

Viral adaptation, vulnerable health care systems and health inequities: Monkeypox as an emerging threat in the Global Health Agenda

Adaptação viral, sistemas de saúde vulneráveis e desigualdades em saúde: Monkeypox, uma ameaça emergente na agenda de Saúde Global

Robert **PAULINO-RAMÍREZ**¹, André Ricardo Ribas **FREITAS**²

ABSTRACT

Due to the increasing number of monkeypox virus (MPXV) cases, WHO declared it a Public Health Emergency of International Concern (PHEIC). The transmission of monkeypox has been described during this outbreak associated with close sexual contact through the skin with infectious lesions. It is not very clear whether this virus is better adapting to human-human transmission, we do not know if the case fatality rate is being lower during the current global spread due to genetic changes in the virus or as an effect of a better understanding of the actual number of mild cases of infections. The emergence of pathogens, particularly the spillover of zoonotic viruses, is not a totally unpredictable phenomenon, the current monkeypox multi-country outbreak was preceded by a progressive increase in the number of cases in recent decades and changes in the epidemiological profile in affected areas of Africa. We must resume the conversation with civil society organizations, bring a more sex-positive health discourse through a healthy and stigma-free scientific dialogue.

RESUMEN

Debido al creciente número de casos del virus de la viruela del simio (MPXV), la OMS lo declaró una emergencia de salud pública de importancia internacional (PHEIC). La transmisión de la viruela del simio se ha descrito durante este brote asociada con el contacto sexual cercano a través de la piel con lesiones infecciosas. No está muy claro si este virus se está adaptando mejor a la transmisión humano-humano, no sabemos si la tasa de letalidad está siendo menor durante la propagación global actual debido a cambios genéticos en el virus o como efecto de una mejor comprensión de el número real de casos leves de infecciones. La aparición de patógenos, en particular la propagación de virus zoonóticos, no es un fenómeno totalmente impredecible, el actual brote de viruela del simio en varios países estuvo precedido por un aumento progresivo en el número de casos en las últimas décadas y cambios en el perfil epidemiológico en las áreas afectadas de África. Debemos retomar la conversación con las organizaciones de la sociedad civil, traer un discurso de salud más sexualmente positivo a través de un diálogo científico saludable y libre de estigmas.

RESUMO

Devido ao número crescente de casos do vírus monkeypox (MPXV, conhecida também como varíola dos macacos), a OMS declarou uma Emergência de Saúde Pública de Interesse Internacional (PHEIC). A transmissão da varíola dos macacos foi descrita durante este

¹ Instituto de Medicina Tropical & Salud Global, Universidad Iberoamericana, Santo Domingo, Dominican Republic. E-mail: <

² Faculdade São Leopoldo Mandic, Curso de Medicina. Campinas, SP, Brasil. E-mail:

Como citar este artigo

Paulino-Ramirez R, Freitas AAR. Viral adaptation, vulnerable health care systems and health inequities: Monkeypox as an emerging threat in the Global Health Agenda. *InterAm J Med Health* 2022;5:e20220247. <https://doi.org/10.31005/iajmh.v5i.247>



surto associada ao contato sexual próximo através da pele com lesões infecciosas. Não está muito claro se esse vírus está se adaptando melhor à transmissão humano-humano, não sabemos se a taxa de letalidade está sendo menor durante a atual disseminação global devido a mudanças genéticas no vírus ou como efeito de uma melhor compreensão do número real de casos leves de infecções. A emergência de patógenos, particularmente o spillover de vírus zoonóticos, não é um fenômeno totalmente imprevisível, o atual surto multipaíses de varíola foi precedido por um aumento progressivo do número de casos nas últimas décadas e mudanças no perfil epidemiológico nas áreas afetadas do África. Devemos retomar a conversa com as organizações da sociedade civil, trazer um discurso de saúde mais sexualmente positivo por meio de um diálogo científico saudável e livre de estigmas.

INTRODUCTION

In public health schools we learnt the concept of endemic diseases, their transmission characteristics, risk groups, and containment measures. However, this “endemic bias” has meant that the discussion on diseases with emerging or re-emerging capacity is often not placed on the health agenda of countries with greater economic resources. Hence, the headlines of the media are often responsible for drawing attention when a pathogen emerges from its pre-established geographical contours. This is always accompanied by the negative effects of stigma and discrimination associated with the disease, country or population most affected.

For this reason, the concept of endemicity of diseases has been associated with the concept of “isolated” or “limited to”, precisely this has been some of the factors associated with the non-importance given to numerous latent zoonotic threats [1]. Several studies have suggested that more than half of current human pathogens have a zoonotic origin [2]. We already know the devastating effects of the Black Death, HIV/AIDS, yellow fever, more recently the Zika virus and currently severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the coronavirus disease 2019 (COVID-19) pandemic, all originating from a spillover from zoonotic species to humans [3-5].

For several years, scientists from numerous research centers in Africa have been drawing attention to the increasing number of cases of monkeypox virus (MPXV) being reported in West Africa [6]. This zoonosis was identified for the first time in captive animals [7], however, cases of this infection had been reported in communities in the Democratic Republic of the Congo (DRC) and more recently its geographical expansion to West African countries [8]. This has caused African scientists on numerous occasions to draw the attention of countries with greater resources to the importance of having vaccines available in the face of an increase in cases, inexistent vaccines stocks that they lack.

MPXV is a member of the *Poxviridae* family with a double-stranded deoxyribonucleic acid (dsDNA), this family is capable to infect numerous animals including mammals, reptiles and birds. MPXV belongs to the subfamily *Orthopoxvirus* the same family as Variola (smallpox virus). MPXV is known to be classified in clades: Central African or Congo, and West Africa, to avoid country- or geographically related stigma, the World Health Organization (WHO) has reclassified the clades reported in the literature as Clade I (previously from the Congo), and Clade II (previously West Africa); from the latter Clade II a and b have diverged [9] (figures 1A and 1B). These latter modifications in the genomic structure of the virus suggest a capacity for adaptability to regions and populations where it did not circulate geographically [10]. Phylogenetic analyzes of *Orthopoxviruses* suggest a range of base pair substitutions of 1-2 substitutions per genome per year, in this sense, human MPXV (hMPXV) cases reported during 2022 when compared to previous genomes (2018-2019) show more than 50 single nucleotide polymorphisms (SNPs) suggesting that during 2020-2021 a series of phenomena occurred that facilitated the incorporation of 6-12 more specific mutations [11].

Factors associated to this viral adaptability are still unknown, however, some studies suggest that it could be influenced by a multi-host ecological complex [12], environmental factors, viral associated APOBEC3-like deaminase mutations [13], and anthropogenic factors [14] that have been associated with the emergence of species spillovers at the animals-humans interface. These phenomena have been described in detail in the outbreaks of West Nile Virus, Zika Virus, avian and swine influenza, Ebola Virus, and of course the Coronaviridae family, of which we already know several with the capacity to cause outbreaks and pandemics [15,16]. Moreover, based on the zoonotic transmission theories proposed by Wolfe et al [17], MPXV has been moving between epidemiological categories IV and V (from animals to humans, and then from humans to humans), with a basic reproductive rate (R0) of >1 which would suggest a capacity

for sustained transmission between humans. However, the latter is still a question to be answered, due to the lack of interest of the scientific community in developed countries, the transmission dynamics “Out of Africa” has not been well established since it required studies of ecology and human behavior in countries where it previously circulated. Some authors suggest that the most likely scenario could be a cryptic transcontinental transmission between humans that was increased after the lifting of restrictions on international circulation caused by COVID-19 [18].

Due to the increasing number of MPXV cases, WHO declared it a Public Health Emergency of International Concern (PHEIC) on July 23, 2022 [19]. As of August 26, 2022, more than 46, 679 confirmed cases (figure 1C), of which the majority correspond to cases in the Americas and Europe [20]. The first human cases outside the African continent were reported in 2003 in an outbreak in the USA; phylogenetic analysis of these cases corresponded to rodents imported from West Africa [21]. These human cases differed in clinical presentation, being milder than those previously reported in Central Africa. Open Reading frames (ORFs) analysis of different MPXV isolates could help us better understand the spillover phenomenon associated to the 2022 cases and the future of this outbreak. It is well described that lethality of some health conditions depends not only on biological factors, but also on structural factors, and the adequate response of health systems [22].

In this sense, during the 2022 outbreak, fatal cases have been reported, mostly from Latin American countries. Current genomic data suggest that the introduction to the American continent was associated with the outbreak in Europe, and therefore corresponding to Clade II a/b, the same cause of more than 13 cases, of which 5 (39%) correspond to Brazil, Mexico, Peru, Ecuador, and Cuba [23]. In recent years, the health systems of Latin American countries have had to respond to the numerous waves of COVID-19, weakening their rapid response structures, and of course all care programs, including those for sexually transmitted and preventable diseases. for vaccines. The health authorities of these countries have also had different emergencies from syndemics, especially arboviral diseases, HIV, tuberculosis, among others. This has caused many governments to redirect efforts in order to mitigate the deleterious effects caused by more than two years of the pandemic [24].

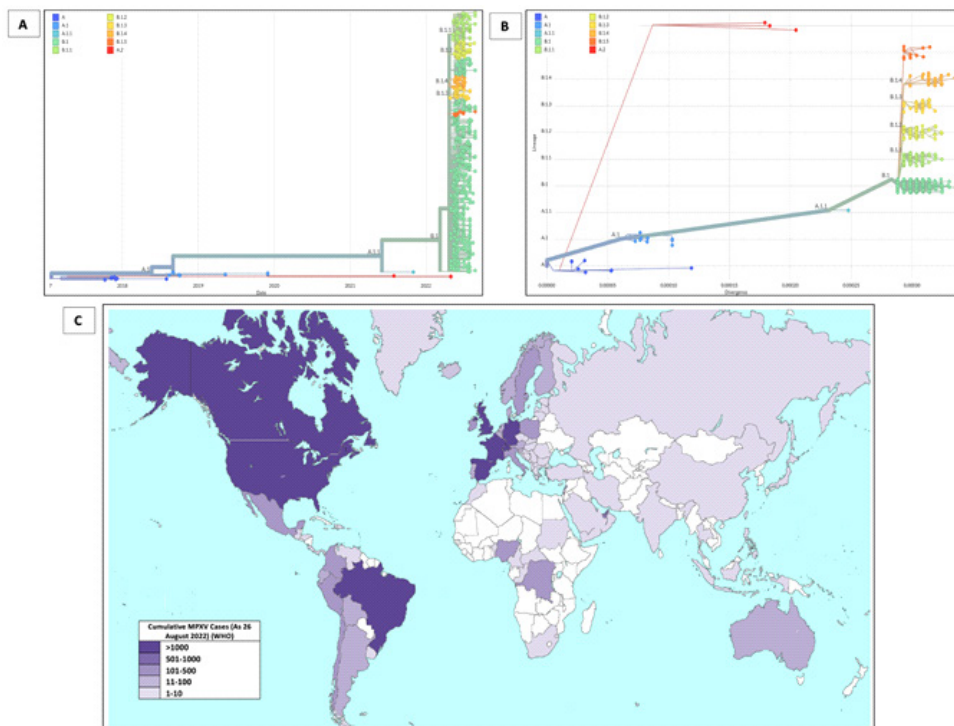


Figure 1 – A. MPXV lineages reported at the GISAID platform (2017-2022); B. Molecular divergence between MPXV clades since 2017. Both phylogenetic trees were constructed using PANGO lineages (A-B). C. Global cumulative confirmed MPXV cases (WHO data as August 2022).

The transmission of monkeypox has been described during this outbreak associated with close sexual contact through the skin with infectious lesions [25] (figure 2). Contact with materials used by people with the infection, such as clothing, sheets, could also be associated with its transmission, sex toys, and salivary transmission [26]. Regarding sexual transmission, the unfortunate network of contacts that has occurred somewhere between men who have sex with men (MSM) has generated immediate media interest and their unique association with such populations, however has not been well established (figure 2). as a sexually transmitted disease, in part because some people have been infected without having had sexual contact, for example in mass activities not related to sexual activities [27]. Therefore, the communicative message of it must be handled very carefully as we are learning during this outbreak.

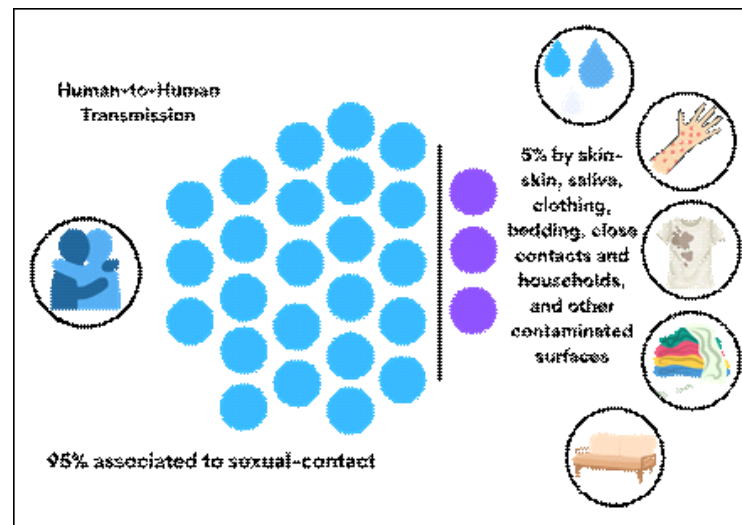


Figure 2 – This figure depicts the most common reported mechanisms of MPXV transmission in the most recent scientific literature obtained from non-previous circulating countries.

On the other hand, clinical patterns during this outbreak shows an atypical lesion pattern, often mimicking sexually transmitted infections (STIs) like those caused by Herpes Simplex Virus (HSV), and Syphilis. For this reason, in several case series reported in the United Kingdom and Spain, it is often described that the confirmed cases were detected in STI care settings, and that the doctors thought precisely of these STIs when differentiating the cases [28,29]. This case series reported that more than 98% of the cases were associated with men identified as gay or bisexual and that 41% lived with HIV, that the most frequent lesions were identified in the genital area, chest, arms and legs, associated always with both inguinal and cervical lymphadenopathy [28,29].

Despite not having specific vaccines and treatments for MPXV infection, some antivirals and vaccines used for Smallpox infection have been authorized for use, however, it is still unknown whether they will work for this and other outbreaks. that may arise [30].

Historically, we have enough examples of the response to other epidemics initially afflicting specific populations, and later spread to the general groups, in this sense, the HIV pandemic is a global health emblem of pitfalls and success that we can emulate. One of those great lessons was precisely that, if we had included the most affected communities early, the stigma and discrimination associated with AIDS would have been less, even today, more than forty years later, we are still trying to eliminate the stigma associated with HIV in gay communities [31]. In the 1980s, the emergence of the HIV pandemic provoked numerous social mobilizations, and the creation of numerous community-based organizations that caused pressure on the rulers of the day to create early response programs and access to medicines. that could save the lives of many[32].

CONCLUSIONS

This current outbreak of MPXV is an emerging phenomenon that we must analyze and respond to in a timely manner, with a global perspective rather than a regional one. This is what the pandemic caused by SARS-CoV-2 has taught us, that “*Quid hic sit*” in Latin, what is there is here, what happens on another continent could always affect the rest of us. We live in an interconnected world, and with increasingly extensive communication networks, which have collaterally been detrimental to our environment; for this reason, the emergence of these global phenomena will continue to rise.

Due to the westernized bias of diseases, this virus and many others require us to understand more clearly their transmission routes and their possible subsequent implications, particularly in other affected populations, such as women, children and those with specific pre-existing diseases. In several situations, we only know the serious and atypical forms of some diseases after the increase in the number of cases that occurred after their emergence, there is no lack of examples such as Zika, West Nile Virus, chikungunya, and others [33,34]. It is not very clear whether this virus is better adapting to human-human transmission, we do not know if the case fatality rate is being lower during the current global spread due to genetic changes in the virus or as an effect of a better understanding of the actual number of mild cases of infections. It is also unclear whether its low transmissibility would extinguish it soon, or whether we should include a new entity to differentiate in health systems, especially in primary care and prevention settings.

The emergence of pathogens, particularly the spillover of zoonotic viruses, is not a totally unpredictable phenomenon. The SARS-CoV-2 pandemic was preceded by the SARS-CoV-1 epidemic and repeated outbreaks of MERS-CoV [35], the global spread of Zika in the second decade of the 20th century was preceded by an epidemic on the small, isolated island of Yap in 2007 which was the first diffuse transmission of the virus in the absence of non-human primate reservoirs [36], the current monkeypox multi-country outbreak was preceded by a progressive increase in the number of cases in recent decades and changes in the epidemiological profile in affected areas of Africa [37]. International health surveillance bodies need to build risk prospecting methods and epidemiological intelligence capable of anticipating these threats so that they can be contained or at least mitigated.

Also due to the patterns of appearance of genital lesions, it is suggested that the use of condoms could be useful for the prevention of anal and oral transmissions. Some more developed countries have been able to start vaccinating, demonstrating once again the existing global health vaccine inequity, in countries where the virus previously circulated there are no vaccines available, and for the moment they have not had access to them either, the same happens with Latin American countries. Consequently, the only tools at hand are containment and education on routes of transmission. However, we still do not know if exposure to the virus will be enough to create prolonged immunity, nor if one dose or two doses of existing vaccines will be necessary to cause herd immunity, or if it is necessary to push further in government investment for a MPXV specific vaccine.

Meanwhile we must resume the conversation with civil society organizations, bring a more sex-positive health discourse where sexual orientation and gender identity are not the reasons why we address diseases, but through a healthy and stigma-free scientific dialogue. Where we can address risk factors, avoiding the many NOs and with a shared responsibility vision. Establish safe spaces with these organizations from where disease risk reduction programs can be implemented, after all, they are the ones that have the knowledge and experience in using the language and cultural skills necessary to avoid generating exclusion from services of health. These organizations are called to create supportive communities, with greater civil society activism. This is what changed the response to HIV in the past and this time we shall not make the same mistake.

REFERENCES

1. Lloyd-Smith JO, George D, Pepin KM, Pitzer VE, Pulliam JR, Dobson AP, Hudson PJ, Grenfell BT. Epidemic dynamics at the human-animal interface. *Science*. 2009 Dec 4;326(5958):1362-7. <https://doi.org/10.1126/science.1177345>
2. Morens DM, Folkers GK, Fauci AS. *Lancet Infect Dis*. 2008;8:710.

3. Morens DM, Taubenberger JK, Fauci AS. A Centenary Tale of Two Pandemics: The 1918 Influenza Pandemic and COVID-19, Part I. *Am J Public Health*. 2021 Jun;111(6):1086-1094. <https://doi.org/10.2105/AJPH.2021.306310>
4. Worobey M, Levy JI, Malpica Serrano L, Crits-Christoph A, Pekar JE, Goldstein SA, et al. The Huanan Seafood Wholesale Market in Wuhan was the early epicenter of the COVID-19 pandemic. *Science*. 2022 Aug 26;377(6609):951-959. <https://doi.org/10.1126/science.abp8715>
5. Pekar JE, Magee A, Parker E, Moshiri N, Izhikevich K, Havens JL, et al. The molecular epidemiology of multiple zoonotic origins of SARS-CoV-2. *Science*. 2022 Aug 26;377(6609):960-966. <https://doi.org/10.1126/science.abp8337>
6. Yinka-Ogunleye A, Aruna O, Dalhat M, Ogoina D, McCollum A, Disu Y, et al. Outbreak of human monkeypox in Nigeria in 2017-18: a clinical and epidemiological report. *Lancet Infect Dis*. 2019 Aug;19(8):872-879. [https://doi.org/10.1016/S1473-3099\(19\)30294-4](https://doi.org/10.1016/S1473-3099(19)30294-4)
7. Von Magnus P, Krag Andersen E, Birkum Petersen K, Birch-Andersen A. A pox-like disease in cynomolgus monkeys. *Acta Path*. 1959;46 (2).
8. Likos AM, Sammons SA, Olson VA, Frace AM, Li Y, Olsen-Rasmussen M, et al. A tale of two clades: monkeypox viruses. *J Gen Virol*. 2005 Oct;86(Pt 10):2661-2672. <https://doi.org/10.1099/vir.0.81215-0>
9. Monkeypox: experts give virus variants new names. World Health Organization (WHO). Available at: <https://www.who.int/news/item/12-08-2022-monkeypox--experts-give-virus-variants-new-names>
10. Di Gennaro F, Veronese N, Marotta C, Shin JI, Koyanagi A, Silenzi A, et al. Human Monkeypox: A Comprehensive Narrative Review and Analysis of the Public Health Implications. *Microorganisms*. 2022 Aug 12;10(8):1633. <https://doi.org/10.3390/microorganisms10081633>
11. Wang, L, Shang, J, Weng, S, Aliyari SR, Ji C, Cheng G, et al. Genomic annotation and molecular evolution of monkeypox virus outbreak in 2022. *J Med Virol*. 2022;1- 7. <https://doi.org/10.1002/jmv.28036>
12. Silva NIO, de Oliveira JS, Kroon EG, Trindade GS, Drumond BP. Here, There, and Everywhere: The Wide Host Range and Geographic Distribution of Zoonotic Orthopoxviruses. *Viruses*. 2020 Dec 30;13(1):43. <https://doi.org/10.3390/v13010043>
13. O'Toole Á, Rambaut A. Initial observations about putative APOBEC3 Deaminase Editing driving short-term evolution of MPXV since 2017. *ARTIC Network*; 2022.
14. Taylor LH, Latham SM, Woolhouse ME. Risk factors for human disease emergence. *Philos Trans R Soc Lond B Biol Sci*. 2001 Jul 29;356(1411):983-9. <https://doi.org/10.1098/rstb.2001.0888>
15. Daszak P, Epstein JH, Kilpatrick AM, Aguirre AA, Karesh WB, Cunningham AA. Wildlife and emerging zoonotic diseases: the biology, circumstances and consequences of cross-species transmission. *CTMI*. 2007;315:463-475.
16. Deming ME, Chen WH. COVID-19 and Lessons to Be Learned from Prior Coronavirus Outbreaks. *Ann Am Thorac Soc*. 2020 Jul;17(7):790-794. <https://doi.org/10.1513/AnnalsATS.202002-149PS>
17. Wolfe ND, Daszak P, Kilpatrick AM, Burke DS. Bushmeat hunting, deforestation, and prediction of zoonoses emergence. *Emerg Infect Dis*. 2005 Dec;11(12):1822-7. <https://doi.org/10.3201/eid1112.040789>
18. Alakunle EF, Okeke MI. Monkeypox virus: a neglected zoonotic pathogen spreads globally. *Nat Rev Microbiol*. 2022 Sep;20:507-508. <https://doi.org/10.1038/s41579-022-00776-z>
19. Nuzzo JB, Borio LL, Gostin LO. The WHO Declaration of Monkeypox as a Global Public Health Emergency. *JAMA*. 2022;328(7):615-617. <https://doi.org/10.1001/jama.2022.12513>
20. World Health Organization. Multi-country outbreak of monkeypox, External situation report #4 - 24 August 2022. [cited 2021 May 19] Available from: <https://www.who.int/publications/m/item/multi-country-outbreak-of-monkeypox--external-situation-report--4--24-august-2022>
21. Centers for Disease Control and Prevention (CDC). Update: multistate outbreak of monkeypox--Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003. *MMWR Morb Mortal Wkly Rep*. 2003 Jul;52(27):642-6.
22. Tambo E, Al-Nazawi AM. Combating the global spread of poverty-related Monkeypox outbreaks and beyond. *Infect Dis Poverty*. 2022;11(80):1-5. <https://doi.org/10.1186/s40249-022-01004-9>
23. Mathieu E, Spooner F, Dattani S, Ritchie H, Roser M- "Monkeypox". [online]. OurWorldInData.org. Retrieved on August 26th, 2022 [citado 2021 abr 21]. Disponível em: <https://ourworldindata.org/monkeypox>
24. Rodriguez-Morales AJ, Lopardo G, Verbanaz S, Orduna T, Lloveras S, Azeñas-Burgoa JM, et al. Latin America: Situation and preparedness facing the multi-country human monkeypox outbreak. *Lancet Reg Health Am*. 2022;13(100318):1-4.<https://doi.org/10.1016/j.lana.2022.100318>
25. Vusirikala A, Charles H, Balasegaram S, Macdonald N, Kumar D, Barker-Burnside C, et al. Epidemiology of early monkeypox virus transmission in sexual networks of gay and bisexual men, England, 2022. *Emerg Infect Dis*. 2022 Aug;28(10). <https://doi.org/10.3201/eid2810.220960>
26. Thornhill JP, Barkati S, Walmsley S, Rockstroh J, Antinori A, Harrison LB, et al. Monkeypox virus infection in humans across 16 countries- April-June 2022. *N Engl J Med* 2022;387:679-691. <https://doi.org/10.1056/NEJMoa2207323>

27. Karan A, Styczynski AR, Huang CH, Sahoo MK, Srinivasan K, Pinsky BA, et al. Human monkeypox without viral prodrome or sexual exposure, California, USA, 2022. *Emerg Infect Dis.* 2022 Aug;28(10):1-2. <https://doi.org/10.3201/eid2810.221191>
28. Tarín-Vicente EJ, Alemany A, Agud-Dios M, Ubals M, Suñer C, Antón A, et al. Clinical presentation and virological assessment of confirmed human monkeypox cases in Spain: a prospective observational cohort study. *Lancet.* 2022 Aug;400(10353):661-669. [https://doi.org/10.1016/S0140-6736\(22\)01436-2](https://doi.org/10.1016/S0140-6736(22)01436-2)
29. Patel A, Bilinska J, Tam JCH, Da Silva Fontoura D, Mason CY, Daunt A, et al. Clinical features, and novel presentations of human monkeypox in a central London centre during the 2022 outbreak: descriptive case series. *BMJ.* 2022;378:e072410. <https://doi.org/10.1136/bmj-2022-072410>
30. Rao AK, Petersen BW, Whitehill F, Razeq JH, Isaacs SN, Merchlsinsky MJ, 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 Jun 3;71(22):734-742. <https://doi.org/10.15585/mmwr.mm7122e1>
31. Budhwani H, Paulino-Ramirez R, Waters J, Bond CL, Ruiz I, Long D, et al. Adapting and pilot testing and HIV and intersectional stigma reducing intervention for Dominican Republic healthcare contexts: Protocol for translational research. *Contem Clin Trials Comm.* 2022 Oct;29(100980):1-6. <https://doi.org/10.1016/j.conctc.2022.100980>
32. Catungal JP, Klassen B, Ablenas R, Lambert S, Chown S, Lachowsky N. Organising care and community in the era of the 'gay disease': Gay community responses to HIV/AIDS and the production of differentiated care geographies in Vancouver. *Urban Studies.* 2021;58(7):1346-1363. <https://doi.org/10.1177/0042098020984908>
33. Hayes EB. Zika virus outside Africa. *Emerg Infect Dis.* 2009 Sep;15(9):1347-50. <https://doi.org/10.3201/eid1509.090442>.
34. Donalisio MR, Freitas ARR, Zuben APBV. Arboviruses emerging in Brazil: challenges for clinic and implications for public health. *Rev Saude Publica.* 2017 Apr;51:30:1-6. <https://doi.org/10.1590/S1518-8787.2017051006889>.
35. Forni D, Cagliani R, Clerici M, Sironi M. Molecular Evolution of Human Coronavirus Genomes. *Trends Microbiol.* 2017 Jan;25(1):35-48. <https://doi.org/10.1016/j.tim.2016.09.001>.
36. Duffy MR, Chen TH, Hancock WT, Powers AM, Kool JL, Lanciotti RS, Pretrick M, et al. Zika virus outbreak on Yap Island, Federated States of Micronesia. *N Engl J Med.* 2009 Jun;360(24):2536-43. <https://doi.org/10.1056/NEJMoa0805715>.
37. Bunge EM, Hoet B, Chen L, Lienert F, Weidenthaler H, Baer LR, et al. The changing epidemiology of human monkeypox-A potential threat? A systematic review. *PLoS Negl Trop Dis.* 2022 Feb;16(2):e0010141. <https://doi.org/10.1371/journal.pntd.0010141>.

Accepted: 04 Sept 2022
Available online: 04 Sept 2022