# Bacterial antibiotic resistance: role of health education in formal and non-formal contexts

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The effectiveness of antibiotics depends greatly on their correct use, for which physicians, retailers and patients contribute. Physicians should direct their conduct towards avoiding the unnecessary use of antibiotics, choosing the least broad-spectrum antibiotic, adequate doses, good timing and the shortest possible duration of the antibiotic course. However, physicians' decisions may be influenced by other factors, such as pressure from patients and families. The general public is mostly unaware of the basic aspects on antibiotics modes of action and is frequently involved in inadequate behaviors, such as self-medication and not following the antibiotic treatment as prescribed. Therefore, education on the correct use of these drugs will be essential for the success of the treatment and prevention of the spread of bacterial resistance.

**Keywords** knowledge attitudes/practices on antibiotic use; antibiotic resistance; teaching interventions

## 1. Relationship between antibiotic use and resistance– impact on educational campaigns

Antibiotics are among the most commonly prescribed drugs, but they are often misused [1,2]. Their unnecessary use contributes to progressive loss of bacterial sensitivity [3], which has clinical and economic impacts [4]. Many issues such as economics, politics, doctor's knowledge/experience, diagnostic uncertainty and pharmaceutical marketing could lead to the irrational use of antibiotics.

Despite ongoing global efforts, antibiotic resistance and the collapse of the antibiotic research-and-development pipeline continues to worsen. Prescription habits are intimately related with emergence of resistance [5]. Indeed, antibiotic resistance is primarily the result of bacterial adaptation to its own exposure. In addition to antibiotic's curative properties, their use naturally selects for preexisting resistant populations of bacteria in nature. Finally we should point that, after billions of years of evolution, microbes have most likely invented antibiotics against every biochemical target that can be attacked – and, of necessity, developed resistance mechanisms to protect all those biochemical targets [6].

Some interventions are set to address the antibiotic-resistance crisis like preventing infections and resistance; refilling antibiotic pipeline by aligning economic and regulatory approaches [7]; preserving available antibiotics and slowing resistance; developing microbe-attacking treatments with diminished potential to drive resistance and developing treatment attacking host targets than microbial targets to avoid selective pressure driving resistance. Transversal to those specific interventions - the knowledge and quality-of-prescription in an individual or institutional manner (through specific and local protocols) – is absolutely fundamental and, as international counseled [8], need to be in continuous improvement. Thus, under- and post-graduate specific scientific antibiotic programs in medical and non-medical grounds are being implemented – as it has been proven to better associate to better standards in quality-of-prescription.

According to these outcomes, it is urgent to encourage health education. Some authors suggest that children need to be educated about antibiotics [9] and several Educations Programs have been developed [10-11]. In 1998, the US Pharmacopeia established Ten Guiding Principles for Teaching Children and Adolescents about Medicines. In our point of view schools are one of the ideal places to promote health education, such as education on bacterial antibiotic resistance. Schools have access to a large population of students and parents, are respected institutions within the communities and, on the other hand, provide the opportunity to reach a large proportion of students in their normal learning environment. In England, it has been a statutory requirement since the introduction of The National Curriculum that children between 7 and 14 years-old are taught about microorganisms. Summarizing, National Education Programs about the dangers of irrational antibiotic use should be priority.

### 1.1. School-teachers

To increase the student knowledge on microorganisms and antibiotics, it will be first necessary that school-teachers have the necessary information. A study performed in New Zealand with primary school teachers belonging to 39 schools showed gaps in the understanding of antibiotics [12]. According to this work, only about 60% of the teachers knew that antibiotics were beneficial only in the treatment of bacterial infections. Several teachers believed that

 

antibiotics are useful for colds and flu, and many did not have knowledge on antibiotic resistance. The same authors conclude that if teachers are responsible to educate children about antibiotics, basic education in respect to antibiotics and resistance will be required for school-teachers [12]. Microbiology educational resources appropriate for pre-school age children, K-12 students, undergraduate and graduate students, and postdoctoral fellows, can be obtained from American Society for Microbiology and the Carnegie Foundation for the Advancement of Teaching [13]. Important and interesting resources could also be obtained in the webpage of Michigan Antibiotic Resistance Reduction (MARR) Coalition. This organization started in 1997 to help reduce unnecessary antibiotic prescribing in Michigan. MARR Coalition "Antibiotics & You" and "High School Biology/Health" curriculum are freely available to teachers. These programs are designed for target audiences, including elementary students $3^{th}$-$6^{th}$ grade, high school student's $9^{th}$-$10^{th}$ grade, and adults [14].

### 1.2. Kindergarten

It is documented that antibiotic education should be initiated in kindergarten. Bush and collaborators suggested that these efforts should begin as early as kindergarten based on observations of successful programs involving young children and their parents [15]. The United States Pharmacopeia Ad Hoc Advisory Committee on Children and Medicines has guidelines for preparation of educational materials about medication for children as young as three years-old. As outlined in the USP Guiding Principles for teaching children and adolescents about medication, education needs to be tailored to their development, capabilities and experience [16].

### 1.3. Basic and secondary schools

A study performed by Jones and co-workers [17] indicate that students as early as the $5^{th}$ grade have distinct images of bacteria and viruses and hold understandings about where germs are found and how they spread. It was been advocated that the natural curiosity of young children about their body functions provides student understandings and build more accurate concepts [17]. Another work documented that children with 6 years and older, begin to identify medications by their brand names and their associated reasons for use. Furthermore, some students are able to distinguish medications and to provide brand names of medications or indications for use [18]. The same authors recommended to include children in discussions about medications because they form opinions about medications at young age and some of these beliefs persist in the adult population. Children as young as 5 years-old agree that following correctly the instructions of medications helps them to get better [19].

In Portugal, Azevedo and colleagues [20] showed that there are marked deficiencies in students' knowledge on antibiotic spectra, indications and correct antibiotic use in $9^{th}$ and $12^{th}$ grade students. A study performed by [21], with $5^{th}$, $8^{th}$ and $11^{th}$ grade students also revealed a common misconception held by students: the belief that "antibiotics can cure viral infections" and large gaps in the function of antibiotics. The same authors performed a study in suburban public schools in the North Carolina with elementary ($5^{th}$ grade), middle ($8^{th}$ grade) and high school ($11^{th}$ grade) students and one point in common to all the student age groups that emerged from the this study was the belief that bacteria caused viral infections. Few students mentioned no differences in the treatment for bacterial or viral infections, and others stated that antibiotics are taken to kill bacteria [21]. It was reported in Thailand, that $12^{th}$ grade student's revealed lack of knowledge in attitudes and behaviors concerning antibiotic use for upper respiratory tract infections. Incomplete course of antibiotic treatment was found in more than 45% of the students, and 50% of them took antibiotics for less than 5 days [22].

A recent work designed in Portugal for $11^{th}$ and $12^{th}$ grade students, entitled "Microbiology recipes" improved the student's conceptualization of antibiotics. When the project began, many students neglected the fact that antibiotics only act on bacteria [23]. However, after a school intervention, most of students stated clearly that bacteria are the only target for antibiotics, and additionally they were able to link antibiotic resistance to improper use of antibiotics [23]. In Moldova, an extensive school-based educational program, (which included peer-education sessions, parents' meetings, and distribution of educational newsletters), was also successful in reduction of antibiotic use for treatment of presumed viral respiratory illnesses [24]. In Europe, a pan-European educational resource was implemented, named e-Bug. This educational resource (e-Bug) aims to reinforce awareness in school children of microorganisms, correct antibiotic use, hygiene and transmission of infection. It has been documented that the curricula of all the countries involved in this project have limited information on antibiotics and their correct use [25]. According to the literature, the Bug Investigator project in England [26], and the peer-teaching program in Moldava [24] are the only national antibiotic educational campaigns that target school children, and teach them how and why antibiotics should be used rationally.

### 1.4. University

A study was developed in Turkey, with University student's from different Faculties with exception of the ones from Faculty of Medicine [27]. The authors showed that the majority of the students (83.1%) took antibiotics for normal cold and 32.1 % to decrease fever. Additionally near 40% of the student's started antibiotics by themselves when they were ill; and during their last infection, between 12% and 27% used the same antibiotic, as previously prescribed by their

doctors. Even though, the Faculties of Dentistry and Pharmacy scored best than the remaining Faculties, they still approve antibiotics against common cold.

There is scarcity of data that how antibiotic resistance is handled at the medical and pharmacy schools and to what manner the concept of antibiotic prescription and antibiotic resistance management is incorporated in the current curriculum. Medical undergraduate curriculum in different countries presents microbiological and antimicrobial pharmacology/pharmacotherapeutics discipline core programs, according to global standards. Some studies addressed the short-term impact of incorporation of these fundamentals of rational therapeutics in medical, dental and pharmacy curriculum. Whenever individual different strategies of teaching (clinical solving problem-based [28]; or more memory-recall based; among others) programs contribute to a more accurate antibiotic use and resistance management, in later professional (short or longer-term) performance, is unknown/unstudied yet. On the other hand, survey-based studies pointed to more objective data and, in 2413 responses from students graduating in 2006-2008 (with complete undergraduate curriculum) from the 25 UK medical schools [29]– the majority (74%) felt that the amount of teaching in this area was "too little" or "far too little". In other words, only 38% felt "confident" about prescription writing and only a minority (35%) had filled in a hospital prescription chart more than three times during training. Similarly, in a multi-center randomized controlled study a short training course in pharmacotherapy designed on the basis of WHO draft manual was administered to 219 undergraduate medical students in Netherlands, Nepal, Nigeria, Australia, India, United States, and Indonesia [30]. In this study, students were taught to generate a standard pharmacotherapeutic approach to common disorders resulting in first choice drugs. The impact of the course measured in three stages showed that both the transfer effect and the retention effect were maintained at least six months after the training session in all seven medical schools, enlightening continuous formation as a powerful tool teaching antibiotic pharmacotherapeutics.

Additionally, Minen *et al* [31] lead a survey on medical students' perceptions and attitudes about antimicrobial use. Most third- and fourth-year students believed that antibiotics are overused and more than 75% would like further education on antibiotic selection, mostly during the third year of the medical curricula. Thus, the authors propose that the medical school curricula should be expanded in the third year to accommodate additional education and training on this problematic.

### 1.5. General Population

The general public is mostly unaware of the basic aspects on antibiotics modes of action and is frequently involved in inadequate behaviors, such as self-medication and not following the antibiotic treatment as prescribed. Therefore, efforts to reduce antibiotic resistance should include educating the population for the appropriate use of antibiotics.

Due to the consequences of irrational antibiotic use, several countries around the world have been assessing the knowledge and attitudes among their populations. A survey in Taiwan [32] in the general population reveled that about half of the subjects considered that physicians advice for antibiotic compliance was poor, 15.3% requested antibiotics for flu-like symptoms, 49.8% failed to comply the prescription regimens, 53.1% were not aware that antibiotic syrups should be refrigerated, 27.1% did not know how to deal with the misuse of antibiotics, 9.3% of pregnant or breast-feeding subjects were not aware of the safety of antibiotics during pregnancy and 30% did not know how to obtain information on antibiotic use. In Germany, a study conducted by Faber *et al* [33] reported that 37.6 % of the population believed that "common cold or flu can be effectively treated with antibiotics" and 8.6 % that "antibiotics should be taken when having a sore throat to prevent more serious illness".

Since the patients' expectations often influence the prescription of antibiotics by physicians, there is an urgent need for education of the general population. Thus, several educational campaigns have been developed around the world. One of them is a novel open access curriculum called GRACE (Genomics to combat Resistance against Antibiotics In Community-acquired lower respiratory tract infections in Europe) that has been developed in the context of a European Union project [34]. This project consists of an e-Learning portal containing a series of post-graduate courses and workshops addressing the issues of community-acquired lower respiratory tracts infections directed for personal learning and to support teaching activities.

A 3-year trial was conducted in Massachusetts by Huang *et al* [35], to determine the impact of a community-wide educational intervention on parental misconceptions which could influence antibiotic overprescribing. Although no significant intervention impact was observed in the population overall, there was a subgroup of parents where there was a significant intervention impact. Another group of authors [36] compared the success of two approaches of providing information to parents, an animated video and a pamphlet. The animated video proved to be highly effective in educating parents on correct antibiotic use and resulted in long-term retention.

A community-based intervention, including consumer information and education of health professionals was developed by Dollman *et al* [37], aiming to reduce antibiotic use for upper respiratory tract infections in South Australia. This intervention was successful in reducing dispensing of unnecessary antibiotics for these infections. Parsons *et al* [38], evaluated the impact of a national campaign developed in the UK National Health Service, to reduce antibiotic prescription on public attitudes and prescribing rates. However, this campaign did not appear to influence the public's attitudes on antibiotic prescribing.

 

## 2. Antibiotic quality-of-prescription and training of healthcare providers

In the United States, there is the global conception that physicians do not use antimicrobial agents properly. On one side, some studies point the problem towards a deficit in acquired based concepts – others more in a lack of recycling-programs. Demonstrating the first, in a Michigan resident physicians population-based survey [39], twenty percent answered that antibiotics were useful in the treatment of the common cold and 30% responded that they would prescribe antibiotics when the diagnosis was not certain - against all recommendations. Furthermore, only 21% knew that there was no resistance to penicillin for *Streptococcus pyogenes*.

On the side of the perception in a continuous need in recycling-programs to obtain better quality-in-prescription, there are actually diverse tools for recycling knowledge. The Network Antibiotic Therapy Test is one of the used in US and this 75-minute videotape test has shown better effect on its users comparing pre- and post-test questions, as demonstrated by Neu HC *et al* [40]. Additionally, it was possible in this study to identify some sub-groups of senior physicians/healthcare providers that were better prepared than others and they were: physicians in practice for one to five years, residents and internists.

In Europe, many other studies assessed the quality of antibiotic prescription in different levels-of-healthcare like primary health centers or, mainly, in emergency-departments (EDs) at hospitals. EDs are a very stressful and under-pressure places where external factors could hardly influence medical judgment and quality of diagnosis and related prescriptions. On the other hand, infection (as trauma) is one of the main final diagnoses performed there – and in reflex – antibiotic prescription as a major global impact. In Spain (Murcia) [41], in a total of 1.057 general adult admissions to ED, 46% were subjected to antibiotic prescription. According to local pre-established protocols, infectious disease of bacterial origin was correctly diagnosed in 40% of the cases, while diagnosis was doubtful or incorrect in the remaining 60% of cases treated with antibiotics. Here, and also against all recommendations, it seems that the context (protective medicine) maximizes the overuse of antibiotics.

Also, in Asia, one survey posing main questions and clinical scenarios about infection and antibiotics performed to rural Vietnam healthcare providers (ranging from 1-year training after medical high school/pharmacist to 5-6 years of post-graduate medical or pharmaceutical training) [42] only 27% demonstrated correct knowledge regarding the consequences of resistance. Seventy-nine per cent would use antibiotics for common colds with fever, and 21% in cases with no fever. Authors concluded in that moment that interventions to change prescribing and dispensing practices should locally be developed. In an interventional point of view, Apisarnthanarak *et al* [43] evaluated the impact of education and an antibiotic control program on antibiotic prescribing practices in a tertiary care teaching hospital in Thailand. After the intervention, there was a 24% reduction in the rate of antibiotic prescription and the incidence of inappropriate antibiotic use was significantly reduced. Consequently, rates of use of third-generation cephalosporins and glycopeptides, the incidence of infections due to methicillin-resistant *Staphylococcus aureus*, extended-spectrum betalactamase-producing *Escherichia coli* and *Klebsiella pneumonia* and third generation cephalosporin-resistant *Acinetobacter baumannii* were all significantly reduced.

Training of dental practitioners in the use of antibiotics in clinical practice is even scarcer. Through an anonymous postal questionnaire sent to National Health Service, with dental practitioners in England and Scotland, just 22.1% from 1338 responders had attended postgraduate courses in the previous 2 years of antibiotic prescribing [44]. Another study from Iran, in an 93-general dentists questionnaire responders, only 29% had fully knowledge (correct answers to all questions) of antibiotic prescriptions protocols in pulpal and periapical disease [45] with a total of 42% of general dental practitioners having full knowledge of antibiotic prescription protocols for persistent or systemic infections cases. A more relevant result from that study was that more recently general dental practitioners had slightly greater knowledge compared to ones with more experience.

In conclusion, antimicrobial resistance that has emerged in the last 50 years will continue to grow in the future. Plus, the number of multi-resistant bacteria will expand and some antibiotics are becoming already obsolete. A multi-faceted strategy will be continuously required to improve antibiotic prescribing and control the emergence of antibiotic resistance. Since many surveys demonstrate that there is insufficient knowledge on correct antibiotic use, and several educational campaigns have been proven successful, it is imperative to continue to invest in the education of students, general public and healthcare professionals, both in formal and informal contexts, as a cornerstone to fight against the antibiotic-resistance crisis.

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