Enferm Infecc Microbiol Clin. 2018;36(5):259–261

Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

Editorial

Crisis of antibiotics: Health professionals, citizens and politicians, we are all responsible☆

La crisis de los antibióticos: profesionales sanitarios, ciudadanos y políticos, todos somos responsables

José Miguel Cisneros Herreros*, Germán Peñalva Moreno

Departamento de Enfermedades Infecciosas, Microbiología y Medicina Preventiva, Instituto de Biomedicina de Sevilla, Hospital Universitario Virgen del Rocío, Sevilla, Spain

The antibiotics crisis has approached slowly and progressively, almost unnoticed, but has now become a serious threat to public health worldwide.[1] In hospitals in developed countries such as Spain, patients are being admitted with serious infections caused by intractable multidrug resistant bacteria (MDR),[2] and up until now their dissemination has been relentless.[3] The mortality, suffering and cost of the infections produced by these bacteria are at their greatest when they are a result of sensitive bacteria. Thus, the mortality of patients with bacteraemia due to carbapenem-resistant Enterobacteriaceae is four times higher than if produced by Enterobacteriaceae susceptible to antimicrobials.[4] If things continue as they are, estimates for the situation in 2050 are terrifying, because MDR infections will produce more deaths than cancer, and a million people will die every year in Europe alone.[5]

Antibiotics are extraordinary drugs because they have saved more lives than any other group of medicinal products, and because they normally cure the illness completely within a few days. However, it is both ignored and forgotten that their ecological impact differentiates them from other drugs because they transcend the patient who receives them and affect society. They do so in such a way that, by prescribing, dispensing, or taking an antibiotic, there is a social responsibility on top of individual responsibility. This is because prescribing, dispensing or carrying out antibiotic treatment poorly increases the risk of resistant bacteria, and, with it, that of transmitting serious and even fatal infections caused by this bacteria to family, friends and the community.

Despite all these data, the antibiotics and bacterial resistance crises are not on the news, nor do they concern society.

What can we do to tackle this situation? We can apply the clinical method as we do everyday. What is the diagnosis? What is the cause? Who is responsible? And what is the most appropriate treatment?

What is the diagnosis? The diagnosis is evident. We are facing an endemic/epidemic situation, as the case may be, of MDR infections as we have never seen before.

What is the cause? Establishing the cause of this situation is more complex because there is multiple causation and the influence of each factor has not been measured. However, the main factor is that microbial resistances are a biological fact, a defence mechanism for bacteria to protect themselves from antibiotics, and the expression of a biological war between the human and bacteria species, that we are losing, because the speed at which bacteria generate resistance is greater than the speed at which we invent new antibiotics.[6] Bacteria are teaching us a genuine lesson that we should imitate, because they have succeeded in working together, exchanging information, plasmids, and resistance genes, and taking advantage of globalisation to disseminate themselves, as borders are of no significance to them. Conversely, humans have accelerated this biological process by using antibiotics excessively and without precision, each working only for him or herself without sharing data, with scant coordination and a reduction in research. This is the reason why the discovery of new molecules has slowed down.

Who is responsible? The responsibility for the antibiotics crisis is shared by health professionals, citizens and politicians, although to varying degrees. The contribution made by countries is very heterogeneous, with Spain occupying a very high position because it ranks among the highest in the world for human consumption of antibiotics.[7]

Professionals are responsible for the antibiotics crisis because the prescription and dispensation of antibiotics is something that can be greatly improved. One in every two prescriptions is inappropriate.[8] This extraordinary figure on lack of quality is a result of the disproportion that exists between the enormous volume of new knowledge about infections, bacteria, new hosts and antibiotics that appears day by day, and the time spent by prescribing physicians on continued training on antibiotics. This gap, which continues to increase, generates uncertainty in the physician, a situation that is perfect for commercial marketing to achieve a multiplier effect on prescriptions. And to all this must be added the

See related article: https://doi.org/10.1016/j.eimce.2016.10.005

☆ Please cite this article as: Cisneros Herreros JM, Peñalva Moreno G. La crisis de los antibióticos: profesionales sanitarios, ciudadanos y políticos, todos somos responsables. Enferm Infecc Microbiol Clin. 2018;36:259–261.

* Corresponding author.

E-mail address: josem.cisneros.sspa@juntadeandalucia.es (J.M. Cisneros Herreros).

anachronistic and unjustifiable absence of the infectious diseases specialisation in Spain, which impedes regulated training of infectious disease specialists and dissemination among peers of criteria for the appropriate use of this health technology that is in danger of extinction. Professionals have also been responsible inasmuch as we do not understand that there is only one way to face this enemy, and that is to work together. Fortunately, this situation is changing.[9]

There is another opportunity for improvement in the dispensing of antibiotics. During this process, which is much more than the sale of a product, the pharmacist must participate by informing the citizen about the correct use of the prescribed antibiotic, reinforcing as part of his or her advice the need to finish the prescribed course, answering any questions and also correcting any prescription errors that may occur. Unfortunately, this does not always happen. In this issue, Guinovart et al. present a study conducted in 220 pharmacies in Tarragona to find out the rate of compliance with the current law that prohibits the dispensation of antibiotics without a medical prescription, and how much advice about appropriate use of antibiotics is given to citizens. The results of the study, carried out between January 2013 and February 2014 are distressing, although consistent with the country's general situation, as the law was violated in 54% of cases.[10] These data confirm those obtained by the same group in previous studies,[11] and highlight the fact that the problem is not anecdotal but structural, and, as indicated in the title, goes well beyond being an administrative problem.

Citizens are also responsible for the antibiotics crisis in that by disregarding medical advice, changing the dose or the duration of the treatment; when they self-medicate; or playing the role of "doctors" and recommending another person take what worked for them; or by not carrying out sanitary measures, such as hand hygiene, or appropriate immunisations, which are fundamental to avoid infections and thus use antibiotics. According to the Eurobarometer, the Spanish are at the bottom of the scale in Europe when it comes to knowledge about antibiotics and infections.[12]

Politicians and central and autonomous health administrations are also responsible for the antibiotics crisis in the following ways: By failing to enforce the law which prevents the sale of antibiotics without a prescription, as the article by Guinovart et al. reveals.[10] By failing to entrust professional leadership with plans to fight against resistances and failing to equip them with the necessary resources to execute these plans.[13] By failing to include information about the prudent use of antibiotics in primary and secondary education curriculums. By failing to create an infectious diseases specialisation, as they have recently been reminded by the European Centre for Disease Prevention and Control (ECDC) after a visit to Spain to evaluate the resistance situation in the country.[14] When the seventeen autonomous communities fail to coordinate their actions in order to face up to this enemy, that to our shame does not understand territories. And, finally, by cutting research budgets.

And what is the solution to this crisis? The two fundamental measures are training and research, and we know how to apply them, but, unfortunately, at present we lack the necessary resources.

Training for citizens and professionals, remembering that we need to innovate to succeed, because what has been done so far has led us to where we are now. We know how to do it: television and PROAs (Programmes for Optimising the use of Antimicrobials). Road safety campaigns on television have been successful, and we can repeat this in schools and on the television. The PROAs, are led by microbiologists, preventionists, pharmacists and infectious diseases specialists who know how to implement them,[15] and we have demonstrated that they are improving the use of antibiotics,[16] and reducing resistances and mortality from serious infections.[17] We should therefore put them in motion without further delay. For this, institutional support with funding to pay for the time required for training, and timely incorporation of developments into diagnostic microbiology is essential.

Public and private, national and European research to increase the budget and develop at the speed at which we need new antibiotics, and also to prioritise research on the main health problems. We have a way to do it through the competitive tenders from the *Instituto de Salud Carlos III* [Carlos III Health Institute] and the Thematic Networks for Co-Operative Research in Health (RETICS) in Spain, and in Europe through public–private consortia such as the 'New Drugs for Bad Bugs' (ND4BB) programme from the 'Innovative Medicines Initiative' (IMI)[18] which already exist.

Together we can tackle the antibiotics and bacterial resistance crises with a chance of success. For this, however, it is essential that we change the current situation and that discussion and plans[19] lead to professional confidence, resources, data and results. If the current situation continues, the threat of return to the pre-antibiotic era will be at closer quarters.

References

1. World Health Organization. Available from: http://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_20-en.pdf [accessed 02.02.18].
2. World Health Organization. Global Antimicrobial Resistance Surveillance System (GLASS) report: early implementation 2016–17; 2017. Available from: http://apps.who.int/iris/bitstream/10665/259744/1/9789241513449-eng.pdf?ua=1 [accessed 02.02.18].
3. Aracil-García B, Oteo-Iglesias J, Cuevas-Lobato Ó, Lara-Fuella N, Pérez-Grajera I, Fernández-Romero S, et al., Grupo español de la European Antimicrobial Resistance Surveillance network (EARS-Net). Rapid increase in resistance to third generation cephalosporins, imipenem and co-resistance in *Klebsiella pneumoniae* from isolated from 7,140 blood-cultures (2010–2014) using EARS-Net data in Spain. Enferm Infecc Microbiol Clin. 2017;35:480–6.
4. Tamma PD, Goodman KE, Harris AD, Tekle T, Roberts A, Taiwo A, et al. Comparing the outcomes of patients with carbapenemase-producing and non-carbapenemase-producing carbapenem-resistant Enterobacteriaceae bacteremia. Clin Infect Dis. 2017;64:257–64.
5. The review on antimicrobial resistance. Charied by Jim O'Neill. Available from: https://amr-review.org/ [accessed 06.02.18].
6. World Health Organization. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics; 2017. Available from: http://www.who.int/medicines/publications/global-priority-list-antibiotic-resistant-bacteria/en/ [accessed 02.02.18].
7. Laxminarayan R, Sridhar D, Blaser M, Wang M, Woolhouse M. Achieving global. targets for antimicrobial resistance. Science. 2016;353:874–5, http://dx.doi.org/10.1126/science.aaf9286.
8. Dyar O, Beović B, Vlahović-Palčevski V, Verheij T, Pulcini C, on behalf of ESGAP (the ESCMID [European Society of Clinical Microbiology and Infectious Diseases] Study Group for Antibiotic Policies). How can we improve antibiotic prescribing in primary care? Expert Rev Anti Infect Ther. 2016;14:403–13.
9. Steering Committees of the Spanish Society of Preventive Medicine, Public Health, Hygiene (SEMPSPH), of the Spanish Society of Infectious Diseases, Clinical Microbiology (SEIMC). Joint Document of the Spanish Society of Infectious Diseases, Clinical Microbiology (SEIMC), the Spanish Society of Preventive Medicine, Public Health, Hygiene (SEMPSPH) for Combating Antimicrobial Resistance. Enferm Infecc Microbiol Clin. 2017;35:139–40 [in English, Spanish].
10. Guinovart MC, Figueras A, Llor C. Selling antimicrobials without prescription – far beyond an administrative problem. Enferm Infecc Microbiol Clin. 2018;36:290–2.
11. Llor C, Cots JM. The sale of antibiotics without prescription in pharmacies in Catalonia, Spain. Clin Infect Dis. 2009;48:1345–9.
12. European Commission. Special eurobarometer 445. Antimicrobial resistance. Available from: https://ec.europa.eu/health/amr/sites/amr/files/eb445_amr_generalfactsheet_en.pdf [accessed 06.02.18].
13. Cisneros JM, Rodríguez-Baño J. ¿Por qué es tan difícil en España conseguir financiación para luchar contra la resistencia a los antimicrobianos? Enferm Infecc Microbiol Clin. 2016;34:617–9.
14. European Centre for Disease Prevention and Control (ECDC). ECDC country visit to Spain to discuss antimicrobial resistance issues. Available from: https://ecdc.europa.eu/en/publications-data/ecdc-country-visit-spain-discuss-antimicrobial-resistance-issues [accessed 31.01.18].
15. Rodríguez-Baño J, Paño-Pardo JR, Alvarez-Rocha L, Asensio A, Calbo E, Cercenado E, et al. Programas de optimización del uso de antimicrobianos en los hospitales españoles: documento de consenso GEIH-SEIMC, SEFH y SEMPSPH. Enferm Infecc Microbiol Clin. 2012;30, e1-22–e1-23.
16. Cisneros JM, Neth O, Gil-Navarro M.V, Lepe JA, Jiménez-Parrilla F, Cordero E, et al., for the PRIOAM team. Global impact of an educational antimicrobial stewardship programme on prescribing practice in a tertiary hospital centre. Clin Microbiol Infect. 2014;20:82–8.

17. Molina J, Peñalva G, Gil-Navarro MV, Praena J, Lepe JA, Pérez-Moreno MA, et al. PRIOAM team. Long-term impact of an educational antimicrobial stewardship program on hospital-acquired candidemia and multidrug-resistant bloodstream infections: a quasi-experimental study of interrupted time-series analysis. Clin Infect Dis. 2017;65:1992–9.
18. Innovative Medicines Initiative (IMI). Available from: http://www.imi.europa.eu/ [accessed 08.02.18].
19. Agencia Española de Medicamentos y Productos Sanitarios (AEMPS). Plan Nacional Resistencia Antibióticos. Available from: https://www.aemps.gob.es/publicaciones/publica/plan-estrategico-antibioticos/home.htm [accessed 05.02.18].