Spate of polio outbreaks worldwide puts scientists on alert

Cases of paralysis in the United States and Israel suggest that vaccine-derived poliovirus has infected many people.

EZRA ACAYAN/GETTY

The virus in live oral polio vaccine occasionally mutates into a dangerous infectious form.

The discovery of poliovirus in New York state, London and Jerusalem this year has taken many by surprise — but public-health researchers fighting to eradicate the disease say it was only a matter of time.

"No country in the world is immune to the effects of polio," says Zulfiqar Bhutta, a global-health researcher at the Aga Khan University in Karachi, Pakistan. "It's all interconnected."

The virus found in these regions is derived from an oral polio vaccine used in some countries. So far, only two cases of polio-related paralysis have been reported, in Jerusalem in February and New York in June (R. Link-Gelles *et al. Morb. Mortal. Wkly Rep.* **71**, 1065–1068; 2022). The New York infection was the first such US case in nearly a decade. But wastewater samples in all three areas suggest that the virus is circulating more widely.

Polio causes irreversible paralysis in less than one in 200 of the susceptible people it infects. So the cases of paralysis suggest that many other people in these regions have been infected, says Walter Orenstein, who studies infectious diseases at Emory University in Atlanta, Georgia. "Cases like that are just the tip of the iceberg," he says. "It's very concerning."

Nature talked to researchers about the scale of the outbreak, and what can be done to stop it.

Why are these outbreaks happening?

Wild poliovirus circulates in only two countries — Afghanistan and Pakistan — where this year nine cases had been reported by June.

But vaccine-derived poliovirus flares up periodically elsewhere, particularly in Africa and Asia. These cases come from a widely used oral vaccine that contains live, weakened virus that sometimes mutates into a dangerous form capable of infecting the nervous system.

Neither the United States nor the United Kingdom use that vaccine, opting instead for an injectable vaccine containing inactivated virus. This vaccine can keep the virus from infecting the nervous system, but it is not as effective as the oral virus at reducing viral shedding and halting transmission, says Raul Andino-Pavlovsky, a microbiologist at the University of California, San Francisco.

High polio vaccination rates in the United Kingdom, Israel and the United States mean that most children will be spared the virus's worst effects (about 94% of US 5- and 6-year-olds are vaccinated). But unvaccinated people are vulnerable to the illness.

"This virus is very, very good at finding unvaccinated individuals," says Orenstein. In the 1990s, a poliovirus outbreak in the Netherlands established a foothold in a community with a relatively low vaccination rate, despite the country's overall vaccination coverage of more than 90%, says Oliver Rosenbauer, a spokesperson for the Global Polio Eradication Initiative of the World Health Organization (WHO) in Geneva, Switzerland. The outbreak resulted in 2 deaths and 59 cases of paralysis, and occurred 14 years after the country's last case of endemic polio.

Has poliovirus spread beyond the regions where it was first identified?

Wastewater surveillance for polio is rare in rich countries; the United Kingdom routinely monitors sewage for the disease only in London and Glasgow. And New York began testing waste water in July, after officials learnt about the case of polio-related paralysis.

So it's unclear how far the virus might have spread. But there is reason to hope that it hasn't gone far: in London, which has been detecting poliovirus in sewage since February, the virus seems to have remained concentrated in the city's north and east, and there have been no reports of polio-related paralysis. "It appears to be fairly localized, even within London," says infectious-disease epidemiologist Nicholas Grassly at Imperial College London.

However, In New York, the virus has been detected in two counties as well as New York City, a geographical spread that is "very concerning", says Orenstein. "It suggests we have had substantial transmission."

The US Centers for Disease Control and Prevention (CDC) will prioritize wastewater surveillance for polio in under-vaccinated communities linked to the paralysis case. "Poliovirus testing from wastewater samples is very labour- and resource-intensive," a CDC spokesperson told *Nature*. But surveillance systems set up to monitor the coronavirus SARS-CoV-2 are working to provide support, she added.

Can the outbreaks be contained?

The United States, Israel and the United Kingdom are all boosting vaccination efforts,

which should fill gaps created during the COVID-19 pandemic. This includes an ambitious effort to vaccinate all one-to-nine-year-olds in London.

This strategy should nip the outbreaks in the bud, says Grassly. But the campaigns in London and New York will use injectable vaccine, so they might not stop virus transmission.

If, in six months or so, wastewater testing suggests that poliovirus has continued to spread, it might be necessary to look at other options, he says. For example, in 2020, the WHO listed a new oral polio vaccine for emergency use.

This vaccine contains weakened poliovirus. But researchers used knowledge of the virus's genome — including how an error-prone enzyme involved in replicating the genome can generate genetic changes — to create a suite of mutations that keep the virus from regaining its ability to infect the nervous system. "It's like putting the virus in an evolutionary cage," says Andino-Pavlovsky, who helped to design the vaccine.

That vaccine has not yet undergone large-scale human testing, and has not been approved by UK or US regulators. But more than 100 million people have received it, says Andino-Pavlovsky, with no signs of vaccine-derived poliovirus emerging.

What is the status of polio outbreaks elsewhere?

Outbreaks in wealthy countries get lots of attention, says Rosenbauer. "But over the past 20 years, we've had many, many serious outbreaks around the world in developing countries."

Rosenbauer says there are encouraging signs that the battle to eradicate polio is making progress, despite the disruption caused by COVID-19. Outbreaks in Yemen and a few countries in Africa are still active, he says, but their range is shrinking.

In places where there is armed conflict, such as areas of Afghanistan and Yemen, vaccination is difficult. "We need the political will to implement a plan to reach all the children in challenging areas," he says. Otherwise, "the disease will come back globally".

By Heidi Ledford

News explainer

ANCIENT TOOTH DNA REVEALS HOW HERPES VIRUS EVOLVED

Teeth from long-dead people and animals are divulging the history of modern-day pathogens.

By Freda Kreier

Ancient DNA extracted from the teeth of humans who lived long ago is yielding new information about pathogens past and present.

Researchers have uncovered and sequenced ancient herpes genomes for the first time, from the teeth of long-dead Europeans. The strain of herpes virus that causes lip sores in people today — called HSV-1 — was once thought to have emerged in Africa more than 50,000 years ago. But data published in *Science Advances* on 27 July[1] indicate that it originated around 5,000 years ago during the Bronze Age.

The findings hint that changing cultural practices during the Bronze Age — including the emergence of romantic kissing — could have factored into HSV-1's meteoric rise.

This and other studies on tooth-extracted DNA are leading to surprising insights into of our shared history with disease, says Christiana Scheib, an archaeomolecular biologist at the University of Tartu in Estonia. "All of the pathogens we have today were once novel infections," she says. "It's important to study ancient DNA so we can understand these past experiences and keep future generations safe from epidemics."

Teeth are treasure chests for ancient DNA because of their ability to protect biological molecules from degradation. In the past decade, scientists have used increasingly powerful sequencing technologies to reconstruct the genomes of long-dead humans and animals — the oldest being a mammoth that died 1.6 million years ago — using DNA found in their teeth.

In the process, they have also sorted through the genetic material of bacteria and viruses preserved in teeth. Molars, incisors and the like have blood vessels in their roots, so when a person or animal dies, these bones become repositories for whatever pathogens were moving through their bloodstream at the time of death.

The realization that teeth are caches for pathogen DNA has opened the study of ancient diseases to "a completely different kind of knowledge than what we could have accessed before", says Martin Sikora, an ancient-genomics researcher at the University of Copenhagen.

DR BARBARA VESELKA

Researchers found herpes DNA in the teeth of an eighteenth-century man.

This genetic information has provided researchers with molecular evidence to pinpoint when and where pathogens were at a given time, Sikora says. In 2013, scientists used DNA extracted from teeth to confirm that the Justinian plague, which swept across the Mediterranean and northern Europe in the sixth century, was the first major outbreak of the plague bacterium *Yersinia pestis*[2]. And in June, a different group of researchers reported that the strain of *Y. pestis* that launched the Black Death — which killed upwards of 60% of people in some parts of Eurasia in the fourteenth century — probably evolved in modern-day Kyrgyzstan, on the basis of DNA from teeth found in that region[3].

Sifting through remains

Studying ancient DNA can also help researchers to learn about the history of less deadly pathogens, such as the strain of oral herpes that currently infects about two-thirds of people under 50 globally. In 2016, Scheib and her colleagues were looking for traces of *Y. pestis* in the 600-year-old tooth of a teenager — who died in the medieval St John's Hospital in Cambridgeshire, UK — when they found genetic sequences that seemed to match those of HSV-1.

Until that point, "there was no published ancient herpes DNA at all", she says. The oldest herpes genome on record had been isolated from someone living in New York in 1925. The