Monkeypox (Mpox)
An Emergence of African Origin

Historical, Clinical, Epidemiological aspects, Reservoir and Current Situation

Antoine Gessain

Unité Épidémiologie et Physiopathologie des Virus Oncogènes

Four main Chapters

1) History, Virus, Genetic variability, Reservoir

2) Clinical and epidemiological aspects of the african classical form

3) First emergence in 2022 and different aspects of the pandemic : *WHO Director-General declares mpox outbreak a public health emergency of international concern*

4) Second emergence in 2024 in DRC and East Africa
WHO Director-General declares mpox outbreak a public health emergency of international concern

Discovery and Isolation of Monkeypox Virus in 1958

FROM STATENS SERUMINSTITUT, DIRECTOR J. ØRSKOV, M.D.

A POX-LIKE DISEASE IN CYNOMOLGUS MONKEYS

By

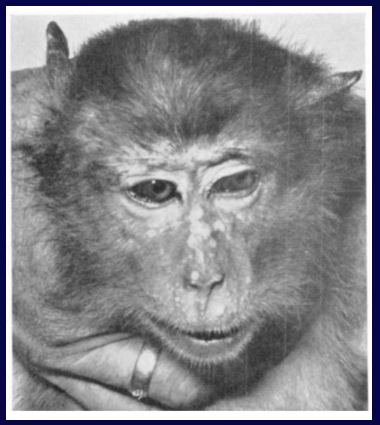
PREBEN VON MAGNUS, ELSE KRAG ANDERSEN,
KNUD BIRKUM PETERSEN and AKSEL BIRCH-ANDERSEN

Received 27.ii.59

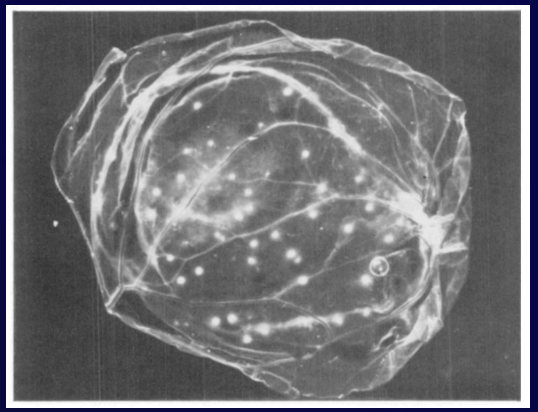
- In 1958 two outbreaks of a spontaneous non-fatal pox-like disease in cynomolgus monkeys have been observed in the colony of this Institute
- Generalized maculopapular rash
- General health quite unaffected with no fatal cases
- Isolation of the virus from pustular lesions in eggs and in tissue culture
- Serologically related to vaccinia virus
- Typical brick-shape appearance of pox virus in EM

It was called monkeypox virus

Acute phase
with typical pustules



Convalescent stage
lesions in healing and scars



Monkeypox virus on the chorio-allantoic membrane with typical discrete opaque foci

First Recognized Human Monkeypox Case in Medical History

Between 1960 and 1968, several other MPX outbreaks were reported in captive monkey colonies in the USA and the Netherlands. No human cases were detected during these outbreaks, despite the death of many affected animals suggesting that humans were not susceptible to monkeypox

Bull. Org. mond. Santé
Bull. Wld Hlth Org. } 1972, **46**, 593-597

A human infection caused by monkeypox virus in Basankusu Territory, Democratic Republic of the Congo *

I. D. LADNYJ,[1] P. ZIEGLER,[2] & E. KIMA [3]

The first case of Monkey pox in human was reported in 1970 as part of the national smallpox surveillance and eradication program then underway in Africa.

This case occured in a nine-month-old-boy who developped a fever, followed two days latter by a centrifugal skin rash.

On Sept 1, 1970, he was admitted to Basankusu hospital, in the DRC with otitis, mastoiditis and painfull cervical lymph nodes. MPXV was isolated from his skin lesions.

He revovered from MPX but developped measles, leading to his death, before discharge.

Human Monkeypox in West Africa 1970-1971

6 cases were reported mostly in children

Bull. Org. mond. Santé / *Bull. Wld Hlth Org.* 1972, **46**, 569–576

Human monkeypox *

STANLEY O. FOSTER,[1] EDWARD W. BRINK,[2] DEANE L. HUTCHINS,[3] JOHN M. PIFER,[4] BERNARD LOURIE,[5] CLAUDE R. MOSER,[6] EVELYN C. CUMMINGS,[7] O.E.K. KUTEYI,[8] REGINALD E. A. EKE,[9] J. B. TITUS,[10] E. ADEMOLA SMITH,[11] JAMES W. HICKS,[12] & WILLIAM H. FOEGE[13]

Table 1. Clinical cases of human monkeypox infection, Liberia, Nigeria, and Sierra Leone, 1970–71

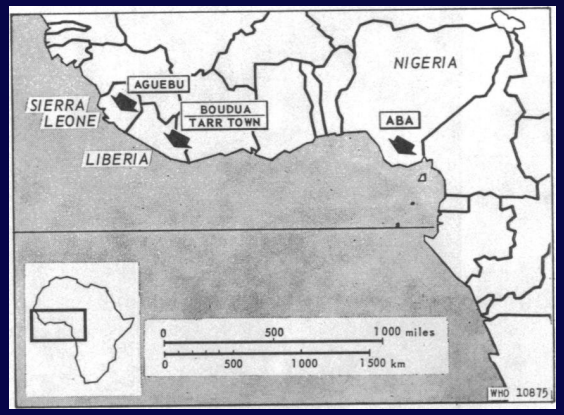
Case	Country	Village	Age	Sex	Vaccination history	Date of rash	Prodrome in days	Severity of rash [a]	Duration of rash (days)
1	Liberia	Boudua	4	F	Negative	13 Sept. 70	3	++	24
2	Liberia	Boudua	4	M	Negative	12 Sept. 70	1	+	4
3	Liberia	Boudua	6	F	Negative	13 Sept. 70	2-3	+	4
4	Liberia	Tarr	9	M	Negative	2 Oct. 70	?	++	21
5	Sierra Leone	Aguebu	24	M	Negative	1 Dec. 70	3-4	+++	28
6	Nigeria	Aba	4	F	Negative	19 May 71	5	+++	26

[a] + Mild
++ Moderate
+++ Severe

Bull. Org. mond. Santé / *Bull. Wld Hlth Org.* 1972, **46**, 633-639

Human infection with monkeypox virus : laboratory investigation of six cases in West Africa *

BERNARD LOURIE,[1] PATRICIA G. BINGHAM,[2] HARMON H. EVANS,[2] STANLEY O. FOSTER,[3] JAMES H. NAKANO,[4] & KENNETH L. HERRMANN [5]



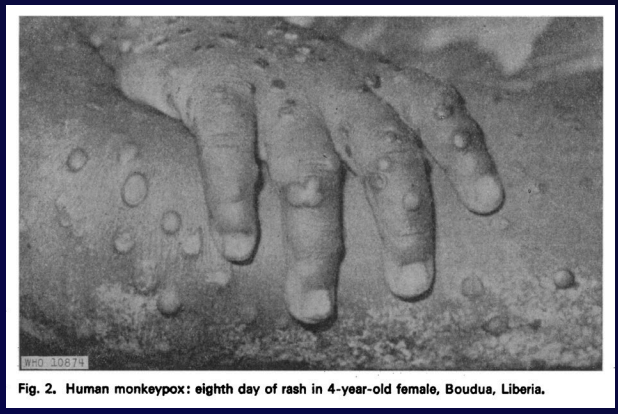
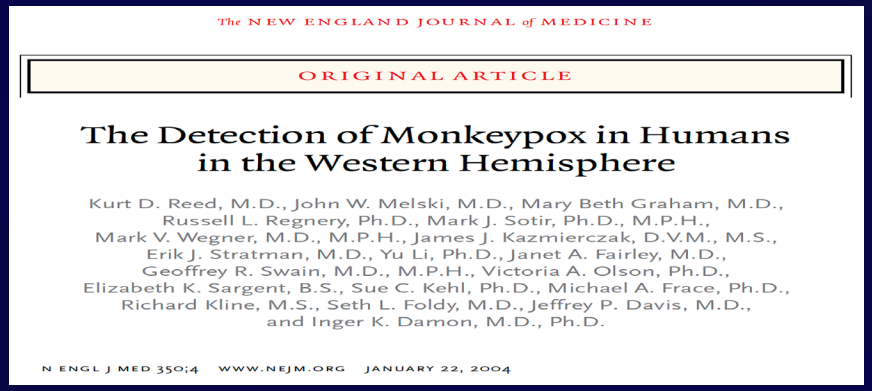


Fig. 2. Human monkeypox: eighth day of rash in 4-year-old female, Boudua, Liberia.

Monkeypox remained an exclusively african disease with sporadic cases in forested areas of central and western Africa and small outbreaks in the human population, mainly in DRC, until 2003 when the first cases out of Africa were reported.

First Monkeypox in Humans out of Africa in 2003



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

The Detection of Monkeypox in Humans in the Western Hemisphere

Kurt D. Reed, M.D., John W. Melski, M.D., Mary Beth Graham, M.D., Russell L. Regnery, Ph.D., Mark J. Sotir, Ph.D., M.P.H., Mark V. Wegner, M.D., M.P.H., James J. Kazmierczak, D.V.M., M.S., Erik J. Stratman, M.D., Yu Li, Ph.D., Janet A. Fairley, M.D., Geoffrey R. Swain, M.D., M.P.H., Victoria A. Olson, Ph.D., Elizabeth K. Sargent, B.S., Sue C. Kehl, Ph.D., Michael A. Frace, Ph.D., Richard Kline, M.S., Seth L. Foldy, M.D., Jeffrey P. Davis, M.D., and Inger K. Damon, M.D., Ph.D.

N ENGL J MED 350;4 WWW.NEJM.ORG JANUARY 22, 2004

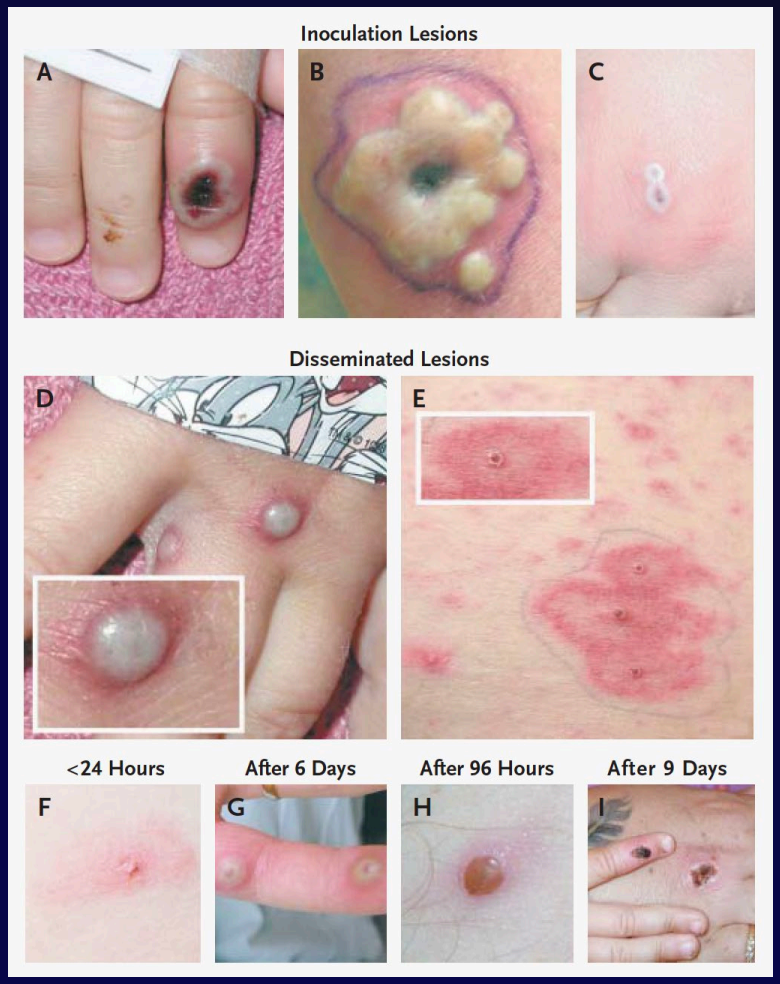
-This event occured in the USA and was linked to the importation of Gambian pouched rats (*Cryceto* from Ghana to Texas.

-These rodents transmitted the virus to prairie dogs housed at the same exotic animal facility. which then infected humans mostly young adults and childr through bites or scratches.

-No deaths, few hospitalisations

- MPXV was isolated by cell culture from 7 patients and one prairie dog.

-

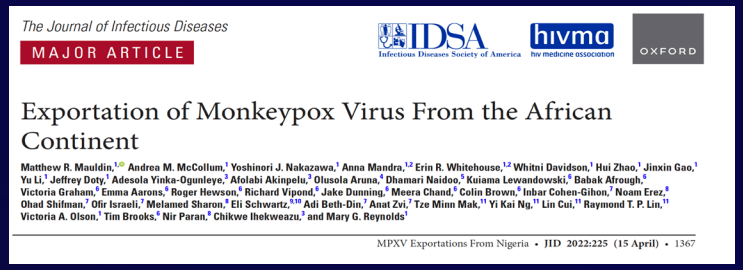


Primary innoculation reactions (A, B, C)

Smallpox-like (D), umbilicated varicella-like (E)

Morphological appearance of lesions over time

First Export of MPXV from the African Continent by Human Hosts in 2018 (UK, Israel and Singapore)



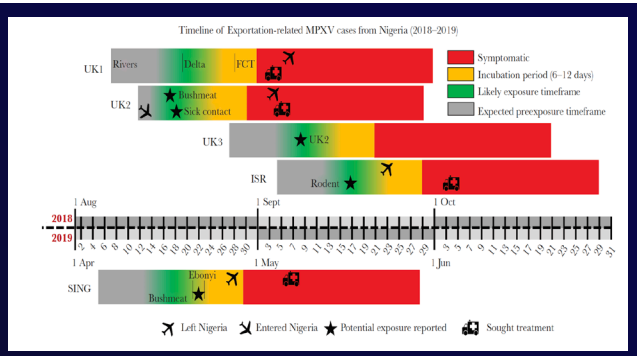
The Journal of Infectious Diseases

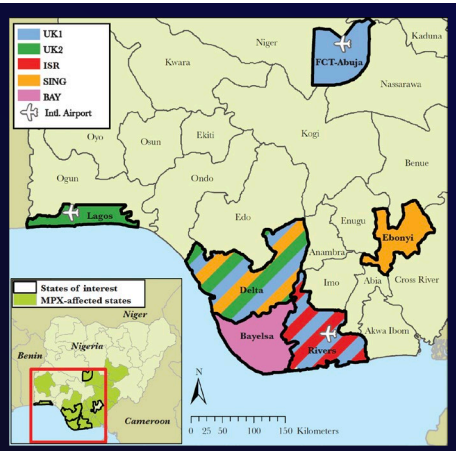
MAJOR ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Exportation of Monkeypox Virus From the African Continent

Matthew R. Mauldin,[1,©] Andrea M. McCollum,[1] Yoshinori J. Nakazawa,[1] Anna Mandra,[1,2] Erin R. Whitehouse,[1,2] Whitni Davidson,[1] Hui Zhao,[1] Jinxin Gao,[1] Yu Li,[1] Jeffrey Doty,[1] Adesola Yinka-Ogunleye,[3] Afolabi Akinpelu,[3] Olusola Aruna,[4] Dhamari Naidoo,[5] Kuiama Lewandowski,[4] Babak Afrough,[6] Victoria Graham,[6] Emma Aarons,[6] Roger Hewson,[6] Richard Vipond,[6] Jake Dunning,[6] Meera Chand,[6] Colin Brown,[6] Inbar Cohen-Gihon,[7] Noam Erez,[8] Ohad Shifman,[7] Ofir Israeli,[7] Melamed Sharon,[9] Eli Schwartz,[9,10] Adi Beth-Din,[7] Anat Zvi,[7] Tze Minn Mak,[11] Yi Kai Ng,[11] Lin Cui,[11] Raymond T. P. Lin,[11] Victoria A. Olson,[1] Tim Brooks,[6] Nir Paran,[6] Chikwe Ihekweazu,[4] and Mary G. Reynolds[1]

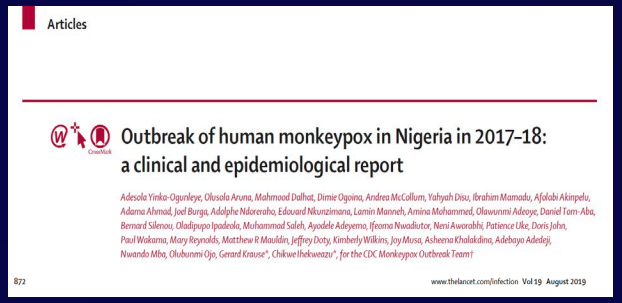




Outbreak in Nigeria 2017/2018

122 confirmed or probable cases in 17 states, median age 29 years, 84% male, 7 deaths (HIV)

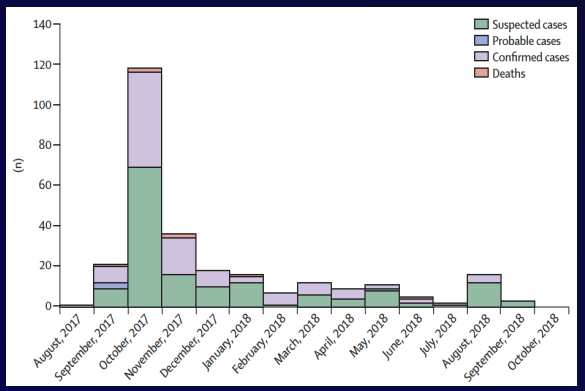
Distribution suggested both primary Zoonosis (+/-) and secondary human-to-human transmission (++ male, young, HIV).



Articles

Outbreak of human monkeypox in Nigeria in 2017–18: a clinical and epidemiological report

Adesola Yinka-Ogunleye, Olusola Aruna, Mahmood Dalhat, Dimie Ogoina, Andrea McCollum, Yahyah Disu, Ibrahim Mamadu, Afolabi Akinpelu, Adama Ahmad, Joel Burga, Adolphe Ndoreraho, Edouard Nkunzimana, Lamin Manneh, Amina Mohammed, Olawunmi Adeoye, Daniel Tom-Aba, Bernard Silenou, Oladipupo Ipadeola, Muhammad Saleh, Ayodele Adeyemo, Ifeoma Nwadiutor, Neni Awarabhi, Patience Uke, Doris John, Paul Wakama, Mary Reynolds, Matthew R Mauldin, Jeffrey Doty, Kimberly Wilkins, Joy Musa, Asheena Khalakdina, Adebayo Adedeji, Nwando Mba, Olubunmi Ojo, Gerard Krause*, Chikwe Ihekweazu*, for the CDC Monkeypox Outbreak Team†



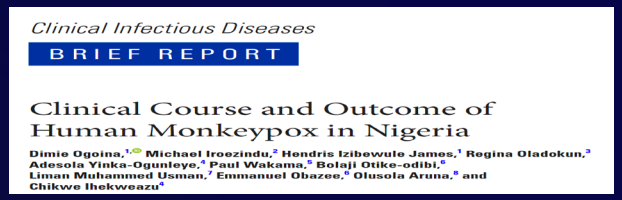
viruses · MDPI

Review

Monkeypox Virus in Nigeria: Infection Biology, Epidemiology, and Evolution

Emmanuel Alakunle [1], Ugo Moens [2], Godwin Nchinda [3,4] and Malachy Ifeanyi Okeke [1,*]

Viruses 2020, *12*, 1257; doi:10.3390/v12111257 www.mdpi.com/journal/viruses

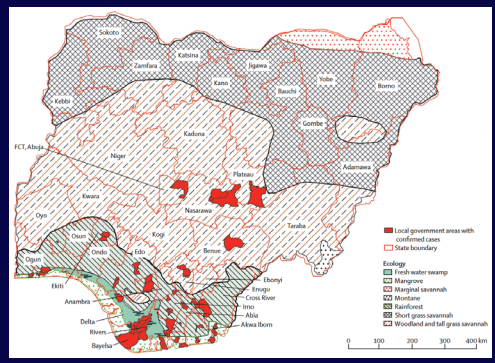


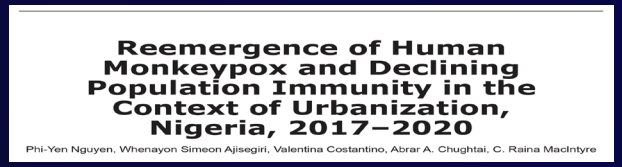
Clinical Infectious Diseases

BRIEF REPORT

Clinical Course and Outcome of Human Monkeypox in Nigeria

Dimie Ogoina,[1,©] Michael Iroezindu,[2] Hendris Izibewule James,[1] Regina Oladokun,[3] Adesola Yinka-Ogunleye,[4] Paul Wakama,[5] Bolaji Otike-odibi,[6] Liman Muhammad Usman,[7] Emmanuel Obazee,[8] Olusola Aruna,[8] and Chikwe Ihekweazu[4]





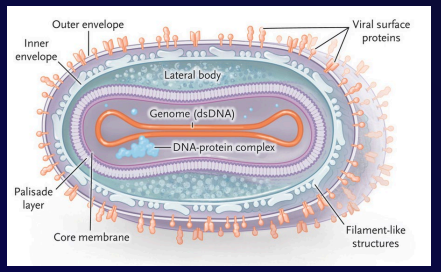
Reemergence of Human Monkeypox and Declining Population Immunity in the Context of Urbanization, Nigeria, 2017–2020

Phi-Yen Nguyen, Whenayon Simeon Ajisegiri, Valentina Costantino, Abrar A. Chughtai, C. Raina MacIntyre

Monkeypox Virus

- *Poxviridae* family,*Chordopoxvirinae* subfamily
- *Orthopox* genus (Variola virus-smallpox, vaccinia virus-smallpox vaccine, cowpox, camelpox and recently isolated poxviruses-Alaskapox)

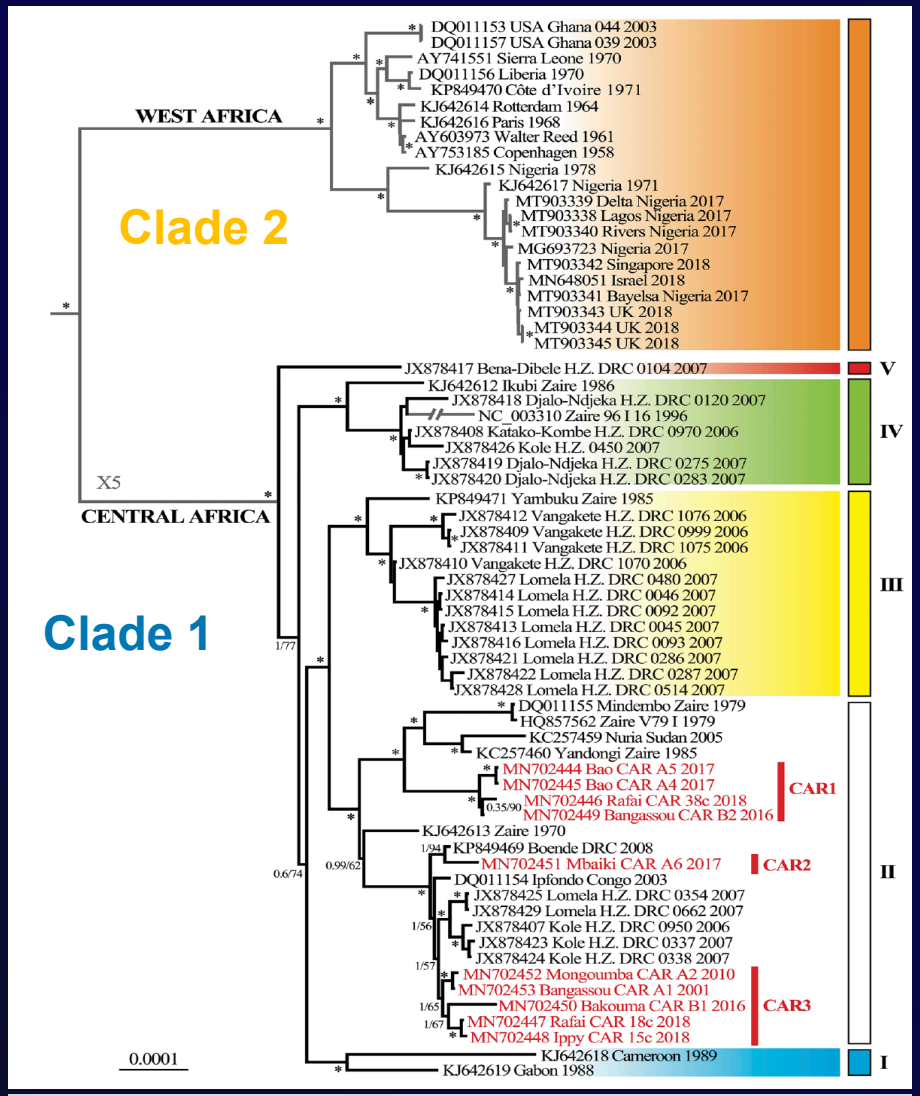
- MPXV is a large enveloped virus
- Each virion encapsulates a core containing a linear double-stranded DNA genome of 200 kilobase pairs encoding approximately 200 proteins



In EM, MPXV has the characteristics of a rectangular or ovoid brick

- Orthopoxviruses are very similar genetically and antigenically, which explains the cross-immunity, with some protection beetween them
- Vaccination against smallpox generally protects against monkeypox (85% in a historical study in Zaire, central Africa)
- This phenomena is one of the factors favoring the emergence of monkeypox

Genetic Variability of Monkeypox



Historically, there are two genetic clades, genomes differ by around 5%, the first being endemic to **Central Africa**, the second to **West Africa**

With the emergence of MPXV outside of Africa, and need to destigmatize the disease and prevent discrimination, definition of 2 clades were done (Clade I and Clade II)

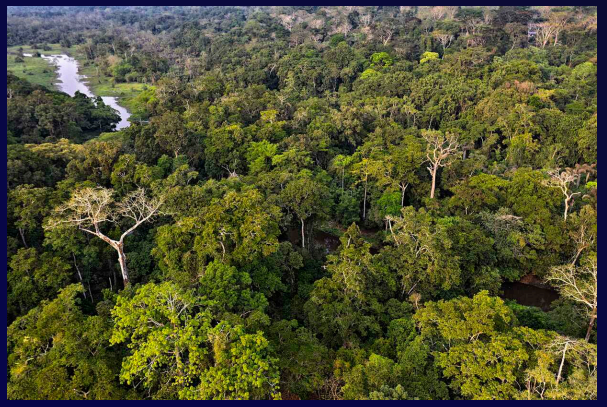
Co-existence of the two clades in Cameroon

Reservoirs of Monkeypox

Cricetomys
giant pouched rats

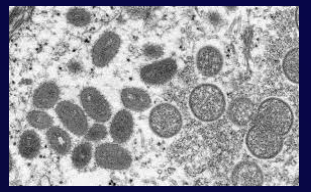
Funisciurus anerythrus

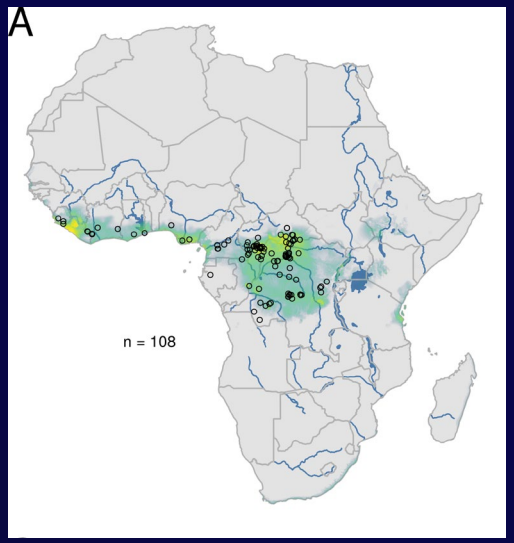
- Monkey pox is a sylvatic zoonosis but the reservoir of MPVX has not yet been clearly identified
- Rodents, including various species of squirell and rats living in the rain forests of Central and West Africa, are among the best candidates
- African apes and monkeys are considered intermediate hosts
- Many animals, including rabbits, prairie dogs, other rodents and monkeys are susceptible to infection in captivity and in the laboratory



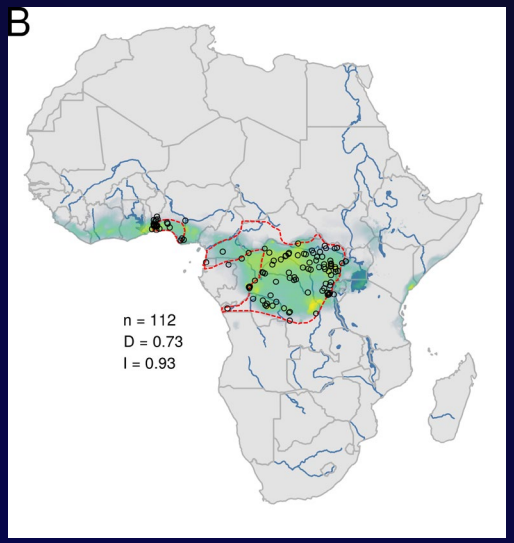
What Are the Most Likely Animal Reservoir Hosts for MPXV?

A Study Based on Ecological Niche Comparison



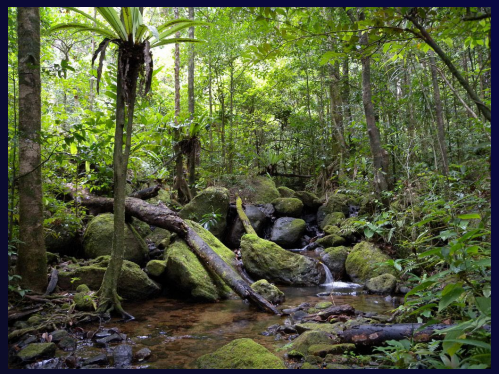


Ecological niche of MPXV



Ecological niche for *Funisciurus anerythrus*

showing the best overlap : Best candidate



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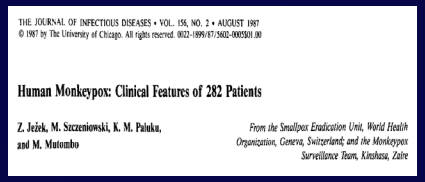
Article

Identifying the Most Probable Mammal Reservoir Hosts for Monkeypox Virus Based on Ecological Niche Comparisons

Manon Curaudeau [1,2], Camille Besombes [3], Emmanuel Nakouné [4], Arnaud Fontanet [3,5], Antoine Gessain [2] and Alexandre Hassanin [1,*]

Viruses **2023**, *15*, 727. https://doi.org/10.3390/v15030727 https://www.mdpi.com/journal/viruses

Curaudeau et al., Viruses 2023

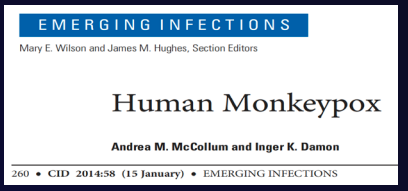

THE JOURNAL OF INFECTIOUS DISEASES • VOL. 156, NO. 2 • AUGUST 1987
© 1987 by The University of Chicago. All rights reserved. 0022-1899/87/5602-0005$01.00

Human Monkeypox: Clinical Features of 282 Patients

Z. Ježek, M. Szczeniowski, K. M. Paluku, and M. Mutombo

From the Smallpox Eradication Unit, World Health Organization, Geneva, Switzerland; and the Monkeypox Surveillance Team, Kinshasa, Zaire

Clinical Features in the African Setting


EMERGING INFECTIONS

Mary E. Wilson and James M. Hughes, Section Editors

Human Monkeypox

Andrea M. McCollum and Inger K. Damon

260 • CID 2014:58 (15 January) • EMERGING INFECTIONS

Based on case descriptions from the 1980 DRC, 2017 Nigeria, Rep. of Congo and CAR epidemics

MPX epidemics in small remote villages in hard-to-reach rural forested areas.

Often in the context of armed conflicts or population movements

Often associated with poor medical infrastructure and limited public health and health care staff resulting in poor patient care and follow-up

Clinical/epidemiological data obtained retrospectively and often incomplete

MPX affects both children and adults and generally has 3 phases :

Incubation; after primary infection, the average 13 days (range 3-34 days)

Prodrome; one to four days high fever, headaches, fatigue and often lymph-nodes (cervical and maxillary). This is distinguishes MPX from chickenpox (varicella)

Eruptive Phase Monkeypox in the African Setting

Lasts 14-28 days

Centrifugal skin lesions appear and evolve through different stages; macules, papules, vesicles and finally pustules.

The lesions are firm, well-delimited and umbilicated, frequently on the palms and soles of the feet (different from chickenpox)

Each patient may have a few to several thousand lesions

Lesions are at the same stage of development

Severity of symptoms/disease are proportional to the density of skin lesions

Evolution into crusts that desquamate leaving areas of hypopygmentation followed by hyperpygmentation

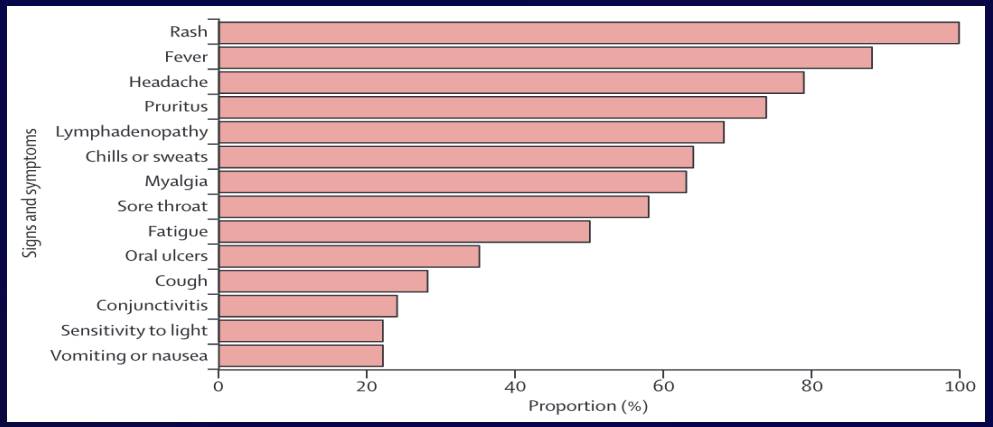
Self-limiting course but clinical sequellae, facial scars are common

Most frequent complications are bacterial skin infections

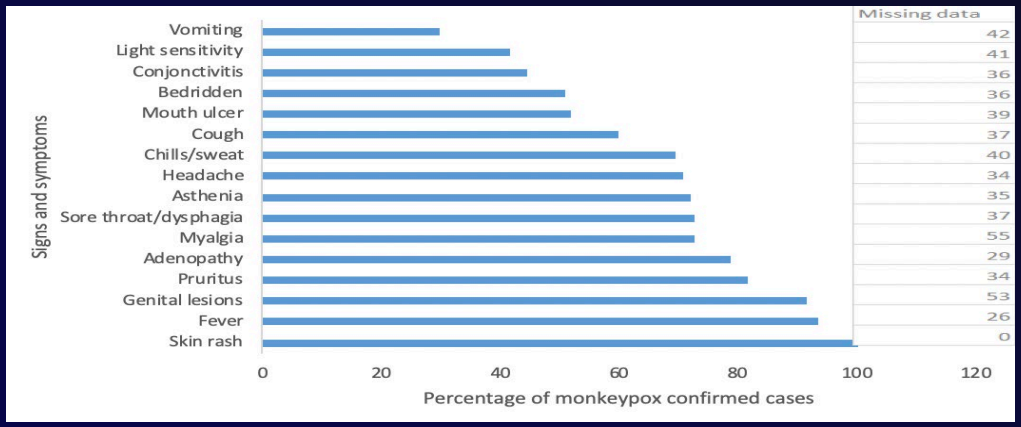
Seems to be more severe in immunocompromized HIV-infected patients

Most Frequent Clinical Signs of Monkeypox in the African Setting

Rash, Fever, Headaches, Pruritus, Lymphadenopathy,..



Frequency of signs and symptoms in people with confirmed monkeypox virus infection in Nigeria 2017-2018 (n=118) Ogunleye et al., Lancet Infectious Disease, 2019



Frequency of signs and symptoms in people with confirmed monkeypox virus infection in the CAR, 2001-2021 (n=99) Besombes et al., EID, 2022

Case Fatality Fate of Monkeypox in an African classical Setting

The overall CFR appears to be lower in patients infected with West African strains (clade II) than in those infected with Central African strains (clade I)

The CFR was 6% in Nigeria but varied from 10-15% in DRC and CAR depending on the study

Death occur mostly in children and young adults with bacterial skin infections and sepsis and in HIV-positive persons without antiretroviral therapy

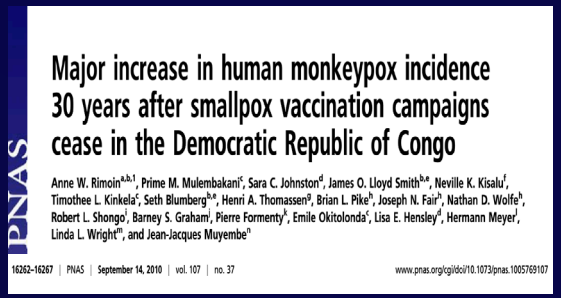
Epidemiological Aspects of Monkeypox in African Settings

Human monkeypox has been reported in ten African countries, with

a very large increase in the number of case cases over the past three decades

The DRC is, by far, the most affected country with a steady increase in suspected cases from less than 500 cases in 2011, more than 2,500 in 2018

Nigeria, Congo, CAR…



PNAS

Major increase in human monkeypox incidence 30 years after smallpox vaccination campaigns cease in the Democratic Republic of Congo

Anne W. Rimoin[a,b,1], Prime M. Mulembakani[c], Sara C. Johnston[d], James O. Lloyd Smith[b,e], Neville K. Kisalu[f], Timothee L. Kinkela[c], Seth Blumberg[b,e], Henri A. Thomassen[g], Brian L. Pike[h], Joseph N. Fair[h], Nathan D. Wolfe[h], Robert L. Shongo[i], Barney S. Graham[j], Pierre Formenty[k], Emile Okitolonda[c], Lisa E. Hensley[d], Hermann Meyer[l], Linda L. Wright[m], and Jean-Jacques Muyembe[n]

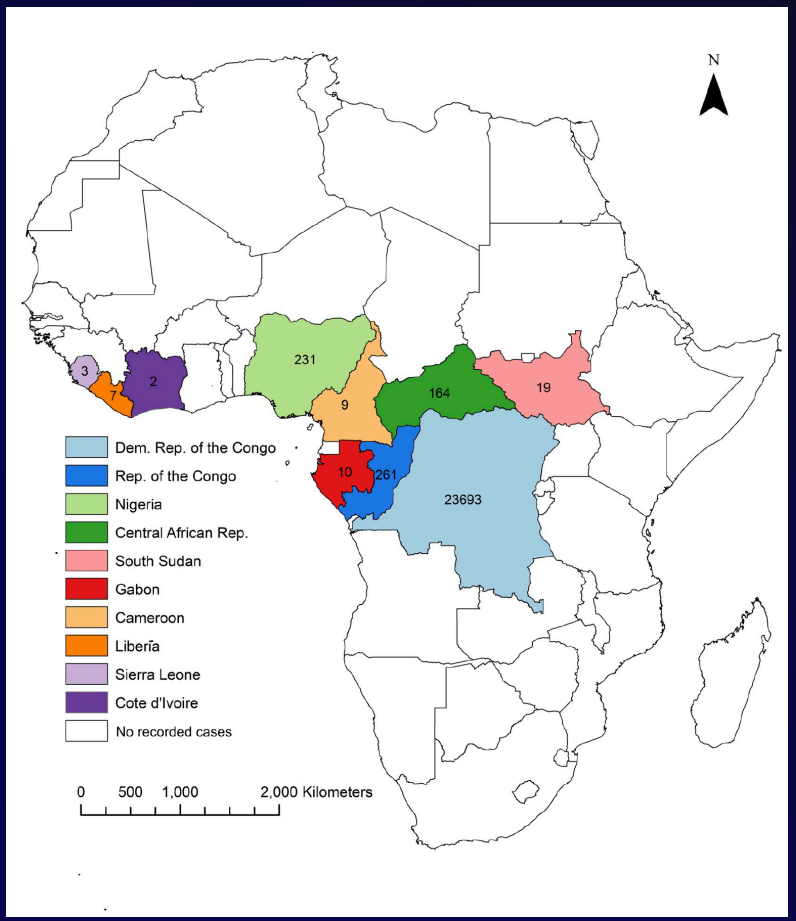
16262–16267 | PNAS | September 14, 2010 | vol. 107 | no. 37 www.pnas.org/cgi/doi/10.1073/pnas.1005769107

Increased ++ in median age at diagnosis over time

- 1970/1980 most cases were in young children
- 2010-2019, median age was 21 years
- 2018/2018 Nigeria 29 years

Large majority no vaccicnated against smallpox

Either too young or born after vaccination was stopped



Map of Africa showing countries reporting human monkeypox cases (1971-2018)

Transmission of Monkeypox in an African Settings

In Africa, both animal-to-person and person-to-person transmission has been documented

Zoonotic transmission via lesions/biological fluids from an infected animal (probably mainly rodents) when hunting, butchering or eating game

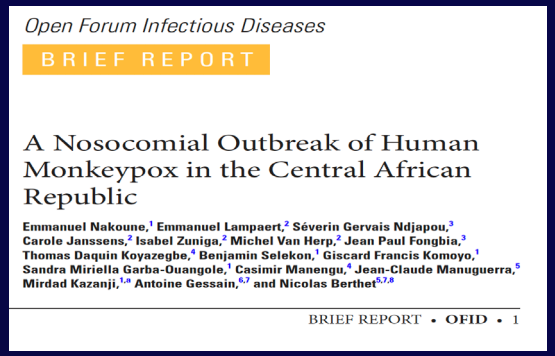
No virological confirmation of interspecies transmission to date

Human-to-human transmission occurs primarly through contact with biological fluids and infected skin lesions of patients

Contaminated materials such as beeding may also be infectious.

The exact origin of transmission is often unknown

Transmission of Monkeypox in a classical African Settings



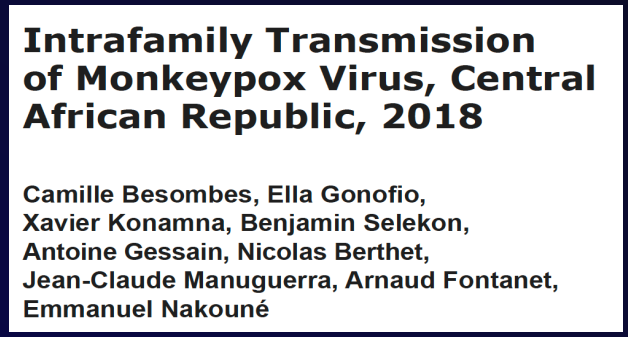
Open Forum Infectious Diseases

BRIEF REPORT

A Nosocomial Outbreak of Human Monkeypox in the Central African Republic

Emmanuel Nakoune,[1] Emmanuel Lampaert,[2] Séverin Gervais Ndjapou,[3] Carole Janssens,[2] Isabel Zuniga,[2] Michel Van Herp,[2] Jean Paul Fongbia,[3] Thomas Daquin Koyazegbe,[4] Benjamin Selekon,[1] Giscard Francis Komoyo,[1] Sandra Miriella Garba-Ouangole,[1] Casimir Manengu,[4] Jean-Claude Manuguerra,[5] Mirdad Kazanji,[1,a] Antoine Gessain,[6,7] and Nicolas Berthet[5,7,8]

Nosocomial and Intrafamilial transmission have been reported



Intrafamily Transmission of Monkeypox Virus, Central African Republic, 2018

Camille Besombes, Ella Gonofio, Xavier Konamna, Benjamin Selekon, Antoine Gessain, Nicolas Berthet, Jean-Claude Manuguerra, Arnaud Fontanet, Emmanuel Nakouné

Sexual transmission poorly documented

www.nature.com/scientificreports

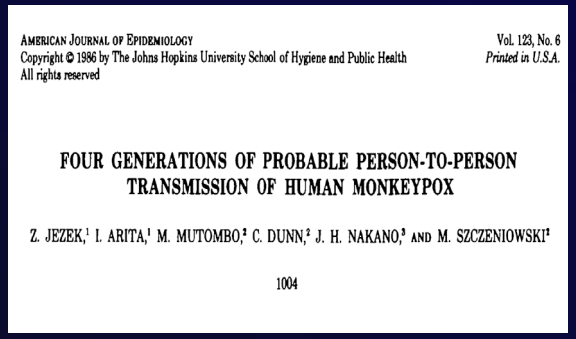
scientific reports

OPEN

Nanopore sequencing of a monkeypox virus strain isolated from a pustular lesion in the Central African Republic

Mathias Vandenbogaert[1,7], Aurélia Kwasiborski[1,7], Ella Gonofio[2,7], Stéphane Descorps-Declère[3], Benjamin Selekon[2], Andriniaina Andy Nkili Meyong[4], Rita Sem Ouilibona[2], Antoine Gessain[5], Jean-Claude Manuguerra[4], Valérie Caro[1], Emmanuel Nakoune[2,9] & Nicolas Berthet[1,6,8]

Scientific Reports | (2022) 12:10768 | https://doi.org/10.1038/s41598-022-15073-1 nature portfolio



AMERICAN JOURNAL OF EPIDEMIOLOGY
Vol. 123, No. 6

Printed in U.S.A.

FOUR GENERATIONS OF PROBABLE PERSON-TO-PERSON TRANSMISSION OF HUMAN MONKEYPOX

Z. JEZEK,[1] I. ARITA,[1] M. MUTOMBO,[2] C. DUNN,[2] J. H. NAKANO,[3] AND M. SZCZENIOWSKI[1]

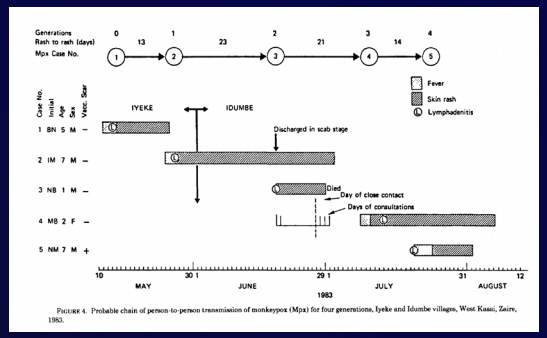


FIGURE 4. Probable chain of person-to-person transmission of monkeypox (Mpx) for four generations, Iyeke and Idumbe villages, West Kasai, Zaire, 1983.

Transmission chains are generally short (max 5-7 events)

Reproduction number R° is estimated between 0.6-1 for Central African clade but lower for the West Arican viruses

International Journal of Epidemiology
© International Epidemiological Association 1988
Vol. 17, No. 3
Printed in Great Britain

The Transmission Potential of Monkeypox Virus in Human Populations

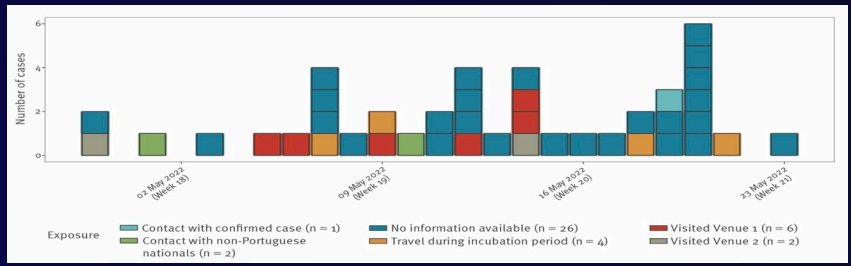
P E M FINE,* Z JEZEK,† B GRAB† AND H DIXON‡

In May 2022, a series of Monkeypox cases were identified in the UK, Portugal and Italy, primarily in Men who have Sex with Men (MSM)

RAPID COMMUNICATION

Ongoing monkeypox virus outbreak, Portugal, 29 April to 23 May 2022

Mariana Perez Duque[1,*], Sofia Ribeiro[1,2,*], João Vieira Martins[1], Pedro Casaca[1], Pedro Pinto Leite[1], Margarida Tavares[3,4,5,6], Kamal Mansinho[7,8], Luís Miguel Duque[9,10], Cândida Fernandes[11], Rita Cordeiro[12], Maria José Borrego[12], Ana Pelerito[12], Isabel Lopes de Carvalho[12], Sofia Núncio[12], Vera Manageiro[12,13], Corrado Minetti[12,13], Jorge Machado[12], Joana M Haussig[14], Roberto Croci[14], Gianfranco Spiteri[14], Ana Sofia Casal[15], Diana Mendes[16], Tiago Souto[17], Sara Pocinho[17], Teresa Fernandes[15], Ana Firme[17], Paula Vasconcelos[17], Graça Freitas[18]



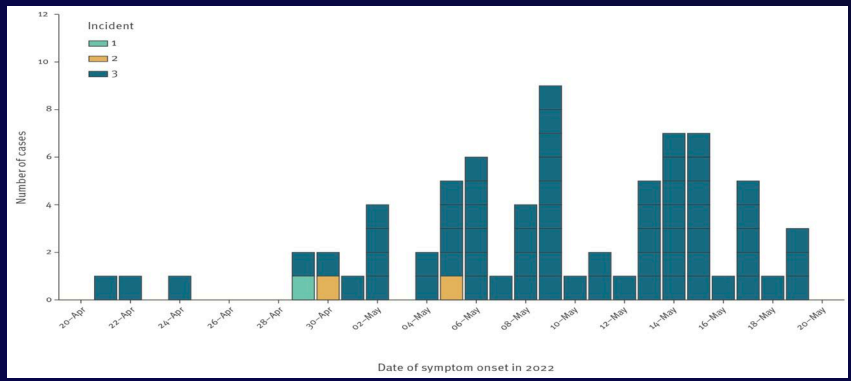
RAPID COMMUNICATIONS

Community transmission of monkeypox in the United Kingdom, April to May 2022

Roberto Vivancos[1,2,3], Charlotte Anderson[1], Paula Blomquist[1], Sooria Balasegaram[1], Anita Bell[1], Louise Bishop[1], Colin S Brown[1,4], Yimmy Chow[1], Obaghe Edeghere[1], Isaac Florence[1], Sarah Logan[5], Petra Manley[1], William Crowe[6], Andrew McAuley[7], Ananda Giri Shankar[8], Borja Mora-Peris[9], Karthik Paranthaman[1], Mateo Prochazka[1], Cian Ryan[1], David Simons[1], Richard Vipond[1], Chloe Byers[1], Nicholas A. Watkins[1], UKHSA Monkeypox Incident Management team[10], Will Welfare[1], Elizabeth Whittaker[9], Claire Dewsnap[11], Allegra Wilson[1], Yvonne Young[1], Meera Chand[1], Steven Riley[1], Susan Hopkins[1,4]

www.eurosurveillance.org 1

Check for updates



RAPID COMMUNICATION

Family cluster of three cases of monkeypox imported from Nigeria to the United Kingdom, May 2021

Gemma Hobson[1], James Adamson[1], Hugh Adler[2,3], Richard Firth[1], Susan Gould[2,3], Catherine Houlihan[4,5], Christopher Johnson[1], David Porter[6], Tommy Rampling[4,7], Libuse Ratcliffe[2], Katherine Russell[8], Ananda Giri Shankar[1], Tom Wingfield[2,3,9]

www.eurosurveillance.org 1

Check for updates

RAPID COMMUNICATIONS

Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022

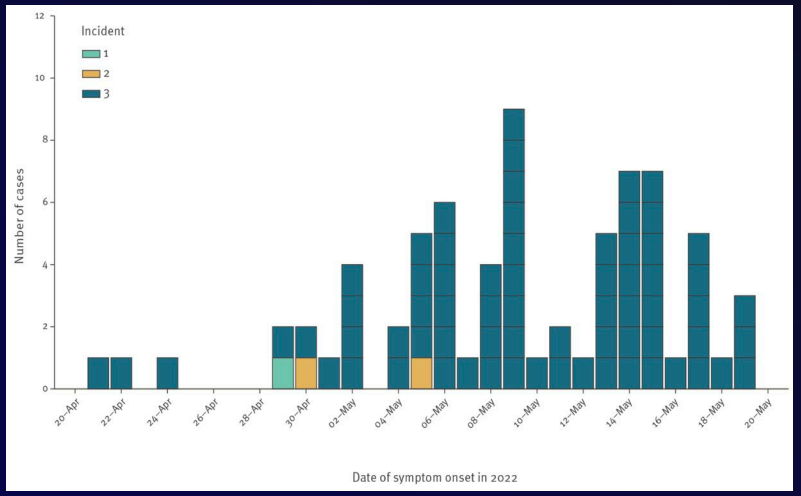
Andrea Antinori[1], Valentina Mazzotta[1], Serena Vita[1], Fabrizio Carletti[1], Danilo Tacconi[2], Laura Emma Lapini[2], Alessandra D'Abramo[1], Stefania Cicalini[1], Daniele Lapa[1], Silvia Pittalis[1], Vincenzo Puro[1], Marco Rivano Capparuccia[2], Emanuela Giombini[1], Cesare Ernesto Maria Gruber[1], Anna Rosa Garbuglia[1], Alessandra Marani[1], Francesco Vairo[1], Enrico Girardi[1], Francesco Vaia[1],

Health authorities rapidly established that we were at the beginning of an outbreak of a new clinical and epidemiological form of monkeypox, different from that observed in Africa

2022 Outbreak of Monkeypox

The first case of Monkeypox in the outbreak was confirmed in the UK on May 6 2022 in a man traveling from Nigeria

Unrelated cases with no documented history of travel to endemic countries were then reported in the UK and Portugal, suggesting undetected local transmission with earlier onset dates of symptoms in late April 2022



WHO declared global health emergency on July 22

By septembre 10, around 80 000 cases of MPX infection have been reported in >100 locations worldwide with >95% in countries not historically endemic (USA, Spain, Brazil and France)

>97% in men who identify as MSM

MPXV has been transmitted primarily in interconnected sexual networks that sustain STIs.

Transmission through Sexual Contacts

Demographic and Clinical Characteristics of the persons with Monkeypox, April-June 2022

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 25, 2022 VOL. 387 NO. 8

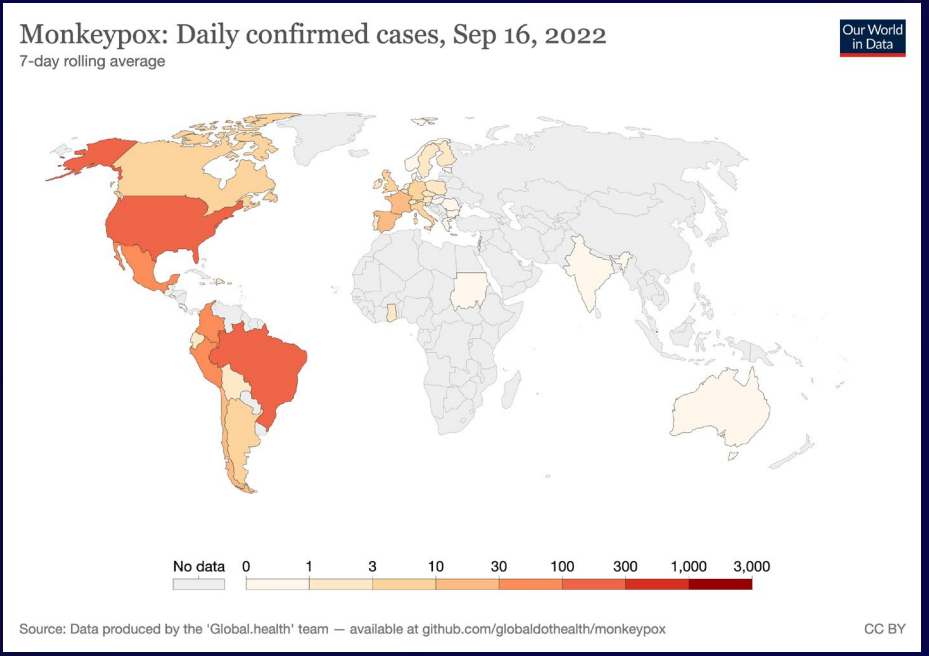
Monkeypox Virus Infection in Humans across 16 Countries — April–June 2022

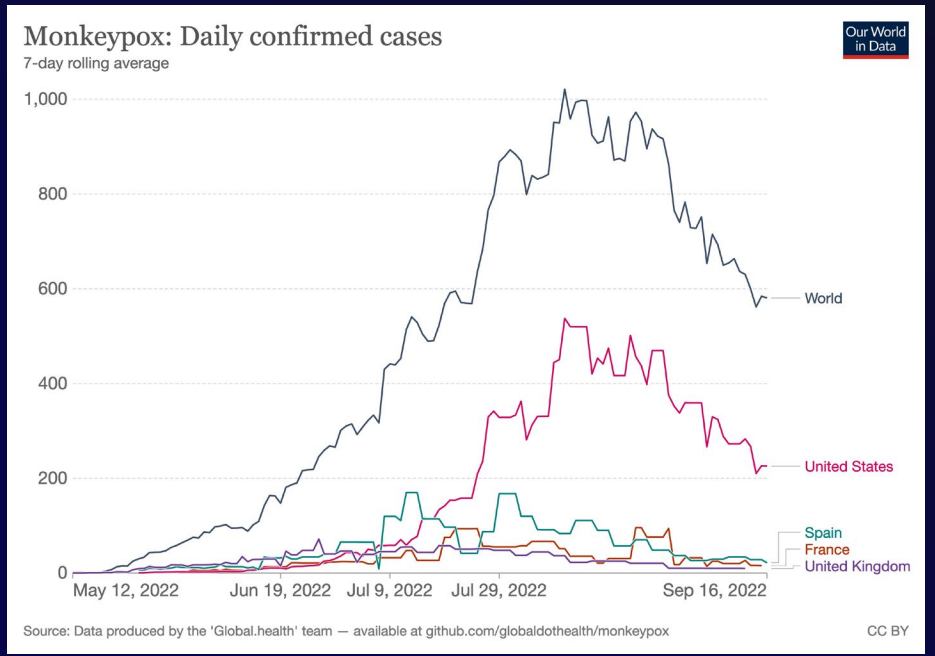
J.P. Thornhill, S. Barkati, S. Walmsley, J. Rockstroh, A. Antinori, L.B. Harrison, R. Palich, A. Nori, I. Reeves, M.S. Habibi, V. Apea, C. Boesecke, L. Vandekerckhove, M. Yakubovsky, E. Sendagorta, J.L. Blanco, E. Florence, D. Moschese, F.M. Maltez, A. Goorhuis, V. Pourcher, P. Migaud, S. Noe, C. Pintado, F. Maggi, A.-B.E. Hansen, C. Hoffmann, J.I. Lezama, C. Mussini, A.M. Cattelan, K. Makofane, D. Tan, S. Nozza, J. Nemeth, M.B. Klein, and C.M. Orkin, for the SHARE-net Clinical Group*

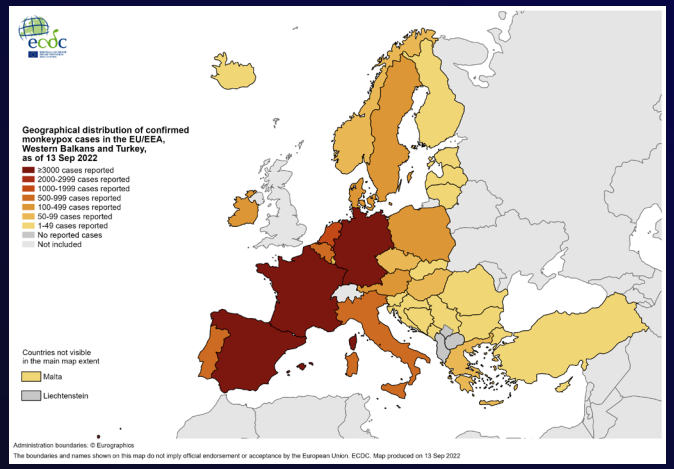
Table 1. Demographic and Clinical Characteristics of the Persons with Monkeypox.*

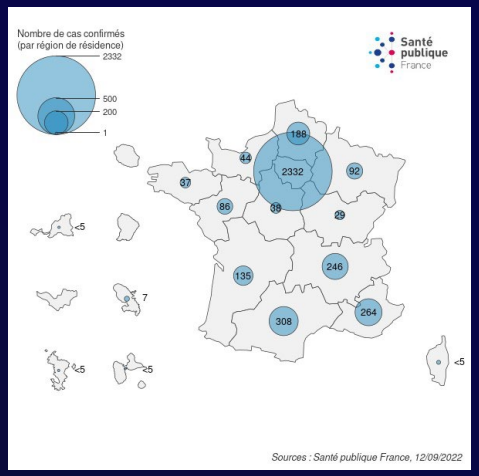
Characteristic	All Persons (N=528)
Median age (range) — yr	38 (18–68)
Sex or gender — no. (%)	
Male	527 (>99)
Female	0
Trans or nonbinary	1 (<1)
Sexual orientation — no. (%)†	
Heterosexual	9 (2)
Homosexual	509 (96)
Bisexual	10 (2)
Race or ethnic group — no. (%)†	
White	398 (75)
Black	25 (5)
Mixed race	19 (4)
Latinx	66 (12)
Other or unknown	20 (4)
HIV positive — no. (%)	218 (41)
HIV negative or status unknown — no. (%)	310 (59)
Use of preexposure prophylaxis against HIV — no./total no. (%)	176/310 (57)
Foreign travel in month before diagnosis — no. (%)‡	147 (28)
Continent of travel — no./total no. (%)	
Europe	132/147 (90)
North America	9/147 (6)
Australasia	0/147
Africa and Middle East	2/147 (1)
Central and South America	2/147 (1)
Not stated	2/147 (1)
Known to have undergone STI screening — no. (%)	377 (71)
Microbiologically confirmed concomitant STI present — no./total no. screened (%)	109/377 (29)
Gonorrhea	32/377 (8)
Chlamydia	20/377 (5)
Syphilis	33/377 (9)
Herpes simplex virus infection	3/377 (1)
Lymphogranuloma venereum	2/377 (1)
Chlamydia and gonorrhea	5/377 (1)
Other or not stated	14/377 (4)
HIV test taken — no./total no. with previously unknown or negative HIV status (%)	122/310 (39)
New HIV infection diagnosis — no./total no. (%)	3/122 (2)
Sexual history not known — no./total no. (%)	122/528 (23)
Median no. of sex partners in previous 3 months (IQR)	5 (3–15)
"Chemsex" reported in the previous month — no. (%)	106 (20)
Reported attendance at a sex-on-site event in the previous month — no. (%)	169 (32)

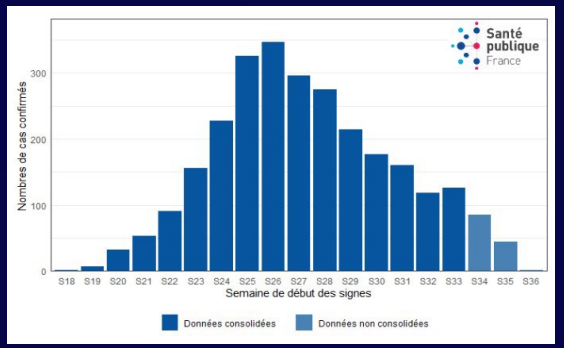
Epidemiological Data on the 2022 Outbreak of Monkeypox











Clinical Aspects of the Monkeypox Outbreak

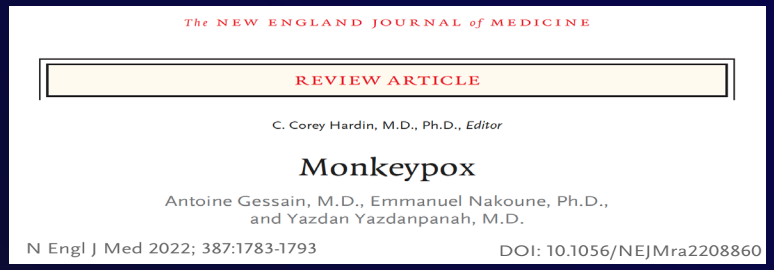
The clinical aspects seem to correspond to the classical presentation (incubation, prodromal and eruptive phase) but with some differences that give rise to a new pattern

Incubation 9.2 days

Lesions are also frequently observed without prodromal phase

The pattern of skin lesions is often unusual

sometimes with only a few painless lesions, but also often in genital, anal and perianal areas (rectitits) and oral lesions (pharyngitis)



The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

C. Corey Hardin, M.D., Ph.D., *Editor*

Monkeypox

Antoine Gessain, M.D., Emmanuel Nakoune, Ph.D., and Yazdan Yazdanpanah, M.D.

N Engl J Med 2022; 387:1783-1793 DOI: 10.1056/NEJMra2208860

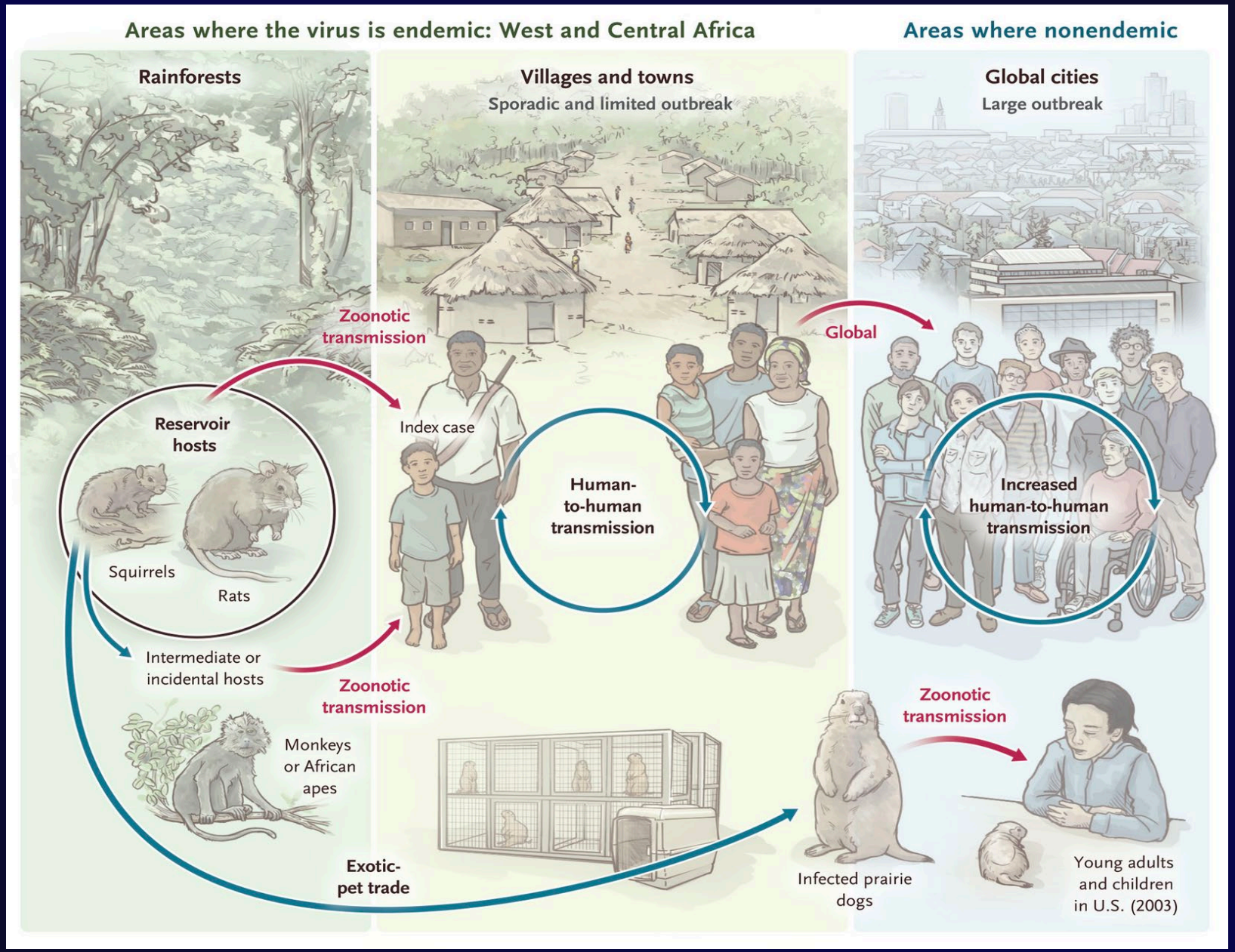
Comparison of the Classical African and the New Clinico-Epidemiological Form of Monkeypox

Table 1. Features of the Classic Form of Monkeypox and the New Clinical–Epidemiologic Form.

Variable	Classic Form, 1970s to the Present	New Clinical–Epidemiologic Form, 2022
Location	Central and West Africa	Countries where monkeypox is not endemic (Europe, North and South America, Middle East, Australia)
Affected population	Children and young adults (age at diagnosis increasing since 1980)	Young men who have sex with men (age, 31–40 yr)
Epidemiologic features	Sporadic cases and epidemics	Pandemic under way since May 2022
Transmission	Contact with infected animal reservoir (probably rodents), followed by human-to-human transmission	Exclusively human-to-human transmission
Dissemination	Mostly intrafamilial and limited nosocomial dissemination	Mostly sexual networking, condomless sex with multiple male partners
Clinical phase	Incubation, prodromal stage, eruption phase with skin lesions	Incubation, prodromal stage (not always present), eruption phase with lesions in an unusual distribution, especially on the genitals
Symptoms	Lesions on the face and extremities, with centrifugal distribution, often associated with cervical or axillary lymphadenopathy	Penile rash, perianal lesions, ulcerative lesions and vesicular rash, painful inguinal lymphadenopathy, pharyngitis, proctitis
Viruses	Central African and West African clades (clades 1 and 2, respectively)	West African variant (clade 3)
Case fatality rate (%)	1–15	0.025

From Gessain et al., New England Journal of Medecine, 2022

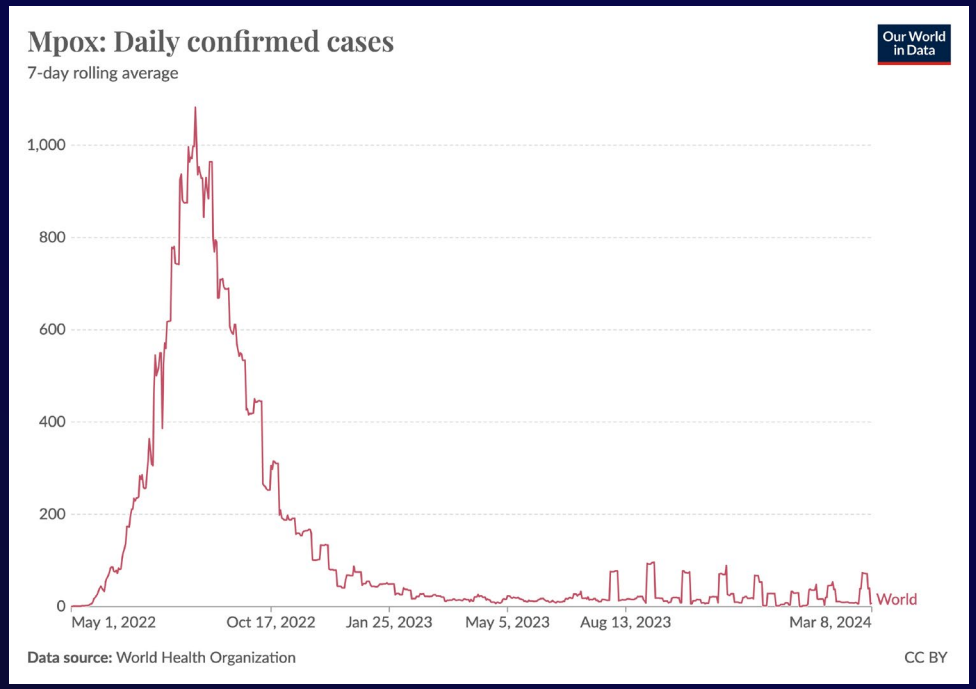
Natural History of Monkeypox

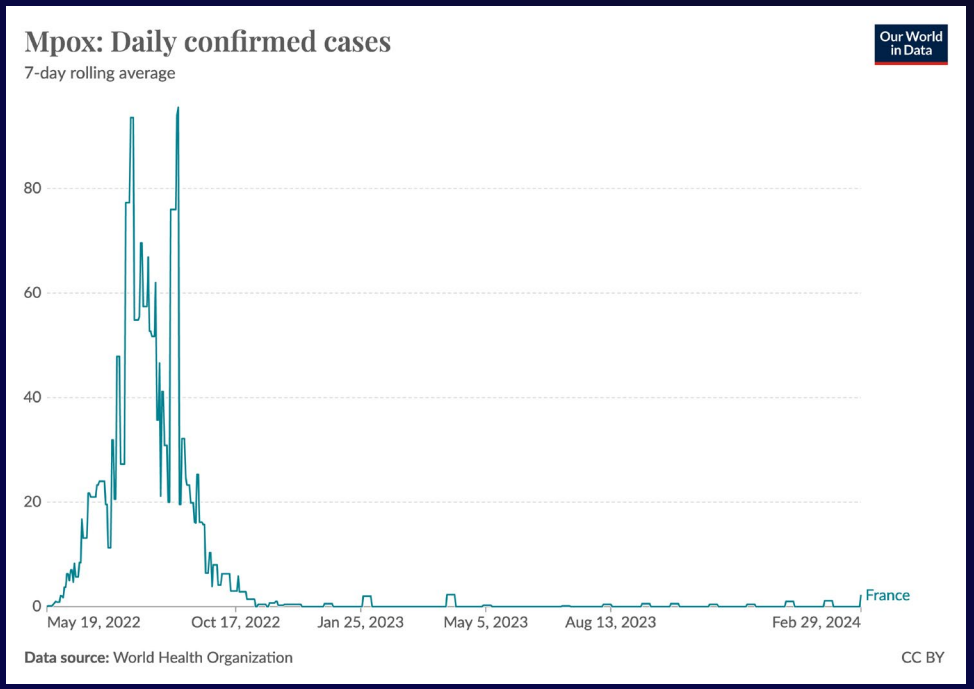


From Gessain et al., NEJM, 2022

Current situation 2024 :

The epidemic is almost over in countries with a high socio-economic level





This is due to **information** and **prevention efforts** and the use of therapeutics and **vaccination** in the **population at risk**

(mainly Gay, Bisexual, MSM with multiple partners)

The epidemic was remarkably controlled by the mobilization of targeted high risk populations with behavioral modifications to avoid Mpxv and the high uptake and effectiveness of anti-smallpox vaccination

MVA–BN is a third generation live attenuated non-replicating modified Vaccinia Ankara vaccine developped by Bavarian Nordic

Use of treatement : Tecovirimat (inhibitor of orthopoxvirus protein P37) and Brincidofovir (inhibitor of viral DNA polymerase led possibly to decrease the duration of viral shedding and illness (not demonstrated).

EMERGING INFECTIOUS DISEASES®
ISSN: 1080-6059
EID Journal > Volume 30 > Early Release > Main Article

Volume 30, Number 5—May 2024

Research

Mpox Diagnosis, Behavioral Risk Modification, and Vaccination Uptake among Gay, Bisexual, and Other Men Who Have Sex with Men, United Kingdom, 2022

Dana Ogaz✉, Qudsia Enayat, Jack R.G. Brown, Dawn Phillips, Ruth Wilkie, Danielle Jayes, David Reid, Gwenda Hughes, Catherine H. Mercer, John Saunders, Hamish Mohammed, and UK Health Security Agency Sexual Health Liaison Group[1]
Author affiliations: UK Health Security Agency, London, UK (D. Ogaz, Q. Enayat, D. Phillips, R. Wilkie, D. Jayes, G. Hughes, J. Saunders, H. Mohammed); The National Institute for Health and Care Research Health Protection Research Unit in Blood Borne and Sexually Transmitted Infections at University College London in partnership with the UK Health Security Agency, London, UK (D. Ogaz, J.R.G. Brown D. Reid, G. Hughes, C.H. Mercer, J. Saunders, H. Mohammed); University College London, London, UK (D. Reid, C.H. Mercer, J. Saunders); London School of Hygiene & Tropical Medicine, London, UK (G. Hughes)

Severe forms

During pandemic >90 000 cases and around 150/200 deaths mostly in HIV infected patients

Articles

Mpox in people with advanced HIV infection: a global case series

Oriol Mitjà*, Andrea Alemany*, Michael Marks*, Jezer I Lezama Mora, Juan Carlos Rodríguez-Aldama, Mayara Secco Torres Silva, Ever Arturo Corral Herrera, Brenda Crabtree-Ramirez, José Luis Blanco, Nicolo Girometti, Valentina Mazzotta, Aniruddha Hazra, Macarena Silva, Juan José Montenegro-Idrogo, Kelly Gebo, Jade Ghosn, María Fernanda Peña Vázquez, Eduardo Matos Prado, Uche Unigwe, Judit Villar-García, Noah Wald-Dickler, Jason Zucker, Roger Paredes, Alexandra Calmy, Laura Waters, Cristina Galvan-Casas, Sharon Walmsley, Chloe M Orkin, on behalf of SHARE-NET writing group

Original research

BMJ Global Health

Mpox (monkeypox) risk and mortality associated with HIV infection: a national case-control study in Nigeria

Adesola Yinka-Ogunleye,[1,2] Mahmood Dalhat,[3,4] Afolabi Akinpelu,[5] Olusola Aruna,[6] Fatima Garba,[7] Adama Ahmad,[5] Adesola Adeleye,[5] Iliya Botson,[5] Bamidele Oluwafemi,[5] Oladipo Ogunbode,[8] Lateefat Amao,[8] Udeme Ekripo,[9] Gambo Gumel Aliyu,[10] Ifedayo Adetifa,[11,12] Chikwe Ihekweazu,[11] Ibrahim Abubakar[2]

Higher mortality in people with more advanced HIV

Among 382 persons with 107 hospitalized, 27 died.

All death occured in people with CD4 counts of less than 200 cells/mm^3

Case fatality rate was 9.4% (8/86) and 20.8% (5/24) overall and in HIV positive cases respectively

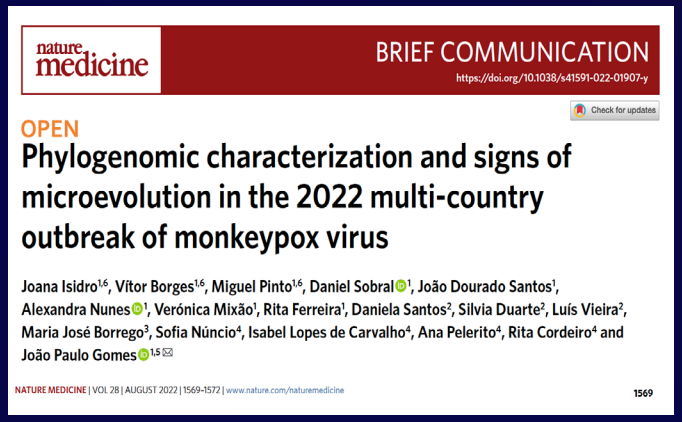
High risk in children dying from Mpox infection irrespective of HIV status

Phylogeny of the Monkeypox Virus Strains of the Outbreak

These MPXV belong to clade 2b, within the formerly West African clade 2

Divergent branch lineage B1descendant from a branch with viruses (A1) associated with exportation of MPXV in 2018/2019 from Nigeria to UK, Israel, Singapore.

The outbreak most likely has a single origin



nature medicine

BRIEF COMMUNICATION

https://doi.org/10.1038/s41591-022-01907-y

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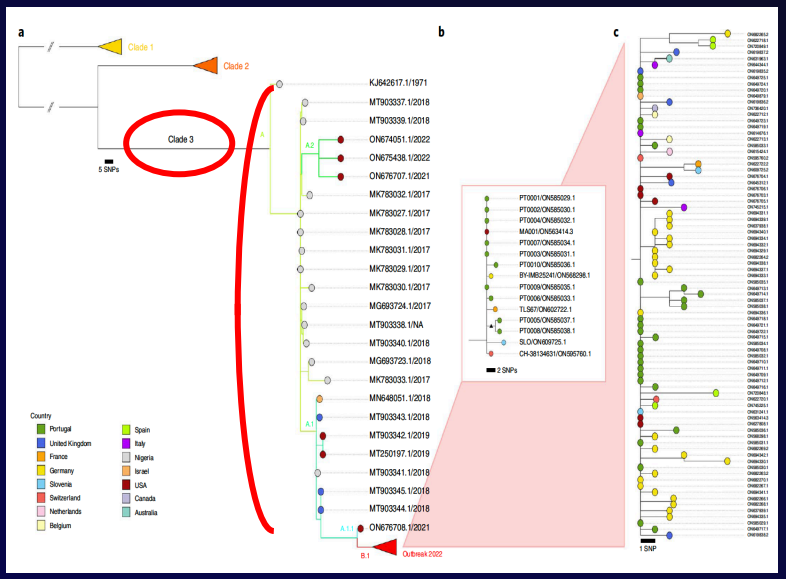
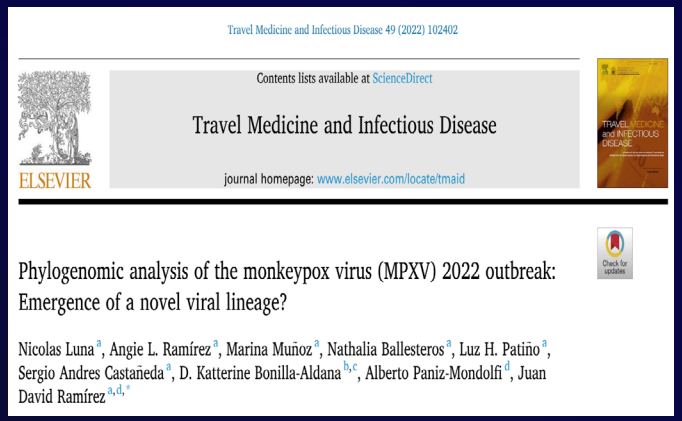
OPEN

Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus

Joana Isidro[1,6], Vítor Borges[1,6], Miguel Pinto[1,6], Daniel Sobral[1], João Dourado Santos[1], Alexandra Nunes[1], Verónica Mixão[1], Rita Ferreira[1], Daniela Santos[2], Silvia Duarte[2], Luís Vieira[2], Maria José Borrego[3], Sofia Núncio[4], Isabel Lopes de Carvalho[4], Ana Pelerito[4], Rita Cordeiro[4] and João Paulo Gomes[1,5]

NATURE MEDICINE | VOL 28 | AUGUST 2022 | 1569–1572 | www.nature.com/naturemedicine





Travel Medicine and Infectious Disease 49 (2022) 102402

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journal homepage: www.elsevier.com/locate/tmaid

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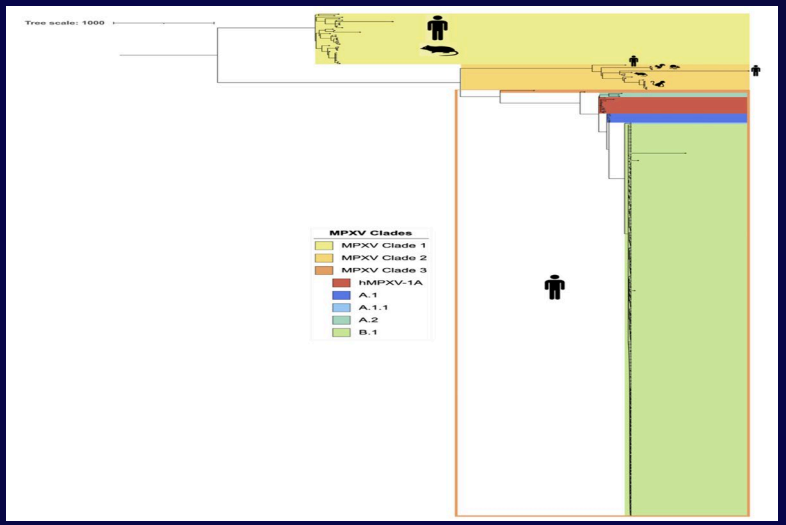
Phylogenomic analysis of the monkeypox virus (MPXV) 2022 outbreak: Emergence of a novel viral lineage?

Nicolas Luna[a], Angie L. Ramírez[a], Marina Muñoz[a], Nathalia Ballesteros[a], Luz H. Patiño[a], Sergio Andres Castañeda[a], D. Katterine Bonilla-Aldana[b,c], Alberto Paniz-Mondolfi[d], Juan David Ramírez[a,d,*]



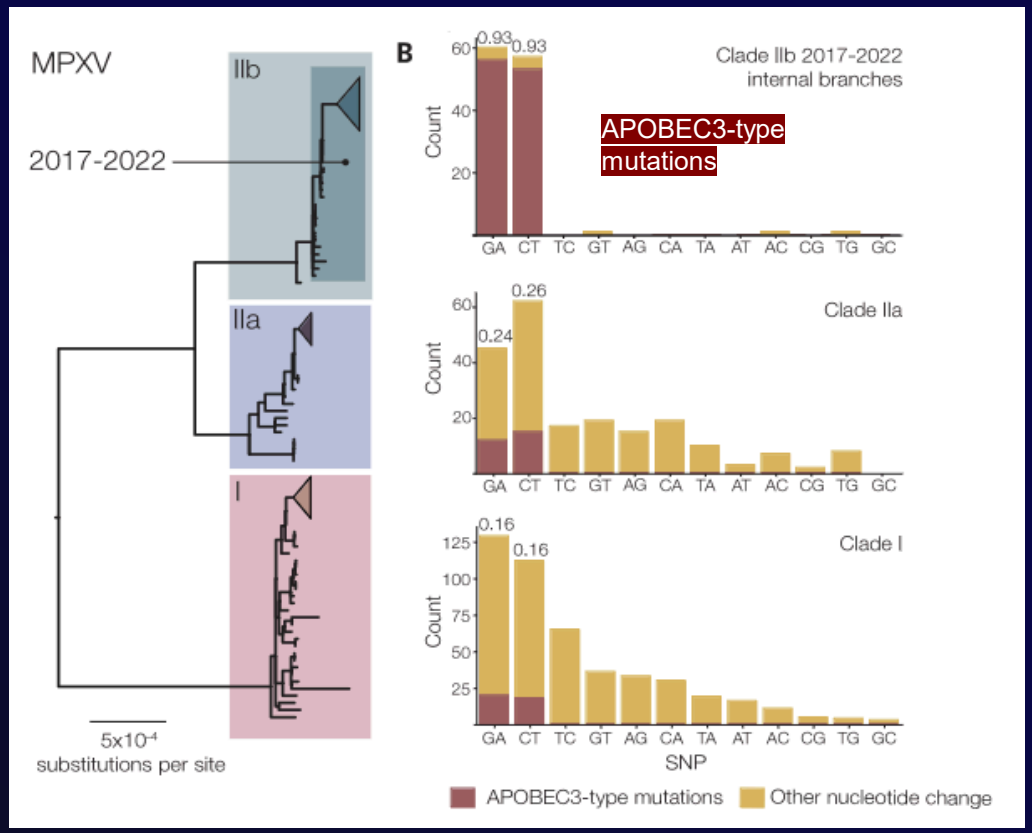
RESEARCH

MPOX

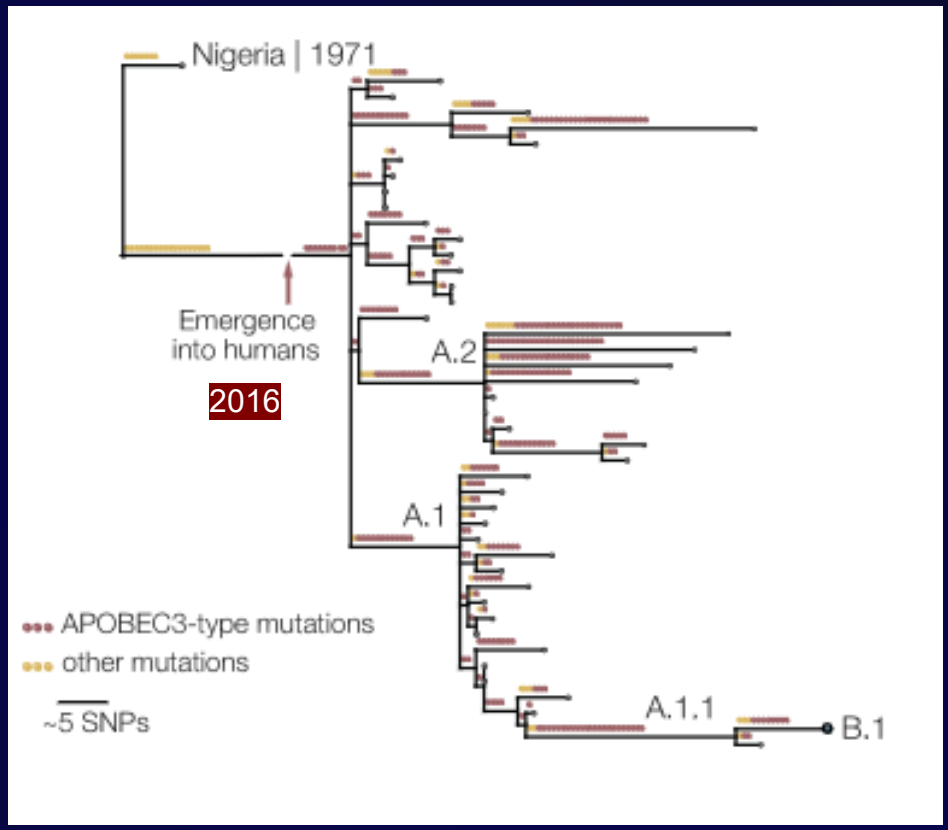
APOBEC3 deaminase editing in mpox virus as evidence for sustained human transmission since at least 2016

Áine O'Toole[1]*, Richard A. Neher[2], Nnaemeka Ndodo[3], Vitor Borges[4], Ben Gannon[5], João Paulo Gomes[4,6], Natalie Groves[7], David J. King[8], Daniel Maloney[1], Philippe Lemey[9], Kuiama Lewandowski[5], Nicholas Loman[7,10], Richard Myers[7], Ifeanyi F. Omah[1,11], Marc A. Suchard[12], Michael Worobey[13], Meera Chand[7,14], Chikwe Ihekweazu[3], David Ulaeto[7]†, Ifedayo Adetifa[3]†, Andrew Rambaut[1]*†

O'Toole *et al.*, *Science* **382**, 595–600 (2023) 3 November 2023



Specific enrichment of APOBEC3-type mutations in MPXV samples collected since 2017



Estimation of the time of MPXV emergence into the human population from the accumulation of APOBEC3-type mutations

medRxiv
THE PREPRINT SERVER FOR HEALTH SCIENCES

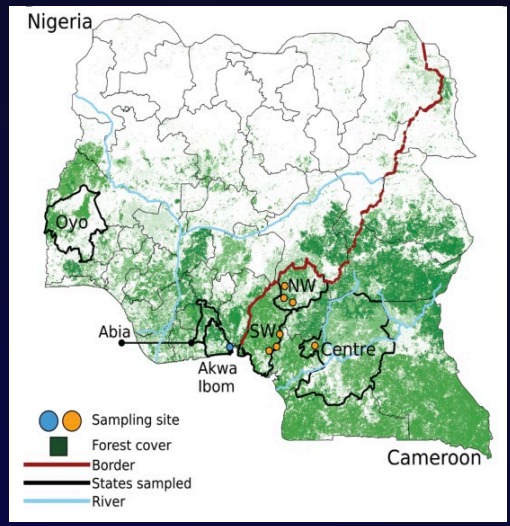
Molecular epidemiology of recurrent zoonotic transmission of mpox virus in West Africa

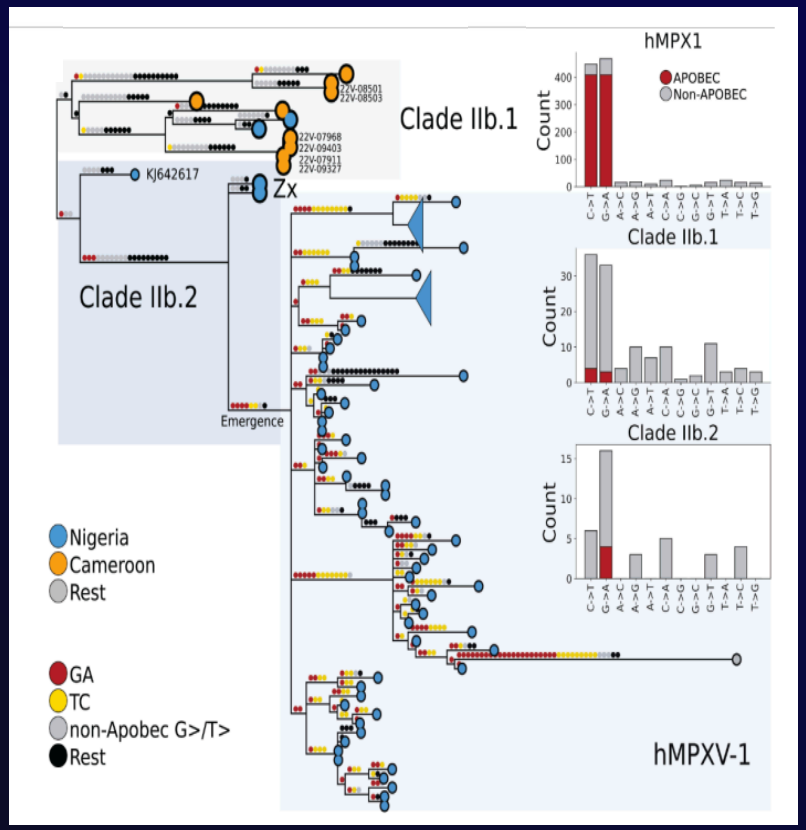
Delia Doreen Djuicy *et al.*

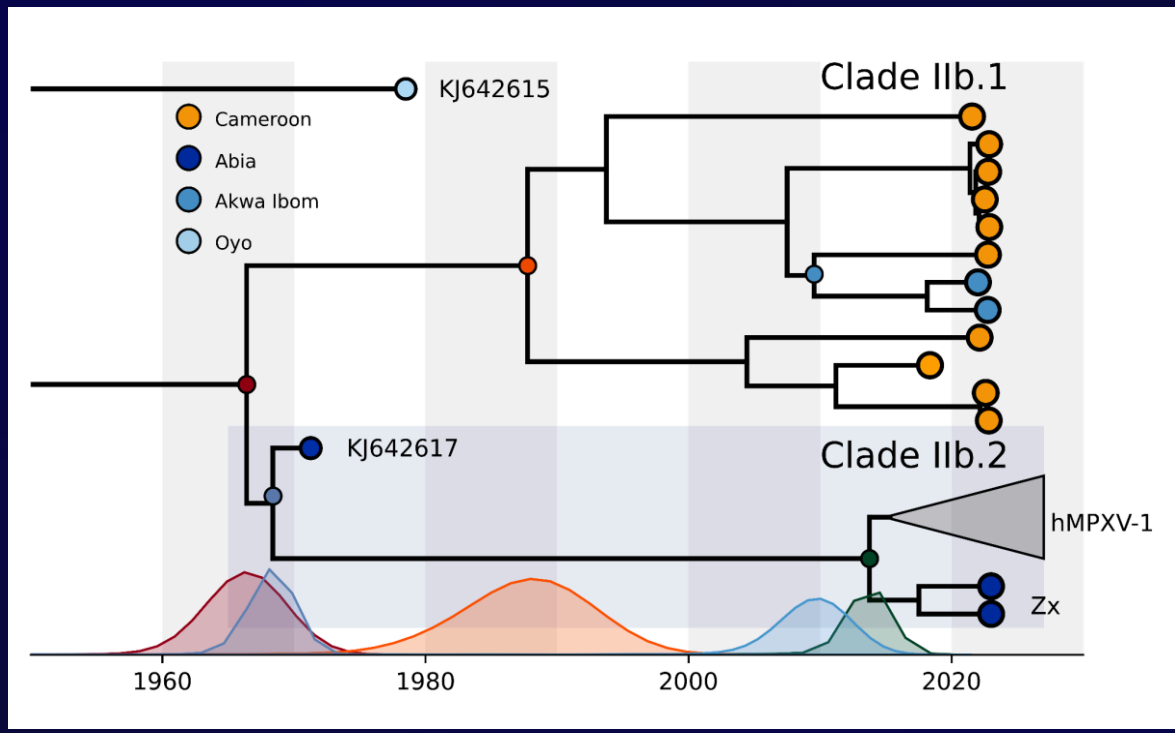
doi: https://doi.org/10.1101/2024.06.18.24309115

Southern Nigeria was the origin of the human pandemic

Still ongoing zoonotic transmission in Cameroon and Nigeria underscoring the continous risk of MPXV (re)emergence







INSTITUT PASTEUR

Situation in DRC 2023/beginning 2024 New outbreak DRC ++

Since Dec. 2022 nationwide monkeypox outbreak with increasing number of suspected cases and deaths.

In 2023, 14,626 cases with 654 deaths, representing a lethality of 4.5%, with documented sexual transmission as well.

In 2024, 3941 suspected cases and 271 deaths, or 6.9% lethality.

Affects mainly children under 5 years old and in the Equateur province.

Group d'Age	Cas Suspect	Décès	Létalité (%)
0 -11 mois	411	56	13.6%
12 - 59 mois	933	114	12.2%
5 -15 ans	922	48	5.2%
>15 ans	924	31	3.4%
Cumul	**3190**	**249**	**7.8%**

TABLEAU 2 : NOMBRE DE CAS SUSPECTS, DECES ET LETALITE PAR GROUPE D'AGE

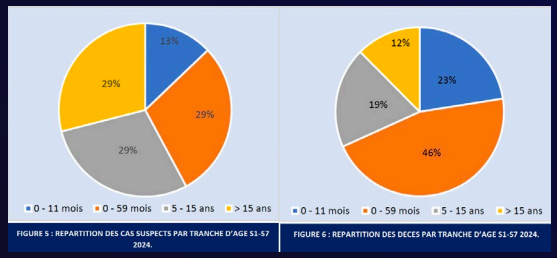


FIGURE 5 : REPARTITION DES CAS SUSPECTS PAR TRANCHE D'AGE S1-S7 2024.

FIGURE 6 : REPARTITION DES DECES PAR TRANCHE D'AGE S1-S7 2024.

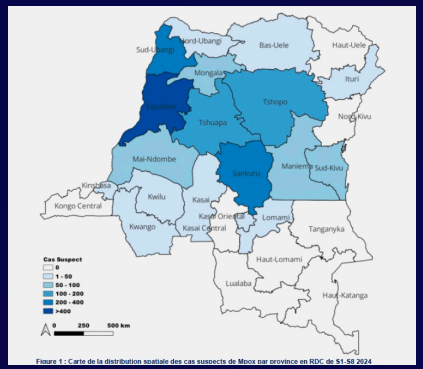


Figure 1 : Carte de la distribution spatiale des cas suspects de Mpox par province en RDC de S1-S8 2024

Province	Cas suspect	Décès	Létalité
Bas-Uele	27	1	3.7%
Équateur	2034	208	10.2%
Ituri	2	0	0.0%
Kasaï	17	0	0.0%
Kasaï oriental	2	0	0.0%
Kinshasa	15	0	0.0%
Kwango	3	0	0.0%
Kwilu	3	0	0.0%
Lomami	2	0	0.0%
Mai Ndombe	92	4	4.3%
Maniema	78	0	0.0%
Mongala	59	1	1.7%
Nord-Ubangi	35	0	0.0%
Sankuru	209	6	2.9%
Sud-kivu	92	1	1.1%
Sud-Ubangi	291	18	6.2%
Tshopo	106	2	1.9%
Tshuapa	123	8	6.5%
Total	**3190**	**249**	**7.8%**

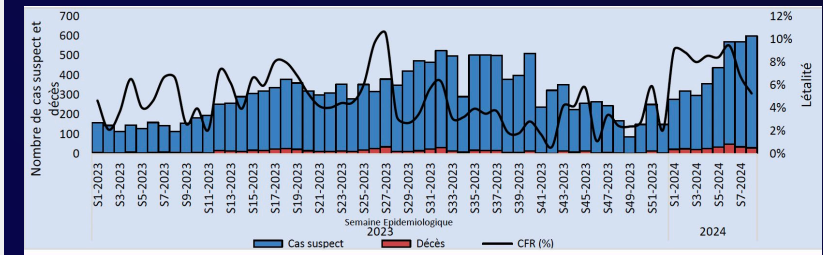


Figure 2 : Courbe épidémiologique des cas suspects, décès et létalité de la variole simienne de S1-2023 à S8-2024.

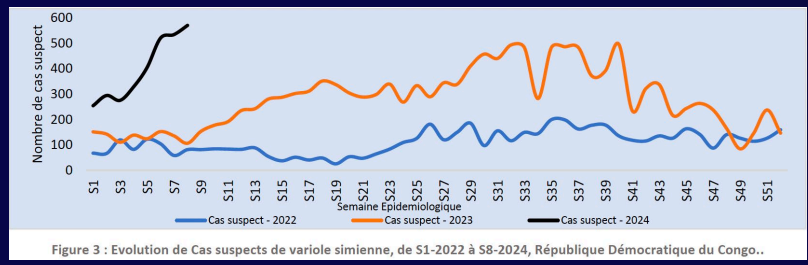


Figure 3 : Evolution de Cas suspects de variole simienne, de S1-2022 à S8-2024, République Démocratique du Congo..

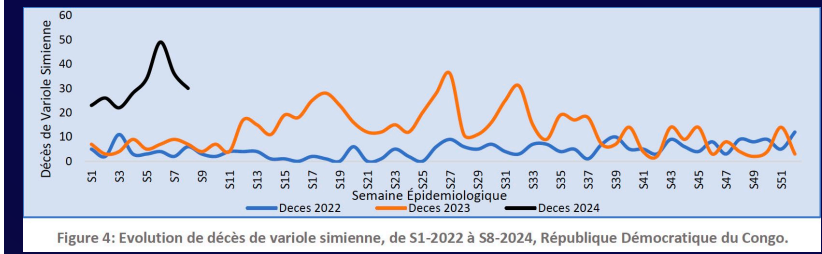


Figure 4: Evolution de décès de variole simienne, de S1-2022 à S8-2024, République Démocratique du Congo.

Epidémiologie et Physiopathologie des Virus Oncogènes

INSTITUT PASTEUR

New epidemic in Kamituga health zone, a densely populated poor mining area in South Kivu province in Eastern DRC beginning in september 2023

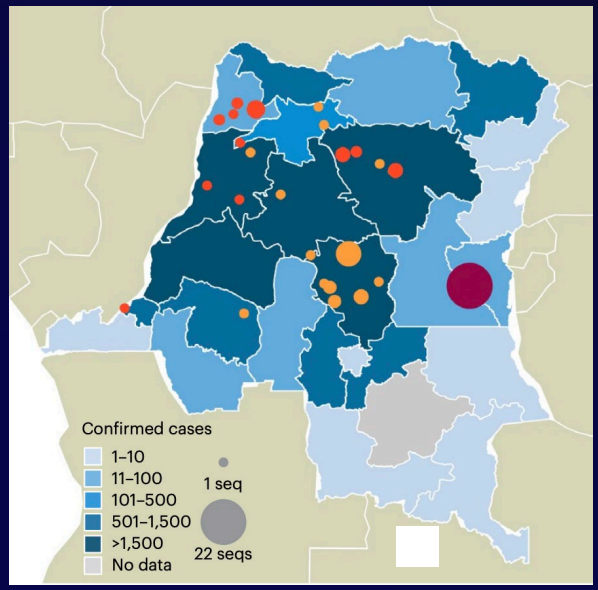
nature medicine

Brief Communication https://doi.org/10.1038/s41591-024-03130-3

Sustained human outbreak of a new MPXV clade I lineage in eastern Democratic Republic of the Congo

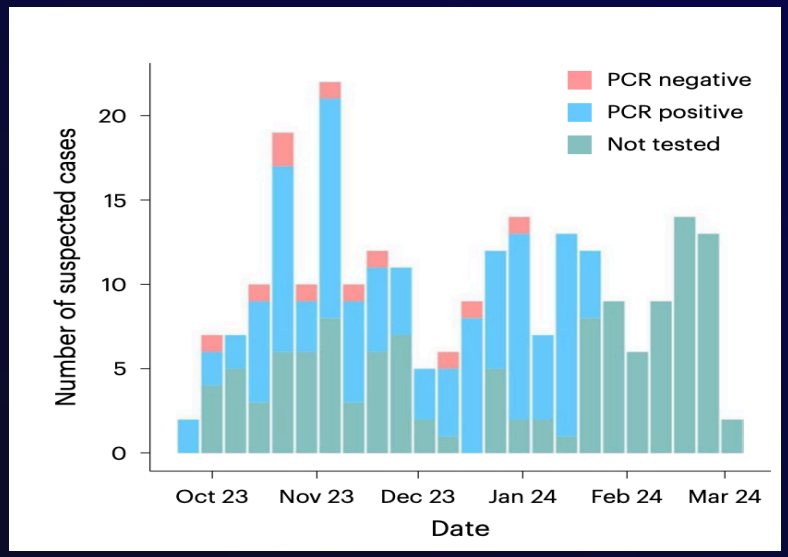
Vakaniaki, E.H., Kacita, C., Kinganda-Lusamaki, E. *et al.*

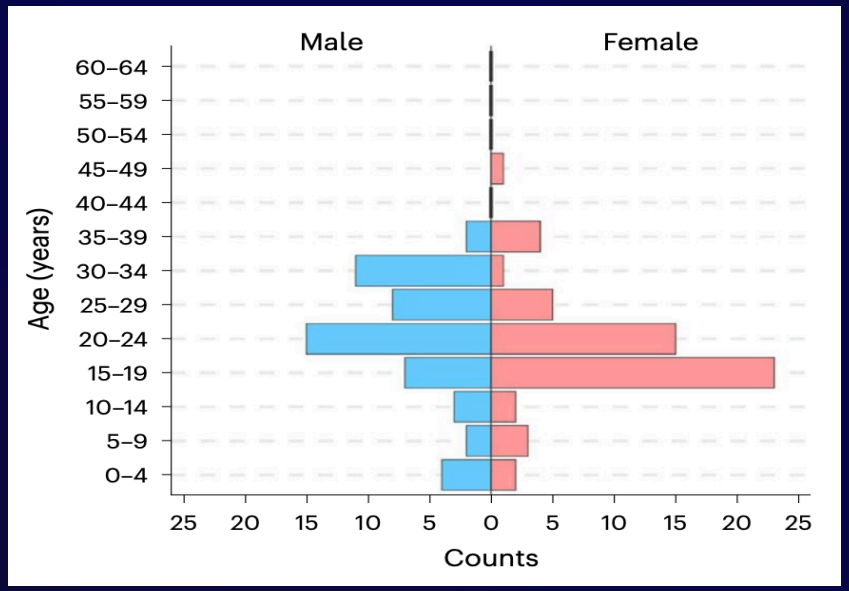
Nat Med **30**, 2791–2795 (2024). https://doi.org/10.1038/s41591-024-03130-3



Kamituga nearby Bukavu city and east african countries (Burundi, Rwanda,..)

241 suspected cases
90% of 119 tested cases MPXV +





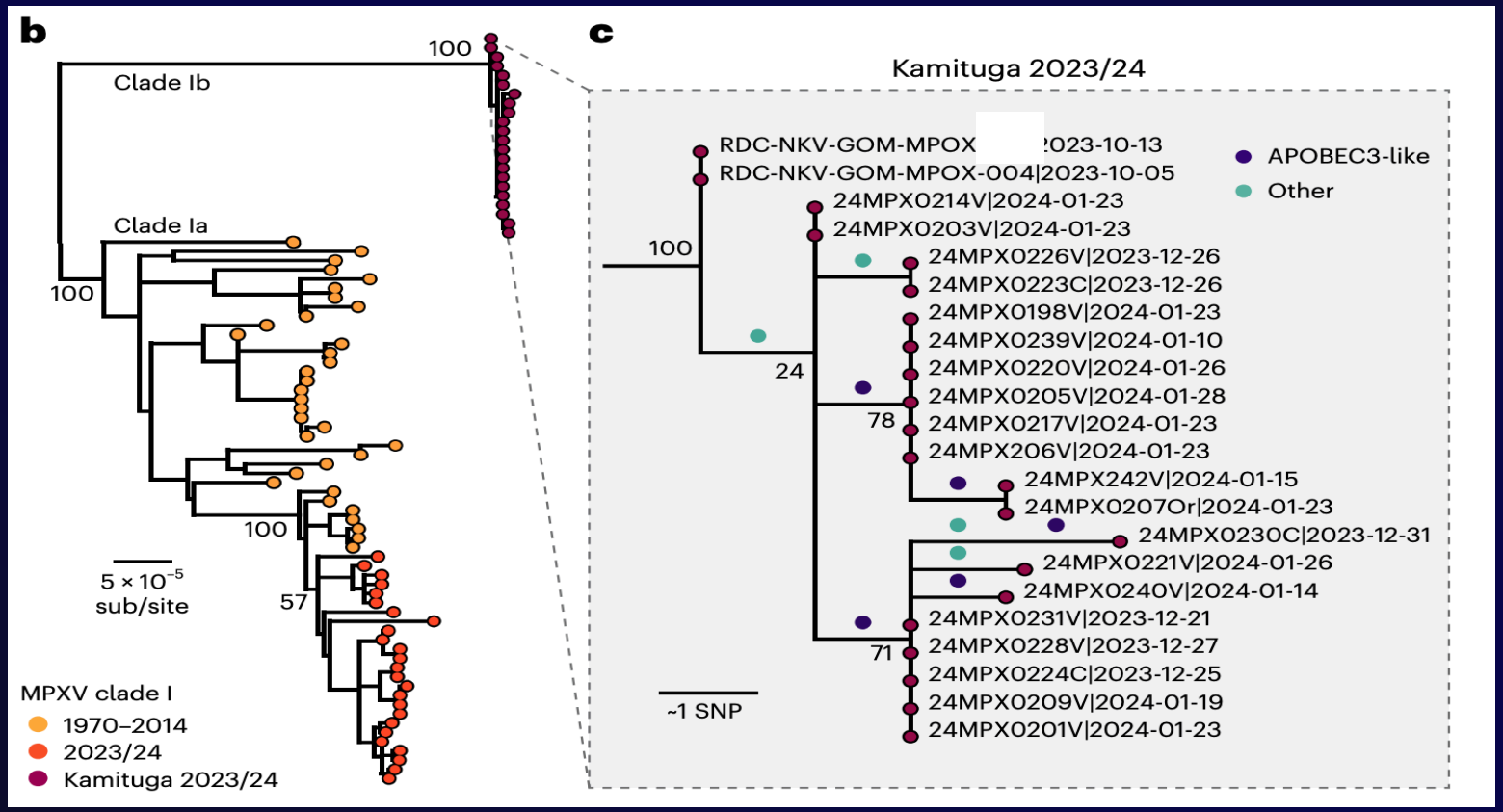
Majority are women

Median age 22 years

Frequent sex workers

Phylogenetic studies demonstrated the existence of a new lineage in the clade 1

The predominance of APOBEC3 mutations support that the entire cluster resulted from human to human transmission and the low genetic diversity indicate a recent outbreak

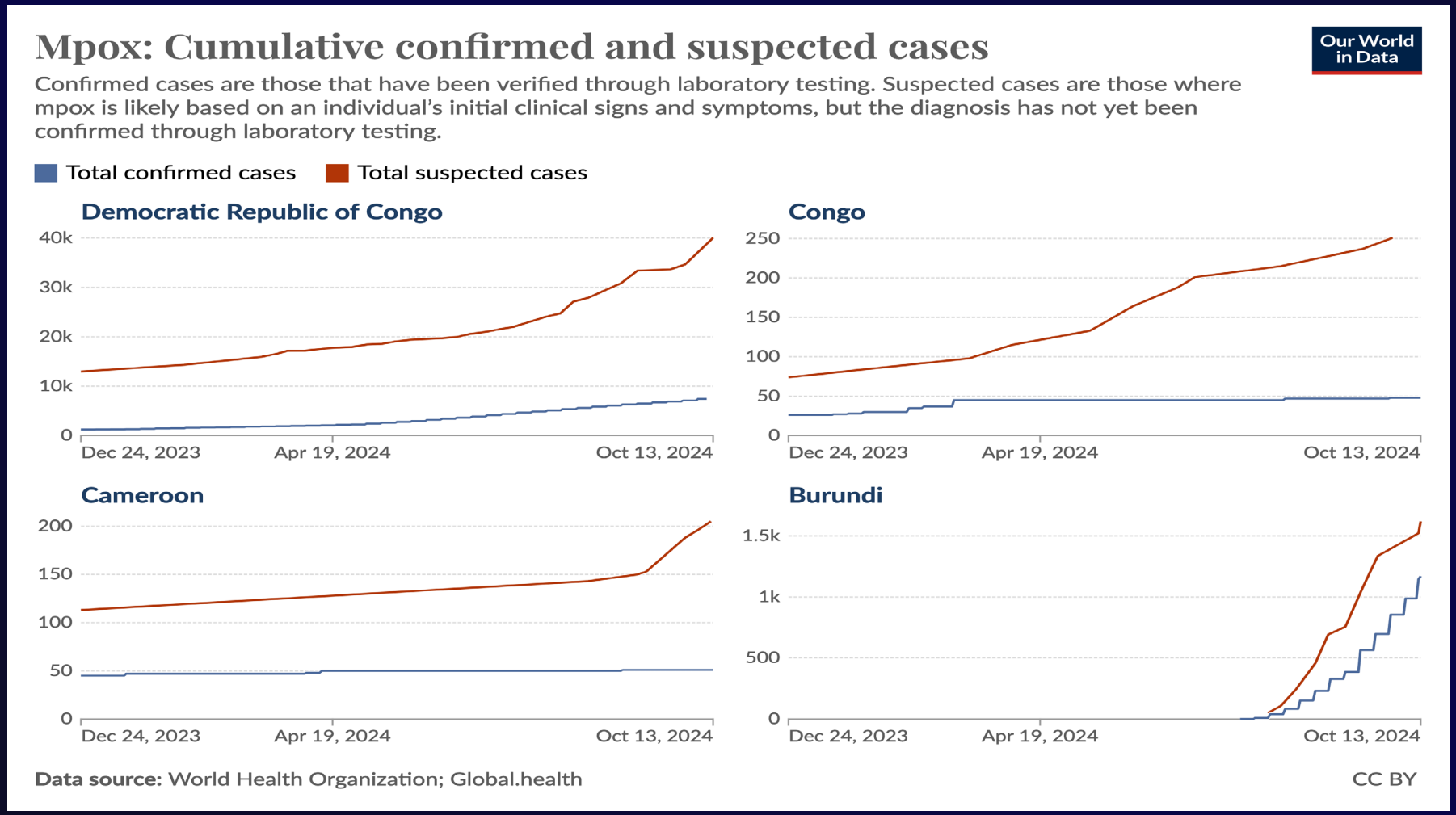


This new lineage was named clade 1b

The situation in Kamituga mirors the 2017/2018 outbreak of clade 2b in Nigeria

WHO declared global health emergency on August 24

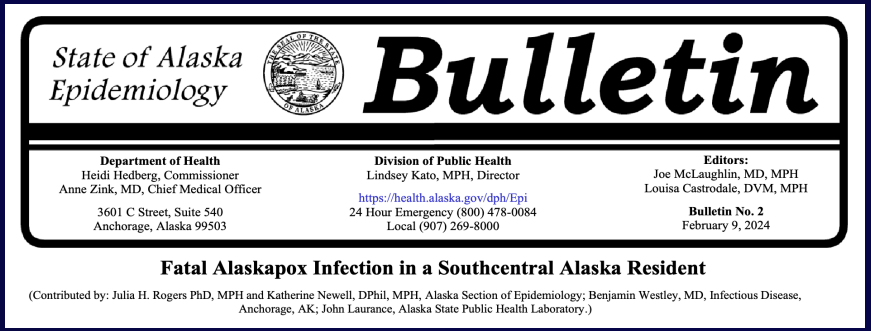
"The emergence of a new clade of mpox, its rapid spread in eastern DRC, and the reporting of cases in several neighbouring countries are very worrying. On top of outbreaks of other mpox clades in DRC and other countries in Africa, it's clear that a coordinated international response is needed to stop these outbreaks and save lives."



Few cases outside Africa

Sweden
Thailand
Germany

Alaska pox



State of Alaska Epidemiology **Bulletin**

Department of Health
Heidi Hedberg, Commissioner
Anne Zink, MD, Chief Medical Officer
3601 C Street, Suite 540
Anchorage, Alaska 99503

Division of Public Health
Lindsey Kato, MPH, Director
https://health.alaska.gov/dph/Epi
24 Hour Emergency (800) 478-0084
Local (907) 269-8000

Editors:
Joe McLaughlin, MD, MPH
Louisa Castrodale, DVM, MPH

Bulletin No. 2
February 9, 2024

Fatal Alaskapox Infection in a Southcentral Alaska Resident

(Contributed by: Julia H. Rogers PhD, MPH and Katherine Newell, DPhil, MPH, Alaska Section of Epidemiology; Benjamin Westley, MD, Infectious Disease, Anchorage, AK; John Laurance, Alaska State Public Health Laboratory.)

In 2024, first report severe case of Alsaka pox infection resulting in hospitalization and death.
Patient with history of drug-immunosuppresion secondary to cancer treatement.
Contact with a stray cat that regularly hunted small mammals and frequently scratched the patient.

Clinical Infectious Diseases

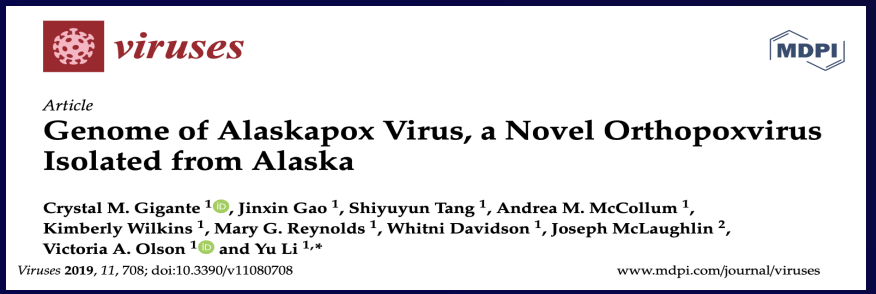
MAJOR ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Novel *Orthopoxvirus* Infection in an Alaska Resident

Yuri P. Springer,[1,5] Christopher H. Hsu,[5,6] Zachary R. Werle,[2] Link E. Olson,[3] Michael P. Cooper,[1] Louisa J. Castrodale,[1] Nisha Fowler,[4] Andrea M. McCollum,[6] Cynthia S. Goldsmith,[7] Ginny L. Emerson,[6] Kimberly Wilkins,[6] Jeffrey B. Doty,[6] Jillybeth Burgado,[6] JinXin Gao,[6] Nishi Patel,[6] Matthew R. Mauldin,[6,8] Mary G. Reynolds,[6] Panayampalli S. Satheshkumar,[6] Whitni Davidson,[6] Yu Li,[5] and Joseph B. McLaughlin[1]

[1]Alaska Division of Public Health, Section of Epidemiology, Anchorage; [2]Tanana Valley Clinic, [3]University of Alaska Museum, and [4]Alaska Division of Public Health, Section of Laboratories, Fairbanks; [5]Epidemic Intelligence Service, Division of Scientific Education and Professional Development, [6]Poxvirus and Rabies Branch, and [7]Infectious Diseases Pathology Branch, Centers for Disease Control and Prevention, Atlanta, Georgia; and [8]Oak Ridge Institute for Science and Education, Tennessee.



viruses MDPI

Article

Genome of Alaskapox Virus, a Novel Orthopoxvirus Isolated from Alaska

Crystal M. Gigante [1], Jinxin Gao [1], Shiyuyun Tang [1], Andrea M. McCollum [1], Kimberly Wilkins [1], Mary G. Reynolds [1], Whitni Davidson [1], Joseph McLaughlin [2], Victoria A. Olson [1] and Yu Li [1,*]

Viruses **2019**, *11*, 708; doi:10.3390/v11080708 www.mdpi.com/journal/viruses

Seven Alaska pox cases have been reported in Residents of the Fairbanks area.

Self-lilmiting illness consisting of a localized rash and lymphadenopathy.

Small mammals tested : four different species mainly « red back voles » -campagnoles à dos rouge

Conclusion

The 2022 and 2024 Mpox outbreaks reminds us that viral emergence is a permanent phenomenon without boundaries and often unpredictable in its nature, its target and magnitude :

a never-ending story?

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