To stop AMR once and for all: stop killing the bugs!

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The solution to AMR is seen overwhelmingly as appropriate stewardship plus the provision of new antimicrobials (such as new antibiotics), which brings with it commensurate challenges of: rapid diagnostics to limit the use of antimicrobials where they will be ineffective and minimizing the use of broad-spectrum and 'last resort' antimicrobials; and setting up a financial reward system for pharmaceutical companies to compensate them for putting efforts in a lower-profit activity such as the search for new antimicrobials, the use of which would be substantially restricted for long periods.

These imperatives tie up the bulk of the effort, facilities, attention, policy and funding in the fight against AMR, but if successful, they are still only a stop gap measure that will delay the 'antibiotic apocalypse' by a decade or two. This apocalypse will come unless the effort is eternally continued, with an endless supply of new antimicrobials.

My concern is that this diverts attention from complementary measures that will greatly slow the development of AMR, and potentially stop it. In NAMRIP (the Network for Antimicrobial Resistance and Infection Prevention, until recently funded by EPSRC via EP/M027260/1), alongside the imperatives listed above, we research such methods, and focus on translating them to the wider world to ensure that our journal papers benefit society. Some of these involve measures to combat infection, and the risk of infection, without changing the wider microbe gene pool. Examples are listed below.

(a) Stop killing the bugs. If we give an antibiotic, or use biocide in a soap, low concentrations eventually enter the sewage and water systems. Here, and in the wider environment, they place natural selection pressures on the billions of microbes which have resided there, and over as little as a few hours can start altering the gene pool so that a greater proportion of that population have resistance to these antimicrobial agents. Serious infections undoubtedly require antimicrobials, but given the stewardship imperative, it is surprising how often our default position is to attempt the routine mass killing of microbes, which fuels AMR. Suppose, instead, that where we can, we use 'trap and release' so that the microbes that were susceptible to our interventions are not removed from the gene pool?

For example, the StarStream and StarSaver devices can wash a microbial biofilm from a wound, and can clean hands, teeth, salad and surgical instruments. They can do this using just cold water, and whilst they can kill microbes if biocide is added to the water, if no such additives are used they wash living microbes away, back into the sewage, soil and wider world. For the vast majority of microbes, their presence in this wider world should be no more alarming than it has been for thousands of years, if we take care of our skin and the breaks in it (see (b)) and have immune systems matched to the level of any infection. If we abandon the default position of killing the microbes, and allow the ones susceptible to removal (e.g. by StarStream's cold water) to remain in the gene pool, then the next time microbes attach to our surgical instruments, guts or wounds, they will be just as susceptible as before to removal. We do not change the microbe gene pool, because we are not providing an opportunity to develop resistance by selection pressure from antimicrobials.

(b) Skin care and food. Healthy skin has provided an effective barrier to the majority or microbes for thousands of years, infection being far more likely if the microbes bypass that barrier through wounds, eyes, mouths, ears, the genitourinary tract etc. Good hand cleaning reduces the likelihood of hands carrying microbes from the wider world into such openings, removing transient bacteria but leaving unharmed the complex microbiome of beneficial bacteria that are key to healthy skin. Damaged skin (even when damage comes from over-vigorous washing) can increase the chance of infection.

A 20-second handwash in warm soapy water, using a simple soap (but avoiding any soap or liquid soap which will pollute the oceans with plastic microspheres) that simply removes most foreign bacteria intact and sends them back into the wider world, usually without significant damage to the natural skin microbiome, will help prevent infection, and preserve the current microbe gene pool (see (a)). It has this advantage over routine use of a bactericidal soap, that will change the gene pool of microbes and promote resistance (as in (a)); or regular alcohol rubs. The imperative to provide a sink with warm water is weakened by the argument that alcohol rubs will suffice (e.g. at music festivals). However, alcohol hand washes do not kill norovirus nor *Clostridium difficile* spores, among others.

Similarly food hygiene without altering the wider microbe gene pool can be achieved by washing without killing the microbes, not just of the food but of the food storage, preparation and transportation facilities. NAMRIP not only researches this, but works to translate it to the food retail sector.

Hands are critical in the transmission of disease because they are in continuous contact with potentially contaminated objects and can transfer microbes, including antibiotic resistant microbes, to relatively vulnerable parts of the body, such as the mucosal surfaces of the eyes, mouth, gut, airway or genital tract. The role of food and hands in transferring microbes from one surface to another is therefore key, and so the use of materials (such as copper) on surfaces that food and hands are likely to touch can reduce this, whilst applying minimal selection pressures if those microbes have sufficient other lower-risk surfaces to colonize in the wider world.

(c) Vaccination. If microbes must be killed, it is better they are killed by our immune system, contained within the body, than by a biocide or antibiotic which leaks back into the sewage system in low concentrations (down sinks and toilets) and so promotes the growth of resistance by changing the microbe gene pool. Vaccination is a key to this, but just as important as finding an effective vaccine, is finding a solution of the problem of delivering it to the right population on a sufficient scale.

Of course there will always be a critically important place for killing microbes. But as our default position, it is not only the cause of AMR, but it is often an avoidable one.