Antimicrobial stewardship: the role of scientists?

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We continue to be warned about the risk of antibiotic resistance. This campaign has targeted medicine and agriculture, asking these industries to pay attention to the risks of widespread resistance and to cut the use of antibiotics wherever possible. However, there has been little to no mention of the widespread use of antibiotics in the scientific research community. As scientists we use antibiotics and antibiotic resistance as fundamental tools for our research; almost all conventional plasmids use an antibiotic resistance gene as a selectable marker, offering us an easy method of screening. With molecular biology and genetics at the heart of many research disciplines, these tools are ubiquitous. Scientists have a responsibility to monitor and reduce our use of antibiotics. With the growth and fast advancement of synthetic biology, it is timely for us to consider other options and to teach the next generation of researchers by example how to truly value antibiotics by using them more responsibly.

Keywords: antibiotic resistance, biological tools, education

Introduction

Following their discovery, antibiotics were heralded as a magic bullet in our fight against the ravages of infectious diseases and they remain an essential component in our therapeutic arsenal. In addition, with molecular biology and genetics at the heart of many research disciplines, the ubiquitous use of antibiotics as tools has also transformed fields of scientific discovery. However, recent influential reports refer to antibiotic resistance as a ‘catastrophic threat’ and ‘a problem so serious it threatens the achievements of modern medicine’. Calls have been made for: manufacturers to stop selling antibiotics as growth promotion stimulators in food-producing animals; better regulation of antibiotic use by veterinarians; new initiatives to stimulate antibiotic research in the pharmaceutical industries; a better educated public that does not misuse or overuse antibiotics; and clinicians to ‘champion the responsible use of antibiotics’. This call to action also includes a request to review and update the curricula of medical schools to ensure the new generations of doctors recognize their pivotal role in the future stewardship of antibiotic use.

Scientists as researchers

The field of biological, health and life sciences is a broad church and clearly not all scientists have the good fortune to be researching antibiotics. In fact it is fair to say that, as a community of scientists, those working within the field of antibiotic research are a small subsection of a much wider research pool. Nevertheless, the time is right for the wider scientific community to take stock and examine their own research practice and the messages, both implicit and explicit, they are providing to the next generation of scientists. A considerable body of scientists across our globe regularly use antibiotics to underpin their own scientific endeavours. Antibiotics have been both the tools and the building blocks that underpinned the rapid expansion of scientific knowledge, technology and literacy we enjoy today. This is especially true in fields linked to or dependent on microbiology, genetics and molecular biology, as exemplified by the burgeoning field of genomic sequence data, including the Human Genome Project. We add an array of antibiotics to a plethora of liquid and solid media to culture our bacteria of choice. Bacteria provide a stepping stone for scientific research and discovery throughout the biological sciences (and beyond). As scientists we are using iterations of the same methods of gene

The roles of scientists

How can scientists contribute to this call to action? Clearly scientists are addressing the need to add to the knowledge base that underpins our current understanding of antibiotic production and the mechanisms of action and resistance. Society is relying on the scientific community to work with pharmaceutical companies to seek effective, new antibiotic targets, to develop quicker, more effective diagnostics and to design new antibiotics and therapeutic measures. On a global scale, recent funding streams have been announced to support these endeavours and a wide range of novel approaches to drug development is being mooted.
selection, manipulation and isolation as those first described more than 40 years ago: in 1973 Stanley Cohen et al.\textsuperscript{24} published one of the first papers describing the construction of biologically functioning plasmids \textit{in vitro}. This plasmid contained a cassette providing resistance to tetracycline. Since then we have grown reliant on the ease and reliability of the different antibiotic resistance markers and selection tools that we manipulate into bacteria, often as a by-product of the molecular biology techniques we use throughout our research.\textsuperscript{23} Indeed, resistance markers are often cloned into broad-host-range plasmids or shuttle vectors with multiple origins of replication, which raises additional concerns about their safety and containment. In addition, antibiotics themselves are cheap, freely available and easy to use. Antibiotic use by the scientific community is ubiquitous and to some extent almost unnoticed.

Let us consider our reliance on this technology. Every time we transform bacteria with an antibiotic resistance marker and screen transformants using antibiotics, we risk releasing antibiotics and new antibiotic (often multi-antibiotic)-resistant bacteria into the environment. The antibiotics we use in the laboratory, such as ampicillin, chloramphenicol and tetracycline, often overlap with the antibiotics used in the clinic and antibiotic resistance genes can effectively provide a pool of bacterial resistance to a range of different antibiotics and antimicrobials.\textsuperscript{23,24} I would like to ask whether this is the type of scientific practice that we want to bequeath to the next generation of scientists. And also, whether in this day and age, scientists’ reliance on antibiotic-based technologies is acceptable, necessary or responsible.

**Scientists as educators**

The next generation of biologists and microbiologists are taught about the mechanisms of antibiotic resistance in formal academic settings. A role of scientists is as educators to the next generation, providing the knowledge needed to understand the scientific basis of the growing threat of antibiotic resistance.\textsuperscript{25} Students are also introduced to the concept of the urgent need for new antibiotics, from the media as well as a teaching and scientific research community that also urges responsible use of antibiotics within our wider society.\textsuperscript{2,26} However, this is often the same community that designs and runs laboratory-based practical classes that have not changed substantially over the last few decades. These ‘cook-book’ practicals often use antibiotics and antibiotic resistance genes as disposable tools. Care is taken to ensure we destroy and safely dispose of the bacteria, but we devote far less attention to the examination or highlighting of what happens (should happen) to the antibiotics that we discard or their long-term impact on the environment.\textsuperscript{27,28}

**Scientists as stewards**

Do we need to stop giving such mixed messages to our young scientists? Should we examine how learning opportunities encompassing antibiotics and antibiotic resistance are incorporated across all university curricula to ensure the information we provide to students at all times is consistent and synoptic? At the very least, should we encourage students and future scientists to use antibiotics more responsibly and sparingly in both educational and research settings, perhaps by agreeing to self-regulate our own reliance on antibiotic-based technology? Maybe the time is right for us to begin to practise what we preach and to develop alternative practical classes where antibiotics and antibiotic resistance are not treated as disposable teaching tools. Examples of alternatives include the Small World Initiative developed by Yale University to crowdsource new antibiotics using undergraduate students in universities across the globe.\textsuperscript{29}

Perhaps the scientific community should begin to provide more support and invest research resources in the development of new technologies that avoid the use of clinically important antibiotics but offer the same benefits and functionality as our current tool set based on antibiotic resistance. Researchers are starting to develop these alternatives.\textsuperscript{30} They are taking advantage of new techniques that often involve synthetic biology, but these alternatives are not widely used and need to be considered and developed further.\textsuperscript{31} Surely this self-scrutiny and assessment of our own practice will give us a better standing when we add our voice to the call for society to use antibiotics more responsibly.

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L. B. is part of the Small World Initiative, developed by Yale University and currently running in more than 40 other Higher Educational Institutions and which has enrolled more than 1000 students across the USA. The programme trained trainers to provide an authentic research project for undergraduate students to address the worldwide health threat of antibiotic resistance. L. B. is currently working with the Society for General Microbiology (SGM) to bring this programme to undergraduate students in the UK. The SGM is taking the project further by including school pupils and the general public (Citizen Science).

**References**


