



Hospitals around the world are treating people for monkeypox.

## HOW DEADLY IS MONKEYPOX? WHAT SCIENTISTS KNOW

The death rate is lower, and symptoms have shifted, compared with past outbreaks.

By Max Kozlov

**T**he global monkeypox outbreak has caused some deaths, but the death rate is lower than expected from historical data – and scientists are breathing a cautious sigh of relief. Of more than **59,000** people confirmed to have had monkeypox infections, at least 22 have died, representing a death rate of about 0.04%. That's significantly less than the 1–3% that has been reported during outbreaks caused by a similar viral strain in West Africa over the past few decades.

All of this has caused researchers to re-evaluate what they thought they knew about severe monkeypox.

In reality, the true death rate is almost certainly higher than current estimates: countries in some parts of the world, including Africa, might not be capturing all deaths during this outbreak because they have limited resources for testing and surveillance. And it could still rise, especially if the virus spreads more extensively among people at high risk of severe disease, such as children, older people and those with severely compromised immune systems, says Andrea McCollum, an epidemiologist who heads the poxvirus team at the US

Centers for Disease Control and Prevention in Atlanta, Georgia.

Still, for the community that has so far been most affected – young and middle-aged men who have sex with men – the disease can be “extremely painful” and has been “causing a lot of suffering”, says Jason Zucker, an infectious-disease physician at Columbia University in New York City who has treated people for monkeypox. The pain arises from distinctive fluid-filled lesions that the disease causes. Although some people have been hospitalized for life-threatening complications such as difficulty breathing or swelling of the brain, Zucker says, it has been more common to see people hospitalized for pain management.

In the current outbreak, clinicians have been seeing fewer lesions overall than in past outbreaks in Africa. But a higher proportion of lesions are appearing on the body's mucosal tissues. Previously, lesions appeared mostly on the skin – on people's hands, feet and faces. Mucosal lesions aren't inherently more severe, but they aggravate sensitive tissue, so they can cause immense pain and interfere with swallowing, eating or drinking when in the throat, or urinating and defecating when in the genital and rectal areas, Zucker says.

These lesions are also more difficult to

identify and characterize than are skin lesions. That means the monkeypox severity scale recommended by the World Health Organization, which uses number of lesions as a proxy for severity of illness, might need some fine-tuning, McCollum says.

### Serious outcomes

So far during the global outbreak, deaths from monkeypox have occurred in at least ten countries, including Brazil, India, Nigeria and Spain. Efforts are under way to understand how the virus contributed to these deaths.

Some people who died – including one in the United States and one in Mexico – were severely immunocompromised and had serious illnesses other than monkeypox. Two people who died in Spain developed encephalitis, or brain swelling, and had no other known risk factors. On the basis of previous monkeypox data, these deaths are “certainly alarming, but not totally surprising”, says McCollum. Encephalitis is a rare but serious complication of many viral illnesses, including those caused by herpes simplex and West Nile virus, and has been known to occur in otherwise healthy people who become infected, Zucker says. It is still not known whether encephalitis from monkeypox happens as a result of the virus infecting brain tissues, or because of an excessive immune response that causes brain swelling.

“We have to move beyond just considering monkeypox a skin and respiratory disease,” says Jonathan Rogers, a neuropsychiatrist at University College London. The monkeypox virus might have evolved since past outbreaks, but scientists are also learning new things about it because of the broader and more geographically diverse population it is now affecting.

More research is needed to understand which individuals are most at risk for developing severe monkeypox – and which routes of transmission might be most dangerous, McCollum says. After a 2003 outbreak in the United States, when a shipment of rodents from Ghana spread the virus to pet prairie dogs in Illinois and infected more than 70 people, researchers noticed that disease severity differed depending on the route of exposure (M. G. Reynolds *et al.* *J. Infect. Dis.* **194**, 773–780; 2006). People who were scratched or bitten by infected animals tended to have more severe disease than did people who were exposed to respiratory droplets and particles from the animals.

Although most infections in the current outbreak have resulted from close sexual contact, McCollum says, the site on the body that the virus first infects – skin versus mucosal tissue – might dictate the severity of disease.

More data are also needed to understand whether the effects of a severe case of monkeypox can linger after an infection clears, Zucker says. “This is not a mild illness,” McCollum says. “It can be quite serious.”