

# Congress Review

## Review of the 31<sup>st</sup> European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) 2021


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**T**HIS YEAR, the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) adapted to the unprecedented challenges of COVID-19 by hosting their first online event. As a consequence, participants at the 31<sup>st</sup> iteration of this world-leading congress on infection were unable to visit Vienna, Austria, which was set to house ECCMID 2021. Rather than viewing the digital congress as an obligation, born of necessity during the pandemic, the ESCMID Committee instead transformed it into an opportunity. The virtual meeting meant that geography was not a barrier to attendance; at a time when open sharing of scientific information from across the world is more important than ever, the increased inclusivity, diversity, and accessibility at ECCMID 2021 was crucial.

Over the course of 4 days, ECCMID broadcast educational workshops, meet-the-expert sessions, symposia, open forums, pipeline

corners, and much more. Presentations spanned across the discipline and included challenges of treating bacterial infections in elderly patients, novel interventions to reduce healthcare-associated infections, innovations in COVID-19 surveillance, the present and future state of influenza and severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) vaccination, biomarkers and predictors for COVID-19 outcome, and the potential of metagenomic sequencing as a first-line diagnostic tool.

ECCMID 2021 incorporated new and innovative ‘fireplace discussions’ with keynote speakers. These sessions provided an opportunity for leading experts in the field of clinical microbiology and infectious diseases to engage with early-career researchers and academics. For example, Michael Houghton, Li Ka Shing Professor of Virology and Director of the Li Ka Shing Applied Virology Institute, University of Alberta, Edmonton, Canada, spoke about the development of a vaccine against the hepatitis C virus. Herman Goossens,



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Professor of Microbiology and Director of the Department of Clinical Pathology at the University Hospital, University of Antwerp, Belgium, gave a talk entitled 'Transcending European Clinical Research in Infectious Diseases Through Collaboration to Break Down Traditional Silos.' These lectures were imperative in promoting the development and exchange of knowledge that is essential for the entire global population.

The 2021 programme was also notable for featuring 5 days of pre-ECCMID content, which covered subjects such as antimicrobial resistance, COVID-19, diagnostic developments, and vaccines. Overall, this supplemented the usual congress with up to 50 additional sessions.

Although there could be no on-site Trainee Association of ESCMID (TAE) Day at this year's annual meeting, ECCMID successfully organised two separate online TAE sessions. The first of these focused on recent publications by ESCMID Young Scientist Members and the TAE Outstanding Awards. The second session allowed young scientists to consult with experienced moderators, in a round-table setting, about future career paths.

Several major awards were presented as part of ECCMID 2021. The ESCMID Young Investigator Awards for Research in Clinical Microbiology and Infectious Diseases were presented to Jason Trubiano, Department of Medicine (Austin Health), University of Melbourne, Australia, and Marit van Gils, Department of Medical Microbiology, Academic Medical Center, University of Amsterdam, the Netherlands. Trubiano and van Gils gave presentations entitled 'The Emerging Role of Antibiotic Allergy Programs in Antimicrobial Stewardship' and

'Lessons Learned from Antibodies Against SARS-CoV-2,' respectively. Furthermore, this year's recipient of the International Sepsis Forum (ISF) ESCMID Sepsis Award was Isis Ricaño Ponce, Radboud University Medical Center, Nijmegen, the Netherlands, who is part of a team integrating -omics technologies (e.g., proteomics, transcriptomics, and metabolomics) with clinical data in order to identify the molecular basis for sepsis heterogeneity. It is hoped that this will facilitate the diagnosis of sepsis and ultimately lead to faster treatment and improved patient outcomes.

The authors of several standout ePosters submitted to ECCMID 2021 have provided summaries of their research, which are shared in this issue of *EMJ Microbiology and Infectious Diseases*. These include a single-centre retrospective study on the impact of reducing the duration of surgical prophylaxis in cardiovascular surgery, evaluation of vaccination effectiveness against SARS-CoV-2 in healthcare professionals, and *Aspergillus* sensitisation in people with severe asthma. Our independent congress review also contains an overview of groundbreaking news stories such as the discovery of antibiotic-resistant bacteria in dog food across Europe, the use of aspirin to reduce the risk of cardiovascular events in individuals with pneumonia, and the increased prevalence of HIV among elderly populations.

Read on for our key scientific insights from ECCMID 2021. We look forward to being part of the international microbiology and infectious diseases community again, hopefully in-person, at next year's congress in Lisbon, Portugal. ■

ECCMID 2021 REVIEWED →

# Antibiotic Resistance Could Be Caused by Commonly Prescribed Classes of Drugs

**P**ROTON pump inhibitors,  $\beta$ -blockers, and antimetabolites, commonly prescribed classes of drugs, could cause antibiotic resistance, especially in the *Enterobacteriaceae* family, despite the fact that they are not antibiotics. A new observational study presented on 10<sup>th</sup> July at ECCMID 2021 stated these antibiotic-resistant bacterial infections could cause extended hospital stays and lead to risk of increased mortality rates.

Bacterial antibiotic resistance is often associated with over-prescription and regular exposure to antibiotics. However, it has been noted that patients diagnosed, and admitted to the hospital, with drug-resistant bacteria show no common recognisable risk factors. Previous studies have identified that commonly used non-antimicrobial drugs (NAMD) play a significant role in antibiotic resistance because of the consequential effect on gut microbiome bacterial composition. The aim of this research was to address the role of NAMD use as a risk factor for infection with antibiotic-resistant bacteria.

The researchers from Tel Aviv Medical Center hospital, Israel, examined data from 1,807 patients diagnosed with upper urinary tract infection, and a positive urine or blood culture of *Enterobacteriaceae*, who were admitted in the hospital over a period of >2 years (from 1<sup>st</sup>

January 2017 to 18<sup>th</sup> April 2019). The researchers then acquired the electronic medical records regarding the previous and current use of 19 NAMDs. The results showed that antimicrobial drug-resistant organisms were found in over half of the collected patient samples (n=944/1,807). Furthermore, approximately one-quarter of samples (n=431/1,807) revealed multi-drug-resistant organisms that were resistant to three or more antibiotic classes.

Interestingly, NAMDs such as selective serotonin reuptake inhibitors for depression symptoms, antipsychotics drugs for mental health, proton pump inhibitors for the reduction of stomach acid,  $\beta$ -blockers for conditions associated with heart problems, and antimetabolites for the treatment of cancer and other inflammatory diseases were all linked to increased antibiotic resistance. Additionally, antimetabolites emerged as the group of drugs with the highest influence on antibiotic resistance.

"Our findings highlight the importance of non-antimicrobial drug exposure as a risk factor for antibiotic resistance," stated lead author Meital Elbaz, Tel Aviv Medical Center. "We urgently need larger studies with more drug classes to confirm the discovery and to clarify the biological link between common prescription drugs and antibiotic resistance." ■



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# Reduction in Antibiotic Outpatient Prescriptions Has Been Noted Across the USA

RESEARCH carried out across more than 1,200 clinics in the USA revealed that the prescribing trends for antibiotics has reduced by 4% per year. The study was presented on 10<sup>th</sup> July 2021 at ECCMID 2021. There are >2.8 million antibiotic-resistant infections occurring every year in the USA, leading to up to 35,000 deaths and 20 billion USD in healthcare costs per year.


Over 9 million veterans receive outpatient care via the Veterans Affairs (VA) facilities, which covers >1,200 outpatient clinics. According to the researchers, this declining trend of antibiotic prescriptions is due to the antibiotic stewardship programmes executed by the Veterans Health Administration (VHA) health system, which began in 2014. According to the World Health Organization (WHO), infections such as pneumonia, tuberculosis, sepsis, gonorrhoea, and food-borne diseases have become difficult to treat as antibiotics become less effective. Shockingly, 266 million courses of antibiotics are prescribed to outpatients in the USA. In 2011, the VHA initiated a National Antimicrobial Stewardship Task Force (ASTF) to help control execution of antibiotic stewardship programmes in the VA and by 2014, the VHA demanded that all of the associated hospitals establish antibiotic stewardship programmes.

To verify the prescribing trend, the researchers of this study examined the data from VA pharmacies

by reviewing the patterns in dispensed antibiotic prescriptions in VA outpatient clinics from 2011 to 2018. Furthermore, they calculated the number of days of therapy (DOT) per 100 outpatient visits for all antibiotics annually and, specifically, the five commonly used antibiotics: doxycycline, azithromycin, amoxicillin/clavulanate, ciprofloxacin, and sulfamethoxazole/trimethoprim.

The results showed that over the period of 8 years, the overall antibiotic prescriptions dispensed declined by an average of 3.9% per year, from 39.6 DOT per 100 visits in 2011 compared with 29.4 DOT per 100 visits in 2018. Additionally, the use of sulfamethoxazole/trimethoprim, commonly used for urinary tract infections, decreased significantly by 7% per year. However, outpatient prescriptions for doxycycline, azithromycin, and amoxicillin/clavulanate between 2011 and 2018 remained the same.

“Use of these three commonly prescribed antibiotics remains high and may be an appropriate target for antibiotic stewardship programmes in the VA to further reduce inappropriate outpatient prescribing,” commented Haley Appaneal, Providence Veterans Affairs Medical Center, Providence, Rhode Island, USA. “It might also help combat resistance if national guidelines took stewardship principles into account when making disease-specific recommendations for antibiotic use.” ■



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## Newly Diagnosed HIV Shows Presence of Risk in Elderly

**P**REVALENCE of HIV in elderly populations is on the rise; approximately 50% of Americans diagnosed with HIV in 2018 were  $\geq 50$  years old. Despite increased awareness, new treatments, and early testing, this life-threatening epidemic still claims millions of lives each year. A common misconception is that older people are not at risk of HIV, which is untrue. Garcia Carcus, from the Central University Hospital of Asturias, Oviedo, Spain, shared the results of a case study in an 83-year-old male with newly diagnosed HIV and explained how “we must debunk beliefs among healthcare professionals that older adults are not sexually active or use drugs” and can also contract this deadly disease.

Carcus examined the medical history of this elderly patient at ECCMID 2021, 9<sup>th</sup>–12<sup>th</sup> July 2021. The patient had a history of heart problems and procedures, including an aortic valve replacement in 2013. He was admitted to a hospital in Spain in July 2019 for a month-long fever and weight loss. Blood tests showed that the patient had low iron, low levels of white blood cells, and impaired kidney function. Moreover, the blood cultures were negative for life-threatening blood infections.

Although the blood tests did not expose any worrying conditions, the imaging of the heart told a different story, showing that the valve replacement was not working and revealing a thickening of small veins characteristic of endocarditis. The doctors prescribed the patient an 8-week course of antibiotics; however, when returning home, the patient's fever continued to worsen.

Finally, the patient's condition required urgent medical attention and he was rushed to the emergency department. The medical staff tested the 83-year-old male for HIV amongst other sexually transmitted infections and the results were positive. He had a very high HIV viral load (180,564 copies/mL) and a CD4 count of 182, indicative of AIDS. This patient is one of the oldest to be newly diagnosed with HIV; luckily,

with antiretroviral treatment, his HIV viral load has decreased, and he recently celebrated his 85<sup>th</sup> birthday.

Interestingly, the doctors believed he contracted the virus at around 70 years old; however, he denied having relations with anyone other than his wife. It is unclear when or how he got HIV, but importantly, as Carcus concluded: “This case serves as a reminder that the elderly are not immune to HIV infection.” Overall, this case report highlights the importance of educating older patients about the risk of unprotected sex and the importance of testing all age groups, including octogenarians. ■





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## Disappearance of Flu and Respiratory Syncytial Virus During COVID-19

COVID-19 rapidly spread from Wuhan, China, to the rest of the world, in the space of a few months. This infectious disease is responsible for millions of deaths around the globe and has led to lasting symptoms in some patients, such as difficulty breathing and the permanent loss of smell. COVID-19 has taken over the headlines in the past year but that is not all this disease has taken over.

A recent study presented at ECCMID 2021, 9<sup>th</sup>–12<sup>th</sup> July 2021, which took samples from Detroit Medical Center and Children's Hospital of Michigan, Detroit, Michigan, USA, aimed to unravel the impact of COVID-19 on the incidence of flu. Siri Sarvepalli, Wayne State University School of Medicine, Detroit, Michigan, and collaborators conducted PCR tests using samples from nasopharyngeal swabs to test for various infections, including severe acute respiratory syndrome coronavirus-2 and the respiratory syncytial virus (RSV). Additionally, swabs were taken from the throat to test for Group A Streptococcus, which frequently occurs after viral respiratory tract infections. The researchers drew comparisons between PCR test results for various infections between September 2019 to February 2020 and September 2020 to February 2021.

The findings showed a significant difference between the 2019–2020 season and the 2020–2021 season in the percentage of influenza and RSV infections in adults and children. In adults, the incidence of influenza A and influenza B were 11.5% and 13.1%, respectively, in 2019–2020. This was strikingly reduced to 0.0% in the later season. The same dramatic absence could be seen in RSV as incidence fell from 9.0% to 0.0%. This stark difference was mirrored in children: 20.2% to 0.0% incidence in influenza B. Interestingly, the prevalence of other respiratory viruses, such as human metapneumovirus, had also decreased. These interesting results were apparent across 42 medical centres in the USA, further confirming the reliability of the data.

The reason for the striking absence of the flu could be due to increased handwashing, social distance measures, and mask-wearing that has occurred during the pandemic. These simple yet effective techniques could be keeping other respiratory viruses at bay. Further to this, as seen in the swine flu pandemic, COVID-19 could be interfering with the ability of other viruses to infect individuals via viral interference. The paper concludes that flu cases are likely to rise again once the pandemic is over, but continuing handwashing and other measures might keep the number permanently low in the future. ■



# Aspirin Shown Effective at Reducing Risk of Cardiovascular Events in Patients with Pneumonia



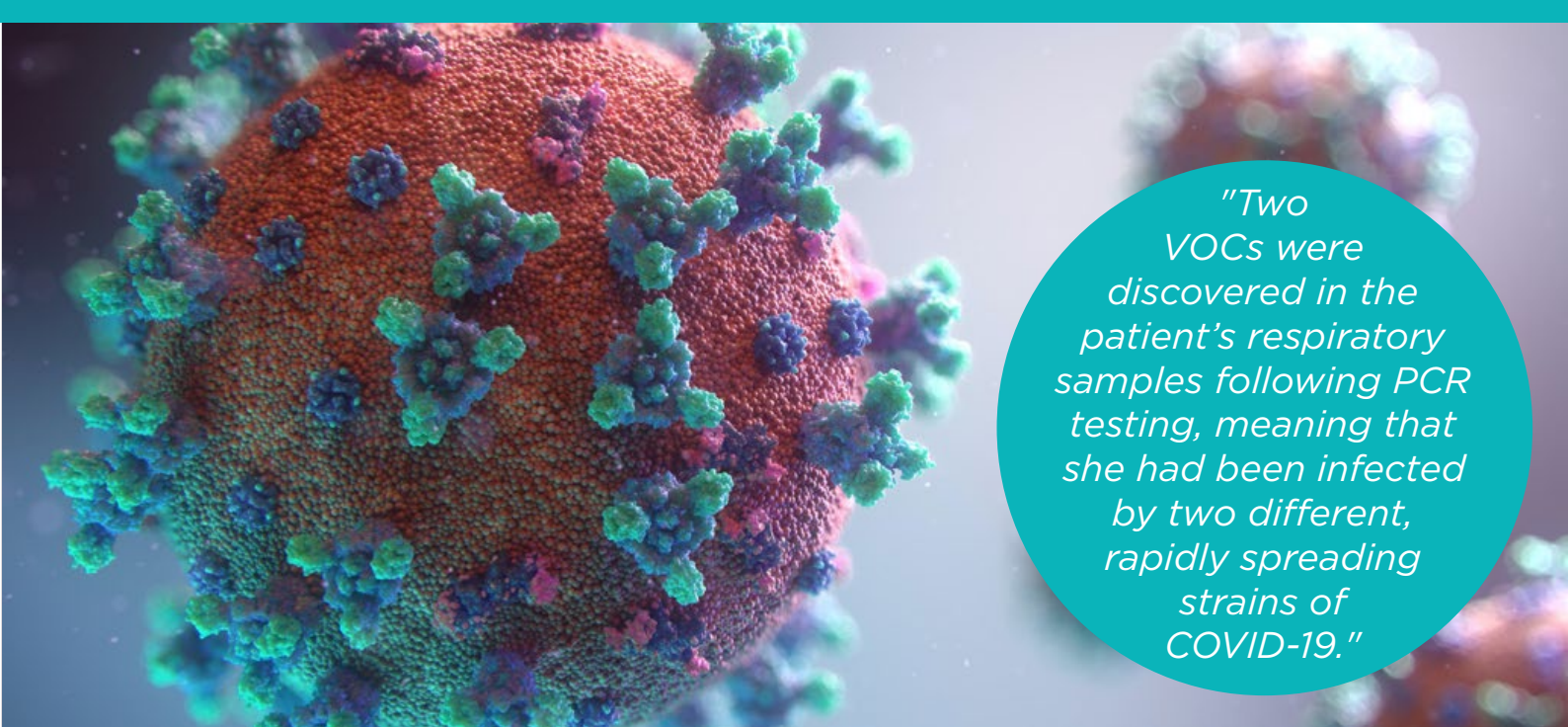
*"This study provides supporting evidence that aspirin use is associated with reduced ischaemic events after pneumonia in a primary care setting."*

**B**RINGING forward findings relating to the interaction between cardiovascular complications and pneumonia, new research presented at ECCMID 2021 revealed that aspirin has the potential to reduce the risk of events such as ischaemic stroke and myocardial infarction (MI) in patients with this condition. The study, conducted by Fergus Hamilton and colleagues at the University of Bristol, UK, investigated the role aspirin might play in primary care settings.

Selection of the participant cohort was conducted from 48,743 patients with pneumonia over the age of 50 years, sourced from the Clinical Practice Research Datalink (CPRD). Primary outcome was defined as occurrence of both ischaemic stroke and MI, and secondary outcome was one of these events happening individually. Researchers uncovered that in the 8,099 aspirin users identified, matched with 8,099 non-users, there was a 36% lower risk of the primary

outcome. Aspirin use was also associated with reduced risk of both secondary outcomes: 30% lower for ischaemic stroke and 54% for MI.

The large sample size allowed investigators to draw strong conclusions about the effective drug profile of aspirin from their findings. The researchers ultimately stated: "This study provides supporting evidence that aspirin use is associated with reduced ischaemic events after pneumonia in a primary care setting." In addition, the authors hinted at the implications of their work: "This drug may have a future clinical role in preventing this important complication." Hamilton went on to highlight the importance of their findings: "This research really paves the foundation for a clinical trial of aspirin in pneumonia, which remains the most common reason for admission to hospital in many countries." ■



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## Woman Infected with Two COVID-19 Variants Simultaneously

COVID-19 has impacted the world since its outbreak in Wuhan, China, in December 2019. The ability of the severe acute respiratory syndrome coronavirus-2 to rapidly mutate has seen the development of multiple variants, making COVID-19 increasingly difficult for the population to overcome. Researchers at the ECCMID 2021 presented a case of a 90-year-old woman with an unremarkable medical history, who was simultaneously infected with two COVID-19 variants of concern (VOC).

The patient, who had not been vaccinated against COVID-19, was admitted to the Onze Lieve Vrouweziekenhuis (OLV) Hospital, Aalst, Belgium, on 3<sup>rd</sup> March 2021 following repeated falls. She tested positive for COVID-19 and experienced no initial respiratory abnormalities. Her condition began to worsen, and she died 5 days later following the rapid development of respiratory symptoms and distress.

Two VOCs were discovered in the patient's respiratory samples following PCR testing, meaning that she had been infected by two different, rapidly spreading strains of COVID-19. The  $\alpha$  strain (B.1.1.7) originated in Kent, UK, and the  $\beta$  strain (B.1.351) from South Africa. A second PCR test confirmed the presence of both strains

through whole genome sequencing and S-gene sequencing techniques.

As this was one of the first cases of simultaneous infection involving two VOCs, Anne Vankeerberghen, lead author and molecular biologist at OLV Hospital explained: "Both these variants were circulating in Belgium at the time, so it is likely that the lady was co-infected with different viruses from two different people." Vankeerberghen added: "Whether the co-infection of the two variants of concern played a role in the fast deterioration of the patient is difficult to say." Previous reports by Brazilian scientists from January 2021 found that two people had also been simultaneously infected with two different strains of COVID-19, but this information is yet to be published in a scientific journal.

Vankeerberghen has posited that the global incidence of cases such as these are underestimated due to a lack of accessible testing options. She stressed the importance of being aware of co-infection rates, and encouraged scientists "to perform fast, easy, and cheap VOC-analysis by PCR on a large proportion of their positive samples, rather than just whole genome sequencing on a small proportion." ■



# Will Current COVID-19 Vaccines Offer Sufficient Protection Against New Variants?

FASCINATING evidence has emerged demonstrating the importance of receiving the second dose of the COVID-19 vaccine. This research was presented at ECCMID 2021, and also discussed the need to review and revise vaccines upon the development of new variants of concern (VOC). Nicole Schneiderhan-Marra and colleagues at the Natural and Medical Sciences Institute at the University of Tübingen, Germany, carried out a study to determine the levels of protection the current generation of vaccines provide against new mutated variants.

Due to the continuous mutation of the severe acute respiratory syndrome coronavirus-2, it is uncertain how effective current vaccines will be in providing protection against new variants. The protection that occurs following vaccination is determined by the levels of 'neutralising antibodies' present in the body. This specific group of antibodies act to defend the body and destroy the virus. Schneiderhan-Marra and colleagues assessed the levels of protection the vaccine provided for different strains through profiling antibodies produced following vaccination in the blood and saliva.

An existing assay, which measured the presence of severe acute respiratory syndrome coronavirus-2 antibodies in the blood, was altered to also detect VOC antibodies. Samples were collected from 23 people who had received two doses of the Pfizer-BioNTech vaccine. Control groups consisting of infected saliva donors, non-infected saliva donors, and infected blood donors were also included.

Analyses showed that the protection against COVID-19 increased significantly following two doses of the vaccine. The study compared the protection levels provided against the original 'wild-type' variant with that provided against the  $\alpha$  and  $\beta$  variants of the virus. Evidence showed that no reduction in protection was found against the  $\alpha$  variant; however, there was a significant

*"Evidence showed that no reduction in protection was found against the  $\alpha$  variant; however, there was a significant reduction against the  $\beta$  variant."*

reduction against the  $\beta$  variant. Schneiderhan-Marra explained: "This shows the importance of constantly updating vaccines to offer maximum protection against different strains of the virus."

With more variants emerging from the continuous mutation of the virus, scientists involved in this study have since adapted their assays to include new VOCs, including the dominant delta strain. Schneiderhan-Marra and colleagues are continuing to develop their research to monitor the emergence of new strains and their impact on current vaccine strategies. ■



# Antibiotic-Resistant Bacteria Found in Dog Food Across Europe



*"The close contact of humans with dogs and the commercialisation of the studied brands in different countries poses an international public health risk."*

**S**URPRISING new evidence has revealed that raw dog food sold across Europe contains antibiotic-resistant bacteria. Presented at ECCMID 2021 on 10<sup>th</sup> July 2021, this novel research discovered multi-drug-resistant bacteria in the products, some of which are identical to 'superbugs' found in hospital patients across Europe. This information has identified raw dog food as an international public health risk that may be encouraging the spread of antibiotic-resistant bacteria.

The World Health Organization (WHO) have labelled antibiotic resistance as one of the greatest public health risks facing humanity, with approximately 700,000 people dying from drug-resistant infections every year. Ana Frietas, Carla Novais, Luísa Piexe, and colleagues from the UCIBIO Faculty of Pharmacy at the University of Porto, Portugal, studied different dog foods sold in supermarkets and pet shops for Enterococci bacteria. These opportunistic bacteria naturally live in the guts of humans and animals but can cause serious infections upon spreading to other parts of the body.

The study analysed 55 samples of dog food of different varieties. Fifty-four percent of samples contained Enterococci bacteria, >40% of which were resistant to erythromycin, tetracycline,

streptomycin, gentamicin, quinupristin-dalfopristin, chloramphenicol, ampicillin, or ciprofloxacin. Twenty-three percent of the bacteria were also resistant to linezolid, which is a critical last-resort antibiotic used to treat serious infections.

Whilst all of the raw dog food samples contained antibiotic-resistant Enterococci, only three of the non-raw samples tested contained the multi-drug-resistant bacteria. Genetic sequencing of the bacteria in the raw samples found that they were genetically identical to bacteria in hospital patients around Europe, as well as bacteria found in farm animals and wastewater in the UK.

Scientists working on this study experimentally transferred the antibiotic-resistance genes found in the dog food samples to other bacteria with success, suggesting that this process could occur naturally with fatal consequences. Frietas explained: "The close contact of humans with dogs and the commercialisation of the studied brands in different countries poses an international public health risk." This research established raw dog food as a source of antibiotic-resistant bacteria that could spread to humans, and encourages pet owners to ensure they disinfect their hands after handling food or faeces. ■



# Dogs May Be Passing Resistance to Vital Antibiotic to Owners

**A**LARMING reports have revealed the presence of the *mcr-1* gene in four healthy humans and two pet dogs. This recent discovery was presented at ECCMID 2021 on 10<sup>th</sup> July 2021, and in both cases found the gene in both the dog and owner. The *mcr-1* gene provides resistance to colistin, a last-resort antibiotic used to treat severe bacterial infections resistant to all other drugs.

Since its initial report in China in 2015, the *mcr-1* gene has been reported in both humans and animals around the world. Due to its established resistance against colistin, there is a risk of this gene combining with drug-resistant bacteria, which would result in the development of an untreatable strain of infection. Juliana Menezes and colleagues at the Centre of Interdisciplinary Research in Animal Health at the University of Lisbon, Portugal, focused their study on whether household pets act as a reservoir of the *mcr-1* gene, facilitating its spread throughout the community.

Scientists tested bacteria in faecal samples from humans and their pets for resistance to colistin. Of the 126 people and 102 cats and dogs, all of the humans and 61 of the pets were healthy. Pets considered 'unhealthy' were suffering from skin and soft tissue infections or urinary tract infections. Eight dogs, three of which were healthy, and four humans were found to be harbouring bacteria with the *mcr-1* gene. All of these 12 samples were found to be resistant to antibiotics.

Genetic analysis of samples indicated that in one case, an *mcr-1*-positive dog with skin and soft tissue infections transmitted the gene to its human. Menezes explained: "While transmission in both directions is possible, it is thought that in this case the gene passed from dog to human." This evidence suggests that pets, particularly dogs, may harbour bacteria with the gene, promoting the overall spread of colistin resistance, which could have fatal consequences as a last-resort antibiotic. ■

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