

11-2-2022

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Recommended Citation

Daley, L. (2022). Monkeypox Fact Sheet. *D.U.Quark*, 7 (1). Retrieved from <https://dsc.duq.edu/duquark/vol7/iss1/12>

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Monkeypox Fact Sheet

By Lance Daley

Published November 2, 2022

What is monkeypox?

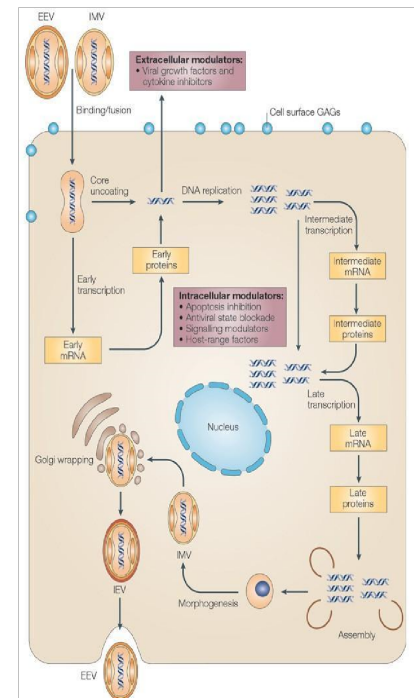
D.U.Quark 2023. Volume 7(Issue 1) Pg. 13-19

Staff Article

Since the beginning of 2020, COVID-19 has presented the world with an unprecedented health crisis, including over six million deaths, extended lockdowns, and supply chain issues accompanying economic slowdowns. In June 2022, a rare virus, human monkeypox, rapidly burst onto the scene amidst the COVID-19 pandemic, prompting the WHO to declare a global health emergency. Daily confirmed monkeypox cases have increased eight-fold in just the month of June alone, and the virus has been confirmed in all inhabited continents.¹ Monkeypox is a zoonotic Orthopoxvirus that causes symptoms similar to smallpox, which include rash, raised skin lesions, high fever, headache, and other symptoms.²

How does the virus infect us?

Monkeypox is a relatively large (200-250 nm), brick-shaped virus containing a double-stranded DNA (dsDNA) genome surrounded by an envelope.³ When someone encounters monkeypox, viral envelope proteins bind to cell membrane receptors to facilitate fusion with and entry into the cell. Although the mechanism of poxvirus entry is not well understood, a 2013 publication from the NIH suggested that MV protein L1 is a receptor-binding protein in



McFadden, G (2005). "Poxvirus tropism." *Nature*. <https://www.nature.com/articles/nrmicro1099>

poxviruses that may trigger fusion with the cell membrane and subsequent entry.⁴ Following entry into the cell, the monkeypox DNA is able to replicate and transcribe in the host cytoplasm in small factories formed by the rough endoplasmic reticulum.⁵ Then, the synthesized viral mRNA transcripts are translated into viral proteins by host ribosomes. Post-translational modifications to viral proteins are applied by the endoplasmic reticulum and Golgi apparatus. Once matured, the newly synthesized viral proteins and replicated DNA associate with each other near the cell membrane. When the new virion is fully assembled, the monkeypox virus buds off the host cell membrane and can infect a new host cell.

What is the prognosis for those infected?

Monkeypox is a self-limiting disease with symptoms lasting around two to four weeks in most individuals.⁶ In the following days or weeks after the initial infection, the virus causes symptoms similar to smallpox and the flu, including fever, chills, headache, fatigue, swollen lymph nodes, and a rash that develops into blisters that can fill with pus and be painful. The mortality rate for monkeypox infections is currently thought to be between 3-6%.⁶ The mortality rate indicates that while most people recover within weeks on their own, those who are immunocompromised, elderly, co-infected with another virus, etc. may not be able to effectively fight off the infection and possibly need antiviral treatment to stop viral replication.

Is there a treatment for monkeypox?

There are currently no curative treatments designed specifically for monkeypox infection. However, due to the genetic similarities between monkeypox and smallpox,

antivirals and vaccines used to treat smallpox may be effective at treating and reducing the spread of monkeypox. One example of an antiviral used to treat poxviruses is Tecovirimat (sold under TPOXX), which reduces viral spread in the host by inhibiting viral p37 protein. p37 plays a role in releasing a newly assembled virus from an infected host, allowing new virus particles to infect new cells.⁷ Two vaccines licensed by the FDA, JYNNEOS and ACAM2000, are also available for reducing potential adverse effects from monkeypox or smallpox infection.⁸ JYNNEOS has been distributed in the U.S. to cities most affected by the monkeypox outbreak, namely New York City. Like the initial COVID-19 vaccines, JYNNEOS is a two-dose regimen that provides weak to moderate protection with the first dose but a robust, longer-term immunological memory with the second dose.⁹ Because of short supply and a relatively low mortality rate, affected communities are currently offering one dose of JYNNEOS to high-risk populations (such as the immunocompromised) and will offer a second dose as supply increases.⁶ Additionally, prior infection with monkeypox or a related Orthopoxvirus will also provide short-term immunological memory but presents a risk for adverse health effects.

How is the virus spreading?

Monkeypox is spread among mammals (zoonotic) through interactions with large respiratory droplets containing the virus. Some ways that monkeypox infection can be transmitted are through physical or sexual contact, lesions, respiratory secretions, contaminated objects, as well as vertical transmission from mother to fetus.⁸ A host is infectious after a one to two week incubation period from first virus contact. Following the

incubation period, the victim will typically experience symptoms for two to four weeks where they are contagious to others. The virus is usually endemic to West and Central Africa, and cases are typically only sporadically observed outside of that region.¹⁰ Because of its endemic nature, monkeypox likely spread globally as a result of travel to and from affected regions in Africa. The introduction of monkeypox to non-endemic areas could potentially lead to volatile outbreaks due to a long infectious period (2-4 weeks) and limited global poxvirus immunity, as the smallpox vaccine was no longer needed and discontinued in the 1970s.

Along with examining the geographical aspects of viral spread, the use of population health statistics can also help illustrate at what rate the virus will spread throughout a population. Reproductive number (R_0) is a useful statistic for virologists that determines the expected number of new cases directly generated from a single case in the population. A value below 1 indicates the viral spread likely will not be sustained since less new infections are being produced from initial infections. A value greater than 1 indicates that a single infection will on average cause multiple new infections, supporting viral spread in a population. In a 2020 study concerning poxvirus spread, the reproductive number for monkeypox was calculated using mathematical modeling to be greater than 1, indicating epidemic potential.¹⁰ The possibility of a monkeypox epidemic is concerning due to the hardships of the ongoing COVID-19 pandemic, as well as the previously addressed lack of immunity in most people to poxviruses due to a lack of exposure.

Viral evolution also plays a direct role in pathogenesis, the viral life cycle, viral spread, and host adverse effects. As of June 3, the CDC suggested that there are at least two different clades of monkeypox virus in new outbreaks occurring outside of Africa.¹⁰ Since then, the CDC has sequenced ten different viral isolates from the outbreak in the U.S. and found that divergent monkeypox lineages exist that differ from those spreading throughout Europe.¹⁰ Despite having a DNA genome, monkeypox virus has accumulated many mutations and unique strains in a short amount of time. This is unexpected since DNA polymerase, a molecule that synthesizes new DNA from a DNA template, has proofreading ability unlike RNA polymerase. In other words, DNA polymerase can fix replication errors that block many new random mutations from occurring. These unlikely mutants potentially arose during endemic infections in Africa or during the current outbreaks across Europe and North America where the spread of the virus helped to facilitate its evolution. Another potential culprit for accelerated viral mutation could be the host's immune enzymes inducing mutations in viruses. Although this evolutionary mechanism is designed to inactivate the virus by generating a deleterious mutation, there is also the opportunity for mutations to accumulate that are beneficial for the virus, including those which increase virulence and viral spread.

The optimal way to minimize the spread and impact of monkeypox virus is to: 1) avoid travel to endemic areas and cities experiencing outbreaks; 2) wear a face covering when in public; 3) quarantine if you have symptoms associated with the virus; 4) stay informed about the current state of monkeypox infections in your area.

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