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Monkeypox Resurgence: Global Health Trends and Strategic Outlook

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Abstract: *Monkeypox, a zoonotic viral disease caused by the monkeypox virus (MPXV), has re-emerged as a significant global public health concern. This review examines the publication Monkeypox in Focus: Current Trends and Future Outlook, which explores the epidemiology, virology, clinical management, and public health implications of MPXV. The first case in a nonendemic country was confirmed on May 6, 2022, leading to over 53,000 cases by September 1, prompting the WHO to declare a public health emergency of international concern. The review emphasizes biosafety strategies in response to the 2022 outbreak, analyzing MPXV's biological features, transmissibility, and variability.*

Using bibliometric analysis, the study highlights a significant increase in monkeypox research, predominantly from the US, indicating a growing interest in this evolving field. The CDC emerged as a key contributor, producing the highest number of related publications. The Journal of Virology received the most citations, underscoring the importance of ongoing research in addressing knowledge gaps and facilitating effective public health interventions.

Particular attention is given to the unique characteristics of the disease, illustrating the need for rapid public health action tailored to the epidemiological differences in current outbreaks, especially in non-endemic regions. The review also considers future research directions in vaccine development and sociopolitical factors influencing decision-making strategies, drawing lessons from the COVID-19 pandemic response. Overall, this work emphasizes the urgent need for coordinated global efforts to manage and control monkeypox effectively.

Keywords: *Monkeypox, Zoonotic diseases, Public health, Virology, Epidemiology, Vaccines, Global outbreaks., Mpox, Orthopoxvirus, Variola minor, Smallpox, Fever, Swollen lymph nodes, Contact transmission, Respiratory droplets, Vaccination, Isolation, Contact tracing, Quarantine*

I. INTRODUCTION

The global response to the recent rise in monkeypox cases has underscored the importance of understanding zoonotic diseases and their impact on public health. Once limited to certain regions in Central and West Africa, monkeypox has now reached pandemic potential, exacerbated by factors such as increasing human-wildlife interactions, weakened herd immunity to smallpox, and globalization. *Monkeypox in Focus: Current Trends and Future Outlook* addresses these concerns by offering an in-depth look into various aspects of monkeypox, from viral structure to epidemiology and management. This review critically analyzes the text to assess its contribution to current monkeypox literature.Viruses are responsible for many medically necessary emerging and reemerging infections and various human and animal infectious disorders. They pose a far more significant threat to global public health today than a century ago [1].Further, since they can spread swiftly, viruses significantly contribute to the morbidity and mortality of infectious diseases globally [2,3]. Human monkeypox is a zoonotic viral disease caused by the monkeypox virus (MPV), capable of transmission between animals and humans and secondary transmission between humans [4,5]. It is a member of the Orthopoxvirus (OPV) genus of the Poxviridae family [4]. Previously, MPV was first identified as a nonhuman pathogenic primate, that is, until human monkey smallpox was reported in the Democratic Republic of the Congo. Clinical expressions of human smallpox were likesmallpox. For instance, in 2003, the United States (US) experienced an outbreak of human monkey smallpox, the first confirmed disease incidence outside of Africa [6,7]. Since then, the cumulative number of cases of monkeypox has steadily increased, and research on this topic has been increasingly

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conducted. However, there is still no comprehensive report to help researchers gain insight and understand global research trends in MPV.

Table 1. Comparison of the characteristics of the classic form of mpox and the new clinical form

Feature	Classic form (1970s to the present)	Current multicenter outbreak (2022 to the present)
Affected area	Central and West Africa	Countries where mpox is not endemic
Epidemiologic characteristics	Occasional cases and epidemics	Global outbreak under way since May 2022
Dissemination	Mostly intrafamilial and nosocomial	Mostly sexual involving men who have sex with multiple partners
Transmission	Direct contact with an infected animal reservoir, followed by person-to-person transmission	Person-to-person transmission
Clinical presentations	Lesions on the face and extremities, commonly linked with cervical or axillary lymphadenopathy	Perianal lesions, ulcerative lesions, penile and vesicular rash, painful inguinal lymphadenopathy, proctitis, pharyngitis
Clinical evolution	Incubation, prodromal stage, eruption phase with skin lesions	Incubation, prodromal stage (not necessary present), eruption phase with skin lesions, especially on the genitals

Bibliometric analysis is a tool for obtaining information and developmental trends about scientific activity in a specific field to collect quantifiable, reproducible, and objective data. This statistical technique is vital owing to its distinct advantages and wide range of applications in various research fields. This scientific approach has been used in multiple disciplines of study, including health sciences and engineering [8–10], to establish different patterns or trends. In this study, the growth rate of publications and the characteristics of research activities (keywords) were calculated, publication patterns (countries and journals) and research hotspot tendencies (citation). Despite the methodological limitations of bibliometric studies, they remain valuable tools for assessing the scientific importance of a selected discipline [8] since the method provides insight into the growth, size, and distribution of scientific literature in the field of interest within a specified time frame [8]. However, there are few bibliometric studies in the field of MPV research. Bibliometric analysis is a novel scientific method that integrates mathematical and statistical approaches with data visualization to determine the overall knowledge structure, development trends, and research priorities in a specific field [6,10]. Additionally, several studies have been published on MPV worldwide [11–19], and findings from such studies have helped to obtain vital information about state-of-the-art research and determine gaps in it. For young researchers to determine research trends and hotspots, the current study employed a method of statistical analysis called bibliometrics to assess the significant evolution of knowledge trends based on published research [6,8,10]. Therefore, in the current study, we conducted a bibliometric analysis of literature on monkeypox published using the Scopus database. The Scopus database was preferred because it provides better coverage of journal abstracts and citations than other databases such as Web of Science and PubMed [20,21]. The analyses comprised the number of annual publications, country contributions, international collaborations, institutions, journals, and authors. Thus, the primary objectives of this study are to identify the highly cited articles in research, their citation rate, and author counts per article. In addition, the study analyzes the significant contributing journals' characteristics, reveals productive authors, shows the most contributing countries and attributes of the most cited papers, and reveals the life cycle of the most cited articles in MPV research. We hope this study can provide a new perspective and reference for future research on MPV.

Over the past months, the emergence and rapid spread of monkeypox virus (MPXV) outside of traditionally endemic countries has led to a new viral global threat. The related impact is compounded by the fact that the coronavirus disease 2019 (COVID-19) pandemic is still an ongoing health challenge.1,2 MPXV is a double-stranded DNA virus, a member of the Orthopoxvirus genus within the Poxviridae family. The virus can be divided into two genetic distinct viral clades: clade I (formerly known as Congo Basin clade) and clade II (former West African clade), which encompasses two phylogenetically distinct subclades, IIa and IIb. The clade I viruses are more virulent, with human case fatality rates during outbreaks in parts of Africa estimated to be around 10%. Clade IIb is responsible for the current global outbreak, although new cases related to clade IIa continue to be reported.3 Other Orthopoxvirus related species pathogenic to

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humans include cowpox virus, variola virus, and vaccinia virus.4 MPXV was first identified in 1958 in a colony of cynomolgus monkeys (Macaca fascicularis) in Copenhagen, Denmark.5 Between 1960 and 1968, several outbreaks involving MPXV as an etiological agent were documented in captive monkeys in the Netherlands and the USA.6 The first case of MPXV in the human population was reported in 1970 in the Democratic Republic of the Congo in a 9-month-old boy.7 Mpox infections remained a disease of the African continent, with sporadic cases diagnosed in forested regions of Central or West Africa and small-scale outbreaks until 2003, when the first cases of infection were reported outside Africa.8,9 In May 2022, a series of mpox cases were reported in Europe, mostly involving men who have sex with men (MSM)10–12 and this emergence has been associated with a steep increase in the number of human mpox infections. When the outbreak of mpox expanded earlier last year, racist and stigmatizing language was observed and reported to World Health Organization (WHO). Following a series of consultations with experts, WHO decided to use a new preferred term named ‘‘mpox’’ as a synonym for monkeypox infection, where both terms will be used simultaneously for one year while ‘‘monkeypox’’ is phased out.13,14 To date, the virus itself remains referred to as MPXV—the International Committee on Taxonomy of Viruses (ICTV) decided to keep the original name to maintain the progress of the scientific literature, at least for now.15 As of 11 April, 2023, more than 86,000 cases of mpox infection and 116 deaths have been reported worldwide, most of which involved individuals living in non-endemic countries.16 Importantly, it has not been formallydemonstrated whether the reported deaths were directly linked with the mpox infection.16 However, the rapid spread of the mpox disease led the WHO to declare the current mpox outbreak a Public Health Emergency of International Concern (PHEIC) on July 23, 2022. Monkeypox is a zoonotic viral disease caused by the monkeypox virus (MPXV), a member of the Orthopoxvirus genus, which also includes variola virus, the causative agent of smallpox. Historically endemic to Central and West Africa, monkeypox has gained prominence due to recent outbreaks in non-endemic regions, raising significant public health concerns. The first confirmed case outside endemic areas occurred in May 2022, leading to a rapid increase in reported cases globally. As of September 2022, over 53,000 cases had been documented, prompting the World Health Organization (WHO) to declare the outbreak a Public Health Emergency of International Concern (PHEIC) (1, 2).

The resurgence of monkeypox underscores the need for a comprehensive understanding of its epidemiology, transmission dynamics, and clinical manifestations. Recent studies have highlighted the potential for human-to-human transmission, which complicates containment efforts (3, 4). Additionally, the ongoing COVID-19 pandemic has strained global health systems, making the management of emerging infectious diseases like monkeypox even more challenging (5).

Research on monkeypox has significantly increased, particularly in the United States, where the Centers for Disease Control and Prevention (CDC) has been a leading contributor to the literature (6). Bibliometric analyses reveal a growing interest in the disease, emphasizing the need for continued investigation into its biological characteristics and public health implications (7). Furthermore, the unusual clinical presentations observed in recent outbreaks indicate substantial knowledge gaps that must be addressed to inform effective public health strategies (8, 9).

This review aims to synthesize current trends in monkeypox research and provide insights into future directions for managing the disease. By examining the historical context, epidemiology, and recent outbreaks through a comprehensive lens, we aim to identify critical areas for intervention and research,
particularly concerning vaccine development and distribution (10).

II. COMPARATIVE ANALYSIS OF MONKEYPOX: A GLOBAL PERSPECTIVE

Monkeypox, a zoonotic viral disease, has gained significant global attention due to its recent outbreak. A comparative analysis can provide valuable insights into its spread, impact, and response efforts across different regions

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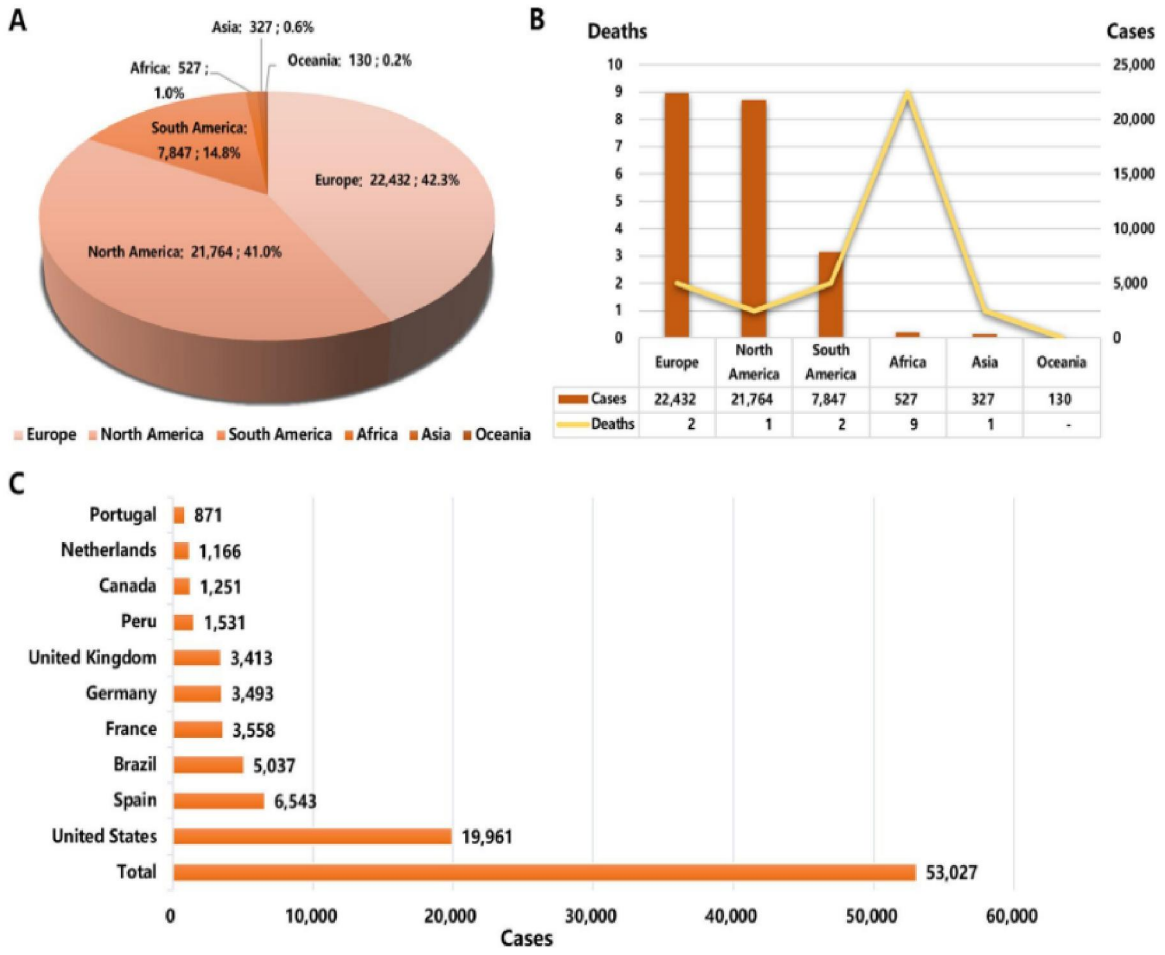

Fig. 1. The global situation of monkeypox confirmed cases. A) The proportion of monkeypox confirmed cases in different continents. B) Confirmed cases and deaths of monkeypox in different continents. C) Top ten countries with the highest monkeypox cases. The source of data statistics from CDC in the United States. (https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html) as of September 2nd, 2022.

Key Areas for Comparison

* Epidemiology:

* Case numbers and trends: Comparing the number of cases, peak periods, and geographical distribution in different countries or regions.

* Transmission patterns: Analyzing the primary modes of transmission (human-to-human, animal-to-human) and any variations observed.

* Risk factors: Identifying common risk factors associated with monkeypox infection, such as sexual behavior, exposure to animals, and underlying health conditions.

*** Public Health Responses:**

* Contact tracing and isolation: Comparing the effectiveness of contact tracing and isolation measures in different countries.

* Vaccination strategies: Evaluating the availability, accessibility, and efficacy of vaccines in various regions.

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* Healthcare infrastructure: Assessing the preparedness of healthcare systems to manage monkeypox cases and prevent further spread.

*** Socioeconomic Impact:**

* Economic burden: Analyzing the economic costs associated with monkeypox outbreaks, including healthcare expenditures, lost productivity, and disruptions to trade and tourism.
* Social stigma: Examining the social stigma and discrimination faced by individuals affected by monkeypox.
* Public perception: Assessing public attitudes and beliefs about monkeypox, including fear, misinformation, and vaccine hesitancy

*** Global Cooperation:**

* International collaboration: Evaluating the extent of international cooperation in sharing information, resources, and best practices for combating monkeypox.
* Global health governance: Analyzing the role of international organizations like the World Health Organization (WHO) in coordinating global responses.

Potential Sources for Comparative Analysis

* World Health Organization (WHO) reports
* Centers for Disease Control and Prevention (CDC) publications
* Peer-reviewed scientific journals
* National health agencies' data and analyses
* Media reports and news articles

By conducting a comparative analysis, researchers and policymakers can identify key lessons learned from the monkeypox outbreak, inform future prevention and response efforts, and contribute to global health security.

III. EPIDEMIOLOGY AND HISTORICAL CONTEXT

The book provides a well-documented historical analysis of the monkeypox virus, tracing its discovery, patterns of human transmission, and association with the smallpox eradication campaign. It also explores early outbreaks and factors contributing to sporadic cases across Central and West Africa, noting the virus's reliance on wildlife reservoirs. In evaluating the current global landscape, the book highlights the significant rise in human monkeypox cases outside endemic regions, offering detailed data on the role of human mobility and urbanization in its spread.

This section of the book successfully outlines the evolving epidemiological trends, supported by up-to-date data and insightful analysis, making it a key contribution to understanding the factors behind monkeypox's global emergence.Host tropism significantly affects the distribution and transmission of viruses among infected hosts. If a virus can infect more hosts or has an adaptive mutation to humans, it will spread widely and even influence public health globally once it crosses the host barrier efficiently.

Even though the reservoir natural host and intermediate host of MPXV have not been recognized thus far [13], the virus is maintained in various mammalian species in endemic areas, including humans, nonhuman primates, and rodents (such as rope squirrels, tree squirrels, Gambia kangaroos, and dormouse) [24,25]. With a variable host spectrum, it seems like that MPXV is provided with the potential to threaten human health. Since rodents were reported to be the source of many monkeypox outbreaks [26,27], they are most likely to be the natural host and play Acbbreviations: R0 = the primary case reproduction number; VARV = variola virus; MPXV = monkeypox virus; SARS-CoV-2 severe acute respiratory syndrome coronavirus 2.a crucial role in the transmission and infection of MPXV. Besides, MPXV is presumed to have a broader range of animal hosts; for example, the first monkeypox case of a dog that might have been acquired through human transmission was reported recently and demonstrated that domesticated dogs could be a vector for MPXV [28].

Additionally, based on currently available data, it appears that VACV and MPXV both have a broad host range, while VARV exhibits a very restricted host tropism . The reason for such a difference remains mysterious. However, it is suggested that the answer might lie in the genetic diversity of those viruses, namely, host range genes. Compared with

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VARV infecting humans exclusively, MPXV has a broader host tropism and an increasing latent ability of widespread transmission genetically.

Monkeypox was first identified in 1958 during two outbreaks in colonies of monkeys kept for research, hence the name. The first human case was recorded in 1970 in the Democratic Republic of Congo (DRC) during a period of intensified effort to eliminate smallpox. Since then, monkeypox has been reported in several other central and western African countries, becoming endemic in some regions Monkeypox is a zoonotic viral disease first identified in 1958, when two outbreaks occurred in laboratory monkeys kept for research in Denmark. The disease itself, however, primarily affects rodents and other small mammals in the rainforest regions of Central and West Africa, where it is endemic. The first human case of monkeypox was recorded in 1970 in the Democratic Republic of the Congo (DRC) during a period of increased smallpox surveillance following the disease's eradication (1). Historically, monkeypox infections were sporadic and mainly confined to remote areas, with only a limited number of cases reported until the early 21st century.

Epidemiological Trends

Over the years, monkeypox has exhibited a clear epidemiological profile characterized by its preferential transmission in tropical rainforest environments. It is primarily transmitted to humans through contact with infected animals, particularly rodents, which serve as the principal reservoir. Secondary transmission can occur through person-to-person contact, particularly via respiratory droplets and skin lesions.

In the DRC, the incidence of monkeypox has notably increased in recent decades. Studies indicated that between 1981 and 1986, a single health zone reported an annual incidence rate of 1.4 to 8.7 cases per 100,000 population (2). By the 2000s, the outbreak frequency and case numbers began to rise, with the WHO reporting a resurgence of monkeypox in Central Africa as early as 2005, indicating broader geographical spread (3).

The most significant change in the epidemiological landscape of monkeypox occurred in 2022, when an unprecedented outbreak emerged globally, with reported cases in several non-endemic countries, including the United States, Canada, and various European nations. This outbreak led the WHO to declare monkeypox a Public Health Emergency of International Concern (PHEIC) in July 2022, representing a significant shift in the epidemiological profile of the disease (4). By late summer 2022, over 50,000 cases had been reported worldwide, prompting increased public health vigilance and response strategies.

Transmission Dynamics

Monkeypox is primarily transmitted through zoonotic events, but human-to-human transmission has been increasingly documented. Direct contact with skin lesions or bodily fluids of infected individuals poses the highest risk, while respiratory droplet transmission can occur during prolonged face-to-face interactions (5). Recent outbreaks have revealed that asymptomatic individuals may also spread the virus, complicating containment efforts. The role of sexual contact in the recent transmission dynamics highlights the significance of health education and targeted public health interventions (6).

Current Epidemiological Insights

The recent upsurge in monkeypox cases in non-endemic areas can be attributed to several interrelated factors, including ecological changes, increased human-animal interactions, and global travel. The disruption of traditional ecosystems, possibly exacerbated by climate change, has led to increased human exposure to wildlife reservoirs of the virus. Globalization and urbanization have further accelerated the spread of infectious diseases, as witnessed during the COVID-19 pandemic (7).

Additionally, vaccine hesitancy and public health system strains resulting from the COVID-19 response present challenges for effective monkeypox vaccination and prevention strategies (8). Currently available vaccines, such as JYNNEOS (MVA-BN), are being utilized in outbreak response efforts, and ongoing research is essential to expand vaccine access and evaluate efficacy in diverse populations (9, 10).

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Virology and Pathogenesis

The book delves deeply into the virology of MPXV, providing a thorough overview of its genetic structure, transmission mechanisms, and pathogenesis. It examines the virus's similarities and differences with other orthopoxviruses, such as smallpox and cowpox, emphasizing the complex factors that contribute to its zoonotic and human-to-human transmission. The discussion on genetic mutations in recent strains and their potential impact on viral behavior is particularly relevant, given the global spread of more virulent forms of the virus.

While the technical language used in these sections can be dense for readers outside of virology, the detailed breakdown of MPXV's biology offers invaluable insight into how it operates at both a molecular and population level.The specific mechanisms involved in monkeypox virus's entry and replication may vary depending on the host cell type and species. Additionally, the virus has evolved to evade host immune responses, further complicating the infection process. Understanding the detailed mechanisms of monkeypox virus's entry and replication is an active area of research, and new insights may continue to emerge. In the context of MPV infection, four distinct viral proteins have been identified as integral components facilitating the attachment of MPV to the host cell, as extensively elucidated by Kaler et al. [21]. The viral binding process involves the interaction of MPV with approximately 11 to 12 transmembrane proteins, which are devoid of glycosylation and have a molecular weight ranging from 4 to 43 kDa [21,22]. Notably, certain poxviruses have been reported to employ laminin and heparin sulfate to augment the attachment process [10,23]. Upon successful attachment and entry into the host cell, MPV initiates DNA synthesis, a critical step that transpires within a concise timeframe of no more than 2 h [24]. Subsequently, MV uncoats within the cytoplasm, as a prerequisite for replication. To ensure uninterrupted viral propagation, MPV efficiently incapacitates the host cell's defense mechanisms through the concerted action of prepackaged viral proteins and enzymatic factors [25]. In the ensuing phases of viral replication, MPV orchestrates the synthesis of early messenger RNA (mRNA) via its DNA-dependent RNA polymerase. The translated early mRNA serves multifarious functions, including facilitating further uncoating, DNA replication, and the generation of intermediate transcription factors [23,25]. Progressing further along the viral life cycle, transcription and translation of intermediate mRNA species transpire, thereby promoting the expression of late mRNAs. Subsequently, the translation of late mRNAs yields both structural and nonstructural proteins. These translated proteins, along with concatenated DNA molecules formed during earlier replication stages, congregate and coalesce to form immature virions (IMVs). These IMVs subsequently mature into MPV and, devoid of an external membrane, initiate infection upon their liberation following host cell disruption [23,26]. Post-formation, these MPV entities undergo intracellular transport facilitated by microtubules, eventually culminating in their fusion with the inner cell membrane to form cell-associated virions (CEVs). The interaction with CEVs triggers actin polymerization and filament development. Finally, these CEVs exit the host cell, now referred to as extracellular enveloped virions (EEVs), marking the culmination of the MPV life cycle [23,27].

The incubation period of MPV is not contagious and has a silent clinical manifestation. It is during the prodromal stage when secondary viremia arises via lymphoid organs to the skin and other tertiary organs, including the eyes, lungs, etc. This is followed by the presentation of symptoms, such as lymphadenopathy, mucocutaneous lesions, etc., making the individual highly infectious during this stage [20].

The pathogenesis of the hMPXV involves viral entry, fusion, replication, and release, during which the virus produces two infectious forms - extracellular enveloped virions (EV) and intracellular mature virions (MV). Whilst MVs are single membrane-bound that are released only during host cell lysis, EVs are specialized MVs that are bound by an antigenically distinct triple membrane (the double membrane is gained by translocation to Golgi bodies) (Realegeno et al., 2020; Mucker et al., 2022a). It has been demonstrated that vaccines and antibodies that fail to produce or target the EV antigens provide lower protection than those including both (Golden et al., 2011; Lustig et al., 2005).

In the context of Orthopoxviruses, two multi-subunit complexes are crucial for completing the viral infectious cycle – GARP (Golgi-Associated Retrograde Protein) and COG (Conserved Oligomeric Golgi) complex (Realegeno et al., 2020). The GARP complex, responsible for retrograde endosomal transport, comprising four vacuolar protein sorting (VPS) genes – VPS51, VPS52, VPS53, and VPS54, all of which were found to be enriched in both CA and WA clades (except VPS53 which is specifically enriched in CA clade) (Realegeno et al., 2017). VPS52 and VPS54 knockout cells

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infected with MPXV have shown a significant decrease in EV yield, thereby confirming their prominent function in virus egress and cell-to-cell spread (Realegeno et al., 2017).

Virology

Monkeypox virus (MPXV) is a member of the Orthopoxvirus genus within the Poxviridae family, which also includes variola virus (the causative agent of smallpox), vaccinia virus (used in the smallpox vaccine), and cowpox virus. MPXV is a large, complex virus that exhibits a double-stranded DNA genome, typically ranging from 197 to 202 kilobase pairs in length (1). The virus is oval or brick-shaped, measuring approximately 200-250 nm in diameter.

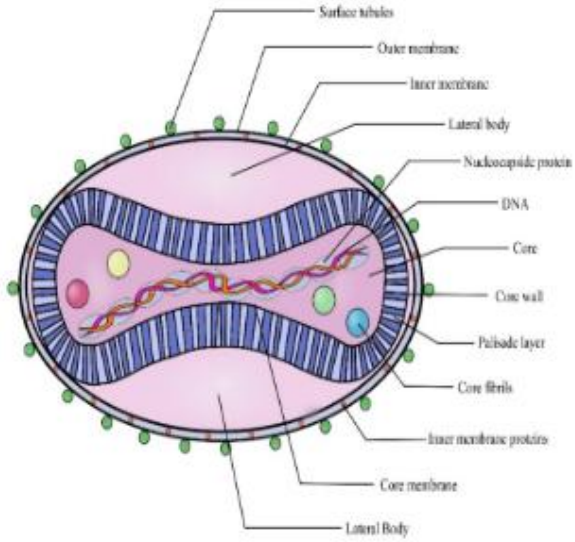

Figure 2. Structural features of a poxvirus virion. The virion is encased in an outer membrane and inner membrane, with surface tubules projecting from the outer surface. Inside, the core contains viral DNA, nucleocapsid proteins, and lateral bodies, surrounded by a core wall and fibrils. The palisade layer provides structural integrity, while inner membrane proteins facilitate viral assembly and infection. This unique design supports the virus's ability to replicate and evade host defenses.

MPXV is categorized into two distinct clades: the Central African clade (also known as the Congo Basin clade) and the West African clade. The Central African clade has been associated with more severe cases and higher mortality rates (2). The clades differ in terms of genetic makeup, virulence, and epidemiological patterns. For instance, while the West African clade has been linked to a recent global outbreak, cases predominantly from the Central African clade have historically been reported in endemic regions (3).

Transmission and Entry

MPXV is primarily transmitted to humans through zoonotic spillover events, often through direct contact with infected animals such as rodents, squirrels, and monkeys. Transmission can occur through bites, scratches, or handling of infected animal tissues (4). The virus can also be spread via respiratory droplets during prolonged face-to-face contact, although this mode of transmission is less common compared to direct contact with lesions or bodily fluids of infected individuals (5).

Once introduced into the human body, MPXV exploits the skin or mucosal entry points to establish infection. The virus binds to cell surface receptors, facilitating entry into host cells through endocytosis (6). After entering the cytoplasm, the viral core is released, leading to the uncoating of the viral genome, which is then transcribed and replicated in the host cell's cytoplasm.

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Pathogenesis

The pathogenesis of monkeypox involves several key stages, beginning with viral entry and replication, followed by systemic dissemination and clinical manifestation of disease.

1. Local Replication: After initial entry, MPXV replicates locally at the site of infection, often resulting in the development of papules or vesicles. This local viral replication is crucial for establishing the initial viral load.
2. Lymphatic Spread: Once the virus has replicated locally, it is released into the adjacent lymphatic vessels and nodes, where it further proliferates. This activates the host's immune response, leading to lymphadenopathy, a notable clinical sign of monkeypox (7).
3. Systemic Infection: Following lymphatic spread, the virus enters the bloodstream (viremia) and disseminates to various organs, including the liver, spleen, and skin. This systemic phase is characterized by the onset of systemic symptoms such as fever, malaise, and myalgia.
4. Skin Manifestations: Skin lesions typically appear 1-3 days after the onset of fever and may progress through several stages: macule, papule, vesicle, pustule, and crusting. The lesions can occur on various body parts, including the face, hands, and genital area. The contagious nature of these lesions is a significant factor in transmission (8).
5. Immune Response: The immune response to MPXV is complex, involving both innate and adaptive arms. Following infection, the host mounts a robust immune response that may influence disease severity. The presence of neutralizing antibodies can help control viral replication, but the virus may evade immune detection through immunomodulatory strategies, contributing to its pathogenesis (9).

IV. CLINICAL PRESENTATION AND MANAGEMENT

The clinical presentation of monkeypox, its course, and potential complications are covered comprehensively in the book. Descriptions of the prodromal phase, characteristic rash, lymphadenopathy, and potential systemic involvement offer a solid foundation for clinicians. Importantly, the text addresses diagnostic challenges in distinguishing monkeypox from other pox-like diseases, such as varicella and syphilis, emphasizing the need for accurate laboratory testing.

Table 2. Clinical characteristics of mpox patients

Reference	Pittman et al.[34]	Yinka-Ogunleye et al.[35]	Huhn et al.[25]	Adler et al.[36]	Patel et al.[30]	Thornhill et al.[37]
Country	Democratic Republic of the Congo	Nigeria	USA	United Kingdom	United Kingdom	International collaborative group (43 sites in 16 countries)
Medical description	216 patients	122 patients	37 patients	7 patients	197 patients	528 patients
Fever	18.5%	79%	87%	42%	61.9%	62%
Rash	99.5%	88%	97%	100%	13.7%	95%
Headache	23.6%	79%	65%	–	–	27%
Myalgia	6.9%	58%	56%	–	31.5%	31%
Malaise	85.2%	50%	–	–	–	–
Sore throat	78.2%	58%	60%	–	16.8%	–
Chill	44.9%	65%	71%	–	–	–
Adenopathy	57.4%	69%	71%	71%	57.9%	56%

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The management strategies discussed include supportive care, the use of antivirals like tecovirimat, and the potential role of newer vaccines, such as the MVA-BN vaccine. The book effectively communicates the limitations in treatment options, especially in resource-limited settings, highlighting disparities in access to care between regions.The clinical presentation of monkeypox consists of three distinct phases: incubation, prodrome, and rash [28]. Following an incubation period of 7–14 days, the 2-day prodrome phase manifests with fever (38.5–40.5 ◦C), chills, myalgia, sore throat, and headaches [2,28]. Notably, lymphadenopathy in the maxillary, cervical, and/or inguinal regions, with inguinal involvement being predominant, occurs in approximately 90% of patients [29]. This lymphadenopathy is characteristic of monkeypox [2]. After the prodromal phase, 0.2 to 1.0 cm lesions and rashes initially appear on the face and oral mucosa, subsequently spreading centrifugally over the body [2], marking the period of highest contagiousness [30]. Oral mucosal involvement can lead to pain and difficulty with oral intake in the later stages [16]. Disease severity is correlated with lesion count, with higher counts indicating an elevated risk of complications, such as ocular infections, respiratory depression, encephalitis, and septicemia [12,31].

A systematic review of MPV cases from 2003 to 2021 revealed confusion, seizures, and encephalitis as symptoms in 2% of cases [10]. Lesions progress through macular, papular, vesicular, pustular, and crusted stages before becoming noncontagious [32]. These lesions are prone to bacterial superinfections, particularly in individuals who are not vaccinated against smallpox [29]. Certain population subgroups exhibit distinctive manifestations. Men who have sex with men may present with anal ulcers and painless genital lesions that spread [33,34]. Vertical transmission of MPV can occur in pregnant individuals, often leading to adverse outcomes, including spontaneous abortions and stillbirths characterized by fetal vesicular lesions, hepatomegaly, and hydrops [35,36]. High viral loads are found in fetal tissue, the umbilical cord, and the placenta due to the virus's ability to breach the syncytiotrophoblast barrier [36]. Young children aged 0–4 years, have a higher fatality rate (14.9%) compared to children over 10 years old (0%). Young children were most affected in the 1970s and 1980s, but the median age of cases has since risen to around39 years old. Further research into pediatric cases may aid in preventing future fatalities in this demographic.

It is also possible for individuals who are infected with MPV to be asymptomatic [37]. A systematic review and meta-analysis demonstrated that 10.2% of monkeypox cases were asymptomatic or clinically silent. These cases were found to either be asymptomatic at the time of testing and develop symptoms later, to not develop symptoms at all, or to have very mild symptoms that were not noticed by the infected individual [37]. MPV has been isolated from urethral and anal samples of asymptomatic individuals, suggesting that asymptomatic cases are able to transmit the virus [37,38]. However, no case of MPV transmission from an asymptomatic individual to a close contact has been definitively confirmed [37]. Future surveillance and research should aim to continue tracking asymptomatic cases and their close contacts to characterize the probability of MPV transmission from asymptomatic individuals. Monkeypox typically presents with a sequence of symptoms that can be grouped into three main stages:

1. Incubation Period:

o The incubation period for monkeypox can range from 5 to 21 days, with an average of 7 to 14 days.

o During this time, the individual may be asymptomatic and not exhibit any signs of infection.

2. Prodromal Phase:

o This phase lasts about 1 to 5 days and involves systemic symptoms such as:

- Fever
- Headache
- Muscle aches
- Backache
- Swollen lymph nodes (lymphadenopathy), which is a key distinguishing feature of monkeypox compared to smallpox.
- Chills and fatigue
- Sore throat

3. Rash Phase:

o The characteristic monkeypox rash usually appears 1 to 3 days after the onset of fever.

o The rash typically progresses through several stages:

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- Macules: Flat, discolored spots appear.
- Papules: Raised bumps develop.
- Vesicles: Fluid-filled blisters form.
- Pustules: The vesicles develop pus.
- Crusts: Eventually, the pustules crust over and scab.

o The rash can appear on various parts of the body, including the face, hands, feet, and genital areas, and may be painful or itchy.
o Lesions can remain for 2 to 4 weeks, with the total duration of illness typically ranging from 2 to 4 weeks.

Management

Management of monkeypox primarily focuses on supportive care, as there is currently no specific antiviral treatment approved for the virus. However, several strategies can be employed:

1. Supportive Care:

o Patients are managed with supportive therapies to alleviate symptoms such as pain and fever.
o Adequate hydration is essential.
o Antipyretics (e.g., acetaminophen) can be administered to reduce fever.
o Pain management may include analgesics.

2. Isolation and Infection Control:

o Patients diagnosed with monkeypox should be isolated to prevent the spread of the virus, especially in healthcare settings.
o Strict infection control measures should be followed to limit transmission, including the use of personal protective equipment (PPE) for healthcare workers.

3. Vaccination:

o Vaccination with live vaccinia virus vaccines (e.g., JYNNEOS or ACAM2000) is recommended for high-risk individuals, including those who may have been exposed to monkeypox or are involved in outbreak response.
o Post-exposure prophylaxis (PEP) with vaccination is most effective when administered within 4 days of exposure but may still provide some benefit up to 14 days post-exposure.

4. Antiviral Treatment:

o While no specific antiviral treatment is approved, antivirals developed for smallpox, such as tecovirimat (TPOXX) and cidofovir, have been used in certain cases.
o These treatments may be indicated in severe cases or for patients at higher risk for complications, such as immunocompromised individuals.

5. Monitoring and Follow-Up:

o Close monitoring of affected individuals is essential, particularly for signs of secondary bacterial infections or complications.
o Healthcare providers should educate patients about the signs of potential complications, such as difficulty breathing or severe skin infections, requiring immediate medical attention.

V. ETHICAL CONSIDERATIONS IN MONKEYPOX RESEARCH AND RESPONSE

The outbreak of monkeypox has raised numerous ethical questions, particularly in terms of research, public health measures, and social justice. Here are some key ethical considerations:

Research Ethics

* Informed Consent: Ensuring that participants in research studies provide informed consent, understanding the potential risks and benefits.
* Privacy and Confidentiality: Protecting the privacy and confidentiality of individuals involved in research, especially those affected by monkeypox.
* Vulnerable Populations: Addressing the ethical concerns related to research involving vulnerable populations, such as healthcare workers, LGBTQ+ communities, and individuals with underlying health conditions.

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Public Health Ethics

* Equity and Justice: Ensuring that public health measures, such as vaccination campaigns and contact tracing, are equitable and do not disproportionately affect marginalized or disadvantaged communities.
* Privacy and Civil Liberties: Balancing the need for public health measures with the protection of individual privacy and civil liberties.
* Stigma and Discrimination: Addressing the ethical concerns related to the potential for stigma and discrimination against individuals affected by monkeypox.

Social Justice Ethics

* Health Disparities: Addressing the underlying social and economic factors that contribute to health disparities and may exacerbate the impact of monkeypox.
* Access to Healthcare: Ensuring that everyone has equal access to healthcare services, including those affected by monkeypox.
* Global Health Equity: Promoting global health equity by ensuring that all countries have the resources and support needed to respond to Monkeypox sir other public health threats

VI. PUBLIC HEALTH IMPLICATIONS AND GLOBAL RESPONSE

One of the strongest aspects of the book is its emphasis on the global public health response. It addresses critical topics such as the importance of surveillance systems, the need for vaccine stockpiling, and global cooperation in controlling outbreaks. The text acknowledges the gaps in the current global response, particularly in regions with poor health infrastructure, and calls for a more equitable distribution of resources, including vaccines and antiviral treatments.

The book's forward-looking perspective includes discussions on the impact of climate change, deforestation, and human encroachment into wildlife habitats, which are likely to drive future zoonotic spillovers. This section underlines the necessity of global preparedness strategies, making it a significant contribution to the discourse on future pandemic prevention.

The rapid spread of MPXV outside endemic regions bears some risk to global public health if it is not contained quickly. The main drivers for the present MPXV global spread include the cessation of smallpox vaccination in 1980 making younger people vulnerable to MPXV infections, the failure to restrain the spread of MPX cases in endemic regions, and an increased likelihood of exportation of the virus to other countries due to globalization and air traffic. Therefore, disease surveillance in endemic and non-endemic regions is essential to control further spread. At this time, it is not clear if the 2022 MPXV differs in host change, transmissibility, or pathology compared to previous isolates. This needs to be urgently established.

The monkeypox virus is an orthopoxvirus that causes mpox (monkeypox), a disease with symptoms similar to smallpox, although less severe. While smallpox was eradicated in 1980, mpox continues to occur in countries of central and west Africa. Since May 2022, cases have also been reported from countries without previously documented mpox transmission outside the African region. Two distinct clades of the monkeypox virus have been identified: Clade I (previously known as the Congo Basin (central African) clade and Clade II (the former west African clade).

Mpox is a zoonosis, a disease that is transmitted from animals to humans, with cases often found close to tropical rainforests where there are animals that carry the virus. Evidence of monkeypox virus infection has been found in animals including squirrels, Gambian pouched rats, dormice, different species of monkeys and others.

The disease can also spread from humans to humans. It can be transmitted through contact with bodily fluids, lesions on the skin or on internal mucosal surfaces, such as in the mouth or throat, respiratory droplets and contaminated objects.

1. Detection of viral DNA by polymerase chain reaction (PCR) is the preferred laboratory test for mpox. The best diagnostic specimens are taken directly from the rash – skin, fluid or crusts, or biopsy where feasible. Antigen and antibody detection methods may not be useful as they do not distinguish between orthopoxviruses. Surveillance and Monitoring:

o The emergence and spread of monkeypox, particularly in non-endemic countries, necessitate enhanced surveillance systems to monitor its incidence and transmission patterns.

o Public health agencies must implement robust epidemiological tracking to quickly identify and respond to outbreaks.

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2. Health Education and Awareness:
o Raising awareness about monkeypox symptoms, modes of transmission, and prevention measures is crucial to empower communities to recognize signs of infection early.
o Public health campaigns should target healthcare workers, vulnerable populations, and the general public to reduce stigma and misinformation associated with the disease.
3. Vaccination Strategies:
o Effective vaccination campaigns are essential to control outbreaks. This includes the use of smallpox vaccines for post-exposure prophylaxis and pre-exposure vaccination for high-risk groups (e.g., healthcare workers, those in contact with infected individuals).
o It's important to assess the availability, distribution, and deployment of vaccines globally, especially in regions at risk.
4. Outbreak Control:
o Strategies for outbreak control should include isolation of infected individuals, contact tracing, and quarantine of exposed persons.
o Collaboration among public health entities is vital to ensure a swift and coordinated response.
5. Equity and Access:
o Addressing disparities in access to healthcare and vaccines is crucial to ensure equitable protection for all populations, particularly in under-resourced regions.
o Vulnerable communities may be disproportionately affected, highlighting the need for targeted interventions.
6. Research and Development:
o Ongoing research into monkeypox, including its transmission dynamics, pathogenesis, and therapeutic options, is essential to strengthen global preparedness for monkeypox and other zoonotic diseases.
o Investments in developing and securing effective treatments and vaccines are necessary to respond swiftly to emerging health threats.
Global Response
1. World Health Organization (WHO) Involvement:
o The WHO has played a key role in coordinating the global response to monkeypox outbreaks, issuing guidelines, and facilitating collaborative efforts among member states.
o The organization has also emphasized the need for international solidarity and resource-sharing in controlling outbreaks.
2. Intersectoral Collaboration:
o A One Health approach, integrating human health, animal health, and environmental sectors, is important for understanding and controlling zoonotic diseases like monkeypox.
o Engagement of veterinary services, wildlife experts, and public health officials is crucial to mitigate risks from animal reservoirs.
3. Global Preparedness Initiatives:
o Organizations such as the Coalition for Epidemic Preparedness Innovations (CEPI) work to ensure that vaccines and therapeutics are researched and developed in anticipation of outbreaks.
o Global health initiatives aim to strengthen healthcare systems in low- and middle-income countries, enhancing their capacity to handle similar health threats.
4. Continuous Monitoring and Assessment:
o Continuous global monitoring of monkeypox cases and transmission patterns helps inform public health responses and modifies strategies as needed.
o Countries are encouraged to report cases and share data to facilitate a better understanding of the epidemiology of monkeypox.
5. Public Health Recommendations:
o Global health bodies recommend that countries develop and maintain response plans for potential monkeypox outbreaks, including disaster preparedness and response frameworks.

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o Periodic drills and training for public health professionals can ensure readiness to handle outbreaks effectively.

VII. CHALLENGES AND FUTURE OUTLOOK

The final chapters of the book take a more speculative approach, discussing the potential evolution of MPXV and its long-term implications for global health. They raise important questions about the intersection of environmental change, globalization, and viral evolution. The authors suggest that a more proactive approach to research and development is necessary to combat future outbreaks, including the advancement of new vaccines and therapeutics.

While the text covers significant ground, it leaves room for further exploration of the socio-political dynamics surrounding public health interventions and the challenges of international cooperation in outbreak responses. Additionally, more focus on the ethical implications of resource allocation during a global health crisis would enhance the book's impact.

Currently, an unusual outbreak of MPXV of the less virulent clade II is occurring outside Africa. Starting in May 2022, independent cases of MPXV infections with local transmissions have been reported. The WHO (World Health Organization) had described 25,047 confirmed cases outside Africa by 2nd August 2022. Of these, 99% were males, with a median age of 36 years. When sexual orientation was reported, 98% were men who have sex with men (MSM) [16]. In July 2022, the WHO declared the global spread of MPXV a public health emergency of international concern (PHEIC).

Although formal proof of clinical vaccine efficacy is lacking, smallpox vaccines are expected to induce a long-lasting immunity against MPXV. The 2022 MPXV infections have been almost exclusively concentrated in the MSM community, most likely through close skin contacts. To contain the outbreak, vaccinations should to be offered to this community, health care workers, and close contacts of MPX patients. The infection is not limited to men, but can be transmitted to anybody by close physical contact. In addition, vaccination campaigns in endemic regions could be envisioned to save lives and eliminate the source of future outbreaks.

Monkeypox had been relatively neglected by global health efforts until the 2022 outbreak, with most cases historically confined to remote areas of Central and West Africa. Surveillance systems in these regions are often underdeveloped, making it difficult to track and respond to outbreaks effectively.

Monkeypox is a zoonotic disease, meaning it is transmitted from animals to humans. The specific animal reservoirs (likely rodents) remain unclear, which complicates efforts to control and prevent outbreaks. As long as animal reservoirs persist, eradicating the virus will be difficult.

Although human-to-human transmission was initially considered limited, the 2022 outbreak showed that it can spread through close physical contact, including skin lesions, respiratory droplets, and contaminated materials. The virus spread in populations previously unexposed to it, highlighting the need for better understanding of its transmission dynamics.

While vaccines developed for smallpox (like the Jynneos vaccine) offer protection against monkeypox, they are not widely available, especially in low-resource settings where monkeypox is endemic. Ensuring equitable access to vaccines during outbreaks remains a challenge, especially when global demand increases.

In the 2022 outbreak, cases were often associated with specific social groups, leading to stigma and fear. Misinformation about transmission and symptoms also spread, making public health efforts more difficult. Stigmatization can reduce willingness to seek care, increasing the spread of the disease.

There are limited treatments available for monkeypox. Tecovirimat (TPOXX) has been used in some cases, but it is not widely available. Supportive care is often the only option in many regions, which can lead to more severe outcomes in areas with underdeveloped healthcare systems.

Strengthening surveillance in endemic regions and globally will be critical. Investment in local health systems, better diagnostic tools, and rapid reporting mechanisms will improve the ability to detect and respond to outbreaks early, potentially preventing further spread.

More research is needed to understand the animal reservoirs of monkeypox and the mechanisms of zoonotic spillover. By identifying the animals that harbor the virus, more targeted interventions (like vaccination of animal populations or habitat management) can be developed to reduce the risk of human infections.

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Developing more specific vaccines for monkeypox or expanding the availability of existing smallpox vaccines is crucial. Ensuring that vaccines are accessible and affordable, particularly in endemic areas, can help manage future outbreaks. Investment in stockpiling vaccines and building capacity for mass vaccination in emergencies is also key.

Addressing the stigma associated with monkeypox is critical to ensuring effective public health responses. Clear, accurate public health messaging that reduces fear and misinformation is essential to encourage testing, vaccination, and safe behaviors. Global cooperation on public health campaigns will be necessary to manage outbreaks that cross borders.

The 2022 outbreak demonstrated that monkeypox is not just a regional concern, but a global one. Coordinated international efforts, supported by organizations like the World Health Organization (WHO), will be essential in responding to outbreaks. Preparing for monkeypox as part of broader pandemic preparedness strategies can help manage future emerging zoonotic diseases.

Investment in research to develop more effective treatments for monkeypox is needed. Broadening access to antiviral drugs like tecovirimat and conducting clinical trials to test their efficacy will help provide more therapeutic options for patients.

1. Underreporting and Surveillance Gaps:

o Many cases of monkeypox may go unreported, especially in endemic regions where healthcare access is limited or public awareness is low.

o Inconsistent surveillance systems make it difficult to track the true incidence and geographical spread of the disease.

2. Stigma and Misinformation:

o Stigmatization of affected individuals, particularly in contexts where monkeypox cases are associated with specific populations or high-risk behaviors, can hinder early detection and reporting.

o Misinformation regarding the disease, its transmission, and safety measures can exacerbate public fear and complicate control efforts.

3. Resource Limitations:

o Many countries, especially low- and middle-income nations, face challenges in healthcare infrastructure, including insufficient access to diagnostics, treatments, and vaccines.

o Inequities in global health resources can lead to unpreparedness in vulnerable regions.

4. Global Health Inequities:

o Disparities in vaccine availability and healthcare access can hinder effective outbreak responses, particularly in regions most affected by monkeypox.

o Marginalized communities may face barriers to accessing care and support.

5. Zoonotic Transmission:

o Monkeypox is a zoonotic disease, meaning animal reservoirs play a crucial role in its transmission. Understanding and managing the dynamics between wildlife and human populations is complex.

o Controlling outbreaks requires a comprehensive understanding of animal-human interactions and wildlife management.

6. Public Health Response Coordination:

o Coordination among various public health sectors and international organizations can be challenging, particularly given differing national priorities and capacities.

o Ensuring a unified response to outbreaks while respecting local contexts can be complex.

Future Directions

1. Enhanced Surveillance Systems:

o Investments in robust surveillance systems, including the use of digital health technologies and community-based monitoring, can improve case detection and tracking.

o Countries should enhance laboratory capacities to facilitate timely diagnostics and reporting.

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2. Public Awareness Campaigns:
o Comprehensive public health education initiatives can help reduce stigma, improve understanding of monkeypox, and encourage timely healthcare-seeking behavior.
o Targeted campaigns should address misinformation and promote preventive measures.
3. Research and Development:
o Continued research into the epidemiology, transmission dynamics, and pathogenesis of monkeypox is essential for developing effective interventions.
o Investment in vaccine and therapeutic research is needed to provide timely responses to outbreaks.
4. Global Collaboration:
o Strengthening international collaboration and partnerships among governments, NGOs, and health organizations can facilitate knowledge sharing and resource distribution.
o Participating in global health initiatives, such as the World Health Organization's plans for outbreak preparedness, can enhance collective response capabilities.
5. Strengthening Health Systems:
o Investment in health infrastructure in low- and middle-income countries is critical to ensure they can respond effectively to current and future outbreaks.
o Building resilient health systems will require a focus on equity, access, and capacity-building.
6. One Health Approach:
o Emphasizing a One Health approach that integrates human, animal, and environmental health can provide a better understanding of zoonotic diseases like monkeypox.
o Collaborative efforts involving veterinarians, ecologists, and public health officials can improve strategies for prevention and control.
7. Policy Development:
o Governments should develop and implement policies focusing on zoonotic disease prevention, including conservation of wildlife habitats and regulation of wildlife trade.
o Policies should also address healthcare access and equity issues to ensure that vulnerable populations receive adequate support.
8. Impact of Monkeypox on Vulnerable Populations
Monkeypox has disproportionately affected certain vulnerable populations, highlighting the importance of addressing health disparities and ensuring equitable access to healthcare.
Key Vulnerable Populations
* LGBTQ+ Communities: Many countries have reported a higher prevalence of monkeypox cases among men who have sex with men. This highlights the importance of targeted public health interventions and addressing stigma within these communities.
* Healthcare Workers: Healthcare workers are at risk of exposure to monkeypox due to their close contact with patients. Adequate personal protective equipment (PPE) and infection prevention and control (IPC) measures are essential to protect their health.
* People with Underlying Health Conditions: Individuals with weakened immune systems or other underlying health conditions may be at higher risk for severe illness from monkeypox. Ensuring access to healthcare and timely treatment is crucial for these populations.
* Children: While cases of monkeypox in children are relatively rare, it's important to monitor the situation and provide appropriate care for those affected.
* Marginalized Communities: Individuals in marginalized communities, such as those living in poverty or with limited access to healthcare, may face additional challenges in preventing and managing monkeypox.
Addressing Health Disparities
To mitigate the impact of monkeypox on vulnerable populations, it's essential to:
* Promote Equity: Implement policies and programs that promote health equity and address social determinants of health.

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* Target Interventions: Develop and implement targeted public health interventions that address the specific needs of vulnerable populations.
* Increase Access to Healthcare: Ensure that everyone has access to quality healthcare services, including those affected by monkeypox.
* Address Stigma and Discrimination: Promote understanding and acceptance of individuals affected by monkeypox to reduce stigma and discrimination.

IX. CONCLUSION

Monkeypox in Focus: Current Trends and Future Outlook is an important and timely contribution to the field of infectious disease research. The book offers a detailed, multidisciplinary examination of monkeypox, presenting both historical context and forward-looking perspectives. It succeeds in integrating virology, clinical insights, public health challenges, and global policy considerations into a comprehensive guide for understanding the monkeypox virus and its future trajectory.Along with the mobilization of populations and international cooperation, emerging and re‐emerging infectious diseases appear more frequently, spread to many nonendemic countries, and constitute a significant threat to human health and global biosafety.

For example, the multi‐country outbreak of monkeypox in 2022 has already “invaded” 6 continents and over 100 countries, with more than 53,000 people from different nations infected. MPXV, causing the 2022 multi‐country monkeypox outbreak, is equipped with a faster speed of microevolution and multi‐patterns of transmission between humans and animals. Presently, many countries are carrying out vaccination, and the

research of therapeutic drugs to prevent and control MPXV infection is accelerating. Cutting off human‐to‐human transmission is our essential goal for preventing and controlling the monkeypox outbreak by keepingsurveillance reservoirs and cases, improving detection technology, and tracing the evolution of MPXV. Our glorious vision is prevention preceding treatment, and strategy before the virus's evolution.

While the dense technical sections may challenge some readers, the book serves as a valuable resource for healthcare professionals, epidemiologists, and policymakers. Its emphasis on global collaboration and preparedness in the face of zoonotic threats makes it particularly relevant in today’s interconnected world. The book provides an essential foundation for future research and underscores the need for continued vigilance against the threat of monkeypox and similar emerging diseases.

The emergence and rapid spread of monkeypox virus (MPV) across the globe presents a complex and evolving public health challenge. MPV, despite its lower fatality compared to smallpox, poses a substantial threat, particularly in regions where cross-protective immunity from smallpox vaccination has waned. The current global outbreak, with its atypical presentation, epidemiological variations, and the emergence of new cases in non-endemic regions, underscores the need for immediate and concerted action. The development and distribution of effective vaccines, such as JYNNEOS, have shown promise in preventing and mitigating MPV infections.

However, there remain critical uncertainties regarding dosing, safety, indications, and contraindications that require further research. Nucleic-acid-based vaccines offer a potential alternative, especially in situations of vaccine supply shortages. These vaccines, inspired by the success of COVID-19 mRNA vaccines, require rigorous evaluation for safety and efficacy. Lessons from the COVID-19 pandemic emphasize the importance of preparedness, clear and transparent communication, and a coordinated global response. Public health systems must strengthen their capacity to detect, respond to, and control emerging viral threats like MPV. This should include bolstering disease surveillance, training healthcare professionals, and adopting a holistic “One Health” approach. Genomic sequencing can aid in understanding the virus’s evolution and spread.

Furthermore, the impact of public health emergencies on healthcare systems, especially in low- and middle-income countries, cannot be underestimated. These systems already have limited resources and are likely strained by the COVID-19 pandemic, so they need proactive measures to prevent further disruption. Lastly, addressing the monkeypox virus outbreak and future viral threats demands a multifaceted approach encompassing research, vaccine development, strengthening healthcare systems, and global cooperation. The current crisis serves as a stark reminder of the need for

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sustained vigilance, investment in public health infrastructure, and a commitment to science-based solutions for safeguarding global health.

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