

What to Know About Monkeypox

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Medical and public health officials are concerned—and puzzled—by the increasing number of confirmed monkeypox cases in countries outside central and western Africa, where the virus is endemic.

In the past 5 years, scientists have confirmed only 8 cases where travelers carried monkeypox to countries outside Africa, including 2 cases last year in the US. Each was linked to a person who had recently spent time in Nigeria, a country that experienced a resurgence in monkeypox starting in 2017. In those cases, the human-to-human spread was limited; 2 family members became infected in one instance, according to the World Health Organization (WHO). One health care worker who had contact with contaminated bedsheets was infected in another case, report experts in an article published in the CDC's *Emerging Infectious Diseases*.

"Monkeypox has never appeared more or less simultaneously across different countries and now continents," Andrea McCollum, PhD, MS, the poxvirus epidemiology team lead at the US Centers for Disease Control and Prevention (CDC), said in an interview with *JAMA*. As of May 21, however, the WHO had confirmed monkeypox among 92 people across 12 countries in Europe and North America, where it is not endemic, with another 28 suspected cases. And unlike the previous cases discovered outside Africa, the current outbreaks have occurred in people with no travel history, suggesting that human-to-human transmission is driving the spread.

Despite the increase in cases and human-to-human transmission, the risk to the general public remains low, according to a briefing by the WHO.

Monkeypox 101

Monkeypox is a zoonotic virus, meaning it is typically transmitted through close contact between an animal and human, often through a bite, scratch, or contact with the rash and with "fomites," material like bedding or clothes contaminated with material from monkeypox lesions. Historically,

human-to-human transmission has been less common. When person-to-person transmission does occur it is believed to be direct contact with lesion material or respiratory droplets.

"This is not COVID," said Capt Jennifer McQuiston, US PHS, DVM, MS, of the CDC's Division of High Consequence Pathogens and Pathology, in a May 23 online media briefing. "We do know a lot about monkeypox from many decades of studying it. And respiratory spread is not the predominant worry. It is contact, and intimate contact, in the current outbreak setting and population."

The virus was first isolated from monkeys in 1958, but the disease wasn't recognized among humans until 1970 when it was diagnosed in an infant in the Democratic Republic of the Congo (DRC), according to the WHO. Since then, monkeypox has become endemic in central and western African countries, which report thousands of cases each year.

Like the smallpox and cowpox viruses, the monkeypox virus is part of the *Orthopoxvirus* genus. But compared with smallpox, monkeypox has a relatively low case fatality rate. People involved in the current outbreaks have been infected with the more mild West African clade, according to CDC officials, which has a case fatality rate of less

than 4%. For people infected with the virulent Central African clade that is more easily spread by human-to-human transmission, the case fatality rate is around 11%. Smallpox, in contrast, is fatal in about 30% of cases.

So far, there have not been any deaths associated with the outbreaks.

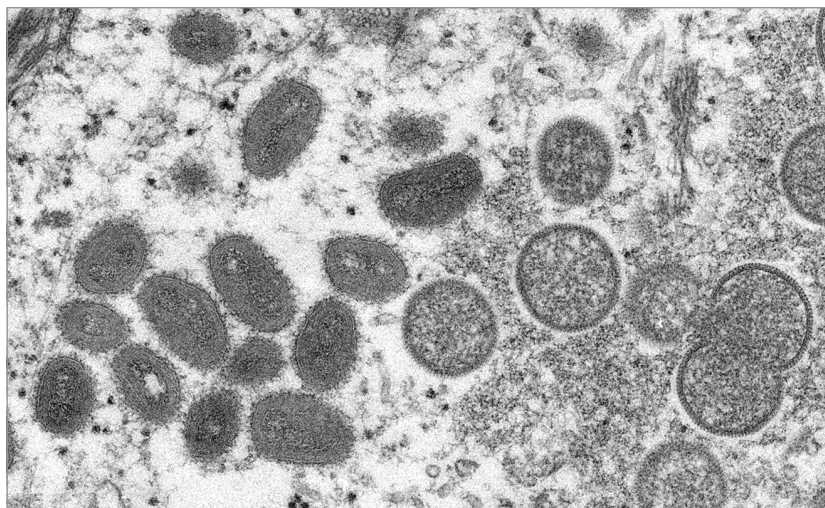
An Altered Presentation

The illness appears to be presenting atypically in the current outbreaks.

Usually, prodromal, or early, symptoms develop 1 to 2 weeks after a person is infected with the monkeypox virus and can include fever, chills, and swollen lymph nodes, according to the CDC. A few days later, a rash develops. Monkeypox lesions then progress through several stages from blister-like lesions to scabs, each lasting 1 to 2 days. After their lesion scabs fall off to reveal healthy tissue underneath, which usually takes 2 to 4 weeks after symptom onset, the individual is no longer infectious.

However, monkeypox appears to be presenting differently among the current patients, Agam Rao, MD, an infectious disease physician and medical officer of the CDC's Poxvirus and Rabies Branch, said in an interview.

"In these new cases, what we're hearing is that those prodromal symptoms might



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be really mild, or not even noticed at all," Rao said. For some patients, the emergence of the rash was the first indication that they were sick.

Additionally, monkeypox symptoms often start in the head region and progress to the patient's arms, legs, palms, and soles. According to Rao, in the current cases—including the [one](#) confirmed in Massachusetts on May 18—the rash has started instead in the genital or perianal region before spreading to the person's extremities. Some patients have presented with proctitis, or inflammation of the rectum, said Rao.

Experts do not currently have evidence that the virus has mutated, according to the WHO. Because the clinical presentation is unusual and cases are rising rapidly, though, continued genomic surveillance is crucial, said Anne Rimoin, PhD, MPH, an epidemiologist at the University of California, Los Angeles, who has studied monkeypox for 2 decades, in an interview.

Why Now?

Monkeypox cases have been increasing since smallpox was declared eradicated in 1980 and that increase has [accelerated](#) over the past decade. Because the smallpox vaccine provides cross-protection from other orthopoxviruses, experts have [suggested](#) that the upward trend in monkeypox cases is due in part to the decline in smallpox vaccinations in the posteradication era. Forty years ago, about [80%](#) of the population was vaccinated against smallpox, according to the WHO. Now, that number is closer to [30%](#).

Increased travel and trade, along with expanding populations, also provide more opportunities for humans to come into contact with the animal reservoirs that harbor the virus. Monkeypox might be found in rodents and nonhuman primates, although experts are still not sure which animals are the natural reservoir. Infected humans can then transmit the disease to others, although this is less common, according to Rimoin.

This combination of factors is "the perfect storm for new disease patterns that we've not seen previously," said Rimoin.

Questions About Transmission

The CDC's Rao said she was concerned but not surprised when she heard of a monkeypox case [diagnosed in the UK](#) in early May in a person who had recently traveled to Nigeria. Given the numbers of monkeypox infec-

tions in recent years, experts expect some small number of sporadic cases.

Then an additional 6 cases were confirmed in the UK about a week later. "That is when we became alarmed, because we haven't seen that kind of transmission," Rao said.

As of May 23, there is a single case of monkeypox confirmed in the US, but 4 additional people have tested positive for an orthopoxvirus, said the CDC's McQuiston. The CDC was investigating whether the virus was monkeypox.

Many of the [confirmed cases so far](#) have been found in people who identify as men who have sex with men, according to the WHO. But it is inaccurate to say that monkeypox is a sexually transmitted infection, David Heymann, MD, DTM&H, said in an interview. Instead, it's likely that some of the current infections have been transmitted sexually "because, by chance, there had been someone who had a lesion in the genital area," said Heymann, a medical epidemiologist and professor at the London School of Hygiene and Tropical Medicine who has served as a director in the WHO on detachment from CDC, and chairman of Public Health England.

"We certainly wouldn't want to make premature conclusions about how it's being transmitted," Rao said. "That could just be harmful to the investigation and also harmful to the communities that are currently affected."

The Tools Available

The CDC is working to ensure that some important tools are available for patients who are infected and have been exposed.

Limited amounts of 2 vaccines are available in the US for adults:

- ACAM2000 was approved in 2007 for immunization against smallpox. [ACAM2000](#) contains a live vaccinia virus and can be used in people exposed to monkeypox if used under an expanded access investigational new drug protocol.
- JYNNEOS, a live, nonreplicating vaccinia virus vaccine, was [approved in 2019](#) by the US Food and Drug Administration for the prevention of smallpox and monkeypox.

Currently, there are 100 million doses of ACAM2000 and 1000 doses of the JYNNEOS vaccine available in the US, said McQuiston. ACAM2000 has some serious potential [adverse effects](#), however. "A decision to use that widely would have to have

some serious discussion behind it," she said in the briefing.

Vaccinations are offered to some close contacts of people infected with monkeypox, said Rao. "Offering it to contacts of contacts is not something that anyone in other parts of the world are doing but it's something to think about."

The smallpox vaccine is not available right now for the general public. And given the limited supply, individual measures to mitigate risk—paying attention to whether sexual partners have genital lesions, for example—is the best approach, said Heymann.

Experts [suggest](#) vaccine administration after exposure can prevent or reduce the severity of disease. The CDC has [guidelines](#) for different exposures, and vaccines are available for qualifying patients and health care workers.

The Scope of the Outbreaks

The main focus now is on identifying all cases, according to Rao. For physicians, that means suspecting monkeypox if a patient has a rash characterized by firm, round lesions sometimes with a fissure in the middle, even if other diagnoses seem more likely, she said.

Physicians should reach out to their local health departments if they believe they have a patient who is infected, Rao said. Those local health departments can then get in touch with the CDC, which is working to get vaccines to patients and close contacts who could benefit.

Patients with monkeypox or suspected to have the virus should be placed in a negative pressure room and health care workers should use standard droplet precautions when treating them, says the CDC's McCollum.

"We have the tools in hand to get this under control," said McCollum. "But I continue to be concerned about increasing case numbers. This is a disease that has potential to cause pretty significant morbidity and mortality." ■

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Note: Source references are available through embedded hyperlinks in the article text online.