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Review

The Latest News for May 2022 All You Need to Know on Monkeypox

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Abstract: Monkeypox virus was named so because of its detection in monkeys in 1958. It belongs to the same family as smallpox and chickenpox viruses. There had been numerous outbreaks of this malady initially in the African continent and other parts of the world. The simultaneous spread in nineteen countries in 2022 has raised some serious concerns.

Monkeypox is no more a rare disease and has the potential for bioweapon use. We discuss the various ways to prevent its spread, treatment options available, diagnosis, and differentiation from other closely related diseases. We also discuss if the present outbreak could be a bioattack or if this disease is here to stay.

The literature suggests that we can effectively manage Monkeypox because of the availability of drugs and vaccination against smallpox. There is also a need for active surveillance against the new resistant recombinant viral strains. The possibility of this outbreak being a bioattack seems remote, although there are questions about the transmission which still need to be answered.

Keywords: Monkeypox; prevention; treatment; endemic; transmission

1. Introduction

After Smallpox, Monkeypox (MPxV)has become a significant orthopoxvirus infection in humans. The Monkeypox virus belongs to Orthopoxvirus genus, which also contains Camelpox, Cowpox, Vaccinia, and Variola viruses.

Recent outbreaks of the MonkeyPox virus in Europe, Australia, and the US (Figure 1) have raised some strong questions. The spread across nineteen countries has indicated that it is not a rare disease anymore. This review tries to address the concerns caused by the recent outbreaks like biological warfare, will it become another COVID, and can it cause death. This article also emphasizes the historical perspective, diagnosis, prevention, treatment, alternative drugs to the mainstream medications, and differentiation between Smallpox, Monkeypox, and Chickenpox based on their clinical presentation. Because the virus was isolated in monkeys, it was termed Monkeypox.

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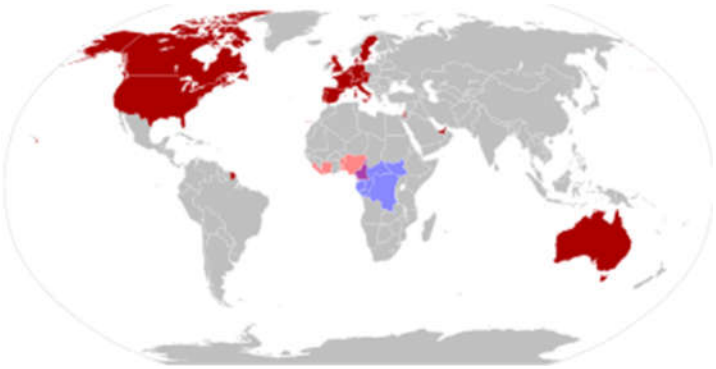

Figure 1. Area with Monkeypox Outbreaks. No known cases; Endemic West African clade; Endemic Congo Basin (Central African) clade; Both clades recorded; West African clade outbreak in 2022.

2. Historical perspective

One of the biggest paradoxes in the world of preventive healthcare was the eradication of smallpox but the advent of Monkeypox (MPX).(Rimoin & Graham, 2011)

In 1958, monkeypox was first documented in Denmark due to a pustular infection in a troop of Singapore-imported monkeys.(Simpson et al., 2020). On September 1, 1970, a nine-month-old boy was hospitalized at the Basankusu Hospital in the Democratic Republic of the Congo as the first documented MPXV incident in the medical literature.(Alakunle et al., 2020) The youngster was the only one infected in the family.

The patient's relatives reported that they sometimes consumed monkeys as gourmet but could not recollect cooking one in the past month. They were also unsure whether the youngster had recently been in contact with a monkey. The analysis revealed that the infant was the sole family member who had not received the smallpox vaccination.

Later six more cases of monkeypox were reported between October 1970 and May 1971 in Liberia, Nigeria, and Sierra Leone.(Alakunle et al., 2020)

WHO confirmed 54 occurrences between 1970 and 1979 (20, 30, 61). Breman et al. described 47 of those fifty-four cases.("The Current Status of Human Monkeypox," 1984)

In 1980 the Global Commission classified MPX for the Certification of Smallpox Eradication as the most significant orthopoxvirus illness in men in the post-smallpox era.(Sklenovská & Van Ranst, 2018)

Historically, monkeypox is confined to the environment of tropical rainforests. In 2005, 49 instances were documented in Sudan outside the rainforests for the first time. Those patients recovered without any fatalities.

2.1.2003. U.S. outbreak

A little girl developed fever and redness after being attacked by a prairie dog during a trade fair near Milwaukee on May 11, 2003.(Anderson et al., 2003) As of June 20, 2003, 71 cases of monkeypox had been documented in the US utilizing electron microscopy and serologic testing. These incidents have been linked to Gambian pouched rats brought from Accra, Ghana, in April 2003 by a Texas-based dealer of exotic animals. It was the first outbreak of Monkey-pox in the US, and there were no fatalities. (*July 15, 2003*, n.d.)

2.2.2017–2019. Nigeria outbreak

According to reports, monkeypox has spread over Southeast and Southern Nigeria, including numerous states in the Southwestern regions of Nigeria. The outbreak began in September 2017 and continues in various states through May 2019.(Bunge et al., 2022)

2.3.2018. United Kingdom cases

Two cases were confirmed in Blackpool, the patient and the medical worker who cared for the patient from Blackpool. On December 3, 2019, a patient traveling from

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Nigeria to the United Kingdom was detected with monkeypox in southwest England, marking the occurrence of a fourth case.

In September 2018, the United Kingdom identified the first-ever incident of monkeypox. It is suspected that the individual, a Nigerian national, caught monkeypox in Nigeria prior to arriving in the United Kingdom.

2.4.2019. Singapore case

A 38-year-old Nigerian male who had come to attend a wedding was admitted to Singapore's National Centre for Infectious Diseases on May 8 after being diagnosed with monkeypox. He was the country's first recorded case. Consequently, 22 hotel staff were quarantined. [59] The patient may be associated with the continuing epidemic in Nigeria.(Yong et al., 2020)

No cases were reported in 2020 due to the spread of Covid and Lassa fever.(Nigeria *Centre for Disease Control*, n.d.) The Covid pandemic resulted in a lockdown and social distancing which may have contributed to minimal or no spread of the MonkeyPox Virus.

2.5.2021. cases

2.5.1. Uk cases

Public Health Wales confirmed three cases of monkeypox originating from the same family on May 24 in the United Kingdom. The Public Health department detected the index case on May 24, following a trip from Nigeria. The second and third incidents were reported on June 2 and June 24, respectively.(*Communicable Disease Threats Report, 27 June-3 July 2021, Week 26*, 2021)

2.5.2. US case

A US returnee from Nigeria was tested with monkeypox on July 14 in the United States. Subsequently, the patient was hospitalized and treated with tecovirimat before being discharged 32 days later.(*A Case of Monkeypox in a Returned Traveler*, n.d.)

2.6.2022. outbreak

In May 2022, the UK Health Security Agency reported multiple incidents of monkeypox in London and northeast England. Both Portugal and Spain recorded numerous incidents during the same month.(*Portugal Identifies Five Monkeypox Infections, Spain Has 23 Suspected Cases | Reuters*, n.d.)

New York City is also investigating a suspected case, admitted to Bellevue Hospital in seclusion.(*New York Investigating Possible Monkeypox Case - but How Much of a Threat Is It?* n.d.)

On May 22 in Quebec, Canada, five documented cases and twenty additional suspect instances are currently being investigated.(Ross et al., 2022)

Two cases were verified in Australia on May 20, one in Melbourne and the other in Sydney. In the Melbourne case, a man in his 30s returned from London on May 16 and is currently hospitalized at Alfred Hospital. In the Sydney instance, a man in his forties has likewise returned from Europe and is isolating himself at home. Each patient exhibits modest symptoms.(*Monkeypox Confirmed in Melbourne and Sydney - ABC News*, n.d.)

Public Health Wales and the Public Health Agency of Northern Ireland reported one case each on May 26, bringing the total number of patients in the United Kingdom to 90.(*Monkeypox Cases Confirmed in England – Latest Updates*, n.d.)

3. Transmission

MPXV may transmit via animals-to-humans and humans-to-humans. Animal-to-human transfer, also known as zoonotic transmission, happens through close contact with or eating any of the biological virus hosts.(Beer & Rao, 2019; Pal et al., 2017)

3.1. Human to Human transmission behaviors

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An increased chance of contracting an MPXV illness can be attributed to the following behaviors:

- Falling asleep in the same room/bed
- Having food in the same dish
- Drinking from the same cup as the primary patient.(Nolen et al., 2015)

Kissing, assistance with toileting and cleanliness, and laundering garments were not significantly associated with contracting the virus.(Nolen et al., 2015)

Transfer of virus among humans may occur via close contact during close sexual intimacy, such as oral, anal, and vaginal sex, hugging, massage, mutual masturbation, kissing, and embracing. Other methods of spread involve handling textiles and things during intercourse that were used by an individual infected with monkeypox, like beddings, towels, etc. More research is being carried out to find the transmission via semen and vaginal secretions.(*U.S. Monkeypox 2022: Situation Summary | Monkeypox | Poxvirus | CDC*, n.d.)

Infection dissemination in hospitals has also been observed, whereas sexual transmission has been hypothesized for infected people with groin and pubic lesions (Ogoina et al., 2019).On May 25, 2022, the CDC asked homosexuals and bisexuals to be cautious considering sexual transmission as one of the means of its spread, especially among homosexuals (Kimball, 2022).

Anne Rimoin and Raina MacIntyre hypothesize in Nature that the higher proportion of MSM infected is the consequence of inadvertent entry to the community, followed by sexual behavior representing "direct contact," as opposed to the virus itself being transferred sexually.(*Monkeypox Goes Global: Why Scientists Are on Alert - PubMed*, n.d.)

Hospital spread can be prevented through the vaccination of medical personnel and using standard precautions.

3.2. Animal to human transmission

Most of the research implies that MPXV enters the human population through encounters with infected wildlife, most likely through eating or handling infected meat. (Beer & Rao, 2019; Hutin et al., 2001) The studies also suggest that the main route of transmission is through cutaneous, mucocutaneous, or airborne droplets

There was no significant danger connected with having pets in the home, discovering animal carcasses around the house, getting into contact with animal feces, being bitten or clawed by an animal, or catching or consuming wild animals according to Nolen et al.(Nolen et al., 2015)

The case-control study by Nolen et al demonstrates that there was a link between sleeping on the floor and an increased risk of infection. Living in a house with a door, eating a duiker(an antelope), and cooking meat from wild animals were recognized as protective factors.(Nolen et al., 2015)

Densely populated areas are more predisposed to the rapid spread of the virus. More people were afflicted with MPXV who had a ground-clearing within 500 m from their house. They had cleared the area for agricultural purposes, increasing their contact with animals. (Hutin et al., 2001; Khodakevich et al., 1988)

Nolen et al. suggest that neither the hunters nor the individuals who prepare the meat but male students were more likely to introduce the virus into a family. The reason could be the lack of small pox vaccination in young children. Due to pre-existing antibodies, older persons may have been impacted to a lower extent than youngsters. (Nolen et al., 2015)

3.3. Human to animal transmission

To date, no such case has been reported.

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4. Types of Monkey Pox virus

There are two strains of the Monkey Pox Virus: the Congo Basin also called Central Africa and the West Africa clades. According to reports, the Congo Basin clade (Central Africa clade) is more aggressive than the West Africa lineages and contributes more to human-to-human transmission.(Kabuga & El Zowalaty, 2019)

	Congo Basin Clade/Central Africa Clade (lineage)(McCollum & Damon, 2014)	West Africa Clade (lineage)(McCollum & Damon, 2014)
T-cell inhibition	Yes	No
Gene inhibiting complement enzymes	Present	Absent
Down-regulate Apoptosis	Yes	No
Silent Transcription genes involving host immunity	Yes	No

5. Reservoirs

Apart from monkeys, several squirrel species like rope squirrels (Funisciurus spp) , tree squirrels (Heliosciurus spp), Gambian rats (Cricetomys spp) , elephant shrews, domestic pigs , sooty mangabey monkey and various mice and rats.(Graphiurus, Xeru,) may serve as a reservoir for the MPXV. The seroprevalence study revealed that squirrels had the highest positivity rate of antibodies against Orthomyxovirus but no definitive reservoir has not been found..(Di Giulio & Eckburg, 2004) Surprisingly, the most frequent animal seized in the traps around the affected individual's residences was a mouse (Mus sp.).(Hutin et al., 2001; Pal et al., 2017)

The virus transmission between mammalian species was established by inoculating a rabbit (family Leporidae) with the MonkeyPox virus following exposure to an infected prairie dog at a veterinary facility.(Di Giulio & Eckburg, 2004)

Reservoir Animals of Monkeypox
Rope Squirrels Figure 2
Gambian Rats (**used to detect land mines in Africa**) Figure 3
Tree Squirrels
Elephant Shrews Figure 4 ("Elephant Shrew," 2022)
Domestic Pigs
Sooty Mangabey Monkeys Figure 5 (Santiago et al., 2005)
Rabbits

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Figure 2. Rope Squirrel (Funisciurus congicus) Reservoir for Monkeypox virus.

Figure 3. Gambian Rat (Cricetomys gambianus) *Reservoir for Monkeypox virus.*

Figure 4. Elephant Shrew (Macroscelididae)("Elephant Shrew," 2022) *Reservoir for Monkeypox virus.*

Figure 5. Sooty Mangabey Monkeys (Cercocebus atys)(Santiago et al., 2005) *Reservoir for Monkeypox virus.*

6. Why now

Thirty years later, the incidence of human MPX in the same region appears to have markedly increased

The causes involve

1. Reduced vaccine-induced protection from the virus,("2005 Robert H. Ebert Memorial Lecture Emerging and Re-Emerging Infectious Diseases," n.d.)

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2. Significant social and population shifts have raised MPX vulnerabilities and the probability of severe disease in humans.("2005 Robert H. Ebert Memorial Lecture Emerging and Re-Emerging Infectious Diseases," n.d.) This happened due to heavy rains and floods which placed people and MPXV-infected animal hosts in close proximity.

3. Periodic military conflicts and associated financial deterioration have driven country populations to migrate for long durations far into the bushland. Consequently, it has disturbed conventional country life and enhanced reliance on hunting for survival, hence increasing contact with animal hosts of MPX.(Simpson et al., 2020)

4. Malnutrition arising from economic constraints and immunodeficiencies such as HIV, organ transplantation, immunosuppressant drugs, and autoimmune diseases, has also led to the recurrence of MPVX.(Simpson et al., 2020)

5. *The virus may evolve into a more virulent strain capable of person-to-person transfer and increases with each recurrence or an outbreak.*("The Current Status of Human Monkeypox," 1984)

6. *The suspension of routine poxvirus immunization after eradicating poxvirus has decreased herd immunity*. The lowered herd immunity increases the susceptibility to MPVX. ("The Current Status of Human Monkeypox," 1984)

7. Increased urbanization of forests by humans, rapid increase in trade, and consumption of wildlife also contribute to the illness.

7. Definition of a Monkeypox case(Di Giulio & Eckburg, 2004)

According to CDC Human monkeypox cases have been categorized into:
Suspect case, Probable case, and a Confirmed case. The criteria for the three cases are:

Case	Criteria	Clinical Features	
Suspect Case	Epidemiological criteria	Fever or Unexplained rash and two more signs or symptoms onset of the first sign or symptom within 21 days of exposure	If both are present it is a suspect case
Probable Case	Epidemiological criteria	Fever AND Pustular rash with the onset of the first sign or symptom within 21 days of exposure	Both constitute a probable case
Confirmed case	Meets laboratory criteria		

7.1. Clinical criteria

The clinical criteria are based on the signs and symptoms and have the following**:**

Clinical Criteria
Fever
Rash: macular, papular, vesicular, or pustular; generalised or localised; discrete or confluent
Other, sweats, headache, backache, lymphadenopathy, sore throat, cough, and/or shortness of breath

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7.2. Epidemiological criteria

Following are the epidemiological criteria established by the CDC following the 2003 outbreak of Monkeypoxirus in the United States. Any one of these constitutes a positive criterion.

Contact (living in a home, stroking or holding, or visiting a pet holding facility such as a pet store or veterinary clinic) to
an exotic or wild mammalian pet (including prairie dogs, Gambian giant rats, and rope squirrels, among others to be assessed on a case-by-case basis) obtained on or after April 15, 2003,
with clinical evidence of sickness (eg conjunctivitis, respiratory problems, and/or rash).
Contact an exotic or wild mammalian pet
with or no clinical signs of illness that have been in touch with a monkeypox-infected animal or a human being in the same house or at the same animal holding facility
Skin-to-skin contact/Face to Face contact with a suspected, probable, or definite human case

7.3. Laboratory criteria

The laboratory criteria include one of the following:

Growth of MPV in culture
Detection of MPV DNA in a patient specimen using PCR.
Electron microscopy reveals virus structure compatible with an orthopoxvirus in the lack of contact with some other orthopoxvirus.
Immunohistochemical evidence of the existence of orthopoxvirus in tissue in the lack of contact with some other orthopoxvirus.

7.4. Clinical features (McCollum & Damon, 2014)

Initial symptoms include fever, widespread malaise, headache, and weariness.

Lymphadenopathy: Lymph nodes that are enlarged are hard and occasionally painful.

Fever: Fever typically subsides on the day of or up to three days after the beginning of the rash.

Rash: Typically, the rash starts initially on the face and then rapidly spreads to the rest of the body. The characteristic lesions frequently manifest as macular, papular, vesicular, and pustular lesions.

Variable numbers of lesions may be seen on a particular subject.

Patients complain of swollen, hard, and painful skin until crusts form [4]. The emergence of a second febrile phase when skin lesions become pustular has been coupled with worsening the patient's physical state.

Complications (McCollum & Damon, 2014)

Pulmonary

Bronchopneumonia,

Vomiting or diarrhea

Neurological

Encephalitis

Sepsis

Eye complications

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Ocular infections
Corneal scarring
Permanent vision loss

Mortality

Eleven percent is the mean case fatality rate of unvaccinated individuals; minors are frequently more susceptible to severe forms of sickness.

Mc Collum and Damon observed substantial problems and repercussions in unvaccinated patients (74 percent) than in vaccinated patients (39.5 percent).(McCollum & Damon, 2014)

7.5. Differentiation from other poxviruses

Comparison of clinical features between human monkeypox, smallpox, and chickenpox (modified from Breman and Henderson)(Breman & Henderson, 2002)

Disease Characteristics	**Monkey Pox**	**Small Pox**	**Chicken Pox**
History			
Recent contact with exotic animal	Yes	No	No
Recent exposure to a patient with vesicular rash	May Be	Yes	Yes
Previous vaccination against smallpox	No (Positive in 10 to 15 percent cases)	Rare	Yes
Incubation period	7 to 17 days	7 to 17 days	10 to 21 days
Prodromal phase	Yes (1-4 days)	Yes(1-4 days)	Yes(0-2days)
Physical Examination			
Prodromal fever	Yes	Yes	Yes
Malaise	Yes	Yes	Yes
Fever	Between 38.5^0 –40.5^0C	Often more than 40^0C	Usually less than 38.8^0C
Lymphadenopathy	Yes	No	N
Headache	Yes	Yes	Yes o
Skin lesions			
Distribution of skin lesions	Centrifugal	Centrifugal	Centripetal
Depth of skin lesions	Superficial	Deep	Superficial
Evolution of skin lesions	Monomorphic* (80%) Pleomorphic (20%)	Monomorphic	Pleomorphic**
Desquamation of skin lesions	22-24 day	14-21 days	6-14 days
Involvement of palms and soles	Yes	Yes	Rare
The appearance of lesions (Figures 6,7,8)	Umbilicated	Umbilicated	Dew Drop

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Complications			
Encephalitis	Less than 1%	Less than 1%	Less than 1%
Pneumonitis	Yes up to 12%	Possible	Yes up to 16%
Ocular complications	Yes up to 5%	Yes up to 9%	None
Secondary Soft tissue infections	Yes	Yes	Yes
Diagnosis			
DNA PCR	Monkeypox Virus	Variola Virus	Varicella Zoster Virus
Electron Microscopy	Pox Virus (Figure 9)	Pox Virus	Herpes Virus
Culture Possible	Yes	Yes	No
Serology	Monkey Pox and Orthopox antibodies present	Small Pox, Orthopox antibodies present	Varicella antibodies present

*Monomorphic: Lesions are in a single stage of development while progressing.

**Pleomorphic: Lesions in different stages of their development while progressing.

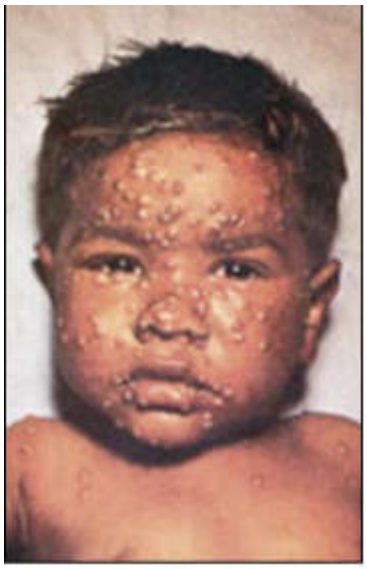

Figure 6. Smallpox rash image (Riedel, 2005).

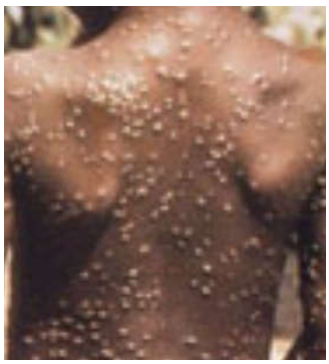

Figure 7. Monkeypox rash ("Monkeypox," 2022).

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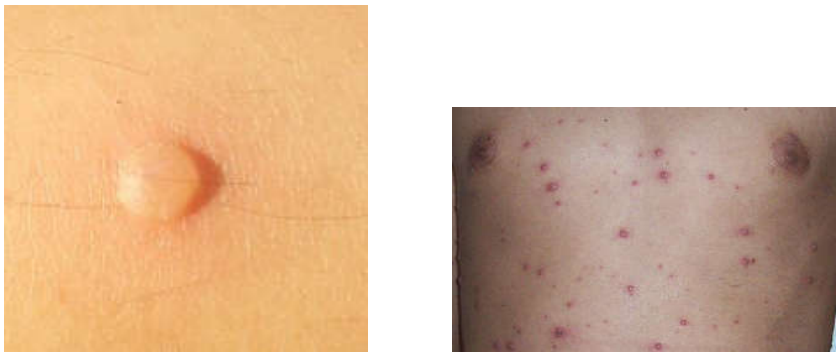

A B

Figure 8. Chickenpox rash (*Chickenpox - Wikipedia*, n.d.).

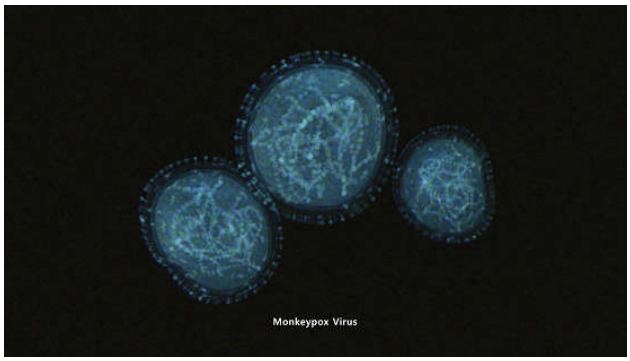

Figure 9. Monkeypox Virus under an electron microscope.

8. Diagnosis

Various diagnostic modalities used for detection of Monkey Pox Virus are:

Diagnostic tests are most successful when combined with clinical and epidemiologic information, such as a patient's immunization history. Lesion exudates on a swab or crust specimens continue to be among the best and least invasive acute patient specimens. Real-time polymerase chain reaction (PCR) is the most accurate diagnostic; however conventional techniques such as viral culture, Immunohistochemistry, and Electron microscopy can also be employed. The table below summarizes the diagnostic tests.

Test	Advantage	Disadvantage
Viral Culture	• Highly specific	Takes several days
Electron Microscopy	• Can be performed on different specimens from the same patient biopsy, scab, and vesicular fluid.	Needs specialized equipment and skilled technicians
Immunohistochemistry	• Can be used in biopsy to detect antigens quickly	Nonspecific
DNA PCR	• Can detect active disease • Highly specific	Expensive
Orthopoxvirus IgG antibodies	• Detects previous exposure to Monkeypox virus • Detects Small Pox Vaccination	Non-specific Requires blood samples Requires cold chain for blood samples
Orthopoxvirus IgM antibodies	• Detects recent exposure to Monkeypox Virus	Non-specific Requires blood samples

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			Requires cold chain for blood samples
Tetracore Orthopox Biothreat Alert	• Detects active disease from a skin lesion • Can be performed at room temperature • Does not require special training	Less sensitive than PCR Non-specific	

9. Treatment

Smallpox vaccines are derived from a fully clonal expansion vaccinia virus. These vaccinations do provide immunity against the Monkeypox virus to a considerable extent. Hence these can be utilized to protect against the Monkeypox virus. The vaccinations are not employed routinely in endemic locations due to concerns of severe unpleasant effects in a demographic with an impaired immune status. The table below summarizes some common side effects, route of administration, and availability of these vaccinations.

Smallpox vaccines	Advantages	Disadvantages	Route of Administration	Trade name	Availability
Live Small Pox (vaccinia virus)	Lesion over the vaccination site Long-term storage	Common side effects Headache, muscle pain, fever, fatigue, nausea Cannot be given to immunocompromised like AIDS, Organ transplants Cannot be given to people with atopic dermatitis, eczema Eye disease on steroids And pregnant females Cardiotoxic effects, Neurological, ocular side effects, and Steven Johnson Syndrome(*ACAM2000 (Smallpox (Vaccinia) Vaccine, Live): Uses, Dosage, Side Effects, Interactions, Warning*, n.d.)	Percutaneous Single-dose (15 pricks with a two-pronged needle in quick succession after dipping it in an injection vial in an area of around 5mm)and revaluate the site after 6-8 days(*Vaccine Administration | Smallpox | CDC*, 2019) Figure 10	ACAM2000(second-generation vaccines)	Licensed in the US
Attenuated vaccinia virus vaccine	No lesion over the injection site Can be used in • Elderly subjects Patients with organ transplants • Clinically immunocompromised	Those allergic to the chicken protein, benzonase, and gentamicin, must not take Imvanex. Common side effects Headache, muscle pain, fever, fatigue, nausea, injection site reactions	The general population (including people with atopic dermatitis) and immunocompromised **without vaccination against smallpox**	Imvanex/MVA BN previously named *Imvamune*	The European Commission has permitted the vaccination of immunocompromised adults and the broader adult

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	patients like AIDS, taking steroids • Can also be used in atopic dermatitis and eczema • Safety experience in mass vaccination due to smallpox outbreaks has been established No-Risk of: • Erythema multiforme • Post-vaccinal encephalitis(EMA, 2018)	like redness, pain, hardness, itching Major side effects Cardiac(Casual relationship) Cannot be used under 18 years pregnant, and lactating(EMA, 2018)	**2 doses** 0.5 ml subcutaneous injection With the second dose after 28 days of the first. Immunocompromised **with vaccination against smallpox** **2 doses** 0.5 ml subcutaneous injection With the second dose after 28 days of the first. General Population including those with atopic dermatitis **with vaccination against smallpox** Single-dose 0.5 ml subcutaneous injection(*Recommendations for the Use of Pre and Post Exposure Vaccination during a Monkeypox Incident*, n.d.)	(second-generation vaccines)	population. Maintained in the Strategic National Stockpile of the United States(McCollum & Damon, 2014)
Attenuated vaccinia virus	Demonstrates a safer profile and fewer adverse reactions than ACAM2000.	The virus can potentially multiply in humans(McCollum & Damon, 2014)	Single Dose	LC16m8 (Third generation vaccines)	Licensed for use in Japan.
Live attenuated vaccine against Smallpox and Monkeypox produced from MVA BN/Imvanex		Cannot be used for Pregnant, breastfeeding, and adolescents less than 18 years Mild side effects like were redness (80.9%), pain (79.5%), induration (70.4%), swelling (67.2%),	Two doses 28 days apart	JYNNEOS	

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				and itching (32.0%) at the injection site; mild systemic effects like fatigue (33.5%), headache (27.6%), muscle pain (21.5%), nausea (9.6%), chills (2%), and diarrhoea (2%). (0.7%), as well as fever (0.5 percent). (C. for B. E. and Research, 2021)	
				Serious Adverse Reactions Cardiac side-effects, Crohn's disease, sarcoidosis, extraocular muscle paresis, and throat tightness(C. for B. E. and Research, 2021)	

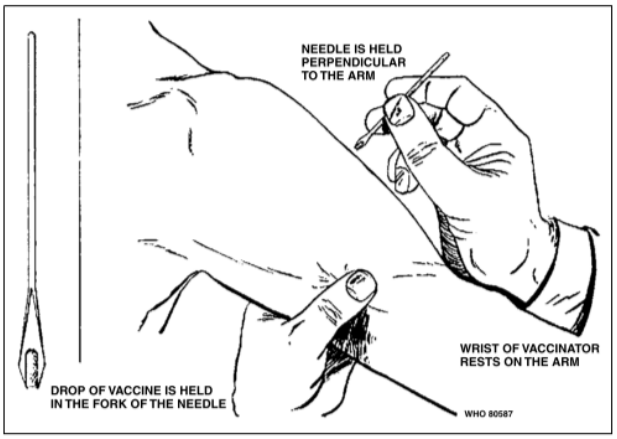

Figure 10. Image showing the technique to inject a smallpox vaccine using a bipronged needle. (Riedel, 2005).

10. Alternatives to Vaccination

Many medications have demonstrated promise as antiviral treatments for Orthopoxvirus species; Table summarises the route of administration, side effects, and the license of these medicines. Some of these medications are still under investigational status. Cidofovir and Brimcidofovir act by inhibiting viral DNA Polymerase, while ST-246 prevents the intracellular virus from escaping the cell.

Drug	Mechanism Of Action	Trade Name	Route of administration	Side-Effects	Stage of Development
Cidofovir	Inhibits viral DNA polymerase	Vistide	Intra-venous	Causes renal damage Prevention of side effects: iv hydration	Already to treat

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				and concurrent administration of Probenecid	1. AIDS patient with CMV retinitis 2. Molluscum Contagiosum infections
CMX-001 (Brincidofovir)	Prodrug of Cidofovir inhibits DNA Polymerase 25 times more efficacy than cidofovir(Alakunle et al., 2020)	Tembexa	Oral	Does not have renal side-effects of Cidofovir Can cause Nausea, Vomiting, and Abdominal Pain (C. for D. E. and Research, 2021)	In developmental stages against Ebola virus, CM virus Used to treat Small Pox(C. for D. E. and Research, 2021)
ST-246 (Tecovirimat)	Inhibits release of intracellular virus	Tpoxx	Oral Less absorbed in fasted individuals (Grosenbach et al., 2011)	CNS toxicity in dogs (Grosenbach et al., 2011)	**Health Canada** approved oral Tecovirimat for the treatment of smallpox in adults and children weighing a minimum of 13 kilograms in December 2021. ("Siga Technologies Inc (SIGA-Q) Quote - Press Release," n.d.) The **US Strategic National Stockpile** contains two million doses of tecovirimat. all pox infections In January 2022, the **Committee for Medicinal Products for Human Use**

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					(CHMP) of the European Medicines Agency (EMA) recommended approving Tecovirimat SIGA for the treatment of orthopoxvirus disease (smallpox, monkeypox, cowpox, and vaccinia complications) in adults and children weighing at least 13kg.(EMA, n.d.)
Other drugs showing promising results					
North-methanocarbathymidine(*Drug Development against Smallpox: Present and Future - PubMed*, n.d.)	Releases active metabolite due to viral thymidine kinase	N-MCT	Used intraperitoneally during animal trial	Has an **advantage** Active against Tecovirimat/Brimcidifovir resistant virus strains	Under investigations in the US
NIOCH-14 (*Drug Development against Smallpox: Present and Future - PubMed*, n.d.)	Prodrug of tecovirimat Easier to produce than Tecovirimat		Oral		Potential new drug as per WHO
KAY-2-41(*Drug Development against Smallpox: Present and Future - PubMed*, n.d.)	Better efficacy than Cidofovir but less than Brimcidofovir or Tecovirimat		Used intraperitoneally during animal trial		Under investigations
Ribavarin and Tiazofurin	IMP dehydrogenase inhibitor Ribavarin might be useful in combination with other drugs like	Rebetol(Ribavarin) Tiazofurine	Ribavarin: Oral inhalation in children Oral in adults	Side effect Ribavarin: Teratogenic, Flu-like syndrome, depression suicidal tendency (when used with	Ribavarin: already used for Hepatitis C, Was previously used for Respiratory

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	Cidofovir(*Potential Antiviral Therapeutics for Smallpox, Monkeypox and Other Orthopoxvirus Infections - ScienceDirect*, n.d.)	interferon for Hepatitis C) Tiazofurin: pleuro-pericarditis, Flu-like syndrome	Syncytial Virus infection in children
C-ca3-Ado and C3-Npc(Alakunle et al., 2020)	SAH(S-adenosylhomocysteine) hydrolase enzyme inhibitor		Not tested in humans due to potential toxicity(*Potential Antiviral Therapeutics for Smallpox, Monkeypox, and Other Orthopoxvirus Infections - ScienceDirect*, n.d.)

11. Prevention

CDC recommends a lot of measures to prevent the spread of the Monkeypox Virus. Some of the strategies for controlling infections with the monkeypox virus:

1. Segregate infected individuals from those who may be susceptible to infection.
2. Scrub your hands with soap and water or use a sanitizer containing alcohol after touching diseased animals or humans.
3. Try not to interact with animals that may be infected (including sick animals or dead animals in areas where monkeypox occurs).
4. Staying away from objects in touch with sick animals or people, like bedding or clothes. (Conventional washing machines, warm water, and detergent can eliminate the MonkeyPox virus.)
5. Utilize the proper personal protective equipment (PPE) when providing care to patients, including a gown, gloves, respirator, and eye protection.
6. Targeted vaccination of high-risk groups like health care workers who treat monkeypox patients and people who spend a lot of time around animal reservoir species in areas where the disease is common could be considered.(Rimoin & Graham, 2011)

The routine measures of surveillance and locating cases in an endemic area are encountered a lot of challenges. Poor technology, lack of finances, sample gathering issues, and medical problems in detecting monkeypox illness are some of the difficulties experienced by monitoring systems.

Post-exposure prophylaxis for monkeypox (PEP) (*Recommendations for the Use of Pre and Post Exposure Vaccination during a Monkeypox Incident*, n.d.)

According to the US Advisory Committee on Immunization Practices (ACIP), individuals exposed to Monkeypoxvirus should be examined by a medical professional. Medical interventions like post-exposure immunization should be decided in agreement with public health officials on case to case basis. The CDC recommends that the smallpox vaccine be administered within four days of contact to effectively avert the initiation of the disease, although it can be administered up to 14 days later. The CDC further recommends, based on ACAM2000, that vaccination administered within 14 days of contact may alleviate the disease manifestations but may not avoid the onset of disease.

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Type of contact that determines post-exposure prophylaxis

Any close contact with a clinical Monkeypox patient, their bodily fluids, or possibly contagious objects (such as clothes or beds) without the use of personal protective equipment

Another form of high-risk exposure involves inhaling dust or droplets while cleaning contaminated spaces; Sharps injuries caused by contaminated equipment or contaminated gloves,

The room inmates or those who have spent at least one night in the same apartment as the Monkeypox case during the infectious phase.

Non-high risk contacts include the Next passenger on an airplane, No direct contact within one meter of the infected case without personal protection equipment kit, and contact with bodily fluids through(Riedel, 2005)h intact skin.

12. Can Monkeypox cause death?

In the majority of cases, the manifestations of monkeypox resolve on their own after a few weeks. However, in certain situations, they might cause medical issues and even fatality.

13. Susceptibility

Monkeypox may cause more severe symptoms and death in neonates, children, and individuals with underlying immunity deficiencies.

13. Could it be biological warfare?

The Centers for Disease Control and Prevention (CDC) in Atlanta has made a list of microbes and ailments that could be utilized as bioweapons. These illnesses are put into three groups based on how they can be used and how they affect public health. Smallpox is in group A, which means it, is easily spread from individual to individual and has a high death rate. Monkeypox is not mentioned in the list of an organism capable of being used for bioterrorism. But some reports suggest that one country had contemplated deploying monkeypox as a biological attack.(*Russia "Planned to Use Monkeypox as a Bioweapon", Report Warned | Metro News*, n.d.)(*Russia Was Planning to Use Monkeypox as Bioweapon, Claims Ex-Soviet Scientist - World News*, n.d.)

Due to human-to-human transmission of monkeypox documented in the previous five years, it can be used as a bioweapon. (Riedel, 2005) However, in the current situation, the possibility of a bio-attack seems remote. Traveling from endemic nations and contact with contaminated animals aren't thought to be causes of any of the recorded incidents so far (as of May 2022) which might raise a suspicion of Monkeypox being used as a bioweapon.

14. Recommendations to prevent such outbreaks in the future(Rimoin & Graham, 2011).

The questions of whether or not to conduct field trials for vaccines and implement vaccination to control MPX in endemic regions will need to be answered periodically by the appropriate stakeholders for each affected region. The authors suggest that the current actions should be taken to inform these decisions:

1. Monitor endemic places for tracking disease occurrence, intensity and rate of person-to-person transmission, and changes in distribution pattern.

2. Identify the alterations linked with transmissibility or virulence of the Monkeypox virus in the genomic pattern.

3. Establish definite intermediate hosts as well as animal reservoirs. A human immunization program may not help prevent the transmission of MPX. The mobility of animals may serve as a proxy for spreading the disease's geographic range.

4. Develop successful, economical treatment options.

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5. There should be allocation of effective vaccines to the endemic regions by the developed countries after conducting a successful trial in the endemic area.

15. Future trends

Emerging new orthopoxviruses that cause diseases in humans, such as the Georgia Caucasus-identified Akhmeta virus and the 2015 discovery of the Alaska-pox virus add urgency to the need for expanded funds for monkeypox research.(Gigante et al., 2019)

16. Conclusion

MonkeyPox is no longer endemic to the African continent. Outbreaks in the past and in May 2022 have demonstrated that it is now a global problem. Newer economic treatment and preventive measures should be sought to tackle it more effectively. Measures should be adopted for frequent surveillance among animal reservoirs to prevent such outbreaks in the future. An increase in outbreaks can lead to a deadlier virus through genetic recombination. Therefore, we need more stringent measures and outlines to prevent MonkeyPox from becoming another COVID or SmallPox.

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