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Opinion

Antimicrobial resistance, society and environment: A glocal syndemic

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1. Glocal context

When antibiotics were first introduced in 1900, it was thought that the war against microorganisms would soon be over and so was proclaimed [1]. But it was rapidly discovered that microorganisms could develop resistance to any of the antimicrobials used to combat them. This emergence and spread of antimicrobial resistance soon became a major worldwide public health emergency [2].

In this opinion, written as an essay supported by a rapid review of key conceptual literature, we argue for an understanding of antimicrobial resistance as a public health emergency, interacting syndemically with other health problems, potentiated by political, social, economic, environmental, behavioural, psychological, and biological mechanisms, with manifestations varying in different contexts, from local community to planetary levels, hence assuming characteristics of a glocal emergency.

By glocal we mean "reflecting or characterized by both local and global considerations". The local being shaped by the global, but the reverse being also valid. It implies that the increasing prominence of continental and global factors is happening simultaneously with growing importance acknowledged for local and regional levels: it points to the interrelation of the global and local contexts contributing to public health in general and, specifically, to antimicrobial resistance (https://www.britannica.com/topic/glocalization) [3].

Syndemic means that two or more health problems co-occur, interact with each other and have common societal drivers. The syndemic approach departs from the biomedical approach of diseases to diagnostically isolate, study, and treat diseases as distinct entities separate from other diseases and independent of social context [4].

2. Syndemics of climate change, malnutrition, infectious diseases, noncommunicable diseases and antimicrobial resistance

Antimicrobial resistance interacts syndemically with other public health emergencies of glocal relevance: climate change, malnutrition, infectious diseases and noncommunicable diseases in diverse environmental, political, and socioeconomic contexts. These emergencies create an ecosystem conducive to the emergence and persistence of antimicrobial resistance (Fig. 1).

3. Climate change

The planet's climate has always varied naturally. The most recent climate changes exceed this natural variability, bringing it closer to situations that can become irreversible.

Scientific evidence has clarified the main One Health effects related to climate change, mediated by the way human organizations deal with air, soil, forests and water pollution, including the oceans, global warming, extreme weather events, droughts, sea level rises and environmental degradation. Climate change interrelates with political, economic, social, demographic and environmental factors to: alter and expand the scale and patterns of animal and human migrations (professional or for leisure, voluntary or forced, spontaneous or planned);

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lead to greater consumption of animal-derived proteins associated with high emissions of greenhouse gases, pollution and acidification of the oceans, misuse of antimicrobials, environmental contamination with waste containing antimicrobial resistant organisms and the transmission of infections between different species, increasing the risk of pandemics and contributing to environmental shocks (e.g. droughts, loss of agricultural crops, lack of pasture for livestock, pests), associated with an environmentally unsustainable development [5]. The human health effects are reflected through food insecurity and malnutrition (undernutrition and obesity), adverse health effects associated with extreme weather events, poor mental health, increase in cancer, cardiovascular and respiratory diseases as well as diseases transmitted by food and vectors, other infectious diseases and several other conditions related to water, pollution and global warming, including antimicrobial resistance (Fig. 1) [6,7].

4. The global syndemic of malnutrition

A commission from *The Lancet* journal [8] has argued that a global syndemic of obesity, undernutrition and climate change has a negative impact on the health of populations on a global scale, despite the particularities of the contexts in which these conditions occur.

Widespread food insecurity and undernutrition coexist with other epidemics, namely HIV/AIDS and tuberculosis, and act as a cause and consequence and amplify the burden of these diseases. Several studies have shown that the interaction between these three conditions worsens the clinical prognosis of patients, increases their mortality, favours therapeutic failure (and the emergence of antimicrobial resistance), and leads to mental disorders [9].

The food industry and inadequate pricing policies and dietary habits play an important role in inducing increased consumption of processed proteins, sugar and sugary products, leading to metabolic changes, obesity, type 2 diabetes, high blood pressure and cardiovascular diseases. Many of these are directly associated with the emergence and spread of antimicrobial resistance [10,11].

5. The double burden of diseases

Progress in fighting poverty, in medicine and in biomedical sciences, in the access to healthcare, increasing vaccination coverage and improved sanitation, have significantly reduced mortality and morbidity related to infectious diseases, leading to a climate of optimism in the second half of the last century that these diseases were practically under control, and attention should focus on noncommunicable diseases [1].

This optimism was justified in the face of demographic (urbanization and urban connectivity, population growth, population density, changes in land use, migration, aging and changes in birth rates), epidemiological and technological transitions (advances that allow cheaper and faster travel and global trade, as well as a loss of readiness of response capacity on the part of health systems, although with an increasing availability of preventive technologies, such as vaccines, and preventive therapeutics using antibiotics) that highlighted the growing importance of noncommunicable diseases as causes of morbidity and mortality worldwide, surpassing the burden attributable to infectious diseases, even in low- and middle-income countries [12].

It turns out that noncommunicable diseases emerge associated with many of the factors that we consider determinants of the occurrence of antimicrobial resistance, namely climate change, nutritional transitions and pollution and are responsible for a significant proportion of infectious diseases [5,12]. It is also known that people with noncommunicable diseases are more susceptible to infections, both in the community and in a hospital environment [2]. Hence, as the prevalence of some of these diseases increases, namely diabetes mellitus, hypertension and respiratory diseases, the incidence of antimicrobial resistance also increases (Fig. 1) [13].

That ungrounded optimism, and the two decades of complacency that followed, including an underfunding of research on new antimicrobials that resulted in a loss of readiness to respond to infectious diseases [2,10,14], was undermined by the emergence in the early 1980s of HIV/AIDS, and associated tuberculosis, suffering successive heavy blows with the emergence and spread of antimicrobial resistance, emerging infections of animal origin (Zika, SARS, MERS, Covid-19), attribution of causality of noncommunicable diseases to infectious agents (association of peptic ulcer with *Helicobacter pylori*, of hepatic

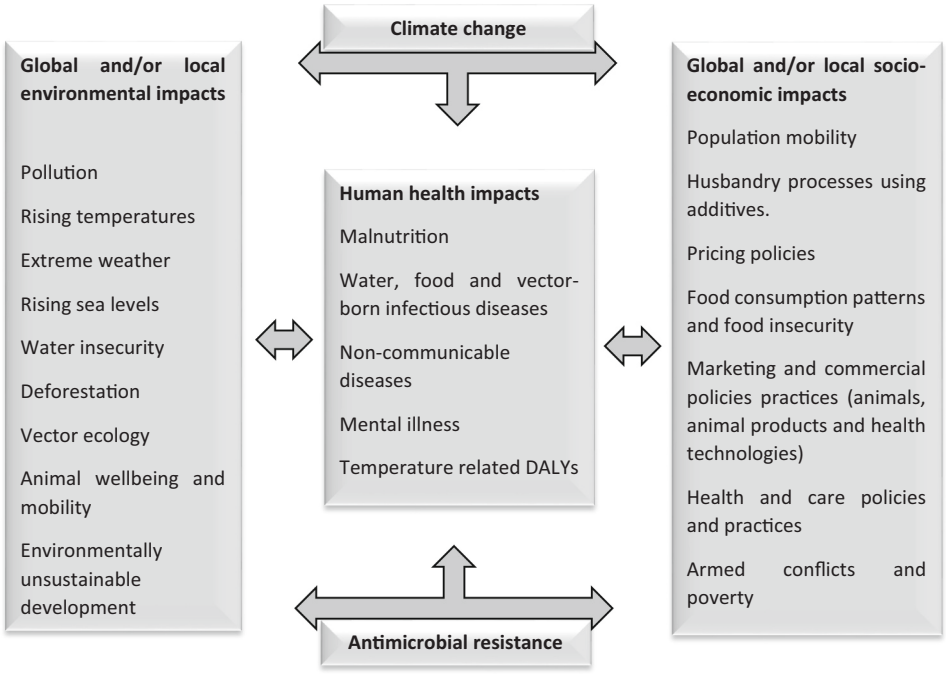

Fig. 1. Syndemics of climate change, malnutrition, infectious diseases, noncommunicable diseases and antimicrobial resistance.

cancer with hepatitis B and C viruses, of Lyme arthritis to *Borrelia burgdorferi* and of cervical cancer to the papilloma virus), re-emergence of diseases considered to be controlled by vaccination (such as measles or polio) and, more recently, public health emergency of international concern and pandemic potential (avian and swine flu, Zika, SARS, MERS, Covid-19) [12,15]. These public health emergencies, disrupt health services and programs, lead to the neglect of other infectious diseases and of noncommunicable diseases, interruption of vaccination programs and failure to treat endemic diseases such as malaria, AIDS or tuberculosis, and divert resources (financial, human and material) to respond to the emergency of the moment. These neglects, disruptions and interruptions result in an increase in the incidence of vaccine-preventable diseases, the burden of endemic diseases in post-emergency periods, worsening of noncommunicable diseases and the burden of infectious diseases and antimicrobial treatments globally. In this context, it is important to highlight the negative impact of the exponential increase in the production of hospital waste on health and the environment. Under these circumstances antimicrobial resistance gains further momentum (Fig. 1) [16].

6. Societal responses

In light of current knowledge, some of the main determinants of the antimicrobial resistance public health emergency are: demographic factors including the urbanization of poverty under poor hygiene and sanitation conditions; the unregulated misuse or overuse of antimicrobial agents in agriculture and farming, potentiating the transfer of resistant microbes to humans via the consumption of animal or vegetables that have been treated with antimicrobial agents; the impact of veterinary services or human health care and cultural practices, including self-medication; close contact between people and between them and animals; unregulated antimicrobial markets; unregulated animal markets, including for exotic animals; handling of animals and carcasses in markets and slaughterhouses without biosecurity conditions; and slaughter of animals on public roads and close to homes in precarious conditions [2]. A substantial body of recent research has also emphasized the risks of war and armed conflicts for antimicrobial resistance.

In addition to these factors, it is worth highlighting: the lack of coherent leadership of organizations with responsibility in the design and implementation of multisectoral policies aimed at the good use of antimicrobials; the marketing of defective, counterfeit or inactive antimicrobials; out of date syndromic approaches to the treatment of febrile syndromes and other infectious diseases, particularly in low- and middle-income countries in both human and veterinary clinics; inadequate management of hospital waste; poor implementation of good practices for infection prevention and control (both in the community and in health structures); limited epidemiological surveillance of both antimicrobial consumption and antimicrobial resistance; and unavailability of diagnostic means that allow the timely identification of the infectious agent and the respective antimicrobial susceptibility testing.

Finally, another barrier in the management of antimicrobial resistance programs comes from the disintegrated approach, in silos of human and animal health, without the involvement and commitment of other related areas such as the environment, industry or commerce, finance, regulation and education, among others.

These more context-dependent factors, also affected by the global determinants already mentioned, strengthen the argument for the glocal nature of antimicrobial resistance.

The multidimensionality of antimicrobial resistance determination and its synergy with concurrent or sequential epidemics or disease clusters in the most diverse populations, which exacerbate the prognosis and burden of disease argues in favour of considering it as a syndemic. The lack of consideration for this syndemic nature of antimicrobial resistance has been one of the limiting factors for the effectiveness of measures taken so far.

Arguing and envisioning antimicrobial resistance as a glocal syndemic provides international, national and local officials and institutions with conceptual tools to design effective responses, for the appropriation of these responses and of the results achieved. These responses should: reflect the ideals of "globalism" - "a belief in universal interdependence that opens new paths to prosperity" [17]; harmonize concepts such as "One Health", "Planetary Health" and Global Health [18]; acknowledge the intense interaction between the global and the local [3]; be rooted in the "here" and "now" of our everyday life, in domains such as politics, economics, culture, family and community [3]; induce a process of "mutual learning and reverse innovation" [15,19]; potentiate the achievement of the sustainable development goals reversing the current environmentally unsustainable development that compromises the ability of future generations to meet their needs locally and globally; and, ultimately, contribute for the sustainable prevention of the emergence and spread of antimicrobial resistance, and safeguard of the scarce antibiotic armament available to treat human and animal infectious diseases.

Declaration of Competing Interest

None reported.

Data availability

No data was used for the research described in the article.

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