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## Letter to the Editor

### Enhanced antibiotic resistance as a collateral COVID-19 pandemic effect?



Sir,

I have read with interest the recent editorial which alerts about the impact of coronavirus disease 2019 (COVID-19) pandemic on antimicrobial stewardship [1].

Antibiotic resistance selection/development is a multifactorial phenomenon in which all factors converge in a common trend: selective antibiotic pressure on micro-organisms [2]. Antibiotics kill susceptible bacteria, so that bacteria possessing or acquiring genes that confer resistance to those antibiotics are selected in a Darwinian manner. Furthermore, while often not considered, non-antibiotic agents, such as biocides or toxic substances, can also contribute to this pressure by favouring the selection/development of resistance to specific antibiotics [3].

Whereas COVID-19 is a viral infection, the pandemic is strongly fuelling direct antibiotic pressure on micro-organisms. It has been reported that 72% of COVID-19 patients attending hospitals have received antimicrobial agents, despite only 8% being co-infected by bacteria or fungi [3]. In addition, several antibiotics have been proposed or explored to treat COVID-19 [1,3]. In addition to the increased pressure exerted on clinical settings, this information on the use of antibiotics to treat COVID-19 is readily accessible to the general public on the Internet and in the daily news and television programmes. The combination of the fear of COVID-19 and the lack of adequate knowledge of the utility of antibiotics has a direct impact on over-the-counter access to antibiotics, especially in low- and middle-income countries with weak antibiotic control measures and limited access to health facilities. In this connection, it has been reported that 68.9% of COVID-19 patients reported the use of antibiotics (mainly azithromycin and ceftriaxone) prior to hospital admission, with a self-medication rate of 33.0% [4]. Moreover, COVID-19 has resulted in an exponential growth in biocide use worldwide, possibly inducing further indirect pressure contributing to the selection of antibiotic-resistant bacteria [3]. This picture has expanded worldwide since the beginning of 2020 and may strongly favour the selection and development of highly resistant micro-organisms, which may in turn aggravate the fragile status of patients attended in certain areas such as intensive care units. Accordingly, fatal co-infections by extremely drug-resistant

and pan-resistant micro-organisms have been reported in COVID-19 patients [5].

Antibiotic resistance has a direct impact on patient outcomes, resulting in increased mortality rates and pessimistic predictions warning of approximately 10 million deaths by 2050 [6]. Antibiotic resistance also has a strong impact on the economy. In a scenario of high levels of antibiotic resistance, the World Bank has predicted direct global healthcare costs of US\$1.2 trillion and a reduction in gross domestic product of 3.8% (US\$6.1 trillion) by 2050 [7]. In this scenario, antibiotic resistance is a formidable threat for achieving the UN Sustainable Development Goals.

Although it would be naive to think that the aforementioned direct and indirect pressures towards selection of antibiotic-resistant micro-organisms will decrease in the near future, or that adequate containment measures will be applied in a general and disciplined manner during the COVID-19 pandemic period, the current panorama requires strong reinforcement of antibiotic control measures. In this scenario, studies focused on determining the evolution of antibiotic resistance levels pre pandemic to the present are of special relevance to establish accurately the effects on therapeutic schedules for bacterial infections during the present pandemic, and are essential to design strategies to mitigate these effects. We cannot afford to further relax the control and containment measures of antimicrobial use.

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