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1 **Environmental side effects of the injudicious use of antimicrobials in the era of**
2 **COVID-19**

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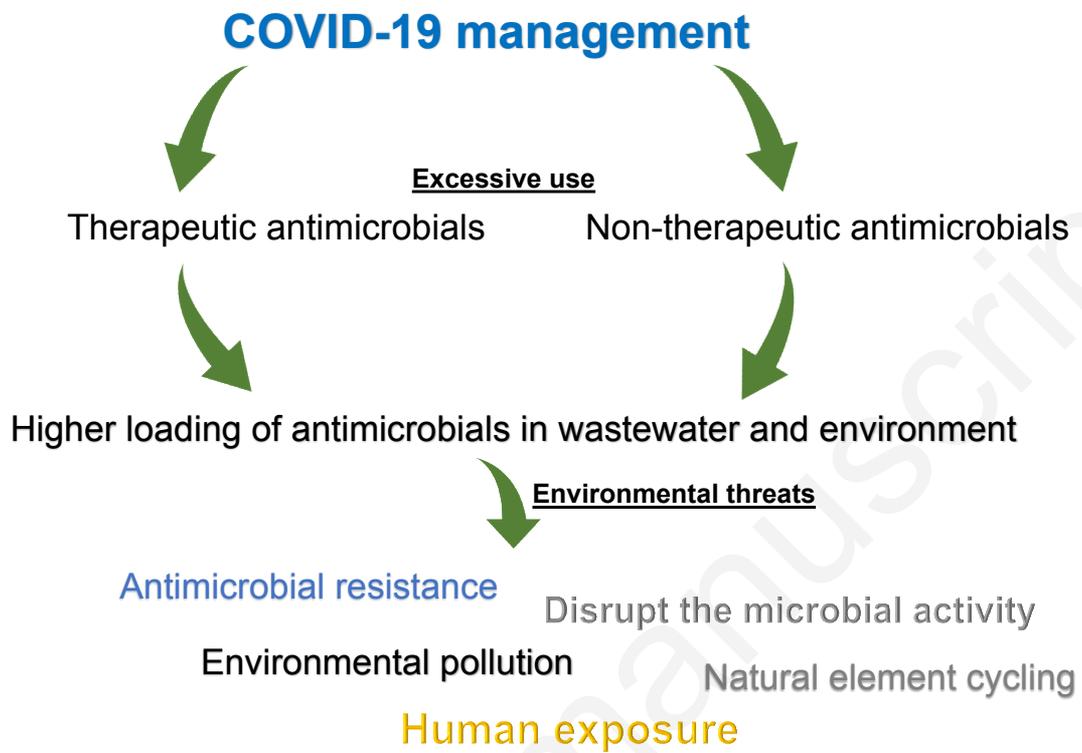
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23 **Abstract**

24 Use of antimicrobials in the treatment and prevention of COVID-19, caused by novel
25 coronavirus SARS-CoV-2, is on the rise. The increased use of antimicrobials can have
26 serious consequences on the environment. Antibiotics have had a reasonable role in
27 bacterial co-infections with regards to the management of COVID-19. However, recent
28 evidences suggest that there has been injudicious prescription of antimicrobials.
29 Moreover, a large number of people are self-medicating with antibiotics in a misguided
30 attempt to protect themselves from the virus. This practice is especially prevalent in
31 developing communities. Although common soaps are effective at inactivating
32 enveloped viruses, such as the SARS-CoV-2, use of antibacterial products bearing
33 biocides has increased during this pandemic. Since current wastewater treatment
34 techniques are unable to offer complete elimination of antibacterial biocides. These
35 compounds can then accumulate in different environmental compartments thus,
36 disrupting the functioning of native microbes. These microbes are involved in the
37 biogeochemical cycling of elements and environmental remediation. In addition, the
38 presence of antimicrobial elements in the environment can stimulate antimicrobial
39 resistance. Concrete actions are needed to address this issue. Development of an
40 antimicrobial policy specific for COVID-19 is urgently needed. Investments into
41 improving wastewater infrastructure as well as public awareness is crucial. Moreover,
42 global monitoring programs and multidisciplinary collaborations are required to
43 understand the environmental impact of this pandemics.

44

45 **Keywords:** COVID-19; Antibiotics in environment; Antibacterial soaps; Antimicrobial
46 resistance (AMR); Wastewater contamination

47

48 **1. Introduction**

49 The ongoing global pandemic of coronavirus disease 2019 (named as COVID-19) is
50 today's most significant health concern. This disease was first reported in Wuhan,
51 China in December 2019. On January 30th, 2020 the World Health Organization (WHO)
52 declared this outbreak a Public Health Emergency of International Concern and on
53 March 11th, 2020 it was characterized as a "pandemic". As of June 30, 2020, this
54 pandemic has infected >10 millions of people and caused >0.5 million deaths. There
55 is a global urgency to develop vaccines to prevent infection and create treatments for
56 this disease. As a response to this pandemic there has been rapid adaptation of
57 infection control and antimicrobial stewardship programs.

58 Use of antibiotics in the treatment and prevention of COVID-19 is rising (Rawson et
59 al., 2020a) despite it being a viral disease (caused by a novel coronavirus—SARS-
60 CoV-2). Therefore, researchers have become increasingly concerned about the in-
61 clinic impacts of COVID-19 on overall levels of antimicrobial resistance (AMR) (Hsu,
62 2020).

63 It is well recognized that excessive use of antimicrobials in medicine and agriculture
64 drives AMR which is a global threat to human, animal and environmental health
65 (Maillard et al., 2020). According to the US Center for Disease Prevention and Control
66 (2019), up to 50% of antibiotic use is not medically justified. This situation is particularly
67 worse in developing communities which have unregulated over-the-counter sales and
68 a weak water and sewage infrastructure. For example, a recent typhoid fever outbreak
69 in Pakistan has been associated to the antibiotic resistance caused by inappropriate
70 use of drugs as well as poor sanitation and contaminated water supplies (Cohen,
71 2018). Recent estimates by UN Interagency Coordination Group on Antimicrobial
72 Resistance (2019) suggest that AMR diseases are responsible for about 700,000
73 annual deaths worldwide. Without concrete action, the death toll could reach up to 10
74 million a year by 2050.

75 The intent of this communication is to highlight the consequences of COVID-19
76 management on the environment. The focus will be on the unnecessary use of
77 antibacterial drugs and personal hygiene products in the treatment and prevention of
78 COVID-19. A brief description of these issues is provided below.

79

80 **2. Excessive use of therapeutic antimicrobials**

81 Antibiotics have reasonable roles in the management of COVID-19 particularly to treat
82 suspected or confirmed bacterial co-infections (Rawson et al., 2020a). The World
83 Health Organization has advised that antibiotics should not be used for the purposes
84 of treating COVID-19 except in the presence of bacterial co-infections (WHO, 2020).
85 However, growing evidence suggest that very high proportion of COVID-19 patients
86 are being unnecessarily treated with antibiotics. Empirical antibiotics were prescribed
87 for 90% of patients despite low confirmation of secondary bacterial infections (<10%)
88 (Lai et al., 2020). Wei et al. (2020) also noted that antibiotics were started on admission
89 in 59% of COVID-19 patients despite the absence of definitive evidence of bacterial
90 coinfection in these patients. Moreover, 98% of these prescriptions were empiric.
91 Similarly, another very recent review of data from covid-19 cases, mostly from Asia,
92 reported that >70% of patients received antimicrobial treatment despite only <10%
93 having bacterial or fungal coinfections (Rawson et al., 2020a). Moreover, the same
94 study found that broad spectrum antibiotics, intended to kill a wide range of bacteria,
95 are being administered. Overuse of these antibiotics can stimulate AMR in the acute
96 care settings (Hsu, 2020; Rawson et al., 2020b). Premature hype surrounding possible
97 treatments for COVID-19 could also spike the prescription of antibiotics. This has been
98 seen for the antibiotic azithromycin in combination with the drug hydroxychloroquine
99 causing shortages in the US (Reardon, 2020). Though unmeasured, there is a
100 possibility of a large number of people taking antibiotics in misguided attempts to self-
101 medicate to protect themselves from the virus. This has the potential to be very
102 prevalent in developing communities where antibiotics can be easily obtained without

103 a prescription. A high proportion of these drugs in bioactive forms is excreted into the
104 wastewater from where they may enter in natural systems (Slater et al., 2011).
105 Release of antibiotic resistant bacteria along with large quantities of antibiotics to the
106 wastewater would spur the AMR and other unintended consequences on the
107 environment. A recent review detailing pharmaceutical pollutants in global aquatic
108 systems found antibiotics as the most-frequently detected compounds (Patel et al.,
109 2019). It should be noted that wastewater is the major hotspot for AMR as it is
110 characterized by extremely high bacterial loads coupled with subtherapeutic antibiotics
111 (Berendonk et al., 2015).

112

113 **3. Excessive use of non-therapeutic antimicrobials**

114 Proper hand hygiene has been recognized as the first line of defense against this
115 pandemic. Therefore, frequent hand-washing with plain soap and water for at least 20
116 seconds has been advised as an impactful way to prevent the spread of COVID-19
117 (WHO, 2020). Soaps contain surfactants that dissolve the lipid-bilayer, an integral part
118 of SARS-CoV-2 envelop, leading to the deactivation of virus. These deactivated viral
119 molecules are then encapsulated within micelles which are then washed away
120 (Chaudhary et al., 2020). A 20-second wash provides sufficient time for the soap
121 molecules to dissolve the lipid-bilayer of the SARS-CoV-2 virus.

122 All regular soaps available in the marketplace have the basic ingredients and chemistry
123 required to disrupt the virus (Chaudhary et al., 2020). Common soaps are effective at
124 inactivating the enveloped viruses such as the SARS-CoV-2 therefore, antibacterial
125 soaps are not required (UNESCO, 2020). The US-Food and Drug Administration
126 (FDA) has also advocated the same and moved to ban 19 antimicrobial chemicals from
127 soaps acknowledging their dangerous impacts (McNamara and Levy, 2016). Despite
128 this, use of antibacterial soaps and disinfectants has increased during this pandemic
129 as evident from sharp increase in their sale worldwide (Matters, 2020). Similar increase

130 in demand for antibacterial products/soaps was noted in the era of 2009 Swine flu
131 (Hickman, 2009; Slater et al., 2011).

132 Antibacterial products contain high amounts of biocides which result in a sharp
133 increase in their presence in wastewater. As a matter of fact, antimicrobial chemicals
134 from soaps could occur in wastewater biosolids (that are land applied as soil
135 conditioners) at multiple orders of magnitude higher than the concentrations of
136 antibiotics (McClellan and Halden, 2010). This may pose severe risks to ecosystem
137 and to the spread of AMR in the environment. In addition to the AMR, persistence of
138 these biocides in the environment is a major environmental threat that calls for suitable
139 remediation (McNamara and Levy, 2016). Moreover, presence of these biocides can
140 sabotage the wastewater treatment processes that rely on microbial activity
141 (McNamara et al., 2014). These compounds may enter into soil system disrupting the
142 functioning of native biota playing crucial roles in biogeochemical cycling of elements
143 and environmental remediation (Patel et al., 2019).

144 **4. Concluding remarks and recommendations**

145 Antibiotic stewardship principles should continue to be applied and promoted in the
146 times of COVID-19 (Huttner et al., 2020). However, development of an antimicrobial
147 policy specific for COVID-19 is urgently needed. For this, coordinated strategies at the
148 individual, health-care and policy levels are essential (Rawson et al., 2020b).

149 Since current wastewater treatment techniques are unable to offer complete
150 elimination of these compounds (Kümmerer et al., 2018; Rodriguez-Mozaz et al.,
151 2020), our daily exposure to various antibiotics, biocides and their active metabolites
152 in environment becomes inevitable. Pollutant input prevention at the production source
153 complemented with wastewater treatment is crucial to ensure water safety (Kümmerer
154 et al., 2018). However, effective input prevention in case of antimicrobials and other
155 pharmaceuticals calls for responsible use of drugs and personal care products by
156 individuals. Intensive information campaigns should be launched to educate the
157 masses about the ecological consequences of misusing antibacterial products. A large

158 portion of the population is creating the habit of regular hand washing as a result of the
159 pandemic. These practices will remain embedded even after the pandemic subsides.
160 Therefore, educating the public about the unwanted effects of
161 antimicrobial/antibacterial products during the pandemic will have the greatest
162 opportunity to instilling change. Governments should ensure that advertising material
163 and message of hygienic products are aligned with COVID-19 guidelines. We also
164 urge researchers to evaluate the environmental consequences of the response
165 measures to COVID-19 by focusing on therapeutic as well as non-therapeutic
166 antimicrobials.

167

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