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Contents

Thrice Monthly Volume 11 Number 19 July 6, 2023

REVIEW

- 4458** Molecular signalling during cross talk between gut brain axis regulation and progression of irritable bowel syndrome: A comprehensive review
Singh SV, Ganguly R, Jaiswal K, Yadav AK, Kumar R, Pandey AK
- 4477** Diffusion tensor imaging in the courtroom: Distinction between scientific specificity and legally admissible evidence
van Velkinburgh JC, Herbst MD, Casper SM

MINIREVIEWS

- 4498** Inequity in the global distribution of monkeypox vaccines
Tovani-Palone MR, Doshi N, Pedersini P
- 4504** Long-term effectiveness, outcomes and complications of bariatric surgery
Gulinac M, Miteva DG, Peshevska-Sekulovska M, Novakov IP, Antovic S, Peruhova M, Snegarova V, Kabakchieva P, Assyov Y, Vasilev G, Sekulovski M, Lazova S, Tomov L, Velikova T

ORIGINAL ARTICLE

Retrospective Cohort Study

- 4513** Age, blood tests and comorbidities and AIMS65 risk scores outperform Glasgow-Blatchford and pre-endoscopic Rockall score in patients with upper gastrointestinal bleeding
Morarasu BC, Sorodoc V, Haisan A, Morarasu S, Bologa C, Haliga RE, Lionte C, Marciuc EA, Elsiddig M, Cimpoesu D, Dimofte GM, Sorodoc L

Retrospective Study

- 4531** Application of cross-migration theory in limb rehabilitation of stroke patients with hemiplegia
Lu YH, Fu Y, Shu J, Yan LY, Shen HJ
- 4544** Analysis of characteristic features in ultrasound diagnosis of fetal limb body wall complex during 11-13⁺ weeks
Ye CH, Li S, Ling L
- 4553** Network pharmacology and molecular docking-based analyses to predict the potential mechanism of Huangqin decoction in treating colorectal cancer
Li YJ, Tang DX, Yan HT, Yang B, Yang Z, Long FX
- 4567** Assessment of functional prognosis of anterior cruciate ligament reconstruction in athletes based on a body shape index
Wang YJ, Zhang JC, Zhang YZ, Liu YH

EVIDENCE-BASED MEDICINE

- 4579** Network pharmacology and molecular docking to explore Polygoni Cuspidati Rhizoma et Radix treatment for acute lung injury

Zheng JL, Wang X, Song Z, Zhou P, Zhang GJ, Diao JJ, Han CE, Jia GY, Zhou X, Zhang BQ

ORIGINAL ARTICLE**Randomized Controlled Trial**

- 4601** Ulinastatin in the treatment of severe acute pancreatitis: A single-center randomized controlled trial

Wang SQ, Jiao W, Zhang J, Zhang JF, Tao YN, Jiang Q, Yu F

- 4612** Fecal microbiota transplantation in patients with metabolic syndrome and obesity: A randomized controlled trial

da Ponte Neto AM, Clemente ACO, Rosa PW, Ribeiro IB, Funari MP, Nunes GC, Moreira L, Sparvoli LG, Cortez R, Taddei CR, Mancini MC, de Moura EGH

SYSTEMATIC REVIEWS

- 4625** Combined medial patellofemoral ligament and medial patellotibial ligament reconstruction in recurrent patellar instability: A systematic review and meta-analysis

Abbaszadeh A, Saeedi M, Hoveidaei AH, Dadgostar H, Razi S, Razi M

CASE REPORT

- 4635** Unique Roberts syndrome with bilateral congenital glaucoma: A case report

Almulhim A, Almoallem B, Alsirhy E, Osman EA

- 4640** CK5/6-positive, P63-positive lymphoepithelioma-like hepatocellular carcinoma: A case report and literature review

Tang HT, Lin W, Zhang WQ, Qian JL, Li K, He K

- 4648** Edaravone administration and its potential association with a new clinical syndrome in cerebral infarction patients: Three case reports

Yang L, Xu X, Wang L, Zeng KB, Wang XF

- 4655** CDKN1C gene mutation causing familial Silver-Russell syndrome: A case report and review of literature

Li J, Chen LN, He HL

- 4664** Hypothetical hypoxia-driven rapid disease progression in hepatocellular carcinoma post transarterial chemoembolization: A case report

Yeo KF, Ker A, Kao PE, Wang CC

- 4670** Metastatic colon cancer treated using traditional Chinese medicine combined with chemotherapy: A case report

Deng CG, Tang MY, Pan X, Liu ZH

- 4677** Rare cause of cerebral venous sinus thrombosis: Spontaneous intracranial hypotension syndrome: A case report

Huang P

- 4684** Integrated Chinese and Western medicine in the treatment of a patient with podocyte infolding glomerulopathy: A case report
Chang MY, Zhang Y, Li MX, Xuan F
- 4692** Morbihan disease misdiagnosed as senile blepharoptosis and successfully treated with short-term minocycline and ketotifen: A case report
Na J, Wu Y
- 4698** With two episodes of right retromandibular angle subcutaneous emphysema during right upper molar crown preparation: A case report
Bai YP, Sha JJ, Chai CC, Sun HP
- 4707** Poststroke rehabilitation using repetitive transcranial magnetic stimulation during pregnancy: A case report
Jo J, Kim H
- 4713** Tuberculosis-induced aplastic crisis and atypical lymphocyte expansion in advanced myelodysplastic syndrome: A case report and review of literature
Sun XY, Yang XD, Xu J, Xiu NN, Ju B, Zhao XC
- 4723** Posterior reversible encephalopathy syndrome following uneventful clipping of an unruptured intracranial aneurysm: A case report
Hwang J, Cho WH, Cha SH, Ko JK

ACADEMIC WRITING

- 4729** Revitalizing case reports: Standardized guidelines and mentorship
Jeyaraman M, Ramasubramanian S, Jeyaraman N, Nallakumarasamy A, Sharma S

ABOUT COVER

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Inequity in the global distribution of monkeypox vaccines

Marcos Roberto Tovani-Palone, Neel Doshi, Paolo Pedersini

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Abstract

Monkeypox (mpox) has been a public health emergency of international concern that emerged in mid-2022 and has spread to 110 countries. The clinical findings of the disease vary according to the seriousness of the cases. Although its case fatality risk has not been high, a significant percentage of patients require hospitalization. In this context, local initiatives were taken to extend the limited supply of vaccines against the disease; however, such measures have not been sufficient to contain the spread of cases and ensure an equitable distribution of health resources. As a result, endemic regions of low-income countries continue to have insufficient access to mpox vaccination. Despite this and considering the global scope of the disease, there is still little discussion in the literature about the difficulties in achieving adequate vaccination coverage rates for the target population of interest. In this article, we briefly discussed general aspects of the disease, including its surveillance, the current global context of challenges for mpox vaccination, and issues on global allocation of health resources as well as proposed related recommendations.

Key Words: Monkeypox; Smallpox vaccine; Health inequities; Vaccination coverage; Vaccination hesitancy; Healthcare financing

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Core Tip: The development and implementation of new global public health policies, to ensure greater equity in global health financing in the short term, may lead to positive impacts in the global distribution of monkeypox vaccines. This would provide safer and more appropriate management of both this outbreak and future pandemics.

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INTRODUCTION

Along with the ongoing coronavirus disease 2019 (COVID-19) pandemic, a recent public health threat has put the world on high alert: the global monkeypox (mpox) outbreak. According to World Health Organization (WHO) data, confirmed cases of the disease exceeded 86000 in April 2023, with a spread across 110 countries and a total of over 110 deaths. Based on WHO regions, the Americas and Europe have been the two most affected regions, accounting for over 90% of all cases. However, as an endemic disease in West and Central Africa, greater attention from local governments and health authorities is needed during the current period[1].

In an attempt to gain greater support, sufficient production of vaccines, more equitable access by the target population, and the implementation of medical countermeasures for coordinated global action aimed at combating the spread of cases of the disease, the WHO declared mpox a public health emergency of international concern in July 2022[2,3]. In light of this, local initiatives were taken to extend the limited supply of vaccines during the early outbreak period. Although dose-saving approaches have been implemented in some countries including the United States, such measures have not been sufficient to contain the spread of the disease[4] and ensure equity in the global distribution of mpox vaccines. As a result, African countries in particular have had insufficient access to these vaccines [5,6].

Although the number of cases reported globally peaked in August 2022[7], an unequal distribution of health resources, negating any equitable prospects, could have the capacity to potentially threaten different regions of the world with significant limitations in this regard. Despite this and considering the global scope of the disease, there is still little discussion in the literature about the difficulties in achieving adequate vaccination coverage rates for the target population of interest. Here, we briefly discussed general aspects of the disease, including its surveillance, the current global context of challenges for mpox vaccination, and issues on global allocation of health resources as well as proposed related recommendations.

ETIOLOGY AND SPREAD OF MPOX

Mpox is a zoonotic viral infection caused by the mpox virus (MPXV). Patients present different symptoms and clinical involvement, which can lead to death in severe cases. Although a smallpox-like rash can be characteristically observed in affected patients[5], the mpox transmission and its case fatality rates are substantially lower compared to smallpox infection[1].

MPXV, in turn, corresponds to a double-stranded DNA orthopoxvirus, belonging to the same genus as smallpox, vaccinia, and cowpox viruses[5]. During the outbreak in 2022, a new lineage and sub-lineages of MPXV were identified. The B.1 lineage, classified as clade IIb for its close relationship to clade II, has been predominant in the worldwide spread of mpox[8,9]. Although this suggests that the current outbreak has a major source of infection[9], knowing how such variants might affect transmissibility, virulence and human adaptation remains a challenge.

TRANSMISSION, DIAGNOSIS, AND CLINICAL COURSE OF MPOX

Among the means of transmission of MPXV, the most common include skin-to-skin and sexual contact [2]. Similar to severe acute respiratory syndrome coronavirus 2, the diagnosis of MPXV infection is primarily made by polymerase chain reaction, using lesion swabs or body fluids[5,10]. Different studies report incubation periods for MPXV ranging from 7-10 d, with most affected patients having systemic disease and approximately 40% progress to complications. Although mpox-related mortality rates are less than 1%, about 1%-13% of cases may require hospitalization, which is expected to significantly

burden health systems[5,11]. Figure 1[2,5,11] illustrates a proposed general mechanism for the transmission cycle and clinical manifestations of mpox in humans.

SURVEILLANCE, CASE INVESTIGATION, AND CONTACT TRACING

According to the latest WHO recommendations published in 2022, the following actions of response to the multi-country outbreak of mpox should be prioritized and implemented: (1) Provide accurate information to people who may be at increased risk of simianpox virus infection; (2) Ensure access to pre- and post-exposure mpox vaccination for at-risk populations; (3) Prevent the spread of MPXV; and (4) Protect vulnerable individuals and frontline healthcare workers. From this perspective, it is imminent that doctors working in private or public settings, including hospital surveillance services, immediately report suspected cases to local and national public health authorities and to the WHO. In suspected cases of the disease, the investigation should consist of a clinical examination of the patient in a well-ventilated single room, using appropriate personal protective equipment. Patients should be questioned about possible sources of exposure, and a safe specimen collection should be obtained and forwarded to the respective laboratories[7].

As soon as a suspected case is identified, identification and tracing of all possible contacts should be initiated. Contacts of probable and confirmed cases must be monitored or self-monitored daily for any signs or symptoms for a period of 21 d from the last contact with confirmed cases or contaminated materials during the infectious period. However, in the absence of symptoms, quarantine or exclusion from work is not required during the monitoring period, which in turn differs from initial recommendations for COVID-19 surveillance. In this stage, asymptomatic contacts are encouraged to practice hand hygiene and respiratory etiquette and to avoid contact with children, immunocompromised individuals, and pregnant women. Moreover, known contacts are advised to avoid sexual contact with others during this period. This is due to the fact that the evidence on the possible transmission of MPXV before the onset of symptoms continues to be reviewed. Therefore, regardless of whether or not symptoms are present, it is strongly encouraged that this advice is followed. Finally, non-essential travel is also discouraged[7].

CURRENT CONTEXT OF MPOX VACCINATION

In the current context of the global mpox outbreak, the non-replicating modified vaccinia Ankara (MVA) vaccine has been one of the most used for both pre- and post-exposure prophylaxis for people at high risk for mpox. This vaccine is commonly administered subcutaneously in two doses, with a 4-wk interval between them. However, given the shortage of vaccine supplies, different countries have authorized single-dose intradermal administration of the MVA vaccine for adults. Thus, a possible increase in vaccine coverage in target groups could be achieved. In this case, only one-fifth of the volume of the subcutaneous route is needed[5]. Recent research conducted by Bertran *et al* [12] demonstrated that a single dose of the attenuated MVA-Bavaria Nordic smallpox vaccine is highly protective against symptomatic mpox, making it a useful tool for controlling disease outbreaks when rapid protection is required[12]. Moreover, the use of the intradermal route may increase immunogenicity and induce antibody responses similar to the subcutaneous route[5].

The main target groups for mpox vaccination in newly affected countries are homosexuals, bisexuals, and others at a higher risk of contracting mpox. Health professionals and people who have had contact with infected individuals have also been included due to the possibility of medium and high risk of exposure to MPXV infection. However, despite the worldwide concern of mpox vaccination for vulnerable populations, adequate access to both antiviral treatment and vaccines remains an obstacle in different endemic countries[5,6]. Even with strong recommendations for the need to increase the coverage of mpox vaccines on a global scale from the Global Alliance for Vaccines and Immunization, the Vaccine Alliance, and the Global Fund to Fight AIDS, Tuberculosis and Malaria, their administration has been made available for the most part to populations in North America and Europe, with a severe limitation of supplies to low-income countries[5].

Although the outbreak has subsided in countries such as the United Kingdom and the United States due to the roll-out of vaccines and therapies as well as changes in awareness and social behavior, the same has not occurred in countries in West and Central Africa. According to the only announcement made in 2022 by the African Centers for Disease Control and Prevention regarding the shipment of mpox vaccines, the African Union should receive a donation of only 50000 doses from South Korea by then. These vaccines may be the first in the continent not intended for research, but the number of vaccines is too small for the target population of mpox vaccination campaigns across the continent[6]. In addition to vaccine shortages, delays in the access of tecovirimat, an antiviral authorized for emergency use to treat severe mpox[13], have also been reported in African countries[6]. It is therefore plausible to affirm that Africa still lacks adequate access to vaccination and antiviral treatment[5,6], which is essential for patients with severe manifestations and people at risk of serious disease[5].

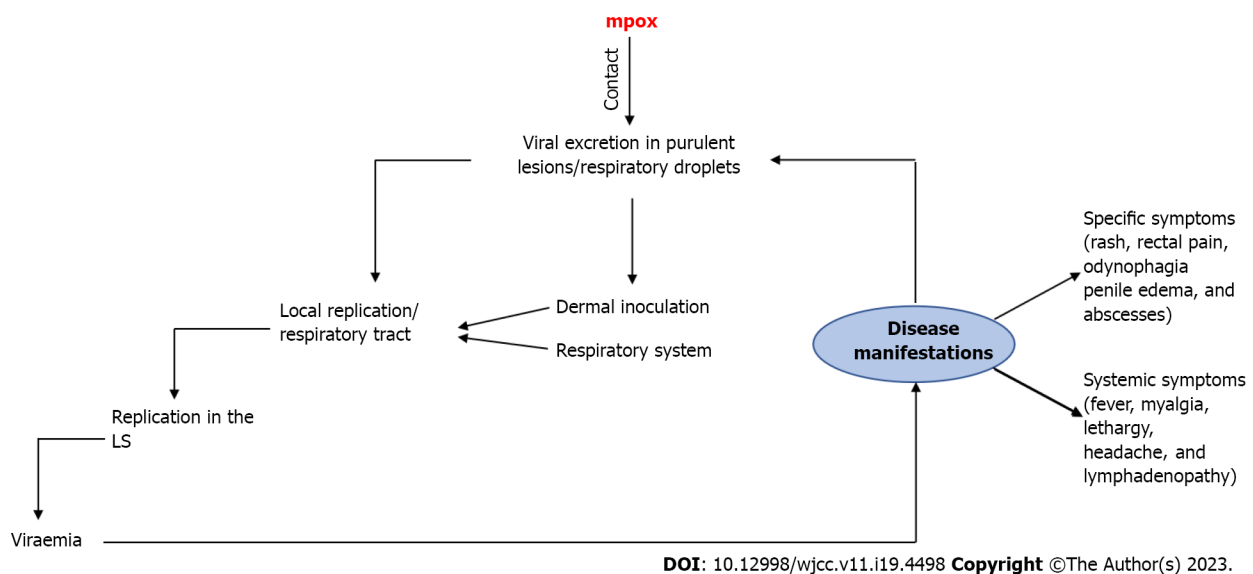


Figure 1 Basic mechanism related to monkeypox in humans. LS: Lymphatic system; mpox: Monkeypox.

However, this was similar to the events that happened during the COVID-19 pandemic when countries in Africa received low numbers of vaccines at a delayed timeframe[14]. It is also possible that cases were underreported[15]. The existence of inequity in the global distribution of mpox vaccines and possible underreporting[6] together with the increase in vaccine hesitancy since the beginning of the COVID-19 pandemic[16] and the resurgence of other previously eradicated infectious diseases[17,18] should call for swift and urgent action. Although mass vaccination of the population is neither required nor recommended for mpox, efforts to contain this global outbreak must focus primarily on ensuring equitable vaccine distribution, with concern focused on low-income and middle-income countries. In addition, other relevant measures must be taken, such as massive global support to enable affected countries to respond equitably and effectively to the outbreak, including increased funding for mpox screening centers. This last action is expected to strengthen the disease surveillance system and contribute to access to both adequate treatment and preventive health services. In short, to effectively control the spread of mpox, broad and efficient measures involving a variety of specific measures (Table 1)[2,4,9] should be implemented.

IMPORTANCE OF GLOBAL ALLOCATION OF HEALTH RESOURCES AMID THE MPOX OUTBREAK

The lack of equity in the global allocation of health resources may impede the implementation of many relevant actions, especially in low-income and middle-income countries. The conclusions of a recent evidence-based review demonstrate that as global health expenditures continue to grow, they remain unequally distributed around the world[19].

As a result of this issue, a worse situation for the mpox outbreak may be expected in several countries beyond what has been reported, particularly in low-income countries. This is due to the potential for underreporting of cases, which may be related to the occurrence of the disease in rural areas[20] in addition to the scarcity of health resources. This context, added to the persistent weaknesses of many health systems, should generate additional limitations that strongly impact the capacity of surveillance systems and the implementation of effective vaccination programs. In order to improve the situation, comprehensive actions, including a planned allocation of financial resources aimed at implementing new interventional measures and surveillance programs using cheap and quick strategies, such as wastewater monitoring of MPXV DNA[9], are also essential.

In addition to countries in Africa not receiving enough mpox vaccines in a timely manner, the recent knowledge gained about MPVX did not change the course of the outbreak in Africa. Therefore, even though there was an increase in world attention focused on MPXV, the resulting benefits were observed, at least initially, in developed countries only. Most research on this topic has been published by researchers based in high-income countries[6], which implies the need for more investments as well as better-targeted funding towards robust and globalized scientific advances aimed at the proper management of the disease and the control of its spread.

Table 1 Key points to contain the spread of monkeypox[2,4,9]

No.	Key points
1	Massive fight against misinformation
2	Strong information campaign strategy
3	Support from global health agencies
4	Effective collaboration with local laboratories, hospitals, and universities
5	Commitment of Ministries of Health of affected countries and partners
6	Implementing genome surveillance
7	Standardized and robust pharmacovigilance
8	Collaborative efficacy studies of vaccines with standardized protocols and data collection tools

Furthermore, even though many uncertainties remain about mpox therapies and comparative data on safety and efficacy related to the treatment of affected individuals, this should be yet another viable opportunity to fund the development of predesigned adaptive trial protocols that may enable faster discovery of effective drugs against viruses with pandemic potential[21].

CONCLUSION

In light of the current situation, the WHO together with other international alliances could play a key role in the development and implementation of global public health policies to ensure greater equity in global health funding in the short term, which should positively impact the global distribution of mpox vaccines as well as provide better management of this outbreak and future health emergencies. Only after building better health systems will be possible to satisfactorily control this and other imminent global emergencies and move closer to meeting the related sustainable development goals[22].

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