

Antibiotics: Between the Tortoise and the Crab

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Editorial

Antibiotics play an important role in both the prophylaxis and treatment of infectious diseases and are a cornerstone of modern healthcare. Antibiotics are lifesaving medicines and have enabled many advances in modern medicine. However, the more they are used, the less effective they become. Thus, the issues of their availability, selection, and appropriate use are of critical importance to the global community. On the other hand, antibiotic overuse is a complex global problem that contributes to antibacterial resistance, loss of diversity in the human microbiome—which can favor the development of chronic diseases such as juvenile idiopathic arthritis, celiac disease, inflammatory bowel disease, diabetes, food allergies, and obesity—and adverse reactions [1–4], with higher rates of morbidity and mortality from resistant infections [5].

Antibiotic resistance is due to improper use. Antibiotics resistance is one of the greatest challenges of the 21st century. In the U.S., antibiotics resistance causes more than 2 million infections and 23,000 deaths per year—the equivalent of a Boeing 747 crashing each week [6].

However, it should be noted that the assessment of the public health burden of antibiotics resistance is underestimated. It is performed through estimates of clinical parameters (mainly crude morbidity and mortality) and economic indicators (direct costs, resource use, and drug spending); Most of these estimates are limited to high-income countries and extract data to fit computational models from national surveillance of clinical samples, prevalence or incidence surveys, and

retrospective cohorts. The high heterogeneity in reporting of surveillance data and the paucity of estimates of the societal effects of antimicrobial resistance (such as reduced productivity due to disease) considerably underestimate the public health burden. Therefore, overall estimates are limited in terms of generalizability of results and predictive values [7].

Antibiotics are associated with adverse events including gastrointestinal disturbances, nephrotoxicity, secondary infections (including yeast infections and potentially fatal *C. difficile*), neurological or psychiatric effects, sensory or motor disturbances, and allergic reactions [4]. Adverse reactions to antibiotics in children result in approximately 70,000 emergency department visits in the U.S. each year, according to CDC estimates. Nearly half of emergency services visits for systemic drug reactions in children under 19 years of age were due to antibiotics. And it should be noted that at least one-third of pediatric antibiotic prescriptions are unnecessary [8].

Antibiotic use is widespread. In the U.S., the likelihood of filling an antibiotic prescription at an outpatient pharmacy was 33% at 1 year, 47% at 2 years, 55% at 3 years, and 62% at 4 years [9]. Antibiotics are overprescribed in all settings [10], and although consumption is on the rise in most countries, this increase is especially in countries forming the BRICS (Brazil, Russia, India, China and South-Africa) group [11].

Furthermore, the use of nonprescription antibiotics is common in many countries, including the U.S. [12]. Self-medication with antibiotics is frequent in developing countries, with an overall prevalence of 39%, and in semi-developed countries. For example, a systematic review including 11 Middle Eastern countries reported that rates of self-medication with antibiotics ranged from 19% to 82%. Attitudes toward self-medication appear to differ among Middle Eastern countries; Gulf countries have much higher

rates compared to other Middle Eastern countries. In Saudi Arabia, for example, self-medication with antibiotics was found to range from 48% to 79% [13].

Global antibiotic consumption has increased across the board, especially during the COVID-19 pandemic. This is partly due to the widespread overuse of antibiotics in hospitalized patients with COVID-19, which may have exacerbated the spread of resistance [14,15], but also in primary care [16].

Moreover, problems of irrational antibiotic use by prescribers not only persist but have intensified following cost-cutting policies for essential medicines [17]. Global consumption of antimicrobial agents in humans is projected to increase by 30% and in animals by 67% over the next 20 years [18].

Although inappropriate antibiotic use is a global problem affecting both developed and developing countries, this problem can present itself differently in each region of the world, depending on the level of economic development and local cultures [19]. According to the UN health agency, antibiotic use ranged from 33% for patients in the Western Pacific region to 83% in the Eastern Mediterranean and African regions. Between 2020 and 2022, prescriptions decreased over time in Europe and the Americas but increased in Africa [20].

Primary care is responsible for around 80% of all antibiotic prescribing in the UK's National Health Service, and these rates likely to be similar worldwide [21]. Acute respiratory infections are the most common reason for antibiotic prescribing in primary care but often do not require antibiotics; nevertheless, these are prescribed very frequently. In most common infections treated in primary care, a considerable proportion of antibiotic prescriptions have durations that exceed those recommended in guidelines. Substantial reductions in antibiotic exposure could be achieved by aligning prescription durations with guidelines [22].

Furthermore, hospitals and doctors' surgeries are not the only places where frequent antibiotic overuse occurs: urgent care centers and retail clinics also contribute. The likelihood of antibiotic prescribing is uniformly higher in urgent care centers than in hospital emergency departments or doctors' surgeries. This applies to both diagnoses for which antibiotics are commonly indicated (e.g., pneumonia, urinary tract infections) and diagnoses for which they are rarely indicated (e.g., viral upper respiratory infections, bronchitis, influenza). Urgent care center visits for these antibiotic-inappropriate respiratory diagnoses result in antibiotic prescriptions in half of cases, compared with 25% of ED visits, 17% of physician office visits, and 14% of clinic visits [23–25].

In this context, significant reductions in antibiotic overuse do not appear possible. For example, the European Union has set targets to reduce antibiotic use, although consumption has

increased between 2019 and 2023, moving away from these goals [26,27].

What can we do? There are many causes of inappropriate antibiotic prescribing. Growing evidence shows that the reasons for inappropriate prescribing have, at least in part, psychological, social, and structural roots, meaning that antibiotic prescribing is as much a reflective behavior of a social structure as it is a scientific decision [4]. Thus, antibiotic prescribing is a complex process influenced by factors affecting healthcare providers, patients, the public, and the healthcare system [28,29].

Antibiotic overuse methods include limiting their use in the livestock industry, promoting health policies in line with antibiotic overuse standards, and adopting stricter clinical prescribing practices for antibiotics used in human therapy [30]. Many governments are trying to develop strategies to curb antibiotic overuse, which include implementing antimicrobial overuse strategies, reducing the burden of infection, improving diagnostics using point-of-care tests (including group A streptococcus rapid antigen detection test, procalcitonin assays, and PCR, with good sensitivity and specificity, and affordable cost), developing new treatments and vaccines, educational interventions for patients and healthcare professionals such as educational materials or standard treatment guides or clinical guidelines, flowcharts/diagnostic cards and simple printed information forms, and public reporting.

Although it should be noted that educational strategies for physicians do not appear to achieve complete and lasting improvements in prescribing habits. "One-size-fits-all" campaigns have shown little impact on increasing public awareness about antibiotic use [31]. Furthermore, the quality of evidence on patient-directed education is limited and has contradictory findings. Mass media campaigns have been associated with reductions in antibiotic use in observational studies, although it is difficult to evaluate causation [4,17].

In any case, it is recognized that patient and healthcare professional education, communication training, point-of-care testing, active monitoring and deferred prescribing, clinical decision support, auditing and feedback, and responsible justification are interventions that can help [4].

In short, the high, unjustified, and dangerous antibiotic prescription rates from before the onset of COVID-19 and afterward are moving very slowly, "like tortoises", toward slight improvements or even worsening, going backward "like crabs."

Antibiotic resistance is one of the greatest public health challenges today and requires a thorough consideration of strategies for addressing it. The main concern with antibiotic

overuse is antimicrobial resistance, where bacteria become immune to antibiotics. There is a risk that even simple infections will be fatal in the future, jeopardizing modern medicine. This could make common infections difficult to treat, leading to increased morbidity and mortality. Due to its impact, antimicrobial resistance requires an investment of 2 to 3.5% of the gross domestic product; if not addressed by 2050, it is estimated that there will be more than 10 million deaths per year [32].

Physicians, healthcare professionals, pharmaceutical industry, businesses, legislators, and researchers should jointly propose methods to overcome this "tortoise or crab" evolution.

Various legal mechanisms could be included, such as develop and enforce laws and guidelines for the use of antibiotics in all sectors; defining curricula in medical and veterinary schools; defining standards and mandatory guidelines for medical and vet antibiotic; reduce the use of antibiotics as growth promoters in livestock and explore alternatives for infection prevention; educate the general public; Implement infection control measures in healthcare settings; establishing a critical resistance rate; establishing; and establishing indicators to monitor the interventions; invest in the development of new antibiotics and alternative treatments; study the mechanisms of resistance, develop new diagnostic tools and treatments; innovation in alternative therapies, such as phages, antibodies, and targeted drugs to counter resistance; and monitor the spread of resistant bacteria to inform public health interventions.

If there is no "hare" (only "tortoise and crab") in this story of antibiotic overuse, let us hope that as in the closest fable "The Tortoise and the Hare", the tortoise wins the race due to his humility, patience, constancy, and perseverance.

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