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POINTS OF REFERENCE

Points of Reference are part of a regular series intended to address emerging or controversial topics of interest to the scientific community.

Impact of Potential COVID-19 Treatment on South African Water Sources Already Threatened by Pharmaceutical Pollution

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After a cluster of human pneumonia cases in Wuhan City (China) on 7 January 2020, a novel coronavirus, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was identified as the causative agent of the disease COVID-19 (World Health Organization 2020). It quickly became a global pandemic and continues to rapidly spread across the world, having infected almost 4 million confirmed cases and caused more than 265 000 deaths at time of publication, far surpassing the total cases of SARS and Middle East respiratory syndrome (MERS).

Currently, health officials are relying on behavioral interventions and quarantines to contain the COVID-19 spread until effective treatment can be developed and deployed. Scientists and researchers are actively working on lifting pressure off countries affected by the COVID-19 pandemic. The use of established drugs developed for other diseases (MERS coronavirus, human immunodeficiency virus [HIV], influenza, hepatitis C, Ebola, and malaria) is being investigated to combat the fast-moving COVID-19 spread (Saey 2020). Research has illustrated similarities between COVID-19 and HIV because host convertase, furin, has the potential to cleave the viral envelope glycoproteins of both viruses. This enhances viral fusion with host cell membranes. Furin is highly expressed in human lungs but also in small intestines and liver and might explain the multiple clinical symptoms observed for COVID-19 patients (Coutard et al. 2020). Lopinavir/ritonavir (HIV treatment), chloroquine phosphate (malaria treatment), ribavirin (broad-spectrum antiviral), arbidol (influenza virus treatment), and interferon- α (hepatitis treatment) are some of the drugs that have been included in the latest version of the "Guidelines for the Prevention, Diagnosis, and Treatment of Novel Coronavirus-Induced Pneumonia," issued by the National

Health Commission of the People's Republic of China for tentative treatment of COVID-19 (Dong et al. 2020). Chu et al. (2004) reported that 41 SARS-infected patients who had been treated with the combined therapy of lopinavir/ritonavir and ribavirin had less adverse outcomes than the 111 who were treated with ribavirin only. In a recent study, lopinavir/ritonavir was orally administered to a COVID-19 patient on day 10 of the illness. The β -coronavirus viral load decreased, and almost no coronavirus titers were detected after the first day of the treatment (Lim et al. 2020). A second-generation HIV-1 protease inhibitor, darunavir, is also being investigated as a potential treatment of COVID-19. It has been proven to inhibit SARS-CoV-2 infection in vitro (Dong et al. 2020). To produce viable results from clinical trials, several thousands of patients have to be recruited.

South Africa has the highest HIV incidence in the world, with an estimated 13.5% (7.9 million) of the population living with HIV and the acquired immune deficiency syndrome (AIDS; Statistics South Africa 2019) and 3.9 million people receiving treatment. This is more than any other country in the world. Several tons of antiretrovirals (ARVs) are prescribed every year in South Africa. In managing this scourge, South Africa's freshwaters became polluted with ARVs because these compounds are partially metabolized and not effectively removed from wastewater by wastewater-treatment plants (Swanepoel et al. 2015). Although not clear at the time of writing, people currently using ARVs may become asymptomatic carriers of SARS-CoV-2 because ARVs possess the ability to curb SARS-CoV-2 infections.

If ARVs and associated drugs such as pain medication, anti-malarials, and antibiotics provide relief and are incorporated into SARS-CoV-2 treatment programs, South Africa, which already has ARV-polluted water, can expect a dramatic increase in the amount of active pharmaceutical ingredients consumed and released to the environment as a "spike" because many more people may now consume increasing amounts of medication. The increase in antibiotics might also exacerbate another

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problem we and the world already face: antibiotic-resistant organisms. The risks posed by high levels of ARVs in the environment are not well understood. May this lead to potential antiviral resistance?

Concerns have also been raised regarding the increased use of personal protective equipment, which involves waste consisting of nondegradable face masks and wipes that end up polluting the environment. Also, chemicals such as triclosan, triclocarbon, and acrylate copolymers in sanitizers may pose environmental problems. Triclosan in water and exposed to sunlight forms dioxins—a group of compounds known to be harmful and to persist in the environment for years (Anger et al. 2013).

The South African health care system experiences enormous strain aiding people living with HIV/AIDS. Poverty, dense living conditions, inadequate sanitation in informal settlements, and customs may also contribute to the spread of COVID-19 in South Africa, producing large volumes of people requiring health care and increasing environmental pollution. This will cause many more people to require the assistance of the already embattled health care system and increase environmental pollution. It is therefore clear that the new COVID-19 disease will influence future studies regarding ARVs in water resources. It is therefore imperative to continuously monitor the occurrence of pharmaceuticals in the natural environment and to continue investigating their effects on the environment as soon as new diseases develop and spread.

Although the world at the time of writing is faced with an enormous challenge in lowering the infections and treating severe cases, we present food for thought for after we have won the war on stopping the spread of this infectious COVID-19 disease: What is the effect of this global event on the natural environment?

Data Availability Statement—Address correspondence to S. Horn (suranie.prinsloo@nwu.ac.za).

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