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Critical Care Update

Monkeypox

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Prelude

Simpson K, Heymann D, Brown CS, et al. Human monkeypox – after 40 years, an unintended consequence of smallpox eradication. *Vaccine*. 2020;38:5077-5081.

Hraib M, Jouni S, Albitar MM, et al. The outbreak of monkeypox 2022: an overview. *Ann Med Surg (Lond)*. 2022;79:104069.

Thornhill JP, Barkati S, Walmsley S, SHARE-net Clinical Group, et al. Monkeypox virus infection in humans across 16 countries – April-June 2022. *N Engl J Med*. 2022;387:679-691.

Smallpox eradication, coordinated by the World Health Organization and certified 40 years ago, led to the cessation of routine smallpox vaccination in many countries. It is estimated that over 70% of the world's population is no longer protected against smallpox and therefore lost immunity to closely related viruses such as monkeypox. Thus, monkeypox is now a re-emerging disease. The vaccinia virus vaccine that eradicated smallpox also protected against other orthopox infections, and if the vaccinia vaccine was given within 4 days of infection, it could modify or prevent the onset of clinical disease. With the elimination of smallpox and the subsequent cessation of routine smallpox vaccination, human monkeypox appeared with increasing frequency in unvaccinated populations. Second-generation smallpox vaccines have been demonstrated to protect against monkeypox.

Variola virus, the causative agent of smallpox, is thought to have adapted to the human host as early as 3,000 to 4,000 years ago. Smallpox immunization has also existed in some form for extended periods of time. The management of viral disease began with Jenner, who produced the cowpox vaccine in 1796 made from a virus that usually caused mild disease transmitted to humans by animal hosts. The vaccination introduced was the basis for the elimination of variola in 1980. Other orthopoxviruses, including the monkeypox virus, are thought to have caused similar mild and sporadic human illness before the introduction of smallpox vaccination and remain in circulation through animal hosts with periodic emergence in human populations. Variola minor was a less common and genetically distinct form of the variola virus. In contrast to the 30% to 50% fatality rate of smallpox, the variola minor fatality rate was less than 1%. Many variola minor patients have felt quite well, were mobile, and were able to infect their contacts, providing protection against variola major. Vaccination and protective variola minor exposure contributed to smallpox elimination and likely reduced the number of other human orthopox infections.

Just as smallpox virus appears to have produced 2 distinct evolutionary varieties or clades, monkeypox displays 2 distinct clades. Monkeypox clades are associated with the Congo Basin and West Africa, with the Congo clade having a reported mortality of about 10%; the West African clade usually displays fatal outcomes in less than 1% of cases, although mortality was observed to be much higher in patients with coincident infection secondary to human immunodeficiency virus (HIV).

As originally noted by Jenner, infection with one orthopoxvirus, cowpox, or vaccinia-derived vaccines offered smallpox protection. Unfortunately, the proportion of smallpox-vaccinated individuals has fallen from over 80% in 1980 to less than 30% today, and in some developing nations, young nonvaccinated individuals exceed 75% of the population. These individuals are clearly susceptible to the monkeypox virus infection.

Monkeypox was first identified in Denmark in 1958 after an outbreak of pustular disease in an animal colony. This animal vector was macaques, which had been imported from Singapore. The first human monkeypox case was identified in the Congo in 1970 as the incidence of smallpox was decreasing. At present, the true burden of monkeypox disease is unknown. Many countries that may harbor monkeypox disease have not included monkeypox screening into routine surveillance systems. In addition, the prevalence of asymptomatic monkeypox infection is not appreciated in human populations. The scope of animal reservoirs of the monkeypox virus and human behaviors that facilitate initial animal-to-human transmission of monkeypox are unconfirmed. One outbreak in the Central United States occurred with 47 confirmed or probable cases, including many children infected by prairie dogs thought to have contracted monkeypox from rodents shipped to the United States from Ghana.

Proposed factors for the emergence or recurrence of monkeypox disease include climate change, exploitation of the rain forest, armed conflicts in disease areas, mobile populations, and reduced herd immunity associated with the discontinuation of smallpox vaccination. Unlike monkeypox, smallpox has no specific animal host, and transmission occurs on a man-to-man basis. Monkeypox may be transmitted to man by animal or human hosts. Serologic surveys in rural portions of West and Central Africa where human monkeypox has occurred suggest the presence of orthopoxvirus antibodies in 12% to up to 15% of children. The mean age of patients was less than 5 years. Cases of monkeypox were linked to animal sources in over 70% of cases. A monkeypox outbreak in the 1990s included 89 persons. Seventy-three percent of these cases were associated with contact with another human case of monkeypox, whereas 27% of cases

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had known contact with an animal vector for monkeypox. Another telling observation from the 1990s data is the identification of 7 new monkeypox cases in man from a single human index case. More recent data from Nigeria associated an outbreak of human monkeypox with heavy rain fall and flooding thought to have brought animal hosts and the human population into closer proximity as both sought a dry environment.

Risk factors for infection with monkeypox are a cause for continued investigation. In approximately 10% of cases, animal contact is confirmed. The prevalence of asymptomatic infection remains unclear. Sexual contact is considered for cases with genital or groin lesions. Other research in Nigeria suggests the importance of animal reservoirs of disease and HIV infection in man. At a high level, control and prevention measures include education and personal hygiene along with the consideration of epidemiology and risk factors. Vaccination is considered for health care workers in treatment facilities but is not widely employed. Human monkeypox is being added to disease surveillance protocols. Additional information regarding transmission between humans and the natural history of dual monkeypox and HIV infection is sought.

Two articles from earlier this year provide important data on epidemiology. A report from May 2022 reports 92 cases worldwide from 13 countries where monkeypox virus was not endemic (ie, not a part of the African continent). In all, 15 countries were reported with confirmed outbreaks. No deaths were reported in this report. Cases were mainly but not exclusively identified among gay and bisexual men 20 to 50 years old. Causality is not clear in this article with respect to monkeypox and an association with sexual behavior. Data from this report suggest an incubation period for monkeypox ranging from 5 days to 3 weeks with symptoms lasting 2 up to 5 weeks. The early symptoms reported included shivers, headache, fainting, and backache. Fever and lymphadenopathy were reported before the development of a rash. Monkeypox cases experienced a rash with clinical features similar to ordinary or milder cases of smallpox. Lymphadenopathy in the neck, groin, and submandibular regions is a particular feature of monkeypox patients in this series. When a rash presented, facial appearance was early with spread of the rash across the trunk and extremities. Individual lesions measured 0.5 to 1.0 cm. Lesions developed crusting with crusts that fell off during healing. A suggested differential diagnosis included water warts, red measles, Rickettsia disease, staphylococcal skin infection, anthrax, mites, syphilis, and a variety of drug reactions. Limiting human exposure to suspect host animals was a recommended first step to reduce monkeypox spread. These authors suggest that human-to-human transmission cannot sustain continued spread of monkeypox without episodic animal contact through bites and abrasions. Where patients are hospitalized, the Centers for Disease Control and Prevention (CDC) recommendations include negative pressure rooms with droplet and contact precautions for health care professionals. Finally, this report shows that monkeypox is less transmissible among humans in comparison to smallpox. The longest chain of infected individuals presented was 6 patients after 1 index case. Although no specific treatment for monkeypox was recommended at this time, the smallpox vaccine was used to prevent progression and reduce the severity of symptoms.

A more extensive epidemiologic data set comes from a report of human cases across 16 countries published in late August 2022. An international collaboration of clinicians contributed a case series to describe the presentation, clinical course, and outcomes of polymerase chain reaction–confirmed monkeypox infections. This report discussed 528 infections diagnosed between April and June 2022 at 43 sites in 16 countries. Remarkably, 98% of the persons with infection were gay or bisexual men; 75% of these men were white, and 41% of this subset of patients had HIV infection. The median age was 38 years. Transmission was thought to occur through sexual activity in 95% of persons with infection. A rash was featured on presentation in 95% of the patients. Seventy-three percent of the patients with a rash had anal and genital lesions, whereas 41% of patients with a rash had mucosal lesions. Systemic complaints included fever, lethargy, myalgia, and headache. Lymphadenopathy was reported in 56% of the individuals affected. Coincident sexually transmitted infections were reported in 109 of the 377 persons who were tested for this problem. When clear exposure history was available for monkeypox, the median incubation time was 7 days. Monkeypox virus DNA was detected in seminal fluid from 29 of the 32 patients in whom seminal fluid was examined. Only 13% of all patients were hospitalized. Hospitalization was required for pain management (typically anorectal), soft tissue superinfection, pharyngitis, eye lesions, acute kidney injury, myocarditis, and infection control requirements. Remarkably, there were no deaths. These authors emphasized the need for screening for monkeypox cases outside areas where the virus has traditionally been endemic and the utilization of rapid identification of cases to contain the spread of this disease.

In this series, the diagnosis of monkeypox was most commonly from swab specimens obtained from skin or genital lesions with throat or nasopharyngeal swab specimens; blood was less commonly tested. Anal or rectal swabs were recommended for patients presenting with anal pain or proctitis. The authors were reassured that there were no serious complications despite the admission of 13% of the patients to hospital. Common reasons for hospitalization were pain and bacterial superinfection. However, rare serious complications such as myocarditis and epiglottitis were also observed; thus, the full spectrum of disease severity and complications must be considered and require further study. Clinical presentation and the severity of monkeypox appeared similar among persons with and without HIV infection. In almost all of the patients in this series with HIV infection, HIV was well controlled. Only a small percentage of patients (5%) received antiviral therapy, most often with cidofovir or tecovirimat. Data on the effectiveness of these drugs in man are still incomplete. Finally, the authors acknowledged that this case series is an observational convenience series and that monkeypox is not a “gay disease” nor is it an “African disease.”

Applied Virology

Titanji BK, Tegomoh B, Nematollahi S, et al. Monkeypox: a contemporary review for healthcare professionals. *Open Forum Infect Dis*. 2022;9:ofac310.

Bunge EM, Hoet B, Chen L, et al. The changing epidemiology of human monkeypox-a potential threat? A systematic review. *PLoS Negl Trop Dis*. 2022;16: e0010141.

CDC. U.S. monkeypox 2022: situation summary. Available at: https://www.cdc.gov/poxvirus/monkeypox/outbreak/current.html. Accessed May 31, 2022.

The *Poxveridae* family consists of double-stranded DNA acid viruses that infect a range of animals, including birds, reptiles, insects, and mammals. The family consists of 2 subfamilies: *Cordopoxvirinae* (18 genera with 52 species) and *Entomopoxvirinae* (4 genera and 30 species). Monkeypox belongs to the *Poxveridae* family, the *Chordopoxvirinae* subfamily, and the genus *Orthopoxvirus*. Several poxvirus species have been shown to cause human infections including variola (smallpox), cowpox, monkeypox, vaccinia, camelpox, Alaskapox, Yaba monkey tumor virus, Tanapox virus, orf virus, pseudocowpox virus, bovine papular stomatitis virus, buffalopox, and molluscum contagiosum viruses. The monkeypox virus has a wide range of potential host organisms that has allowed it to circulate in wild animals for prolonged periods of time while sporadically causing human disease through spillover events. More importantly, orthopoxviruses exhibit immunologic

cross-reactivity and cross-protection; thus, infection with any member of the genus provides some protection from infection with any other member of the same genus.

Orthopoxviruses are large viruses with a bricklike structure and a genome consisting of 200 to 500 thousand base pairs that code for over 200 genes. Many of the genes encoded by the orthopoxvirus genome are not essential for virus replication in cell culture but might play important roles in the host antiviral response. All poxviruses complete their replication cycle in the cytoplasm of infected cells via complex molecular pathways. Intracellular replication has been well characterized for the vaccinia virus, which was used to develop the vaccine that helped to eradicate smallpox. Features of the replication cycle are similar for all poxviruses. The infection cycle can be initiated by 2 distinct forms of the virus: the intracellular mature virion and the extracellular enveloped virion, which differ in their expression of surface glycoproteins. Glycosaminoglycans, which are commonly expressed on the surface of mammalian cells, are thought to be crucial for binding of the virion onto the cell membrane, although all cellular receptors are not fully characterized.

Smallpox is estimated to have caused millions of fatalities worldwide and is 1 of the most dreaded infections in human history. This experience serves as a reminder that orthopoxviruses are significant pathogens. Although the origins of smallpox are unclear, evidence suggests that the variola virus may have evolved from a rodent poxvirus thousands of years ago. The increasing danger of orthopoxvirus infections such as the monkeypox virus has long been recognized. Unfortunately, as we have noted, discontinuation of smallpox immunization decades ago significantly reduced global population immunity against smallpox and other orthopoxviruses. The conditions summarized previously raise the possibility that under appropriate circumstances, an increase in human infections, and decreased long-term immunity because of the absence of vaccination, an orthopoxvirus such as the monkeypox virus could acquire the ability to more effectively pass between humans and cause larger outbreaks.

The transmission of monkeypox in endemic and nonendemic settings includes animal-to-human transmission via bites and scratches from infected animals. The preparation and handling of infected animal products may also result in viral transmission. The definitive animal reservoir of the monkeypox virus has not been identified. The virus has been isolated from several animal species, including small mammals and nonhuman primates. When the monkeypox virus has been isolated from wild animals, those animals demonstrated poxlike lesions suggesting active monkeypox virus infection. It is not known whether asymptomatic carriage of monkeypox virus occurs in an animal reservoir. The examination of wild animals in endemic regions detected several animal species with antibodies to orthopoxvirus in the absence of virus in the blood stream on polymerase chain reaction testing. The transmission of virus between humans is thought to occur via direct skin-to-skin contact with lesions on the skin as well as indirect contact with contaminated materials including bedding or clothing. Transmission may also occur at proximity through the exchange of respiratory secretions that contained live virus.

Contact tracing is crucial to controlling the spread of monkeypox. Patients with monkeypox should be interviewed to identify contacts for tracing. The types of contact include face-to-face contact, direct physical contact including sexual contact, and contact with contaminated fomites such as bedding or other objects with shared use. In the health care setting, anyone who has had contact with the patient (eg, staff, roommates, and visitors) should be identified. If someone is exposed to a person with monkeypox, they should be monitored for symptoms such as fevers, chills, rash, and lymphadenopathy for 21 days after the last exposure and offered vaccination where appropriate. Individuals with suspected or confirmed monkeypox should be isolated in a private room apart from other family members and pets. Patients should also avoid close contact with others while they are infectious. Isolation should continue until all cutaneous lesions have resolved and a new layer of skin has formed beneath sites where lesions were present. Waste from monkeypox carriers is considered a pathogen that is life-threatening or a cause of permanent disability. As such, handling and management of clinical waste should be done in accord with hazardous materials management regulations. The greatest concern for human-to-animal transmission is with pet rodents. Although it is possible that transmission may occur with other pets such as dogs and cats, this risk is not clearly defined and should be further evaluated. Current recommendations include quarantine for pet rodents for 21 days and the exclusion of infection through testing.

Therapy

Rizk JG, Lippi G, Henry BM, et al. Prevention and treatment of monkeypox. *Drugs*. 2022;82:957-963.

Adler H, Gould S, Hine P, et al. Clinical features and management of human monkeypox: a retrospective observational study in the UK. *Lancet Infect Dis*. 2022;22:1153-1162.

The mainstay of clinical management for typical monkeypox infection is supportive care. Supportive care includes the maintenance of adequate fluid balance due to the risk of increased insensible fluid losses from the skin, decreased oral intake, vomiting, or diarrhea. Other measures including hemodynamic support, supplemental oxygen or other respiratory care, and treatment of bacterial superinfection of skin lesions should be considered when indicated. Another aspect of supportive care that has been described with other infections is the management of ocular complications, specifically resulting from corneal scarring, possibly with loss of vision. When eye lesions are a concern, potential approaches to consider include early ophthalmology consultation, application of topical lubricants, topical ocular antibiotics for bacterial superinfection, and possibly topical antivirals. Patients with confirmed or suspected disease should be isolated. Clinicians encountering suspects with monkeypox infection should wear personal protective equipment, including face shields, goggles, gowns, and gloves. Surfaces in the patient room should be decontaminated. A high index of suspicion is very important to support the identification of potential cases. Rapid confirmation through testing during isolation of individuals with suspected or confirmed disease is vital. Public health authorities should be notified for contact tracing and mobilization of other components of public health response. Antiviral agents and immune therapies should be considered for individuals with moderate or severe symptoms or who are thought to be at high risk for progression to severe disease.

At the present time, there are no US Food and Drug Administration (FDA)-approved treatments specifically for monkeypox. However, there are antiviral agents with known activity against monkeypox including cidofovir, brincidofovir (a lipid conjugate prodrug of cidofovir), and tecovirimat. In addition to antiviral agents, vaccinia immune globulin given intravenously has been previously approved by the FDA for the treatment of complications due to vaccinia vaccination, such as progressive vaccinia and severe generalized vaccinia. Currently, tecovirimat, cidofovir, and vaccinia immune globulin intravenous are available from the Strategic National Stockpile under expanded access investigational new drug protocols held by the CDC for the treatment of orthopox infections in an outbreak scenario. In the United States, these medications may be accessed through the CDC via requests from state or territorial health departments. The available agents for orthopox infections are summarized in the following paragraphs.

Cidofovir was approved by the FDA in 1996 for the management of patients with retinitis caused by cytomegalovirus in association with AIDS. Cidofovir has broad antiviral

activity against viruses from different families including herpes, adenovirus, and orthopox viruses. Brincidofovir was approved by the FDA for the treatment of smallpox in 2021. It has also been used for cytomegalovirus infections, adenovirus, and other orthopox infections. This agent was used as part of a combination therapy protocol in a patient developing leukemia after smallpox vaccination. This drug has also been used in the treatment of a transplant recipient with cowpox infection. One noted complication of brincidofovir use is elevated liver enzymes, which led to the cessation of therapy. Cidofovir blocks viral DNA synthesis through the inhibition of DNA polymerase. It may be given intravenously, and off-label use includes topical administration at vesicular lesions. A typical dose is 5 mg/kg once weekly for 2 or more doses with coincident probenecid. The side effects noted include nephrotoxicity, neutropenia, decreased intraocular pressure, nausea, and vomiting. Brincidofovir is given orally at a dose of 4 mg/kg once weekly for 2 doses with a maximum of 200 mg of drug per dose. The side effects of this agent include abdominal pain, nausea, vomiting, diarrhea, elevated liver enzymes, and increased bilirubin.

Tecovirimat was approved by the FDA in 2018 for the treatment of smallpox infection. It was approved in Europe in 2022 for the treatment of smallpox and cowpox. Tecovirimat has also been used as a prophylactic agent to prevent the development of progressive vaccinia in a patient who had already received smallpox vaccination and was diagnosed with leukemia after vaccination. Tecovirimat was used while the patient was receiving chemotherapy for leukemia. Tecovirimat has also been used for keratoconjunctivitis due to cowpox and travel-associated monkeypox in the United States since 2021. An expanded access protocol is now in place in the Central African Republic. The mechanism of action for tecovirimat includes the inhibition of protein VP37, which prevents the creation of variants that can be released from an infected host cell; thus, replication is prevented, and dissemination within the host is limited. A variety of intravenous and oral dosing regimens allow administration of the drug for 14 days with protocols based on patient weight.

Vaccinia immune globulin intravenous was approved by the FDA in 2005 for the treatment of complications due to vaccination for vaccinia virus. Before this, vaccinia immune globulin was administered as an intramuscular injection. The FDA subsequently approved intravenous administration of vaccinia immune globulin after several published reports of efficacy for orthopox infections. Vaccinia immune globulin intravenous has been used in a patient with inflammatory bowel disease who developed infection after exposure to vaccinia-rabies glycoprotein recombinant virus used in animal bait to help control the spread of rabies in the animal population. Intravenous vaccinia immune globulin provides passive immunity through orthopox-specific antibodies collected from pooled human plasma taken from persons immunized with smallpox vaccine. Doses of 6,000 U/kg to 9,000 U/kg as a single dose are given. Doses may be repeated based on patient symptoms. FDA approval is directed toward complications of vaccinia vaccination (progressive vaccinia, severe generalized vaccinia). The noted side effects include systemic infusion reactions and injection site reactions. Antibody infusion is contraindicated in persons with immunoglobulin A deficiency and possible immunoglobulin A hypersensitivity.

Overall, the natural history of monkeypox infection in humans is mild to moderate disease with a self-limited course for many patients. Antiviral therapy should be considered for severe illness requiring hospitalization or when ocular, oral, or perineal involvement is identified. Antiviral therapy should also be considered in patients at higher risk for progression to severe viral illness such as the immunocompromised patient group, children less than 8 years of age, pregnant or breastfeeding persons, and in the presence of atopic dermatitis or other active exfoliative skin conditions. The most practical clinical experience is with tecovirimat, which is the preferred antiviral drug. Ideally, treatment for monkeypox infection should be given in the context of a clinical trial to generate long-term evidence that could inform future treatment strategies. The coordination of treatment with infectious disease specialists and public health authorities is encouraged.

Epilogue

Sherwat A, Brooks JT, Birnkrant D, Kim P. Tecovirimat and the treatment of monkeypox – past, present, and future considerations. *N Engl J Med*. 2022;387:579-581.

Lane HC, Fauci AS. Monkeypox – past as prologue. *N Engl J Med*. 2022;387:749-750.

The current monkeypox outbreak provides a new set of challenges to patients as well as the medical and biomedical research communities. It is noteworthy that there appears to be a recent change in the epidemiology of monkeypox in Africa, where cases are now occurring in new geographic areas, perhaps facilitated by changes in the climate and deforestation leading to changes in the environmental interface between humans and animal reservoirs. At the time of the largest demographic survey of monkeypox disease, approximately 14,000 cases had been reported in the world; approximately 2 weeks later, that number had doubled. We can hope that lessons learned during the responses to HIV/AIDS and coronavirus disease 2019 (COVID-19) help us to organize a more efficient and effective response to monkeypox, and the response to monkeypox should, in turn, help us to prepare a response to the inevitable next emerging or re-emerging infectious disease with pandemic potential. The challenge to public health and research communities during this time of emergency response is to demonstrate efficient and equitable availability and distribution of existing countermeasures to individuals in need of them while conducting rigorous studies to define what clinical efficacy may be for these measures, demonstrate any safety concerns, and guide optimal utilization.

A more extensive comparison of the situations at the start of the AIDS, COVID-19, and global monkeypox outbreaks reveals striking similarities and differences. For example, in the case of AIDS, the etiologic agent was unknown, and there were no effective specific counter measures at that time. Today, we know the cause of AIDS and have effective therapies. However, it took years to reach that point, and a vaccine is lacking. In the case of COVID-19, the etiologic agent was quickly identified. However, effective countermeasures were lacking. Today, we have more effective diagnostics, vaccines, and therapies for COVID-19 after approximately 1 year of intense research and development. In the case of monkeypox, the etiologic agent has been known for decades. There is 1 vaccine available for monkeypox under a new drug license that incorporates live virus vaccines. This agent is in the Strategic National Stockpile. In addition, 2 drugs including tecovirimat and brincidofovir have been licensed for the closely related virus variola, which causes smallpox. Studies of monkeypox and its animal reservoirs have been ongoing in Africa, and a placebo-controlled trial of tecovirimat may start in the Congo. Clinicians and other health care workers should follow this work with interest.

Summary Points

- When smallpox immunization was common, monkeypox was not a pathogen causing significant risk. However, the proportion of smallpox-vaccinated individuals has fallen from over 80% in 1980 to less than 30% today, and in some developing countries, young nonvaccinated individuals exceed 75% of the

population. These individuals are also susceptible to monkeypox infection.

- Factors contributing to the emergence or recurrence of monkeypox disease include climate change, exploitation of the rain forest, armed conflicts in disease areas, mobile populations, and reduced herd immunity associated with the discontinuation of smallpox vaccination.
- Incubation for monkeypox ranges from 5 days to 3 weeks with symptoms lasting from 2 to 5 weeks. Early symptoms include shivers, headache, fainting, and backache. Fever and lymphadenopathy may precede the development of rash. Lymphadenopathy in the neck, groin, and submandibular regions is a particular feature of monkeypox patients in recent series. When rash presented, facial appearance was early with later spread of the rash along the trunk and extremities.
- Limiting human exposure to suspect host animals is a recommended initial step to reduce monkeypox spread. Human-to-human transmission cannot sustain the continued spread of monkeypox without animal contact. Where patients are hospitalized, CDC recommendations include negative pressure rooms with droplet and contact precautions along with full protective apparel for health care professionals.
- Although mortality is uncommon in some series, common causes for hospitalization were pain and bacterial superinfection of lesions. Rare serious complications such as myocarditis and epiglottitis have also been observed; thus, the full spectrum of disease and complications must be considered in the monkeypox patient and require further study. Although many reported patients have homosexual behavior and many animal vectors begin in Africa, it is important to note that monkeypox is not a “gay disease” or an “African disease.” Contact tracing is crucial to controlling the spread of monkeypox. The types of contact include face-to-face contact, direct physical contact including sexual contact, and contact with contaminated fomites such as bedding or other objects with shared use.
- At present, the mainstay of clinical management for a typical monkeypox infection is supportive care. Supportive care includes the maintenance of adequate fluid balance, hemodynamic support, respiratory care, and treatment of bacterial superinfection of skin lesions. Assess patients for ocular complications, particularly resulting from corneal scarring. Patients with confirmed or suspected disease should be isolated. Clinicians encountering patients with suspected monkeypox infection should wear personal protective equipment, including face shields, goggles, gowns, and gloves. Surfaces in the patient room should be decontaminated.
- The natural history of monkeypox infection in man is mild to moderate disease with a self-limited course. Antiviral therapy should be considered for more severe illness requiring hospitalization or ocular, oral, or perineal involvement. Antiviral therapy should also be considered in patients at higher risk for progression to severe viral illness such as the immunocompromised patient group, children less than 8 years of age, pregnant or breastfeeding persons, and in the presence of atopic dermatitis or other exfoliative skin conditions specific for monkeypox. Antiviral agents with known activity against monkeypox include cidofovir, brincidofovir, and tecovirimat. In addition to antiviral agents, vaccinia immune globulin may be given intravenously. This agent was previously approved by the FDA for the treatment of complications due to vaccinia treatment.

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