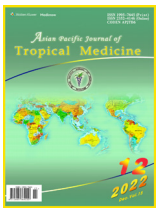

Perspective

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# New variola (mpox) in Brazil: Epidemiological update and perspectives

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New variola (NV)–mpox (monkeypox)–is a zoonosis caused by the mpox virus, which belongs to the genus *Orthopoxvirus* in the family Poxviridae. This disease, in the present year (2022), has caused several cases and deaths around the world, including Brazil[1]. The group of poxviruses, in which the species that causes NV is included, consists of agents widely distributed in nature. Due to their considerably large size, they were among the first viruses to be microscopically visualized. The Poxviridae family is capable of infecting epithelial and connective tissue cells. Currently, such a viral family is classified as a genome lineage composed of double-stranded DNA, completely independent of the host nucleus[1].

In the total of 28 genera described in the scientific literature, only four are, up to the present moment, capable of infecting human beings: (1) *Orthopoxvirus*; (2) *Molluscipoxvirus*; (3) *Parapoxvirus*; and (4) *Yatapoxvirus*[2]. Orthopoxviruses are the best known among the poxviruses, since they comprise smallpox, which causes smallpox, a disease that devastated a large part of the world's population throughout the 20th century, but which has been considered eradicated since 1980[1]. Orthopoxviruses, along with viruses of the genus *Molluscipoxvirus*, are the only two genera of the Poxviridae family specific to humans. *Molluscipoxvirus* is the cause of the disease known as molluscum contagiosum. Molluscum contagiosum consists of a dermatological disease that commonly affects children, attacking only human basal keratinocytes. The other two types of poxvirus (*Parapoxvirus* and *Yatapoxvirus*) are considered zoonoses, with low infectivity and isolated occurrence[2].

NV (mpox) is a tropical zoonosis with a marked increase in the incidence rate today. After the eradication of human smallpox, it became the most important *Orthopoxvirus* disease for public health in the world[1,2]. Endemic in West and Central Africa, it has mild symptoms and signs, similar to those of human smallpox. The disease was first described in Africa and later spread to other countries through travelers, causing small outbreaks[3,4].

In 2022, NV reached global notoriety due to the increased incidence of cases, with occurrences in 12 countries. The first records in the United Kingdom and Portugal were related to the occurrence of the disease among men who have sex with men, which contributed to the emergence of stigma for this often marginalized community[5]. However, transmission of the virus occurs through several routes, such as contact with fluids and injuries from infected animals (and possibly the consumption of contaminated meat)[3], human-to-human spread due to direct contact with secretions, lesions, and even handling objects (fomites) of a person infected, in addition to vertical transmission *via* the placenta and contact with droplets exhaled by animals (human or not) infected. Thus, sexual contagion is not the only possible route of infection, and it is important to mention the increased risk for health professionals through respiratory droplet transmission, given the closer contact with the sick ones.

NV was described in 1958, when it triggered two outbreaks of a disease similar to human smallpox in monkeys kept for research purposes. The first human case was recorded in 1970 in the Democratic Republic of Congo, during a period of intensified efforts to eliminate smallpox. The symptoms and signs originally described included fever, chills, headache, myalgias, feelings of exhaustion, swollen lymph nodes, and skin lesions, first on the face and later on to other parts of the body, including the genitals. During pregnancy, the virus can lead to different complications, triggering congenital smallpox and even the baby's death[6-8].

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In the current outbreak (2022), the biggest concern is related to the notification of new cases of the disease in hitherto non-endemic areas. Unlike the brief episodes of NV previously described, since the beginning of May 2022, the world has faced the emergence of several reported cases, creating an alert regarding the level of lack of control that NV is currently at. There are several hypotheses to explain the spread of the disease, but (1) the easy transmission–as previously mentioned–and (2) the limited significance of borders in the contemporary world-which represent, as a rule, little more than the delimitation of territories, which facilitates the contact of people from different parts of the world-seem to be determining factors in the current state of dissemination of the disease[9]. The reality is that, for the first time, several cases were reported and confirmed in places where there was no record of endemic NV, in addition to the fact that numbers are increasing in places where the disease was endemic[10].

After the first descriptions of NV epidemiological data by the World Health Organization (WHO), in May 2022, new suspicions and confirmations emerged in other countries. According to a recent report prepared by WHO with data received on 09/05/2022 and published on 16/11/2022, there is a moderate endemic global risk, considering the European region the only one at high risk. Until the present moment, 79411 laboratory-confirmed cases and 50 deaths have been described in the 110 monitored territories. The number of occurrences is highest in America and Europe, with approximately 98.36% of confirmed cases of NV. However, region of the Americas holds 60% of deaths[11–13].

Brazil reported the first eight suspected cases on June 8, 2022, in Ceará, Mato Grosso do Sul, Rio Grande do Sul, Rondônia, Santa Catarina and São Paulo[7]. The first confirmed case was detected at the Institute of Infectious Diseases Emilio Ribas, through a swab taken on eruptions presented by a 41-year-old male patient, with a history of recent travel to Spain and Portugal. The genome sequencing, carried out to help in understanding the transmission of the virus, was shown to be aligned with the sequences of Germany, Spain, USA and Portugal, with the identification of 3 unique SNPs in comparison with the updated US-CDC genome [according Claro *et al*: "(Accession Nº ON563414.3): GA->AA (10118; non-synonymous), TC->TT (15004; synonymous) and GA->AA (169928; non-synonymous)"][5]. The identified G->A and C->T mutations, like those described in the new Brazilian MPXV genome, may be a result of APOBEC3 deaminase editing[5], which makes it possible for other cases to be diagnosed by polymerase chain reaction (PCR).

According to data collected by the WHO on 15/11/2022, Brazil has a total of 9655000 confirmed cases and 12 deaths. The analysis of Figure 1, which contains information on cases over time in Brazil, shows that the number remains stable, with an average of approximately 13 cases per day and from the second half of July, period of school holidays in the country, the number grows dramatically, reaching peaks of 410 cases. This fact corroborates the data regarding the mode of contagion and dissemination of the disease. The growth in notifications can also be explained by the increased testing of suspects. It is also worth mentioning that the visible peaks in the graph validate the data on the manifestations and severity of the disease, characterized by a self-limited and mild condition, which explain the decreasing of case number that the peak is showing[7,14].

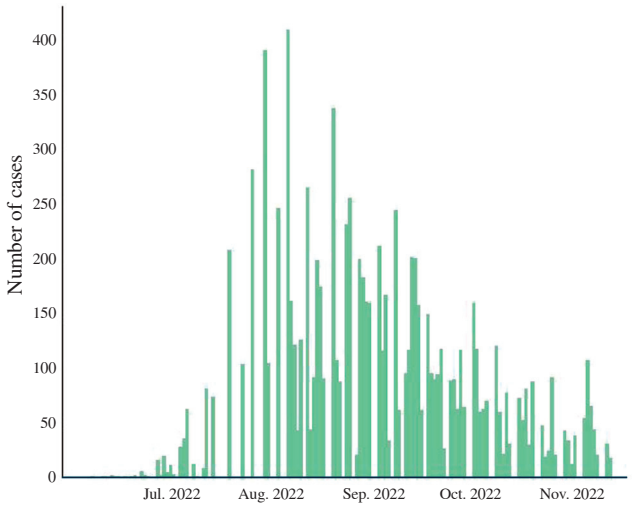


**Figure 1.** Number of new variola (mpox) cases over months in Brazil in 2022.

Most of the infected population comprises young adults, probably because this age group does not include those vaccinated against human smallpox (in fact, once the disease was eradicated, vaccination was discontinued). It is important to highlight that NV has a long incubation period: once infected, the individual can take from six to thirteen days for the prodromes, and this period can be extended to three weeks. The first clinical manifestations are nonspecific, and it is important to consider the differential diagnoses so that the case is notified as soon as possible. From the first to the fifth day of the state period, complaints of fever, headache, asthenia, fatigue, myalgia, low back pain and lymphadenopathy are common, the latter being a very useful finding for the differential diagnosis. Approximately three days after the appearance of the initial manifestations, skin eruptions appear[12,13], which begin centrifugally: they settle on the extremities of the body and on the head and only afterwards-depending on the viral load and the impairment of the immune system affected individual-appear on the trunk, cornea and genital region (at least 30% of cases). Lesions begin as macules, progressing to papules and pustules, which eventually rupture and become crusts. All skin lesions, including crusts, are infectious (*i.e.*, transmission only ends when the lesions disappear completely). The period from onset of symptoms to their

end lasts from two to four weeks. Complaints are usually mild, but injuries can become painful depending on the affected body part. Occasionally, secondary (bacterial) local infections also occur, which can progress to systemic conditions[1,7].

As soon as NV is suspected, the PCR is indicated. The samples include the vesicular secretion or the crust, being extremely important to observe the biosafety protocols for the collection and transport of the material. To obtain the material–preferably from the secretion of pustular and vesicular lesions–a swab is used, which must be placed in a dry tube. It is recommended the collection be performed in two different skin areas. In the case of obtaining the scab, it is important to perform it in the initial healing phase, since there is a greater probability of detecting the viral genome[9,10].

Treatment of the disease is based on relieving symptoms, in addition to addressing possible complications. Antiviral agents with potential for the treatment of NV have been sought, with emphasis on the following drugs: brincidofovir, cidofovir and tecovirimat. Among these, cidofovir has broad activity against many viruses including orthopoxviruses, with dramatic resolution of lesions described in some patients who used the drug. Brincidofovir–a drug with broad activity against DNA viruses–was approved by the Food and Drug Administration (FDA) in 2021 for the treatment of smallpox. Tecovirimat-a drug that acts against orthopoxviruses, but which does not have notable activity against other DNA viruses-was also approved for the treatment of smallpox, in 2018, by the FDA[15].

Because it is a virus transmitted by contact with infected individuals, the best form of prevention is to avoid it. Personal protection measures such as the use of masks covering the nose and mouth and frequent hand hygiene are equally useful for preventing the disease. In case of suspected infection, the healthcare professional should promptly contact the agency responsible for testing and case reporting. Currently, there is a vaccine developed against NV, which was approved in 2019 in Canada, the United States and the European Union. Once made available in Brazil, there is no evidence to recommend it to the general population, as NV infection does not have severity rates that justify universal vaccination at this time. For the public at high risk of infection, the vaccine has a two-dose application scheme. If the immunobiological is applied three days after exposure-and, in some cases, even seven days after the probable contagion-, there may be a drastic reduction in the progression of the disease[1,2,7,16].

In Brazil, the Unified Health System plays a fundamental role in epidemiological control, diagnosis, treatment and prevention of different diseases[17], including NV. It is worth mentioning in this context, bill 1917/22 that includes the vaccine against the disease in the National Immunization Calendar[18].

Although it is not usually a fatal disease, NV can cause serious complications, especially in immunosuppressed individuals, with the possibility of death, such as those described in Brazil. Thus, the dissemination of reliable scientific information is crucial for society to understand its role in preventing the disease–supporting control actions–, in addition to preventing the emergence of unacceptable prejudices in democratic, secular, and pluralistic societies. People from the LGBTQIAP+ community (lesbian, gay, bisexual, transgender, queer, intersex, asexual, pansexual) cannot be characterized as the great villains in the transmission of the disease, since they are not the only ones who acquire and transmit the pathogen[19]; in fact, the risk of contagion is more related to the multiplicity of partners than to sexual orientation. Indeed, every effort to counteract the stigmatization of the LGBTQIAP+ community–stemming from initial reports of association with same-sex relationships–must be undertaken, in order to prevent different social segments from being placed in a vulnerable situation in health services[20]. Moreover, the link between NV and monkeys is also fallacious–and potentially generating violent actions against these animals–, since the main hosts of the virus are not apes, but rodents, and the adoption of alternative nomenclature for the disease[21], as we tried to achieve in this article (use of the terms "new smallpox" or "mpox").

The development of care actions, involving the diagnosis, treatment, prevention, and rehabilitation of the sick (for which the Unified Health System becomes essential)[20–22], and of critical positions towards any form of discrimination, whether directed at humans or not humans, constitute the great challenges for the management of the new smallpox in Brazil.

## Conflict of interest statement

The authors declare that there are no conflicts of interest.

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## Authors' contributions

ACEE, MCC, APG and RSB designed the study; MEQSB, LMS and WP collected the data; ACEE and MEQSB analyzed the data; ACEE, MCC, APG and RSB searched the literature and wrote the manuscript; MCC and RSB edited and revised manuscript according to journal's instructions; ACEE, MCC and RSB edited and controlled the final version of the manuscript. All the authors approved the final version of the manuscript.

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