Path of least resistance

Antimicrobial resistance threatens the effective treatment of a wide range of infections, and GPs have a crucial role to play in the leading the fight back, says Dr Bianca Potterton

Antimicrobial resistance (AMR) is one of the greatest threats to human health that exists in our times. It is an emergent public health crisis on an enormous scale and the problem is set to increase. Antimicrobial resistance may be defined as the ability of an organism to grow and survive in the presence of high levels of antimicrobials.[1] This resistance threatens the effective prevention and treatment of a range of infections caused by bacteria, viruses, fungi and parasites. While hospital-acquired infections account for the highest mortality, community-acquired infections are on the increase as treatment options become increasingly limited.

Antibacterial resistance (ABR) to all classes of antibiotics has developed. Among hospital-acquired infections perhaps the most well-known is methicillin-resistant *Staphylococcus aureus* (MRSA), which causes wound and blood stream infections.

Resistance has developed among the enterobacteriaceae, the family of gram-negative bacteria, including *Escherichia coli* and Klebsiella. *Klebsiella pneumoniae*, which causes pneumonia, urinary tract infections and septicaemia, has developed resistance against the third generation cephalosporins, including resistance conferred by extended-spectrum beta-lactamases (ESBLs) and third generation carbapenems, such as meropenem and ertapenem. *E coli*, which causes urinary tract infections and septicaemia, has developed resistance against trimethoprim, the fluoroquinolones (for example, ciprofloxacin) and the third generation cephalosporins (such as Cefixime and Cefotaxime). MRSA, klebsiella and *E coli* can be spread from the healthy host in the community into hospitals.

Community-acquired bacterial infections include streptococcus pneumonia, salmonella, shigella and gonorrhoea. *Strep. pneumoniae*, a common cause of pneumonia, meningitis and otitis media, has developed resistance to penicillin. Salmonella and shigella, which cause foodborne diarrhoea and septicaemia, are resistant to the fluroquinolones. *Neisseria gonorrhoeae* has decreased susceptibility to the third generation cephalosporins. Candidiasis, a common fungal infection responsible for oral/genital infections and additionally line infections in hospital, has developed resistance against fluconazole.

In addition to creating community and hospital-acquired infections, which will be largely untreatable, another sinister implication of antimicrobial resistance is the impact upon the success of clinical outcomes within areas in which antibiotics play a major role, such as organ transplants and chemotherapy.

Antimicrobial resistance contributes to a significant global burden of disease; 3.6% of new TB cases and 20.2% of previously treated cases are estimated to have multidrug-resistant TB (MDR-TB). Artemisinin-based combination therapy has begun to make inroads into controlling the spread of malaria; artemisinin-resistant strains have now been identified in Cambodia, Myanmar, Thailand and Vietnam. Anti-retrovirals have revolutionised the treatment of HIV in the past decade; it is now estimated that 10%–17% of patients without prior anti-retroviral therapy in Australia, Europe, Japan and the USA are infected with virus resistant to at least one antiretroviral. Antiviral drugs have become important tools for the treatment of epidemic and pandemic influenza, but there is now widespread resistance to adamantine antivirals within currently circulating A(H1N1) and A(H3N2) viruses. Although the frequency of oseltamivir resistance in currently circulating influenza viruses is very low, the rapid spread of oseltamivir resistance in the former seasonal A(H1N1) viruses demonstrates the need for increased vigilance and surveillance.[2]

What can be done about this? In short, there is much that can be done, and much to do.

The first step is assessing the scale of the problem. In order to do this, the WHO recently collated up-to-date information on resistance surveillance and data for a set of nine bacteria–antibacterial drug combinations from 129 member states, and detailed this in its 2014 report, *Antimicrobial Resistance: Global Report on Surveillance*. The report highlighted major gaps in antibiotic resistance surveillance, and the urgent need to strengthen global collaboration. Following on from the report, the WHO is developing a global plan to reduce the impact of antimicrobial resistance.

In December 2013, the pan-European Joint Planning Initiative on Antimicrobial Resistance (JPI APR) set out a Strategic Research Agenda which was devised to coordinate European research on AMR. Taking into account the numerous players involved, the JPI APR set out six priority areas:

- Therapeutics (the development of novel antibiotics and alternatives)
- Diagnostics (improved treatment and prevention of infections through better diagnostics)
- Surveillance
- Transmission dynamics
- The environment (tackling environmental risks such as the use of antibiotics in animal husbandry)
- Interventions (designing and testing interventions to prevent acquisition, transmission and infection caused by AMR).

In order to coordinate research and promote collaboration, the JPI APR is developing a publicly accessible database of research activities within the EU.[3]

In the UK, the *UK Five Year Antimicrobial Resistance (AMR) Strategy 2013 – 2018* was published in 2013. This sets out seven steps to reduce antimicrobial resistance, and there is some overlap with the JPI APR:

- Improving infection prevention and control
- Optimising prescribing practice
- Improving professional education, training and public engagement
- Developing new drugs, treatments and diagnostics
- Better access to and use of surveillance data
- Better identification and prioritisation of antimicrobial research needs
- Strengthening international collaboration. [4]

This is a big problem that is not going away. As front-line clinicians, GPs have a profoundly important role to play in terms of reducing antibiotic misuse and educating our patients. We are often placed in the situation where a patient demands an antibiotic for a suspected viral illness. Should we hold our ground, and perhaps spend one more minute of precious consulting time educating our patients about why we are being careful about prescribing antibiotics? The answer is clearly yes, because the implications of not doing so are huge and the outcome potentially catastrophic.

References

1. Strategic Research Agenda: Joint Programming Initiative on Antimicrobial Resistance, 2013
2. Antimicrobial Resistance: Global Report on Surveillance, The World Health Organization, 2014
3. Strategic Research Agenda: Joint Programming Initiative on Antimicrobial Resistance, 2013
4. UK Five Year Antimicrobial Resistance (AMR) Strategy 2013 – 2018, Department of Health, 2013