PIECING TOGTHER THE PUZZLE: MUSINGS ON AN INTERDISCIPLINARY RESEARCH WORKSHOP

By Alex Williams

Although antimicrobial resistance (AMR) threatens to herald the rise of untreatable infections, such extreme cases of resistance are still relatively uncommon. However, the case I'm about to describe vividly illustrates why the Medical Research Foundation has invested £2.85m in establishing the National AMR PhD Training Programme, and why it has placed the concept of interdisciplinary research at its core.

In September 2016 a woman in her seventies from Washoe County, Reno, Nevada, succumbed to a bacterial infection resistant to the entire arsenal of antibiotics available to clinicians battling for her life. The defunct drugs comprised 26 antibiotics including carbapenems; a class of antibiotic reserved specifically for the treatment of antibiotic resistant infections.

Klebsiella pneumoniae was identified as the causal agent of the infection. *K. pneumoniae* is a species of bacteria associated with a range of environments, such as soil, water and the human gut. It has even been suggested that *K. pneumoniae* plays a significant role in shuttling antibiotic resistance genes between the wider environment and

the clinic. AMR is therefore an environmental challenge which is not confined to hospitals.

As late as June 2016 the woman had visited India where she had undergone multiple operations to address a fracture in her right femur. It is quite possible that during this period she acquired the *K. pneumoniae* strain carrying the carbapenemase resistance gene NDM-1 (New Delhi metallo-beta-lactamase -1); a gene which is thought to have originated in India. AMR is therefore a geographical challenge which is unfurling on a regional, national and international scale.

Washoe County has carried out surveillance for multi-drug resistant bacteria since 2010 and healthcare professionals who were in contact with the patient were subsequently monitored for signs of infection transmission. It is also unclear whether the patient visited India under the pretext of medical tourism. AMR is therefore as much about understanding human behaviour as microbiology.

The Medical Research Foundation has recognised AMR is an interdisciplinary challenge, and in addition to fully funding 18 PhDs in AMR it organised a residential training workshop open to existing PhD students studying any AMR-related topic. It is through the latter initiative that I shared a wonderful week in Bristol with over one hundred researchers working on AMR in the broadest sense.

How do you cultivate an appreciation for interdisciplinary research in a week? In short, you begin with the people. The cohort is a mosaic of disciplines; encompassing students in engineering researching bio-mimetic materials that emulate the bacterial cell-busting properties of caddisfly wings, bio prospectors chasing antibiotic lead compounds across glaciers, social scientists characterising the opinions of vets and farmers on antibiotic use in agriculture, and microbiologists probing the microbiome of hospital sinks for clues behind the spread of antibiotic resistance genes in healthcare settings. Understandably, this variety was mirrored in the roster of experts who delivered talks throughout the week; NHS healthcare professionals, global investigators, environmental scientists, veterinarians and social scientists were all represented.

However, when it comes to instigating interdisciplinary thinking, placing people in a room together is rarely sufficient. Even enquiring minds can find themselves congregating with others who share their niche area of expertise. Strolling around Bristol I came across an example of street art by Jody Thomas depicting a figure with their head buried in a bouquet of flowers- to me it resonated as a great metaphor. A PhD can be a very isolating experience where you take a topic, and following intensive literature review and experimentation burrow down into a tightly bounded box which ultimately becomes the content of your PhD. You are often actively encouraged to fight against the desire to expand the breadth of your research, lest you become overwhelmed by the myriad avenues to pursue. I emphatically believe this to be the case with a

sprawling subject like AMR. There is a danger then that students become so fixated on the bouquet before their eyes which they know so well, that they become oblivious to, or even reluctant to engage with the research outside their immediate subject of study. I for one know that I have gone to conferences and zealously hunted down exhibitors who have displayed work closely aligned with mine, almost to the complete exclusion of all else. Such a stance could be highly damaging in the long-run with respect to collaborative endeavours, yet the damage is difficult to quantify, since lost opportunities are precisely that, lost.

Thankfully the organisers facilitated interdisciplinary thinking very effectively. This was primarily achieved by dividing the cohort across three challenge themes. These included 1) Evaluating the use of diagnostics to combat AMR; 2) Challenges and considerations for the antibiotics development pipeline, and finally 3) AMR in the environment. Teams were assembled with the express intention of pulling attendees out of their respective comfort zones; those like myself examining environmental AMR found themselves delving into the world of diagnostics and drug discovery, while those embedded in the clinic ventured out to visit Wyndhurst dairy farm. Our task was to produce a briefing document and presentation summarising the critical aspects of our challenge theme.

Our sense of investment in the outputs was further galvanised by the fact that they would be submitted as evidence to the Health and Social Care committee, with the potential to be placed before the inquiry on the implementation of the National AMR Strategy.

The group I was placed in was charged with evaluating the current and future role of rapid diagnostic technologies. As part of our introduction to diagnostics we were treated to a tour of the Southmead Infection Sciences diagnostics laboratory. Here we witnessed the power of automation. We watched the hypnotic procession of ceiling-mounted carriages, laden with dozens of biological samples, snake their way to processing stations on a track system spanning multiple floors. We watched Petri dishes slide along conveyor belts undergoing sorting, saw how MALDI-TOF mass spectrometry is continuing to revolutionise bacterial identification in under twenty minutes, and discovered how antibiotic doses and combination therapies are being optimised to treat different infection types using inventive physical models affectionately termed 'jam jars'.

The most rewarding aspect of the week was no single piece of information gleaned from a lecture, or any one new contact forged, but the prospect of an enduring network that has been built between a wide array of researchers tackling a common problem from a multitude of angles- it is the feeling of being enmeshed within a larger whole where you know you can call on a community of colleagues eager to hear your perspective and offer their own.

The team; from left to right: Sylvia Rofael (UCL), Sarah Golding (Surrey), Mary McCarron (Ulster), Alex Williams (Nottingham), Anna York (Warwick) and Lorna Pate (Edinburgh).