Monkeypox

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Continuing Education Activity

Monkeypox is a zoonotic orthopoxvirus that incidentally causes disease in humans similar to smallpox, although with notably lower mortality. This virus is clinically relevant because it is endemic to western and central Africa, with outbreaks in the Western Hemisphere related to the exotic pet trade and international travel. This activity reviews the evaluation and management of monkeypox infections in humans and highlights the role of the interprofessional team in caring for patients with this condition and minimizing disease outbreaks.

Objectives:

- Describe the epidemiology of monkeypox.
- Review the presentation of a patient infected with monkeypox.
- Identify common complications of monkeypox.
- Summarize the role of the interprofessional healthcare team in monkeypox disease prevention and mitigation measures.

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Introduction

Monkeypox virus was first isolated and identified in 1958 when monkeys shipped from Singapore to a Denmark research facility fell ill.[1] However, the first confirmed human case was in 1970 when the virus was isolated from a child in the Democratic Republic of Congo suspected to have smallpox.[2]

Coincident immunity to monkeypox virus was previously achieved with vaccinia vaccination; however, eradicating smallpox and subsequent lack of vaccination efforts paved the way for monkeypox to gain clinical relevance.[3] Furthermore, because most cases of monkeypox occur in rural Africa, suspected underreporting may translate to an underestimation of the potential threat of this pathogen.[4]

Etiology

Monkeypox is from the family: *Poxviridae, s*ubfamily: chordopoxvirinae, genus: orthopoxvirus, and species: Monkeypox virus.

On electron microscopy, the monkeypox virus is relatively large (200-250 nanometers). Poxviruses are brick-shaped, surrounded by a lipoprotein envelope with a linear double-stranded DNA genome.[5][6] Aside from their reliance on host ribosomes for mRNA translation, poxviruses include all necessary replication, transcription, assembly, and egress proteins in their genome.[7][5]

Epidemiology

Monkeypox is a zoonotic disease endemic to central and western Africa and most concentrated in the Democratic Republic of Congo. Although first identified in captive monkeys (hence the name), the available data suggests African rodents as the natural reservoir. Infections have occurred in squirrels, rats, mice, monkeys, prairie dogs, and humans.[4][8] Currently, two genetically distinct clades have been identified. The Congo Basin (Central African) clade is reported more frequently than the West African clade and has documented cases of human-to-human transmission, whereas the West African clade does not.[4]

Sporadic clusters and cases of human monkeypox have occurred outside of Africa. In 2003, Gambian giant rats imported from Ghana infected co-habitant prairie dogs sold as household pets in the Midwestern United States. This resulted in fifty-three human cases of monkeypox.[9] In October 2018, one case occurred in a man who traveled from Nigeria to Israel.[10] In May 2019, one case occurred in a man who traveled from Nigeria to Singapore.[11]

In May 2021, a family returned to the United Kingdom after traveling to Nigeria, and three family members became infected with the monkeypox virus.[12] The sequential timing of symptom development in each case within the family (day 0, day 19, day 33) could represent human-to-human transmission. In July 2021, one case occurred in a man who traveled from Nigeria to Texas.[13] In November 2021, one case occurred in a man who traveled from Nigeria to Maryland.[14] As of May 2022, one case of human monkeypox in a man who returned to Massachusetts from Canada is under investigation as well as clusters of human monkeypox in the United Kingdom.

Precise prevalence and incidence are difficult to establish given suspected shortcomings in disease reporting and confirmation. However, both metrics have increased since the discontinuation of routine smallpox vaccination.[4][15] Demonstrated risk factors for monkeypox infection are living in heavily forested and rural areas of central and western Africa, handling and preparing bushmeat, caregiving to someone infected with monkeypox virus, and not being vaccinated against smallpox.[15][16] Male gender has also been correlated with infection risk. However, this may be confounded by the cultural norm that men frequently hunt and contact wild animals.

Transmission can occur through contact with bodily fluids, skin lesions, or respiratory droplets of infected animals directly or indirectly via contaminated fomites. Although human-to-human transmission has previously been limited, mathematical modeling in the context of decreasing herd immunity to orthopoxviruses reflects an increasing threat of disease spread between humans.[17] The Centers for Disease Control and Prevention (CDC) recommends isolation in a negative pressure room and standard, contact, and droplet precautions in the healthcare setting with escalation to airborne precautions if possible.

Pathophysiology

Following viral entry from any route (oropharynx, nasopharynx, or intradermal), the monkeypox virus replicates at the inoculation site then spreads to local lymph nodes. Next, an initial viremia leads to viral spread and seeding of other organs. This represents the incubation period and typically lasts 7 to 14 days with an upper limit of 21 days.

Symptom onset correlates with a secondary viremia leading to 1 to 2 days of prodromal symptoms such as fever and lymphadenopathy before lesions appear. Infected patients may be contagious at this time. Lesions start in the oropharynx then appear on the skin. Serum antibodies are often detectable by the time lesions appear.[18] Rash progression is described in more detail in the History and Physical section.

History and Physical

Historical clues for monkeypox infection such as recent travel to endemic areas, interaction with wild animals imported from endemic areas, and providing care to an infected animal or human help build a differential diagnosis, but clinical features are critical.

Initial symptoms include fever, headache, myalgia, fatigue, and lymphadenopathy, a key differentiating feature of monkeypox from smallpox. After 1 to 2 days, mucosal lesions develop in the mouth closely followed by skin lesions of the face and extremities (including palms and soles) and are centrifugally concentrated. The rash may or may not spread to the rest of the body, and the total number of lesions may vary from a small amount to thousands.[19]

Over the following 2 to 4 weeks, the lesions evolve in 1 to 2-day increments through macular, papular, vesicular, and pustular phases. Lesions change synchronously and are characterized as firm, deep-seated, and 2 to 10 mm in size. Lesions remain in the pustular phase for 5 to 7 days before crusts begin to form. Crusts form and desquamate over the subsequent 7 to 14 days, and the condition resolves around 3 to 4 weeks after symptom onset in most cases. Patients are no longer considered infectious after all crusts fall off.[20]

Evaluation

The CDC established case definition criteria for human monkeypox during the 2003 outbreak in the United States. However, the same criteria are not necessarily as valuable in endemic areas. The specificity of the epidemiological criteria decreases as the potential exposure of the population to infected mammals or humans increases. In addition, the specificity of the clinical criteria decreases as the prevalence of similar illnesses increases, as is the case with chickenpox, given the lack of routine varicella-zoster vaccination in Africa.[21] Although clinical and epidemiologic criteria remain under review and may differ by situation and geographic location, confirmation of human monkeypox infection requires laboratory evidence.[22]

Considering the similarities between human monkeypox infection and smallpox, the “Acute, Generalized Vesicular or Pustular Rash Illness Protocol” created by the CDC with the addition of lymphadenopathy to requisite primary criteria could be used to determine which patients warrant further testing.[19]

Monkeypox infection can be confirmed via isolation in viral culture or PCR for monkeypox DNA from a patient specimen. Alternatively, tests indicating the presence of Orthopoxvirus in a patient specimen, barring patient exposure to another of the same genus, can be sufficiently diagnostic, such as visualization on electron microscopy, immunohistochemical staining for orthopoxvirus antigens, serum studies for anti-orthopoxvirus IgM (indicating recent exposure) and IgG (indicating prior exposure or vaccination).[19]

Treatment / Management

Currently, there are no specific clinically proven treatments for monkeypox infection. As with most viral illnesses, the treatment is supportive symptom management. There are, however, prevention measures that can help prevent an outbreak.

The infected individual should remain in isolation, wear a surgical mask, and keep lesions covered as much as reasonably possible until all lesion crusts have naturally fallen off and a new skin layer has formed. For severe cases, investigational use can be considered for compounds with demonstrated benefit against orthopoxviruses in animal studies and severe vaccinia vaccine complications. The oral DNA polymerase inhibitor brincidofovir, oral intracellular viral release inhibitor tecovirimat, and intravenous vaccinia immune globulin have unknown efficacy against the monkeypox virus.[19]

For individuals exposed to the virus, temperature and symptoms should be monitored twice per day for 21 days because that is the accepted upper limit of the monkeypox incubation period. Infectiousness aligns with symptom onset; therefore, close contacts need not isolate while asymptomatic. In some cases, post-exposure vaccination with modified vaccinia, Ankara vaccine (smallpox and monkeypox vaccine, live, non-replicating) is recommended. Contact between broken skin or mucous membranes and an infected patient's body fluids, respiratory droplets, or scabs is considered a "high risk" exposure that warrants post-exposure vaccination as soon as possible. According to the CDC, vaccination within four days of exposure may prevent disease onset, and vaccination within 14 days may reduce disease severity.

The replication-defective modified vaccinia Ankara vaccine is a two-shot series, four weeks apart, with a superior safety profile compared to first and second-generation smallpox vaccines. Unlike live vaccinia virus preparations, administering modified vaccinia, Ankara does not create a skin lesion or pose a risk of local or disseminated spread.[19] In addition, clinical trials have shown that modified vaccinia Ankara is safe and stimulates antibody production in patients with atopy and compromised immune systems, which are known contraindications to live vaccinia administration.[16]

Identifying the potential benefits and drawbacks of preventative monkeypox vaccination in endemic communities requires more thorough data collection and feasibility analysis. Access to medical care, testing capabilities, and infrastructure limits the ability to make informed decisions about best addressing this neglected tropical disease.[4][16][23]

Differential Diagnosis

- Smallpox
- Generalized vaccinia
- Disseminated zoster
- Chickenpox
- Eczema herpeticum
- Disseminated herpes simplex
- Syphilis
- Yaws
- Scabies
- Rickettsialpox
- Measles
- Bacterial skin infections
- Drug-associated eruption[8][19]

Prognosis

There are two distinct clades of the monkeypox virus. The West African clade has a more favorable prognosis with a case fatality rate below 1%. On the other hand, the Central Basin clade (Central African clade) is more lethal, with a case fatality rate of up to 11% in unvaccinated children. Aside from potential scarring and discoloration of the skin, the remainder of patients typically fully recover within four weeks of symptom onset.[4]

Complications

- Bacterial superinfection of skin
- Permanent skin scarring
- Hyperpigmentation or hypopigmentation
- Permanent corneal scarring (vision loss)
- Pneumonia
- Dehydration (vomiting, diarrhea, decreased oral intake due to painful oral lesions, and insensible fluid loss from widespread skin disruption)
- Sepsis
- Encephalitis

- Death[23]

Deterrence and Patient Education

Education of patients and healthcare workers in regions where the monkeypox virus is endemic is of the utmost importance. Local containment is the best defense against the worldwide spread. Historically, the monkeypox virus has a limited ability to spread between humans. Nonetheless, the waning population of people vaccinated against smallpox paves the way for an increased prevalence of human monkeypox, increasing viral mutation opportunities. Therefore, improving patient recognition of this disease, reporting fidelity, and access to diagnostic capabilities are critical actions for collecting the data necessary to gain a deeper understanding of and strengthened defense against monkeypox.[4][16]

Enhancing Healthcare Team Outcomes

The spread of infectious diseases requires a susceptible population and opportunities for transmission. Individual and herd immunity to monkeypox, previously achieved through widespread vaccinia vaccination, has declined since the 1980s, increasing human susceptibility to outbreaks.[3] [Level 3] In addition, interim sociopolitical and ecological changes in endemic regions likely increased human exposure to animal reservoirs.[15] [Level 5]

Although relatively rare outside of central and western Africa, the aforementioned recipe for disease spread coupled with the wildlife trade and availability of international travel has resulted in cases in other parts of the world. Due to the range of monkeypox disease severity, an infected patient may present to the emergency department, urgent care, or primary care setting. The ability of an interprofessional team of physicians, nurses, virologists, veterinarians, and public health experts to promptly identify monkeypox infection in humans and animals, implement protective measures, and initiate public health reporting creates a bulwark against a devastating outbreak. [Level 5]

Review Questions

- Access free multiple choice questions on this topic.
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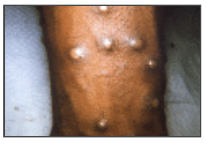

Figure
Pathology, Maculopapular lesions, arm, Smallpox Virus, Pustular phase, Variola major and minor. Contributed by Dr. John Noble, Jr., The Centers for Disease Control and Prevention (CDC)

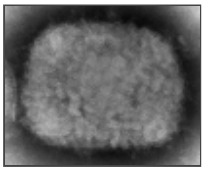

Figure
Poxvirus under electron microscopy. Public Health Image Library #22663

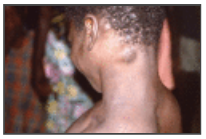

Figure
Cervical lymphadenopathy in a child with monkeypox. Public Health Image Library #12778

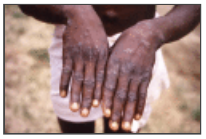

Figure
Monkeypox lesions on hands. Public Health Image Library #12763

Figure

Monkeypox lesions on palms. Public Health Image Library #12761

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