that can help optimise processes. Our regulatory team has expertise in food safety legislation in the UK, EU and rest of the world.

About the author

Peter obtained his BSc in Agricultural Science from the University of Leeds and a PhD in Plant Pathology from the University of Hull. Before joining Leatherhead in 2001, he worked for the Natural Resources Institute undertaking development work on food processing and food security projects in Central & South America, Africa and South East Asia. Peter has many years' experience working in microbiological research, development and training. His specialist areas are food safety systems including HACCP, microbiology and mycology. He is particularly interested in confectionery and snack foods, sauces and dressings, hot and cold beverages and dried foods. At Leatherhead, Peter undertakes troubleshooting audits and investigations for clients, is an expert witness and delivers food safety-related sessions on training courses.

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Leatherhead Food Research provides expertise and support to the global food and drink sector with practical solutions that cover all stages of a product's life cycle from consumer insight, ingredient innovation and sensory testing to food safety consultancy and global regulatory advice. Leatherhead operates a membership programme which represents a who's who of the global food and drinks industry. Supporting all members and clients, large or small, Leatherhead provides consultancy and advice, as well as training, market news, published reports and bespoke projects. Alongside the Member support and project work, our world-renowned experts deliver cutting-edge research in areas that drive long term commercial benefit for the food and drink industry. Leatherhead Food Research is a trading name of Leatherhead Research Ltd, a Science Group Company.

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