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Review Article

A Detailed Insight of Monkey Pox Virus Infection in Adolescent

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ABSTRACT

Background: Smallpox-like symptoms are seen in the viral zoonotic illness known as monkeypox. In the current outbreaks being reported, the World Health Organization (WHO) claims that this is the first instance of chains of transmission being documented in Europe without known epidemiological connections to West or Central Africa. On August 7, 2022, the WHO reported a total of 27,815 confirmed cases in over 89 countries, with the majority of those affected experiencing monkeypox for the first time. The objective of this article is to provide a succinct overview of the monkey pox, its transmission mechanisms, and available preventative methods in adolescents. **Materials and Methods:** Several databases, including WHO guidelines, PubMed, Bentham Science, and Elsevier, were used to compile the data for the article following a thorough analysis of the various research findings connected to monkey pox infection, pathogenesis, and available treatments. **Results:** Monkeypox is a zoonotic orthopoxvirus that causes disease in humans similar to smallpox. Complications are more likely in children and the immunocompromised. Treatment is largely symptomatic. The first-line treatment for monkeypox, including in kids and teenagers, is tecovirimat. **Conclusion:** We came to the conclusion from this review that adolescents and adults both transmit the monkey pox virus. The most common sign of monkeypox in kids and teens is a rash that starts out as maculopapular lesions and turns into vesicles, pustules, and then scabs, just like diseases in adults. Children and adolescents who have been exposed to individuals with suspected or confirmed monkeypox may benefit from Post-Exposure Prophylaxis (PEP) with vaccination, immune globulin, or antiviral medicine.

Keywords: Pathogenesis of Monkey Pox, Treatment of Monkey Pox, Complication, Prevention and Management of Monkey Pox, Vaccination of Monkey pox, WHO guidelines for Monkeypox.

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INTRODUCTION

In contrast to the devastating COVID-19 pandemic, which the world has only recently begun to recover from, the discovery of the fatal disease monkeypox in the US and Europe has alarmed many nations and wreaked havoc. According to the World Health Organization, there have been 3413 confirmed cases of monkeypox and one fatality (WHO).[1]

The monkeypox virus, which is a member of the Orthopoxvirus genus, Chordopoxvirinae subfamily, and Poxviridae family, is the culprit behind monkeypox, a currently uncommon zoonotic illness. A smallpox-like illness is similar to monkeypox disease, which is closely linked to the variola virus (smallpox virus), occurring primarily in forested parts of central and west Africa. According to historical data, a smallpox vaccination with the vaccinia virus (another Orthopoxvirus) provided about 85% protection against monkeypox. However, systematic immunization against smallpox was no longer recommended after the disease was eradicated in 1980, and it has been forty years since the last Orthopoxvirus vaccine program.[2-5] A moderate virus called monkeypox is spread by the ferocious wild animals of Africa. The illness was first identified when two pox outbreaks occurred in colonies of monkeys held for research at a research facility in Copenhagen, Denmark in 1958.[6] On September 1, 1970, a nine-month-old child was admitted to the Basankusu Hospital in the Democratic Republic of the Congo, marking the first human MPXV case in recorded medical history (at that time, known as the Republic of the Congo). A virus similar to MPXV was isolated from the boy's smallpox-like illness.[7-10] Between October 1970 and May 1971, six human MPXV cases were reported in Liberia, Nigeria, and Sierra Leone. Ten MPXV cases were reported between 1971 and 1978, with the first index MPXV case in Nigeria being reported in 1971. Since then, thousands of human cases of monkeypox have been documented in 15, with 11 of those locations being in Africa. Monkeypox has been brought to Singapore, Israel, the US, the UK, and the Philippines.[11] On August 7, 2022, the WHO reported a total of 27,815 confirmed cases in over 89 countries, with the majority of those affected experiencing

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monkeypox for the first time. It is unknown, however, if children are more susceptible to monkeypox than adults or whether adult patients experience different clinical consequences. Even though there isn't much known about monkeypox in children, patients infected with Clade I of the monkeypox virus have shown that children under the age of 8 are more likely to have severe cases. In the past, endemic areas have reported cases of monkeypox in kids and teenagers. Once an illness manifests, it is anticipated that the clinical presentation will resemble that of adults. Additionally, severe monkeypox sickness can affect anyone who has immune-suppressing illnesses or specific skin diseases such as eczema. The virus that is responsible for the 2022 Multinational Monkeypox Outbreak belongs to Clade IIb, which normally produces less severe illness than Clade I.[12] Children were more likely than adults to be hospitalized in an intensive care unit during an outbreak of monkeypox in the US in 2003, which was brought on by rats imported from Ghana, according to research published in the journal Clinical Infectious Diseases. The report states that over a third of the 37 confirmed patients were less than 18. But in a large outbreak that occurred in Nigeria in 2017, very few illnesses in children were found. A systemic study of case data from outbreaks between 1970 and 2019 found that the virus is mostly spread by personal contact with contagious sores or fluids. This is different from previous outbreaks. In this review, we'll give a thorough overview of teenage monkeypox. This article's overall goal is to raise awareness of the dangers of infection.

VIROLOGY

The Monkey Pox morphology indicates that viral particles are ovoid or brick-shaped particles with a geometrically corrugated lipoprotein outer membrane around them. These traits are shared by other Orthopoxviruses. The 200 by 250 nm size range of the monkey pox virus is well recognized.[13,14] The outer membrane serves to protect the densely populated core of the membrane, which is home to numerous enzymes, double-stranded DNA, transcription factors, and other components. The core is defined as biconcave and contains lateral bodies on either side because of an artefact caused by fixation during electron microscopy.[15,16] The Congo strain and the West African strain of monkeypox are the two varieties. The Congo strain is deadlier than the West African strain. The Congo strain has a 10% mortality rate compared to the West African strain's 1% fatality rate.

EPIDEMIOLOGY

Since humans were the first to become infected by the virus through close contact with infected animals, monkeypox has most likely been present in Sub-Saharan Africa for thousands of years. The reservoir of MPXV is currently unidentified. Evidence, however, points to monkeys as incidental hosts, much like humans, and indicates that the reservoir is most likely one or more rodent or squirrel species that reside in the secondary forests of central Africa. Monkeypox was not recognized as a distinct infection until 1970, after smallpox had been completely eradicated from Zaire (the current Democratic Republic of Congo [DRC]), where it had previously been common. During the global push to get rid of monkeypox, a lot of people got vaccinated in central Africa. This is thought to have temporarily decreased the number of people who got monkeypox. The incidence of human monkeypox may have temporarily dropped in central Africa as a result of mass vaccination during the global eradication campaign, but the illness has since returned due to a lack of immunity in succeeding generations and a rise in reliance on hunting for sustenance in areas devastated by civil war.[17] Between 1 January 1998 and 31 December 2002, the DRC Ministry of Health received reports of 1265 monkeypox cases throughout Africa; 215 of those cases led to the collection of specimens. Of these 215 cases, PCR and viral culture studies revealed that MPXV was the root cause in 88 of them. The patient ages of the laboratory-confirmed cases ranged from 10 months to 38 years, with a mean age of 16.5 years and a median age of 15.5 years. 73.6 percent of patients were under the age of ten, and 73.2 percent were over the age of 25.[18]

It was discovered that MPXV was to blame for a cluster of illness cases that occurred in the US Midwest in the summer of 2003.[19] This marked the discovery of MPXV for the first time in the Western Hemisphere. During an outbreak, 37 of the 72 reported human patients had their cases confirmed in a lab.[20,21] It was thought that native prairie dogs (Cynomys species) kept alongside rodents brought from Ghana in western Africa were the primary cause of the outbreak because the majority of the infected humans became ill after interacting with pet prairie dogs.[22] Since the latest disease outbreak news on June 17 was published, 1310 additional cases have been recorded, and eight other nations have also reported cases. A 30-year-old man who travelled to Kerala from the United Arab Emirates last month has tested positive for monkeypox, making him the fifth case of the virus in the southern state and the seventh overall, according to state Health Minister Veena George. The 30-year-old man who came from the United Arab Emirates on July 27 and landed at Kozhikode Airport is being treated for monkeypox at the Manjeri Medical College in Malappuram, according to information given to the health minister.[23]

Monkeypox has so far been linked to over 27,814 cases worldwide. Nine confirmed cases of monkeypox have been reported in India. Figure 1 shows the 3413 lab-confirmed cases and 11 deaths that have been reported to WHO since January 1 from 89 countries and territories in six WHO Regions.

In epidemiological week 31 (from 1 to 7 August), there were 6217 new cases recorded worldwide, up 19% from week 30 (from 25 to 31 July) (5212 cases). The WHO European region (53%) received the majority of the notifications of cases over the previous four weeks, followed by the Americas (46%), the Eastern Mediterranean Region (1%), and the Western Pacific Region (1%). Nigeria recorded one fatality during the second quarter of

2022.[24] The ten nations with the largest number of cases recorded globally as of August 7 are the United States (7510), Spain (4577), Germany (2887), the United Kingdom (2759), France (2239), Brazil (1721), the Netherlands (959), Canada (957), Portugal (710), and Italy (505). Together, these nations account for 89% of cases around the world.[25] The latest outbreak of monkeypox has distinct clinical symptoms than the previous one. Traditional signs and symptoms of human monkeypox include monomorphic pustular rashes and uncommon genital lesions.[26]

PATHOGENESIS OF MONKEY POX IN ADOLESCENTS

In the past, endemic areas have reported cases of monkeypox in kids and teenagers. Once an illness manifests, it is anticipated that the clinical presentation will resemble that of adults. It is unknown, however, if children are more susceptible to monkeypox than adults or whether adult patients experience different clinical consequences. The infectious phase of the monkeypox virus begins with exposure to the host's oropharyngeal or respiratory mucosa, much like the smallpox virus does. Following viral entry, the monkeypox virus multiplies at the inoculation site; during human-to-human transmission, the inoculation sites are the oropharyngeal and respiratory mucosa. The viral load increases during primary viremia and then disseminates to the nearby lymph nodes. In secondary viremia, the viral load spreads through the circulatory system to distant lymph nodes and organs. The entire process replicates the incubation phase, which can last up to 21 days but usually lasts seven to fourteen days. As the clinical symptoms of monkeypox do not appear during the incubation stage, this period is not contagious. Clinical manifestations and symptoms of monkeypox can be linked to the prodromal stage.

This is mainly because symptoms including mucocutaneous lesions, lymphadenopathy, and other ambiguous symptoms are present during the prodromal stage, which is the most contagious.[27] Figure 2 depicts direct contact with infected people's mucocutaneous lesions as well as direct contact with contaminated objects or surfaces.

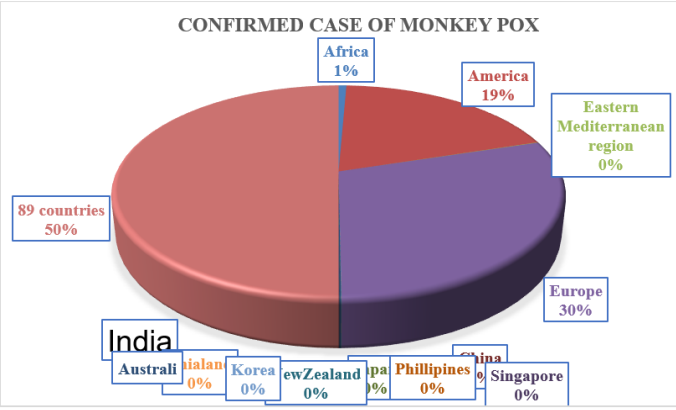

Figure 1: The WHO reports widespread prevalence of the monkey pox virus worldwide from 1 January 2022 to 7 August 2022.

TRANSMISSION IN ADOLESCENT

Animal to adolescent transmission

It first affects animals in the wild before moving on to people. There are various ways that the virus might spread. Especially when the animal is sick or dead, intimate personal contact with an infected animal can spread the infection.[28] As shown in Figure 2, there are several ways that monkeypox can spread from animal to human. Primary transmission can happen through bites or scratches from infected animals, contact with exposed blood or bodily fluids from infected people, consumption of contaminated animals when hunting, cooking, or eating, and direct contact with cutaneous or mucosal lesions from infected people.[29,30]

Human to human transmission (or human-to-children)

Transmission in children and adults is remarkably comparable. Close contact with respiratory droplets, direct contact with cutaneous lesions of the infected person, as well as contact with contaminated objects or surfaces, can all result in human-to-human transmission (secondary transmission).[31,32] Additionally, the placenta and skin-to-skin contact between an infected parent and the child before, during, or after delivery are two ways the virus can spread from a pregnant woman to her foetus.[33]

In addition to the obvious carriers of the virus, there are several hidden ones. One of the greatest contributors to this "silent spreader" category is those who are asymptomatic. In contrast to other silent spreaders like those who purposefully do not test themselves and try to suppress it before others or those who, despite showing symptoms, do not take the necessary precautions, asymptomatic individuals are unaware that they are carrying a significant amount of the virus and are equally capable of infecting others. A person who has the infection but doesn't have any symptoms is almost as likely to spread it as someone who does have symptoms.[34]

CLINICAL FEATURES

According to WHO, the most prevalent indication of monkeypox in children and adolescents is a rash that develops from maculopapular lesions to vesicles, pustules, and finally scabs, much like infections in adults.[35] The monkeypox rash can be confused with other rash conditions that are frequently diagnosed in kids, such as varicella (chicken pox), hand, foot, and mouth disease, measles, scabies, molluscum contagiosum, herpes, syphilis (including congenital syphilis), allergic skin rashes, and drug eruptions. Monkeypox co-infections are possible. When deciding which etiologies should be examined, clinical judgement should be utilised; monkeypox testing should be done on children and adolescents who exhibit symptoms and indications that are

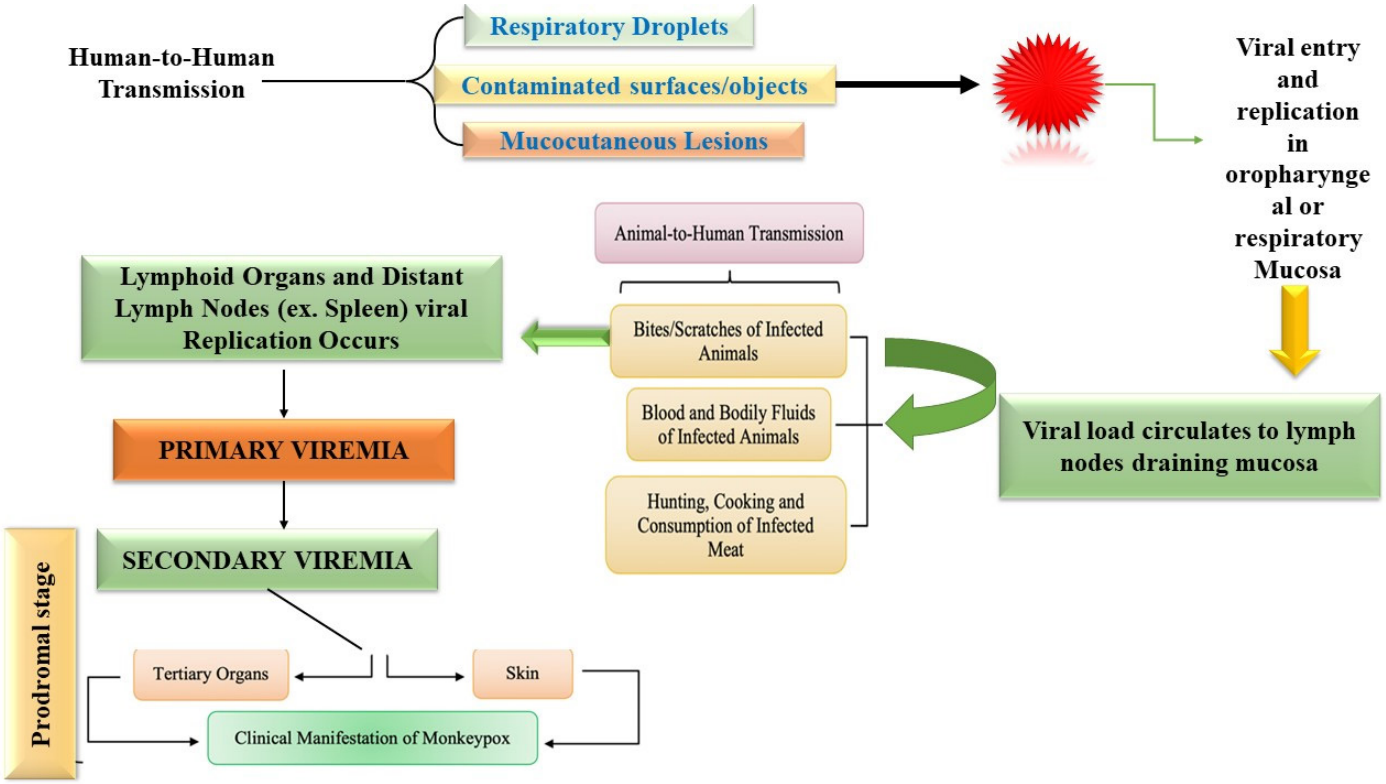

Figure 2: Pathogenesis of Monkey Pox-Human-to-Human and Animal-to-Human Transmission of Monkey pox virus.

possibly caused by monkeypox, especially if those youngsters meet epidemiological requirements.[36] The various symptoms and complications of monkey pox virus are shown in Figure 3.

Before symptoms appear, the monkeypox virus has a 21-day latency period. The signs and symptoms of monkeypox are milder than those of smallpox. Fever, headache, discomfort in the muscles, exhaustion, and swollen lymph nodes are some of the symptoms of monkeypox. After experiencing these symptoms, individuals get skin rashes, which typically begin on their face before spreading to other body parts. The rashes become bigger until they form a scab and go away. The WHO has issued a warning that it may cause a number of medical complications, including bacterial superinfection of soft tissues, eye infection, scarring, pneumonia, sepsis, cellulitis, respiratory distress, encephalitis, dehydration, and excruciating anogenital sores.

Participants in this epidemic commonly report experiencing rectal pain and penile swelling, according to the research paper. The study is based on 197 men who tested positive for monkeypox, 196 of them had sex with another man or identified as gay, bisexual, or both. Based on the study's findings, which are related to the newly asserted symptoms, 56% of lesions are found in the vaginal region and 42% in the perianal region. Lesions have been found in close proximity to the vaginal area for the first time. The lesions have previously only ever been noticed on other parts of the body, such as the head, arms, and legs. Between 2007 and 2011, the head and limbs were where the lesions were most frequently observed. During the previous monkeypox outbreak in Nigeria, which took place in 2017–2018, lesions were mostly discovered on the face, legs, and trunk. Potential carriers of the monkeypox virus include lesions in the form of body fluids and respiratory droplets. The lesions begin to from one to three days following the onset of a fever.[37,38] Figure 4 shows the several stages of lesions that appear during monkeypox.

The clinical manifestation of cases of monkeypox connected with this epidemic has been unexpected compared to earlier reports: many cases in newly affected areas are not presenting the classically characterized clinical picture for monkeypox (fever, swollen lymph nodes, followed by centrifugal rash). Among the peculiar traits mentioned are the possibility of one or more lesions. In certain cases, skin lesions are absent, but there may still be anal pain and non-spreading bleeding lesions in the vaginal or perineal/perianal region. Other times, lesions could show up before a person experiences a fever, a cold, or other physiological symptoms (absence of prodromal period).[39]

LABORATORY DIAGNOSIS

Monkeypox is the most likely diagnosis because the illness typically affects isolated communities in tropical African rain forests. It's crucial to distinguish between chickenpox and other skin conditions since the latter manifests itself as successive harvests of lesions that are always apparent at varying stages of development. Due to the similarities between the monkeypox and varicella-zoster viruses, it might be difficult to diagnose an infection with the virus. Recently, a study investigated the

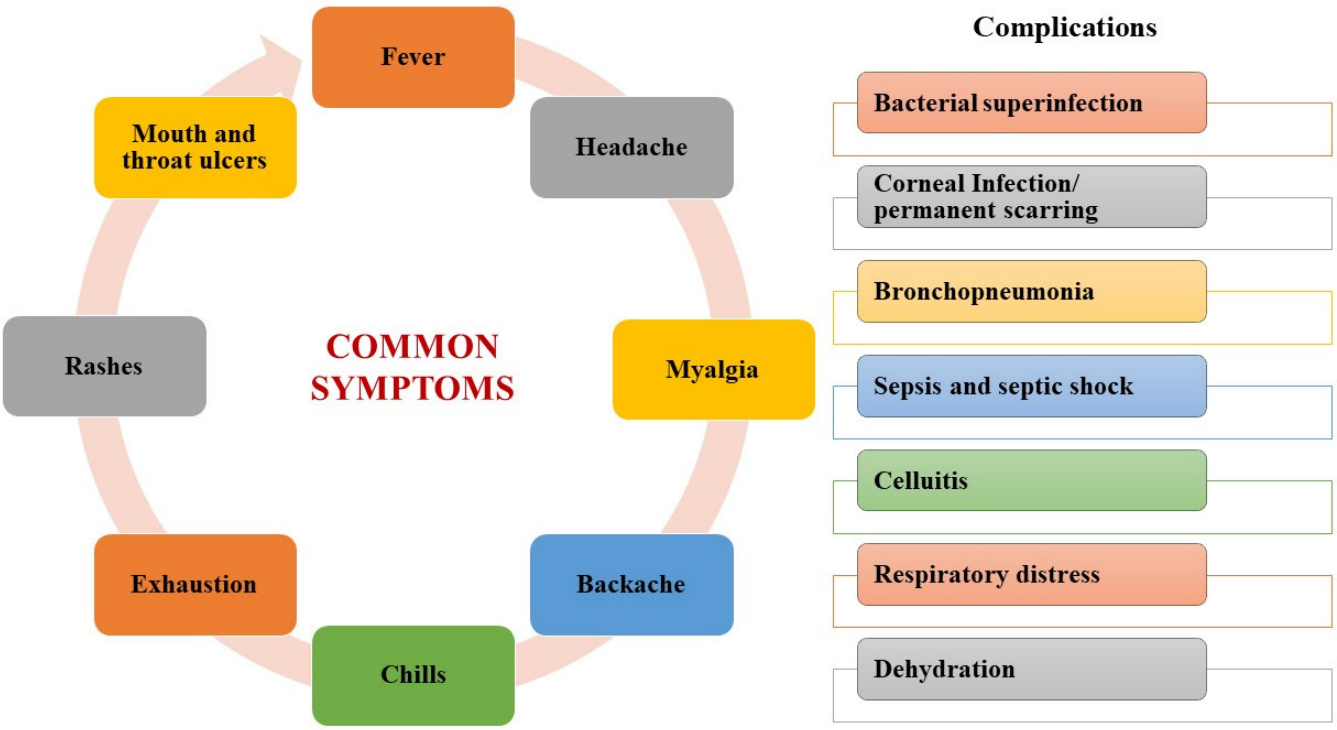

Figure 3: Symptoms and Complication of Monkey Pox Virus in Adolescents.

effectiveness of the different approaches for the laboratory diagnosis of monkeypox.

Electron microscopy

The distribution of chickenpox is "centripetal," as opposed to smallpox, with more lesions on the trunk than on the face and extremities. Scabs can be sent to a reference lab for an accurate diagnosis, which can identify an Orthopoxvirus and distinguish it from the varicella virus.

Real-time quantitative Polymerase Chain Reaction (PCR) assay: In recent years, there has been a rise in the utilization of panorthopoxvirus or MPXV-specific targets.[40,41]

Highly automated GeneXpert MPX/OPX methodology Recently, it was claimed that a laboratory diagnostic test that can be used on-site and on both humans and animals has been developed.[42,43]

ABICAP

ABICAP is the name of an immune-filtration technology (Antibody Immuno Column for Analytical Processes). In contrast to conventional enzyme-linked immunosorbent tests (ELISAs), this uses a gravity-driven flow-through antigen capture ELISA and lateral flow.[44,45]

DNA restriction analysis can be used to identify the virus and it can be cultivated in tissue culture. It is best to obtain a viral culture from an oropharyngeal or nasopharyngeal swab. A sample of the ceiling of an intact vesiculopustular or a skin biopsy

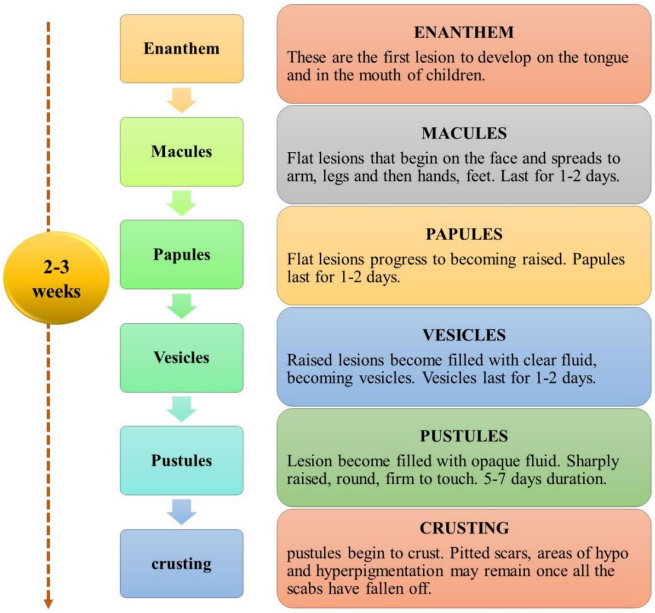

Figure 4: The several stages of lesions that appear during monkeypox.

specimen of the vesiculopustular rash should be examined. It is possible to get tissue for PCR of DNA sequence-specific for the monkeypox virus. It is possible to examine paired sera for acute and convalescent titers. The most effective serum for detecting the monkeypox virus infection was serum obtained more than 5 days after rash onset for IgM detection or more than 8 days

after rash onset for IgG detection.[46] Based on virus isolation or PCR detection of the virus from a clinical specimen, instances of monkey pox were confirmed (skin biopsy or throat culture). People were thought to have a likely case of infection if they had fever and a rash within 21 days of being exposed to monkey pox, had serum that was positive for Orthopoxvirus immunoglobulin Mz (IgM), but didn't have any clinical specimens that were positive for the virus through culture or PCR.[47]

TREATMENT

No specific treatments have yet been applied to the monkeypox virus. Doctors advise segregating the patients in a hospital to treat any recurring symptoms and stop the disease from spreading. In the US, vaccinations against smallpox are given to those who have monkeypox and are 85% effective. The first-line treatment for monkeypox, including in kids and teenagers, is tecovirimat. Post-Exposure Prophylaxis (PEP) with a vaccine, immune globulin, or antiviral medicine can help protect children and teens who have been around people with suspected or confirmed monkeypox.

Oral drugs

Antivirals and vaccinia immune globulin have also been shown to be effective in curing monkeypox in patients. The antiviral medication tecovirimat, which was originally developed to treat smallpox and is now marketed under the brand name TPOXX, could theoretically hasten the resolution of monkeypox sickness and improve outcomes. There are some antiviral drugs listed in Table 1 that are used in the treatment of monkeypox infection and the mechanism is Figure 5.[48,49]

Vaccines

Smallpox immunization appears to reduce the severity of infection symptoms and protect against the monkeypox virus.[53,54] Currently, the US Strategic National Stockpile has three smallpox vaccinations (SNS). The Aventis Pasteur Smallpox Vaccine (APSV) could be used for smallpox under an Investigational New Drug (IND) program, together with JYNNEOSTM (also known as IMVAMUNE, IMVANEX, MVA-BN), and ACAM2000®. The two-dose Jynneos immunization can be administered to children and adolescents using the single patient expanded access experimental new pharmaceutical approach, although there is a limited supply available. Even though the ACAM2000 vaccine has been linked to negative side effects and isn't recommended for babies younger than 12 months or kids and teens with certain health problems, it can still be given as part of an exploratory protocol.

PREVENTION

Prevention of animal to human

Animal outbreaks can be prevented by improved infection control techniques, such as routine screening and isolation of newly affected animals. Better hygiene practices are necessary to prevent the virus from spreading to fomites, which can then serve as a source for future infections. In order to protect animals, vaccination with the vaccinia virus may be an option. Care must be taken to house these species separately because diseases have been linked to mixing Asian monkeys with primates from Africa. To stop spreading the infection, anyone who has been exposed to the monkeypox virus should stay away from all animals, especially children's.[55] When there is an outbreak, the spread of the monkeypox virus can be stopped by isolating the affected animals and tracking down their contacts for at least six weeks after the last exposure. The areas where these animals have been housed need to be carefully cleaned and disinfected. It is necessary to follow the detailed guidelines provided by the state, local, or CDC Web sites. A monkeypox patient should seek medical attention, carefully protect his face with a mask, prevent contact with infected animals, and track down any interactions they may have had recently. The areas where these animals have been housed need to be carefully cleaned and disinfected.

Prevention of human to human (Adolescents)

Clinicians should exercise their professional judgement when deciding what tests to order and take into account the patient's history of contact with individuals who have a confirmed or probable case, close relationships with MSMs, or travel that puts them in danger. When a patient may have monkeypox, doctors should call their jurisdictional health department. The recommendations state that children with monkeypox should cover their skin lesions and refrain from touching or scratching them Children with immune-compromising disorders should avoid close contact with those who have monkey pox, but if

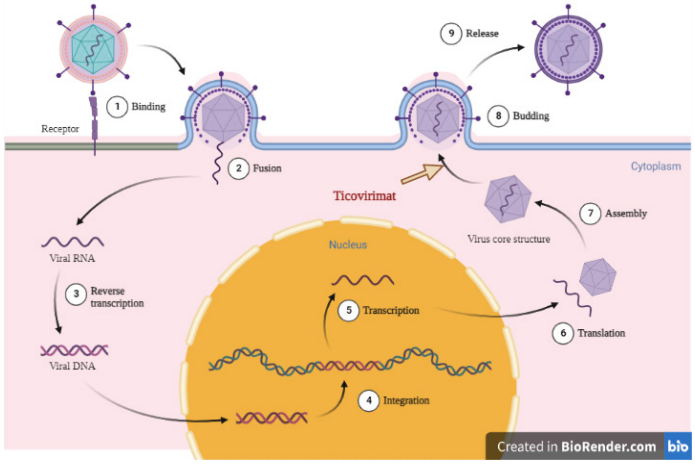

Figure 5: Mechanism of action of anti-viral drugs used for the treatment of monkey pox infection.

Table 1: Lists of Medicines used for the Treatment of Monkeypox Infection along with mechanism of action.

Drug Name	Category	Mechanism of Action	Ref.
Cidofovir	Antiviral	Inhibit viral DNA polymerase	50
Ribavirin	Antiviral	IMP dehydrogenase inhibitor	50
HPMA	Antiviral	DNA polymerase inhibitor	50
ANO	Antiviral	Blocks the translation of viral mRNAs	51
C3Npc A	Antiviral	SAH hydrolase inhibitor	51
N-MCT	Antiviral	Nucleoside analog inhibitor	51
KAY-2-41	Antiviral	Nucleoside analog inhibitor	52
NIOCH-14	Antiviral	Blocks the release of intracellular virus from the cell	52

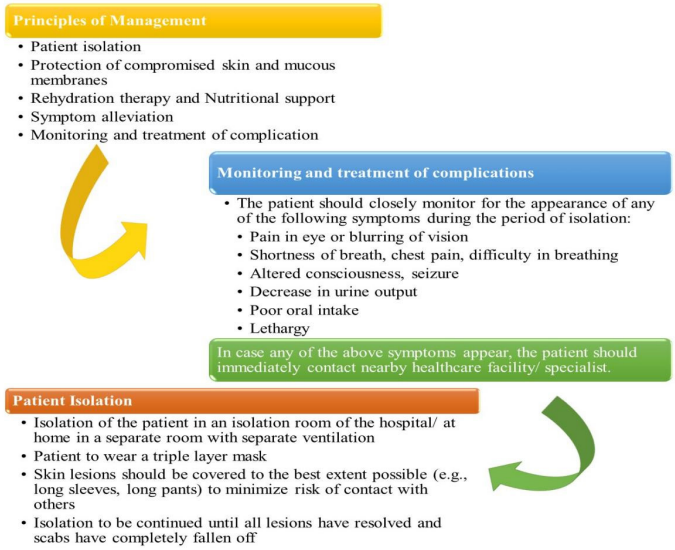

Figure 6: The fundamental rule for managing isolated patients, treating patients for complications, and preventing the spread of the monkey pox virus.

this is not possible, they should use a mask or respirator that fits properly.

It is preferable if there is only one caregiver for a child who has monkey pox, and skin-to-skin contact should not be made with the rash. When interacting with a caregiver, a kid with monkeypox over the age of two should wear a mask that fits comfortably, and the caregiver should wear gloves when touching bandages or clothing. For neonates of adults with suspected or confirmed monkeypox, the CDC suggests early washing and taking PEP into account. Aside from staying in a different room, they should also keep their distance from the infected person. Breastfeeding should be postponed while the baby is in isolation, and moms should be encouraged to pump and discard milk.

As seen in Figure 6, the fundamental concept of patient monitoring and patient isolation also plays a significant role in the prevention of the monkey pox virus in adolescents.

FUTURE PROSPECTS

A new study suggests that the presence of a gene encoding the Golgi-Associated Retrograde Protein (GARP) complex in a monkeypox virus strain that is infected may raise the risk of severe illness. The same study shows that figuring out which host cells are needed for a virus to grow could help scientists make medicines that fight viruses.

According to a new analysis, the precise mode of transmission of the human monkeypox virus is unknown. Even though there hasn't been a confirmed source of the monkeypox virus, the same study suggested that close contact with wild animals, which could lead to bites, and eating bush meat could be risk factors for infection.[56]

CONCLUSION

It is important to remember that several of the nations with verified cases of monkeypox during the epidemic in May 2022 do not have an endemic monkeypox population, and the patients had no travel ties to endemic regions. However, in view of the devastation brought on by the COVID-19 pandemic, it is imperative to thoroughly investigate the public health consequences and pandemic potential of monkeypox. In order to ensure public health readiness and create defenses against potential threats, it will be helpful to have a better understanding of the factors influencing the transmission of this virus. The likelihood of underreporting must also be taken into account because the majority of cases occur in rural Africa, a continent with weak health infrastructure and few resources. This review led us to the conclusion that the monkey pox virus is transmitted by both adults and adolescents. The most prevalent sign of monkeypox in children and adolescents is a rash that, like illnesses in adults, progresses from maculopapular lesions to vesicles, pustules, and finally scabs. Tecovirimat is the first-line medication for monkeypox, including in children and teenagers. Children and teenagers who have been exposed to people who have monkeypox, whether suspected or confirmed, may benefit from post-exposure prophylaxis (PEP) with vaccines, immune globulin, or antiviral medication.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

WHO: World Health Organization; **PEP:** Post Exposure Prophylaxis; **COVID-19:** Coronavirus 2019; **GARP:** Golgi-Associated Retrograde Protein; **APSV:** Aventis Pasteur Smallpox Vaccine; **IND:** Investigational New Drug; **MPXV:** Monkey Pox Virus; **DRC:** Democratic Republic of Congo; **PCR:** Polymerase Chain Reaction; **AICAP:** Antibody Immuno Column for Analytical Processes; **ELISAs:** Enzyme-Linked Immunosorbent Tests.

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