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Human Monkeypox Virus: A Systematic Review

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Abstract

A zoonotic orthopoxvirus called monkeypox unintentionally causes an illness in humans that is similar to smallpox, but with significantly lower mortality rates (1). Historically, the condition was thought to be uncommon and self-limiting, but the new isolated reports show different results. Human monkeypox cases have become more common and more widely distributed geographically in recent years. Therefore, there is a critical need to concentrate on developing surveillance capabilities that will yield useful data for creating suitable preventative, Operational readiness, and responsiveness (2). In this article, we reviewed the taxonomy, transmission of disease within animals and humans, diagnosis, treatment, and prevention of monkeypox. Monkeypox has been determined to pose substantial risks to humans, therefore risk management and community involvement during outbreaks are to be studied.

Keywords: Monkeypox, Monkeypox virus, Orthopoxvirus, zoonotic disease, MVA-BN, LC16, ACAM2000, Pre-exposure prophylaxis, post-exposure prophylaxis, Risk management, Lesion.

Introduction:

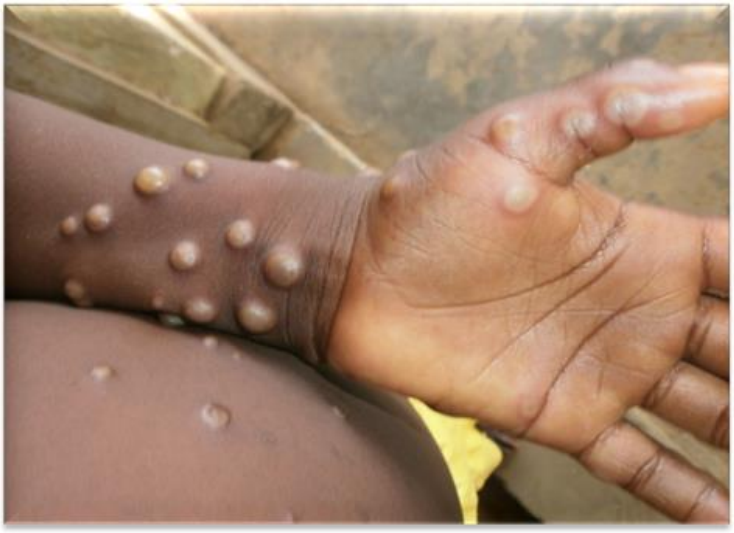

Figure 1: monkeypox lesions on the body of an infected person

Monkeypox, presently an unprecedented zoonotic disease is a result of the monkeypox virus, a member of the genus Orthopoxvirus, family Poxviridae, and subfamily Chordopoxvirinae (3). Along with the variola virus, which causes smallpox, the cowpox virus, and the vaccinia virus, the monkeypox virus is one of the four orthopoxvirus species that are dangerous for humans (2). Zoonosis is a disease that spreads from animals to people, such as monkeypox. Cases are frequently seen close to tropical rainforests where the virus is spread by animals. The monkeypox virus is contaminated in a variety of animals, including Gambian poached rats, squirrels, rare species of monkeys, dormice, and others (14).

In 1959, the monkeypox virus was first found and isolated when monkeys fell sick after transportation from Singapore to a research facility in Denmark. However, the virus was isolated from the first known human instance of smallpox in a nine-month-old boy who was believed to have it in the Democratic Republic of the Congo in 1970 (1).

A sooty mangabey in the Ivory Coast and a rope squirrel in the Democratic Republic of the Congo (DRC) are the only two wild animals from which the virus has been isolated. The primary transmission pathways are assumed to be composed of respiratory excretions, saliva, or coming into contact with lesion exudate or crust material. Viral exposure can also occur through the passing of feces (2).

The variola virus (smallpox virus), which produces a condition similar to smallpox, and the monkeypox virus are closely related (3). Although the clinical signs of smallpox and monkeypox are remarkably similar, the early-onset lymph node enlargement that commonly occurs with the onset of fever distinguishes monkeypox from smallpox(2).

History:

In a Danish laboratory, monkeypox was initially identified as a primate infection in 1959. Between 1958 and 1968, eight more laboratory outbreaks were linked to monkeypox(4). The initial human instance was discovered in 1970 in August in a community located in a tropical rainforest in Equateur province, Democratic Republic of the Congo (4).

Cameroon, the Democratic Republic of the Congo, South Sudan, Cote d'Ivoire, Nigeria, Liberia, Benin, Sierra Leone, the Central African Republic, and Gabon are the 11 African nations where there have been recorded occurrences of human monkeypox since 1970 (14).

Outbreaks of chicken pox and monkeypox that coexisted in 1996–1997 may have been resulting from the varicella virus, which had an unusually high attack rate and a reduced case fatality ratio. This may have contributed to actual or apparent alterations in transmission dynamics (14).

On a global scale, a significant public health issue is monkeypox. The United States of America saw its first monkeypox outbreak outside of Africa in 2003, due to contact with pet prairie dogs who were infected. (14).

There have been more than 500 suspected cases, a case mortality rate of about 3%, and over 200 confirmed cases in Nigeria since 2017. This outbreak in the US led to the development of more than seventy cases of monkeypox. Travelers from Nigeria to various countries like Israel, the United Kingdom, Singapore, United States of America have also been noted to have monkeypox. Numerous non-endemic nations reported lots of cases of monkeypox in May 2022 (14).

Method:

International guidelines for conducting and reporting systematic reviews were followed when conducting this study. In this systematic review, we report the taxonomy, epidemiology, risk communication, and community engagement, diagnosis, signs and symptoms, treatment and prevention, and vaccination for monkeypox.

Taxonomy:

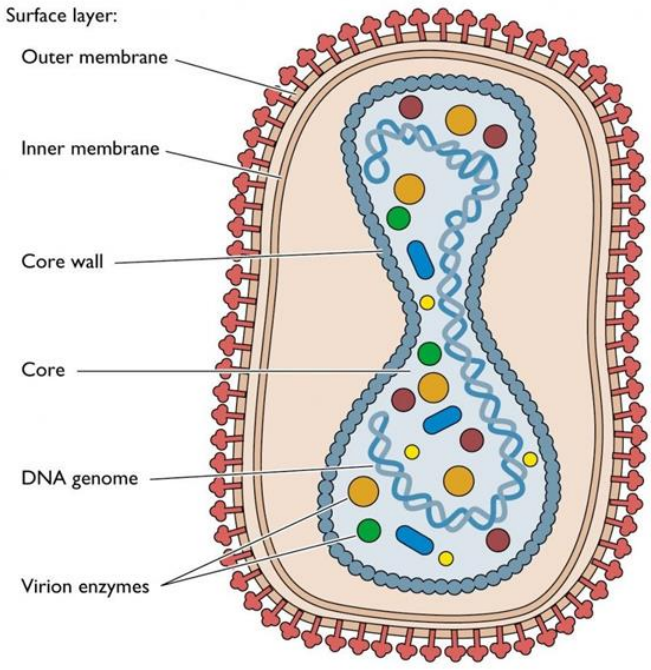

Figure 2: Taxonomy of monkeypox virus

The orthopoxvirus that causes monkeypox differs genetically from other Poxviridae family members which include the ectromelia, vaccinia, cowpox viruses, camelpox, and variola ((5). The poxviruses are the most substantial and intricate viruses. The virion has a diameter of roughly 200 nm and is structured like a brick. A dumbbell-shaped core and two unidentified "lateral bodies" are surrounded by an exterior membrane made of tubular lipoprotein subunits that are organized erratically. The viral DNA and related proteins are located in the core. Cellular lipids and various virus-specific polypeptides are present in an envelope (4) (20).

Serologically, the Monkeypox virus and variola are closely linked, and cannot be consistently distinguished from one another (5). However, certain antisera can distinguish between monkeypox and smallpox by the use of particular viral antigens (5) (6). These antibodies against monkeypox were 1st utilized to identify the monkeypox virus reservoir in central African wild monkeys (5).

In 2001, researchers revealed a genetic comparison of the monkeypox virus and variola contagion. The Monkeypox contagion genome's core region, which is 96.3 percent identical to the variola contagion's, encodes pivotal enzymes and structural proteins. The Monkeypox contagion genome's terminal regions, which law for acridity and host-range factors, are veritably different. Analysis of smallpox and Monkeypox contagion genomes demonstrate that monkeypox contagion is a separate species that diverged from an orthopoxvirus ancestor without the help of the variola contagion (5).

Host and Reservoir: The monkeypox contagion has been set up to be vulnerable to a variety of animal species. This comprises rope squirrels, dormice, tree squirrels, Gambian swelled rats, non-human primates, and other species (14). still, the main source of mortal infection is still unknown. Multitudinous epidemiological studies from the Democratic Republic of the Congo have suggested that squirrels, particularly Funisciurus anerythrus, living in agrarian regions, are the main carriers of viral transmission to girding habitations. In one study, Funisciurus spp. squirrels showed a lesser rate of monkeypox virus seropositivity (24%) than other studied creatures, similar to Heliosciurus spp. squirrels (15%) and primates (8%). Indeed, lesser positivity rates in these squirrels were set up in an after-seroprevalence exploration carried out as part of the inquiry into the epidemic in the Democratic Republic of the Congo in February 1997 (39 – 50% in Funisciurus spp. and 50% in Heliosciurus spp.). Also, this study set up that 16 of the Gambian giant rats examined had monkeypox virus exposure evidenced by serology. The infection of a rabbit of the family Leporidae following contact with a sick champaign canine at a veterinary clinic proved that the contagion can be transmitted between the common North American mammal species. In one US case, this rabbit was allowed to be the original pestilent source. 3 On June 11, 2003, the CDC and the US Food and Drug Administration concertedly issued an order banning the importing of any rodents from Africa for the time being in a trouble to stem the further spread of the monkeypox virus to humans and other species (5).

Cell cycle: It's unknown whether the smallpox contagion has a unique cell-face receptor. Once within the cell, the poxviruses replicate in the host cell's cytoplasm. The poxviruses, in discrepancy to other DNA contagions, render the several enzymes demanded viral genome recap and replication. The virion and tube membrane fuse and the viral core is also discharged into the cytoplasm. The viral transcriptase starts to recap. Within twinkles of infection, functional limited and polyadenylated runner RNAs(mRNAs) can be created

without splicing because of recap factor, circumscribing and methylating enzymes, and a poly(A) polymerase. The uncoating of the core is finished by the polypeptides created by the restatement of these mRNAs. Before viral DNA conflation starts, a recap of roughly 100 genes spread throughout the genome takes place. DNA polymerase, thymidine kinase, and other enzymes necessary for genome replication are exemplifications of early proteins (4). The list of particular viral proteins to distinct protagonist regions regulates the recap of intermediate and late genes. Circumscribed regions of the cytoplasm are where virion assembly takes place. A double membrane is acquired by an intracellular mature contagion when it proceeds toward the trans- Golgi network or early endosomes on microtubules. This intracellular enveloped contagion peregrination via microtubules to the cell face, where the tube membrane fuses with the external membrane, allowing the contagion to exit the cell through exocytosis. still, the maturity of patches isn't wrapped and is latterly liberated by cell breakdown. Although both types of patches are contagious, it appears that the enclosed patches play a more significant part in the propagation of the contagion throughout the body because they're more snappily absorbed by cells (4) (19).

Transmission: Beast-to-human (zoonotic) transmission can do from direct contact with the fleshly fluids, blood, or cutaneous lesions or mucosal lesions of infected creatures. An implicit threat component is the consumption of sick animal products and undercooked meat. People who live in or close to timbers may be laterally or minimally exposed to diseased creatures (14). mortal- to- mortal transmission can affect by close contact with the skin sores of an infected individual, respiratory passages, or recently defiled objects. Because drop respiratory patches typically involve extended face-to-face contact, family members, health professionals, and other close associates of current victims are more at risk. In the most recent period, the number of transmissions between people in a community's longest proven chain of transmission rose from 6 to 9. Transmission can also occur during intimate contact during labor and after delivery or via the placenta from mother to fetus (which might result in congenital monkeypox) (14). According to a study of case series of monkeypox contagion infection in humans across 16 nations reported over two months sexual intimate contact was the most constantly suspected route of monkeypox viral transmission in 95 of the cases. Out of 528 people, 406 had a sexual history; out of these 406 people, the median number of coitus mates in the former three months was 5, 147 i.e., 28% had reported traveling overseas in the month before to opinion, and 103 ii.e.,20% had gone to events with further than 30 people, similar as Pride fests. Overall, 106 people i.e., 20% reported having" chem sex" (i.e., coitus with medicines like mephedrone and demitasse methamphetamine) in the former month, while 169 i.e., 32% were known to have visited coitus-on-point establishments during that time. Anal, oral mucosal lesions and primary vaginal which may be the inoculation location, were found to have a high risk of sexual transmission (7).

Results

Diagnosis:

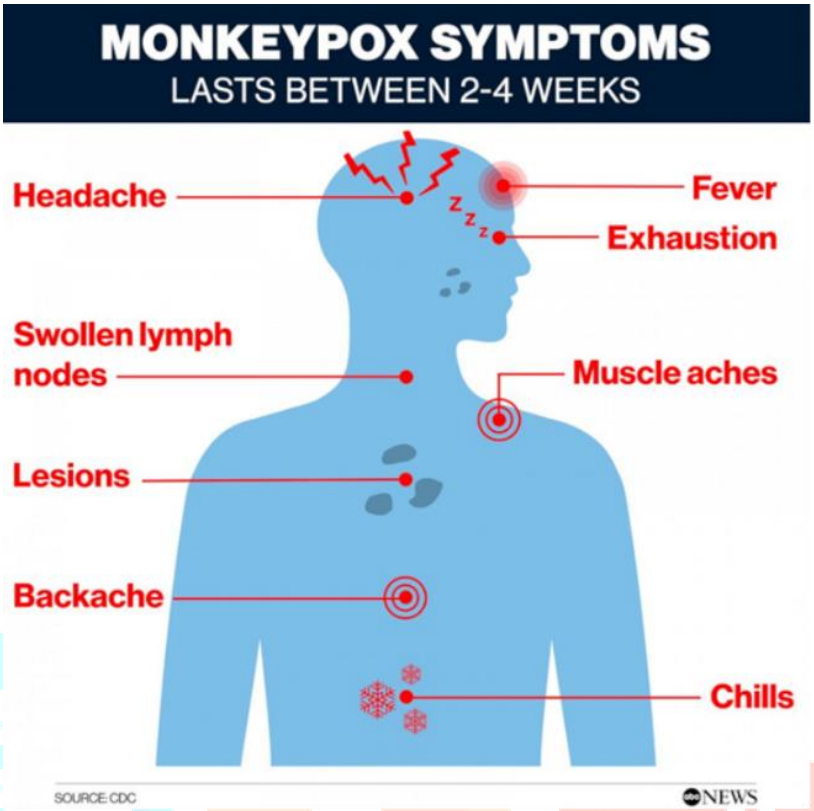

Figure 3: Symptoms of monkeypox

Although monkeypox can take anywhere between 5 and 21 days for symptoms to manifest, the typical incubation period for monkeypox is 6 to 13 days.

Two distinct stages of the infection:

1. The first five days of the invasion period are marked by myalgia (muscle aches), fever, severe headache, severe asthenia (lack of energy), back pain, and lymphadenopathy (swelling of the lymph nodes).
2. A day or two after the fever first appears, the skin eruption frequently begins. The face and limbs are more likely to develop the rash than the trunk. The face is affected in 95% of instances, while the palms of the hands and the bottoms of the feet are affected in 75% of cases. In 70% of cases, oral mucous membranes, genitalia, and the conjunctivae are also affected in addition to the cornea. From macules, which are flat, firm lesions, the rash progresses to papules, which are stiff, slightly elevated lesions, then to vesicles, which are transparent fluid-filled lesions, further to pustules, which are lesions with a yellowish fluid core, and then crusts that become dry and eventually crumble. The number of lesions can be somewhere between several hundred to several thousand.

Corneal infections, sepsis, bronchopneumonia, secondary infections, and encephalitis with resultant vision loss are some of the problems associated with monkeypox. The case fatality ratio of monkeypox has historically fluctuated between 0 to 11% in the general population; it has been greater among small children. The case fatality rate lately hovered between 3 and 6%. (14).

Anyone who meets the requirements for a suspected case should receive diagnostics. The decision to test should take into account epidemiological and clinical factors as well as the possibility of infection. Monkeypox can be difficult to differentiate based just on the clinical appearance, particularly for individuals with an atypical appearance, due to the variety of illnesses that can produce rashes on the body and the fact that clinical presentation might be more frequently unusual. Hence, it's crucial to take into account further possible sources of an extensive rash or isolated skin lesions (8).

Laboratory staff must be trained in the packaging, proper wearing and removal of personal protective equipment (PPE), specimen collection, transport, and storage, as well as the use of sufficient standard operating procedures (SOPs). When analysing routine clinical specimens from patients diagnosed with monkeypox or suspected of having it, precautions should be followed depending on risk analysis to reduce the potential for laboratory transmission. Skin abrasion material, such as swabs of the exudate or lesion's surface, roofs of many lesions, or crust around the lesion are the suggested specimen type for monkeypox laboratory confirmation. Make sure sufficient viral DNA is collected by forcefully swabbing the lesion. Swabs may be utilized dry or after being put in a viral transport medium (VTM). Ideally, two lesions of the same type with diverse appearances and from different body areas should be analysed, should be collected in a single tube. Vesicular fluids, lesions, and crusts should not be combined in the same tube. It is recommended to also obtain an oropharyngeal swab along with a sample of the lesion. Conventional tests such as immunohistochemistry, viral isolation from a clinical sample, and electron microscopy are still valid methods, yet, they require sophisticated lab apparatus and knowledgeable technicians (9).

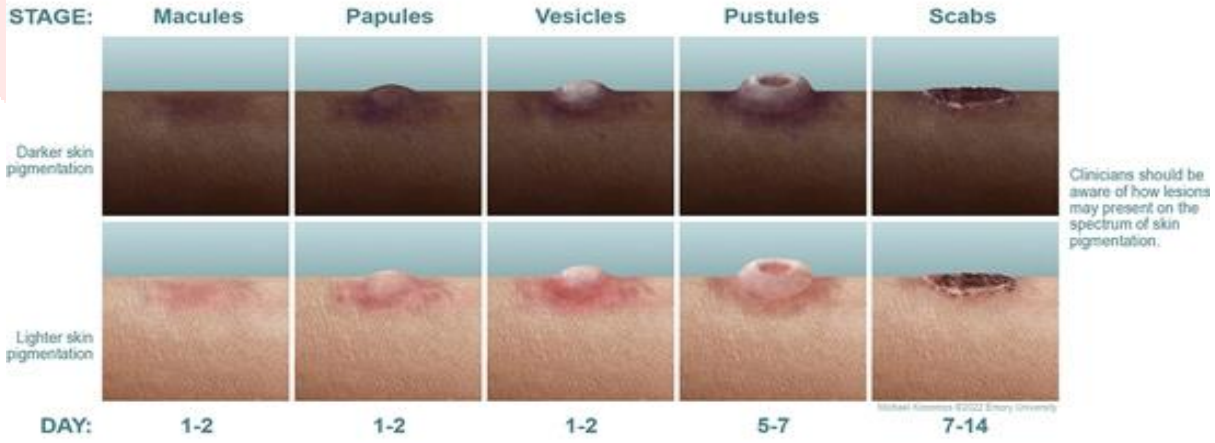

Figure 4: Skin lesions appearance on the spectrum of skin

The present outbreak is still being investigated, thus collecting additional research specimens can be considered provided the relevant ethical review board approves and there is enough laboratory and medical expertise for their secure, storage collection, and handling. Considering the clinical appearance, especially the lesions' locations, these may include semen, vaginal swabs, rectal, and/or urine. EDTA blood may aid in the detection of the monkeypox virus but may not contain the amount of virus detected in lesion samples due to any viremia occurring early in the course of infection, often in the prodromal stage and before skin lesions

become obvious. Only when clinically necessary and only by trained staff, should take a sample of a lesion be considered as the macular stage develops. It is not necessary to collect these additional specimen categories outside of research settings because they are not intended for routine diagnostic uses. The diagnosis of monkeypox should not be made solely based on plasma or serum antibody detection. However, if test findings from tested samples are ambiguous, the initial sample is taken within the 1st week of illness, and detection of IgM in recently acutely ill individuals or IgG in matched serum specimens can help with the diagnosis when administered at least 21 days apart. Serological testing may be hampered by recent immunization.

Within an hour of collecting, specimens should be chilled or frozen, and They should be delivered to the lab as soon as feasible. For reliable diagnostic testing, proper specimen handling and storage during transportation are crucial. Depending on the form of transport employed, specimen transportation must adhere to all applicable national and/or international rules, including the UN Model Regulations, and should be transported as category A, UN2814 "infectious substance, affecting humans". Within an hour of collection, samples obtained for the MPXV examination should be frozen (-20 °C or lower) or chilled (2-8 °C). Specimens ought to be stored at -20 °C or below if the transport time for the sample to be analysed is more than 7 days. At -70°C, longer-term specimen storage greater than 60 days from the collection is advised. When there is no immediate access to a cold chain, it might be taken into consideration that virus DNA found in Skin lesion substances is largely stable if kept in a chilly, dark setting.

The identification of specific viral DNA sequences using real-time/traditional polymerase chain reactions (PCR) is the basis for nucleic acid amplification testing (NAAT), which is used to confirm MPXV infection. Some procedures have two phases, where the initial PCR reaction finds OPXV but cannot identify the species it belongs to. A second step can then be taken to precisely detect MPXV, which may be PCR-based or involve sequencing. Clinical and epidemiological data should be taken into account when MPXV infection is confirmed. MPXV infection has been proven by positive OPXV PCR test results followed by MPXV PCR and/or sequencing confirmation, or by positive MPXV PCR test results in suspected cases. (8).

Even for well-equipped, high-impact healthcare systems networks specializing in infectious diseases, human monkeypox presents particular difficulties so care should be taken accordingly (10).

Discussion:

In addition to the DRC, monkeypox is known to be endemic in ten other African nations. Before it was brought into the USA in 2003, it was believed that the sickness was restricted to a certain region of the African continent. The incidence of monkeypox cases has increased recently, along with a wider geographic occurrence, as seen by the summary of recorded cases (2).

Treatment and prevention:

As stated by the Centre for Disease Control and Prevention (CDC), Supportive treatment is frequent enough for individuals with a monkeypox viral infection at this time because no specific medications are available. Antivirals, smallpox vaccines, and vaccinia immune globulin (VIG), which are all available after consulting with the CDC, have, however, been used to manage tiny outbreaks.

The World Health Organization strongly advises its member nations to take into account the current multi-nation monkeypox outbreak when convening their national immunization technical advisory groups (NITAGs) to review the available data and formulate recommendations for vaccine use that are appropriate to their specific national contexts.

Mass vaccination is not advised in cases of monkeypox epidemics. At this time, vaccination is not advised for the general public. According to Public health, authorities should implement a robust surveillance and containment strategy to ensure isolation, thorough case investigation and, care as well as thorough contact tracing and monitoring, according to the WHO interim guidance on Surveillance, investigation, and contact tracing for monkeypox. This will make it easier to determine who is most at risk for infection and, thus, who should receive vaccinations first.

For contacts of cases, post-exposure prophylaxis (PEP) is recommended with an appropriate second or third-generation vaccine, ideally, 4 days after the initial exposure (and up to 14 days if no symptoms are present), to stop the disease from developing. According to the type of potential exposure, the interaction of people with definite/likely/suspected monkeypox are at a greater risk of exposure. Monkeypox transmission necessitates protracted close contact with a person who is exhibiting symptoms. Brief contacts and those carried out while wearing the proper protected personal equipment (PPE) by conventional procedures are not typically in high danger and don’t need post-exposure prophylaxis (PEP).

It is advised to monitor high-level exposures and to get PEP vaccinated. It includes

1. Skin-to-skin contact without protection between a person's skin lesions, bodily fluids, contaminated objects, or mucous membranes.
2. Performing any procedures that would cause oral secretions, cutaneous lesions, or resuspended dry exudates to produce aerosols without protective gear inside a patient's room or within 6 feet of a patient (11).

A recommendation for monitoring and an informed clinical decision would be made in the event of a medium risk of exposure.

1. Being at least 6 feet away for three hours or longer from a patient who is not wearing a surgical mask (11).

Monitoring is advised for low or unclear exposures, but no post-exposure prophylaxis is advised. It includes

1. Contact a case that is known, likely, or suspected.
2. Isolation from the symptomatic case while in an outside setting.
3. Workers in the laboratory who handle routine clinical blood samples or other materials unrelated to monkeypox testing (12).

Pre-exposure prophylaxis (PrEP): As determined by national public health authorities, PrEP is advised for outbreak response team members healthcare professionals at high exposure risk, laboratory people dealing with orthopoxviruses, and clinical laboratory personnel conducting monkeypox diagnostic tests. Select individuals who run the risk of exposure to orthopoxviruses at work are advised to get vaccinated by the Advisory Committee of Immunization Practices (ACIP). It is advised that anyone working in a research facility, a clinical lab performing orthopoxvirus diagnostic testing, or a member of a specified response team who may be subjected to orthopoxviruses at work get immunized.

MVA-BN, LC16, or ACAM2000 are vaccination alternatives that can be considered for authorized or off-use for post-exposure or pre-exposure monkeypox prophylaxis. The reactogenicity, safety, and risk of adverse events connected to vaccination should be considered during the need-risk-benefit analysis for vaccine selection. Non-replicating (MVA-BN) or minimally replicating (LC16) vaccinations should be used for individuals for whom replicating vaccines may be regarded as a precaution or are not recommended. This affects youngsters, pregnant or nursing mothers, and those with immunological deficiencies, immunosuppressive treatments, or atopic dermatitis. The application of ACAM2000, LC16, or other equivalent smallpox immunizations using bifurcated needles, as well as information on subcutaneous injection of the MVA-BN monkeypox vaccine, must be made sure of by national health authorities (12).

Risk management and community involvement:

Unprecedented monkeypox outbreaks in numerous nations with no obvious travel connections to regions where monkeypox generally occurs raise the possibility of increased human-to-human transmission. The difficulty and need for effective communication increase when disease transmission patterns change. Most instances of monkeypox in newly affected areas, though not all of them, are currently seen in men who have intercourse with men (MSM). It should be avoided at all costs to stigmatize this or any other afflicted demographic. The spread of disease may be accelerated in crowds like concerts and festivals where individuals are or may be in intimate contact. It is important to use planned events and gatherings that have preventative and control mechanisms in place to engage audiences and deliver useful public health messages (13).

The main goals of risk management and community involvement activities for monkeypox are to manage risk perception, increase awareness, uphold confidence in health authorities and intervention strategies, and actively communicate to help those who are at risk make decisions that will keep them and others around them safe from infection and serious illness. The right balance between being educational and targeted to greater risk groups while avoiding stigmatization or excluding other people or groups who could be at risk must be struck by risk management and community involvement programs (13).

Conclusion

In particular, about viruses like monkeypox that we have identified as significant threats to people, it is crucial to begin preventing epidemics and preparing for them. Monkeypox poses a major health danger to people who live in endemic regions where the virus is known to spread, such as the Democratic Republic of the Congo and other African countries. However, it is also a problem for the security of world health, as the USA outbreak in 2003 demonstrated. To halt enhanced transmission virulence or efficiency, appropriate and effective interventions must be implemented immediately, as well as active surveillance operations. (2)

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