Infectious Diseases

Poc (Pox), a term for various infectious diseases in the history of public health and epidemiology: the dreaded *Smallpox*, the almost unknown *Alastrim* and the *Mpox*

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Summary

Introduction. *In 2022, the appearance of cases of Mpox outside the countries where the disease is endemic, and of some cases of human-to-human transmission, alerted the scientific community to a virus that is closely related to the smallpox virus. Mpox is a zoonosis and can be transmitted to humans. Following the eradication of smallpox in 1980 and the subsequent cessation of smallpox vaccination, it is emerging as the most important Orthopoxvirus in terms of public health impact.*
Methods. *In outlining the current situation of Mpox in the world, the authors frame the virus responsible within a broader reflection on the Orthopoxvirus family, focusing particular attention on the Variola virus, which formerly caused millions of deaths.*
Discussion. *Since Edward Jenner initiated the practice of vaccination, a progressive and careful vaccination campaign has led to the eradication not only of human smallpox but also of a minor form, called Alastrim, which was caused by the same virus. The mode of transmission of Mpox has been debated. At first, it seemed that the disease mainly, though not exclusively, affected men who had sex with other men. This conviction has been partially revised and the WHO recently changed the name of the disease from Monkeypox to Mpox, thereby alleviating the stigma involved.*
Conclusion. *The recent human cases of Mpox have prompted greater surveillance and research into the biology of MPXV and other closely related poxviruses. Studies have focused on the natural history of the virus, its transmission, pathogenesis, host interactions and evolution, and on the development of drugs and vaccines to prevent its spread.*

Background

In May 2022, the first cases of monkeypox (*Mpox*) were reported in countries where the disease is not endemic [1].
As of 5 June 2023, a total of 87,929 laboratory-confirmed cases of *Mpox* and 146 deaths have been reported to WHO. Since May 2022, a high percentage of these cases have been reported from countries without previously documented transmission of *Mpox*. It is the first time that cases and infections have been reported in countries without direct or immediate epidemiological links to areas of West or Central Africa [2].
The monkeypox virus is an *Orthopoxvirus* that causes a disease with symptoms similar to smallpox, although less severe. *Orthopoxvirus* is a genus of dsDNA viruses in the Poxviridae family that infect mammals.
Monkeypox virus (MPXV) is a double-stranded DNA virus. It is normally associated with rodents and occasionally spreads to humans. The emergence of cases in countries not normally affected by *Mpox* has brought to the attention of society a family of viruses which includes the terrible *Variola virus*, or smallpox virus, which killed millions of people for centuries [3].
Smallpox is an extremely contagious, severe infectious disease, with a historical fatality rate of around 30%. The disease is transmitted from person to person, as there are no other reservoirs in nature. It has been dreaded since ancient times, owing to both its high mortality and the fact that survivors were left with disfiguring marks all over their bodies.
Although there is evidence of smallpox dating back thousands of years, the timing of the appearance of the causative agent of the *Variola virus* and the way it evolved have caused quite a few controversies among scholars.
In 2016 Hendrik Poinar, a biologist specialized in ancient DNA has reconstructed the family tree of the *Variola virus* extracted from a 17th century Lithuanian mummy and established that the common ancestor appeared in modern historical times, between 1530 and 1645 [4].
Smallpox was eradicated in 1980, thanks to an intensive worldwide vaccination program.
Vaccination is a method of preventing smallpox, devised in 1796 by the English physician Edward Jenner (1749-1823) [5], who presented it in his book *The Origin of the Vaccine Inoculation* (1801) [6]. Having observed that people who had recovered from "*cowpox*" did not

contract "*smallpox*", Jenner deduced that the former disease could confer protection against the latter [7]. He began vaccinating healthy people by injecting material from a cowpox pustule. After developing the disease, the vaccinated person became immunized for both cowpox and human smallpox. This result was due to the similarity of the antigens of the two viruses: antibodies active against cowpox were also active against smallpox [8,9].
The smallpox vaccine was created by using viruses of the same species of *Orthopoxvirus*: *Cowpox virus* and *Vaccinia virus* (VACV), which do not cause human smallpox but elicits cross-immunity which protects the vaccinated individual against possible attack by the *Variola virus*.
Cowpox virus, *Vaccinia virus* and *Variola virus*, the cause of smallpox, are all closely related immunologically. For this reason, both VACV and CPXV determine immunity to smallpox.
VACV was the first animal virus to be purified and chemically analyzed. It was also the first virus to be genetically engineered, the recombinant viruses being utilized in vaccines against other infectious diseases" [10, 11].
Today, 200 years after the death of Edward Jenner, the world is still indebted to him for this fundamental discovery, which enabled smallpox to be eradicated and inspired the creation of vaccines against many other diseases.
Although the smallpox virus (*Variola virus*) has been eradicated worldwide, it is still preserved in some laboratories, and the possibility that it may be accidentally or deliberately reintroduced could have catastrophic consequences. In the event of biological attack, devastating smallpox epidemics could spread elsewhere but thankfully World Health Organization (WHO) and some countries like Italy have in their stocks important stash of vaccine.
There are 12 known *Orthopoxvirus* species, four of which can infect humans: *Variola virus* (VARV), *i.e.* the virus of human smallpox and *Alastrim*; *Monkeypox* (*Mpox*) *virus*, *Cowpox virus* and the *Vaccinia virus* used for smallpox vaccination.
The term *variola* derives from the Latin *varius* (spotted) or *varus* (pimple): it was used for the first time in the sixth century by Bishop Marius of Avenches (Switzerland), when smallpox had already become endemic in Europe. In the Anglo-Saxon world, in the 10th century, the word poc or pocca, a bag or a pouch, described an exanthematous disease. With the appearance of syphilis in Europe at the end of the 15th century, writers began to use the prefix small to distinguish *variola*, *smallpox*, from *syphilis*, the great *pox* [12].

Mpox: a long-term global threat?

With the eradication of smallpox in 1980, and the subsequent cessation of smallpox vaccination, *Mpox* has emerged as the most important *Orthopoxvirus*, in terms of its possible public health impact; the case-fatality rate of the Congo basin strain is ≤ 10%, while that of the West African strain is < 1% [13].
The first MPXV genome sequences from the outbreak were reported from Portugal on May 19, 2022, and multiple additional sequences, which can shed light on virus circulation, are now available.
Initial phylogenetic analyses indicated that the 2022 outbreak was caused by the virus belonging to the clade MPXV II (former West African clade), which is less severe than clade I (former Congo Basin clade). These analyses have led to think that the current outbreak was caused by the recent introduction of the virus into communities in non-endemic MPXV countries. However, further studies that include additional MPXV genome sequences point to a different scenario [14].
Current data on the spread of cases outside countries where the virus is normally endemic suggests that *Mpox* could pose a long-term global threat.
On 23 July 2022, the Director-General of the WHO, Thedos Adhanom Ghebreyesus, issued an international public health alert regarding cases of monkeypox [15]. Indeed, within a few months, the number of individuals infected by monkeypox increased exponentially.
Mpox is a zoonosis, that is transmitted from animals to humans, with cases often found close to tropical rainforests where there are animals that carry the virus.
"The disease can also spread from humans to humans, through contact with bodily fluids, lesions on the skin or on internal mucosal surfaces, such as in the mouth or throat, respiratory droplets and contaminated objects" [16].
In humans, *Mpox* begins with non-specific symptoms, such as fever, headache, chills, asthenia, enlarged lymph nodes and muscle pain. Within three days, a rash appears, first involving the face and then spreading to other parts of the body, including the hands and feet. The skin lesions evolve in the form of papules, then vesicles, pustules and finally crusts. In most people, *Mpox* lasts for two to four weeks and heals completely.
Prior to the 2022 outbreak, the majority of cases of monkeypox had been reported in people living in central and western Africa. Almost all of the cases identified in subjects living outside Africa were linked to travel to countries where the disease was endemic or were due to contact with sick animals brought from Africa. Within a few months, the disease aroused interest in Europe and the United States.
The interest of the scientific community also focused on the modes of transmission of the disease, which seemed to affect mainly, though not exclusively, men who had sex with other men [17].
Although direct contact through sexual activity appears to have been the main mode of transmission during the 2022 outbreak, recent studies have shown that "Human-to-human transmission of monkeypox virus can occur through respiratory secretions, direct contact, vertical transmission, percutaneous transmission, or indirect contact through fomites" [18].
This declaration also seems to have curbed, to some

degree, the stigmatization of people affected by this disease.

Therefore, it is important "to disseminate precise communication to the entire population that must not be directed only to high-risk groups, *i.e.*, MSM, people living with HIV/AIDS (PLWHA), and the lesbian, gay, bisexual, transgender, and queer (or questioning), plus other sexual and gender identities (LGBTQI+ community)" [19].

At the same time, the WHO changed the name of the disease from Monkeypox to *Mpox*, as the term 'monkeypox' could be discriminatory, stigmatizing and misleading.

Indeed, when the outbreak of monkeypox expanded earlier this year, racist and stigmatizing language online, in other settings and in some communities was observed and reported to the WHO.

Thus, "Following a series of consultations with global experts, the WHO will begin using a new preferred term "*Mpox*" as a synonym for monkeypox. Both names will be used simultaneously for one year while "monkeypox" is phased out [20].

Discovered in 1958 in colonies of captive-bred research monkeys, the virus came to be known as "monkeypox", although the source of the disease was unknown. The first case of animal-to-human zoonotic MPV transmission was registered in 1970 in Zaire (now the Democratic Republic of Congo, DRC) in a 9-month-old baby boy [21-24]. Over the years, a few cases of monkeypox were recorded outside Africa, such as an outbreak in the United States of America in 2003 due to animals imported from Ghana [25] and sporadic travel-related cases registered in the UK, Singapore and Israel [26]. The WHO Bulletin reported over 6200 confirmed cases and 9400 suspected cases in 2020 and 2021, respectively [27, 28].

Moreover, these data are probably underestimated, owing to the lack of robust surveillance systems in endemic regions. However, little attention was paid to this disease until the WHO Director-General's international public health alert in July 2022.

In addition, as the African countries where the virus is endemic are developing countries, they have little or no possibility to monitor and report cases of monkeypox, the clinical symptoms of which resemble those of some other widespread diseases, such as syphilis and chickenpox. This lack of rigorous health surveillance may facilitate the spread of the epidemic.

In addition to *Mpox*, the Cowpox and Vaccinia viruses, which are used in vaccines against smallpox and are normally responsible for zoonoses, can also infect humans.

Alastrim, a disease that spread rapidly everywhere

Thanks to the extraordinary vaccination campaign implemented worldwide, not only human smallpox has been eradicated but also the clinically less serious form, *Alastrim* [29,30]. The name *Alastrim* is of Brasilian origin, being derived from a Portuguese word meaning to spread or strew about.

This term, introduced in the scientific language in 1910 by the Brazilian doctor Emilio Ribas, in the Portuguese language indicates "something that spreads rapidly everywhere" [31, 32].

Alastrim was also known as pseudovariola or whitepox, Kaffir pox [33] and by various other names.

Variola minor produced a milder illness with case-fatality rates of 1% or less, as opposed to 30% in the case of *Variola virus*. This is why it was used in antiquity in the variolation technique.

De Korte described it as "Cafri fever" for the first time in the late 19th century in South Africa. And in 1897 Chapin witnessed its presence in the United States of America. *Variola minor* became the prevalent variety in America, Europe and some areas of eastern and southern Africa [12].

In 1921, *Alastrim* struck Jamaica [34] and in November 1922 it appeared in French Guiana, where many cases were mistaken for chickenpox, given the many points of similarity between the two diseases. In a 1924 article by Stéphen Chauvet, a physician of internal medicine at the Paris Hospitals, *Alastrim* was described as an almost unknown disease, unmentioned in pathology textbooks. "Some seaports visited by steamships from Central America and the Antilles (Bordeaux, Saint Nazare, le Havre) have recently seen cases of an eruptive disease hitherto completely unknown in France, *Alastrim* […]" [35].

At the time of Dr. Chauvet, *Alastrim* also raised an important diagnostic problem: that of his relationship with smallpox, asserted by some and denied by others. From this theoretical problem important practical deductions necessarily arose regarding the curative and preventive treatment and the choice of prophylactic sanitary measures.

Clinically, after an incubation period of 10-14 days (like that of *Variola maior*), which however in some cases is reduced to 7 days, the infected person developed dermatitis.

The lesions were initially erythematous, subsequently papular, and then papulo-vesicular; in the following 1-2 days, centrally umbilicated pustular lesions appeared. The papules, which were fewer than in cases of *Variola maior*, first appeared on the face and then on the trunk, without itching. In addition to the skin lesions, the patient presented general malaise, digestive disturbances and a slight fever, which disappeared when the rash appeared (Fig. 1).

In his article, Stéphen Chauvet stated that *Alastrim* had a "*predilection for the black race*", unlike smallpox, smallpox and chickenpox, which "*affect all races without distinction*". However, the editorial staff of the journal inserted a note, specifying that: "*This article was in composition when Dr. Léon Bernard presented some preliminary clarifications on Alastrim to the Paris Academy of Medicine (October, 1923): this author now*

Fig. 1. Patient affected by Alastrim (from Chauvet S. L'Alastrim. 1924)

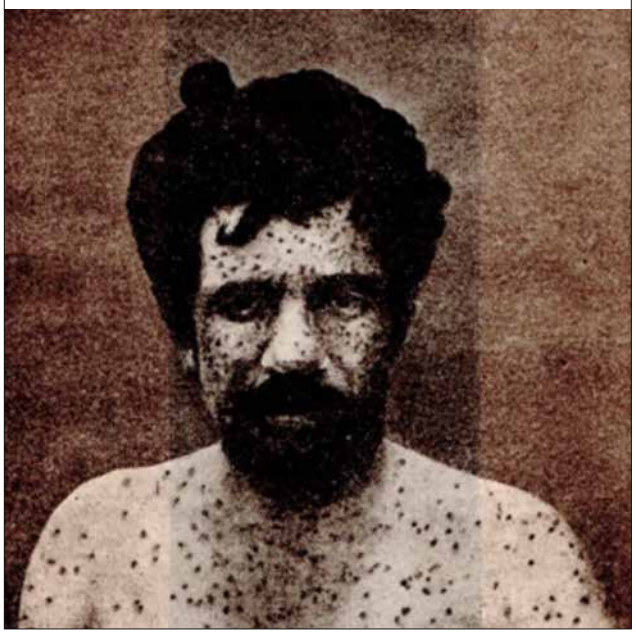
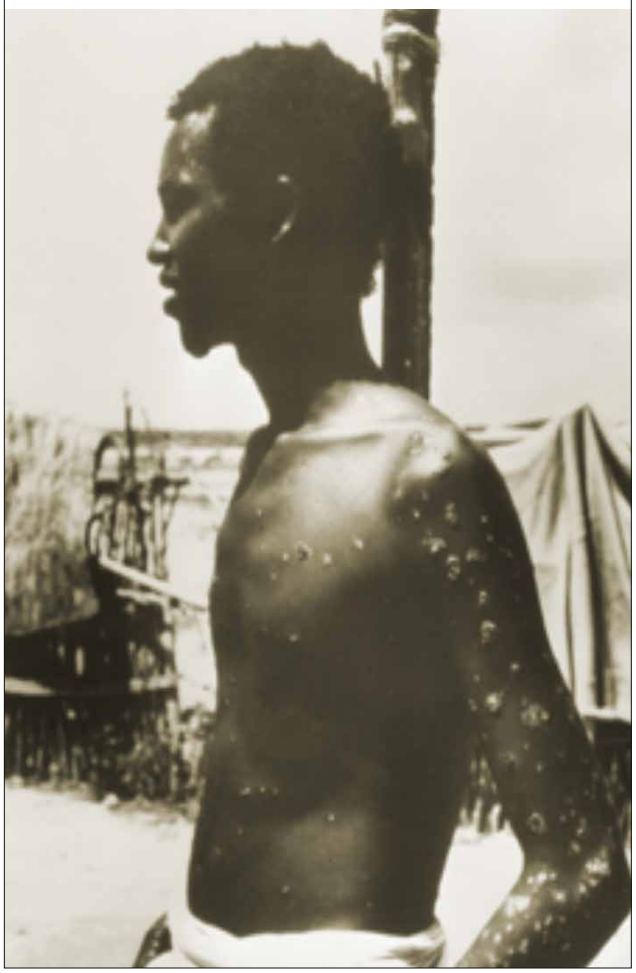


Fig. 2. Ali Maow Maalin, 1977, while infected with Alastrim (Wikipedia commons - public domain)



states that only negroes are affected. In reality, this statement, which Dr. Bernard absolutely insisted on, is completely wrong; the white race is affected just like blacks. Perhaps, as Dr. Blin observes, the black race is particularly sensitive; it is, however, more likely that blacks are affected more frequently owing to their lack of hygiene. We note that the photographs presented by Dr. Stéphen Chauvet in this article show a white sailor affected by Alastrim" [35].

Clearly, the content of this note and the terminology used are absolutely unacceptable. Nevertheless, the note shows that *Alastrim* long remained an almost unknown disease, so much so that doubts were raised as to whether the virus responsible actually belonged to the *Orthopoxvirus* family. Indeed, the linear double-stranded DNA sequences of the *Alastrim* virus genome were only determined in the 1960s [36].

Conclusion

It was precisely this virus that infected Ali Maow Maalin (1954-2013) (Fig. 2), the last person to be infected with *Variola minor*.

On 22 October 1977, Maalin, who was occasionally involved in smallpox vaccination campaigns organized by the WHO in Somalia, developed fever and headache, and was given antimalarial drugs. Four days later, a rash typical of smallpox appeared. However, presuming that Maalin had been vaccinated against smallpox, the doctors assumed he had chickenpox. After a few days, the symptoms began to indicate smallpox infection. However, not wishing to be placed in solitary confinement, Maalin did not report himself as a probable smallpox patient; he therefore came into contact with numerous individuals. Eventually, the diagnosis of smallpox caused by *Variola minor* became clear, and was confirmed by laboratory tests. Containment measures were immediately implemented, first in the Merca region, where Maalin lived, and later throughout Somalia. On April 17, 1978, a communiqué from the WHO office in Mairobi stated: "Search complete. No cases discovered. Ali Maow Maalin is the world's last known smallpox case" [37].

Thus ended the story of smallpox, which, on 8 May 1980, was declared by the WHO to have been eradicated from the world! [38] And so it was *Alastrim* - a disease caused by the minor form of the *Variola virus* and far less well-known than human smallpox - that closed the story of an evil that had afflicted humanity since the dawn of time, striking terror into people's hearts.

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Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

DO and MM conceived the study; DO designed the study; MM and DO drafted the manuscript. DO, MM and NLB performed a search of the literature.
All authors revised the manuscript; NLB and MB critically revised the manuscript. All authors have read and approved the latest version of the paper for publication. Furthermore: DO: conceptualization, and MM, DO, NLB: methodology, validation, and data curation; NLB, MB: formal analysis; MM and DO: original draft preparation; MM: review, DO editing.

References

[1] Saxena SK, Ansari S, Maurya VK, Kumar S, Jain A, Paweska JT, Tripathi AK, Abdel-Moneim AS. Re-emerging human monkeypox: A major public-health debacle. J Med Virol 2023;95:e27902. https://doi.org/10.1002/jmv.27902.

[2] World Health Organization - 2022 Mpox (Monkeypox) Outbreak: Global Trends.Available at: https://worldhealthorg.shinyapps.io/mpx_global/ (Accessed on: June 20, 2023).

[3] Bunge EM, Hoet B, Chen L, Lienert F, Weidenthaler H, Baer LR, Steffen R. The changing epidemiology of human monkeypox-A potential threat? A systematic review. PLoS Negl Trop Dis 2022;16(2):e0010141. https://doi.org/10.1371/journal.pntd.0010141

[4] Duggan AT, Perdomo MF, Piombino-Mascali D, Marciniak S, Poinar D, Emery MV, Buchmann JP, Duchêne S, Jankauskas R, Humphreys M, Golding GB, Southon J, Devault A, Rouillard JM, Sahl JW, Dutour O, Hedman K, Sajantila A, Smith GL, Holmes EC, Poinar HN. 17th Century Variola Virus Reveals the Recent History of Smallpox. Curr Biol 2016;26:3407-12. https://doi.org/10.1016/j.cub.2016.10.061

[5] Martini M, Bifulco M, Orsini D. Smallpox vaccination and vaccine hesitancy in the Kingdom of the Two Sicilies (1801) and the great modernity of Ferdinand IV of Bourbon: a glimpse of the past in the era of the SARS-COV-2 (COVID-19) pandemic. Public Health 2022;213:47-53. https://doi.org/10.1016/j.puhe.2022.09.012

[6] Jenner E. On the Origin of the Vaccine Inoculation. Med Phys J 1801;5:505-8.

[7] Jenner E. An inquiry into the causes and effects of the variolae vaccinae: a disease discovered in some of the western counties of England, particularly Gloucestershire, and known by the name of the cow pox. Springfield [Mass.]: Re-printed for Dr. Samuel Cooley, by Ashley & Brewer 1802.

[8] Orsini D, Martini M. From inoculation to vaccination: the fight against smallpox in Siena in the 18th and 19th centuries, Le Infezioni in Medicina 2020;(4):634-41.

[9] Bifulco M, Di Zazzo E, Pisanti S, Martini M, Orsini D. The nineteenth-century experience of the kingdom of the two Sicilies on mandatory vaccination: An Italian phenomenon? Vaccine 2022;40:3452-4. https://doi.org/10.1016/j.vaccine.2022.04.052

[10] Smith GL. Genus Orthopoxvirus: Vaccinia virus. In: Mercer, AA, Schmidt A, Weber O, eds. Poxviruses. Birkhäuser Advances in Infectious Diseases. Birkhäuser Basel 2007. https://doi.org/10.1007/978-3-7643-7557-7_1

[11] Ahmed SF, Sohail MS, Quadeer AA, McKay MR. Vaccinia-Virus-Based Vaccines Are Expected to Elicit Highly Cross-Reactive Immunity to the 2022 Monkeypox Virus. Viruses 2022;14:1960. https://doi.org/10.3390/v14091960

[12] Henderson DA, Moss B. Smallpox and Vaccinia (Chapter 6). In: Vaccines. 3rd ed. Philadelphia: Saunders 1999.

[13] Isidro J, Borges V, Pinto M, Sobral D, Santos JD, Nunes A, Mixão V, Ferreira R, Santos D, Duarte S, Vieira L, Borrego MJ, Núncio S, de Carvalho IL, Pelerito A, Cordeiro R, Gomes JP. Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus. Nat Med 2022;28:1569-72. https://doi.org/10.1038/s41591-022-01907-y. Erratum in: Nat Med 2022;28:2220-1.

[14] Dumonteil E, Herrera C, Sabino-Santos G. Monkeypox Virus Evolution before 2022 Outbreak. Emerg Infect Dis2023;29:451-453. https://doi.org/10.3201/eid2902.220962.

[15] World Health Organization (WHO). WHO Director-General's statement at the press conference following IHR Emergency Committee regarding the multi-country outbreak of monkeypox - 23 July 2022. Available at: https://www.who.int/director-general/speeches/detail/who-director-general-s-statement-on-the-press-conference-following-IHR-emergency-committee-regarding-the-multi--country-outbreak-of-monkeypox--23-july-2022 (Accessed on: June 20, 2023).

[16] World Health Organization - 2022 Mpox (monkeypox). Available at: https://www.who.int/health-topics/monkeypox#tab=tab_1. (Accessed on: June 20, 2023).

[17] Antinori A, Mazzotta V, Vita S, Carletti F, Tacconi D, Lapini LE, D'Abramo A, Cicalini S, Lapa D, Pittalis S, Puro V, Rivano Capparuccia M, Giombini E, Gruber CEM, Garbuglia AR, Marani A, Vairo F, Girardi E, Vaia F, Nicastri E; INMI Monkeypox Group. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. Euro Surveill 2022;27:2200421. https://doi.org/10.2807/1560-7917.ES.2022.27.22.2200421

[18] [18] Mitjà O, Ogoina D, Titanji BK, Galvan C, Muyembe JJ, Marks M, Orkin CM. Monkeypox. Lancet 2023;401:60-74. https://doi.org/10.1016/S0140-6736(22)02075-X. Erratum in: Lancet.2022;400:1926.

[19] Baldovin T, Girolametto G, Geppini R, Bordignon M, Alaibac M. Preventing and fighting stigma: a lesson from the first Mpox in Veneto region of Northeast Italy-A case report. Front Public Health 2023;11:1141742. https://doi.org/10.3389/fpubh.2023.1141742

[20] World Health Organization. WHO recommends new name for monkeypox disease - 28 November 2022. Available at: https://www.who.int/news/item/28-11-2022-who-recommends-new-name-for-monkeypox-disease (Accessed on: June 20, 2023).

[21] Cho CT, Wenner HA. Monkeypox virus. Bacteriol Rev 1973;37:1-18. https://doi.org/10.1128/br.37.1.1-18.1973

[22] Breman JG, Kalisa R, Steniowski MV, Zanotto E, Gromyko AI, Arita I. Human monkeypox, 1970-79. Bull World Health Organ 1980;58:165-82.

[23] Marennikova SS, Seluhina EM, Mal'ceva NN, Cimiskjan KL, Macevic GR. Isolation and properties of the causal agent of a new variola-like disease (monkeypox) in man. Bull World Health Organ 1972;46:599-611.

[24] Jezek Z, Fenner F. Melnick JL. Human monkeypox. Monographs in virology (vol. 17). Basel, Switzerland: Karger 1988.

[25] Gross E. Update on emerging infections: news from the Centers for Disease Control and prevention. Update: Multistate outbreak of monkeypox--Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003. Ann Emerg Med 2003;42:660-2; discussion 662- 4. https://doi.org/10.1016/s0196064403008199

[26] Bunge EM, Hoet B, Chen L, Lienert F, Weidenthaler H, Baer LR, Steffen R. The changing epidemiology of human monkeypox-A potential threat? A systematic review. PLoS Negl Trop Dis 2022;16:e0010141. https://doi.org/10.1371/journal.pntd.0010141

[27] World Health Organization. Regional Office for Africa. Weekly bulletin on outbreak and other emergencies: Week 4: 18–24 January 2021. World Health Organization, Regional Office for Africa 2021. Available at: https://apps.who.int/iris/handle/10665/338891 (Accessed on: June 20, 2023).

[28] World Health Organization. Regional Office for Africa. Weekly bulletin on outbreak and other emergencies: Week 4: 17–23 January 2022. World Health Organization, Regional Office for Africa. 2022. Available at: https://apps.who.int/iris/handle/10665/351164 (Accessed on: June 20, 2023).

[29] Alastrim (Variola minor). In: Jawetz E, Melnick JL, Adelberg KA. Medical Microbiology. Padova: Piccin Editore 1973, p. 621.

[30] Shchelkunov SN, Totmenin AV, Loparev VN, Safronov PF, Gutorov VV, Chizhikov VE, Knight JC, Parsons JM, Massung RF, Esposito JJ. Alastrim smallpox variola minor virus genome DNA sequences. Virology.2000;266:361-86. https://doi.org/10.1006/viro.1999.0086

[31] Ribas, E. Alastrim, amaas or milk-pox. Trans. Roy Soc Trop Med Hyg 1910;4:224-32.

[32] Torres CM. Further Studies on the Pathology of Alastrim and Their Significance in the Variola-Alastrim Problem. Proc R Soc Med 1936;29:1525-40. https://doi.org/10.1177/003591573602901201

[33] Mukerji BK. A Case of Alastrim (Kaffir Pox). Ind Med Gaz 1924;59:89-90.

[34] Maccallum WG, Moody LM. Alastrim in Jamaica. American J Epidemiol 1921;1:388-409. https://doi.org/10.1093/oxfordjournals.aje.a118044

[35] Chauvet S. L'Alastrim. Una nuova malattia eruttiva. La Rassegna di clinica, Terapia e Scienze affini 1924;XXIII(3):123.

[36] Shchelkunov SN, Totmenin AV, Loparev VN, Safronov PF, Gutorov VV, Chizhikov VE, Knight JC, Parsons JM, Massung RF, Esposito JJ. Alastrim smallpox variola minor virus genome DNA sequences. Virology 2000;266:361-86. https://doi.org/10.1006/viro.1999.0086

[37] Jonathan B. Tucker, Scourge: The Once and Future Threat of Smallpox. Grove Press, 2002, pp. 117-8.

[38] Parodi A, Martini M. History of vaccine and immunization: Vaccine-hesitancy discussion in Germany in XIX century. Vaccine 2023;41:1989-93. https://doi.org/10.1016/j.vaccine.2023.02.029

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