editorial

Wastewater monitoring comes of age

Methods for monitoring wastewater for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and emerging variants have risen to prominence during the COVID-19 pandemic. Routine monitoring of wastewater should be deployed around the world to mitigate the spread of pathogens, both old and new.

In late June 2022, wastewater surveillance in London, UK, identified poliovirus on consecutive occasions, which indicated a provisional outbreak and prompted health officials to instigate catch-up vaccination campaigns to prevent infections in the unvaccinated that can lead to paralysis in some cases (less than 5 out of every 1,000 people infected). For years, wastewater monitoring has been routinely implemented in many regions as an early warning system to identify and rapidly mitigate the spread of many pathogens, including norovirus, hepatitis viruses and salmonella — and more recently SARS-CoV-2 — in addition to poliovirus.

In the UK, the last case of wild polio was reported in 1984, and the UK was declared polio-free in 2003. By 2020, most of the world was considered by health agencies to be poliovirus-free. Such declarations belie the complexities of viral epidemiology and the global inequalities in public health. In Pakistan and Afghanistan, for example, poliovirus is still endemic, and there are numerous other countries where poliovirus routinely circulates. As long as poliovirus is found anywhere, it is a potential problem everywhere. As the recent outbreak in London highlights, even regions where disease is unlikely owing to high rates of vaccination should maintain vigilance in screening and immunization efforts.

There are two vaccines used against poliovirus today, each of which has pros and cons. The oral polio vaccine (OPV) is a live attenuated virus vaccine that is used across much of the developing world. Although the OPV prevents disease and transmission, the weakened virus can, very rarely, revert to a neurovirulent form referred to as vaccine-derived poliovirus (VDPV), which has the potential to spread and lead to infections that result in paralysis. The other vaccine, the inactivated polio vaccine (IPV), is used in higher-income countries. It confers strong protection against disease without the risk of reversion, but it does not prevent transmission. Like most high-income countries, the UK exclusively administers the IPV today. Investigation of the outbreak detected in June indicated that the virus found in sewage samples was VDPV, likely brought to London by people who had been previously vaccinated by the OPV in another country. Although such transmission does not pose a threat to anyone who is vaccinated, it puts those who are vulnerable, such as children too young to be fully immunized, at risk of infection.

One way to detect polioviruses that are spreading without causing symptoms in regions declared free of the virus is through epidemiological surveillance of wastewater. At wastewater treatment facilities, sewage from an entire region is combined, such that culturing, PCR or metagenomics-based sampling of a single wastewater sample can detect the presence of pathogens at the population level. What this approach lacks in terms of individual patient-level specificity, it makes up for by sampling large swathes of the population. Perhaps more importantly, this approach can detect the presence of circulating pathogens before patients present to clinicians with symptoms, thereby giving public-health experts time to mount defences before outbreaks occur.

Accurate detection of viruses from wastewater samples can be challenging[1]. Larger quantities of sewage sludge are typically filtered to remove debris, before viruses can be concentrated through filtration techniques, flocculation, precipitation or centrifugation. Concentration techniques can damage genomic material or cause the build-up of substances that inhibit molecular analyses like PCR. Sewage also contains an abundance of other microbes and viruses that can confound results or lead to false positives, as well as human DNA, which in turn raises concerns about privacy.

Despite these challenges, wastewater surveillance has been instrumental in controlling past outbreaks of poliovirus. Between 2013–2014, after 25 years without a case, Israel detected wild poliovirus in wastewater samples. More recently, in March 2022, poliovirus was detected in sewage samples from Jerusalem and surrounding regions. In both instances, the authorities dealt with the outbreaks with campaigns to vaccinate those not already fully immunized, which curtailed further spread of the virus. Rapid detection enabled by wastewater surveillance was crucial to stop the disease caused by poliovirus: in the 2013–2014 outbreak in Israel there were no cases of paralysis, and in 2022, there was only one case of paralysis in an unvaccinated child. Similarly, after the recent outbreak in London, increased public messaging about poliovirus and vaccination schedules in children, many of whom have fallen behind as a result of the COVID-19 pandemic, has thus far prevented any cases of paralysis.

For an ongoing and rapidly evolving pandemic such as that of COVID-19, wastewater surveillance[2,3] can be used both to detect the presence or absence of the virus, as well as the emergence and transmission of new variants that are more transmissible or immune-evading. SARS-CoV-2 variant detection necessitates pinpointing low-abundance, subtly different genomes from amidst a confounding mix of genomic material. In this issue of *Nature Microbiology*, Jahn and co-authors report a bioinformatics method named Co-Occurrence adJusted Analysis and Calling (COJAC) that detected the local spread of Alpha, Beta and Gamma variants in SARS-CoV-2 RNA amplicon sequencing from wastewater samples in two cities in Switzerland. COJAC scans for read pairs with multiple variant-specific mutations to enable detection. Similarly, reporting in *Nature*, Karthikeyan and co-authors describe an optimized approach for the concentration of viruses from wastewater, and software for variant deconvolution informed by high-resolution, long-term clinical and wastewater sequencing[4]. Their tool, called Freyja, uses a library of single-nucleotide-variant frequencies as molecular barcodes for each lineage of SARS-CoV-2 in the global phylogeny and detects variants from SARS-CoV-2 RNA amplicon sequencing. Both tools rely on databases of known variants, so neither has yet been used to detect the emergence of new variants of concern.

There are additional limitations to approaches for wastewater surveillance for SARS-CoV-2 and other pathogens. While treatment plants can report back on pathogens present in millions of people via wastewater collection, this type of surveillance is a blunt instrument. Wastewater surveillance cannot pinpoint infected individuals, transmission, or account for the interconnectedness of modern society or the mobility of the populations in any given region. Infected people could merely be passing through, unwittingly spreading a pathogen and confounding wastewater detection efforts, because the index case might have moved on from a region by the time the pathogen is detected.

The drawbacks of wastewater surveillance are offset by the foresight that approaches such as COJAC and Freyja provide. Both methods detected outbreaks more than two weeks before the first positive clinical tests were reported. Another advantage is that wastewater surveillance is more economical than clinical testing: it effectively screens large numbers of people in just a few samples, and doesn't require clinician-led sampling. Wastewater surveillance is not just for viruses. It can be used to detect other microbial pathogens[5], antimicrobial resistance[6], or chemical water contaminants[7]. Furthermore, these tools are not limited to wastewater treatment facilities, and could be applied to samples from other settings such as transport hubs, hospitals, schools, workplaces and leisure facilities[8]. Apart from public-health applications, the data generated by wastewater surveillance might be useful for researchers investigating community trends and the efficacy of health policies and non-pharmaceutical interventions.

To enable implementation of public-health measures as soon as they are needed, and to intervene against the spread of infectious disease, any strategy that enables economical, early and efficient detection is key, and these methods seem to fit the bill. Wastewater surveillance is poised to become embedded in public-health strategies across the globe — at least 55 countries[9] track SARS-CoV-2 in wastewater already — but it needs to be shown to be practical and informative in both high- and low-income countries. This is especially true for regions without ready access to COVID-19 vaccines, so as to prevent against new waves of variant infection, because unchecked transmission anywhere is a problem everywhere. ❐

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References

1. Farkas, K., Hillary, L. S., Malham, S. K., McDonald, J. E. & Jones, D. L. *Curr. Opin. Environ. Sci. Health* **17**, 14–20 (2020).
2. Vogel, G. *Science* https://doi.org/10.1126/science.adb1932 (2022).
3. Schmidt, C. *Nat. Biotechnol.* **38**, 917–920 (2020).
4. Karthikeyan, S. et al. *Nature* https://doi.org/10.1038/s41586-022-05049-6 (2022).
5. Ko, K. K. K., Chng, K. R. & Nagarajan, N. *Nat. Microbiol.* **7**, 486–496 (2022).
6. Hendriksen, R. S. et al. *Nat. Commun.* **10**, 1124 (2019).
7. Jung, J. K. et al. *Nat. Biotechnol.* **38**, 1451–1459 (2020).
8. Nordahl Petersen, T. et al. *Sci. Rep.* **5**, 11444 (2015).
9. Ahmed, W. et al. *Sci. Total Environ.* **805**, 149877 (2022).