Commentary

Expired and unwanted pharmaceuticals: The hidden environmental legacy of COVID-19

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The World Health Organization declared the novel coronavirus disease (COVID-19) a global pandemic on 11 March 2020 (WHO 2020). Now two years into the pandemic, there have been more than 370 million confirmed cases, including 5.7 million deaths around the globe, making it the largest public health crisis in the past hundred years (WHO 2022). With the recent emergence and spread of new variants (DeSimone 2021; WHO 2021; Wang and Han 2022), global weekly new infections have surged to above 20 million cases since the beginning of 2022 (WHO 2021b). The eradication of the novel coronavirus remains a distant goal in a near future.

Therapeutic agents, most notably synthetic pharmaceuticals, play a pivotal role in managing the global public health crisis. Sales of prescription and over-the-counter drugs surged in Europe, Brazil, and North America since the onset of the pandemic (Smith and Elsayed 2020). The strong demand for pharmaceutical products persisted in regions experiencing re-emergent outbreaks with massive new infections. In India, pharmaceutical sales were boosted through the second quarter of 2021 as the 'second wave' of COVID-19 swept across the country, resulting in year-on-year growth of 134% in anti-infectives (Leo 2021). In the United States, sales of pharmaceutical drugs reported strong growth in 2020, with the largest increases recorded in antivirals (78.3%), hormones (16.7%), and diabetes (11.5%) compared with the previous year (Tichy et al. 2021). Pharmaceuticals used for treating mental disorders also experienced high demand. In December 2020, more than 42% of adults (n = 3,904) surveyed by the U.S. Census Bureau reported depression or anxiety (Abbott 2021), and 34.0%–71.5% of healthcare workers in China reported mental disorders related to COVID-19 (Moses 2020).

While concerns have been raised on the discharge of sanitary wastes containing antiviral drugs and metabolites, which are often inadequately treated at municipal wastewater treatment plants and pose threats to the receiving aquatic environments (Kumar et al., 2020; Kuroda et al., 2021), a wider and potentially more far-reaching issue has been overlooked. The enormous quantities of pharmaceuticals dispensed to or purchased by the general public that are left unused or expired throughout the COVID-19 pandemic may have created an unintended yet massive legacy of potent bioactive substances that are destined for the environment (**Fig. 1**). These include expired, unused (e.g., from recovered or deceased owners), and excess pharmaceuticals due to over-prescription, patient incompliance, panic buying, or stockpiling (i.e., hoarding). Without proper management and regulatory oversight, these may culminate an ecological disaster given their enormous quantities and prominent toxicities to aquatic and terrestrial biota.

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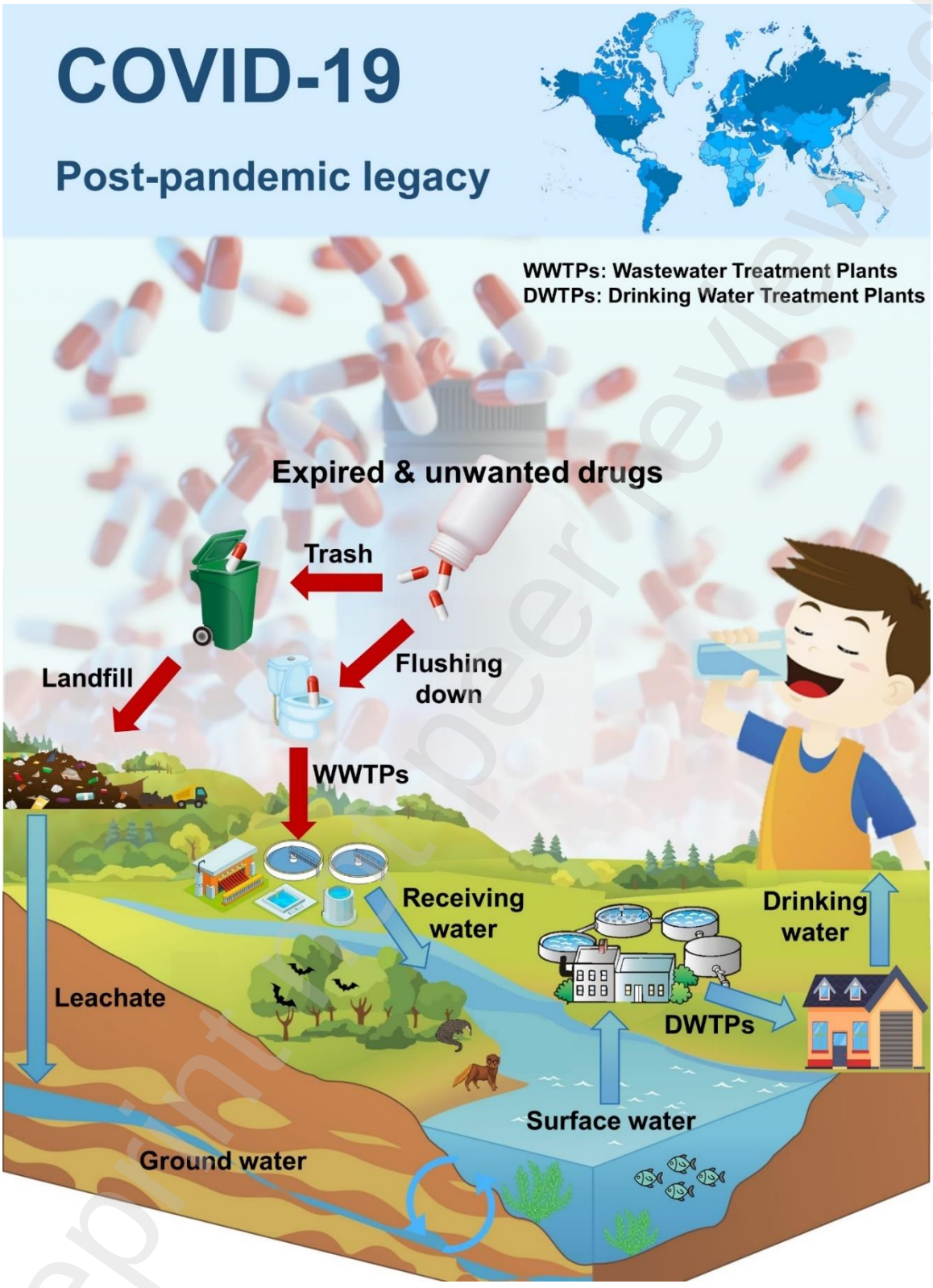

Fig. 1 An enormous quantity of pharmaceuticals dispensed to or purchased by the general public are left unused or expired throughout the novel coronavirus (COVID-19) pandemic, creating a hidden and toxic environmental legacy that requires urgent regulatory oversight for safe disposal.

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In an awakening paper, Daughton and Ternes described pharmaceuticals as 'agents of subtle change' (Daughton and Ternes 1999). Since then, numerous studies have reported their adverse effects and risks on environmental and public health. Pharmaceuticals constitute a notorious class of anthropogenic wastes with high toxicities and persistence in the environment if disposed of inappropriately (Aydın 2021; Manocha 2020; Nibamureke and Wagenaar 2021). At parts per trillion levels, those bioactive substances can elicit biological responses in aquatic or terrestrial biota (Nakada et al. 2006; Miège et al. 2009; Velpandian et al. 2018), bioaccumulate, and pose risks to humans through food and drinking water (Wee et al., 2020). Unwanted household pharmaceuticals, in particular, pose longstanding challenges to environmental regulators due to their low collection rates and improper disposal by owners (Law et al. 2015; Manocha 2020). An earlier survey of U.S. households revealed that about two-thirds of prescription drugs remained unused after being dispensed to patients (Law et al. 2015). As a result of not knowing how to properly dispose of unwanted drugs, close to one in three (29%) Americans would place their unused or expired medications in the trash, and about one in four (26%) flushed them down the drain (Stericycle 2020). Surveys in developing countries painted an even bleaker picture. A recent survey in India (n = 956) showed that the majority of the survey respondents threw their unused or expired medicines in the trash (73%) or flushed them down the drain (20%), and only 6% returned their unused medicines to local pharmacies (Manocha 2020). Similar findings were reported in China where both awareness and collection programs are lacking for managing unwanted pharmaceuticals in households (Anonymous 2022).

A significant portion of pharmaceuticals thrown into household trash ends up in municipal solid waste landfills. A recent report by the U.S. Environmental Protection Agency stated that more than 50% of municipal solid wastes were landfilled across the country (EPA 2021a). Under the selected pressure exerted by pharmaceuticals, landfills provide favorable environments for the growth of antimicrobial resistance in microbes, which can transmit antibiotic-resistant genes to other pathogens that eventually reach their surrounding outer environments through leachates or bioaerosols (Anand et al. 2021). Leakages from landfills or inappropriate management of leachates are known to cause pollution in adjacent groundwater (US GAO 2019; Yu et al. 2020). Active pharmaceutical ingredients have been detected at elevated or alarming levels in groundwater near municipal landfill sites (Velpandian et al., 2018). Meanwhile, pharmaceuticals flushed into sewers often show persistence to biological treatment processes at wastewater treatment plants, where removal efficiencies vary wildly for pharmaceutical compounds (Kuroda et al. 2021; Nakada et al. 2006; Miège et al. 2009). Reported removal rates for COVID-19 drugs ranged from less than 6% to 47–92% for antivirals and antibiotics approved for treating COVID-19 and bacterial co-infections (Kuroda et al. 2021). Much of the pharmaceutical compounds and transformational products are accumulated in the sludge (Tarazona et al. 2021), which can re-enter the environment via the application of biosolids on agricultural soils, a widespread practice in EU member states and OECD countries (ECHA 2019; OECD 2022).

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In light of their adverse effects and risks, regulatory bodies have taken actions to mitigate the inappropriate disposal of unwanted pharmaceuticals in households. While those efforts received overall positive responses, they achieved varying degrees of success in the past and now, under the impact of COVID-19, have either been hindered or come to a stall (DEA 2020). Furthermore, these programs are only available in countries and regions with stringent environmental regulations. Prior to COVID-19, Sweden was the only member state in the EU requiring that, by law, all unused drugs must be returned to local pharmacies (Meddisposal 2021; SMPA 2019). In most countries, there is no such mandate in place, and participation in these programs requires voluntary efforts (DHTGA 2019; EPA 2021b). Like other waste recycling programs (Zand and Heir 2021; U Michigan 2020), lockdowns, reduced trips, and the perceived risk of infection at public facilities during COVID-19 could severely hinder the will and actions of the public to return their unwanted pharmaceuticals to collection points. The National Prescription Take Back Day, the largest collection event for expired and unwanted prescription drugs in the U.S. that is held twice a year, was canceled on 25 April 2020 due to the ongoing COVID-19 pandemic (DEA 2020). While the event was resumed in October 2020 and 2021, the number of collection sites were among the lowest compared with those in the past five years, and the total weight of drugs (ca. 372 tons) collected in the most recent event was the lowest since April 2016 (DEA 2022).

While recent discussions focused on the mounting wastes of single-use plastics (e.g., face masks) discarded into the environment during COVID-19, a less visible and perhaps more toxic environmental legacy is the enormous amounts of excess and unwanted pharmaceuticals that are left with individual owners in common households. US House Committee reported that prescription drug spending exceeded US$500 billion a year and was growing three times faster than inflation rates even prior to the current pandemic (Kovner 2020). Around the globe, an estimated total of US$1,270 billion were spent on pharmaceuticals in 2020 (Mikulic 2021). With the active community transmission of COVID-19 and strict infection prevention and control measures in place, it will not be surprising to find that the old 'throw-in-the-trash' and 'flushing-down-the-drain' methods gained favor again in common households in the current pandemic. We call for regulators to promote the awareness of the public to keep or dispose of their unwanted pharmaceuticals in a safe manner and, where resource permitting, initiate or reinstate drug take-back programs in communities (e.g., at vaccination sites). As an emergency response, pharmaceutical companies and public health authorities can provide households with paid mail-back envelopes to collect non-liquid pharmaceutical products for centralized treatment or safe disposal (e.g., incineration with medical wastes). Meanwhile, we urge individuals not to throw their expired or unwanted pharmaceuticals into the household trash or flush them into the toilet, and when necessary to do so, do these in a safe manner by following the instructions to reduce their harm and impact on the environment (FDA 2018, 2020).

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