

Persistence or... Resistance?

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Port J Pediatr 2019;50:9-10

DOI: <https://doi.org/10.25754/pjp.2019.16251>

Antibiotics and resistance share a common history. Penicillinase, one of the enzymes that confer resistance to bacteria against penicillin was discovered in 1940, before the introduction of the antibiotic for therapeutic purposes, by two members of Fleming's team.¹ The same occurred seven years before the clinical application of sulfonamides, when one of the specific resistance mechanisms of bacteria against this substance was identified. Resistances, therefore, exist innately in the genetic code of many microorganisms: the resistome.²

In the age of antibiotics, bacterial infection is no longer an "acceptable" cause of death. However, the use of antibiotics, often administered abusively and indiscriminately, has contributed to the selection of resistant strains that are progressively less sensitive to several (or all) currently available antibiotics. I must cite Burke: "Despite the multifactorial nature of antibiotics resistance, the central issue remains quite simple. The more you use it, the faster you lose it".³

Some microorganisms first considered to be multidrug-resistant have become even less susceptible and have become extensively drug-resistant and then pandrug-resistant (when they are non-susceptible to all agents in all antimicrobial categories): the superbugs.⁴ This reality is causing high morbidity and mortality both in the community and at the hospital level. The multidrug-resistant *Mycobacterium tuberculosis* is a paradigmatic example of this evolution, responsible for "new" epidemics in both developed and developing countries. Other agents associated with health care, such as *Campylobacter* spp, methicillin-resistant *Staphylococcus aureus*, and carbapenemase-producing *Enterobacteriaceae*, among others, are responsible for prolonged periods of hospitalisation and high costs. In some cases, these strains acquire greater virulence and transmissibility. Resistance becomes a true virulence factor.⁵

Less than half of all antibiotics produced by industry are used to treat humans. The rest are used in the agro-food industry both in the prevention and treatment of

diseases in animals and plants. Nature, acting through human hands, becomes a reservoir of multi-resistant agents that will be difficult to eradicate.⁵ Doctors seem to have little concern about this. Can we continue to ignore the impact of this practice on the development of antibiotic resistance? Should not we take some kind of action?

The scientific community has shown increasing concern about this problem in children. The number of papers indexed in PubMed on antimicrobial resistance in paediatrics quadrupled in 30 years (Fig. 1), but we continue with extremely high inappropriate prescription rates.⁶ It is, therefore, essential to publish papers like the one published in this issue, pointing out solutions to mitigate "bad prescription".⁷ On the one hand, it is noted that there are still significant differences in prescription among the various specialties but, on the other hand, a simple intervention can change the prescribing "habits". It remains to be seen how this change can be made even more effective and lasting. In emergency services where clinicians are pressured to prescribe antibiotics, viewed as the solution to all infectious diseases, what are the most effective actions to reduce (and improve) paediatric prescription?

After it was first published in 1996,⁸ the concept of the antibiotic stewardship programme has evolved, and much has been written on this subject. Currently, antibiotic stewardship programmes can be defined as a coherent set of actions which promote using antimicrobials responsibly. They encompass a set of actions aimed at the rational use of antibiotics reducing their global use, particularly of broad-spectrum antibiotics. These actions need to be planned by national and international health authorities and need to be implemented at the national, regional, and local level.⁹ In this sense, the World Health Organization offers an eight-hour free online course, whose modules include learning material on stewardship opportunities on multiple types of infections.¹⁰

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Received: 21/12/2018 | Accepted: 28/12/2018

In Portugal, the first national antimicrobial resistance programme was created in 2010, which is aimed at reducing the emergence of microorganisms resistant to antimicrobials, notably through the judicious use of antibiotics. This programme was quickly merged with the national infection control programme of the Direção Geral da Saúde in a single programme for the prevention and control of infections and resistance to antimicrobials. They addressed the same goal on two fronts, preventing infection and cross-transmission of microorganisms and avoiding the emergence of resistance.^{11,12} The report published in 2017 shows some benefits of this programme. The overall consumption of antibacterials in Portugal in primary health care remains at a high level, although below the European average (21.6 vs 21.9 daily doses per 1000 inhabitants per day, respectively), but it has been decreasing both in hospitals and in the community, along with antimicrobial resistance.⁶

The Direção Geral da Saúde provides a set of clinical guidelines (*normas de orientação clínica*) for various conditions. However, in paediatrics, only four of them guide the choice of antibiotics in specific situations (tonsillitis, acute otitis media, urinary tract infection, and community acquired pneumonia). All were published more than three years ago. This is clearly insufficient. Concerns about the costs of antibiotic stewardship programmes, the difficulties in implementing them in intensive care units (including paediatric and neonatal), as well as in the developing countries are challenges that cross the literature.

As paediatricians, we must persist in the improvement of our daily practice. We have to fight against the use of broad-spectrum antibiotics, we should use the old antibiotics that are still effective and, finally, we must resist the prescribing pressure imposed by children's carers so that antibiotic resistance does not persist.

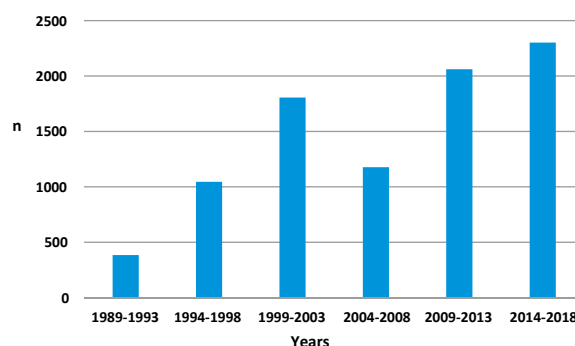


Figure 1. PubMed indexed publications on “children” and “antibiotic stewardship” in the last 30 years.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

Funding Sources

There were no external funding sources for the realization of this paper.

Acknowledgments

The author thanks to Joaquim Pinheiro and Luís Lito for reviewing the manuscript.

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