Inspiring STEM undergraduates to Tackle the AMR Crisis

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Running Title: Inspiring STEM undergraduates to Tackle the AMR Crisis

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One Sentence Summary: In addition to the traditional research-led lecture, different teaching approaches using multiple modes of instruction can be used in a biology-centric department to incorporate antimicrobial resistance as a topic into an undergraduate curriculum.

Abstract

To address the growing problem of antimicrobial resistance (AMR) it is necessary to invest in, inspire and attract future generations of scientists to this research area. Undergraduate education should be a focus for attention and efforts should be made to ensure that students are afforded opportunities to actively engage with AMR. We illustrate how as a topic, AMR provides opportunities to deliver effective research-led teaching in addition to traditional teaching methods. We have used a selection of case studies to illustrate how students can be engaged with AMR using a variety of research-led approaches to develop the required skills for biology-centric students. In addition we indicate how these skills map to the UK Quality Assurance Framework and the Vision and Change report developed by the American Association for the Advancement of Science.

Introduction

Recent media attention has raised public awareness towards the major societal concern of antimicrobial resistance (AMR). Dame Sally Davies the Chief Medical Officer in the UK (2011) referred to AMR as '*one of the greatest threats to modern health*'. This growing awareness has led to many new reports, (Shallcross and Davies 2014)(Earnshaw *et al*. 2009)(President's Council of Advisors on Science and Technology 2012) and funding streams and initiatives (http://www.mrc.ac.uk/research/initiatives/antimicrobial-resistance/; http://www.niaid.nih.gov/topics/antimicrobialresistance/Pages/default.aspx). The televised Longitudinal prize award particularly caught the public imagination in the UK, resulting in AMR being the focus of a £10 million research prize (https://longitudeprize.org/) . Recently, this dire warning also attracted the attention of the current UK Prime Minister, David Cameron. He called for a review to investigate both the multifaceted problem of increasing AMR as well as the diminishing investment in new antimicrobial discovery. A report (2015) has been published as a direct output of this review: 'Tackling a global health crisis: the initial steps' (The Review on Antimicrobial Resistance 2015). It proposes a series of interventions to stimulate antimicrobial development to be underpinned by commercial activity. These initial proposals include a call to '*Invest in the people who will solve the problem'* and that '*It is crucial to train the next generation of doctors, scientists, microbiologists, pharmacologists, medicinal chemists and biochemists, as well as economists, social scientists and vets, among others*.'

The Role of STEM Graduates

Tackling the international threat of AMR must involve the next generation of Science Technology Engineering and Maths (STEM) graduates. In the UK this is reflected in the Quality Assurance Agency benchmarks statements for Biosciences and Biomedical Sciences taught in Higher Education. The subject benchmark statement for Biosciences includes a paragraph specifically relating to antibiotics; '*the biosciences have much to contribute to the health and wealth of the nation. Fundamental understanding of diseases, for example, the role of microorganisms, together with the development of […] antibiotics, has saved many lives'* (Quality

Assurance Agency for Higher Education 2007a). Similarly the benchmark statement for Biomedical Science degree draws attention to the major health risk of antibiotic resistant bacteria (Quality Assurance Agency for Higher Education 2007b).

Modern society relies heavily on STEM and is dependent on STEM graduates to address global problems such as AMR. Yet evidence suggests that fewer school-aged children are choosing STEM subjects as a career path (Donghong and Shunke 2010) even though the state-mandated National Curriculum was introduced to schools in 1989 to ensure that science was a core subject from the age of 5-16 years. This is a concern as research by the UK Science Council suggests that in 2017 over 58% of jobs will require skills in STEM subjects (The SCORE partnership 2011). However, this recruitment problem is not restricted to school pupils. Recent reports have highlighted a similar trend in undergraduate populations with students choosing not to major in the sciences on both sides of the Atlantic in the UK and the USA. Economic projections indicate that, in the US, there is a predicted shortfall of more than 1 million new STEM graduates over the next decade (President's Council of Advisors on Science and Technology 2012). The Engage to Excel report (2012) outlined issues with uninspiring undergraduate courses, difficulties with developing maths skills and an unwelcoming atmosphere within faculties as factors that encourage students to switch to non-STEM disciplines.

Tackling the growing problem of AMR will depend on the interest of future generations of STEM graduates to provide solutions. Stimulating interest and awareness of the complexity of this problem within an undergraduate curriculum is desirable. Clearly, one way we can do this is to examine how we embed research about AMR in university curricula.

The Role of Research-Led Teaching

The importance of the links between research and teaching in undergraduate education has been viewed as a priority for student education with a report by the UK Department for Education and Skills in 2004 stating "*it is important to see this as an issue about ensuring that research-informed teaching takes place in all HEIs*". The links between research and teaching have been debated and critiqued. Boyer *et al.* (1997) examined the relationship between teaching and research in HEI curricula. They also considered the benefits that a curriculum that combines research and teaching can bring to students and faculty members of staff, while considering how research and teaching can be embedded and facilitated. Griffiths (2004) followed by Healey (2005) developed a Teaching-Research Nexus. It has two axes that highlight the role of active student engagement in the process and differentiated between understanding the physical processes involved with research as opposed to learning about the results of research outputs. Within this nexus students experience four relationships of Teaching-Research links in their subject-based departments. This Teaching-Research Nexus can be considered in terms of AMR (Figure 1):

- Research-Based teaching with students as active participants, where students are actively engaged as researchers and the teaching is designed around inquiry-based activities. The division between teacher and student is minimised. In science curricula, this has conventionally been delivered as the final year research project, which can be focussed on projects assessing AMR mechanisms or potential new antibiotic discoveries. (Case Study 1 and 4)
- Research-Orientated teaching where the student is a recipient of teaching. The students learn about research processes that underpin new knowledge. The division between teacher and student is apparent. In science curricula, this learning has conventionally been delivered as laboratory practicals that may use antibiotic resistance marker methodologies. This can also be delivered in classes that develop critical analysis of the primary research literature in the field of AMR. (Case Study 3 and 5)
- Research-Led teaching, in which the student is the passive recipient of knowledge and information about research findings that can often be related to the research interest of the staff delivering the teaching. The division between teacher and student is apparent. In science curricula, this has conventionally been delivered in a lecture format where lecturers have the opportunity to inform students about the latest research in the field of antibiotic discovery.

- Research-Tutored teaching involves the student as an active participant. In science curricula this has conventionally been delivered in ‘Oxford style’ tutorials where students actively engage with tutors within discussions about research findings and may produce papers or essays focussed on antibiotic discovery. The division between teacher and student is minimised. (Case Study 2)

Embedding research into biology undergraduate curricula was also addressed in The Vision and Change in Undergraduate Biology Education report in 2009 (Bauerle *et al*. 2011). The report recommends the use of innovative pedagogy along with integration of authentic research experiences and building key skills in mathematics to encourage student engagement and retention in STEM. It uses case studies to illustrate how to successfully embed enquiry-based teaching within undergraduate programmes. Interestingly, the Engage to Excel report (President’s Council of Advisors on Science and Technology 2012), also recommends replacing standard laboratory courses with discovery based research courses to engage and excite students with empirical research. Below, we also use case studies to illustrate how different approaches using multiple modes of instruction can be used in biology-centric departments, to incorporate AMR as a topic into an undergraduate curriculum in addition to the Research-Led traditional lecture.

In summary

The study of AMR can be incorporated into undergraduate biology-centric curricula using a variety of various educational approaches that map to the Teaching-Research Nexus and offer alternatives to the traditional lecture. These different approaches have the potential to be adapted to different curricula and to attract the interest of future generations of doctors, scientists, microbiologists, pharmacologists, medicinal chemists and biochemists to provide solutions to this growing problem. We also believe that other curricula including postgraduate curricula, which incorporate different aspects of AMR may benefit from a similar scrutiny and mapping exercise.

Moreover, it is also important that the interest of potential STEM graduates towards AMR is captured prior to University. Therefore we suggest that there is scope to use aspects of these different approaches and modes of instruction illustrated in the case studies to incorporate AMR teaching into schools. (http://www.sgm.ac.uk/outreach/small-world-initiative/)

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Table 1 Case Study 1: Stakeholder perspectives in the Antimicrobial Resistance Crisis (University of East Anglia)

Research-Based Teaching

Science undergraduates benefit from taking an issues-based approach to understand how advances in science and technology concerning AMR impact upon society (Bowater, 2013) (Bauerle et al., 2011). An effective way to introduce this to curricula is via interactive, small-group teaching (Springer et al., 1999). A two-hour workshop session allows students to explore the multifaceted problem of AMR. Firstly, students are provided with a short, tutor-led introduction to revisits and reinforces student's previous learning on antibiotic targets and AMR mechanisms. Next students are introduced to the dual problem of increasing AMR and the diminishing investment in new antibiotic discovery. The tutor actively encourages students to produce a list of key stakeholders required to tackle these dual problems; pharmaceutical companies, general practitioners, the agricultural industry, policy makers and members of the public are often proposed. Students divide into small groups that represent key stakeholders in order to answer:

- how and why their stake-holder contributes to this global crisis
- what steps could be taken to provide solutions to this global crisis from the viewpoint of the stakeholder and society in general.

The tutor encourages students to undertake online research during the session to find the information and evidence required to develop arguments. Students are required to capture and share their group learning using short presentations to the whole workshop group within the final plenary session. During the session student engagement with this global issue was generated as evidence by the fact that all students contributed to the discussion during the final plenary. In addition students suggested initiatives to address AMR such as labelling food to indicate their possible levels of antibiotics. After the session, students write a short report to reflect on their own learning. Students were sufficiently interested to engage in further research outwith the workshop as indicated in by their reflective reports that provided evidenced of additional reference to the research literature surrounding AMR. Student evaluation comments of the session included '*this was a particularly interesting session, as it not only educated us on the issues but truly hit home as to* *how difficult it is to come up with a solution giving us a proper understanding of this issue*.'

Table 2 Case Study 2: Critical Analysis of AMR literature with a social media presence (University of Strathclyde)

Research-tutored teaching

Final year undergraduates benefit from learning how to critically appraise the literature, enabling them to develop skills and knowledge not only on research outcomes but also how certain methodologies can be employed to answer a research question (Quality Assurance Agency for Higher Education, 2007a)(Quality Assurance Agency for Higher Education, 2007b)(Bauerle et al., 2011). One of the best ways to facilitate this kind of learning is via student participation and cooperative problem solving opportunities using a discussion based delivery (Knight and Wood, 2015). Active discussion between students can be encouraged and facilitated by the tutor through the use of social media such as Twitter - active learning has been shown to improve student learning outcomes (Knight and Wood, 2005) and extending this conversation beyond the classroom (http://www.academiccommons.org/2014/07/21/teaching-with-twitter-extending-the-conversation-beyond-the-classroom-walls/).

Final year Microbiology students are firstly tutored in how to read and appraise a scientific paper and to critically analyse the work. Next they are provided with a selection of research papers and asked to choose a paper that interests them. The 'Twitter-handle' (Twitter name) of the author(s) is provided to the student(s) and the authors are informed their paper is chosen. Papers are selected from the literature by the tutor to reflect the breadth of work related to AMR, from molecular mechanisms of both resistance and biosynthesis, antibiotic discovery, biotechnology etc. All class papers are available to students, to encourage them to read widely, followed by a period of student-centred learning where the class critically appraise the papers they are studying. Students are also encouraged to 'tweet' the authors with questions relating to their work. Tutors facilitate and stimulate discussion amongst the class and with the authors of the papers and potentially the wider scientific community through tweets and the use of class-specific #Hashtags. During the class presentations (Journal club style) the class are encouraged to tweet about their research on the papers, and through the use of #hashtags these can form a useful resource to influence student revision. There is also potential to 'Storify' (https://storify.com) with the class #hashtag to provide an automated summary of all tweets containing that #hashtag and email or tweet this to the class. The presentations normally last 20-30 minutes and have time for discussion following the presentation. Students can be assessed on their presentation skills and critical analysis skills. There is also the potential to use peer-marking approaches with this format. Anecdotally, from our work students who engage with Twitter discussion generally score higher marks on the class, but this likely reflects their overall level of engagement in the subject. A more detailed trial of 125 students also showed a correlation between Twitter use and grades (Junco et al., 2011). We found using this approach as with a face-to-face discussion based delivery still encourages variable engagement from students. In addition Twitter engagement from the paper authors can also be variable. Suggesting papers from authors who you know will engage through Twitter is a solution to this issue. However we also noticed that shy students or students who are uncomfortable with sharing their Twitter handles with a tutor, can be encouraged to set up a class-specific account for themselves thereby facilitating greater inclusion in online discussions as oppose to face-to-face discussion settings. As tutors we could clearly observe that students found the discussions stimulating and it enable wider engagement - where students explain the subject to the wider public following a question. Clearly the format of Twitter also encourages students to be succinct and ask their questions in 140 characters.

Table 3 Case Study 3: Learning the skills of a scientist; Writing papers about AMR

University of Strathclyde

Research-orientated teaching

Students, while learning within a course often develop abstract and theoretical skills within microbiology. However, there is a need to introduce greater problem-solving, analytical skills and writing skills to undergraduate courses (Quality Assurance Agency for Higher Education, 2007a)(Quality Assurance Agency for Higher Education, 2007b)(Bauerle et al., 2011). Traditional essay writing, whilst useful for the former, often does not enable acquisition of the skills that a practicing scientist requires – such as data analysis and paper writing (Coil et al., 2010). To develop these skills a data analysis and paper writing assignment for undergraduate students was constructed. The students are presented with a detailed scenario that describes how 'they' are a scientist who has completed a series of experiments and sequenced a gene responsible for AMR in a specific organism. The students are provided with appropriate data, a DNA sequence (the gene of interest), a series of numerical data (growth curves, qRT-PCR etc) and some *in vivo* data. The students are also provided with the 'Instructions for authors' for a scientific journal, such as 'Microbiology' (http://www.sgm.ac.uk/publications/journals/microbiology.cfm), and a sample paper from the journal, to enable them to see how a manuscript is put together for that journal. They are asked to go and write the manuscript (with the exception of a materials and methods section). This process requires the students to use a range of skills they have learned during their degree – bioinformatics, statistics, data visualization, literature searching, critical analysis etc. The students engage well with the work, often describing it as 'challenging but enjoyable', and they generally achieve good marks as they engage well with the assignment. Interestingly we noticed that the way students approach the task reflects their own interests; students with biochemistry interests often focus on the protein and align the translated sequence, picking out active sites; immunology students often focus on the interaction with the host; and microbiologists can focus on the AMR mechanisms.

Overall the assessment is amenable to any subject and allows students to learn skills that they can see will be useful to them as scientists. Moreover, by supplying appropriate data, assessments of this kind allow students to develop the analytical skills required to develop a deep understanding of AMR.

Table 4 Case Study 4: The Small World Initiative (originated in Yale University)

Research-based teaching

Student retention and engagement is more likely if students take part in authentic research experiences at an early stage in STEM curricula (President's Council of Advisors on Science and Technology, 2012) (Bauerle et al., 2011). The Small World Initiative (SWI), developed at the Center for Scientific Teaching at Yale, is designed as an undergraduate research course where students are used to crowd source the search for new antibiotics (http://smallworldinitiative.org/about#about). Initially first year students' culture soil microbes and screen for antibiotic activity against the human pathogens that are currently causing concern because of their growing resistance to Antimicrobials: the so called ESKAPE pathogens (*Enterococcus faecium* [E], *Staphylococcus aureus* [S], *Klebsiella pneumoniae* [K], *Acinetobacter baumannii* [A], *Pseudomonas aeruginosa* [P] and *Enterobacter* Sp. [E]; Boucher et al., 2009), thus addressing a real-life problem. Using standard laboratory protocols, students are encouraged to design their own experiments, analyse data and produce presentations about their research project. Providing students with opportunities to experience the excitement and process of research in the first years of Higher Education in university and colleges provides a positive, realistic reflection of science, resulting in higher retention rates within STEM fields. The SWI is currently running at more than 59 diverse institutions across the United States (including state universities, community colleges and non-traditional universities), United States Territories and internationally within Puerto Rico, Belize, Malaysia and The United Kingdom. Preliminary evaluation data based on pre and post SWI questionnaires and course tests suggests that taking part in the SWI can increase undergraduate student academic performance and encourage student engagement (Slone, 2015)(Caruso et al., 2015). Currently the SWI is being adapted for used within School University partnerships to encourage STEM participation in school pupils at a pre-university stage. (http://www.sgm.ac.uk/outreach/small-world-initiative/)

Table 5 Case Study 5: Exploring Antibiotic action; a laboratory investigation (Newcastle University)

Research Orientated Teaching

Developing effective laboratory skills is a key element of undergraduate Bioscience and Biomedicine degree programmes (Quality Assurance Agency for Higher Education, 2007a)(Quality Assurance Agency for Higher Education, 2007b) (Bauerle et al., 2011). Embedding opportunities to develop confidence in mathematics is also desirable (President's Council of Advisors on Science and Technology, 2012). We constructed a series of laboratory experiments focused on the action of β-lactam antibiotics using the Gram-positive bacterium *Bacillus subtilis* as a model organism. Three practical sessions were integrated into this experiment:

1. Bacterial sensitivity to antimicrobial compounds – using a disc diffusion assays with eight antibiotics tested against six *B. subtilis* strains with or without mutations in the genes encoding the penicillin binding proteins)
2. A Minimum Inhibitory Concentration (MIC) using microplate assays with one antibiotic against the six *B. subtilis* strains from experiment 1.
3. Identification of β-lactam targets – Bocillin (Fluorescent Penicillin from Invitrogen) is used in a competition assay with SDS-PAGE detection. Each student challenges the six strains of bacteria with their antibiotic and then Bocillin.

Students use the individual data sets to develop an understanding of how bacteria react to antibiotics and to semi-quantitatively estimate the minimum number of antibiotic molecules needed to kill a single cell. They also integrate the different data sets into a written report. Students are supported throughout this process using seminars focussing on the maths that underpin the data analysis of MIC calculations and effective scientific report writing including the importance of self-editing their own report writing. Students have shown that they are able to effectively integrate three data sets in order to produce a scientific report. Students recognise that this set of microbiology practical sessions allows them to develop practical microbiology skills and a confidence in their maths and writing skills.