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Mpox: a global public health emergency

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Just when the world is recovering from the devastation from covid-19 pandemic, it is on the brink of another viral outbreak – this time it's a pox virus. On August 14, 2024, the World Health Organization declared a global public health emergency related to the ongoing outbreak of mpox in the Democratic Republic of Congo. Mpox (previously referred to as monkeypox) is a viral zoonotic infection that is caused by monkeypox virus and results in a rash similar to that of smallpox. However, historically, person-to-person spread outside the household and mortality from mpox are significantly less than for smallpox.

Virology

Monkeypox virus is an orthopoxvirus that is in the same genus as variola virus (the causative agent of smallpox) and vaccinia virus (the virus used in the available smallpox vaccines).

Two distinct strains of monkeypox virus have existed in different geographic regions of Africa, as suggested by epidemiologic, animal, and molecular evidence.[1] Clade I has been responsible for disease in the Congo basin, having higher mortality (up to 10%) whereas clade II has been isolated in West Africa and is less virulent (mortality <0.1%).[2] Both clades have been further subclassified into a and b groups. Monkeys and humans are incidental hosts; the reservoir is likely to be certain rodents.

Epidemiology

Monkeypox virus was first isolated in Denmark in 1958 from a colony of laboratory monkeys from Singapore that were going to be used for polio virus research.[3]

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Monkeypox virus was first identified as a cause of disease in humans in the 1970 in what is now the Democratic Republic of the Congo (DRC). Since the discontinuation of smallpox immunization, which also protects against mpox, cases of mpox have generally occurred in Central and West Africa.

There was an outbreak of human mpox in the United States in 2003 associated with infected prairie dogs who were exposed to imported animals from Africa.[4] After that, sporadic cases were reported in several previously nonendemic countries, mostly related to travel from Africa.

However, in May 2022 a global multi-country outbreak was recognized; this outbreak was associated with person-to-person transmission, especially homosexual young males, mostly due to clade II mpox virus. This outbreak was reduced in late 2022. But in early 2023, another global outbreak started with more virulent clade Ib virus and still spreading worldwide. Till August 2024, it has spread to 115 new countries other than 7 previously affected ones and infecting almost 1,00,000 population worldwide, including our neighboring countries India and Pakistan.[5]

Transmission

Human-to-human transmission of monkeypox virus can occur through several routes. These include: 1. Close contact with infectious skin lesions like close intimate contact during sexual activity or patient handling.[6] 2. Indirect contact with infectious fluid (eg, on contaminated linens). 3. Percutaneous inoculation via needlestick injuries from supplies used to collect cutaneous lesion samples. 4. Large respiratory droplets. For this to occur, prolonged face-to-face contact may be required (eg, within a six-foot radius for e"3 hours in the absence of personal protection equipment [PPE]). Animal-to-human transmission may occur through

contact with an infected animal's bodily fluids or through a bite.

Clinical features

Infections caused by mpox can be classified as either systemic or localized (at the site of virus entry). The type of infection depends on the species of mpox and the route of entry. The incubation period can vary from 4 to 21 days.

Systemic manifestations are fever, headache, sore throat, myalgias, regional lymphadenopathy followed by a characteristic rash. Systemic symptoms typically last one to five days. The skin eruption usually occurs between one to two days before and three to four days after the onset of the systemic symptoms and continues for two to three weeks, although rashes without systemic illness have been reported.

The rash associated with mpox progresses through several stages: macule, papule, vesicle, pseudo-pustule. The lesions eventually crust over, and these crusts dry up and then fall off. Lesions may be painful or itchy. Frequently the lesions are concentrated around the anogenital, oral, and perioral areas, suggesting the site of inoculation. Severe diseases, including a necrotizing form of mpox, may be seen in the context of advanced HIV. Other complications include bronchopneumonia, sepsis, myocarditis, encephalitis etc.[7]

Diagnostic work-up

The diagnosis of mpox should be suspected in patients who present with a rash or other symptoms that could be consistent with mpox and have epidemiologic risk factors for infection.

When evaluating a patient with suspected mpox, varicella zoster virus (presenting as chickenpox or herpes zoster), herpes simplex, syphilis, smallpox, and other poxvirus infections should be included in the differential diagnosis.

A diagnosis of mpox can be confirmed by demonstration of orthopoxvirus DNA (eg, by polymerase chain reaction [PCR] testing or next-generation sequencing of a clinical specimen) or through isolation of monkeypox virus in culture from a clinical specimen.

Serologic testing for monkeypox virus can be used to support a diagnosis of mpox and may be particularly helpful if viral testing is not able to be performed. Patients with mpox typically have detectable levels of anti-orthopoxvirus IgM antibody during the period of 4 to 56 days after rash onset. The CDC developed an IgM capture and an IgG enzyme-linked immunosorbent assay (ELISA) that demonstrated recent monkeypox virus infection. Serum IgM and IgG antibodies were detected five and eight days after onset of rash, respectively.[8] People presenting higher IgM and IgG levels have shown faster viral clearance and more rapid clinical resolution

Clinical management

Management of patients with mpox involves supportive care as well as antiviral therapy for select patients. Most immunocompetent patients with mpox have mild disease and will recover without medical intervention.

Hospitalization may be warranted for those who have or are at risk of dehydration (eg, nausea, vomiting, dysphagia, sever tonsillitis), those who require more intensive pain management, and those experiencing severe disease or complications.

Several antivirals may be useful for the treatment of mpox. However, none of the recommended agents are US Food and Drug Administration (FDA)-approved for this indication. During the outbreak that began in 2022, tecovirimat was the agent most used in USA and Europe, since it was available through an expanded access investigational new drug (EA-IND) protocol held by the CDC.[9] However, data supporting the efficacy of antiviral therapy for patients with mpox are limited and not readily available in most countries including Bangladesh. Antiviral therapy is indicated for the following groups of patients with confirmed or suspected mpox patients – 1. Severely immuno-compromised, (like HIV patients, hematological or other malignancy, chemotherapy or radiotherapy receiving patients, organ transplant recipients or patients on immunosuppressive drugs or steroids etc.), 2. Active skin conditions (psoriasis, eczema, burn etc.), 3. Pregnant or lactating patients, Persons <18 years of age, regardless of illness severity or underlying comorbidities at presentation and 4. Patients with protracted or life-threatening manifestations of mpox.

Secondary bacterial infections can occur in patients with mpox. The patient should receive appropriate antibiotic coverage in addition to antiviral therapy; regimens should generally include agents that are used to treat

soft tissue infections (eg, those that cover both staphylococcal and streptococcal species).

Vaccine

There are two available vaccines that can reduce the risk of developing mpox. The modified vaccinia Ankara (MVA) vaccine (JYNNEOS in the United States, IMVANEX in the European Union, and IMVAMUNE in Canada) and ACAM2000 vaccine. Vaccination is expected to provide protection regardless of clade. The MVA vaccine is made from a highly attenuated, nonreplicating vaccinia virus. It is administered as two doses four weeks apart. In the United States, JYNNEOS is approved for the prevention of smallpox and mpox. It is now recommended as a routine vaccine in people at risk for mpox (pre-exposure prophylaxis) and as post-exposure prophylaxis, within four days of exposure whenever possible, although vaccination can be considered for up to 14 days after an exposure.[10]

Disease course

Most patients with mpox have a self-limited illness. In the 2022 global outbreak, rare deaths have been reported. By contrast, in Central Africa, where infection is caused by a different strain (clade I), the fatality rate has been reported to be as high as 10 percent; severe disease is more commonly seen in children and immuno-compromised patients.

Infection prevention and control

The risk of transmitting monkeypox virus to others in both health care and community settings can be mitigated through implementation of infection prevention and control measures. These recommendations are based on guidance from the United States Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO).

All individuals with confirmed exposures to mpox should monitor for signs and symptoms for 21 days. Contacts who remain asymptomatic can continue routine daily activities. If symptoms develop, they should immediately self-isolate.

A patient with suspected or confirmed mpox should be triaged promptly to a single-person (private) room with dedicated toileting facilities. Patients should don a facemask, when possible, if any individual enters the room. Personal protective equipment (PPE) is required for all health care personnel (HCP) interacting with a patient with suspected or confirmed mpox or interacting with the patient's environment.

Persons with mpox should be considered infectious until all lesion scabs have fallen off and re-epithelialization has occurred, which typically lasts two to four weeks.[11]

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