An Overview of Monkey-pox Disease

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Abstract: Monkeypox is a rare self-limiting viral zoonosis (a virus transmitted to humans from animals) with symptoms in humans similar to those seen in the past in smallpox patients, although less severe. Monkeypox virus (MPV) causes monkeypox disease. The virus belongs to the family: Poxviridae; Subfamily: Chordopoxvirinae; Genus: Orthopoxvirus. MPV was first identified in laboratory monkeys at State Serum Institute in Copenhagen, in 1958. The first human case of MPV was detected in 1970, in Zaire (Democratic Republic of the Congo—DRC) after smallpox eradication in the country. The primary disease symptoms include: Demonstration of characteristic prodromal illness for 2 days before the onset of rash with fever, malaise, and lymphadenopathy by most patients. Almost 90% of patients infected with monkeypox develop lymphadenopathy, which is the key feature distinguishing human monkeypox from smallpox. Typical monkeypox rash begins as maculopapular lesions of 2-5 mm in diameter; the rash becomes generalized in distribution in most cases, spreading in centrifugal pattern. Skin lesions progress from papules to vesicles, and pustules followed by umbilication, scabbing, and desquamation over a period of 14-21 days. Skin lesions are observed on mucous membrane, in the mouth, on tongue, and on genitalia. Monkeypox disease mortality rate in Africa is about 10%. The most recent outbreak of Monkeypox disease occurred in 2017, in Nigeria. This paper is a comprehensive review of the: pathology, pathogenesis, epidemiology, signs and symptoms, diagnoses and prevention of monkeypox disease.

Keywords: Orthopoxvirus, Lymphadenopathy, Rodents, Exposure routes, Extracutaneous, Infection

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1 Introduction

Monkeypox is an orthopoxvirus that is closely related to smallpox and exhibits a similar pustular rash [1]. Monkeypox virus (MPV) is the pathogenic agent for monkeypox disease. The consequences range from asymptomatic infections to severe, fatal illness. Monkeypox disease is a smallpox-like viral infection caused by a virus of zoonotic origin [2]. The virus belong to the family: Poxviridae; subfamily: Chordopoxvirinae; and genus: Orthopoxvirus. Morphologically, the virion: enveloped shaped, slightly pleomorphic; dumbbell-shaped core with lateral bodies [3]. Between 140-260 nm in diameter by 220-450 nm in length. MPV is a nucleic acid: linear, double-stranded DNA virus; genome length: ~197 kb in length bp. MPV is resistant to common phenolic disinfectants. But it can be inactivated with polar lipophilic solvents, such as chloroform, and at low pH [4]. Complete inactivation of the closely related vaccinia virus occurs in 2-3 hours at 60°C or within minutes following exposure to 20 nM caprylate at 22°C; however, MPV is more resistant than vaccinia to solvent-detergent treatment [5]. It has an incubation period of 7-17 days (mean of 12 days). Other members of the Orthopox genus include Variolavirus (smallpox virus), Vaccinia virus (smallpox, vaccine virus), Ectromelia virus, Camelpox virus, and Cowpox virus [6].

The identification of monkeypox virus is based on biological characteristics and endonuclease patterns of viral DNA [7]. In contrast to smallpox, monkeypox virus can infect rabbit skin and can be transmitted serially by intra-cerebral inoculation of mice. The four orthopox viruses that may infect man produce macroscopically characteristic lesions on the inoculated chorioallantoic membrane of an embryonated chicken egg [8]. The maximum or 'ceiling' temperature at which the viruses can proliferate in the chorioallantoic membrane differs for monkeypox and smallpox [8]. These viruses differ also in the ability to multiply in different tissue culture cells. However, at present the clearest results are obtained by the endonuclease restriction patterns of the virus DNA [9]. Some genetic variability has been noted between monkeypox viruses isolated from West and Central African regions [10]. Genome studies have revealed strong evidence regarding monkeypox virus being a non-ancestral to variola virus. This may be important in view of the fear expressed by some researchers that variola might again evolve from monkeypox virus [11]. In the pre-molecular era, significant efforts were made to distinguish the four viruses by serological reactions. These were delicate studies, since the viruses share most antigens [11, 12, and 13]. Some results were obtained using absorbed sera in agar gel diffusion tests, but they were rapidly superseded by the studies on biological characteristics and DNA restriction patterns [12]. The development of relatively specific antigens has been extremely useful for serological surveys in human and animals. In the field, rapid presumptive diagnosis of infection caused by viruses belonging to the orthopoxvirus group is necessary, as is differentiation from chickenpox, as confusion is possible on clinical grounds [14]. For this purpose, it is recommended that scabs of the lesions are sent, without transport medium, to the diagnostic laboratory. Electron microscopic examination of this material will allow the differentiation of Orthopox and Herpes viruses [15]. Poxviruses can be detected in more than 95% of the scabs, whereas varicella-zoster virus could be detected in only half of the material from cases of chickenpox, meaning that electron microscopy negative specimens are very unlikely to be monkeypox [16].

1.1 Etiology
Monkeypox results from infection by the monkeypox virus, a member of the genus Orthopoxvirus in the family Poxviridae (subfamily Chordopoxvirinae) [3]. Two clades of monkeypox viruses, the West African and Congo Basin viruses have been identified. The Congo Basin viruses are more virulent [5]. Monkeypox virus is closely related to some other orthopox viruses such as variola (smallpox) virus, and it cannot be distinguished from these viruses in some laboratory tests [17].

1.2 Classification and Characterization of Monkeypox Virus

Poxviruses are the largest vertebrate viruses known, infecting humans, and other vertebrates (species of sub-family Chordopoxvirinae), and arthropods (species of sub-family Entomopoxvirinae) [18]. There are around 70 known species of pox viruses spread among 28 genera and two sub-families (the Chordopoxvirinae and the Entomopoxvirinae). The virions contain a linear double-stranded deoxyribonucleic acid (dsDNA) genome and enzymes that synthesize messenger ribonucleic acid (mRNA). They multiply in the cytoplasm of the host cells [19].

The Chordopoxvirinae consists of around ten genera including the genera which are genetically and antigenetically related [20]. The genus Orthopox virus comprises camelpox, cowpox, ectromelia, monkeypox, racoonpox, skunkpox, taterapox, Uasingishu (pox virus of Horses in Kenya), vaccinia, variola and volepox. African swine fever viruses were also known to share some properties of the poxviruses [21].

Many poxviruses are associated with a specific vertebrate species, which indicates that the transmission of these viruses occurs preferentially among a specific vertebrate species [22]. Nevertheless, accidental transmission into a different vertebrate species can occur [22]. There was no resultant clinical-pathological condition noted in the infected host to be further maintained in this ‘aberrant’ species. The orthopox viruses which can infect humans include variola, vaccinia, cowpox and monkeypox viruses [18]. Variola virus is a virus which only infects humans and the Vaccinia virus is a vaccine strain that does not exist in nature and is used to treat small pox. Vaccinia virus originated in the 18th Century from an unknown vertebrate species [23].

1.3 Historical background and Epidemiology of Monkeypox Disease

Monkeypox is typically found in the Central and West African rain forests. MPV was first identified in 1958, in a group of sick laboratory monkeys (Macacacynomolgus),at State Serum Institute in Copenhagen. The first known human case occurred in1970 in the Equateur province of Zaire (now known as the Democratic Republic of Congo (DRC)) when a 9-year-old boy developed smallpox like illness which was confirmed as human monkey pox by the World Health Organization [24]. Monkeypox was limited to the rain forests of central and western Africa until in June 2003, when the first cases in the Western Hemisphere were reported [21]. The source of this single outbreak was small mammals imported from West Africa. Prairie dogs housed in pet stores in close proximity to these infected small mammals became infected and transmitted the infection to humans [21]. Multiple persons were infected in the Midwestern United States who had developed fever, rash, respiratory symptoms, and lymphadenopathy following exposure to ill pet prairie dogs (a rodent of Cynomys species) infected with the monkeypox virus. The only outbreak of human monkeypox reported outside Africa occurred in the United States in 2003. The virus entered North America in exotic African rodents imported as pets, and spread to pet prairie dogs, which were highly susceptible to infection [25]. This virus subsequently infected approximately 70 people who had been in contact with these animals [25].
A direct contact or exposure with ill, prairie dogs (a group of herbivorous burrowing rodents), showing signs of profuse nasal and ocular discharge, dyspnoea, lymphadenopathy, and muco-cutaneous lesions was noted among the cases reported. Another interesting observation noted among those cases was the presence of a common animal distributor where prairie dogs were housed or transported along with African rodents from Ghana [26].

People living in or near the forested areas may have indirect or low-level exposure, possibly leading to subclinical infection. The disease is rare and only known to be indigenous to the rain forests of western and central Africa. The first known human case came after the eradication of smallpox, possibly because of the subsequent unmasking of the infection [27]. Surveillance reports from 1981-1986 documented 338 cases in the DRC (out of a 1982 estimated population of 5 million). In the 1996-1997 outbreaks in the DRC, the attack rate was 22 cases per 1000 population. Human infection with monkeypox has not been reported in West Africa since 1978. However, monkeypox continues to exhibit a robust emergence in the DRC, with sporadic occurrences of disease in neighboring countries [2]. In 2003, 11 cases and 1 death were reported from the DRC and 10 cases with no deaths were reported from Sudan in 2005[28]. In United States, no cases occurred until the late spring 2003 outbreak in the Midwestern states. Between May 16 and June 20, 2003, 71 suspected cases of monkeypox were investigated. Mortality/morbidity rash burden, hospitalization rates and illness severity (a global score incorporating degree of incapacitation, need for nursing care and rash burden) were used to define human disease [28].

In the African epidemics, 90% of the patients were children younger than 15 years. In the US outbreak, of the confirmed cases in 2003 (n = 35), 11 patients were younger than 18 years and 24 were older. Although the highest age-specific incidences and the greatest number of cases occur among persons younger than 15 years, a trend toward increasing incidence among persons aged 15-30 years has been seen in recent years [25]. It has been hypothesized that cessation of smallpox vaccination may be a factor in the increasing incidence in this age group. An annual crude incidence rate of human monkeypox of 0.63/10,000 population was inferred. Those at high risk were young unvaccinated children (especially boys) and adult women. Approximately one third of the infections were estimated to be sub-clinical [19]. The increase in cases was ascribed to the effect of the civil war which had led to increased hunting for forest animals that carry monkeypox, particularly squirrels. With changes in lifestyle due to increasing urbanization, and intensified agricultural activities replacing hunting and trapping, the chances of contracting monkeypox, either from the primary reservoir or intermediate hosts, will decrease [11].

Several documented outbreaks have occurred in Central and West Africa close to tropical rain forests where humans have frequent contact with infected animals. The 2003 outbreak in the US, as a result of virus introduction through infected exotic pets, resulted in 37 laboratory-confirmed cases. No cases have been reported in the US since that outbreak. In Africa, the reported mortality rate is about 10% among patients with disease [19, 28]. Genomic sequencing of monkeypox strains isolated from the Americas, western and central Africa’s, has noted the existence of two distinct clades of the virus. The isolates from the United States were found to be identical with the western African strains. The clinical course of the disease among people infected with the western African strain was observed to be milder with minimum human-to-human transmission as compared to those infected with isolates from central African region [25].
### Table 1  
**Timeline of Human Cases of Monkeypox Disease**

<table>
<thead>
<tr>
<th>Period</th>
<th>Cases reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>1958-1969</td>
<td>Sporadic outbreaks in captured monkeys (Zoo research centre)</td>
</tr>
<tr>
<td></td>
<td>Europe, USA</td>
</tr>
<tr>
<td>1970</td>
<td>First human case (9 years old boy, Zaire) DRC</td>
</tr>
<tr>
<td>1970-1980</td>
<td>59 cases: Zaire (DRC), Cameroon, Cote d’ivoire, Liberia, Nigeria, (Most [80% 48</td>
</tr>
<tr>
<td></td>
<td>Sierra Leone cases) were from Congo (DRC).</td>
</tr>
<tr>
<td>1981-1986</td>
<td>404 cases 386 (95%) from Congo (DRC)</td>
</tr>
<tr>
<td></td>
<td>Cameroon (1) Gabon (100, Congo (2).</td>
</tr>
<tr>
<td>1993-1995</td>
<td>No case reported</td>
</tr>
<tr>
<td>1996-1997</td>
<td>511 case in 54 villages with peaks of transmission in August</td>
</tr>
<tr>
<td>1996</td>
<td>(51 Cases), March 1997 (40 cases) and August 1997 (71 cases)</td>
</tr>
<tr>
<td>2003</td>
<td>70 cases (USA)</td>
</tr>
<tr>
<td>2017</td>
<td>74 cases (Nigeria)</td>
</tr>
</tbody>
</table>

Source [29, 24]

#### 1.4 Common Human Exposure Routes and Transmission modes

Common human exposure routes includes: respiratory, percutaneous, and permucosal exposures to infected monkeys, zoo animals, prairie dogs, and humans. Likelihood of secondary transmission include: direct contact with body fluids, respiratory droplets, or with virus-contaminated objects, such as bedding or clothing. Period of human-to-human transmission is during the first week of the rash [30]. Longest chain of documented human-to-human transmission was five generations (four serial transmissions). African rodents are the major vector and reservoir of infection. It is a zoonotic virus with primary transmission believed to occur through direct contact with infected animals or possibly by ingestion of their inadequately cooked flesh. Inoculation may be from cutaneous or mucosal lesions on the animal, especially when the skin barrier is compromised secondary to bites, scratches, or trauma. Transmission can also occur from animal reservoirs from Western Africa (prairie dogs, rabbits, rats, mice, squirrels, dormice, monkeys, porcupines, gazelles). Additionally, direct cutaneous (skin-to-skin) or respiratory contact with an animal or person who is infected can transmit the infection [31].

#### 2 Risks factors to MPV disease, and Likelihood of Clinical Disease

In Africa, people coming in contact with infected animals. A close association with wild animals leading to bites, and consumption of bush meat could be potential risk factors to acquire monkeypox virus infection [29]. Risk factors are very lower in the US, based on animal import controls established in 2003. The likelihood of the disease include a high percentage of exposed individuals develop clinical disease. In addition, serological evidence of infection has been reported in about 3% of asymptomatic household contacts of MPV symptomatic individuals studied between 1980 and 1984 in DRC [24].
3 Hosts and Reservoirs

Although rodents are believed to be the major reservoir in Africa, a 2010 study reaffirmed that several species of forest-dwelling rodents are at risk of developing Orthopox virus (including monkeypox) infection [22]. Serological surveys suggest that many animals are infected with MPV under natural conditions, including squirrels, non-human primates, and rats. Several epidemiological studies from the Democratic Republic of Congo have implicated squirrels (especially Funisciurus anerythrus) inhabiting agricultural areas as primary candidates to sustain viral transmission among people in nearby settlements. In one environmental survey, Funisciurus spp. squirrels had a higher rate of MPV seropositivity (24%) than other animals that were tested, including Heliosciurus spp. squirrels (15%) and primates (8%) [12]. A subsequent seroprevalence study done as part of the investigation of the outbreak in February 1997, in the Democratic Republic of Congo showed even higher positivity rates in these squirrels (39—50% in Funisciurus spp. and 50% in Heliosciurus spp. squirrels). In addition, 16% of Gambian giant rats tested in this study had serological evidence of MPV exposure [32]. The infection of a rabbit (family Leporidae) after exposure to a diseased prairie dog at a veterinary clinic confirmed the transmissibility of the virus between mammal species common in North America. Little is known about co-infection with MPV and HIV [19].

Two genera of African squirrels, Funisciurus spp. (rope squirrels), and Heliosciurus spp. (sun squirrels), have high seroprevalence rates, and have been suggested as possible maintenance hosts or vectors in Africa [26].

4 Symptoms and Diagnosis

4.1 Primary Disease Symptoms

In humans, the signs and symptoms of monkeypox are similar to smallpox, but usually milder. Approximately 12 days after exposure, symptoms of fever, headache, backache, muscle aches and extreme tiredness occur. Swelling of the lymph nodes also occurs with monkeypox [28]. One to three days (or longer) after the fever starts, a rash begins. This rash develops into raised bumps filled with fluid. The bumps progress to become crusts and scabs before they fall off. Most patients demonstrate characteristic prodromal illness for 2 days before the onset of rash with fever, malaise, and lymphadenopathy [28, 25]. Almost 90% of patients infected with monkeypox develop lymphadenopathy, which is the key feature distinguishing human monkeypox from smallpox. Typical monkeypox rash begins as maculopapular lesions of 2-5 mm in diameter; the rash becomes generalized in distribution in most cases, spreading in centrifugal pattern. Skin lesions progress from papules to vesicles, and pustules followed by umbilication, scabbing, and desquamation over a period of 14-21 days [25]. Skin lesions are observed on mucous membrane, in the mouth, on tongue, and on genitalia. In addition to skin lesions, extracutaneous manifestations, such as secondary skin and/or soft-tissue infection (19% of cases), pneumonitis (12%), ocular complications (4%-5%), and encephalitis (<1%), were also observed [19]. No hemorrhagic form of monkeypox has been described in humans. Among individuals with smallpox vaccination history, the rash is milder and more likely to be pleomorphic. Pediatric patients are more likely to be hospitalized in an intensive care unit [19]. Typical clinical presentation of human monkeypox in a child is presented in Fig.1.

The clinical presentation of human monkeypox was described primarily among children and adolescents identified in central and West African regions. The disease was characterized as a viral
prodrome fever with chills, headache, myalgias, and back pain lasting for 1–3 days, followed by a maculopapular exanthematous eruption. The rash was predominantly monomorphic with a centrifugal distribution, progressing to vesicular, pustular, and finally developing crusts during a 2- 3-week period. Clinicians should consider monkeypox in people with fever, cough, headache, myalgias, rash or lymph node enlargement within 3 weeks after contact with prairie dogs or giant Gambian rats [5].

Monkeypox viral infection can cause a syndrome clinically like smallpox but was noted to be less infectious and clinically milder. Fever could be the first symptom (usually 38.5-40.5°C). The febrile illness may often be accompanied by chills, drenching sweats, severe headache, backache, myalgia, malaise, anorexia, prostration, pharyngitis, shortness of breath, and cough (with or without sputum). Lymphadenopathy might appear within 2-3 days after the fever in most cases [4]. In the 2003 outbreak, 47% of patients had cervical lymphadenopathy, with nodes measuring several centimeters in diameter [8]. In the exanthematous stage, most infected people develop a rash within 1-10 days after the onset of fever. The rash often starts on the face and then spreads to the rest of the body, and could persist for 2-4 weeks until all lesions have turned to crusts. Encephalitis with immunoglobulin M (IgM) was observed in the cerebrospinal fluid [11].

In the exanthematous stage, within a body region, lesions evolve synchronously over 14-21 days, like the development of lesions with smallpox. However, unlike smallpox, skin lesions may appear in crops [11]. In contrast to smallpox, the lesions do not have a strong centrifugal distribution. Lesions progress from macules to papules to vesicles and pustules; the face, the trunk, the extremities, and the scalp are involved. Lesions may appear both in covered and uncovered areas. Lesions may be seen on the palms and the soles. Necrosis, petechiae, and ulceration may be features and pruritus may also occur. Pain is unusual, and, if it occurs, it is often associated with secondary bacterial infection. In patients who have been previously vaccinated against smallpox, a milder form of disease occurs. In children, the lesions may appear as non-specific, erythematous papules that are 1-5 mm in diameter and suggestive of arthropod bite reactions [33].

4.2 Diagnosis of MPV diseases

The geographic location of the patient is important in the diagnosis of monkeypox, since the disease is known to occur mostly in remote villages, in the tropical African rain forests [34]. It is also important to differentiate the lesions of monkeypox from that of smallpox and chicken pox during clinical diagnosis. The latter appears in successive crops so that lesions at various stages of development are visible at any time. In contrast with smallpox, the distribution of chickenpox is ‘centripetal’ with more lesions on the trunk than on the face and extremities. Identification of infection with monkeypox virus is complex due to its similarities between smallpox virus, and, varicella-zoster viruses [35].

The characteristic skin lesions are suggestive of monkeypox, and histopathology provides supportive evidence. The diagnosis can be confirmed by virus isolation or polymerase chain reaction assay (PCR) [36]. Monkeypox virus can be recovered in mammalian cell cultures, and may be identified using PCR followed by restriction fragment- length polymorphism (RFLP) analysis or sequencing. Monkeypox-specific PCR assays are available in some laboratories, and a DNA oligonucleotide microarray can identify this virus rapidly and specifically. PCR can also be performed directly on clinical samples [37].

No FDA-licensed blood donor screening test exists [12]. Currently, CDC uses cell culture or chick chorioallantoic membrane isolation in conjunction with a DNA-based assay for the diagnosis of orthopox virus infection. Several DNA-based tests and sequencing are useful. Serological tests are not
useful for the diagnosis of acute infection [19]. For definitive diagnosis, scabs can be forwarded to a reference laboratory where electron microscopy may confirm the presence of an Orthopox virus and differentiate this virus from varicella virus. The virus can be cultured in tissue culture and identified by DNA restriction analysis [6].

A viral culture should be obtained from an oropharyngeal or nasopharyngeal swab. A skin biopsy specimen of the vesiculopustular rash or a sample of the roof of an intact vesiculopustular should be analyzed. Tissue for PCR of DNA sequence-specific for the monkeypox virus may be obtained [31]. Paired sera for acute and convalescent titers may be analyzed. Serum collected more than 5 days for IgM detection or serum collected more than 8 days after rash onset for IgG detection was most efficient for the detection of the monkeypox virus infection [1]. A Tzanck smear can help differentiate monkeypox from other non-viral disorders in the differential diagnosis. However, a Tzanck smear does not differentiate a monkeypox infection from smallpox or herpetic infections [26].

Monkeypox cases were confirmed based on virus isolation or detection of the virus by polymerase chain reaction (PCR) from a clinical specimen (skin biopsy or throat culture). Individuals who presented with fever and rash within 21 days of exposure to monkeypox and had serum positive for orthopox immunoglobulin M (IgM), but did not have culture- or PCR-positive clinical specimens, were classified as having a probable case of infection [4]. The most reliable clinical sign differentiating monkeypox from smallpox and chickenpox is enlarged lymph nodes, especially the submental, submandibular, cervical, and inguinal nodes. Regarding exanthema, nonspecific lesions and inflammation of the pharyngeal, conjunctival, and genital mucosae have been observed [3].

Morand and Morand [10], observed that although clinical recognition of monkeypox is the first step in diagnosis, the definitive diagnosis can however only be done in the laboratory where the virus can be identified by a number of different tests which include:

i. Enzyme-linked immunosorbent assay (ELISA)
ii. Antigen detection tests
iii. Polymerase chain reaction (PCR) assay
iv. Virus isolation by cell culture

The swabs of lesions, fluid samples or crusts are most appropriate for laboratory.

5 Treatment and Prevention

5.1 Treatment

There is no specific treatment for monkeypox other than supportive care to prevent complications [19]. In Africa, people who had previously received the smallpox vaccine had a lower risk of monkeypox. The Centers for Disease Control and Prevention (CDC) [25], developed guidelines explaining when smallpox vaccine should be used to protect against monkeypox. When a case of monkeypox has been confirmed, the investigators, veterinarians, animal control workers and healthcare personnel involved may be advised to receive the smallpox vaccine.

No proven treatment for humans but animal studies shows effectiveness of antiviral treatment either with cidofovir or with a related acyclic nucleoside phosphonate analog. In animals, treatment with antiviral compounds is more effective in reducing mortality than the therapeutic use of smallpox vaccine. The Centers for Disease Control and Prevention (CDC) [19] recommended smallpox vaccination within 2 weeks, ideally before 4 days, after a significant, unprotected exposure to a diseased animal or a confirmed human case. Data from the African outbreaks suggested that prior smallpox
vaccination confers 85% protection from monkeypox viral infection. Efficacy of vaccination was noted to be prolonged with protection noted even several years after vaccination, and the incidence of complications being reduced [11].

Multiple pathogen reduction steps used in the fractionation process have been shown to be robust in removal of enveloped viruses. Treatment with solvent-detergent and pasteurization has been effectively used for inactivation of vaccinia virus and may be useful for monkeypox. Nanofiltration of plasma may be effective in the removal of monkeypox virus [9].

5.2 Prevention

Vaccinia immunization is approximately 85% effective in preventing human monkeypox disease, and CDC [19], recommends its use for exposed people up to 14 days after the exposure. Improved infection control measures, including the regular screening, and isolation of newly infected animals will certainly help in preventing outbreaks among animals. Better hygiene habits are warranted to avoid spreading of the virus on fomites which then become a source for newer infections [39]. Vaccination with vaccinia virus could be choice to protect animals. Because infections have been reported in Asian monkeys mixed with primates from Africa, care must be taken to house these species separately. Anyone who has been exposed to monkeypox virus should avoid contact with animals, particularly rodents and non-human primates, to stop transmitting the virus [40].

Avoid contact with prairie dogs or giant Gambian rats that appear ill. Prairie dogs with monkeypox had missing patches of fur, lesions on their skin, and respiratory symptoms (discharge from eyes or nose). Wash your hands thoroughly following any contact with sick animals. It is important that ill prairie dogs should not be released into the wild. If the prairie dog has a disease, it could infect wild prairie dogs [41].

During an outbreak, monkeypox viral spread may be controlled by quarantining (at least for six weeks from the date of the last exposure) the infected animals and tracing of their contacts. Areas where these animals have been kept should be cleaned and disinfected thoroughly. Although vaccinia immunization has proven effective, in the prevention of monkeypox disease, general vaccination of people in the endemic areas is not recommended [42]. This is because human infection with monkeypox virus is a rare disease; no benefit would be derived from vaccination with vaccinia virus. Furthermore, smallpox vaccination cannot be undertaken in populations with high prevalence of HIV infection because of the risk of serious complications [29]. The U.S. Centers for Disease Control and Prevention (CDC)[25], recommends disinfection of contaminated surfaces with 0.5% sodium hypochlorite or other EPA approved high level disinfectants. Incineration or autoclaving is appropriate for some contaminated materials. Burial without decontamination is not recommended.

5.2.1 Prevention measures

Nalca et.al. [44] and NCDC [29], enumerated important measures in MPV prevention to include:

i. Preventing spread of the virus through restrictions on animal trade: Potentially infected animals should be isolated from other animals and placed into immediate quarantine. Animals that may have come in contact with an infected animal should be quarantined, handled with standard precautions and observed for monkeypox symptoms for 30 days. Isolate infected patients from others who could be at risk for infection. Avoid direct contact with animals that could harbor the virus including sick or dead animals especially in areas where monkeypox occurs. Avoid contact with any material that has been in contact with a sick animal.
ii. Reducing the risk of infection in people: During human monkeypox outbreaks, close contact with other patients is the most significant risk factor for transmission of infection. In the absence of specific treatment or vaccine, the only way to reduce infection in people is by raising awareness of the risk factors and educating people about the measures they can take to reduce exposure to the virus. Surveillance measures and rapid identification of new cases is critical for outbreak containment.

iii. Controlling infection in health-care settings: Health-care workers caring for patients with suspected or confirmed monkeypox virus infection, or handling specimens from them, should implement standard infection control precautions. Samples taken from people and animals with suspected monkeypox virus infection should be handled by trained staff working in suitably equipped laboratories.

iv. Maintaining general hygiene: Always wash hands with soap and water after contact with infected animals. Regular hand washing after caring for, or visiting sick people. Wear protective equipment (hand gloves, etc) when taking care of ill people and thoroughly cook all animal products before eating.

![Fig. 1 Typical clinical presentation of human monkeypox in a 7 years old child of Sankuru District, Democratic Republic of Congo](image)

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