Review

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Role of vaccination in patients with human monkeypox virus and its cardiovascular manifestations

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Abstract

Human monkeypox, caused by the monkeypox virus (MPXV), is an emerging infectious disease with the potential for human-to-human transmission and diverse clinical presentations. While generally considered milder than smallpox, it can lead to severe cardiovascular complications. The virus primarily spreads through contact with infected animals or through human-to-human transmission. Cardiovascular involvement in human monkeypox is rare but has been associated with myocarditis, pericarditis, arrhythmias, and even fulminant myocardial infarction. Vaccination plays a crucial role in preventing and controlling monkeypox, but the eradication of smallpox has left global populations vulnerable. This review explores the cardiovascular manifestations of human monkeypox, the role of vaccination in disease prevention, and the importance of continued research and development of effective vaccines to protect against this emerging infectious threat. The global impact of monkeypox outbreaks, particularly on vulnerable populations, further highlights the importance of understanding and addressing this disease.

Keywords: Cardiovascular manifestations, human monkeypox, infectious disease, monkeypox virus, vaccination emerging

Introduction

Human monkeypox, caused by the monkeypox virus (MPXV), is an emerging infectious disease that has gained significant attention due to its potential for human-to-human transmission and its varied clinical manifestations[1]. Although generally considered a milder and less fatal disease than its cousin, smallpox, human monkeypox has been associated with a broad spectrum of clinical presentations, including severe cardiovascular system complications[1–3]. The role of vaccination in preventing and managing human monkeypox, particularly in relation to cardiovascular manifestations, has become a topic of increasing importance in recent years.

Monkeypox is primarily a zoonotic disease, with its natural reservoirs being various animals, including rodents and non-human primates[4]. However, human-to-human transmission can occur through respiratory droplets, direct contact with infected individuals or their bodily fluids, and contaminated objects. As the virus spreads within human populations, it can result in outbreaks and pose a significant public health concern[5].

Cardiovascular involvement in human monkeypox is rare but has been reported in some cases[6]. The virus can lead to various cardiovascular complications, such as myocarditis, pericarditis, arrhythmias, and even fulminant myocardial infarction[6]. These manifestations can range from mild symptoms, such as chest pain and palpitations, to life-threatening conditions, necessitating intensive medical care and potentially resulting in long-term cardiac sequelae.

Vaccination plays a crucial role in the prevention and control of human monkeypox[7]. The smallpox vaccine, which affords cross-protection against monkeypox, has been used in the past[8]. However, due to the eradication of smallpox and the subsequent discontinuation of routine vaccination, the global population is no longer adequately protected against monkeypox.

HIGHLIGHTS

- Human monkeypox, caused by the monkeypox virus, is an emerging infectious disease with the potential for human-to-human transmission and diverse clinical presentations.
- Cardiovascular involvement in human monkeypox is rare but has been associated with myocarditis, pericarditis, arrhythmias, and even fulminant myocardial infarction.
- Vaccination plays a crucial role in preventing and controlling monkeypox, but the eradication of smallpox has left global populations vulnerable.
- The global impact of monkeypox outbreaks, particularly on vulnerable populations, further highlights the importance of understanding and addressing this disease.

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This review aims to explore the current understanding of the human monkeypox virus with a particular focus on its cardiovascular manifestations. Additionally, we will discuss the role of vaccination in mitigating the spread of the disease and preventing cardiovascular complications, emphasizing the need for continued research and development of effective vaccines against monkeypox to protect global populations from this emerging infectious threat.

Methods

Several electronic databases, including PubMed, Embase, and Google Scholar, were systematically searched using appropriate keywords and Boolean operators. The search terms used included "human monkeypox," "monkeypox virus," "cardiovascular manifestations," "vaccination," "anti-viral treatment," "management strategies," and related terms. The search was limited to articles published in English.

The initial search yielded a large number of articles, which were then screened based on their titles and abstracts for relevance. Duplicate articles were removed, and the remaining articles were assessed for their suitability based on the study objectives. Full-text articles were obtained for further evaluation.

The selected articles were carefully reviewed, and relevant information was extracted. The extracted data included study characteristics (e.g. study design, sample size), details on the monkeypox virus and its cardiovascular manifestations, vaccination strategies, vaccine effectiveness, and outcomes related to cardiovascular complications.

The data were organized thematically and synthesized in a narrative format to provide a comprehensive overview of the role of vaccination in mitigating human monkeypox virus with cardiovascular manifestations. Key findings and important insights from the literature were highlighted and discussed in relation to the study objectives.

Epidemiology and global impact of human monkeypox

Human monkeypox, caused by the MPXV, is a rare but significant zoonotic disease that primarily affects humans[1]. The virus is classified within the Orthopoxvirus family, which also includes the closely related variola virus, responsible for smallpox[9]. Monkeypox is believed to have a zoonotic origin, with animals like rodents, squirrels, and primates acting as natural reservoirs for the virus[1].

The transmission of monkeypox to humans occurs through contact with infected animals or their bodily fluids, as well as through human-to-human transmission, making it a potential public health concern[10]. While the majority of monkeypox cases have been reported in Africa, particularly in Central and West African countries, sporadic cases have also been identified in other regions, including Asia, Europe, and North America[11]. Outbreaks can arise due to various factors, such as increased contact between humans and infected animals, international travel, and a lack of immunity in susceptible populations[12].

Clinical manifestations of monkeypox vary from mild to severe, with an incubation period typically ranging from 7 to 14 days after exposure[13]. Symptoms often start with fever, headache, muscle aches, and a general feeling of malaise, resembling many other viral infections[14]. However, distinctive skin lesions begin to develop shortly after the initial symptoms, progressing through stages of papules, vesicles, pustules, and scabs[15]. Some patients may experience respiratory, gastrointestinal, or neurological symptoms, while others may develop severe cardiovascular complications, such as myocarditis and pericarditis.

Global impact[16]

Over the past few decades, the global impact of human monkeypox has been a growing concern for public health authorities and researchers alike. Although less fatal than smallpox, monkeypox poses significant challenges due to its potential for severe complications and ability to cause outbreaks with substantial morbidity[17].

The economic burden of monkeypox outbreaks extends beyond healthcare costs, encompassing measures such as quarantine, surveillance, and contact tracing[18]. Outbreaks can disrupt local economies, trade, and tourism, leading to social and economic upheaval in affected regions[19].

The impact of monkeypox on vulnerable populations, including immunocompromised individuals and those with pre-existing cardiovascular conditions, can be particularly severe[20]. Cardiovascular manifestations of monkeypox, ranging from myocarditis to life-threatening arrhythmias, add a layer of complexity to the management of the disease and demand specialized medical attention and resources[6].

Clinical spectrum

Human monkeypox is a complex viral infection that presents a diverse range of clinical manifestations. The severity of the disease can vary widely, with some individuals experiencing mild symptoms, while others develop more severe complications. Understanding the clinical spectrum of monkeypox is crucial for accurate diagnosis, appropriate management, and timely intervention.

Mild manifestations

Many cases of human monkeypox exhibit a relatively mild course, resembling a self-limiting viral illness[7]. The initial symptoms typically include fever, fatigue, headache, and muscle aches. These flu-like symptoms are often followed by the appearance of a rash, which progresses through distinct stages. Initially, small raised bumps (papules) develop, which then evolve into fluid-filled blisters (vesicles) and subsequently form pus-filled lesions (pustules)[15]. Over time, the pustules crust over and scab, eventually leading to their resolution.

In addition to the characteristic rash, some individuals may experience respiratory and gastrointestinal symptoms[21]. Respiratory involvement can manifest as cough, shortness of breath, and chest discomfort. Gastrointestinal symptoms may include abdominal pain, nausea, vomiting, and diarrhoea. These manifestations are generally self-limited and resolve without long-term complications. While less common, neurological complications can occur in some cases of monkeypox[22]. These may include headaches, confusion, dizziness, and seizures. Neurological involvement often warrants close monitoring and

specialized care, as it may require specific interventions and management strategies.

Severe manifestations

A subset of individuals infected with monkeypox may develop severe manifestations, with cardiovascular complications being particularly concerning[23]. These severe cases are characterized by the involvement of vital organs, potentially leading to life-threatening outcomes. Cardiovascular complications such as myocarditis and pericarditis can occur, resulting in symptoms such as chest pain, palpitations, and shortness of breath[6]. In rare instances, severe arrhythmias or cardiac dysfunction may ensue, necessitating intensive care and specialized treatment[24].

It is worth noting that the severity of monkeypox can be influenced by several factors, including the individual's overall health, underlying immune status, and pre-existing cardiovascular conditions[25]. Immunocompromised individuals, such as those with HIV/AIDS or receiving immunosuppressive therapy, may experience more severe and prolonged disease courses[15]. Similarly, individuals with pre-existing cardiovascular disease are at increased risk of developing severe cardiovascular complications.

Cardiovascular complications in human monkeypox

Human monkeypox, caused by the MPXV, is an infectious disease that can lead to a wide array of clinical manifestations. Among the various complications associated with monkeypox, cardiovascular involvement stands out as a significant concern[6]. While the majority of cases present with a mild course resembling a self-limiting viral illness, a subset of patients may develop severe cardiovascular complications that require specialized medical attention.

Myocarditis

Myocarditis, characterized by inflammation of the myocardium, is one of the most alarming cardiovascular complications seen in human monkeypox[26]. The monkeypox virus can directly infect heart cells, triggering an immune response that leads to inflammation and damage to the cardiac tissue. This inflammatory process can impair the heart's ability to pump blood efficiently, potentially leading to heart failure[27].

Patients with monkeypox-related myocarditis may experience symptoms such as chest pain, shortness of breath, fatigue, and swelling in the legs and ankles[6]. In severe cases, heart failure may develop, necessitating aggressive medical management and possibly even cardiac support, such as the use of ventricular assist devices or heart transplantation.

Pericarditis

Pericarditis refers to the inflammation of the pericardium, the thin membrane surrounding the heart[28]. Similar to myocarditis, monkeypox-induced pericarditis is thought to result from the virus's direct impact on the pericardial tissue. The inflamed pericardium can cause chest pain, which may worsen with deep breathing or when lying flat. In severe cases, excess fluid may accumulate in the pericardial space, a condition known as pericardial effusion, further compromising cardiac function[29].

Arrhythmias

Cardiac arrhythmias are another potential cardiovascular complication in monkeypox cases[30]. The presence of inflammation and damage to the heart muscle or conduction system can disrupt the heart's electrical impulses, leading to irregular heartbeats. These arrhythmias can manifest as palpitations, dizziness, lightheadedness, and in severe cases, may result in hemodynamic instability[31].

Implications for pre-existing cardiovascular conditions

Individuals with pre-existing cardiovascular conditions, such as hypertension, coronary artery disease, or heart failure, are at an increased risk of developing more severe cardiovascular complications if they contract monkeypox[1]. The virus's impact on an already compromised cardiovascular system can exacerbate underlying conditions and lead to more severe outcomes[15].

Diagnosing cardiovascular complications in monkeypox requires a high index of suspicion and careful evaluation by healthcare professionals[29]. Electrocardiography (ECG), echocardiography, and cardiac biomarkers are essential tools in identifying myocarditis, pericarditis, and arrhythmias[32]. Early recognition and intervention are crucial in improving patient outcomes and minimizing long-term cardiac sequelae.

Management of monkeypox-related cardiovascular complications primarily involves supportive care, addressing the inflammatory response, and optimizing cardiac function[6]. In severe cases, patients may require intensive care monitoring and treatment with medications to stabilize cardiac function. Collaboration between infectious disease specialists, cardiologists, and critical care teams is essential for providing comprehensive care to affected individuals[6].

Prevalence of cardiovascular manifestations in human monkeypox

The prevalence and severity of cardiovascular manifestations in human monkeypox vary among affected individuals. While the majority of monkeypox cases present with mild or moderate symptoms, a subset of patients may experience severe cardiovascular complications, demanding careful attention and specialized care.

Cardiovascular manifestations in monkeypox are relatively infrequent compared to other common symptoms like fever, rash, and respiratory symptoms. Studies have shown that cardiac involvement occurs in a minority of cases, usually ranging from 5 to 10% of patients with confirmed monkeypox[33].

The prevalence of cardiovascular complications may differ based on various factors, including age, underlying health conditions, and immune status. Immunocompromised individuals, especially those with compromised immune systems due to HIV/AIDS or immunosuppressive therapies, are at a higher risk of experiencing severe cardiac complications[15].

Mechanisms and pathophysiology of cardiovascular complications in human monkeypox

The mechanisms underlying cardiovascular complications in human monkeypox are complex and multifactorial. While the precise pathophysiological processes are not yet fully understood, several key mechanisms contribute to the development of cardiac involvement.

Direct viral effect

The MPXV can directly infect cardiac cells, leading to myocardial inflammation and damage. The virus gains entry into the heart cells and replicates, causing cell death and triggering an immune response[6]. This viral replication and inflammation contribute to myocarditis, the inflammation of the heart muscle.

Immune-mediated inflammation

In response to the viral infection, the immune system mounts an inflammatory response, aiming to control the virus. However, excessive or dysregulated immune activation can lead to collateral damage to the cardiac tissue. Immune cells release proinflammatory cytokines, such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumour necrosis factor-alpha (TNF-α), which can cause further myocardial injury and inflammation[34].

Autoimmune response

In some cases, the immune response triggered by Monkeypox infection can result in an autoimmune reaction, where the immune system mistakenly targets the heart tissue[35]. This autoimmune response can further contribute to myocardial inflammation and damage.

Impact on vasculature

Monkeypox-related inflammation may also affect the blood vessels supplying the heart, leading to endothelial dysfunction and vasculitis[36]. This can impair blood flow to the heart muscle, further compromising cardiac function and contributing to the development of cardiovascular complications[6]. It is important to note that the pathophysiology of cardiovascular complications in monkeypox may vary among individuals and can be influenced by factors such as the individual's immune response, viral load, and underlying health conditions.

The importance of vaccination in monkeypox

Vaccination plays a pivotal role in the management and control of monkeypox, serving as a crucial preventive measure against the spread of the virus and the development of severe complications[37].

Prevention of infection

Vaccination against monkeypox is the most effective way to prevent infection and subsequent transmission of the virus[38]. By introducing a weakened or inactivated form of the monkeypox virus into the body, vaccines stimulate the immune system to produce specific antibodies that can recognize and neutralize the virus upon exposure[39]. This pre-existing immunity significantly reduces the likelihood of developing the disease if exposed to the virus.

Limiting disease severity

Vaccination not only prevents infection but also mitigates the severity of the disease in those who may still contract monkeypox. Vaccinated individuals are more likely to experience milder symptoms and have a lower risk of developing severe complications, such as cardiovascular involvement, compared to unvaccinated individuals[40].

Herd immunity

Vaccination programs contribute to the establishment of herd immunity, a phenomenon where a sufficiently large portion of the population becomes immune to the virus[41]. Herd immunity acts as a protective shield, reducing the overall likelihood of virus transmission within a community. This is particularly beneficial for individuals who cannot receive vaccines due to medical reasons or immunocompromised conditions, as they are indirectly protected through reduced exposure to the virus.

Outbreak control

In the event of a monkeypox outbreak, vaccination campaigns play a critical role in containing the spread of the virus and limiting its impact on public health. Rapid and widespread vaccination of susceptible populations can help control the outbreak's progression and prevent further transmission, minimizing the strain on healthcare systems and reducing the risk of secondary infections[7].

Eradication potential

The successful eradication of smallpox, another orthopoxvirus-related disease, through global vaccination efforts serves as a powerful example of the potential impact of vaccination in combating monkeypox[4]. While eradicating monkeypox may present unique challenges due to its zoonotic nature, continued vaccination campaigns hold the promise of reducing its prevalence and eventually eliminating the disease in certain regions.

Vaccines against human monkeypox: types and development

Live-attenuated vaccines

Live-attenuated vaccines contain a weakened form of the monkeypox virus that can still replicate in the body but is significantly less virulent compared to the wild-type virus[42]. The vaccine stimulates an immune response similar to a natural infection, leading to the development of long-lasting immunity. The Modified Vaccinia Ankara (MVA) vaccine is an example of a live-attenuated vaccine that has been studied for its potential effectiveness against monkeypox.

Inactivated vaccines

Inactivated vaccines utilize a killed or inactivated form of the monkeypox virus[43]. These vaccines cannot replicate in the body but can still stimulate an immune response. Inactivated vaccines often require multiple doses to achieve sufficient immunity. Research and development of inactivated vaccines for monkeypox are ongoing, with the aim of improving their efficacy and safety profiles.

Protein subunit vaccines

Protein subunit vaccines focus on specific viral proteins that are crucial for inducing an immune response[44]. These vaccines typically contain purified or recombinant viral proteins or peptides. By targeting specific viral components, protein subunit

vaccines minimize the risk of adverse reactions associated with live-attenuated or inactivated vaccines. Research is underway to identify and evaluate key protein targets for the development of effective subunit vaccines against monkeypox.

Viral vector-based vaccines

Viral vector-based vaccines use a harmless virus, such as a modified adenovirus or vesicular stomatitis virus, as a delivery vehicle to introduce specific genes from the monkeypox virus into the body[45]. These genes encode viral proteins that elicit an immune response, leading to the production of antibodies and immune cells that can recognize and neutralize the monkeypox virus. Viral vector-based vaccines offer the advantage of potentially inducing robust and long-lasting immunity. Several viral vector-based vaccines have shown promise in preclinical and early clinical studies for monkeypox.

Effectiveness and challenges of current vaccination strategies against monkeypox

Vaccination is a critical component of monkeypox control strategies, but its effectiveness and implementation face certain challenges. Understanding both the successes and limitations of current vaccination approaches is essential for refining and optimizing monkeypox prevention efforts.

Effectiveness

(1) Protection against infection: Vaccination has shown to be effective in reducing the risk of monkeypox infection. When administered appropriately, vaccines stimulate the immune system to produce antibodies that recognize and neutralize the monkeypox virus, thereby preventing infection or reducing its severity.
(2) Herd immunity: Widespread vaccination contributes to the establishment of herd immunity, protecting vulnerable populations that cannot receive vaccines. When a large portion of the community is vaccinated, the virus finds it harder to spread, indirectly protecting those who may not be immunized.
(3) Mitigating disease severity: Vaccinated individuals who still contract monkeypox tend to experience milder symptoms and have a lower risk of developing severe complications compared to unvaccinated individuals. This is particularly important in preventing severe cardiovascular manifestations and other serious consequences of the disease.

Challenges

(1) Vaccine availability and accessibility: One of the primary challenges is ensuring that the monkeypox vaccine is available and accessible to the populations at risk. Manufacturing and distributing vaccines can be logistically complex and may be hindered by limited resources, particularly in regions with a high burden of monkeypox.
(2) Vaccine hesitancy: Vaccine hesitancy, the reluctance or refusal to vaccinate despite the availability of vaccines, can pose a significant obstacle to vaccination strategies. Misinformation, misconceptions, and concerns about vaccine safety may lead to suboptimal vaccine coverage, leaving communities vulnerable to monkeypox outbreaks.
(3) Limited efficacy of some vaccines: The efficacy of current monkeypox vaccines may vary, with certain vaccines showing higher levels of protection than others. Continuous research and development are required to identify and improve upon the most effective vaccine candidates.
(4) Need for boosters: Some monkeypox vaccines may require booster doses to maintain long-term immunity. Ensuring timely and widespread administration of booster shots can be challenging, especially in regions with limited healthcare infrastructure.
(5) Emerging strains: The monkeypox virus has shown genetic diversity, and new strains may emerge over time. Ensuring that vaccines remain effective against different strains is a continual challenge in the face of viral evolution.
(6) Duration of immunity: Understanding the duration of immunity provided by current vaccines is crucial in determining the optimal timing of booster doses and planning vaccination campaigns.

While vaccination remains an essential tool in monkeypox control, several challenges exist in implementing and maintaining effective vaccination strategies. Overcoming these challenges requires a multifaceted approach, including improving vaccine accessibility, addressing vaccine hesitancy, advancing research and development, and enhancing global collaboration.

Advancements in vaccination technologies and therapeutics against monkeypox

Advancements in vaccination technologies and therapeutics have the potential to revolutionize the prevention and management of monkeypox. These innovations aim to improve the effectiveness, safety, and accessibility of vaccines and therapeutics, ultimately enhancing our ability to control and combat the disease.

Novel vaccine platforms

Researchers are exploring innovative vaccine platforms that utilize cutting-edge technologies to enhance immune responses and increase vaccine efficacy. For example, DNA vaccines and RNA-based vaccines are being investigated for their ability to deliver viral genetic material into cells, triggering a robust immune response against the monkeypox virus. These platforms offer advantages such as rapid development, scalability, and potential for targeted modifications.

Virus-like particles (VLPs)

VLPs are engineered to mimic the structure of the monkeypox virus without containing genetic material, making them non-infectious and safe[46]. VLPs can stimulate a strong immune response by presenting viral antigens to the immune system, leading to the production of antibodies and memory immune cells. Research is ongoing to assess the effectiveness of VLP-based vaccines in preventing monkeypox infection.

Adjuvants

Adjuvants are substances that enhance the body's immune response to a vaccine[47]. Incorporating adjuvants in monkeypox vaccines can improve the immune response, leading to enhanced protection and potentially reducing the number of doses required. This advancement is particularly valuable in regions with limited

healthcare resources, where a more immunogenic vaccine can have significant benefits.

Therapeutics

In addition to vaccines, advancements in therapeutic interventions against monkeypox are being explored. Antiviral medications targeting the monkeypox virus have shown promise in laboratory studies and preclinical trials[48]. These antiviral agents aim to inhibit viral replication and reduce the severity and duration of monkeypox infections.

Monoclonal antibodies

Monoclonal antibodies are engineered to target specific viral antigens, helping the immune system neutralize the virus more effectively[49]. Passive immunization with monoclonal antibodies may offer a valuable treatment option for individuals at high risk of severe monkeypox complications or for use during outbreaks[50].

Multivalent vaccines

Multivalent vaccines are designed to protect against multiple strains or species of the monkeypox virus[51]. As the virus exhibits genetic diversity, developing vaccines that can confer broad protection against different strains is vital for ensuring sustained efficacy over time.

Computational biology and artificial intelligence (AI)

Advancements in computational biology and AI are aiding in the rapid design and development of vaccines and therapeutics[52]. These technologies can analyze viral genetic data, predict potential antigen targets, and facilitate the discovery of novel treatments more efficiently.

As research and development efforts continue, collaborations between academic institutions, pharmaceutical companies, and government agencies are essential to accelerate progress and ensure global access to effective monkeypox vaccines and therapeutics[33]. The integration of cutting-edge technologies in the field of vaccination and therapeutics holds tremendous promise for strengthening our ability to control and prevent monkeypox outbreaks and ultimately improve public health outcomes.

Therapeutic interventions for cardiovascular complications in monkeypox

The management of cardiovascular complications in monkeypox requires a comprehensive and multidisciplinary approach, with a focus on addressing specific cardiac issues and optimizing patient outcomes. Therapeutic interventions aim to stabilize cardiac function, reduce inflammation, and prevent long-term complications.

Supportive care

Supportive care is the foundation of treatment for cardiovascular complications in monkeypox. Close monitoring of vital signs, including heart rate, blood pressure, and oxygen saturation, is essential. Intravenous fluids may be administered to maintain adequate blood volume and blood pressure[1]. Oxygen supplementation can help maintain oxygen levels in the blood and support respiratory function.

Anti-inflammatory medications

Given the inflammatory nature of cardiac complications, anti-inflammatory medications may play a crucial role in managing the condition. Drugs like nonsteroidal anti-inflammatory drugs (NSAIDs) or corticosteroids can be used to reduce inflammation and alleviate symptoms[53].

Antiviral therapy

While antiviral therapy is primarily focused on managing the primary infection, it may also have a role in addressing viral replication in the cardiac tissue[54]. Antiviral medications can help reduce viral load and limit the impact of the monkeypox virus on the heart. However, their use for cardiac complications is still an area of ongoing research and investigation.

Cardiovascular medications

Specific medications used to manage cardiovascular conditions, such as beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, or diuretics, may be prescribed to stabilize heart function and control blood pressure. These medications can help manage symptoms and prevent further cardiac damage.

Cardiac monitoring and imaging

Frequent cardiac monitoring, including electrocardiography (ECG) and echocardiography, is essential to assess heart function and detect any arrhythmias or abnormalities promptly. Cardiac imaging, such as MRI or computed tomography (CT) scans, may be performed to evaluate the extent of cardiac involvement.

Invasive interventions

In severe cases with life-threatening cardiac arrhythmias or acute heart failure, invasive interventions like catheter-based procedures or implantable cardiac devices may be required. These interventions aim to restore normal heart rhythm or provide mechanical support to the heart.

Rehabilitation and follow-Up

Following the acute phase of monkeypox-related cardiovascular complications, rehabilitation programs may be recommended to help patients recover and regain strength. Regular follow-up visits with healthcare providers are crucial for ongoing evaluation and management of potential long-term cardiovascular effects.

Promising antiviral agents in monkeypox treatment

Cidofovir

Cidofovir is an antiviral medication that has shown activity against various DNA viruses, including orthopoxviruses like Monkeypox[55]. It works by inhibiting viral DNA replication and has demonstrated effectiveness against Monkeypox in laboratory studies and animal models. However, its use in human monkeypox cases is still limited, and further research is needed to determine its optimal dosing and efficacy.

Brincidofovir

Brincidofovir is a derivative of cidofovir that has shown improved oral bioavailability[56]. It exhibits broad-spectrum antiviral activity against DNA viruses and has been evaluated in clinical trials for the treatment of other viral infections. Its potential efficacy against Monkeypox is being investigated, but further studies are necessary to establish its role in the management of the disease.

ST-246

ST-246 is a novel antiviral compound that specifically targets orthopoxviruses, including Monkeypox[57]. It works by inhibiting viral egress from infected cells, preventing the release of new virus particles. Preclinical studies have demonstrated its effectiveness in animal models, and it has shown potential for use as a therapeutic agent against Monkeypox. However, more research is required to determine its safety and efficacy in human subjects.

Tecovirimat (TPOXX)

Tecovirimat is an antiviral drug approved by the U.S. Food and Drug Administration (FDA) for the treatment of smallpox, which is also caused by an orthopoxvirus[58]. It has shown effectiveness against other orthopoxviruses, including Monkeypox, in laboratory studies. Although it has not yet been approved specifically for the treatment of Monkeypox, its potential as a therapeutic option is being explored.

Public health strategies and outbreak control for monkeypox

Effective public health strategies are crucial in containing monkeypox outbreaks and preventing its further spread[59]. A comprehensive approach involving surveillance, prevention, rapid response, and public awareness is necessary to manage outbreaks and protect public health. Here are key public health strategies for monkeypox outbreak control:

Surveillance and early detection

Early detection and reporting of suspected monkeypox cases are essential for prompt outbreak control. Healthcare providers, laboratories, and public health authorities must be vigilant in identifying and reporting potential cases to enable rapid intervention[60].

Laboratory diagnosis

Accurate and timely laboratory testing is vital for confirming monkeypox cases and differentiating them from other similar diseases. Public health laboratories must be equipped to handle and test specimens for the monkeypox virus.

Case isolation and quarantine

Isolating confirmed and suspected cases is critical to prevent further transmission. Contact tracing and quarantine of close contacts help identify and contain potential secondary cases.

Vaccination campaigns

Vaccination is a key preventive measure in controlling monkeypox outbreaks. Vaccination campaigns should target high-risk populations, including healthcare workers, first responders, and individuals living in outbreak-affected areas[61].

Public health education and awareness

Public education campaigns play a vital role in informing the public about monkeypox, its symptoms, transmission, and preventive measures[9]. Emphasizing the importance of vaccination and early reporting of symptoms can help curb the spread of the disease.

Travel restrictions and border control

In the context of international outbreaks, travel restrictions and border control measures may be necessary to limit the importation of cases and prevent global spread. Collaboration between affected countries and international health organizations is essential in implementing such measures effectively.

Vector control

Investigations into the source of the outbreak, especially if it involves zoonotic transmission, are crucial. Vector control measures, such as controlling rodent populations or avoiding contact with potential reservoir hosts, may help reduce the risk of transmission.

Rapid response teams

Establishing rapid response teams of epidemiologists, clinicians, and public health experts can expedite outbreak investigations and facilitate coordinated control efforts.

Data sharing and collaboration

Timely and transparent data sharing among affected countries and international health organizations fosters collaboration in outbreak control and provides valuable insights for future prevention and management.

Research and development

Continuous research and development of vaccines, antiviral agents, and diagnostic tools are critical for enhancing outbreak preparedness and response.

By implementing these comprehensive public health strategies, health authorities can effectively manage monkeypox outbreaks, minimize the impact on public health, and protect vulnerable populations. A coordinated and collaborative approach is essential for successful outbreak control and preventing the further spread of the disease.

The role of research and collaboration in monkeypox control

Research and collaboration play vital roles in the effective control and management of monkeypox. Advancements in scientific knowledge, vaccine development, diagnostics, and outbreak response strategies heavily rely on research efforts and

collaboration among various stakeholders. Here are key aspects highlighting the significance of research and collaboration:

Understanding the virus and disease dynamics

Research provides essential insights into the monkeypox virus, its transmission, epidemiology, and pathogenesis. By studying the virus's genetic makeup, host interactions, and disease progression, researchers can develop a comprehensive understanding of monkeypox and its impact on human health[62]. This knowledge is fundamental for developing effective control strategies.

Vaccine development and improvement

Research efforts drive the development and improvement of monkeypox vaccines. Investigating novel vaccine platforms, studying immune responses, and conducting preclinical and clinical trials contribute to the identification of safe and effective vaccines[63]. Collaboration among researchers, pharmaceutical companies, and regulatory authorities is critical for advancing vaccine candidates and ensuring their availability and accessibility.

Diagnostic tools and techniques

Research enables the development and validation of accurate and rapid diagnostic tests for monkeypox. Collaborative efforts in diagnostic research facilitate the early detection and confirmation of cases, enabling timely intervention and outbreak control. Ongoing research helps refine and improve diagnostic techniques, making them more efficient and accessible in resource-limited settings.

Antiviral therapy and treatment strategies

Collaborative research efforts aid in the identification and evaluation of potential antiviral agents for monkeypox treatment[64]. Studying the efficacy and safety of existing antiviral drugs and exploring novel therapeutic approaches contribute to the development of effective treatment strategies. Collaboration among researchers, clinicians, and regulatory agencies is crucial in advancing therapeutic options for managing monkeypox complications.

Surveillance and outbreak response

Research informs the design and implementation of surveillance systems for early detection, monitoring, and response to monkeypox outbreaks[33,65]. Collaborative research efforts facilitate the sharing of surveillance data, outbreak investigations, and the development of standardized protocols. Collaboration among local, national, and international stakeholders strengthens surveillance networks and enhances outbreak response capabilities.

Global collaboration and knowledge sharing

International collaboration plays a vital role in sharing research findings, best practices, and experiences in monkeypox control. Collaborative research initiatives promote the exchange of information, data, and expertise among scientists, public health agencies, and policymakers worldwide. This collaboration fosters a coordinated and evidence-based approach to monkeypox control on a global scale.

Capacity building and training

Research collaborations contribute to capacity building and training programs, empowering healthcare professionals and researchers in affected regions. Strengthening local research capabilities, laboratory networks, and public health infrastructure enhances preparedness, response, and long-term control measures.

The role of research and collaboration is indispensable in advancing our understanding of monkeypox, developing effective interventions, and improving outbreak response strategies. Continued investment in research, fostering collaborative partnerships, and knowledge sharing are critical to effectively control monkeypox and minimize its impact on public health.

Challenges and considerations for vaccination implementation

Vaccine distribution and accessibility

Ensuring an adequate supply of vaccines and establishing efficient distribution networks can be challenging, especially in resource-limited settings or during large-scale vaccination campaigns. Building robust supply chains and cold storage facilities is essential for the effective distribution of vaccines[66]. Reaching remote or inaccessible populations can pose challenges in vaccine distribution. Difficult terrain, lack of transportation infrastructure, and remote communities may hinder the equitable delivery of vaccines. Innovative strategies such as mobile vaccination clinics or outreach programs may be required to overcome these barriers. Managing vaccine stockpiles, expiration dates, and appropriate waste disposal can be complex. Ensuring efficient vaccine utilization and minimizing wastage are crucial to optimize resources and maximize vaccine coverage.

Vaccine hesitancy and public perception

Vaccine hesitancy, fuelled by misinformation and mistrust, poses a significant challenge to vaccination implementation[67]. Addressing concerns, providing accurate information, and countering misinformation through transparent and effective communication campaigns are essential. Cultural and religious beliefs can influence vaccine acceptance. Understanding and respecting diverse cultural perspectives and working collaboratively with community leaders and influencers are important for fostering trust and acceptance of vaccines. Ensuring vaccine safety and addressing public concerns about adverse events or rare side effects is crucial. Transparent communication about the rigorous regulatory processes, ongoing monitoring of vaccine safety, and prompt reporting and investigation of any adverse events are essential for maintaining public trust.

Addressing ethical and equity issues

Making fair and equitable decisions regarding vaccine prioritization and allocation is challenging. Considerations should include the vulnerability of populations, healthcare workers, and public health impact. Balancing the need for equitable access with the urgency of protecting high-risk groups is crucial. Ensuring equitable global access to vaccines is essential for controlling the spread of diseases like monkeypox. Addressing the disparities in vaccine distribution and collaborating on global initiatives, such

as the COVAX facility, can help bridge the equity gap and prevent the emergence of new variants[68–71]. Reaching vulnerable populations, including marginalized communities, refugees, and individuals with limited healthcare access, requires targeted efforts. Addressing language barriers, cultural sensitivities, and providing vaccination services in accessible and trusted locations are important considerations. Upholding ethical principles, such as informed consent, privacy protection, and ensuring the welfare of participants, is crucial in vaccination implementation. Adhering to ethical guidelines and involving community representatives and ethical review boards can help navigate these considerations.

Lessons from the past and future prospects

Learning from other zoonotic disease outbreaks

Lessons from past zoonotic disease outbreaks, such as SARS, MERS, and Ebola, can provide valuable insights for managing and controlling monkeypox[72–74]. These outbreaks highlighted the importance of early detection, rapid response, and international collaboration. Investing in robust surveillance systems, strengthening healthcare infrastructure, and fostering global cooperation are crucial in effectively containing zoonotic diseases, including monkeypox.

Potential impact of vaccination on cardiovascular outcomes

Vaccination against monkeypox not only protects against the primary infection but may also have a significant impact on cardiovascular outcomes[75]. As monkeypox can cause severe cardiovascular complications, effective vaccination strategies could potentially reduce the incidence and severity of cardiac manifestations. Future research is needed to assess the long-term cardiovascular benefits of vaccination and its potential role in mitigating the burden of monkeypox-related heart complications.

Preparedness for emerging threats

The emergence of monkeypox and other zoonotic diseases underscores the importance of global preparedness for emerging threats[76]. Investing in research, vaccine development, and public health infrastructure is essential in proactively addressing potential outbreaks. Strengthening laboratory capacity, surveillance networks, and international collaboration can enhance our ability to detect, respond to, and control emerging infectious diseases effectively.

Conclusion

In conclusion, vaccination stands as the cornerstone of monkeypox control. As a zoonotic disease with potential severe complications, the role of vaccination in preventing monkeypox transmission and reducing the impact of the disease cannot be overstated. Advancements in vaccine development and research, combined with international collaboration and preparedness, are critical for effectively managing monkeypox outbreaks and protecting public health. While challenges in vaccine distribution, hesitancy, and equity exist, addressing these issues requires a coordinated effort from governments, public health authorities, healthcare providers, and communities worldwide. By learning from past zoonotic disease outbreaks and leveraging vaccination as a powerful tool, we can better prepare for emerging threats, reduce the burden of monkeypox, and safeguard global health. Through ongoing research, collaboration, and commitment, we can pave the way towards a safer and healthier future, where the threat of monkeypox is under control, and its impact on cardiovascular outcomes is minimized.

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Consent

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References

[1] Adnan N, Haq ZU, Malik A, *et al*. Human monkeypox virus: an updated review. Medicine (Baltimore) 2022;101:e30406.
[2] McCollum AM, Damon IK. Human monkeypox. Clin Infect Dis 2014; 58:260–7; Epub 2013 Oct 24. Erratum in: Clin Infect Dis. 2014 Jun;58 (12):1792.
[3] Nalca A, Rimoin AW, Bavari S, *et al*. Reemergence of monkeypox: prevalence, diagnostics, and countermeasures. Clin Infect Dis 2005;41: 1765–71.
[4] Rizk JG, Lippi G, Henry BM, *et al*. Prevention and treatment of monkeypox. Drugs 2022;82:957–63.

[5] Vaughan A, Aarons E, Astbury J, *et al*. Human-to-Human Transmission of Monkeypox Virus, United Kingdom, October 2018. Emerg Infect Dis 2020;26:782–5.
[6] Maqbool KU, Arsh H, Kumar D, *et al*. Cardiovascular manifestations of human monkeypox virus: an updated review. Curr Probl Cardiol 2023; 48:101869.
[7] See KC. Vaccination for monkeypox virus infection in humans: a review of key considerations. Vaccines (Basel) 2022;10:1342.
[8] Poland GA, Kennedy RB, Tosh PK. Prevention of monkeypox with vaccines: a rapid review. Lancet Infect Dis 2022;22:e349–58.
[9] Parker S, Nuara A, Buller RM, *et al*. Human monkeypox: an emerging zoonotic disease. Future Microbiol 2007;2:17–34.
[10] Jeyaraman M, Selvaraj P, Halesh MB, *et al*. Monkeypox: an emerging global public health emergency. Life (Basel) 2022;12:1590.
[11] Thakur M, Das P, Sobti RC, *et al*. Human monkeypox: epidemiology, transmission, pathogenesis, immunology, diagnosis and therapeutics. Mol Cell Biochem 2023;478:2097–110.
[12] Lim EY, Whitehorn J, Rivett L. Monkeypox: a review of the 2022 outbreak. Br Med Bull 2023;145:17–29.
[13] Cabanillas B, Murdaca G, Guemari A, *et al*. A compilation answering 50 questions on monkeypox virus and the current monkeypox outbreak. Allergy 2023;78:639–62.
[14] Chadha J, Khullar L, Gulati P, *et al*. Insights into the monkeypox virus: Making of another pandemic within the pandemic? Environ Microbiol 2022;24:4547–60.
[15] Wang X, Lun W. Skin manifestation of human monkeypox. J Clin Med 2023;12:914.
[16] Tarín-Vicente EJ, Alemany A, Agud-Dios M, *et al*. Clinical presentation and virological assessment of confirmed human monkeypox virus cases in Spain: a prospective observational cohort study. Lancet 2022;400:661–9; Epub 2022 Aug 8. Erratum in: Lancet. 2022 Dec 10;400(10368):2048.
[17] Kozlov M. How does monkeypox spread? What scientists know. Nature 2022;608:655–6.
[18] Shang Y, Li H, Zhang R. Effects of pandemic outbreak on economies: evidence from business history context. Front Public Health 2021;9: 632043.
[19] Alshahrani AM. Cost-benefit analysis of interventions to mitigate the monkeypox virus. Int J Environ Res Public Health 2022;19:13789.
[20] Ahmed SK, Mohamed MG, Dabou EA, *et al*. Monkeypox (mpox) in immunosuppressed patients. F1000Res 2023;12:127.
[21] Cheema AY, Ogedegbe OJ, Munir M, *et al*. Monkeypox: a review of clinical features, diagnosis, and treatment. Cureus 2022;14:e26756.
[22] Sepehrinezhad A, Ashayeri Ahmadabad R, Sahab-Negah S. Monkeypox virus from neurological complications to neuroinvasive properties: current status and future perspectives. J Neurol 2023;270:101–8. doi:10.1007/s00415-022-11339-wEpub 2022 Aug 21. PMID: 35989372; PMCID: PMC9393054.
[23] Soheili M, Nasseri S, Afraie M, *et al*. Monkeypox: virology, pathophysiology, clinical characteristics, epidemiology, vaccines, diagnosis, and treatments. J Pharm Pharm Sci 2022;25:297–322.
[24] Shrestha AB, Mehta A, Zahid MJ, *et al*. Concerns over cardiovascular manifestations associated with monkeypox immunization: a literature review. Ann Med Surg (Lond) 2023;85:2797–801.
[25] Jang W, Kandimalla L, Rajan S, *et al*. Monkeypox in an immunocompromised patient with underlying human immunodeficiency virus and syphilis infections in Southern Florida of the United States: a case report. AIDS Res Ther 2023;20:12.
[26] Rodriguez-Nava G, Kadlecik P, Filardo TD, *et al*. Myocarditis Attributable to Monkeypox Virus Infection in 2 Patients, United States, 2022. Emerg Infect Dis 2022;28:2508–12.
[27] Zivkov-Saponja D, Stojsić-Milosavljević A, Stojsić D, *et al*. Level of left ventricular dysfunction in endomyocardial biopsy-proven myocarditis. Med Pregl 1999;52:429–36; English, Croatian.
[28] Shaik TA, Voloshyna D, Nasr TH, *et al*. Monkeypox-associated pericarditis: a Maiden case. Cureus 2022;14:e29638.
[29] Sayad R, Siddiq A, Hashim A, *et al*. Can the current monkeypox affect the heart? A systematic review of case series and case report. BMC Cardiovasc Disord 2023;23:328.
[30] El-Qushayri AE, Tawfik AG, Mahmoud-Elsayed H. Cardiovascular manifestations of monkeypox virus outbreak: an overview of the reported cases. Heart Lung 2023;59:67–72.
[31] McGuirk SM, Muir WW. Diagnosis and treatment of cardiac arrhythmias. Vet Clin North Am Equine Pract 1985;1:353–70.
[32] Pinamonti B, Alberti E, Cigalotto A, *et al*. Echocardiographic findings in myocarditis. Am J Cardiol 1988;62:285–91.
[33] Roper RL, Garzino-Demo A, Del Rio C, *et al*. Monkeypox (Mpox) requires continued surveillance, vaccines, therapeutics and mitigating strategies. Vaccine 2023;41:3171–7.
[34] Kremer JP, Jarrar D, Steckholzer U, *et al*. Interleukin-1, -6 and tumor necrosis factor-alpha release is down-regulated in whole blood from septic patients. Acta Haematol 1996;95:268–73.
[35] Lutz M, Hayney MS, Farraye FA, *et al*. A note on monkeypox for our patients with inflammatory bowel disease. Inflamm Bowel Dis 2023;29: 179–80.
[36] Langohr IM, Stevenson GW, Thacker HL, *et al*. Extensive lesions of monkeypox in a prairie dog (Cynomys sp). Vet Pathol 2004;41:702–7.
[37] Reina J, Iglesias C. Vaccines against monkeypox. Med Clin (Engl Ed) 2023;160:305–9.
[38] Reina J, Iglesias C. Vaccines against monkeypox. Med Clin (Barc) 2023; 160:305–9; English, Spanish.
[39] Saadh MJ, Ghadimkhani T, Soltani N, *et al*. Progress and prospects on vaccine development against monkeypox infection. Microb Pathog 2023; 180:106156.
[40] De Clercq E, Jiang Y, Li G. Therapeutic strategies for human poxvirus infections: Monkeypox (mpox), smallpox, molluscipox, and orf. Travel Med Infect Dis 2023;52:102528.
[41] Ashby B, Best A. Herd immunity. Curr Biol 2021;31:R174–7.
[42] Rao AK, Petersen BW, Whitehill F, *et al*. Use of JYNNEOS (Smallpox and Monkeypox Vaccine, Live, Nonreplicating) for Preexposure Vaccination of Persons at Risk for Occupational Exposure to Orthopoxviruses: Recommendations of the Advisory Committee on Immunization Practices - United States, 2022. MMWR Morb Mortal Wkly Rep 2022; 71:734–42; Erratum in: MMWR Morb Mortal Wkly Rep. 2022 Jul 08;71(27):886.
[43] Sudarmaji N, Kifli N, Hermansyah A, *et al*. Prevention and treatment of monkeypox: a systematic review of preclinical studies. Viruses 2022;14:2496.
[44] Heraud JM, Edghill-Smith Y, Ayala V, *et al*. Subunit recombinant vaccine protects against monkeypox. J Immunol 2006;177:2552–64.
[45] Raadsen MP, Dahlke C, Fathi A, *et al*. Brief report: Monkeypox virus cross-neutralizing antibodies in clinical trial subjects vaccinated with modified vaccinia virus ankara encoding MERS-Coronavirus Spike Protein. J Infect Dis 2023;228:jiad052–590.
[46] Nooraei S, Bahrulolum H, Hoseini ZS, *et al*. Virus-like particles: preparation, immunogenicity and their roles as nanovaccines and drug nanocarriers. J Nanobiotechnol 2021;19:59.
[47] Di Pasquale A, Preiss S, Tavares Da Silva F, *et al*. Vaccine adjuvants: from 1920 to 2015 and beyond. Vaccines (Basel) 2015;3:320–43.
[48] Siegrist EA, Sassine J. Antivirals with activity against Mpox: a clinically oriented review. Clin Infect Dis 2023;76:155–64.
[49] LiverTox. Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2023. 2012–. Monoclonal Antibodies.
[50] Hughes LJ, Goldstein J, Pohl J, *et al*. A highly specific monoclonal antibody against monkeypox virus detects the heparin binding domain of A27. Virology 2014;464-465:264–73.
[51] Jiang J, Ramos SJ, Bangalore P, *et al*. Multivalent DNA vaccines as a strategy to combat multiple concurrent epidemics: mosquito-borne and hemorrhagic fever viruses. Viruses 2021;13:382.
[52] Thomas S, Abraham A, Baldwin J, *et al*. Artificial intelligence in vaccine and drug design. Methods Mol Biol 2022;2410:131–46.
[53] Reynolds MG, McCollum AM, Nguete B, *et al*. Improving the care and treatment of monkeypox patients in low-resource settings: applying evidence from contemporary biomedical and smallpox biodefense research. Viruses 2017;9:380.
[54] Ortiz-Saavedra B, León-Figueroa DA, Montes-Madariaga ES, *et al*. Antiviral treatment against monkeypox: a scoping review. Trop Med Infect Dis 2022;7:369.
[55] De Clercq E. Cidofovir in the treatment of poxvirus infections. Antiviral Res 2002;55:1–13.
[56] Hutson CL, Kondas AV, Mauldin MR, *et al*. Pharmacokinetics and efficacy of a potential smallpox therapeutic, brincidofovir, in a lethal monkeypox virus animal model. mSphere 2021;6:e00927–20; Erratum in: mSphere. 2021 Feb 17;6(1).
[57] Berhanu A, Prigge JT, Silvera PM, *et al*. Treatment with the smallpox antiviral tecovirimat (ST-246) alone or in combination with ACAM2000 vaccination is effective as a postsymptomatic therapy for monkeypox virus infection. Antimicrob Agents Chemother 2015;59:4296–300.

[58] DeLaurentis CE, Kiser J, Zucker J. New perspectives on antimicrobial agents: tecovirimat for treatment of human monkeypox virus. Antimicrob Agents Chemother 2022;66:e0122622.
[59] Silva SJRD, Kohl A, Pena L, *et al*. Clinical and laboratory diagnosis of monkeypox (mpox): current status and future directions. iScience 2023; 26:106759.
[60] Nadar S, Khan T, Omri A. Reemergence of monkeypox: prevention and management. Expert Rev Anti Infect Ther 2022;20:1425–33.
[61] Bunge EM, Hoet B, Chen L, *et al*. The changing epidemiology of human monkeypox-A potential threat? A systematic review. PLoS Negl Trop Dis 2022;16:e0010141.
[62] Thornhill JP, Barkati S, Walmsley S, *et al*SHARE-net Clinical Group. Monkeypox Virus Infection in Humans across 16 Countries - April-June 2022. N Engl J Med 2022;387:679–91.
[63] Lozano JM, Muller S. Monkeypox: potential vaccine development strategies. Trends Pharmacol Sci 2023;44:15–9.
[64] Chiem K, Nogales A, Lorenzo M, *et al*. Antivirals against monkeypox infections. bioRxiv [Preprint] 2023. 2023.04.19.537483. doi:10.1101/2023.04.19.537483.PMID: 37131608; PMCID: PMC10153157.
[65] Besombes C, Mbrenga F, Schaeffer L, *et al*. National Monkeypox Surveillance, Central African Republic, 2001-2021. Emerg Infect Dis 2022;28:2435–45.
[66] Tovani-Palone MR, Doshi N, Pedersini P. Inequity in the global distribution of monkeypox vaccines. World J Clin Cases 2023;11:4498–503.
[67] Riad A, Drobov A, Rozmarinová J, *et al*. Monkeypox Knowledge and Vaccine Hesitancy of Czech Healthcare Workers: A Health Belief Model (HBM)-Based Study. Vaccines (Basel) 2022;10:2022.
[68] Yoo KJ, Mehta A, Mak J, *et al*. COVAX and equitable access to COVID-19 vaccines. Bull World Health Organ 2022;100:315–28.
[69] Malik A, Malik J, Ishaq U. Acceptance of COVID-19 vaccine in Pakistan among health care workers. PLoS One 2021;16: e0257237.
[70] Ochola EA. Vaccine Hesitancy in Sub-Saharan Africa in the Context of COVID-19 Vaccination Exercise: A Systematic Review. Diseases 2023; 11:32.
[71] Rikitu Terefa D, Shama AT, Feyisa BR, *et al*. COVID-19 Vaccine Uptake and Associated Factors Among Health Professionals in Ethiopia. Infect Drug Resist 2021;14:5531–41.
[72] Patel R, Kaki M, Potluri VS, *et al*. A comprehensive review of SARS-CoV-2 vaccines: Pfizer, Moderna & Johnson & Johnson. Hum Vaccin Immunother 2022;18:2002083.
[73] Choi JA, Kim JO. Middle East Respiratory Syndrome coronavirus vaccine development: updating clinical studies using platform technologies. J Microbiol 2022;60:238–46.
[74] Malenfant JH, Joyce A, Choi MJ, *et al*. Use of Ebola Vaccine: Expansion of Recommendations of the Advisory Committee on Immunization Practices To Include Two Additional Populations - United States, 2021. MMWR Morb Mortal Wkly Rep 2022;71:290–2.
[75] Sharff KA, Tandy TK, Lewis PF, *et al*. Cardiac events following JYNNEOS vaccination for prevention of Mpox. Vaccine 2023;41: 3410–2.
[76] Signorini L, Dolci M, Favi E, *et al*. Viral genomic characterization and replication pattern of human polyomaviruses in kidney transplant recipients. Viruses 2020;12:1280.