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Monkeypox: A current emergency global health threat

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Abstract:

Monkeypox (MPXV) is an emerging zoonotic disease carrying a global health threat. Using a multi-disciplinary approach, we review the current MPXV virus infection outbreak including virology, prevention, clinical presentation, and disaster management. MPXV is caused by a double-stranded deoxyribonucleic acid virus. Despite its clinical similarities with smallpox, it is less severe with low mortality. Human-to-human transmission occurs through prolonged direct or close contact, or through blood, body fluids, or mucosal lesions. Risk groups include frontline health workers who care for MPXV patients, household members of an infected patient, and men who have sex with men. Skin lesions are usually, but not always, at the same stage. They may affect the face followed by the distal extremities with fewer lesions on the trunk (centrifugal distribution). Lesions may involve the mouth, genitalia, conjunctiva, and rectum. The majority of cases are mild. Nevertheless, the disease may have long-term effects on the skin, the neurological system, and the eye. Vaccination against MPXV is available but meanwhile should be limited to those who are at high risk. Those vaccinated against smallpox (usually older than 40 years) might be immune against MPXV. Infectious diseases are without borders. If proper action is not taken, there is considerable risk that MPXV will be entrenched worldwide. Our world has a delicate balance between animals, environment, and humans reflecting the need for a "one globe, one health approach" to address this risk. Following the principles of disaster management and using the lessons we have learned from the COVID-19 pandemic will reduce the impact of the MPXV outbreak.

Keywords:

Emergency, human monkeypox, orthopoxvirus, pandemic, public health, transmission, vaccine

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Introduction

Zoonotic diseases continue to be a serious global public health threat. The last encountered is the monkeypox (MPXV) disease. It is caused by a deoxyribonucleic acid (DNA) virus belonging to the orthopoxvirus genus, similar to smallpox. It can be transmitted from animals to humans and from humans to humans. The general symptoms and signs of MPXV disease are similar to the eradicated smallpox disease but are less severe with a much lower death rate.

Since 2019, the primary global focus was on the control of the COVID-19 pandemic through preventive methods and vaccination, despite the shortage of vaccines in low-income countries. The sudden outbreak of MPXV caused anxiety of facing another pandemic. This was exacerbated by the spread of misinformation, misdiagnosis, and inadequate safety measures. It is time to apply what we have learned from the COVID-19 pandemic, which has revealed the weaknesses in the public health

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infrastructure, shortage of the public health task force, and shortages of the organizational capacities.[1] Historically, MPXV was first identified in a Danish laboratory in 1958.[2] The first case in humans was described in 1970 in the Democratic Republic of the Congo (formerly Zaire).[3] Zoonotic outbreaks of orthopoxviruses occurred before. Cowpox has been reported in several European countries, and camel-pox in Africa, the Middle East and Asia.,[4-6] In 1796, Edward Jenner pioneered the concept of vaccines with the development of a cowpox vaccine tested in a child. This was further developed to fight smallpox which was finally eradicated in 1980.[7]

Some may assume that we have learned lessons from our global previous experiences including the smallpox epidemic, the COVID-19 pandemic; the smallpox vaccination, epidemiological prevention, and the public health responses; and that we are now adequately prepared to handle the spread of another serious viral global pandemic. Unfortunately, this is still not the case. Much remains to properly respond to this current outbreak. Interrupting the transmission of MPXV from animals to humans is essential to contain this disease, otherwise, human infections will continue to occur as we witness. The initial assessment of the limited MPXV outbreak in Africa indicated that it should be contained using the "one globe one health" approach to stop its spread keeping the balance between man, animals, and the environment. Knowledge about MPVX is relatively low among healthcare workers. Profound knowledge is essential for reducing human transmission, adopting proper infection control policies, and supplying proper personal protective equipment and isolation, facilities.[8] In this review, we will summarize our understanding of this topic, using a multidisciplinary approach, from a public health, virological, clinical and disaster medicine perspectives to have health care professionals more aware of this new global health emergency.

The Perplexities of the Monkeypox Virus Outbreak

MPXV is a rare zoonotic viral disease which is endemic in the West and Central Africa. The first case was diagnosed in Congo in 1970. Subsequently, the disease spread to infect children and adults during the period of 2010-2019. This might be due to the cessation of smallpox vaccination, which previously provided some cross-protection against MPXV, or alternatively due to genetic mutations that increased transmission outside the endemic areas. Nevertheless, there is no scientific evidence to support these suggestions.[9] The largest previous MPXV outbreak occurred in Nigeria during 2017-2018. Travellers from UK and Israel, who had the disease, were linked to travel to endemic areas. MPXV in America was previously linked back to rodents (hosts of the virus) imported from Ghana. On July 23, 2022, the World Health Organization (WHO) declared the MPXV outbreak as a "public health emergency of international concern". The Center for Disease Control and Prevention in the United States (US) has reported a total of 72,874 confirmed cases of MPVX globally as of October 13, 2022 with only 28 deaths (a mortality of <1 in every 3000 cases) [Figure 1]. Out of this, 27,096 were from the USA. The US president has already declared MPXV a public health emergency.[10] This alarming increase in MPVX infection has triggered the importance of intensifying public health surveillance, epidemiological investigation of cases and close contact tracing to launch public health measures on early detection and prompt response.

Risk of Infection and Mode of Transmission

Almost half of the world's population has no immunity against orthopox viruses. Preventive measures should be adopted to protect vulnerable communities, especially young children, and to prevent transmission from those already affected. Vulnerable unexperienced communities who were not previously exposed to the virus are at a higher risk of infection.[11,12] The WHO risk assessment implies that vaccination against smallpox might be cross-protective against MPXV. Nevertheless, immunity from smallpox vaccination will only be present in those older than 40 years, with varying ages depending on the country, because smallpox vaccination programmes ended worldwide in 1980 after its eradication.[13]

We must acknowledge that the natural reservoir of MPXV has not been well-identified. There are different possible means of MPXV transmission from animals to humans. Animal transmission may occur via

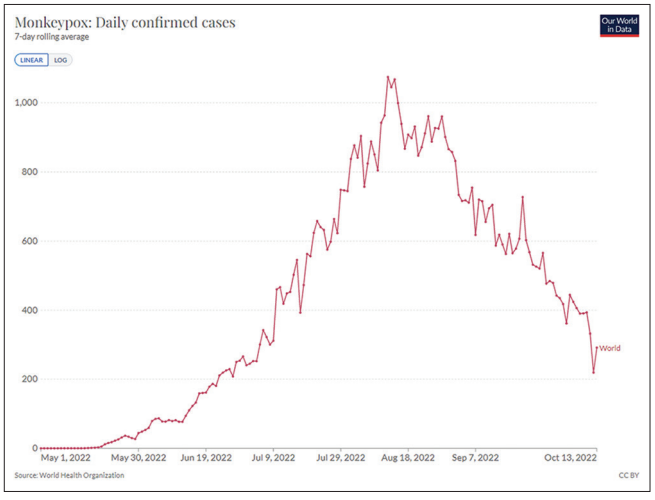

Figure 1: Seven-day rolling daily average confirmed cases of monkeypox worldwide as of October 13, 2022. Source: Edouard Mathieu, Fiona Spooner, Saloni Dattani, Hannah Ritchie and Max Roser (2022)-"Monkeypox." Published online at OurWorldInData.org. Retrieved from: "https://ourworldindata.org/monkeypox " (Online Resource) (Accessed on October 15, 2022)

contact with infected animals, their body fluids, lesion materials, and respiratory droplets. However, there are multiple wild and domestic animals in Africa that act as reservoirs for the disease including rope squirrels, and tree squirrels. Eating inadequately cooked meat or other products of infected animals is a possible risk factor. There was an increased contact between humans and the reservoir animals of the disease because of continued deforestation. Furthermore, civil wars pushed the refugees to move deeper into forests and hunt wild animals like monkeys and rodents for food. Human to human transmission may occur through prolonged or close contact, either directly or through blood, body fluids, or cutaneous/mucosal lesions. Most cases in Europe and other countries were found in men who had sex with men.[14,15] MPXV reminds us of the early stages of HIV which was recognized in the eighties with the similar modes of transmission.

Control and Prevention

Establishing an active surveillance system that rapidly identifies the index case and close contacts is important to contain the outbreak. Those at high-risk should be identified including frontline health care workers, infected household members, and those suspected or confirmed to pose a risk of infection. Active community health education and awareness about the risk factors for MPXV infection and measures to reduce its exposure should be implemented. It is interesting to note that the scientific impact of Edward Jenner's work in 1796 is still useful today. Smallpox vaccination provides about 85% of the recipient's protection against MPXV infection. In the US, two vaccines, namely JYNNEOS and ACAM2000, have been approved for the prevention of MPXV.[16,17]

Virological Characteristics

The orthopoxviruses, including the MPXV virus, are large brick shaped viruses with a virion size of around 200-450 nm with varying length DNA genomes [Table 1]. This makes them large enough to be viewed even by a light microscope.[18] At the center of the virion is the nucleoprotein core which protects the tightly packed linear double-stranded DNA genome [Figure 2], and also contains the viral DNA-dependent RNA polymerase required for replication.[19,20] The core is surrounded by an outer membrane which is studded with microtubules. The orthopox viruses are unusual DNA viruses in that they replicate within the cytoplasm of the infected cells rather than the nucleus.[18,21] Virions enter the cell through endocytosis or hemifusion with the plasma membrane before undergoing two sequential uncoating processes to release the viral DNA for replication. Virions are packaged within the cytoplasm where most remain

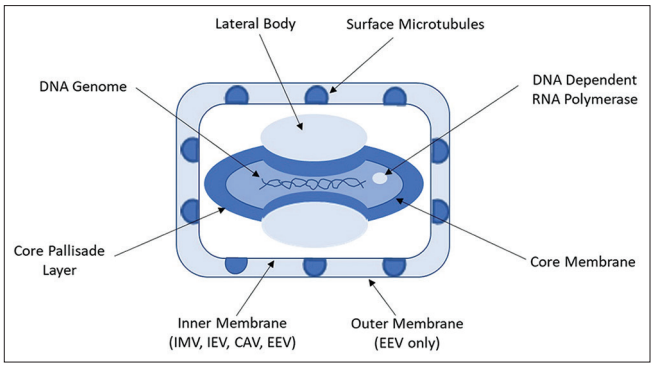

Figure 2: An illustration demonstrating the Monkeypox Virion structure. CAV: Cell Associated Virion, EEV: Extracellular Enveloped Virion, IEV: Intracellular enveloped virion, IMV: Intracellular mature virion (Illustrated by Dr Emma A. Davies, Consultant Clinical Scientist, Department of Virology, Manchester University NHS Foundation Trust, Manchester, UK)

as intracellular mature virions [Figure 3]. However, a proportion of them become intracellular enveloped virions through the acquisition of a further membrane. These double membrane virions can migrate to the cell surface on actin filaments and go on to infect other cells as cell-associated virions or cause systemic viral spread as extracellular enveloped virions which have been released from the cell membrane.[18,22]

MPXV virus is a member of the chordopoxvirinae subfamily of the poxviridae family. This subfamily, which includes the orthopoxviruses, can infect chordates.[23] The MPXV virus dsDNA genome consists of three distinct regions: (1) the conserved central region, (2) the left terminal region, and (3) the right terminal region.[21,23-25] There are 190 nonoverlapping genes within the genome, 90 of these are found in the conserved region. These conserved genes have more than 90% sequence similarity across all orthopoxviruses. They encode the structural proteins and essential components for protein processing and virion assembly.[21,23,25,26] The terminal genome regions encode the non-essential proteins which impact virulence, host range or interaction with the host immune system.[23,24]

Poxviruses and MPXV infectious ability are related to their manipulation of the host immune system. Virulence factors found in the variola virus have homologs in MPXV, with 83.5-93.6% sequence similarity, the majority of which are postulated to affect the host immune response.[21,22] Suppression of the immune response may account for the reduced case-fatality rate compared with smallpox. Nevertheless, it may also increase the time to clearance of the virus, therefore, improving transmission rates.[26] Suppression of the immune response can occur through different mechanisms: (1) suppression of the protein kinase R pathway and of the complement binding pathway,[26,27] (2) reduction of the binding of the host Interleukin (IL)-1 receptor and IL-1 cytokine response pathways,[25,26] (3) inhibition of the inactivation of both

Table 1: Comparison between orthopoxviruses and chickenpox

	Monkeypox	Smallpox (variola)	Cowpox	Camelpox	Alaskapox	Chickenpox
Family	Poxviridae	Poxviridae	Poxviridae	Poxviridae	Poxviridae	Herpesviridae
Genus	Orthopoxvirus	Orthopoxvirus	Orthopoxvirus	Orthopoxvirus	Orthopoxvirus	Varicellovirus
Approximate genome size (kb)	197	186	222.5	205	210.8	125
Genome composition	Linear dsDNA	Linear dsDNA	Linear dsDNA	Linear dsDNA	Linear dsDNA	Linear dsDNA
Number of genes	190	200	223	211	206	71
Virion size	200–250 nm	250–350 nm	250–350 nm	265–295 nm	Unknown	150–200 nm
Virion shape	Brick	Brick	Brick	Brick	Brick	Spherical
Incubation period	5–21 days	7–19 days	8–12 days	2–3 weeks	Unknown	10–21 days
Average clinical syndrome	2–4 weeks	21 days	6–12 weeks	30–40 days	3 weeks	4–7 days
Transmission	Lesion fluid contact Droplet/fomite Respiratory secretions	Lesion fluid contact Airborne/droplet	Contact with infected animals or their body fluids	Contact with infected animal or their body fluids	Unknown-likely infected animals	Lesion fluid contact Droplet/fomite
Animal reservoir	Uncertain Possibly rodents	None	Rodents	Camels	Unknown	None
Intermediate animal host	Small mammals	None	Cows Domestic cats	None	Unknown	None
Case fatality rate	Clade I~10.3% Clade II a/b~3.6%	Variola minor~1% Variola major~30%	2 reported deaths	No reported deaths	No reported deaths from 4 known cases	1–14 years=1/100,000 15–19 years=6/100,000 >19 years=21/100,000

DNA: Deoxyribonucleic acid, dsDNA: Double-stranded DNA

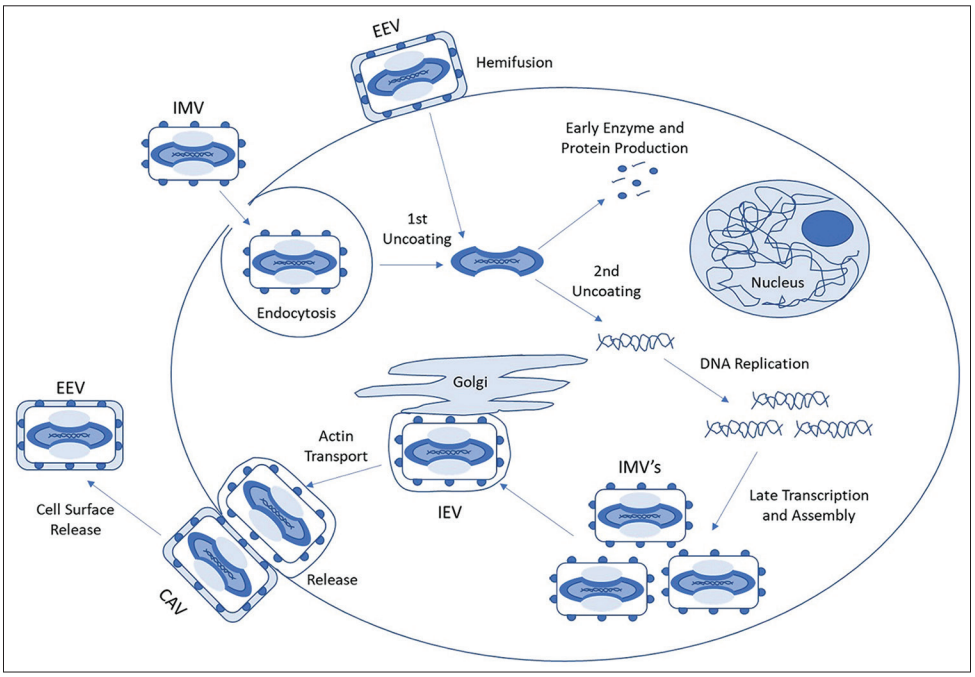

Figure 3: An illustration demonstrating the Monkeypox Replication Cycle. CAV: Cell Associated Virion, EEV: Extracellular Enveloped Virion, IEV: Intracellular enveloped virion, IMV: Intracellular mature virion *(Illustrated by Dr Emma A. Davies, Consultant Clinical Scientist, Department of Virology, Manchester University NHS Foundation Trust, Manchester, UK)*

CD4+ and CD8+ T-cells, and[28] (4) mutations in the key areas for antibody response generation including the B21 protein and the OPG210.[24,29,30]

Despite the clinical similarities between MPXV and smallpox disease, they are not phylogenetically closely related.[31] MPXV viruses do not cluster with any other

orthopoxvirus, although they are most closely related to vaccinia and cowpox.[21,23,31] MPXV genetics explains its morbidity and mortality. Until recently there were two clades of African MPXV viruses; West African and Central African.[31] The Central African clade, now known as Clade I, is the oldest and contains five subgroups of virus.[25] According to historical phylogenetic analyses, a single group of West African clade viruses developed to become Clade II. This in turn split into two groups: (1) Clade IIa (the historical West African strains) and Clade IIb, which was responsible of outbreaks from 2017/2018 onwards.[24,25,30] (2) Clade IIb was briefly known as Clade III. There is major difference in case-fatality rate of Clade I (>10%) and Clade IIa/b a (<1%).[29] The 2022 MPXV outbreak is caused by a B.1 lineage virus which belongs to West African Clade IIb. It has possibly emerged from a single introduction into Europe from an endemic country in March 2022.[24,29,30] The B.1 lineage diverged from the A.1 lineage viruses which formed part of the old Clade II and was associated with exportation from Nigeria to multiple countries in 2018-19. The B.1 lineage viruses contain an average of 50 single nucleotide polymorphisms over the A.1 lineage suggesting rapid accumulation of genetic changes over a short period of time.[29,30] APOBEC3 editing of the genome possibly contributes to this phenomenon. It has mutation rates 6-12-fold higher than the 1-2 substitutions per genome per year which was previously observed. It is unclear if this has contributed to increased transmission or virulence of the virus.[24,29,30] Isidro *et al*.[29] suggested an ongoing APOBEC3 driven evolution in MPXV virus during human-to-human transmission of B.1 lineage virus.

Vaccination

There are two types of vaccines: the inactivated vaccines and live attenuated vaccines. The former type has killed or nonliving parts of the microbes while the latter type contains living weakened microbes.[32] Both types trigger the innate immune system. The immune system is divided into the innate/general resistance system and the adaptive system interacting with each other to provide an effective immune response.[33] Both JYNNEOS and Modified Vaccinia Ankara (MVA) are live attenuated, non-replicating viruses which produce neutralizing antibody responses in humans for the prevention of smallpox and MPXV.[34]

The Advisory Committee on Immunization Practices (ACIP) recommend the vaccination of individuals who have a high risk of contracting orthopoxviral infections (including MPXV) like healthcare workers.[35] ACAM2000 was the only available vaccine in 2015.[36] In 2021, ACIP permitted the use of JYNNEOS as prophylaxis for the high-risk group. It is also safe for immunocompromised and as booster doses. These two vaccines are available now. The booster doses are recommended on regular basis for those having continued occupational risk. Other high-risk workers without ongoing occupational risk, such as public health response team members, should have a booster dose only after a high-risk event. Any species of orthopoxvirus can provide cross-protection against the other species including MPXV, variola, vaccinia, cowpox, akhmeta, and alaskapox.[37] Almost all cases of vaccinia virus among previously vaccinated individuals were among those who had incomplete booster doses.[37,38] The WHO`s interim guidance on June 14, 2022 recommended a judicious use of the old as well as the second-and third-generation vaccines of smallpox, some of which may be useful for MPXV, one of which, MVA -Bavarian Nordic, has been approved for the prevention of MPXV.[39] In the United Kingdom, a modified smallpox vaccination, called MVA, was offered to people at high risk. Because of its limited supply, it is recommended to be used only in susceptible people and those with high risk to reduce the spread of the infection in the community.[40]

A recent systematic review of 18 studies, including three randomized controlled trials, indicated that JYNNEOS provides slightly better prevention compared with ACAM2000 with fewer side effects. Accordingly, JYNNEOS was recommended as an alternative to ACAM2000 for primary vaccination response team members, laboratory personnel, and healthcare workers who care for orthopoxviruses patients. Furthermore, high-risk occupationally exposed individuals to virulent orthopoxviruses, such as MPXV and variola viruses, were recommended for a booster dose of JYENNEOS every 2 years following the two primary doses of the same vaccine. On the other hand, high-risk occupationally exposed individuals to less virulent orthopoxviruses, such as cowpox virus or vaccinia virus, were recommended for a booster dose of JYENNEOS every ten years following the primary vaccination. Finally, ACIP recommended, that occupationally exposed persons can take the JYNNEOS vaccine as booster doses when the primary doses were ACAM2000.[37]

Clinical Presentation

Following exposure, MPXV disease starts with an incubation period of 3-17 days during which the person has no symptoms. This is followed by 2 to 4 weeks of active viral infection. At the beginning of this period, infected individuals typically exhibit a nonspecific prodrome of fever, chills, malaise, headache, sore throat, and cough that precedes the rash by 1-4 days. At the onset of fever and almost 1-2 days prior to rash development, patients develop a generalized or

localized lymphadenopathy in the neck, axilla, and groin. This is a distinctive clinical sign of MPXV disease when compared with smallpox and chickenpox.[41] Nevertheless, with the current 2022 outbreak, prodromal symptoms including lymphadenopathy are often mild or nonexisting or may appear after the onset of the rash. Clinicians are strongly advised to be alert about these atypical features and test patients with rash consistent with MPXV regardless of whether the rash was preceded by a typical prodrome.[14,41-44]

The classic rash of MPXV disease presents with lesions at the same stage (similar to smallpox) but can also present with lesions appearing in crops of different stages (similar to chickenpox) particularly among smallpox vaccinated individuals.[45] The rash typically progresses every 1-2 days through four stages: macules, papules, vesicles, and pustules, and lastly scabbing over and peeling. The rash starts on the face and then involve the whole body with a centrifugal distribution (lesions concentrated on the face and distal extremities (hands and feet), and fewer lesions on the trunk) [Figure 4]. Lesions may also involve mucosal surfaces including the mouth, genitalia, conjunctiva, and rectum and is often associated with itching (especially in the healing stage) and pain at the site of lesions resulting in tenesmus (painful defecation) and dysphagia (painful swallowing).[41]

With the current 2022 outbreak, skin and mucous membrane lesions may present simultaneously without a preceding prodrome. In some patients, the mucocutaneous lesions are the only manifestation. Moreover, fewer lesions (<10) are frequently noted in the penile, anorectal, and oropharyngeal areas and sometimes it is just a single painful lesion. Rash is not always present on the palms and soles.[41,42,44]

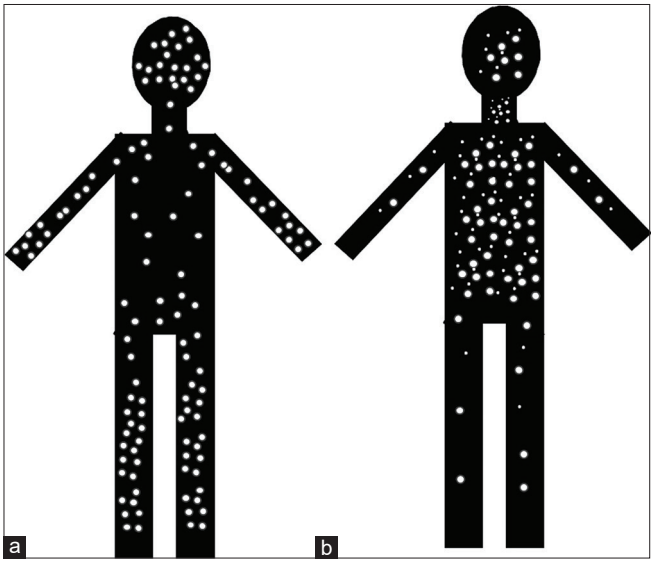

Figure 4: The monkeypox skin lesions usually, but not necessarily, are of the same stage which start on the face and then involve the whole body with a *centrifugal distribution* (a). The lesions become concentrated on the face and distal extremities (hands and feet) with fewer lesions on the trunk. The centripetal distribution of the skin lesions involves the face and trunks with fewer lesions on the extremities. This is usually seen in chickenpox disease (b).(*Illustrated by Professor Fikri Abu-Zidan, Professor of Disaster Medicine, The Research Office, College of Medicine and Health Sciences, United Arab Emirates University*)

Although most patients with MPXV disease have mild illness, severe disease and complications can occur and include secondary bacterial infection of the lesions, dehydration from desquamation of skin with fluid loses, pneumonia, visual impairment, encephalitis, and death. The risk factors for severe disease include young age (children), having >100 lesions (grave and plus grave severity) [Figure 5], dysphagia from mucosal lesions, and underlying comorbidities such as cancer, immunodeficiency (HIV or chemotherapy), eczema and other skin conditions, and diabetes.[41,45,46]

There are several diseases that may resemble MPXV rash including dermatological conditions such as smallpox, chickenpox, hand-foot-mouth disease, scabies, and measles as well as sexually transmitted infections including syphilis, herpes simplex virus infection and chancroid (haemophilus ducreyi infection).[41] Differentiating MPXV from these differential diagnoses is a challenging task. Clinicians are strongly advised to obtain careful history and detailed physical examination for all suspected cases. History should include travel history, sexual history, contact with infected persons, and smallpox vaccination. Physical examination must be thorough and include a full skin and mucosa exam (mouth, eye, and genitalia) as well as examining other systems to rule out any complications of MPXV or any of the differential diagnoses.[41,47,48]

Diagnosis

When evaluating patients with suspected MPXV disease, clinicians must consider testing for other differential diagnoses in addition to testing for MPXV (orthopoxvirus). Routine investigations include testing nonlesion specimens (e. g., blood for complete blood count, electrolytes, renal and liver functions, and urine analysis and culture) and lesion specimens for varicella, herpes viruses or other sexually transmitted infections, when clinically indicated.[41]

Testing for MPXV requires obtaining samples from at least 2-3 lesions (surface, exudate, or crust). Two swabs need be taken from each lesion and preferably from different body sites and from lesions at different stages. Sterile and synthetic swabs (e. g., Dacron) but not cotton swabs must be used to collect samples. Swabs should be sent to the laboratory in the viral transport media. Using needles and other sharp instruments to unroof or aspirate the lesions is associated with the risk of sharps injury and

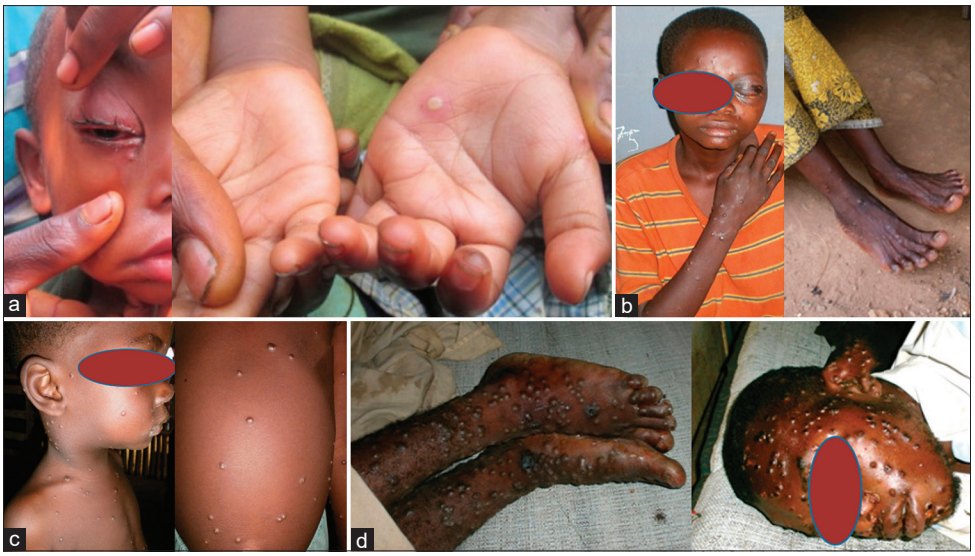

Figure 5: Spectrum of rash burden experienced by different individuals with acute monkeypox, Democratic Republic of the Congo. Lesion counts are based on whole-body estimates performed by trained health care personnel.(a) "benign", 5–25 lesions (plus ocular involvement); (b) "moderee", 26–100 lesions [plus ocular involvement]; (c) "grave", 101–250 lesions (plus lymphadenopathy); (d) "plus grave", >250 lesions.(Photo credits: (a) Jacque Katomba; (b and d) Gregoire Boketsu; (c) Toutou Likafi). Reproduced from Reynolds *et al*. Viruses. 2017;9:380 which is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons. org/licenses/by/4.0/)

must be avoided. Throat swabs can also be obtained if there are pharyngeal lesions or if the patient is a contact of a confirmed case with a possible prodrome syndrome but without a typical rash. Testing should be done while wearing appropriate personal protective equipment.[49,50] Nucleic acid amplification testing (NAAT), such as real-time or conventional polymerase chain reaction are the currently recommended tests for diagnosing MPXV. NAAT can be generic to orthopoxvirus or specific to MPXV virus which is desirable.[51]

Management

Infection control measures

Healthcare professionals caring for patients with suspected or confirmed MPXV disease should wear appropriate personal protective equipment including N95 respirator or higher, gloves, gown, eye goggles and shoe protector. Patients should wear a surgical mask and cover their exposed lesions for source control. Contaminated surfaces (e. g., gurney) must be disinfected. The hospital infection control officer and infectious diseases physician should be promptly informed. Public Health Department must be also notified as per local policies.[41,47]

Treatment

Supportive care including rehydration and pain control are the mainstay treatment for patients with MPXV disease. Antibiotics can be prescribed for treating secondary bacterial infections of skin lesions or conjunctivitis if present. However, certain patients including those with severe disease (e. g., encephalitis, pneumonia, larger number of lesions or having lesions at anatomic sites that increase the risk of stricture such as pharynx and rectum) and those at high risk for severe disease (e. g., HIV, transplant patients, children, and pregnant women) may benefit from a specific antiviral treatment. Currently, there is no specific treatment approved for treating MPXV. However, antivirals developed for smallpox or other orthopoxviruses may have some benefit. Nevertheless, data proving the effectiveness of these antivirals in patients with MPXV are currently lacking. Potential antivirals include tecovirimat (also known as TPOXX, ST-246), intravenous vaccinia immune globulin and cidofovir.[41]

Disaster Management

A medical disaster is a situation in which the available urgently needed resources are less than those required for adequate medical care."[52,53] At present, the MPXV outbreak did not reach this status compared with COVID-19 pandemic because of multiple reasons: (1) the infection rate is much lower (2) the mode of transmission is different, and (3) the disease is less severe with very low mortality.[54] The health systems in different countries worldwide could accommodate this situation. Nevertheless, having the WHO declaring it as a global public health emergency indicates the seriousness of the issue. There is risk that mortality will increase if more vulnerable people are affected like those having comorbidities, pregnant women, and children.[55] Accordingly, it will be safer to apply the principles of disaster management in the current MPXV outbreak. Disaster management has four phases. These are: (I)

Preparedness which includes building up the proper infrastructure, prepare its needed resources, have a clear plan for response, and train staff on this plan; (II) Mitigation by reducing the impact and effects of the disaster; (III) Response by establishing a command centre that coordinates the response activities through proper communication. This includes accurate triage, proper decontamination, safe and quick transport, and proper patients' medical care; and finally, (IV) recovery by restoring the normal community functions.[53,56,57] Figure 6 illustrates these stages. Line A represents the normal capacity and resources of a health care system to address the maximum number of patients it can manage. During a disaster, the system tries gradually to increase its capacity overtime (Line B, dashed line). The solid white line curve represents a disaster in which the number of patients is more than the capacity. This occurred in the early period of the COVID-19 pandemic. Following the principles of disaster management will reduce the impact of the MPXV outbreak. We will highlight these phases as reflected in the current MPXV outbreak.

Preparedness

The most effective strategy for preparedness for infectious pandemics is to strengthen the public health infrastructure including an active surveillance system, continuous and effective training on managing infectious pandemics, and supplying the needed resources including personal protective equipment laboratory and diagnostic methods, and facilities to isolate infected patients.[54,58,59] This should be thought of and planned globally. The risk that MPXV will be entrenched worldwide is considerable because of easy, relatively cheap, and fast transportation methods.[55] Our world has a delicate balance between animals, environment, and humans reflecting the need for a "one globe, one health approach". Trade in wild animals for food consumption or as pets taken from the wild endangers public health and must be addressed globally before repeated animal born infectious pandemics threaten the human existence.[60] Preparedness for infectious disasters is more challenging in developing countries.[57,61] The COVID-19 pandemic has clearly demonstrated that inequality of resources between developing and developed countries slows the speed of vaccination in the low-income countries.[62]

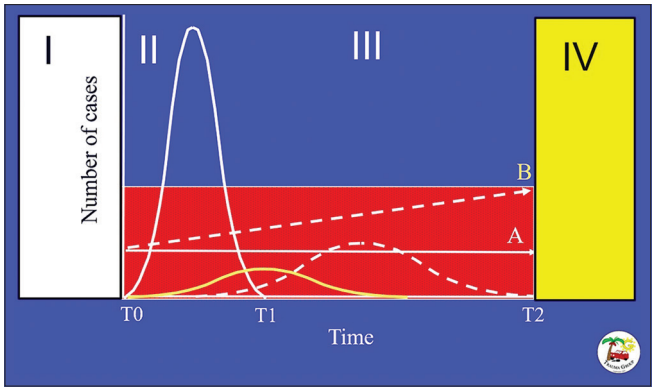

Figure 6: The four stages of a disaster include: I = preparedness, II = mitigation, III = response, and IV = recovery. Line A represents the normal capacity and resources of a healthcare system. During a disaster the system tries gradually to increase its capacity (Line B, dashed line). The solid white line curve represents a disaster situation (T0 = start, T1 = end); Mitigation is represented by dashed white curve (T0 = start, T2 = end). The monkeypox outbreak is similar to the yellow curve.(*Illustrated by Professor Fikri Abu-Zidan, Professor of Disaster Medicine, The Research Office, College of Medicine and Health Sciences, United Arab Emirates University*)

Mitigation

Efforts at this stage aims to reduce the spread of infection to flatten the pandemic curve. Infected patients are treated over a longer period to match the health care capacity without affecting the care of other patients. Line B (dashed white curve) at Figure 6 represents the situation during the late period of the COVID-19 Pandemic. The MPXV outbreak did not reach a disaster situation [Figure 6, yellow curve]. Current strategies to contain the global spread of the MPXV outbreak includes active surveillance, contact tracing of cases, and isolation of infected persons. As stated by the WHO, mass vaccination for MPXV is not recommended at this moment but might take place later.[39] At present, prophylactic vaccination should be implemented for high risk and exposed subjects. This includes frontline healthcare workers, laboratory personnel, clinicians caring for symptomatic patients, and the public health team involved in active surveillance. Contacts of cases are recommended to have postexposure preventive vaccination with second-or third-generation vaccine, as early as possible, within 2-4 days of first exposure to prevent the onset of the disease within 14 days in the absence of symptoms.[63]

Response

Having a disaster within another disaster needs unique measures to be considered. Management of a recent major train collision in Kuala Lumpur, Malaysia during the peak of the COVID-19 pandemic has highlighted this important point.[64] Although the two disasters were of different nature (trauma and infectious disease), occurring at the same time needed certain considerations. It is important to be flexible and innovative to address both at the same time. There should be a disaster management plan for any suspected highly contagious infectious pandemic. This should include a strong command system which will organize all hospital activities during the pandemic, identify the required resources, define priorities

of the needed supplies, and coordinate actions to be taken.[64,65] Health care providers should protect themselves by wearing N95 masks, gloves, gown, and eye protectors, when examining or treating confirmed or suspected MPXV patients. These precautions are very effective in preventing the transmission of the virus.[54]

Triage is essential when responding to infectious disasters in the emergency department and dealing with an influx of a large number of patients. It depends on recognition and isolation of infected patients. Patients having the current MPXV outbreak can be difficult to triage. Many of them have nonspecific symptoms without any epidemiological links.[55] Furthermore, other diseases can present with fever and rash like MPXV. Triage in this case will depend mainly on proper clinical history by collecting selective relevant data and clinical findings which includes the stage and distribution of skin lesions. Nevertheless, over-triage can be counterproductive, spreads fear and consumes resources.[66] Visual safety patients' tools, computer programs, and website information have been developed to help nurses and emergency physicians to triage and manage MPXV patients.[47,67-69] Early case notification, data collection, valid scientific reporting, and community public health guidance through proper communication and media is essential for both prevention and recovery.[61] Vaccination is very effective in preventing infectious diseases and is part of the preparedness stage if indicated. For example, the USA army vaccinated deployed soldiers to Asia in 2002 as a precaution against smallpox.[70]

Recovery

Recovery of a community from a disaster depends on its resilience, capacity to prepare before the disaster occurs, and its response to the disaster with a structured command while maintaining the community function.[71] This requires reflection on own lessons learned during similar disasters.[62] The MPXV outbreak came within the COVID-19 pandemic when the community resources have been depleted. Communities are exhausted both psychologically and economically and are afraid of having another lengthy painful experience similar to the COVID-19 pandemic.[72] MPXV may cause long-term facial skin scars.[73] [Figure 7] and neurological effects. Some patients may have altered consciousness and seizures. The virus may have neuroinvasive effect by crossing the blood – brain barrier through the circulatory macrophages and monocytes or through the olfactory epithelium.[74] Eye lesions are indicative of a severe disease. Almost 50% of those having conjunctivitis become bed-ridden. Patients may have corneal scarring and even permanent vision loss.[75]

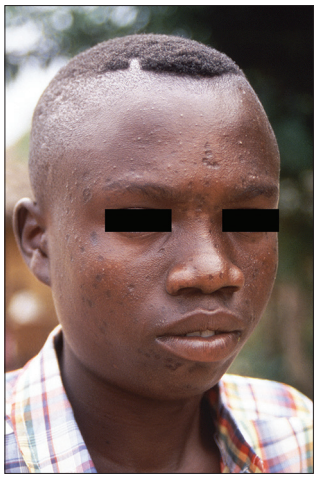

Figure 7: A young man who had recovered from monkeypox infection and developed permanent skin scars on his face. This image was taken from the Public Health Image Library, Centers for Disease Control and Prevention, image number 12,777, provided by Brian W. J. Mahy Available on https://phil.cdc.gov/Details.aspx?pid = 12777 (Accessed on 3rd of October 2022). This image is in the public domain and thus free of copyright restrictions

Conclusions

MPXV is an emerging zoonotic disease caused by a DNA virus which can transmit from human to human through prolonged direct or close contact, or through blood, body fluids, or mucosal lesions. Risk groups include frontline healthcare workers, household members of an infected patient, and men who have sex with men. Skin lesions are usually at the same stage with centrifugal distribution. Although its clinical presentation is usually mild, the disease may have long-term effects on the skin, eye, and neurological system. Vaccination is available for those who are at high risk. We should follow the principles of disaster management using what we have learned from the COVID-19 pandemic so as reduce the impact of the MPXV outbreak. If proper action is not taken using the "one globe, one health approach", there is considerable risk that MPXV will be entrenched worldwide.

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Author contributions

All autors have contributed to the idea. Mohamud Sheek-Hussein retrieved the literature on the public health section and vaccination and wrote it. Ahmed Alsuwaidi retrieved the literature on the clinical management section and wrote it. Emma Davies retrieved the literature on the virology section, wrote it, and drew two of the illustrations. Fikri Abu-Zidan supervised the project, retrieved the literature on the disaster medicine section and wrote it, organized

the structure of the manuscript, drew two of the illustrations, and repeatedly edited the manuscript. All authors read and approved the final version of the paper. All authors have contributed equally to this manuscript.

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None declared.

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