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Human monkeypox: epidemiology, transmission, pathogenesis, immunology, diagnosis and therapeutics

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Abstract
"Zoonoses" describe diseases that may be acquired by humans from animals. Due to the constant contact between humans and other animals, many infectious diseases are disseminated. This may happen via direct contact, such as bites or scratches, or by indirect contact, such as when eating bush meat or using contaminated animal parts. Monkeypox disease is one such zoonotic infection which is now emerging as a disease of global concern, and the World Health Organization has already labelled it a public health emergency. The virus is related to other orthopox viruses and may be further classified into two genetically separate clades, the West African and the Central African. The latter is far more pathogenic than the former. Utilizing virotransducer and virostealth proteins, the virus is able to control the host's T-cell-mediated responses and impede the release of cytokines and chemokines.Monkeypox may be treated with tecovirimat, cidofovir, or brincidofovir, and prevention with the vaccination JYNNEOS is recommended. The disease's fast global expansion warrants concern despite the fact that it is less fatal than that caused by the variola virus. Before the sickness reaches catastrophic proportions, we must draw on our prior experiences and act prudently. This article serves as an introduction to the monkeypox virus and its associated pathology, treatments, diagnostics, and preventative measures.

Keywords Diagnosis · Immunomodulation · Pathology · Monkeypox · Treatment · Vaccines

Introduction

Until recently, monkeypox was only known to exist in Africa, but it has now been confirmed in more than ninety non-African countries, impacting over seventy-nine thousand individuals in just a few months. It is highly concerning that the virus has started to arise in different populations throughout the world, in places where it is unusual for it to do so. The United States of America is the worst-hit country with 28,999 reported cases and 11 deaths till date, that is, 16 November 2022 [1]. Next in the list is Brazil with 9637 reported cases. Rising occurrences of monkeypox have undoubtedly raised concerns, particularly at a time when the entire world is still healing from the pandemic shock of COVID-19. The World Health Organization (WHO) issued a global public health emergency of concern proclamation on 23 July 2022 to the ongoing monkeypox pandemic. Considering the aforementioned information, the purpose of this review paper is to familiarize the readers to the monkeypox illness, its epidemiology, pathology, diagnosis, and current therapeutic options.

Methodology

In order to write this review article, more than 200 research papers were obtained from the different search engines like Google, Science Direct, NCBI Library; websites of important organizations like WHO, CDC, and news reports, etc., using keywords like epidemiology of monkeypox, diagnosis of monkeypox, therapeutics of monkeypox disease, vaccines for prophylaxis of monkeypox, differences between monkeypox and other orthopox viruses, differences between monkeypox and smallpox, differences between monkeypox and chickenpox, differences between monkeypox and

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COVID-19, etc. After reading all the articles obtained from the above-mentioned sources, around 100 articles were short-listed and the information gathered from them is summarized in the form of the present review article. The map showing the geographical distribution of the monkeypox disease has been created using the data wrapper software (Fig. 1). Rest all figures have been prepared using the latest version of the Microsoft powerpoint software.

The monkeypox virus

The monkeypox virus (MPXV) is a member of the Poxviridae family, specifically the Chordopoxvirinae subfamily, and it is a double-stranded DNA virus that is enveloped and is brick shaped. The virus was first discovered in primates in 1958 [2] in a laboratory in Denmark. The term "Monkeypox virus" comes from the fact that the virus was first discovered in monkeys. However, the name is misleading since monkeys are the incidental and not the natural hosts of the virus.

Different clades of the monkeypox virus

There are two clades of the virus which differ in their pathogenicity, modulation of host immune responses and rate of transmission. The monkeypox virus clade found in the Congo Basin is more fatal than the one found in West Africa. Central Africa's case fatality rate was 10.6%, far higher than the 3.6% rate seen in the West African clade. As a whole, monkeypox is becoming more significant around the globe [3]. The Basin clade is more prone to spread and has historically caused more severe cases. The current monkeypox epidemic seems to have originated in the West Africa clade. Cameroon, which separates the two groups geographically, is the only country where both viral clades have been found [4].

Comparison of the genomes of monkeypox virus and the smallpox virus

Genetic analysis shows that the monkeypox virus is distinct from other members of the Poxviridae family, such as variola, vaccinia, ectromelia, camelpox, and cowpox. In 1958, researchers at Copenhagen's Statens Serum Institute identified it as the agent responsible for a smallpox-like illness in cynomolgus monkeys [2]. For the first time, anything like this was uncovered. It was recognized as a novel species of orthopox virus after culture on embryonated eggs revealed pocks that resembled those of the variola virus but had other biological properties different from those of the variola virus. In 2001, a genetic comparison of MPXV and variola virus was published [5]. The essential enzymes and structural proteins are encoded by the core region of the MPXV genome, which shares 96.3% of its sequence with the variola virus. But the MPXV terminal regions that code for virulence and host range features vary greatly across strains. When comparing the MPXV genome to other orthopoxvirus genomes, it has been found that the central genomic regions are conserved and the terminal regions vary. For details, readers may refer to the work done by Shchelkunov and coworkers [5]. As with every other orthopox virus, it possesses a distinct surface epitope composition, different polypeptides, specific DNA cleavage sites, and various modifications in the double-stranded DNA genome's long terminal repeats. The detailed genomic analysis shows that MPXV evolved from an orthopox viral progenitor apart from variola virus. The variola virus cannot easily be generated from MPXV since MPXV is not the variola virus's direct ancestor (or vice versa). This and other data allayed worries that MPXV

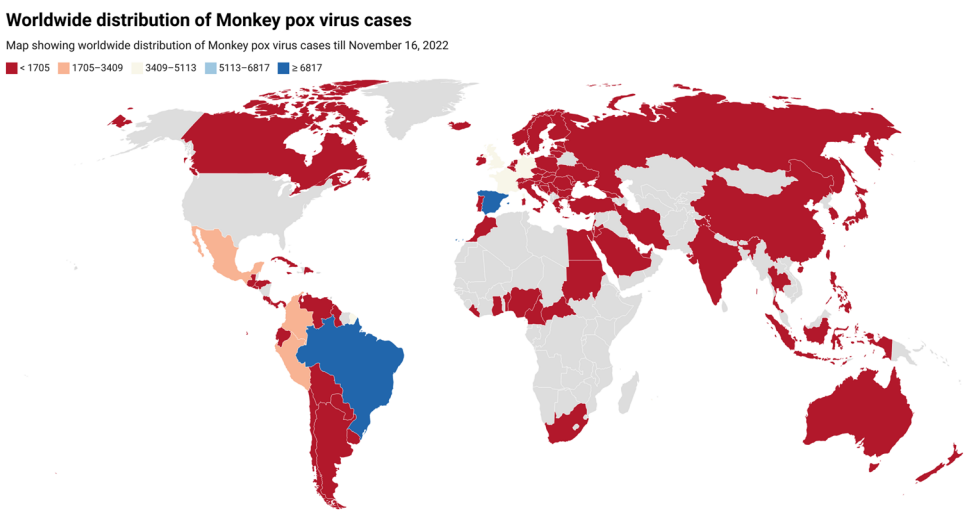

Fig. 1 Map showing worldwide distribution of MPXV cases till 16 Nov 2022. The map has been created by using data wrapper software

would transform into variola virus and reaffirmed faith in the long-term effectiveness of the smallpox immunization programme.

Similarities and differences between the monkeypox virus and the chickenpox virus

Chickenpox is caused by Herpes virus which has no correlation with the orthopox viruses but the clinical presentation of monkeypox and chickenpox appear similar which is why sometimes the disease may be misdiagnosed. However, as compared to the monkeypox, chickenpox has a brief, moderate prodrome, a mild clinical course, seldom causes lymphadenopathy, and often causes pleomorphic skin lesions to grow in a centripetal pattern, with a very low death rate [6, 7].

Epidemiology of the monkeypox disease

Between 1970 and 1979, epidemiological investigations were done in the rain forest regions of sub-Saharan Africa, where they discovered 47 cases of human monkeypox. Of these 47 occurrences, the Democratic Republic of the Congo (DRC) was responsible for 38, followed by Cameroon, the Central African Republic, Gabon, Cote d'Ivoire, Liberia, Nigeria, and Sierra Leone (together accounting for 11 incidences) [8]. Each event in the DRC had similarities that pointed to animal interaction as the likely cause; each also occurred near tropical rain forests. Of the 47 infections, only 7 were fatal. Transmission from a vulnerable person to another is the most likely explanation for illness in four of the instances. The probability of secondary transmission is 7.5% among close relatives and 3.3% among all susceptible contacts. The majority of documented instances since 1980 have come from the Democratic Republic of the Congo. For the purpose of gauging the potential of a monkeypox epidemic in central Africa, the World Health Organization (WHO) conducted surveillance in the Democratic Republic of the Congo (DRC) between 1981 and 1986 [9].

Only 13 occurrences from 1986 to 1992 were documented in the literature, and no cases from 1993 to 1995 were reported. But in Kasai-Oriental province, DRC, during 1996 and 1997, more than 500 probable cases of monkeypox were recorded [10, 11]. In spite of the fact that only a small percentage of these cases were confirmed by laboratories, the high prevalence of secondary cases (78 per cent) and the low mortality rate (one per cent to five per cent) suggest that the vast majority were in fact instances of varicella. Until 2001, when 31 individuals with monkeypox in 7 distinct illness clusters were documented in the DRC's Equateur region, there had been no fresh reports of suspected monkeypox cases.

In total, 10 African nations and 4 other nations had then subsequently reported cases of human monkeypox. Examples include Nigeria, where the illness returned after a 40-year absence in the past decade, and the United States, where an epidemic happened in 2003. The number of cases grew at least ten times, and from young children (4 years old) in the 1970s to young adults (21 years old) in 2010–2019 [12].

The 2022 monkeypox outbreak

The current outbreak is an illustration of how quickly the virus may be transmitted by intimate contact with infected wounds. Since the beginning of May 2022, cases of the sickness have also been reported in a number of countries in which it was not endemic. Till date (16 Nov 2022) more than 79,655 cases have been recorded worldwide and less than two per cent cases are from Africa, rest all are from the non-African countries where the disease is not prevalent otherwise [1]. This is a cause of concern. By now, the disease has spread in six continents leaving just Antarctica where no case has been reported so far. These include 12 African and 93 non-African countries. The majority of reported cases had no connection to travel to an endemic nation [12]. The worldwide distribution of monkeypox cases is summarized in Table 1 and Fig. 1.

Transmission of the monkeypox virus

Squirrels (particularly *Funisciurus anerythrus*) living in agricultural regions have been identified in several epidemiological studies from the Democratic Republic of the Congo as the main carriers of viral transmission among local populations [13]. *Funisciurus* spp. squirrels showed a higher rate of MPXV seropositivity in an earlier research compared to other animals tested [14]. Gambian rats and many other non-primate and primate mammals have also been found to be seropositive [15, 16]. In conclusion, it has been determined that several animal species are vulnerable to the monkeypox virus and may serve as reservoir for the same.

Zaire was the first place where the monkeypox virus, a zoonotic orthopox DNA virus, was found in humans, back in 1970. After being discovered as a zoonotic illness in the 1970s, the MPXV virus began a pattern of frequent transmission from its reservoir hosts to humans. The transmission rate among humans was low. Most cases of this zoonosis have been documented in the Democratic Republic of the Congo among very young rural boys who

Table 1 Worldwide distribution of MPXV cases till 16 Nov 2022

S. No.	Region	Country	No. of confirmed cases	First case reported	References
1	Asia	Georgia	2	July 2022	[1, 38]
		India	17*	July 2022	[1, 39, 40]
		Indonesia	1	August 2022	[1, 41]
		Iran	1	August 2022	[1, 42]
		Israel	262	May 2022	[1, 43]
		United Arab Emirates	16	May 2022	[1, 44]
		Thailand	12	July 2022	[1, 45]
		Philippines	4	July 2022	[1, 46]
		Japan	7	July 2022	[1, 47]
		Qatar	5	July 2022	[1, 48, 49]
		Saudi Arabia	8	July 2022	[1, 50]
		South Korea	2	June 2022	[1, 51]
		Singapore	19	July 2022	[1, 52]
		Lebanon	18	June 2022	[1, 53]
		China	1	September 2022	[1, 54]
		Bahrain	1	September 2022	[1, 55]
		Jordan	1	September 2022	[1, 56]
		Taiwan	4	July 2022	[1, 57]
2	Europe	Turkey	12	June 2022	[1, 58]
		Andorra	4	July 2022	[1, 59]
		Germany	3671	May 2022	[1, 60]
		Croatia	29	June 2022	[1, 61]
		Lithuania	5	August 2022	[1, 62]
		Luxembourg	56	June 2022	[1, 63]
		Malta	33	May 2022	[1, 64]
		Cyprus	5	August 2022	[1, 65]
		Ireland	210	May 2022	[1, 66]
		Moldova	2	August 2022	[1, 67]
		Monaco	3	July 2022	[1, 68]
		Latvia	6	June 2022	[1, 69]
		Italy	915	May 2022	[1, 70]
		Czechia	70*	May 2022	[1, 71]
		Montenegro	2	July 2022	[1, 72]
		Finland	42	May 2022	[1, 73]
		France	4102	May 2022	[1, 74]
		Greece	85	June 2022	[1, 75]
		Norway	93	May 2022	[1, 76]
		Netherlands	1240	May 2022	[1, 77]
		Hungary	80	May 2022	[1, 78]
		Iceland	16	June 2022	[1, 79]
		Austria	325	May 2022	[1, 80]
		Poland	212	June 2022	[1, 81]
		Portugal	948	May 2022	[1, 82]
		Romania	45	June 2022	[1, 83]
		Russia	2	July 2022	[1, 84]
		Spain	7377*	May 2022	[1, 85]
		Sweden	212	May 2022	[1, 86]
		Switzerland	546	May 2022	[1, 87]
		Estonia	11	June 2022	[1, 88]
		Belgium	785*	May 2022	[1, 89]
		Bosnia and Herzegovina	9	July 2022	[1, 90]

Table 1 (continued)

S. No.	Region	Country	No. of confirmed cases	First case reported	References
		Bulgaria	6	June 2022	[1, 91]
		Serbia	40	June 2022	[1, 92]
		Slovakia	14	July 2022	[1, 93]
		Slovenia	47	May 2022	[1, 94]
		Denmark	191	May 2022	[1, 95]
		Gibraltar	6	June 2022	[1, 96]
		Ukraine	5	September 2022	[1, 97]
		United Kingdom	3703	May 2022	[1, 98]
3	Africa	South Africa	5	June 2022	[1, 99]
		Central African Republic	12	March 2022	[1, 100]
		Liberia	3	2018	[1, 101]
		Cameroon	16*	December 2019	[1, 102]
		Benin	3	June 2022	[1, 103]
		Ghana	107*	June, 2022	[1, 104]
		Morocco	3	June 2022	[1, 105]
		Nigeria	624*	1970	[1, 106]
		Sudan	18*	July 2022	[1, 107]
		Egypt	1	September 2022	[1, 108]
		Democratic Republic of the Congo	206	1970	[1, 11]
		Mozambique	1*	October 2022	[1, 109]
4	North America	Canada	1444	July 2022	[1, 110]
		Costa Rica	16	July 2022	[1, 111]
		Martinique	1	July 2022	[1, 112]
		Cuba	8*	August 2022	[1, 113]
		Mexico	3007*	May 2022	[1, 114]
		Jamaica	16	August 2022	[1, 115]
		Greenland	2	August 2022	[1, 116]
		Panama	21	July 2022	[1, 117]
		Guadeloupe	1	July 2022	[1, 118]
		Guatemala	111	August 2022	[1, 119]
		Honduras	10	August 2022	[1, 120]
		Bermuda	1	July 2022	[1, 121]
		Dominican Republic	52	July 2022	[1, 122]
		Bahamas	2	June 2022	[1, 123]
		Barbados	1	July 2022	[1, 124]
		Saint Martin	1	August 2022	[1, 125]
		United States	28,999*	July 2022	[1, 126]
		El Salvador	17	September 2022	[1, 127]
5	South America	Argentina	808	May 2022	[1, 128]
		Aruba	3	July 2022	[1, 129]
		Chile	1243	June 2022	[1, 130]
		Colombia	3630	June 2022	[1, 131]
		Paraguay	7	August 2022	[1, 132]
		Peru	3299	June 2022	[1, 133]
		Guyana	2	August 2022	[1, 134]
		Bolivia	248	August 2022	[1, 135]
		Ecuador	311*	July 2022	[1, 136]
		Brazil	9637*	June 2022	[1, 137]
		CuraÃ§ao	3	August 2022	[1, 138]
		Uruguay	14	July 2022	[1, 139]
		Venezuela	10	June 2022	[1, 140]

Table 1 (continued)

S. No.	Region	Country	No. of confirmed cases	First case reported	References
6	Oceania	New Caledonia	1	July 2022	[1, 141]
		New Zealand	33	July 2022	[1, 142]
		Australia	141	May 2022	[1, 143]
7	Antarctica	No confirmed cases yet			

*Countries where death cases have been reported

participate in small-game hunting [17]. The virus may be transmitted from animals to humans by eating of bush meat, coming in contact with the body parts or body fluids of infected animals, respiratory droplets, etc.

However, the 2017 Nigerian epidemic was concentrated amongst adult males between the ages of 25 and 40 who were residents of urban or periurban areas and had no discernible contact with animal reservoirs. This might be because of sexual transmission among males. Numerous studies indicate that keeping infected people isolated reduces the spread of disease. A person can contract monkeypox virus through a variety of sexual or non-sexual contact-related methods. The latter include coming into direct contact with wounds of an infected person; coming into contact with objects and surfaces that have been contaminated by an infected person; and coming into contact with respiratory droplets or oral fluids from an infected person. Monkeypox virus may be able to penetrate the placenta, although the consequences of infection during pregnancy are yet unclear. The transmission of virus among men is corroborated by scientific testing that revealed MPXV qPCR positivity in MSM seminal fluid from Germany and other nations [18]. The different transmission routes by which the monkeypox virus can spread from animals to humans or humans to humans are summarized in Fig. 2.

Pathology and clinical features

Like other poxviruses, monkeypox has a pathogenesis that is distinguished by pronounced intracytoplasmic eosinophilic inclusions in epithelial cells [19]. The epidermis may also exhibit hyperplasia, keratinocyte necrosis, and ballooning degeneration. Ulceration and neutrophils, eosinophils, and multinucleated giant cells follow the lymphocytic inflammation seen in the dermis. As well, vascular inflammation (vasculitis) is evident.

Monkeypox in humans starts with a brief (2–3 day) febrile prodrome and proceeds to a broad rash with monomorphic, well-defined, deep-seated, and often umbilicated pustules [20]. Most skin lesions tend to show up on the face and the palms of hands and bottoms of feet. During the pustular phase, the visual features of monkeypox rash lesions clearly suggest an infection caused by the orthopox virus.

The incidence and severity of certain clinical characteristics are independent of sex, age, or vaccination status. Pre-eruptive and eruptive are the two stages of the illness's clinical course, accordingly [21].

Pre-eruptive stage. There aren't many chances to study patients in the pre-eruptive stage since they often seek guidance or medical assistance after several days of sickness, when lymph nodes have swelled and skin eruptions have begun. It is feasible to pinpoint the onset of the fever and rash by inquiring from the patients. It has been observed that the patient temperature ranges from 38.5 to 40.5 ℃ and reaches its peak during the second day of the illness. The patients generally experience extreme weakness, fatigue and back ache. Fever is the second most common symptom, with a headache (sometimes frontal, but often broad) being the most common symptom overall. Several people have lymph node enlargement before they develop a rash.

Eruptive stage. Except for the face, the skin rash manifests itself first on other regions of the body, such as the forearms. Lesions went through the same stages as smallpox, starting as macules and progressing through papules, vesicles, pustules, and finally umbilication, drying, and desquamation. In specific circumstances, there might have been a few or several thousand skin lesions. Vaccinated individuals had considerably fewer lesions than unvaccinated patients. In most cases, higher fever, more severe symptoms, and longer illness corresponded to higher lesion densities.

Lymph node enlargement is the only clinical indicator that may differentiate human monkeypox from smallpox and chickenpox.

The way monkeypox is currently presenting itself is also novel. Most instances of the present worldwide pandemic, including those in Nigeria, manifest as an ulcerating genital rash rather than the more widespread lesions that were seen in previous epidemics [22]. The generalized pustular rash, which is frequently mild, comes before the genital rash in clinical presentations that occur outside of Africa [23, 24]. According to this depiction, the genital area is an initial infection site that causes a discrete rash before occasionally progressing to a subsequent, disseminated illness.

Monkeypox is usually a short-lived infection, with symptoms often disappearing within two to four weeks. Severe cases are associated with the extent of virus exposure, the

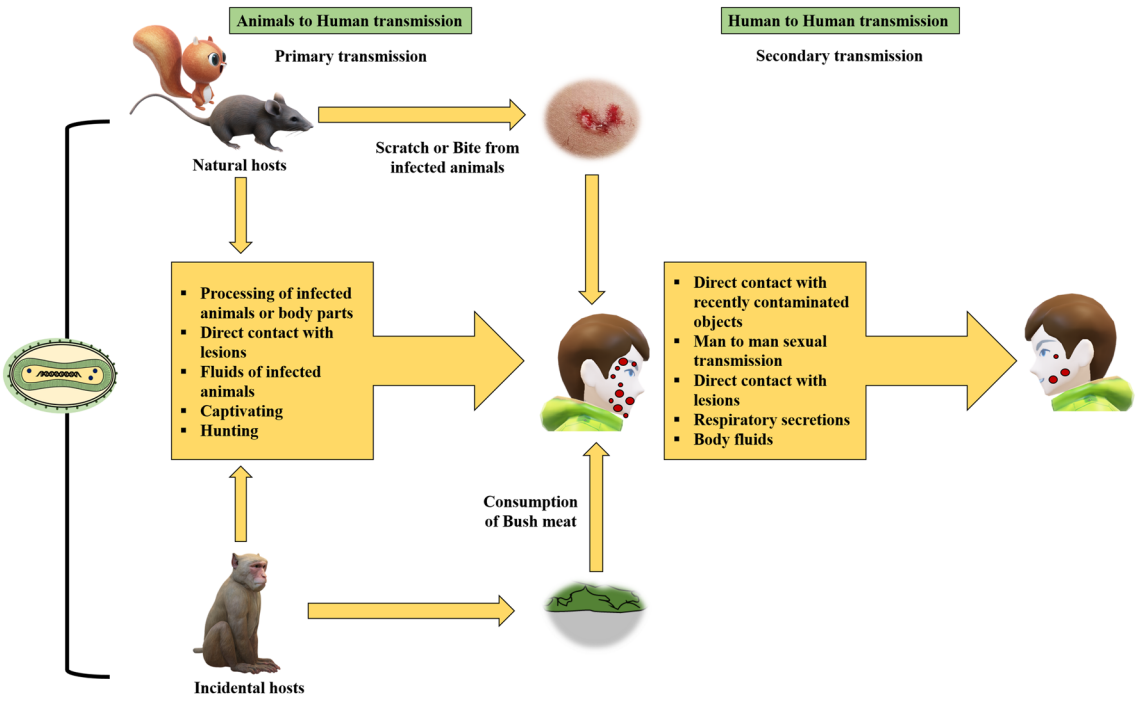

Fig. 2 Different routes of animal–human and human–human transmission of MPXV

patient's state, and the kind of difficulties and are more common in children. Having immunological deficiencies may make matters worse. Although smallpox immunization proved protective in the past, but people who were vaccinated more than 40 years ago may now be more vulnerable to monkeypox. Monkeypox complications can include secondary infections, bronchopneumonia, sepsis, encephalitis, and corneal infections with subsequent vision loss [25].

In the general population, the case fatality ratio of monkeypox has traditionally varied from 0 to 11%; it has been greater in young children [4].

Diagnosis

Polymerase chain reaction, often known as PCR, is now generally accepted as the gold standard for laboratory testing due to its reliability and sensitivity. Monkeypox is no exception to this rule and is best diagnosed by real-time PCR conducted on fluid isolated come from skin lesions. This fluid can also be used for viral culture, another reliable diagnostic test but this consumes longer time as compared to RT-PCR. Biopsy samples from lesions can also be used for viral detection by electron microscopy or immunohistochemistry. The serum IgG and IGM levels can also be used for detecting present or past infection [26]. However, the serological investigations do not offer any promise of monkeypox-specific infection because orthopox viruses are cross-reactive. Also, people immunized with smallpox vaccines may give false positive results [4].

Therapeutics

In the absence of any treatment option available for the monkeypox disease, FDA approved. Oral tecovirimat is currently being used as an emergency drug for the severely infected patients. Tecovirimat (TPOXX) is a drug approved by FDA for the treatment of smallpox but since the symptoms of both the diseases overlap, the drug is being used for treating MPXV-infected patients also. However, the FDA approval for the same is still pending and the clinical trials for testing the drug efficacy are going on. It is noteworthy that tecovirimat is recommended for severe cases only. As per CDC, if the drug is given to milder cases, the monkeypox virus is likely to develop resistance against it [27]. Brincidofovir and cidofovir are other drugs used for monkeypox treatment. Both the drugs stop the viral replication by inhibiting DNA polymerase enzyme. Tecovirimat on the other hand interferes with the viral envelope formation [28]. The former is lesser nephrotoxic as compared to the latter [29]. Another antiviral drug NIOCH-14 which is known to stop viral

replication by serving as nucleoside is in clinical trials and approval is anticipated soon [30]. In addition to the treatment, the patients need to be fed and hydrated to keep their nutritional health in good shape [25]. Figure 3 summarizes the mode of action of different drugs used in the treatment of the monkeypox disease.

Immunomodulation by MPXV

Human cells obtained from monkeypox patients are resistant to T-cell receptor-mediated T-cell activation, meaning they cannot produce inflammatory cytokines. These findings point to the possibility that monkeypox generates a modulator that dampens T-cell responses in the host. It is now known that MPXV manipulates host immune responses via virotransducer and virostealth proteins. The former changes the cell's ability to respond to infection, while the latter decreases the virus's immunological recognition molecules, allowing it to elude the immune system. Moreover, unlike West African strains, Central African monkeypox strains preferentially downregulate host responses, including apoptosis in the host [31]. Extracellular proteins, known as viromimic proteins, function as viroreceptors to imitate cytokine and chemokine receptors, preventing glycoprotein receptors from binding, and as virokines to imitate cytokines and chemokines, disrupting host immune activation pathways and inhibiting viral reproduction [32]. Weaver and Issacs (2008) enumerated many genes encoding distinct proteins of monkeypox virus important for regulation of host immune responses, such as MOPICE in the Congo clade of monkeypox virus, which suppresses the host complement enzymes. The readers might consult the works of Weaver and Issacs (2008) for information on the remaining genes of orthopox viruses responsible for modulating the host immune responses [33].

Vaccination

The smallpox vaccination has been found in several studies to be around 85% effective at preventing monkeypox [4]. Dryvax, the smallpox vaccine of the first generation, has been rendered unusable because of the adverse side effects it may cause [34]. Similar is the case with ACAM2000, the second-generation vaccine. Recently, a third-generation vaccine developed from the Ankara strain of the modified attenuated vaccinia virus was approved for use in the prevention of monkeypox. The vaccine is marketed under the name JYNNEOOS [35, 36]. Moreover, clinical studies for the VAC6 vaccine, a vaccination of the fourth generation, are now underway [37]. All these vaccines are made from vaccinia virus since it provides cross-protection to the orthopox viruses. However, the vaccination is recommended only for immunocompromised people or for the frontline health workers who are at risk of high exposure. Because vaccinations are in short supply, it is not advised for healthy people to be vaccinated.

Future perspective

These international outbreaks of monkeypox will probably grow more frequent over time since population immunity won't likely increase significantly in the foreseeable future. For monkeypox, a vaccination (JYNNEOS) is now available, but there is a need to look for more promising vaccine candidates. Similarly, although the treatment options are available but drug resistance might be a problem in the near future. Therefore, novel therapeutic strategies are required such as nanoparticle-based targeted drug delivery, etc. Also, the viral zoonoses are becoming a serious health issue and there is an urgent need to change our behaviour towards animals. Wild animals should remain undisturbed in their habitat, and the health of domesticated animals should be regularly monitored for any kind of pathogenesis. Also, the animals should be bred in clean and hygienic conditions to eliminate the pests like rats which can act as reservoir hosts.

Conclusion

The international outbreak has again highlighted global health inequities. In contrast to COVID-19, monkeypox did not spring upon suddenly. An unusual virus that travelled from forest species in the Democratic Republic of the Congo to villagers who hunted the animals was first discovered decades earlier.

Monkeypox is closely related to smallpox. They both belong to the same family of viruses. A smallpox infection or smallpox vaccination provides excellent protection against both smallpox and monkeypox. In other words, protection against smallpox also cross-protects against monkeypox. Since, the major population was either vaccinated for smallpox or survived an infection back in 1970s, they had some sort of immunity towards monkeypox too. However, the globe ceased immunizing individuals against smallpox in the late 1970s. Thankfully, the spread of the disease ceased among people. Therefore, immunity to smallpox and monkeypox has drastically decreased during the past forty years.

When infection does affect humans, it can be clinically difficult to identify from the chickenpox and smallpox. Severe lymphadenopathy is the most useful diagnostic clinical sign of human monkeypox; nonetheless, laboratory analysis is required for a firm diagnosis. We saw that the

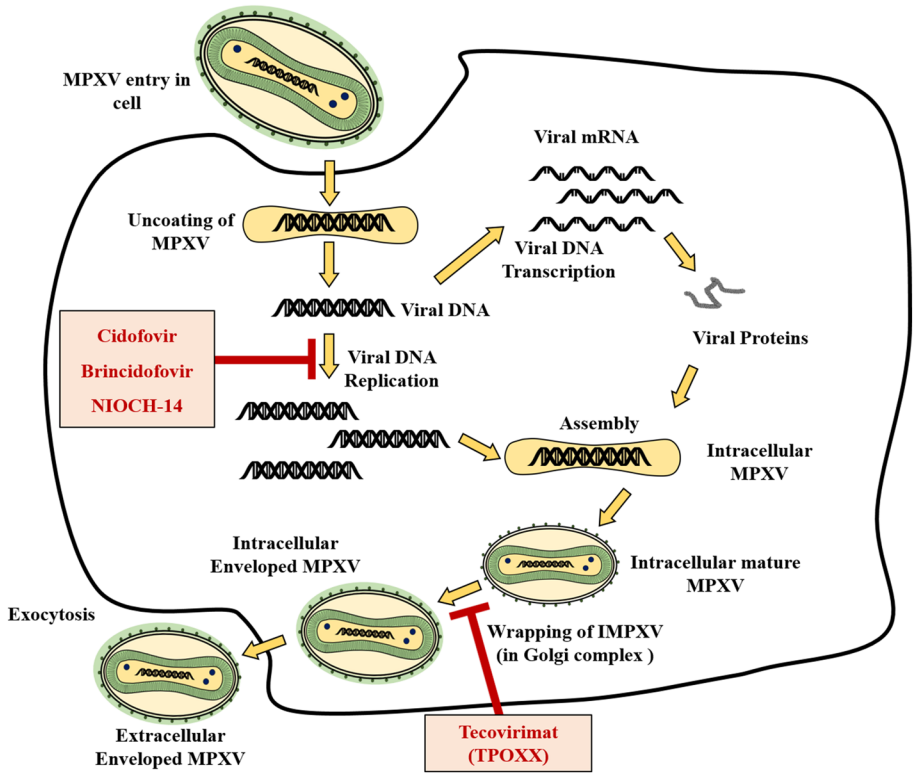

Fig. 3 Treatment options for the monkeypox disease, and their underlying mechanisms of action. Brincidofovir and cidofovir stop the viral replication by inhibiting DNA polymerase enzyme. Tecovirimat on the other hand interferes with the viral envelope formation. Another antiviral drug NIOCH-14 is known to stop viral replication by serving as nucleoside

monkeypox virus has two clades: West African and Congo Basin. The latter causes a more serious condition. Though it was first observed in monkeys and since rodents, not monkeys, appear to be the disease's primary natural reservoir in terms of both absolute numbers and percentages, the name "monkeypox" is rather imprecise.

The current 2022 outbreak has shown us that the stakes are really high now. A weak link anywhere is a threat everywhere. Since population immunity won't likely increase significantly in the foreseeable future, immunising people who have come into contact with sick individuals by vaccinating them as well as accelerating our trials on currently underway therapeutics and not forgetting about making diagnostics broadly accessible must be our main focus right at the moment.

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Data availability Enquiries about data availability should be directed to the authors.

Declarations

Conflict of interest The authors declare no competing interests.

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