

Rising Monkeypox Cases and Decreased Smallpox Immunity Raise Concerns of Potential Pandemic

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Dear Editor

Monkeypox is a zoonotic virus that can spread rapidly among humans and poses a serious threat to public health. The first case of monkeypox virus (MPV) was reported in a nine-month-old child in the Democratic Republic of Congo in 1970, and between 1970 and 1979, over 48 cases were reported in six African countries (3). The MPV has recently re-emerged and has caused concerns among health authorities, particularly as the world continues to grapple with the COVID-19 pandemic (1, 2).

Between May 4 and July 12, 2022, over 10,000 new cases of MPV were reported from non-endemic areas worldwide. However, this number may be underestimated, due to limited access to the MPV diagnostic facilities in certain regions. Monkeypox is primarily transmitted through contact with infected animals, as well as direct contact (sexual or skin), respiratory droplets, and shared items such as towels and bedding. The symptoms of monkeypox are similar to those of smallpox, but monkeypox is milder and presents as high fever, headache, lymphadenopathy, and systemic blisters and rashes. The death rate of monkeypox is about 1% to 10% (4, 5).

In contrast, smallpox is a highly contagious airborne disease caused by the variola virus (VAV). There are two forms of smallpox: variola major (Asiatic smallpox) with mortality rate of 20-45% and a weakened form called variola minor with mortality

rate of 1-2% in Europe and America. The case fatality rates are approximately 30% overall, and survivors often suffer from significant morbidity, including blindness and skin scarring. The last naturally occurring case of smallpox was reported in Somalia in 1977. Given the risks posed by both monkeypox and smallpox, health authorities need to remain vigilant and take appropriate measures to prevent the spread of these diseases (6).

In January 2022, Tecovirimat in capsule form (dosage 200mg) was approved by the European Medicines Agency (EMA) as the first treatment for monkeypox (7). The monkeypox vaccine is also available for the patients who were exposed to the virus to enhance the antibody production and stop the spread of the virus (8). Also, DNA, mRNA, viral vector, and nanoparticle-based vaccines are all suitable platforms for making a favorable vaccine against the MPV. These platforms can deliver immunogenic proteins of MPXV, which can elicit protective immunity against MPXV (9). DNA vaccines are more stable, easier to transport, with shorter development and production timeline, making them a cost-effective alternative, however, mRNA vaccines have shown impressive effectiveness in studies, but they come with certain challenges, such as the need for cold-chain storage. Moreover, a relatively higher cost can make their distribution challenging in developing countries and remote areas (9).

Unlike MPV, which affects animals, poxvirus infections affect humans and can be fatal. Smallpox, a type of human-infecting poxvirus that has caused numerous deaths in the past, was eradicated in 1977 through vaccination efforts worldwide. However, the discontinuation of smallpox vaccinations has left over 70% of the global population unvaccinated, making them susceptible to the smallpox and other related viruses (10).

Based on the early genetic data, there are some differences between VAV and the MPV. However, despite these differences, the central genomic regions of both viruses, which contain crucial codes to produce enzymes and structural proteins, are almost identical. On the other hand, the terminal genomic regions, which involve codes for the virulence and host domain factors, differ significantly.

Recently, there has been a global outbreak of monkeypox that has become a public health concern. It appears that people's immunity against VAV is also protective against MPV. This is because smallpox vaccine can make people highly resistant to the MPV (11).

The global spread of the monkeypox pathogen can be attributed to the international travel and increased susceptibility to VAV (re-emergence). Another reason for the increase in MPV cases could be that people are now less immune to smallpox as smallpox vaccination is no longer available. The smallpox vaccine also protects against MPV (12). During the 1970s and 1980s, MPV was common among unvaccinated children. However, as time passed, the average age of MPV patients increased because children born after the smallpox eradication were more vulnerable (13).

There is concern for the increasing prevalence of human immunodeficiency virus (HIV)-infected patients who are not able to receive the smallpox vaccine. Of note, other immunodeficiency conditions in which, the vaccine does not elicit an adequate immune response can predispose these patients to smallpox infection. This has raised concerns about the potential for a smallpox pandemic. Furthermore, the rise in the monkeypox cases, especially in people with weakened immune systems, may lead to further virus mutations and persistence in different communities, increasing the likelihood of infection as the population ages.

The transmission patterns of MPV have been changed over time and they may cause the virus to spread more easily. The disease is more common in men who have sex with other men, and it can spread like a sexually transmitted disease. Additionally, mutations in MPV may enhance the spread of the virus.

The smallpox vaccine can provide protection against MPV in about 85% of people. However, since the last smallpox vaccine was given over 30 years ago, the level of immunity against smallpox has decreased. Adults between the ages of 21 and 40 who have not received the human typhoid vaccine have been found to have a higher rate of monkeypox infection. This suggests that MPV could continue to spread within the human population, increasing the likelihood of infection as the population ages (11).

As the number of MPV cases increases worldwide, there is a need to develop more effective vaccines and drugs against MPV infection. This requires a focus on factors such as vaccine development, distribution infrastructure, vaccination implementation speed, vaccination coverage, health messaging, and non-pharmacological interventions. The worldwide commitment to controlling monkeypox is essential, and it is recommended that the disease be closely monitored and studied. Additionally, early diagnosis and treatment are critical, and physicians should be vigilant in identifying the rashes.

It is also important to consider the risk of bioterrorism involving the VAV, given its previous implementation in the Soviet biological weapons program (14). With the current unrest in the world and the ongoing war in Ukraine, it is necessary to pay attention to this risk.

Overall, the rise in monkeypox cases, the changing in transmission patterns, the decreased immunity against smallpox, and the potential for bioterrorism using the human poxvirus are all reasons to pay close attention to the situation and take action to control the spread of these viruses.

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Ethical Considerations

There is nothing to declare. This study is a letter to the editor.

Authors' Contributions

R.K: Idea design, writing-original draft preparation; M.F: writing-review and editing; S.J: writing—review.

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Conflict of interest

The authors declare that there is no conflict of interest.

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We accept the liability of the scientific integrity of the manuscript contents.

Consent

This is a Letter to the editor and does not require Consent.

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