Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
At the end of February, 2021, the state government of Victoria, Australia, issued a warning indicating that fragments of SARS-CoV-2, the novel coronavirus that causes COVID-19, had been detected in the wastewater from the western suburbs of Melbourne. As the state only had 15 known active cases of the disease at that time, most of which were linked to the outbreak in a quarantine hotel earlier in the month, the unexpected finding led to a call for increased alertness. While it is possible that the virus material was shed by a recovering patient no longer considered infectious, the state authorities announced that “anyone who has been in these suburbs and has any symptoms of COVID-19 from 20 to 22 February is urged to get tested”.

Meanwhile in France, as the government there was desperately trying to keep infection rates under control and avoid a third nationwide lockdown, cities like Orléans turned to their water facilities to find out their fate and to be able to fine-tune their local and regional responses and testing efforts. French authorities were also on the lookout for those “variants of concern” that threatened to undermine the measures taken and the vaccine efforts.

Variants are also being sought in the sewage in many places in the USA, where the world’s worst death toll from the pandemic is still increasing and the risk of mutations is biggest simply because the virus has had so many replication cycles in which mutations may happen. Wastewater analyses in the US state of Missouri, for instance, found traces of the ‘UK’ variant, B.1.1.7, in more than a dozen locations by the end of February, although only one clinical case involving this variant had been reported by that time.

Thus, whether the COVID-19 pandemic is suppressed successfully, hovering on the brink of resurgence, or running out of control, the past few months have shown that there is valuable epidemiological information to be found in sewage.

**European advances**

Wastewater is already being monitored for SARS-CoV-2 in many places around the world. While there is no indication that the disease can be transmitted via the water infrastructure, at least half of the patients affected are found to shed virus material with their stools, making sewage a valuable data source. Researchers at the University of California, Merced, USA, are maintaining a global data summary site covering, as of March 3, updates from 50 countries and more than 1,300 monitoring sites (https://arcg.is/1aummW or via @COVIDPoops19 on Twitter).

However, different countries move at very different speeds in recognising the usefulness of the method in setting policy. Thus, when experts from five European countries connected in February for a virtual conference on the topic, hosted by Technologieiland Hessen at Wiesbaden, Germany, all agreed on the usefulness of the method, but only the delegation from the Netherlands could report that wastewater results were already being used to inform the public and guide policy at the national level. Switzerland was at that point moving towards using the data in determining the reproduction number (R value) of the virus, while, in Germany, the UK and Sweden, efforts remained more limited to specific locations and had not become a visible part of the official response yet.

In the UK, for instance, Andrew Singer from the Centre for Ecology and Hydrology at Wallingford leads a project that was launched in July 2020 aiming to establish wastewater monitoring as a tool in the fight against the pandemic. He reported that monitoring capacity is being increased to cover up to 80% of the population in England. Currently, samples for coronavirus analyses are taken several times a week from the influx of 44 water treatment plants in England, 28 sites in Scotland and 21 in Wales. Separate, specific monitoring projects around the world are demonstrating that the detection of SARS-CoV-2 in wastewater can uncover both incidence trends and new variants before they become apparent in the clinic. A more systematic use of the methodology could also help fight other diseases and avert pandemics in the future. Michael Gross reports.

**Water works:** Samples taken from the raw sewage entering water treatment plants can be used to monitor the spread of infectious diseases, including COVID-19. The image shows aeration tanks at a water treatment plant in Upper Providence, Pennsylvania, USA. (Photo: Montgomery County Planning Commission/Flickr (CC BY-SA 2.0).)
projects of near-source tracking were focused on sensitive locations, including schools, prisons and care homes.

“Initially, the sampling efforts were run as a proof of principle, but now these work strands are transitioning into a dataset that directly helps to inform public health action, among other datasets that are collected,” Singer explains. “Sequencing is a very important part of the sewage surveillance effort. Wastewater offers insight into the changing prevalence of different variants within a location and the wider range of variants circulating in a population from a single sewage sample. We can monitor the prevalence of variations within a location and assess the movement of the variants across the country. This is a very new capacity and will grow significantly in the coming weeks.”

Javier Martin from the National Institute for Biological Standards and Control (NIBSC), Potters Bar, UK, and colleagues published the first scientific assessment of the UK effort in October (Viruses (2020) 12, 1144), and an official report was presented to the UK government’s Scientific Advisory Group for Emergencies (SAGE) in December. Martin and colleagues concluded in their paper: “Environmental surveillance could be used for the early detection of peaks in virus transmission for public health interventions to be timely implemented”.

The events in the following months suggest, however, that this didn’t happen, resulting in January becoming the deadliest month in the UK pandemic yet.

In the Netherlands, projects to monitor wastewater for SARS-CoV-2 started as early as February 2020, even before the first cases were diagnosed in the country. David Calderón from Delft University of Technology told the conference about the analytical methodology developed there, which includes a concentration step using electronegative membranes. Concentrated viral RNA is transcribed to cDNA for PCR tests. The Delft laboratory tests simultaneously target three different genes of the coronavirus, to avoid missing any variants that may have mutated in a site required for recognition by one of the PCR primers.

A year into the effort, the method is now well established to the extent that the country’s official coronavirus dashboard, which is freely accessible online, includes a map updated weekly with details of SARS-CoV-2 in the wastewater of different regions. Experts in the Netherlands have been able to monitor the success of policy changes such as lockdowns and reopenings much closer to real time than clinical data would allow. They have also been able to apply sequencing technology to identify new variants from the wastewater samples before these were detected in patients.

Improving methods
Detection of SARS-CoV-2 in wastewater is currently a qualitative assay based on the same PCR technology as the clinical tests. Given the lack of understanding of how much viral material patients shed and how that amount changes over the course of their infection, results cannot pin down in absolute terms how many people are infected.

However, with improved standardisation of sample preparation and testing methods, and the use of correlation with clinical data as a tool to normalise results, one can imagine that at least rough quantitative results based on population statistics should become a possibility.

In New Zealand, where the wastewater surveillance method is used to watch out for any cases slipping through the tight net of quarantine measures, experts have estimated that the detection limit for the mild cases that might escape medical attention might be on the order of 10 cases per 100,000 population.

An increasing number of data management tools is also becoming available to connect wastewater data to other types of information, such as clinical and contact-tracing data. For instance, the ‘Surveillance Outbreak Response Management and Analysis System’, or SORMAS for short (https://sormas.org/), originally developed at the Helmholtz Centre for Infection Research at Braunschweig, Germany, for the management of contacts during outbreaks of Ebola in Africa, has already been adapted for the use against COVID-19 with the addition of a new module for the specifics of this disease. This system saw early use in Ghana and Nigeria, even before these countries were touched by the pandemic, and is now also being set up in European countries including France, Germany and Switzerland.

Other tools address the complexities inherent in the network structures of urban sewers, as well as the phylogenetics of the virus variants. With the sheer scale of the pandemic and the number of parameters involved, epidemiological monitoring is also becoming a major challenge in terms of the management of big data.
Polio and parasites

Before the COVID-19 pandemic, the main success story of wastewater-based epidemiology was its contribution, alongside the successful vaccination programme, towards the WHO effort to eradicate poliomyelitis (polio). The WHO reports that case numbers have declined by more than three orders of magnitude, from an estimated 350,000 cases in more than 125 endemic countries in 1988 to 175 reported cases in 2019. Of three known poliovirus types, two have been declared extinct, while the surviving type 1 still affects two countries, namely Pakistan and Afghanistan.

In countries where eradication is considered successful, surveillance of wastewater can help to confirm the absence of the disease and could give an early warning in case it might return. Following an outbreak that happened in Israel in 2013 and led to a vaccination campaign using attenuated live virus vaccines, Yakir Berchenko from the Ben-Gurion University of the Negev at Beer-Sheva, Israel, and colleagues used the opportunity to calibrate the wastewater findings against the known amounts of virus dispatched in the vaccination programme (Sci. Transl. Med. (2017) 9, eaaf6786). The authors conclude that their quantitative correlations between these datasets can help both with certifying the absence of infection cases and with containment efforts where they are needed.

Other waterborne pathogens that warrant surveillance of wastewater include bacteria like Vibrio cholerae, viruses like Norovirus and Adenovirus species, and protozoan parasites such as Cryptosporidium and Giardia, which cause diarrhoea. Una Ryan at Murdoch University at Perth, Australia, and colleagues recently reviewed the monitoring efforts against the protozoa in the context of the SARS-CoV-2 surveillance (Parasitol. Res. (2021) https://doi.org/10.1007/s00436-020-07023-5).

The authors call for increased integration of wastewater monitoring with other methods, including clinical testing, case reporting and public health campaigns. They note that good efforts have been made in this direction in the fight against the COVID-19 pandemic, concluding that: “Based on this precedent, similar collaboration in relation to the monitoring of protozoan and other pathogens in wastewater is highly desirable”.

Much of the work on waterborne pathogens in sewage is motivated by the fear of transmission via water provision, especially in the developing world where availability of clean drinking water is a major factor determining public health.

By contrast, wealthier countries have also found time to scrutinise their water systems for chemicals that are neither infectious nor particularly polluting, such as residues of illicit drugs, pharmaceuticals and care products, and for alcohol.

Phong Thai at the University of Queensland in Brisbane, Australia, and colleagues have recently improved methods to quantify population-wide estimates of alcohol consumption by calibrating ethyl sulphate measurements obtained (before the pandemic) from the National Wastewater Drug Monitoring Program and covering more than half of the Australian population against sales statistics (Environ. Sci. Technol. Lett. (2021) https://doi.org/10.1021/acs.estlett.1c00065).

Preventing future pandemics

With the intense focus now placed on wastewater-based epidemiology in the fight against the COVID-19 pandemic, it is to be hoped that standards and methods now optimised may help to stop future outbreaks of an infectious disease from becoming a global pandemic.

The genome sequence of SARS-CoV-2 was released on January 10, and this immediately led to the development of PCR tests capable of detecting the virus. Initially, most countries only used these tests for people with symptoms seeking medical help. Countries like Italy were overwhelmed by the first wave of the epidemic, as the spread through carriers with mild or no symptoms was recognised much too late.

If the tests had been used on wastewater systematically, local clusters could have been contained efficiently, much like Australia is currently using them to spot any new infections arising.

Given the increasing disturbance of wildlife habitat by human activities, further outbreaks of zoonotic diseases caused by coronaviruses and other pathogens are to be expected (Curr. Biol. (2020) 30, R191–R194). Sampling sewage may not appear to be the most glamorous application of modern science, but in future zoonotic disease outbreaks its systematic use can save us a lot of trouble.

Michael Gross is a science writer based at Oxford. He can be contacted via his web page at www.michaelgross.co.uk