Antimicrobial Resistance: New Issues (inspired by an article in the Biomedical Scientist September 2021 on AMR)

What is Antimicrobial Resistance? Antimicrobial Resistance, or AMR, describes when microbes, such as bacteria, viruses, fungi, and parasites, develop mechanisms to protect them from antimicrobials, allowing them to resist their actions. Antibiotic resistance, a subset of AMR describing when bacteria evolve to resist antibiotics (thus making the infections caused by them more difficult to treat – these bacteria are known as 'superbugs'), is a growing concern, partly due to antibiotic misuse and overuse. Other drivers of AMR recognized by WHO include lack of access to clean water, sanitation and hygiene (WASH) for both humans and animals; poor infection and disease prevention and control in health-care facilities and farms; poor access to quality, affordable medicines, vaccines and diagnostics; lack of awareness and knowledge; and lack of enforcement of legislation. WHO also classify AMR as one of the greatest public health threats.

Emerging Issues, Developments and Research (2021):

- Feeding dogs raw food. Researchers at the University of Porto (Portugal) have found the bacteria enterococci in raw dog food (they sampled 55 varieties of dog food from supermarkets and pets hops and found 54% contained the bacteria). Some of the bacteria were genetically identical to bacteria isolated from hospital patients in the UK. Moreover, greater than 40% of the bacterial samples were resistant to a range of antibiotics, include ampicillin ciprofloxacin, and 23% were also resistant to the 'last resort' antibiotic linezolid. The close contact of humans with dogs therefore poses major health risks. Also, notably, the majority of the bacteria were found in raw dog food samples, and so researchers are proposing that authorities raise more awareness of the risks of feeding raw diets to pets, as well as to manufacturers of dog food. Feeding raw meat to puppies was found by researchers at the University of Bristol to be a factor in puppies carrying antibiotic resistant bacteria – and, in a further study of the transmission of antibiotic resistant bacteria between animals and humans, it was found that the resistant organisms within the dog food actually remain and are excreted in their feces.
- Rapid antimicrobial susceptibility testing. The University of Bristol have been working with the company Vitamica to develop diagnostic technology that can show whether or not an antibiotic is suitable against a particular bacteria. Rapid AST can inform doctors which antibiotics will be effective for an individual's specific infection within one hour, in contrast to the usual 48 hours required when growing bacteria. The technology uses lasers to detect tiny fluctuations within individual bacteria, indicating whether or not the cells are alive (which would indicate the antibiotic has not successfully been able to kill the bacteria). Other European companies have also developed their own rapid AST

mechanisms, for example bioMerieux and Specific Diagnostics, who have developed a patented Rapid AST system called REVEAL, which provides information for bloodstream infections within five hours.

- Subscription style payment models. The NHS has developed a subscription style payment model for antibiotics, which is providing more incentivization for pharmaceutical companies to develop new drugs. This was launched in July 2019. Following a rigorous process with expert clinical input, two treatments, Cefiderocol (Fetcroja) manufactured by Shionogi, and ceftazidime with avibactam (Zavicefta) manufactured by Pfizer, were selected as the first drugs to be made available to patients for a subscription based model and will be undergoing an evaluation process in order to be ready for early 2022. The idea of the payment approach is to move away from paying for individual packs of antimicrobials and, instead, make an annual payment based on the health benefits to patients and the value to the NHS. This model is thought to benefit both health systems and industry - NHS patients will be able to benefit from a secure supply of new antimicrobial drugs, while pharmaceutical companies will be able to reliably forecast their return on investment, and are motivated to invest in research in antimicrobials.
- Inhibitors as a way of tackling AMR. At the University of Bristol, researchers are investigating new approaches to fight antibiotic resistance, including the development of inhibitors to be co-administered with antibiotics, in order to restore their effectiveness against resistant strains. This is achieved by developing synthetic chemicals designed to get into the bacteria and block resistance enzymes – however, suitable inhibitors are only available for a small number of resistance enzymes, and therefore there are few infections they can be used to target.
- Climate change and AMR. Antibiotics are produced by bacteria and fungi in the environment, and so climate change actually enables AMR and the spread of infectious diseases. Many researchers are advocated for change at a policy level, emphasizing the need for more understanding of the links between climate change and AMR, and curriculum changes for medicine allowing for more knowledge of AMR for future doctors. Dr Tina Joshi is a lecturer at Plymouth University and has examined the interaction between climate change and AMR in great detail. In her lectures on the subject, she focuses on recent studies suggesting links between increasing temperatures and the spread of AMR, as well as factors like poverty and the stifled economic growth due to climate change. Sanitation and health has already been proven to be a bigger factor in AMR than the use of antibiotics (which is more of an issue in developing countries) – lack of effective sanitation offers a breeding ground for drug resistant microbes to spread. Joshi also calls for improved sanitation within hospitals, in both more and less developed countries.
- A connection between AMR and arthropods. Oxford researchers have found evidence of connections between AMR bacteria and these creatures, and have published their findings in an article in Nature Microbiology. Some of their key findings include

approximately 20% of the files, cockroaches, spiders, moths and ants tested were found to be carrying resistance to the 'last resort' drug carbapenem, and another 70-80% were carrying extended spectrum cephalosporin resistance. They believe that by 2080, there could be approx. 50,000 trillion flies carrying carbapenem resistance and spreading AMR across the planet.

What Is The UK's Action Plan for AMR? The UK published a 20 year vision for antimicrobial resistance, entitled 'Contained and controlled', in 2019. The vision was for a world in which antimicrobial resistance is 'effectively contained, controlled and mitigated' by 2040, and the publication suggests the UK will contribute to the global effort for containing and controlling resistance through new diagnostics, therapies, vaccines and interventions, better use of antimicrobials in all sectors, and a lower burden of infection, minimized transmission, and better treatment of resistant infections. While the UK has been advocating for AMR to be addressed or years, the previous 2013-2018 strategy has not prevented the increase of drug resistant infections. However, the strategy did help reduce antibiotic use in humans and food producing animals (for example, there was a 40% decrease in sales of veterinary antibiotics from 2012 to 2017, and a 7.3% decrease in human antibiotic use from 2014 to 2017), and achieved improved, coordinated research, greater awareness, and helped to secure global commitments to address resistance(such as the UN General Assembly and UN Environment Program resolutions, and G7 and G20 declarations). Some of the key points in the 2019-2024 UK action plan against AMR are to reduce human infection, help increase access to clean water and sanitation, reduce animal infections, minimize the spread of AMR in the environment, and increase food safety. There is also a focus on optimizing the use of antimicrobials across all sectors, greater surveillance of AMR, and more investment in research of new therapies, diagnostics, and vaccines. Some specific points within these areas include improving training of health and social care workers in hand hygiene in order to improve infection prevention, developing a single UK portal as a source of data and information on AMR for greater research and overall surveillance, promoting the TARGET toolkit to support antimicrobial stewardship, to help ensure appropriate prescription of antibiotics, and ensuring all NHS hospitals have electronic prescribing systems within the electronic health record by 2025 (and that these systems support and drive good antimicrobial stewardship by coding, auditing and providing feedback for surveillance) – among many other initiatives.