Review Article

An clinical overview on Monkeypox: Prevention and prevalence with current status and future prospects in clinical management

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Abstract

Monkeypox is a zoonotic viral infection caused by the monkeypox virus. It belongs to the ortho poxvirus genus in the poxviridae family and can infect humans as well as other animals. It is a DNA virus with an enclosed double standard. Since the virus was first identified in macaque monkeys in 1958, it has been referred to as "monkeypox." The initial signs and symptoms are a fever, headache, and muscle aches. When instances of monkeypox began to rise in the 1970s and the smallpox vaccine program was terminated, the world took note. Recently, there has been a notable outbreak of the monkeypox virus in central Africa, and the infection's threat to public health is constantly growing. As of right now, the monkeypox virus has been classified into two genetic clades: the clades of western and central Africa. The most common clinical manifestation seen in people with monkeypox is mucocutaneous presentation. Despite the lack of a proven, safe treatment, antivirals, which were first developed for use in smallpox patients—are being used to treat monkeypox. In severe cases, medication like Tecovirimat may be administered. We have discussed a number of subjects in this article, including outbreaks, immunizations, therapies, transmission, and worldwide prevalence, in an effort to improve understanding of monkeypox and to set the stage for future research.

Keywords: Monkeypox, orthopox, zoonotic, tecovirimat, immunization, vaccination, smallpox, iymphadenopathy, encephalitis

Introduction

Monkeypox is a zoonotic disease caused by the monkeypox virus which belongs to Orthopoxvirus genus, Poxviridae family, Chordopoxvirinae subfamily, and is the causative agent of monkeypox illness. The genetic material of this virus is linear double-stranded DNA, which is found in the cytoplasm of infected cells. Viruses are hosted by a variety of rodent species and nonhuman primates. It has been discovered that a wide range of animal species, including non-human primates, rope and tree squirrels, dormice, Gambian pouched rats, and others, are sensitive to the MPXV. In 1958, a case of monkeypox was reported among monkeys transported from Singapore to Denmark. Magnus et al. (1959) colleagues originally discovered the monkeypox virus as the causative agent of pox infection in monkeys in 1959. On September 1, 1970, the Democratic Republic of the Congo reported the first human case of monkeypox infection. The victim was a 9-month-old boy who was the only person in his family who had not had a smallpox vaccination. The virus that causes monkeypox, which is related to smallpox, was first identified in humans in the 1970s and was endemic in some regions of Africa (Bunge et al., 2022).

The virus that causes monkeypox was first identified in monkeys in a Danish laboratory, hence the name. MPXV cases and clusters have been recorded simultaneously for the first time in both endemic and non-endemic nations across a wide variety of geographical locations (Karem et al., 2007). Based on the results of genome sequencing and clinical presentation, two clades of monkeypox virus isolates were identified. Clade 1 of the monkeypox virus produced multiple outbreaks in the Democratic Republic of the Congo between 1981 and 2017, with high death rates ranging from 1 to 12% (Aplogan et al., 1998). Very few cases of human monkeypox were reported in West Africa throughout this time, but in 2017, there was a significant outbreak in Nigeria with 122 cases of the monkeypox virus clade 2 that were

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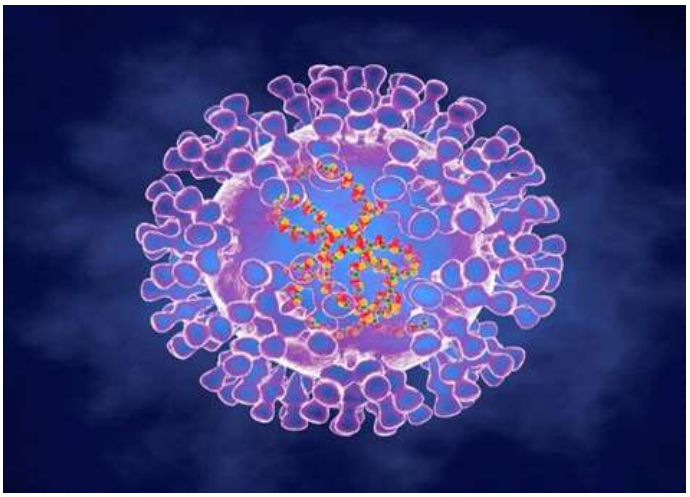

Figure 1: Structure of Monkeypox virus

verified by PCR (Heymann et al., 1998). A rodent virus known as monkeypox mostly spreads among specific rats in Africa. The viruses have an oval, brick-like shape, and their viral DNA is encased in a lipoprotein layer. Based on biological characteristics and the viral DNA's endonuclease sequence, the monkeypox virus is identified (Ladnyj et al., 1972).The main difference between smallpox and monkeypox is that the former presents with fever, malaise, back pain, headaches, and muscular aches, whereas the latter does not . As of right now, there is no proven, safe cure for monkeypox (Philpott, 2022).

The orthopoxvirus genus also includes three other species that are pathogenic The orthopoxvirus genus also to humans; these are the variola virus, cowpox virus, and vaccinia virus. Monkeypox is closely related to smallpox but has a striking distinguishing feature of an early lymphadenopathy. The virus is transmitted from human to human by droplet infection contact with lesions, fomites, and via the placenta as well. There are numerous smallpox vaccinations that offer some immunity against MPX. Through early case recognition, diagnosis, and treatment, public health initiatives can stop the spread of mpox from person to person. People who live in or visit the home of someone who has mpox are advised to wear a well-fitting mask, refrain from touching potentially contaminated surfaces, practice good hand hygiene, avoid sharing eating utensils, clothing, bedding, or towels, and follow home disinfection guidelines (Arita et al., 1985).

Epidemiology

Human monkeypox was first identified in 1970 in the village of Basankusu in the Democratic Republic of the Congo. In DRC/Zaire, a second abrupt outbreak of human sickness was identified between 1996 and 1997. A minor outbreak of human monkeypox emerged in the US in 2003 among owners of prairie dogs as pets (Huang et al., 2022). The infant developed hemorrhagic lesions in a centrifugal pattern resembling smallpox, along with a fever. In August 2022, the World Health Organization declared it as a Public Health Emergency of International Concern. The first two cases of monkeypox were reported in India in the 2nd week of July 2022 in Kerala, and both these patients had arrived from the Middle East. The first reported monkeypox death on July 30, 2022, in India, was of a 22-year-old male from Kerala .Humans can contract the virus by coming into intimate contact with bodily fluids like mucus, saliva, or skin lesions that are carriers of the virus (Breman et al., 1980).

Since the beginning of May 2022, more than 3000 instances of the MPXV virus have been reported in more than 50 nations spread over five regions. As opposed to West or Central Africa, where the monkeypox virus is widespread, the majority of verified cases with a travel history reported visits to Europe and North America. Of these cases, 17% of the victims were children under the age of ten (Huang et al., 2022). In 2003, 71 human cases of monkeypox were discovered in the USA, which attracted some interest from around the world. More than 78,000 cases have been documented in more than 100 countries by November 2022, and several clinical research have revealed that the illness may have unique epidemiological and clinical features (Harris, 2022).

Seven cases of monkeypox were reported in the UK between 2018 and 2021, four of which were linked to travel from endemic countries. Two Nigerian travellers who were returning were diagnosed with monkeypox in July 2021 in Texas and Maryland, respectively (Vaughan et al., 2020) .

A total of 80,249 laboratory-confirmed cases of monkeypox had been reported worldwide in the 2022 outbreak, and as of November 17, 2022, over 106 countries in the WHO regions have reported 53 deaths. Since the World Health Organization [WHO] declared a Public Health Emergency of International Concern [PHEIC] in 2022, India has reported 30 cases of monkeypox [Mpox] as of August 2022. Over 20,000 cases overall [over 5000 confirmed cases] in 2024, with over 600 deaths, although testing rates rose to over 40% .The number of human cases of monkeypox documented throughout the last three decades has increased . Three family members contracted the mpox virus when the family returned to the UK in May 2021 from their trip to Nigeria (Likos et al., 2005).

One case included a man who went from Nigeria to Texas in July 2021. One case happened in November 2021 and involved a man who went to Marylan from Nigeria. According to the report, the majority of cases of monkeypox occur in people under 40, with a median age of 31. This clarifies how travellers contribute to the global

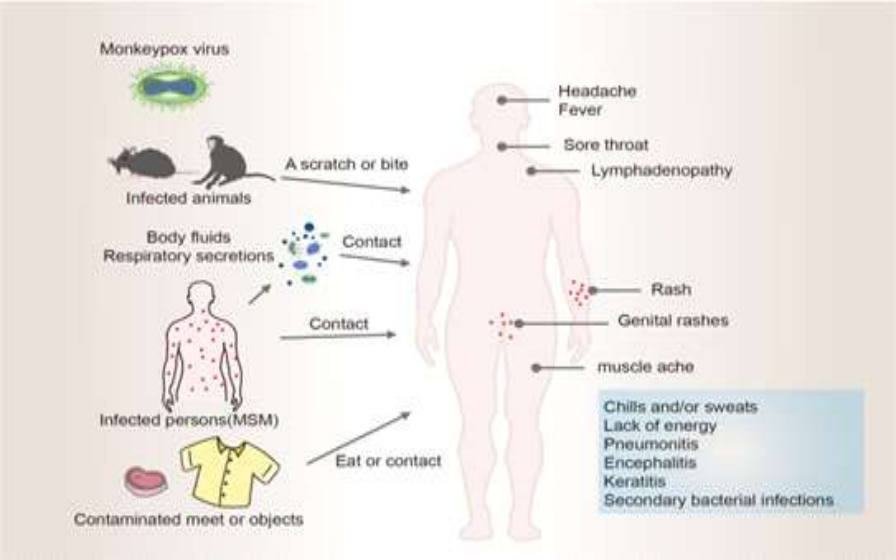

Figure 2: Proposed mechanism for the spread of the monkeypox virus throughout the body and its relation to the transmission route

spread of infectious disease epidemics in new areas (European Centre for Disease Prevention and Control 2022).

Etiology

The genus orthopoxvirus, which causes monkeypox, is the source of the disease. It is also caused by a group of viruses that also causes chicken pox and small pox .Close contact with an animal or human who is infected can spread the virus. Although the source of the monkeypox virus is uncertain, rodents or squirrels in central Africa are believed to be it.

The mpox virus is relatively large (200–250 nanometers) when viewed under an electron microscope. Brick-shaped poxviruses have a linear double-stranded DNA genome and are encased in a lipoprotein envelope. Poxviruses have all the replication, transcription, assembly, and egress proteins required for mRNA translation in their genome, aside from their need on host ribosomes. Monkeypox infections in humans are dependent on a few risk factors (Petersen et al., 2019). The primary cause of the decline in cross-protective immunity is the smallpox vaccination campaign's termination. The younger age group is now the most vulnerable to the virus as a result. The growing intimate contact between humans and the virus's reservoir hosts is another important element linked to the rising prevalence (CDC.11 May 2015).

Additionally, it has been proposed that eating bush meats may increase your risk. Male gender, civil wars, farming, deforestation, farming, refugee displacement, climate change, demographic shifts, and population migration are other influences (Sklenovská and Van Ranst, 2018). A different study proposed that climatic change, rain forest exploitation, declining herd immunity, transboundary migration, and geopolitical conflicts in disease areas are common factors contributing to the resurgence of human monkeypox. Other unintentional factors contributing to the increase in monkeypox prevalence and incidence, particularly in northern Nigeria, include ignorance, poverty, hazardous customs, and other factors. According to recent studies, bodily fluids such as urine, saliva, semen, and faces, as well as swabs collected from the oropharynx and rectum, had significant virus loads, indicating that sexual transmission is a key mode of infection (Tom and Anebo, 2018).

Pathogenesis

The virus that causes monkeypox can infect airway epithelial cells in the respiratory tract and keratinocytes, fibroblasts, and endothelial cells in the skin, resulting in both productive and cytopathic infection. Mature virions with a single lipid membrane are produced by viral replication, gene expression, and virion assembly in the cytoplasm of the host cell. These are then released as extracellular virions with an extra envelope (Realegeno et al., 2017). The virus replicates in the respiratory epithelium during the incubation period (up to post-challenge day 4) in the non-human primate models of respiratory acquired, clade 1 monkeypox virus. After that, it moves to the regional lymph nodes and lymphoid organs, such as the tonsils, spleen, liver, and colon, where it amplifies until day 6. At last, on day 8, the virus is found in the blood, and it continues to grow in concentration until day 10, at which point it causes extensive skin and mucous membrane sores (Tree et al., 2015).

The only information available on human skin inoculation is that which came from variolation, or immunization against the variola or vaccinia viruses, which caused lesions that were localized to the site of entry. Similar to this, during the 2022 outbreak, individuals who contract the

monkeypox virus through sexual contact typically have localized oral and anogenital lesions (Català et al., 2022). According to immunochemistry, the virus is present in the cytoplasm of every keratinocyte in the infected epidermis, but not in the unaffected epidermis. T lymphocytes with CD4+ and CD8+ components make up the majority of the lymphocytic infiltration (Maronese et al., 2022).

Transmission

Animal to human: Humans can acquire monkeypox from animals through body fluids or bites. Animals reported include squirrels, rats, and monkeys (WHO 2022).

This may happen by, Direct Contact: Coming into contact with an infected animal's blood, body fluids, or skin/mucosal sores. Eating undercooked meat or other animal products that have been infected is considered consumption. Getting bitten or scratched by an animal is also a diseased. Numerous rodents and primates are among the animals known toharbor the monkeypox virus. Human to animal transmission is more likely to occur in hunters, farmers, and residents near wildlife. Preventing contact with possibly sick animals is a vital step in lowering the risk of infection (Shaheen et al., 2022).

Human-to-human and animal-to-human transmission are both possible. Despite the fact that the monkeypox virus has been isolated from a number of rodents and non-primate animals in Africa, including dormice, rope, tree, and Gambian rats, as and squirrels (Learned et al., 2005).

Symptoms

Monkeypox is an uncommon virus that is similar to smallpox but less deadly. Among the first symptoms include fever, chills, headaches, backaches, swollen lymph nodes, and fatigue.

A rash normally develops on the face and moves to other parts of the body in a span of one to three days. Red spots on the skin may develop into raised bumps or painful red papules packed with pus after contracting monkeypox (Hagan et al., 2022). According to study, monkeypox normally takes six to thirteen days to incubate. Symptoms that may manifest include fever, sore throat, enlarged lymph nodes, backache, muscle soreness, lesions around the mouth and eyes, vesicular rash, which can cause pruritus (itching) or lesions on any part of the body (including the area around the genitalia and anus) (Ježek et al., 1988). Reports from the European Region indicate that the West African variant of the virus has killed about 1 in 100 afflicted people. A more severe course of the disease may be experienced by tiny children, pregnant women, and chronic patients whose systems are unable to generate an appropriate immune response (Pastula et al., 2022).

Complications

In the past, sepsis, bronchopneumonia, eye infections, and neurological symptoms have been reported as serious side effects of monkeypox infections. Ocular involvement can manifest as keratitis, which can cause corneal scarring and blindness, conjunctivitis, and sores on the eyelids. In a comprehensive analysis of research published between 2003 and 2021, neurological clinical characteristics like encephalitis, seizures, and disorientation were noted in around 2% of instances of monkeypox. Cerebrospinal fluid PCR assays revealed no poxvirus DNA, despite radiographic imaging in some encephalitis patients being consistent with severe demyelinating encephalomyelitis (Thornhill et al., 2022).

Figure 3: Symptoms and Prevention of monkeypox virus

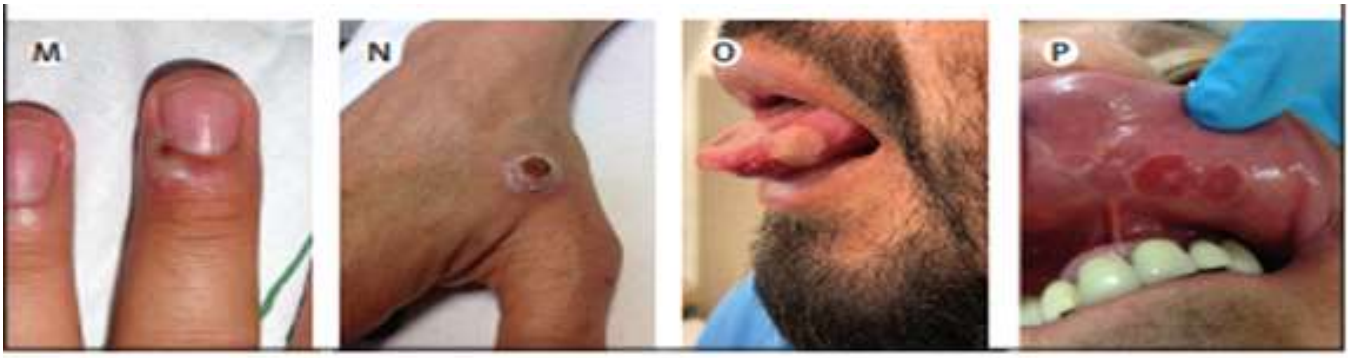

Figure 4: Monkeypox clinical presentations and differential diagnosis. Hand lesions caused by monkeypox {M} and Orf virus infection {N}, monkeypox lesions on the tongue {O} and aphthous ulcer on the labial mucosa {P} (Reynolds et al., 2017).

In Nigeria, reports of mental health problems such as depression and even suicide have been made. However, it is unclear if these illnesses are due to the neurological tropism of the monkeypox virus or if stigma and isolation play a more significant role. A few sporadic cases of myocarditis, epiglottitis, peritonsillar abscesses, rectal wall perforation with associated abscess in patients with proctitis, and hemophagocytic lymph histiocytosis are among the novel (albeit rare) severe complications linked to the 2022 outbreak.

Other less serious yet more frequently mentioned issues in 2022 include pain during bowel movements or rectal soreness.

Bacterial superinfection of skin, Permanent skin scarring, Hyperpigmentation or hypopigmentation, Permanent corneal scarring (vision loss), Pneumonia, Dehydration (vomiting, diarrhea, decreased oral intake due to painful oral lesions, and insensible fluid loss from widespread skin disruption), Sepsis, Encephalitis, Death (Yuan et al., 2022).

Common Complications

Secondary bacterial infections (e.g., pneumonia, sepsis), Skin infections (e.g., abscesses, cellulitis), Respiratory complications (e.g., bronchopneumonia, respiratory failure), gastrointestinal problems (e.g., diarrhea, abdominal pain), Eye complications (e.g., conjunctivitis, keratitis), and Orthopedic issues (e.g., arthritis, osteomyelitis) are the common complications reported.

Severe Complications

Septicemia (bloodstream infection), Meningitis (inflammation of the brain and spinal cord), Encephalitis (brain inflammation) Respiratory failure, Cardiac complications (e.g., myocarditis, pericarditis), Multi-organ failure and premature birth (Breman et al., 1980) are the severe complications reported.

Outbreaks

Monkeypox, a zoonosis, has been recorded since early May 2022 in at least 30 non-endemic countries including Spain, the United States, Germany, the United Kingdom, France, and Canada. As of 21 July 2022, the cumulative number of confirmed cases exceeded 15,000 globally. On 23 July 2022, the World Health Organization (WHO) declared monkeypox a Public Health Emergency of International Concern (PHEIC) due to outbreaks in multiple countries and continents. The Public Health Agency of Canada (PHAC) reported 1,410 cases of monkeypox as of 14 October 2022, mostly occurring in Quebec, Ontario, and British Columbia .The unusual outbreak emerged in non-endemic areas of the world associated with transmission among gay, bisexual, and other men who have sex with men (gbMSM). Although at the time of writing this paper, the epidemic was declining, there remains a pressing need to understand the epidemic and potential control methods (Yuan et al., 2022).

The former is more virulent with reported fatality rates in Africa of 10% for the Central Africa clade and 3.6% for the West African clade. The incubation period ranges from 5 to 21 days, after which infected individuals may initially have flulike symptoms, then, 1–3 days later, a characteristic skin rash develops. The recovery period may take 2–4 weeks. In the recent outbreak, there are atypical clinical observations (Petersen et al., 2019).

In Canada, control is based on vaccines and non-pharmaceutical interventions including recommendations for testing and isolation of cases, and, where possible, tracing of contacts. In June 2022, the National Advisory Committee on Immunization (NACI) released a guideline on using an orthopoxvirus (Imvamune R) vaccine with potential efficacy against monkeypox (Yuan et al., 2022). WHO also expressed concerns that more infections could arise in Europe and elsewhere due to private and social gatherings during festivals, parties, and holidays. In fact, in the United States, many cases were reported linked to large social gatherings, such as pride events, pool parties, and bathhouses. Consequently, it is essential to assess the effect of gathering events on monkeypox transmission to inform public health on the most effective control measures (Bass et al., 2013).

Previous Monkeypox Outbreaks

When the first instance of monkeypox virus (MPXV) was found in 1970 in the Democratic Republic of the Congo (DRC), it became well-known. MPXV was first detected in 1958 as pox-like skin outbreaks among cynomolgus monkeys. One human MPXV stain was collected from a 9-month-old infant who had a haemorrhagic, centrifugally distributed rash that was connected to cervical lymphadenopathy. Since, it was once thought to be smallpox due to the case-based resemblance, but it was quickly determined to be a different orthopoxvirus variant (Bass et al., 2013).

Prevention of Future Outbreaks

Coordinated, multidisciplinary international efforts are needed to contain and prevent any future outbreaks of monkeypox. Reducing the virus transmission from rodents and primates in endemic areas is crucial but extremely difficult. Large-scale health awareness programs should be launched to inform the public about the dangers of eating undercooked meat and avoiding contact with possible animal reservoir species. The bushmeat trade cannot be completely stopped, both culturally and commercially, but animal-to-human transmission can be reduced by handling animals carefully and wearing protective gear, surgical masks, and gloves (Li et al., 2006).

The COVID-19 pandemic has brought to light the shortcomings of public health systems around the globe and the lack of readiness to handle any upcoming widespread disease outbreaks.

Diagnosis

It's critical to be vigilant about monkeypox. The symptoms of this sickness can occasionally be somewhat peculiar, particularly in the context of the 2022 pandemic. These samples have very accurate PCR results. However, because they can react similarly to other viruses, testing by serology or culture isn't always as accurate (Saijo et al., 2008; Di Gennaro et al., 2022). PCR is the most reliable method of confirming that it is indeed monkeypox! According to a 2006 study, there are several tests that can identify the monkeypox virus 100% of the time. Furthermore, when compared to real viral samples, Light Cycler quantitative PCR (LC-qPCR) eibits more than 90% sensitivity and accuracy. Surprisingly, 14 out of 15 blood samples in that investigation yielded positive results, indicating the presence of the virus. Thus, keep yourself educated and don't be afraid to consult a healthcare professional if you have any questions or concerns (Adler et al., 2022). The assessment of clinical appearance and a detailed medical history should be part of be taken into account. Nonetheless, the results of the lab tests should support the final diagnosis. This is due to the extensive range of differential diagnoses that exist for acute rash when the patient presents with non the evaluation process for monkeypox. To aid in the diagnosis, a history of visiting an endemic region, engaging with a wild animal from an infected area, or caring for a differential diagnoses that exist for acute rash when the patient presents with non-specific symptoms (such as fever, headache, myalgia, asthenia (Russo et al., 2023).

Treatment

Antiviral medications

Thus, several antiviral medications were investigated for smallpox in animals. They may also be beneficial for monkeypox! Human studies have been conducted, although their precise effectiveness is still unknown (Chan-Tack et al., 2021).

Tecovirimat

The first antiviral that comes to mind for treating smallpox is tecovirimat. It may be referred to as TPOXX or ST-246. This medication is effective for children and adults weighing three kilograms or more. It is regarded as the greatest option for medical care. In cases of severe illness, physicians may combine Tecovirimat and Brincidofovir. Tecovirimat inhibits the virus by interfering with the VP37 protein. This aids in preventing the virus from developing and dispersing from infected cells (Chittick et al., 2017).

Brincidofovir with Cidofovir

In June 2021, brincidofovir received approval in the US to treat smallpox. It's fantastic that there's an oral option. Given that it might be less harmful to the kidneys than cidofovir, it might be safer. These drugs also obstruct a significant portion of the virus's DNA processing (Smee, 2008). The effectiveness of brincidofovir against monkeypox in animals has not been thoroughly studied, yet it has demonstrated good efficacy against other viruses of a similar nature. As for cidofovir, at this time there are no clinical trials concerning its impact on human monkeypox. However, studies have indicated that it is effective against harmful infections in monkeypox-affected animals (Gruber, 2022). Cidofovir must be administered via IV in addition to regular saline and probenicid in order to be used. A doctor may advise resting and maintaining hydration until the infection clears up for patients with minor symptoms. In more severe situations, physicians could substitute antiviral medications.

Vaccination

The smallpox vaccine has gone through three generations of medical technology but only the second and third smallpox vaccine generations-ACAM2000, a mild vaccine, and IMVANEX, a live vaccine-are now approved. Smallpox vaccinations have gone through three generations of medical technology, It doesn't happen again. This vaccine can be administered either before or after exposure to improve disease transmission and dissemination (ideally

within 4 days of exposure), or in high-risk groups to avoid infection and disease (Hatch et al., 2013). ACAM2000 should not be used by immunocompromised individuals, those with skin conditions, people with heart conditions, or pregnant women. MPOX has an Expanded Investigational New Drug Application from the Centers for Disease Control (CDC) (Ogoina et al., 2019).

A third-line vaccination called IMVANEX is derived from the MVA vaccine. Although there are insufficient clinical data to support the use of vaccinations to prevent influenza in people, they have been demonstrated in animal models to elicit humoral and immunological responses as well as to offer therapeutic protection against serious illness and mortality. Generally speaking, the MVA vaccination is safer than ACAM2000 (Rizk et al., 2022).

Even though the vaccination is mostly utilized in North America and Europe, it is still inaccessible in many African nations.

Challenges in India and other developing countries:

Monkeypox is becoming a serious threat to global health as it can easily cross borders and spread. One major problem is that the tests to confirm monkeypox cases are very sensitive and are usually found only in a few specialized labs in certain countries. Many suspected cases are already reported, especially in Africa, where the Democratic Republic of the Congo and Nigeria the highest number of infections. However, these countries struggle with poor healthcare, lacking both trained medical staff and the necessary testing supplies. Additionally, the smallpox vaccine, which could provide protection against monkeypox, was stopped in the 1970s after smallpox was declared extinct. While some medicine and vaccines exist, not much research has been done since then (Edghill-Smith et al., 2005). The tests available today are designed for various related viruses, meaning they cannot specifically identify monkeypox, which confuses results with past smallpox vaccinations. For example, data from Nigeria shows that about 20% of patients who tested negative for monkeypox actually had antibodies from other viruses. To better understand and control the spread of monkeypox and related viruses, more research is urgently needed (Hammarlund et al., 2003; Miura et al., 2022).

Conclusion

The majority pox is, a viral zoonotic illness occur in Central and West Africa. It presents clinically like smallpox, which was declared and destroyed in 1980. Study demonstrates the evolutionary character of the monkeypox virus, which is the known cause of monkey pox. The COVID-19 experience that is still going on epidemic has made the demand for health awareness worldwide. Be ready for any pandemics or epidemics in the future. Therefore, it is appropriate to begin constructing structures to reinforce the current system of disease surveillance and reporting vital to combating infectious disease outbreaks around the world.

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