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What do we need to know about the monkeypox virus infection in humans?

O que precisamos saber sobre a infecção humana pelo vírus monkeypox?

¿Qué debemos saber sobre la infección humana por el virus de monkeypox?

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The first reported monkeypox virus infection in humans occurred in 1970 in Zaire (present-day Democratic Republic of the Congo) and affected a 9-month-old child [1]. Monkeypox is a classic zoonosis, as most infections in humans occur due to the contact with infected animals. In recent years, human-to-human transmission became more frequently reported, increasing the global concern about its spreading potential [2].

Over the last five decades, the number of reported human cases increased, especially in Democratic Republic of the Congo and Nigeria, where this disease is endemic and transmitted by small mammals. Although the wild reservoirs of infection are not fully known, forest squirrels and wild rodents stand out among them [3]. Monkeypox is not a typical monkey disease, even though it was observed for the first time in 1958 in these animals. The mean age of people infected with this disease increased from 4 (1970) to 21 years old (2010-2019). This increase in the number of cases may be due to the discontinued application of the smallpox vaccine, which provided cross-protection against monkeypox, the genetic evolution of the virus, or environmental factors, such as deforestation, which increased the number of synanthropic rodents and its interaction with humans [4].

Before the current epidemic "outside Africa", the last outbreak of this disease occurred in Nigeria in 2017-2018. Before this outbreak, most cases of monkeypox affected children and occurred in rural areas, which shows a transmission mode mainly associated to contact with animals [2,5]. However, the 2017-2018 outbreak presented a high number of cases in urban areas and among young men, similarly to the current epidemic. This change in the epidemiological profile raised the hypothesis that human-to-human transmission is probably becoming more frequent. Simultaneously, the relatively high frequency of genital lesions among patients suggest the possibility of transmission by prolonged sexual contact [2,5,6].

Outside Africa, the first cases of humans infected by monkeypox appeared in 2003 in the United States, after the importation of African rodents. From 2018 to 2021, the United Kingdom, the United States, Singapore, and Israel reported outbreaks of this disease associated with trips to Nigeria and their indexes were attributed to animal-to-human transmission [7].

Since May 2022, non-endemic regions have been reporting monkeypox outbreaks; thus, the World Health Organization (WHO) declared Public Health Emergency of International Concern (PHEIC) on July 23, 2022 [8]. Until August 24, 2022, at least 100 countries had already reported more than 45,000 cases – most of them in the United States, Spain, Brazil, Germany, the United Kingdom, France, Peru,

Canada, and Netherlands – and 12 confirmed deaths [9]. Although some cases were related to trips to African endemic regions, the rapid emergence of new cases and the broad geographical spread suggest that the monkeypox virus was probably already circulating and human-to-human transmission was not identified [10]. To date, most confirmed cases in the current outbreak occurred among young men (mean age of 36 years old) [10]. In those cases in which patients declared their sexual orientation, 95.8% involved men who had sexual contact with other men [10]. Some current monkeypox outbreaks are related to situations that enhance its spread – the so-called super-spreaders [11] – in which one or a few individuals transmit the infection to a high number of secondary cases, such as large-scale events, festivals, and raves [12,13].

The sequenced genomes of cases in Belgium, France, Portugal, and the United States were similar to cases that occurred outside Africa in 2018 and 2019, which were related to trips to Western Africa [14]. These cases presented an estimated 3.6% fatality rate, in opposition to the 10% fatality rate in Central Africa [4]. This similarity favors the hypothesis that the current epidemic outside Africa started from an individual who was infected while visiting African endemic regions, however, the hypothesis of the existence of a cryptic extended transmission period involving humans or animals in non-endemic countries after the viral introductions from previous years cannot be excluded [14]. The size of the monkeypox genome (six times bigger than the SARS-CoV-2 genome) and the lack of investment in a structure that allows an appropriate genomic surveillance in African countries hinders studies on African lineages for the analysis of genetic mutations, which could explain the current unprecedented spread of this virus outside Africa [13]. After years alerting about the spread of monkeypox in Africa, overcoming inequality of investment to develop resilient and integrated local laboratory systems in African countries as a support to face new health crises is an urgent challenge for global health [13,15].

The monkeypox virus is an orthopoxvirus with a clinical presentation similar to the smallpox virus. After an incubation period of five to 21 days, a nonspecific acute febrile syndrome occurs – a period of great potential for contagion [16]. Fever, myalgia, asthenia, headache, and adenomegaly may last from one to five days. Similarly to chickenpox, polymorphous skin rashes emerge one to three days after the onset of fever, mainly in the face and mouth, and spreads centrifugally, including palms and soles of the feet. Cutaneous and mucosal lesions, with variable number and confluence, tend to evolve sequentially from macules, papules, vesicles, pustules to crusts [16,17]. In this epidemic, the variations in clinical presentation have been reported as genital, perineal, perianal, mouth, and eye lesions, the coexistence of lesions in different stages of progression, skin rashes emerging before fever, anorectal pain, and bleeding [16]. Smallpox, chickenpox, herpes zoster, measles, syphilis, scabies, and allergic reactions are possible differential diagnoses. Monkeypox tends to be self-limited, with complete elimination of the infection from two to four weeks. Secondary infection, bronchopneumonia, encephalitis, and sepsis are the complications reported. Children, pregnant women, immunocompromised people, and people with a history of atopic dermatitis or eczema have an increased risk of developing severe forms of the disease [17,18].

Monkeypox virus is transmitted by direct and prolonged contact with secretions eliminated by skin and mucosal lesions, body fluids, or respiratory droplets of infected people or animals. The transmission ends when crusted lesions disappear and a new layer of healthy skin is formed [16]. Different from SARS-CoV-2, poxviruses can survive long periods outside the body, on surfaces such as contaminated sheets and door handles, allowing the transmission through fomites [16]. Transplacental transmission is possible, as well as the transmission by scratches or bites of infected animals or during the preparation, handling, and consumption of meat or products derived from these animals. Although the virus was detected in several body fluids, including semen, sexual transmission is yet to be fully understood [9].

The polymerase chain reaction, followed by sequencing, is the gold standard for the diagnosis. The examination is preferably performed with samples of fragments or secretion of skin lesions (vesicles and pustules). Blood samples can be used, but they usually provide inconclusive results due to the short periods of viremia [17]. Serological antigen and detection tests are useful in specific situations (detection of IgM or IgG in paired tests), but they can provide false-positive results in people immunized against smallpox [17,18]. Therapeutic measures are aimed to symptom relief and prevention of complications. No specific medication exist to treat monkeypox, but some antivirals used for smallpox have recommended for patients with more severe forms of the disease and mucosal involvement [19].

Smallpox immunization is about 85% effective for preventing monkeypox [20,21]. However, smallpox was considered eradicated in 1980 and, since then, the systematic immunization was discontinued [5]. WHO do not currently recommend mass immunization and the transmission of this disease must be contained by health surveillance measures, including the early diagnosis of cases, their isolation and treatment, and contact tracing [22]. Anti-orthopoxvirus vaccines are recommended for people at higher risks of infection, such as close individuals, health professionals, and laboratory professionals [20,22]. The inequity in the availability of these vaccines is a serious global health problem, as the COVID-19 pandemic clearly showed [23]. Immunization doses have been stored only in Northern Hemisphere countries, therefore, African countries affected by monkeypox does not have the necessary access to such vaccines to tackle epidemics throughout the continent [5].

Surveillance actions are essential to tackle and to contain the spread of monkeypox [16,24]. Nowadays, the rapid diagnosis of cases for isolation and treatment, contact tracing to prevent further transmission, protection of health professionals under greater exposure to the disease, identification of risk groups, and implementation of effective control measures are the main goals of health surveillance [16]. The immediate notification of suspected cases is crucial for the success of actions to control the spread of monkeypox [20]. As most infections present mild symptoms and few clinical signs (adenopathy and localized skin rashes), the search for health care may not occur, increasing the difficulties in containing the epidemic. Emergency communication campaigns for the general population and specific training for health professionals, as well as the establishment of care flows and diagnoses, implementing clinical and therapeutic protocols, organizing a unified information system, strengthening epidemiological and genomic surveillance actions, and investing in research, are essential to allow appropriate actions to tackle the epidemic [16,24].

From an individual point of view, the main prevention measures concern avoiding contact with infected individuals or animals. In households with suspected cases of monkeypox, people must not share personal items and feeding devices, but must wear masks, regularly sanitize hands, and, if possible, use a separate bathroom and clean and disinfect all surfaces [25]. Infected, confirmed, or suspected patients must be isolated and people involved with personal and health care must wear personal protective equipment and eventually be vaccinated [25]. The households of infected people must undergo an appropriate disinfection process [26].

The Brazilian Ministry of Health created a special Situation Room on May 23, 2022, to monitor the epidemiological situation of monkeypox in Brazil and worldwide, to analyze cases, to prepare technical documents to promote public actions, and to standardize information, reporting, and research flows [27]. The Brazilian Health Regulatory Agency (ANVISA) created a specific technical standard for health services in order to control possible nosocomial outbreaks [28]. On July 11, 2022, the activities of the Situation Room were discontinued and its assignments were transferred to the Department of Chronic Diseases and Sexually Transmitted Infections of the Brazilian Ministry of Health [27].

Until August 25, 2022, in Brazil, 4,216 cases of monkeypox were confirmed in 24 Federative Units (UF) – most of them in São Paulo, followed by Rio de Janeiro, Minas Gerais, Goiás, and the Federal District. Almost 5,000 suspected cases were being investigated in 26 UF [29].

Historically, the conditions for a sustained maintenance of the transmission of monkeypox among humans is considered limited [30]. This limitation would be lower due to the possibility of introducing the virus into the human population, since spillover events are relatively common and mainly because the potential for transmission – expressed by the basic reproduction number of the infection (R_0) – is insufficient to sustain this transmission [30]. The R_0 for monkeypox, regarding human-to-human transmission, can be expressed as the average number of new infections caused from the introduction of an infected individual into a totally susceptible population. To spread, an infection needs to present $R_0 > 1$; otherwise it will tend to disappear. However, even though a value of R_0 around 0.8 was estimated for populations not vaccinated and living in rural areas – which suggest difficulties in the spread of monkeypox – we can consider that $R_0 > 1$ may exist in specific situations and populations, allowing its spread among humans [30,31]. Estimates corrected for immunity conferred by smallpox vaccination reached R_0 values from 1.46 to 2.67 [31]. According to the preliminary estimates of the current epidemic, $R_0 = 1.29$ (95%CI: 1.26-1.33) [32]. Considering the current rapid spread of monkeypox worldwide, valid estimates of R_0 are essential for a forecast more focused on its development in the short-, medium-, and long-term [33].

The PHEIC declaration was met with antagonistic views, mainly because the WHO Emergency Committee voted against the measure [8]. On the one hand, the declaration recognizes the unusual situation, strengthens the need for international coordination to tackle it, encourages governments to consider the problem with due seriousness, and favors fundraising. On the other hand, arguments state that this measure is more symbolic than effective and particularly worrying in a situation of pandemic fatigue [8]. In any case, Brazil failed to tackle the COVID-19 pandemic, although its structural conditions could offer a more effective response in health emergencies. May the negative lessons help to build a new story based on better public health practices and the best scientific evidence.

Contributors

All authors contributed to the study conception, writing and revision of the text and approved its final version to be published.

Additional informations

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