### The world this week

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The monkeypox virus (shown here in a coloured transmission electron micrograph) is closely related to the smallpox virus.

# MONKEYPOX GOES GLOBAL: WHY SCIENTISTS ARE ON THE ALERT

Researchers are trying to understand why the virus, a less-lethal relative of smallpox, has cropped up in so many populations around the world.

#### By Max Kozlov

s *Nature* went to press, almost 600 confirmed or suspected cases of monkeypox, a rare viral disease seldom detected outside Africa, had been reported in at least 30 non-African countries in the course of a few weeks. The emergence of the virus in separate populations around the world, in locations where it doesn't usually appear, has alarmed scientists – and sent them racing for answers.

"It's eye-opening to see this kind of spread," says Anne Rimoin, an epidemiologist at the

University of California, Los Angeles, who has studied monkeypox in the Democratic Republic of the Congo for more than a decade.

The virus is called monkeypox because researchers first detected it in laboratory monkeys in 1958, but it is thought to transmit to people from wild animals such as rodents, or from other infected people. In an average year, a few thousand cases occur in Africa, typically in the western and central parts of the continent. But cases outside Africa have previously been limited to a handful that were associated with travel to Africa or with the importation of infected animals. The number of cases detected outside of Africa in the past few weeks alone has already surpassed the total number detected outside the continent since 1970, when the virus was first found to cause disease in humans. This rapid spread is what has put scientists on high alert.

But monkeypox is no SARS-CoV-2, the coronavirus responsible for the COVID-19 pandemic, says Jay Hooper, a virologist at the US Army Medical Research Institute of Infectious Diseases in Fort Detrick, Maryland. It doesn't transmit from person to person as readily, and because it is related to the smallpox virus, there are already treatments and vaccines on

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hand to curb its spread. So although scientists are concerned – because any new viral behaviour is worrying – they are not panicking.

Unlike SARS-CoV-2, which spreads through tiny airborne droplets called aerosols, monkeypox is thought to spread from close contact with bodily fluids, such as saliva from coughing. That means a person with monkeypox is likely to infect many fewer close contacts than is someone with SARS-CoV-2, Hooper says. Both viruses can cause influenza-like symptoms, but monkeypox also triggers enlarged lymph nodes and eventually causes distinctive fluid-filled lesions on the face, hands and feet. Most people recover from monkeypox in a few weeks, without treatment.

On 19 May, researchers in Portugal uploaded the first draft genome of the monkeypox virus that was detected there to an online database, and other genomes have since followed. Gustavo Palacios, a virologist at the Icahn School of Medicine at Mount Sinai in New York City, emphasizes that more data are still needed before many conclusions can be drawn.

What researchers can tell from these preliminary genetic data is that the strain of the monkeypox virus detected so far is related to a viral strain predominantly found in West Africa. This strain causes milder disease and has a lower death rate – about 1% in poor rural populations – compared with the one that circulates in Central Africa (which can have a death rate of up to 10%). But exactly how much the strain causing the current outbreaks differs from the one in West Africa – and whether the cases popping up in various countries are linked to one another – remains unknown.

Answers to those questions could help researchers to determine whether the sudden uptick in cases stems from a mutation that allows monkeypox to transmit more readily than it did in the past, and whether each of the outbreaks traces back to a single origin, says Raina MacIntvre, an infectious-diseases epidemiologist at the University of New South Wales in Sydney, Australia. Unlike SARS-CoV-2, a rapidly evolving RNA virus whose variants have regularly eluded immunity from vaccines and previous infection, monkeypox is caused by a relatively large DNA virus. DNA viruses are better at detecting and repairing mutations than are RNA viruses, which means it's unlikely that the monkeypox virus has suddenly mutated to become adept at human-to-human transmission, MacIntyre says.

#### 'Deeply concerning'

Still, for monkeypox to be detected in people with no apparent connection to one another suggests that the virus might have been spreading silently – a fact that Andrea McCollum, an epidemiologist who heads the poxvirus team at the US Centers for Disease Control and Prevention in Atlanta, Georgia, calls "deeply concerning". Unlike SARS-CoV-2, monkeypox rarely goes unnoticed when it infects a person, in part because of the skin lesions it causes. If monkeypox could spread asymptomatically, it would be especially troubling, because that would make the virus harder to track, McCollum says.

Another puzzle is why almost all of the case clusters include men aged 20–50, many of whom are men who have sex with men (MSM). Although monkeypox isn't known to be sexually transmitted, sexual activity certainly constitutes close contact, Rimoin says. The most likely explanation for this unexpected pattern of transmission, MacIntyre says, is that the virus was coincidentally introduced into an MSM community, and has continued circulating there. Scientists will have a better idea of the origin of the outbreaks and the risk factors for infection once an epidemiological investigation, which could take weeks, is complete.

#### **Containment strategies**

Scientists have been keeping an eye on monkeypox ever since an eradication campaign for smallpox wound down in the 1970s. Once smallpox was no longer a threat, thanks to worldwide vaccinations, public-health officials stopped recommending smallpox inoculation – which also kept monkeypox at bay. With each year that has passed since smallpox's eradication, the population with weakened or no immunity to these viruses has grown, MacIntyre says.

There have been a few monkeypox outbreaks since then. The Democratic Republic of the Congo, for example, has been grappling with the virus for decades, and Nigeria has been experiencing a large outbreak, with over 500 suspected and more than 200 confirmed cases, since 2017, when the country reported its first case in some 40 years.

Public-health authorities are not powerless against monkeypox. As a precaution against bioterrorism, countries such as the United States maintain a supply of smallpox vaccines. However, these probably wouldn't be deployed on a large scale to tackle monkeypox, McCollum says. Health-care workers would probably instead use a method called ring vaccination to contain the spread of the virus: this would vaccinate the close contacts of people who have been infected with monkeypox, to cut off any routes of transmission.

On the basis of the data that she has seen so far, McCollum thinks the current outbreaks probably won't necessitate containment beyond ring vaccination. "Even in areas where monkeypox occurs every day," she says, "it's still a relatively rare infection."

## 'MIND BLOWING' ANCIENT SITES UNCOVERED IN THE AMAZON

The urban centres are the first to be discovered in the region, challenging archaeological dogma.

#### **By Freda Kreier**

ysterious mounds in the southwest corner of the Amazon Basin were once the site of ancient urban settlements, scientists have discovered<sup>1</sup>. Using remote-sensing technology to map the terrain from the air, they found that, starting about 1,500 years ago, ancient Amazonians built and lived in densely populated centres, featuring 22-metre-tall earthen pyramids, that were encircled by kilometres of elevated roadways.

The complexity of these settlements is "mind blowing", says team member Heiko Prümers, an archaeologist at the German Archaeological Institute, headquartered in Berlin.

"This is the first clear evidence that there were urban societies in this part of the

Amazon Basin," says Jonas Gregorio de Souza, an archaeologist at the Pompeu Fabra University in Barcelona, Spain. The study adds to a growing body of research indicating that the Amazon – long thought to have been pristine wilderness before the arrival of Europeans – was home to settlements and agriculture well before that. The discovery was published on 25 May in *Nature*<sup>1</sup>.

#### A shift in thinking

Humans have lived in the Amazon Basin – a vast river-drainage system roughly the size of the continental United States – for around 10,000 years. Researchers had thought that before the arrival of Europeans in the sixteenth century, all Amazonians lived in small, nomadic tribes that had little impact on the world around them. And although early European visitors described a landscape filled