# Monkeypox (Mpox)

# An Emergence of African Origin

# Deciphering an epidemic

Pr Antoine Gessain

Unité Épidémiologie et Physiopathologie des Virus Oncogènes

# Africa, land of Viral Emergence

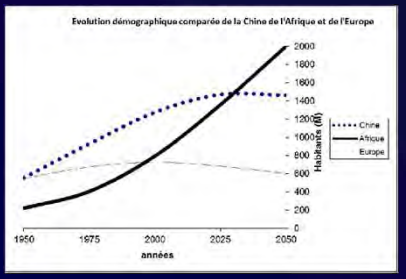



•Cradle of Humankind

Prehistoric (Lucy, Toumaï, Abel, etc.) Historical ("Out of Africa" migration, etc.)

•Major ecological changes with transformation of natural ecosystems (deforestation, intensive agriculture /livestock farming, climate change, mining,..)

• Population expansion and conflicts (regional and extra-African migrations/population movements)




• Rapid epidemiological transition

•High biodiversity, particularly at the animal level, a source of potential reservoirs of microbes



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# Viral Emergence of African Origin and Inter-species Transmission

**Zoonoses: diseases or infectious agents transmitted from animals to humans**

**>70% of emerging infectious diseases are zoonotic (HIV/AIDS, Ebola, COVID-19, Zika, Nipah/Hendra, Dengue, West Nile, etc.)**

Animal reservoirs and modes of transmission are very various

Rodents



bats



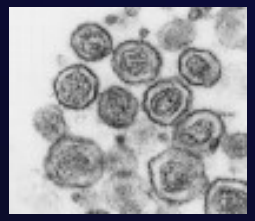
Apes/monkeys



Birds

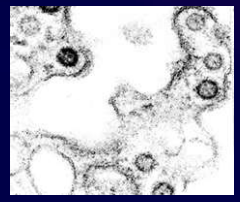


Contact with infected biological fluids: Blood, saliva, urine, feces, aerosols, etc. Bites, wounds, skin contact, respiratory/inhalation, insect bites, etc.....



## Retrovirus and associated diseases

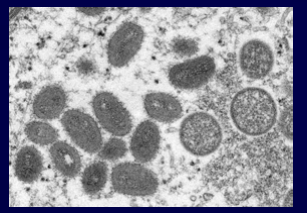
**(HIV/AIDS, HTLV-1/ATL and HAM/TSP and Foamy virus)**





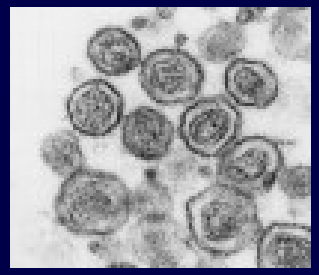
## Ebola virus and associted diseases

## Monkeypox virus and Mpox

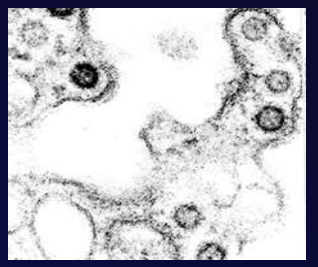
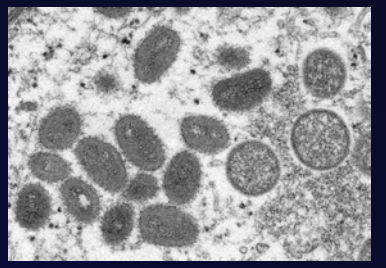




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# EPVO unit

*The main studies concern :*

- *Oncogenic viruses in humans and associated hematological and neurological diseases : HTLV-1/ATL, TSP/HAM,. HHV-8/Kaposi sarcoma and Merkel cell polyoma-virus and cutaneous cancer*
- *Emerging Viruses of zoonotic african origin (Chikungunya, Zika, Foamy viruses,* ***Monkey-pox,*** *Ebola…),*

# To study interspecies transmission ("spill-over") from monkeys/apes to human, the High-risk Populations consist of Hunters of Apes or Monkeys living in Central Africa







Indeed, because of their genetic, physiological, and even some behavioural similarities, NHPs are the sources of viruses (retroviruses SIV, STLV-1/2/3/4, SFV) that can infect humans and thus pose a significant threat to human population.

# Transmission of simian retroviruses in natural settings

Hunting non Human primates in the wild



Handling NHP pets



Butchering of wild game for consumption





Studies performed in

# Cameroon and Gabon



5000 plasmas and BC of adults tested (specific serology, PCR, sequences) in a retrospective study in general rural population including Pygmees or Bantus living close to NHPs habitats and a prospective study focused on more than 300 individuals who reported direct contacts (bites, wounds,..) with NHPs, mainly during hunting activities

## From the field to the laboratory









## STLV-3/HTLV-3

**Retrovirology** BioMed Central

Short report Open Access

**Discovery of a new human T-cell lymphotropic virus (HTLV-3) in Central Africa**

Sara Calattini[†1], Sébastien Alain Chevalier[†1], Renan Duprez[1], Sylviane Bassot[1], Alain Froment[2], Renaud Mahieux[†1] and Antoine Gessain[*†1]

**New Strain of Human T Lymphotropic Virus (HTLV) Type 3 in a Pygmy from Cameroon with Peculiar HTLV Serologic Results**

**Sara Calattini,[1,a] Edouard Betsem,[1,3] Sylviane Bassot,[1] Sébastien Alain Chevalier,[1] Renaud Mahieux,[1,4] Alain Froment,[2] and Antoine Gessain[1]**

[1]Unité d'Epidémiologie et Physiopathologie des Virus Oncogènes, URA CNRS 3015, Département de Virologie, and [2]Institut de Recherche pour le Développement, Musée de l'Homme, Paris, France; [3]Faculté de Médecine et des Sciences Biomédicales, Université de Yaoundé I, Yaoundé, Cameroun; [4]Department of Microbiology, Immunology and Tropical Medicine and Department of Biochemistry, The George Washington University Medical Center, Washington, DC

**The Journal of Infectious Diseases 2009; 199:561–4**

## STLV-4/HTLV-4

*Clinical Infectious Diseases*

BRIEF REPORT

**Zoonotic Transmission of Two New Strains of Human T-lymphotropic Virus Type 4 in Hunters Bitten by a Gorilla in Central Africa**

**Léa Richard,[1,2,3] Augustin Mouinga-Ondémé,[1] Edouard Betsem,[1,2,5,a] Claudia Filippone,[1,2,3] Eric Nerrienet,[1] Mirdad Kazanji,[4,c] and Antoine Gessain[1,2]**



## Simian Foamy Viruses

OPEN ACCESS Freely available online PLOS PATHOGENS

**Frequent and Recent Human Acquisition of Simian Foamy Viruses Through Apes' Bites in Central Africa**

**Edouard Betsem[1,2,3]*, Réjane Rua[1,2], Patricia Tortevoye[1,2], Alain Froment[4], Antoine Gessain[1,2]***

**Abstract**

Human infection by simian foamy viruses (SFV) can be acquired by persons occupationally exposed to non-human primates (NHP) or in natural settings. This study aimed at getting better knowledge on SFV transmission dynamics, risk factors for such a zoonotic infection and, searching for intra-familial dissemination and the level of peripheral blood (pro)viral loads in infected individuals. We studied 1,321 people from the general adult population (mean age 49 yrs, 640 women and 681 men) and 198 individuals, mostly men, all of whom had encountered a NHP with a resulting bite or scratch. All of these, either Pygmies (436) or Bantus (1085) live in villages in South Cameroon. A specific SFV Western blot was used and two nested PCRs (*polymerase*, and LTR) were done on all the positive/borderline samples by serology. In the general population, 2/1,321 (0.2%) persons were found to be infected. In the second group, 37/198 (18.6%) persons were SFV positive. They were mostly infected by apes (37/39) FV (mainly gorilla). Infection by monkey FV was less frequent (2/39). The viral origin of the amplified sequences matched with the history reported by the hunters, most of which (83%) are aged 20 to 40 years and acquired the infection during the last twenty years. The (pro)viral load in 33 individuals infected by a gorilla FV was quite low (<1 to 145 copies per $10^5$ cells) in the peripheral blood leucocytes. Of the 30 wives and 12 children from families of FV infected persons, only one woman was seropositive in WB without subsequent viral DNA amplification. We demonstrate a high level of recent transmission of SFVs to humans in natural settings specifically following severe gorilla bites during hunting activities. The virus was found to persist over several years, with low SFV loads in infected persons. Secondary transmission remains an open question.

**Citation:** Betsem E, Rua R, Tortevoye P, Froment A, Gessain A (2011) Frequent and Recent Human Acquisition of Simian Foamy Viruses Through Apes' Bites in Central Africa. PLoS Pathog 7(10): e1002306. doi:10.1371/journal.ppat.1002306

**Editor:** Jeffrey Lifson, SAIC-Frederick, United States of America

**Received** June 3, 2011; **Accepted** August 24, 2011; **Published** October 27, 2011

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**Funding:** E. Betsem was personally supported by the "Service de Coopération et de l'Action Culturelle (SCAC), of the French embassy in Yaounde, and also by the Institut Pasteur in Paris, the "Association Vaincre Cancer Prevention" and the Institut National pour le Cancer. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Competing Interests:** The authors have declared that no competing interests exist.

* E-mail: antoine.gessain@pasteur.fr (AG); edouard.betsem@pasteur.fr (EB)

13350 jvi.asm.org Journal of Virology p. 13350–13359 December 2012 Volume 86 Number 24

**Genetic Characterization of Simian Foamy Viruses Infecting Humans**

**Réjane Rua,[a,b,c] Edouard Betsem,[a,b,d] Sara Calattini,[a,b,e] Ali Saib,[e] and Antoine Gessain[a,b]**

Unit of Epidemiology and Physiopathology of Oncogenic Viruses, Department of Virology, Institut Pasteur, Paris, France[a]; Centre National de la Recherche Scientifique (CNRS), URA 3015, Paris, France[b]; Université Paris Diderot; Cellule Pasteur, Paris, France[c]; Faculty of Medicine and Biomedical Sciences, University of Yaounde I, Yaounde, Cameroon[d]; and CNRS UMR7212/INSERM U944, Hôpital Saint-Louis, and Conservatoire National des Arts et Métiers, Paris, France[e]

## STLV-1/HTLV-1

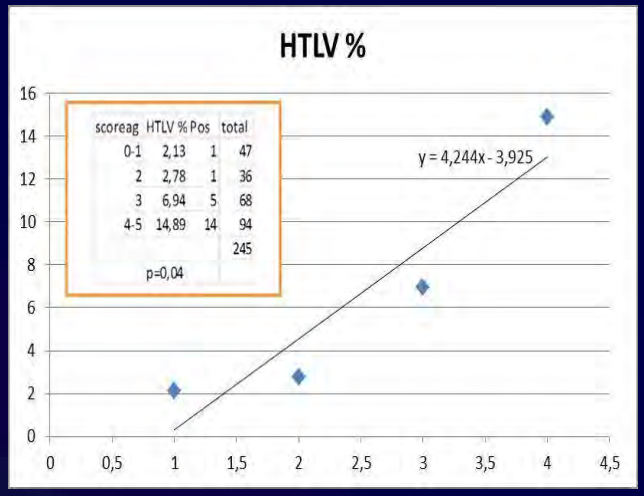
**Clinical Infectious Diseases Advance Access published April 1, 2015**

MAJOR ARTICLE

**A Severe Bite From a Nonhuman Primate is a Major Risk Factor for HTLV-1 Infection in Hunters From Central Africa**

**Claudia Filippone,[1,2] Edouard Betsem,[1,2,3] Patricia Tortevoye,[1,2] Olivier Cassar,[1,2] Sylviane Bassot,[1,2] Alain Froment,[4] Arnaud Fontanet,[5,6] and Antoine Gessain[1,2]**

[1]Institut Pasteur, Unité d'Epidémiologie et Physiopathologie des Virus Oncogènes, Département de Virologie, and [2]CNRS, UMR 3569, Paris, France; [3]Faculté de Médecine et des Sciences Biomédicales, Université Yaoundé I, Yaoundé, Cameroun; [4]Institut de Recherche pour le Développement, Musée de l'Homme, [5]Institut Pasteur, Unité de Recherche et d'Expertise Epidémiologie des Maladies Emergentes, Département d'Infection et Epidémiologie, and [6]Conservatoire National des Arts et Métiers, Paris, France





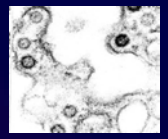

HTLV-1 infection was associated to the severity of the bite

# FROM NHPs TO HUMANS: THE NATURAL HISTORY

## Different steps leading to possible retroviral emergence

NON HUMAN PRIMATES

HUMANS



FOAMY ? STOP

Very few studied cases

HUMANS

? STOP HTLV-3/4

Very few studied cases

HUMANS

CONTACTS (bites, cuts, wounds…)
~ 50% rural population adults

TRANSMISSION (saliva, blood, other fluids…)
Innate immunity

PERSISTENCE in HOST
viral replication lymphocytes
Restriction factors

For SFV emergence, transmission rate is not the limiting factor

TRANSMISSION (sexual, nursing, blood…)
HIV/HTLV-1/2

DIFFUSION (sex, drug users, traveling…)
HIV/HTLV-1/2

EPIDEMIC / ENDEMIC
HIV-1 HTLV-1/2

Studies are ongoing what will be the future story for HTLV-3, HTLV-4 and Foamy viruses in Humans ?



# Monkeypox: a new viral emergence of African origin



## ACIP 2013

Détection de la circulation d'*orthopoxvirus* simiens en Afrique centrale,

Emmanuel Nakoune, Mirdad Kazanji, Nicolas Berthet, Jean Claude Manuguerra, Antoine Gessain

Clinical, epidemiological and virplogical aspects in CAR


Case Report

Maculopapular lesions in the Central African Republic


Open Forum Infectious Diseases

BRIEF REPORT

A Nosocomial Outbreak of Human Monkeypox in the Central African Republic


scientific reports

OPEN Genomic history of human monkey pox infections in the Central African Republic between 2001 and 2018

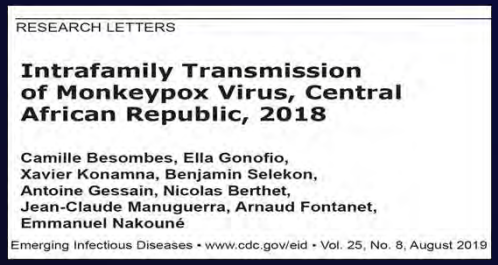

scientific reports

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

## ANR, PTR, Fondation SCOR 2018

A. Fontanet, E. Nakoune, A. Gessain, A. Hassanin, T. Giles-Vernick, JC Manuguerra...

Multidisciplinary work: epidemiological, animal reservoir, serological, anthropological and virological diagnosis in CAR


RESEARCH LETTERS

Intrafamily Transmission of Monkeypox Virus, Central African Republic, 2018

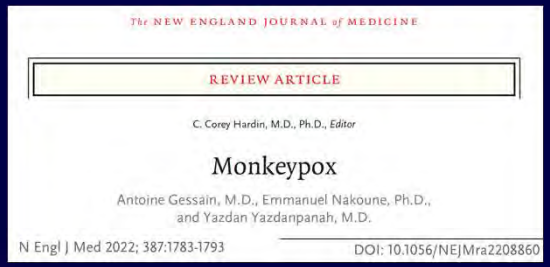
Camille Besombes, Ella Gonofio, Xavier Konamna, Benjamin Selekon, Antoine Gessain, Nicolas Berthet, Jean-Claude Manuguerra, Arnaud Fontanet, Emmanuel Nakouné

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 25, No. 8, August 2019


National Monkeypox Surveillance, Central African Republic, 2001-2021.

Besombes C, Mbrenga F, Schaeffer L, Malaka C, Gonofio E, Landier J, Vickos U, Konamna X, Selekon B, Dankpèa JN, Von Platen C, Houndjahoue FG, Ouaimon DS, Hassanin A, Berthet N, Manuguerra JC, Gessain A, Fontanet A, Nakouné-Yandoko E

Emerging Infectious Diseases, 03 Nov 2022, 28(12):2435-2445


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

# Four Main Chapters

1) History, Virus, Genetic Variability, Reservoir

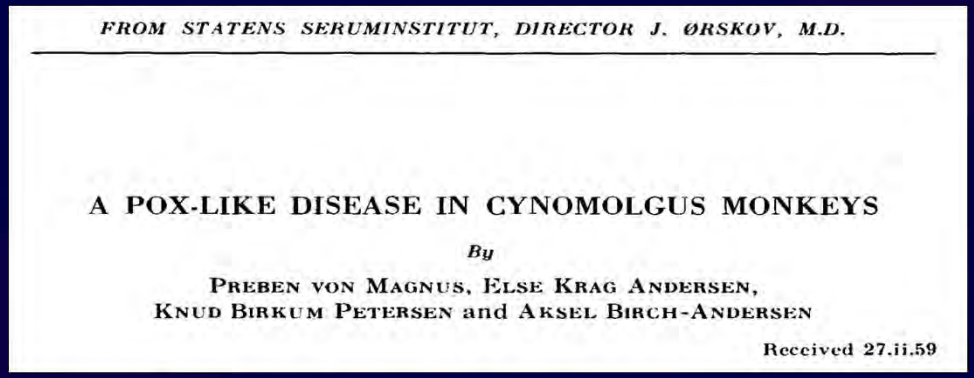
2) Clinical and Epidemiological Aspects of the Classical African Form

3) First Emergence in 2022 and Different Aspects of the Pandemic: WHO Director-General Declares the MPOX Epidemic a Public Health Emergency of International Concern

4) Second Emergence in 2024 in the DRC and East Africa: WHO Director-General Declares the MPOX Epidemic a Public Health Emergency of International Concern: Current Situation

Animal Reservoir

# 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

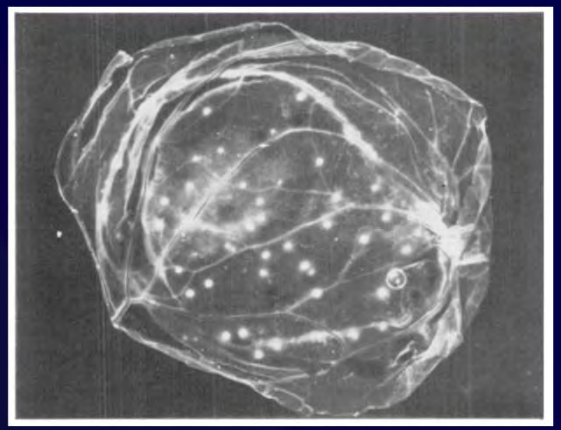


**Acute phase**
with typical pustules





**Convalescent stage**
lesions in healing and scars



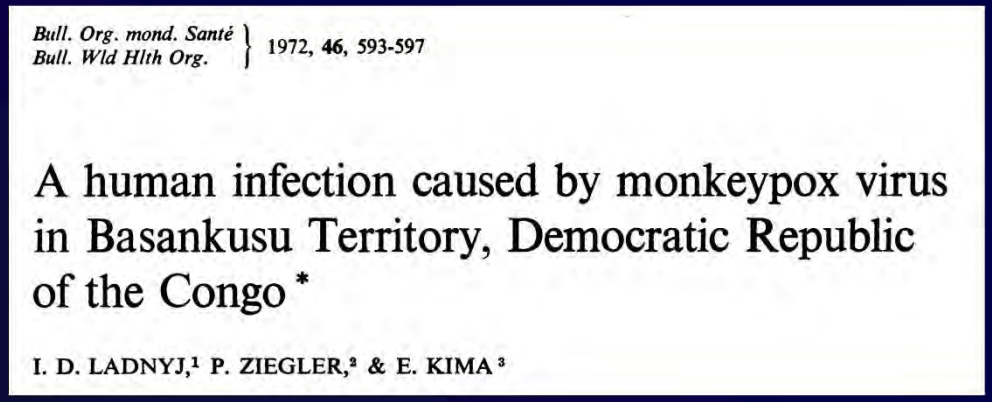
Monkeypox virus on the chorio-allantoic membrane with typical discrete opaque foci



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# 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

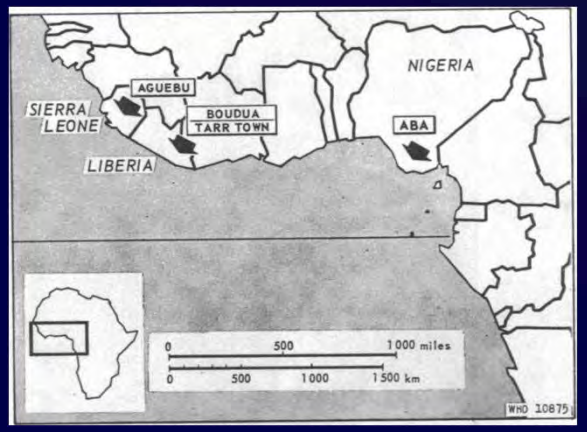
| Case | Country | Village | Age | Sex | Vaccination history | Date of rash | Prodrome in days | Severity of rash[a] | Duration of rash (days) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Liberia | Boudua | 4 | F | Negative | 13 Sept. 70 | 3 | ++ | 24 |
| 2 | Liberia | Boudua | 4 | M | Negative | 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]



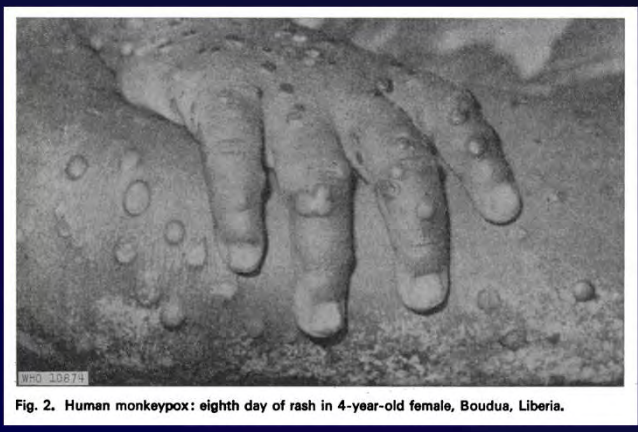
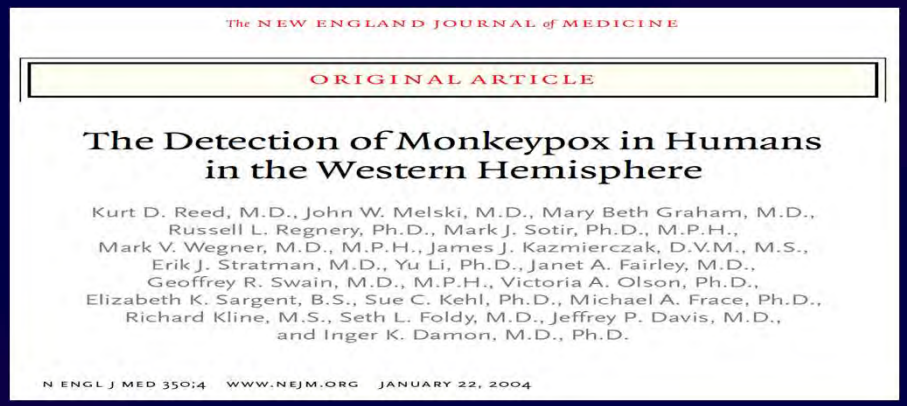




Fig. 2. Human monkeypox: eighth day of rash in 4-year-old female, Boudua, Liberia.

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.



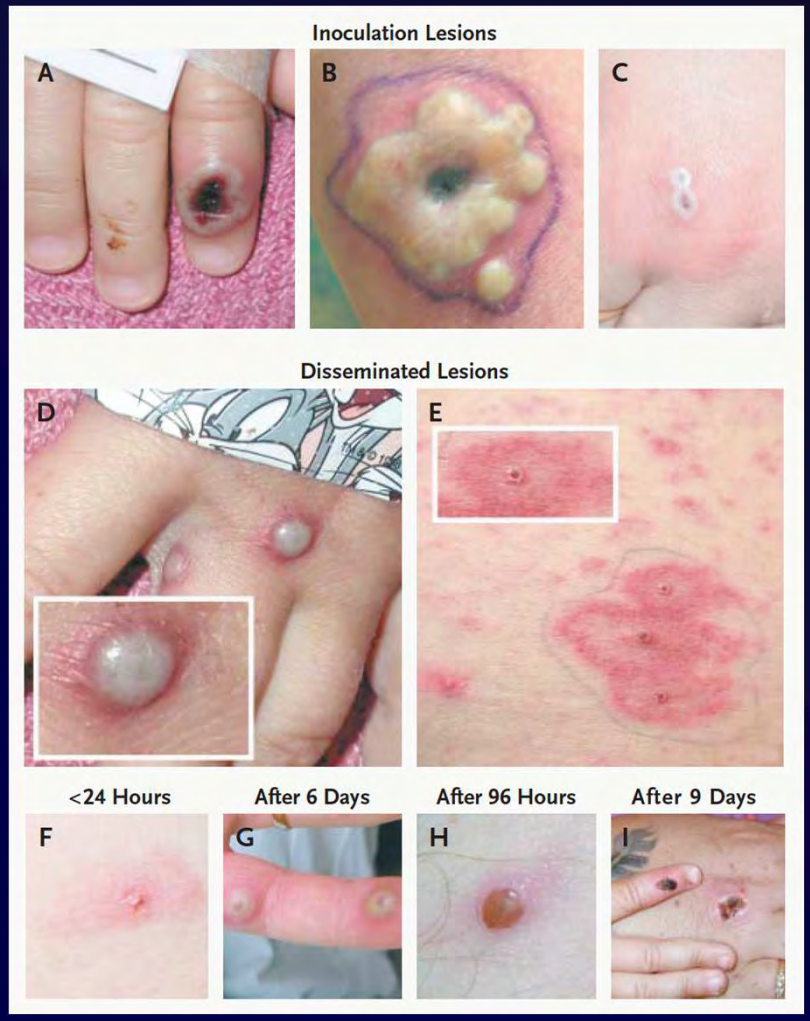
-These rodents transmitted the virus to prairie dogs housed at the same exotic animal facility. which then infected humans mostly young adults and childr through bites or scratches.



-No deaths, few hospitalisations

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

-

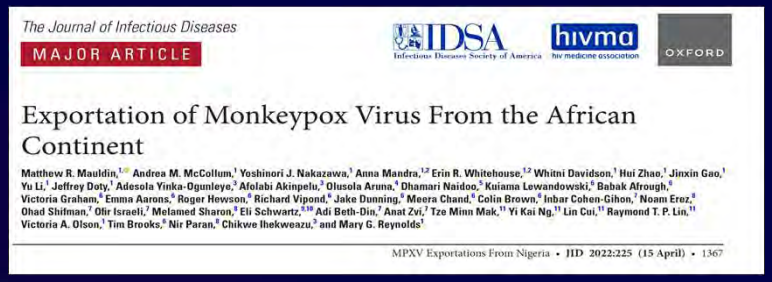



Primary innoculation reactions (A, B, C)

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

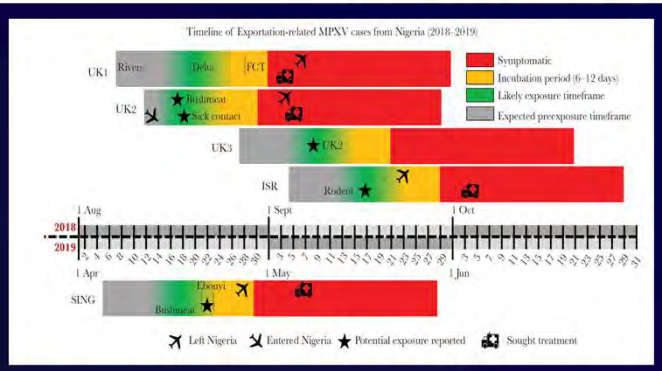
MAJOR ARTICLE

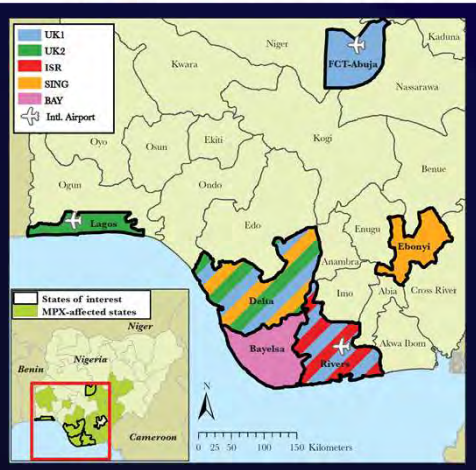
IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Exportation of Monkeypox Virus From the African Continent

Matthew R. Mauldin,[1,a] 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,[2] Afolabi Akinpelu,[2] Olusola Aruna,[2] Dhamari Naidoo,[3] Kuiama Lewandowski,[4] Babak Afrough,[4] Victoria Graham,[4] Emma Aarons,[4] Roger Hewson,[4] Richard Vipond,[4] Jake Dunning,[5] Meera Chand,[6] Colin Brown,[6] Inbar Cohen-Gihon,[7] Noam Erez,[8] Ohad Shifman,[7] Ofir Israeli,[7] Melamed Sharon,[8] 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,[4] Nir Paran,[8] Chikwe Ihekweazu,[2] 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).

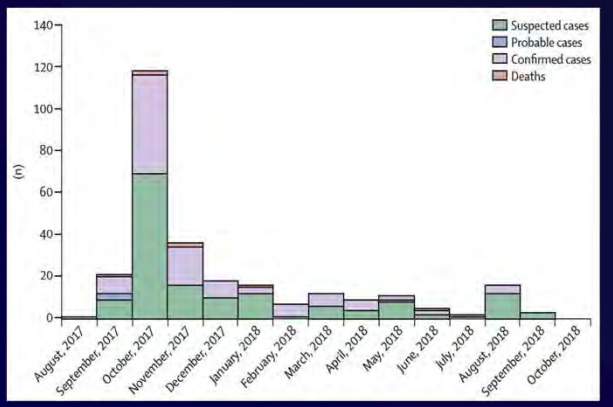


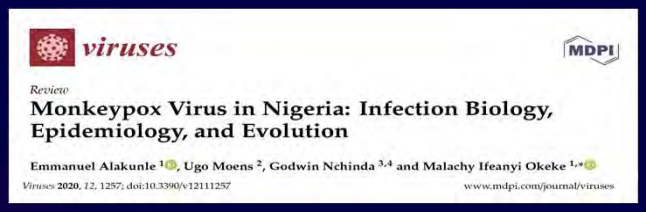
Articles

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 Ndzerarho, 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, Ashcena Khalakdina, Adebayo Adedeji, Nwando Mba, Olubunmi Ojo, Gerard Krause*, Chikwe Ihekweazu*, for the CDC Monkeypox Outbreak Team†





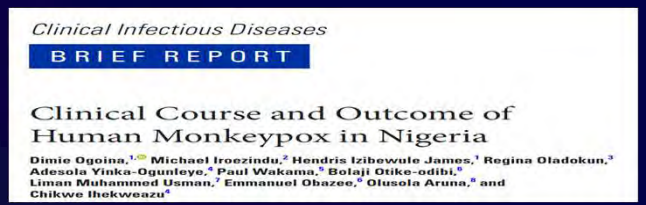
viruses · MDPI

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

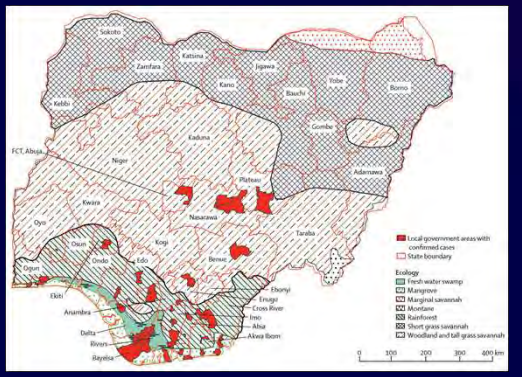


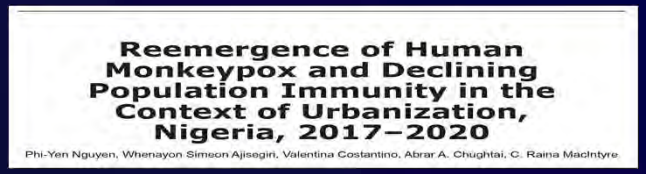
Clinical Infectious Diseases

BRIEF REPORT

Clinical Course and Outcome of Human Monkeypox in Nigeria

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



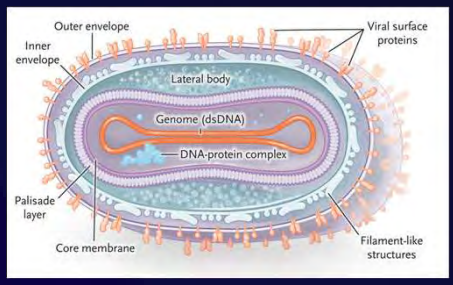



Reemergence of Human Monkeypox and Declining Population Immunity in the Context of Urbanization, Nigeria, 2017–2020

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
- Highly conserved genes are present in the central portion of the genome (important for viral replication), whereas less conserved genes present in the terminal repeat play a role in virus-host interaction

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

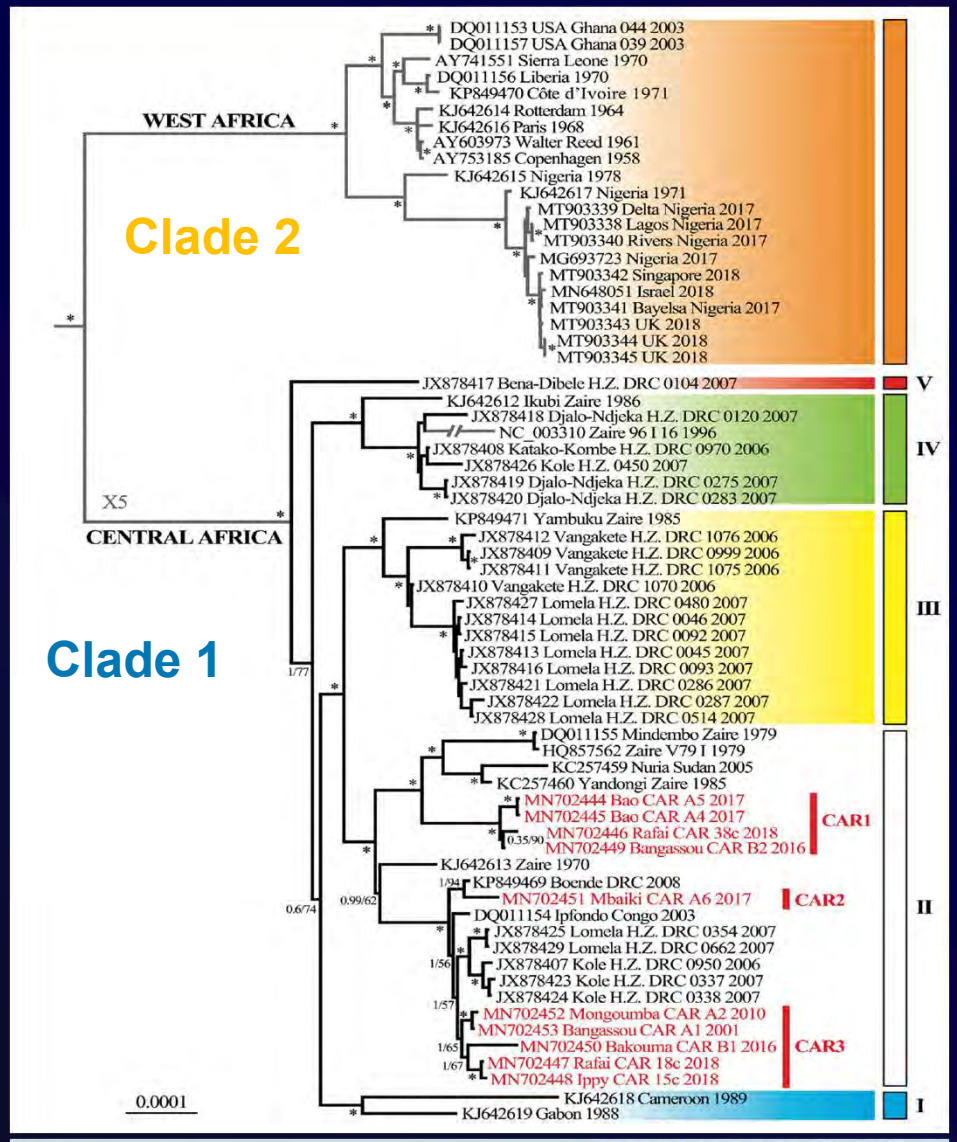


- Orthopoxviruses are very similar genetically and antigenically,

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





www.nature.com/scientificreports

scientific reports

OPEN

Genomic history of human monkey pox infections in the Central African Republic between 2001 and 2018

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



INSTITUT PASTEUR

# Reservoirs of Monkeypox





*Cricetomys* *giant pouched rats*



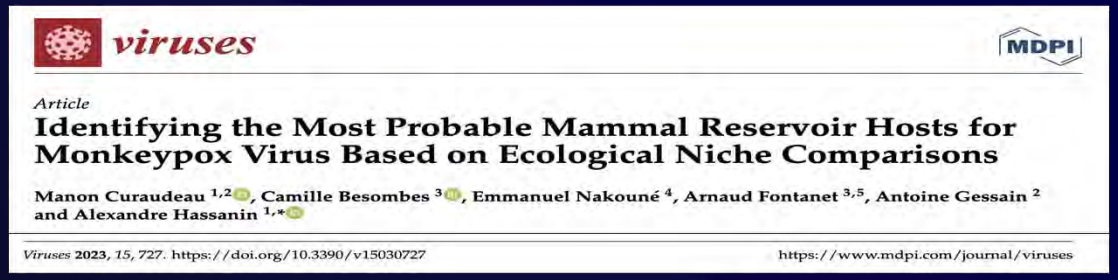


*Funisciurus anerythrus*

- Monkey pox is a sylvatic zoonosis but the reservoir of MPVX has not yet been clearly identified
- Rodents, including various species of squirrel 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







viruses

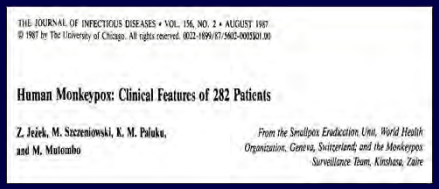
MDPI

*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

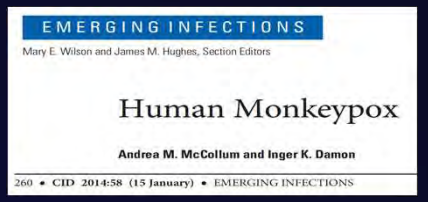

THE JOURNAL OF INFECTIOUS DISEASES • VOL. 156, NO. 2 • AUGUST 1987
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Human Monkeypox: Clinical Features of 282 Patients

Z. Jezek, 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

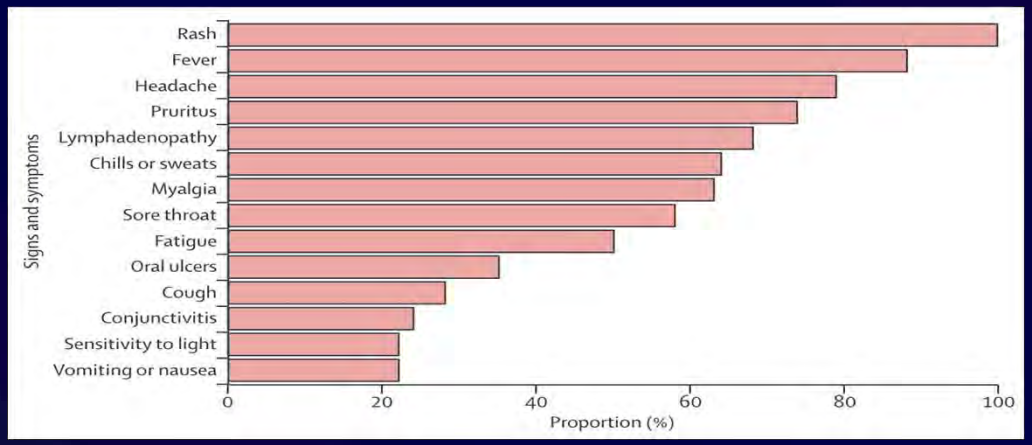
Seems to be more severe in immunocompromized HIV-infected patients



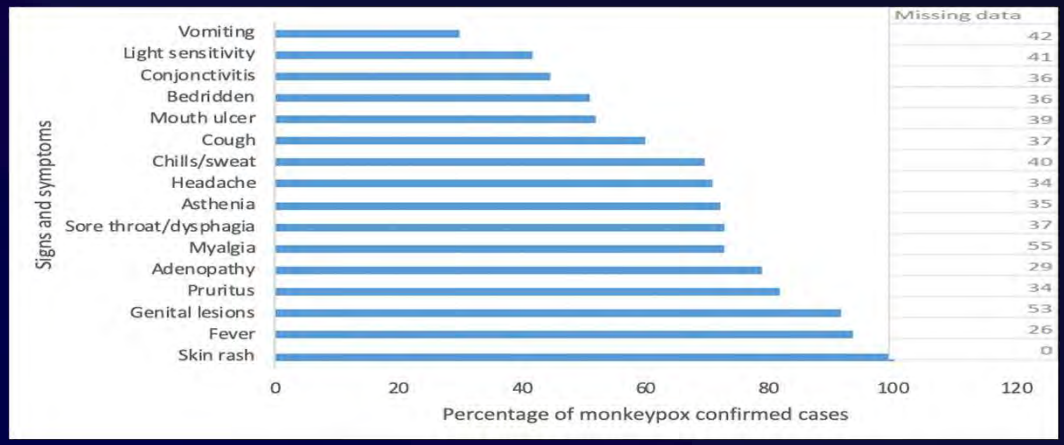


# Most Frequent Clinical Signs of Monkeypox in the African Setting

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

Importance of child care (rehydration, AB therapy, renutrition, etc.

# 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]

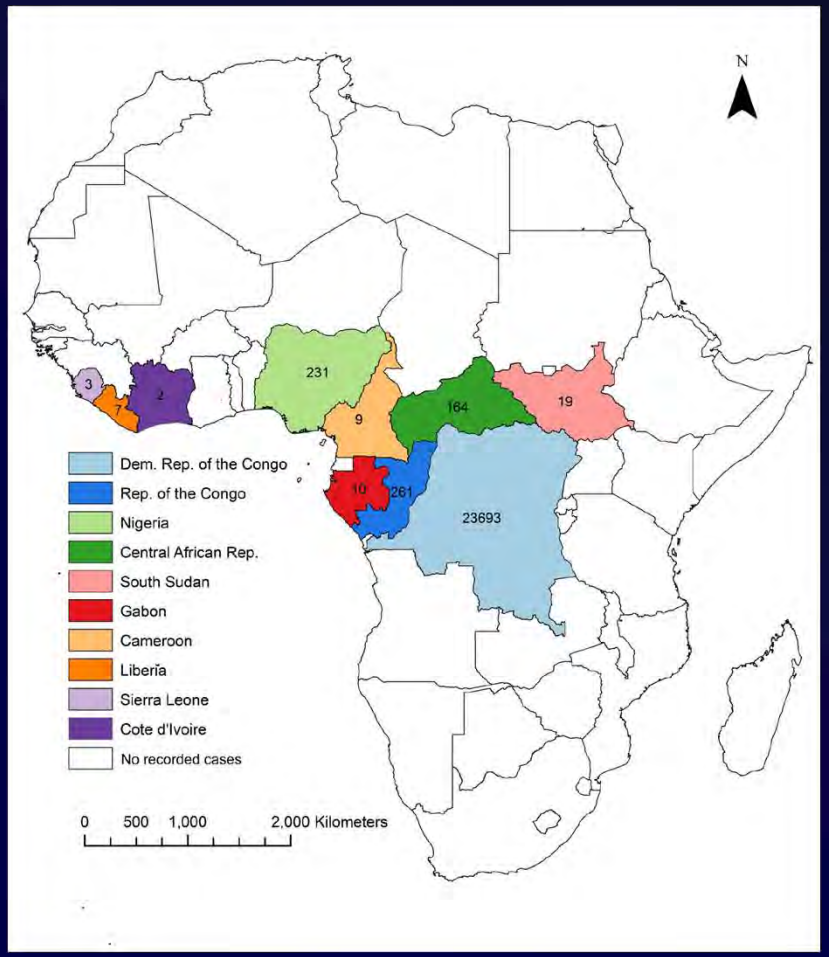
16262–16267 | PNAS | September 14, 2010 | vol. 107 | no. 37 www.pnas.org/cgi/doi/10.1073/pnas.1005769107

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

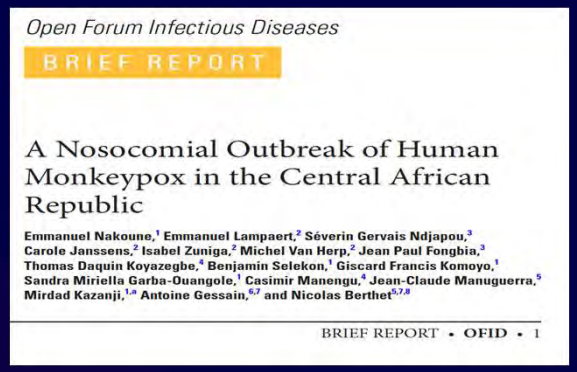




Contaminated materials such as beeding may also be infectious.

The exact origin of transmission is often unknown

# Transmission of Monkeypox in a classical African Settings



*Open Forum Infectious Diseases*

BRIEF REPORT

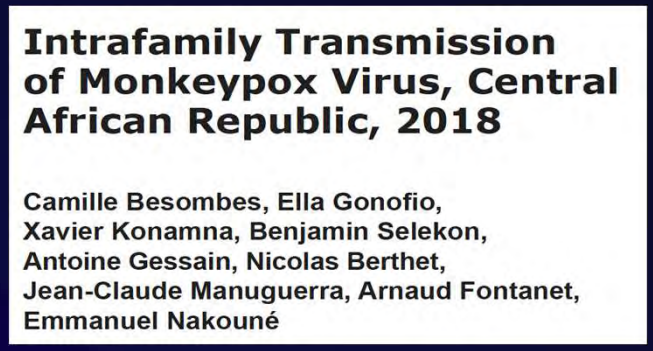
A Nosocomial Outbreak of Human Monkeypox in the Central African Republic

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[6,7,8]



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

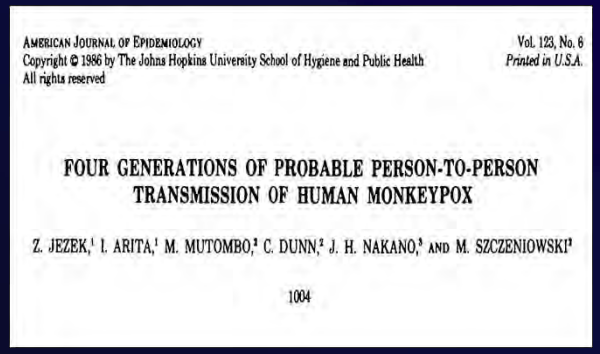
**scientific** reports

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[1], Valérie Caro[1], Emmanuel Nakoune[2,8] & Nicolas Berthet[1,6,8]

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

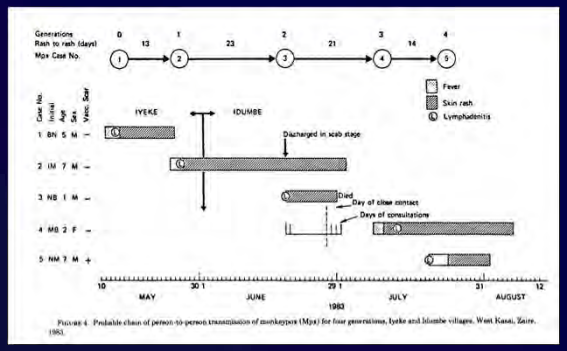


AMERICAN JOURNAL OF EPIDEMIOLOGY Vol. 123, No. 6
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FOUR GENERATIONS OF PROBABLE PERSON-TO-PERSON TRANSMISSION OF HUMAN MONKEYPOX

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






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. Range from 4-6 for smallpox



International Journal of Epidemiology Vol. 17, No. 3
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**The Transmission Potential of Monkeypox Virus in Human Populations**

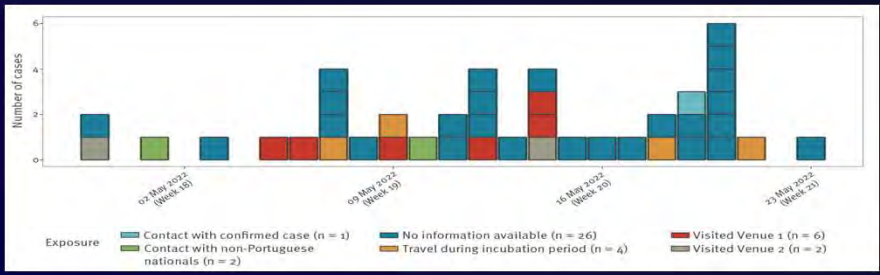
P E M FINE,* Z JEZEK,† B GRAB† AND H DIXON‡

# 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]

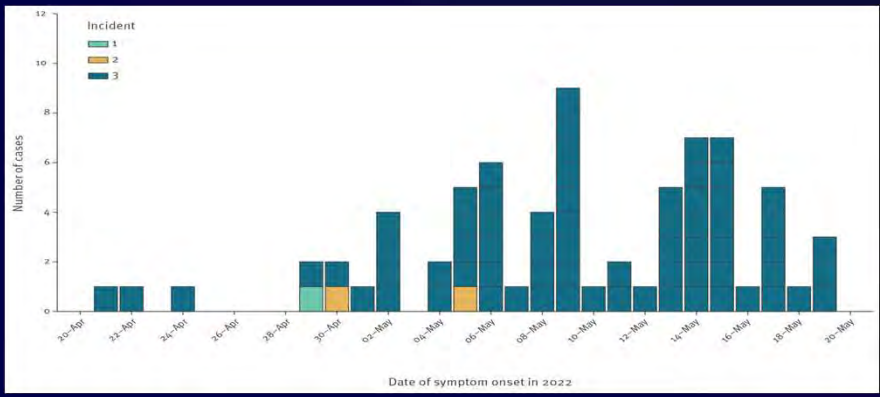



RAPID COMMUNICATIONS

## 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




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

RAPID COMMUNICATIONS

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

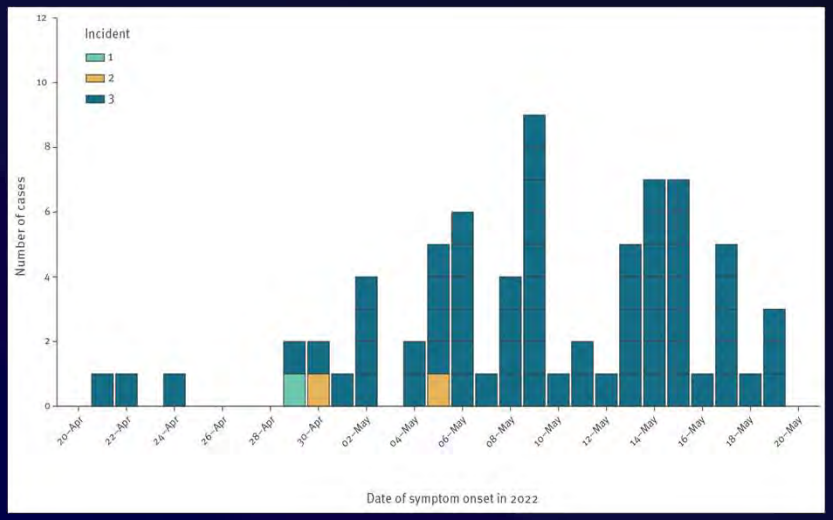
Andrea Antinori[1], Valentina Mazzotta[1], Serena Vita[1], Fabrizio Carletti[1], Danilo Tacconi[2], Laura Emma Lapini[2], Alessandra D'Abramo[1], Stefania Cicalini[1], Daniele Lapa[1], Silvia Pittalis[1], Vincenzo Puro[1], Marco Rivano Capparuccia[3], Emanuela Giombini[1], Cesare Ernesto Maria Gruber[1], 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

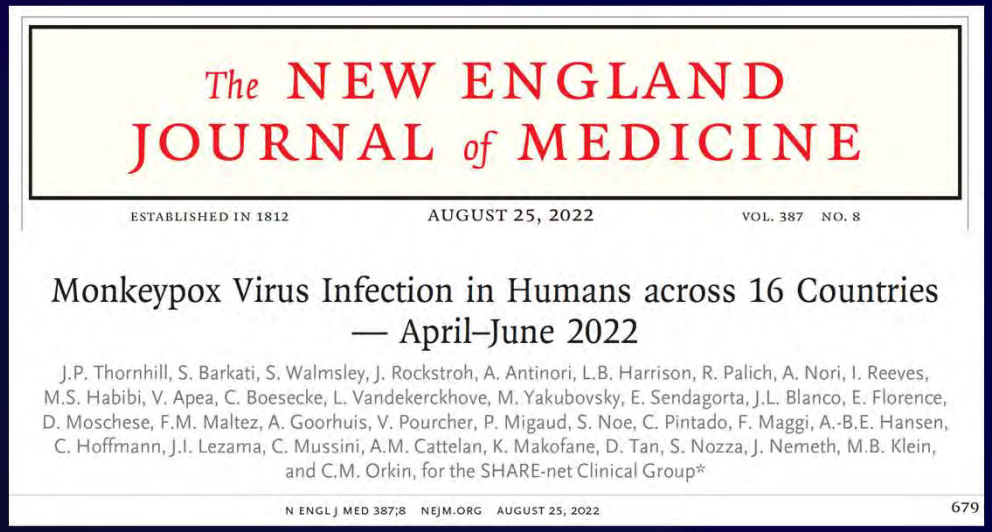
By septembre 10, around 80 000 cases of MPX infection have been reported in >100 locations worldwide with >95% in countries not historically endemic (USA, Spain, Brazil and France)

>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

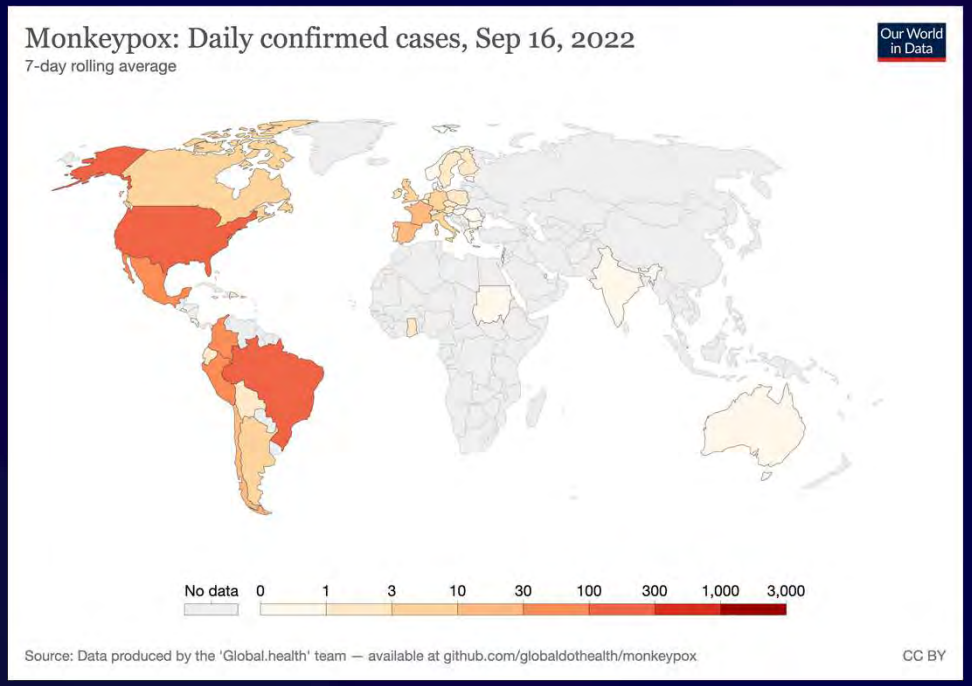
J.P. Thornhill, S. Barkati, S. Walmsley, J. Rockstroh, A. Antinori, L.B. Harrison, R. Palich, A. Nori, I. Reeves, M.S. Habibi, V. Apea, C. Boesecke, L. Vandekerckhove, M. Yakubovsky, E. Sendagorta, J.L. Blanco, E. Florence, D. Moschese, F.M. Maltez, A. Goorhuis, V. Pourcher, P. Migaud, S. Noe, C. Pintado, 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*

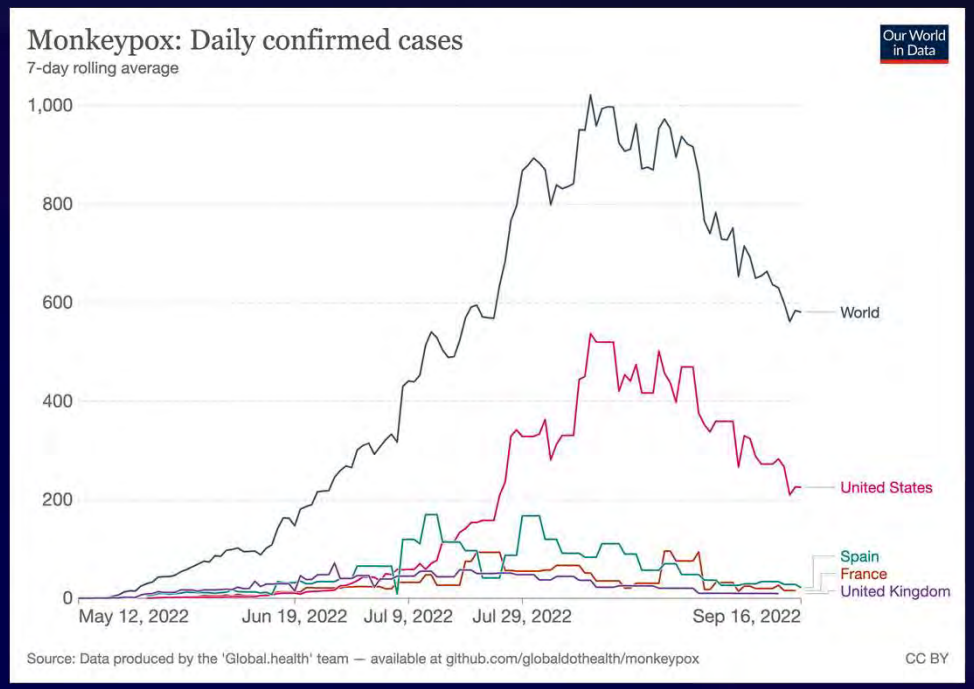


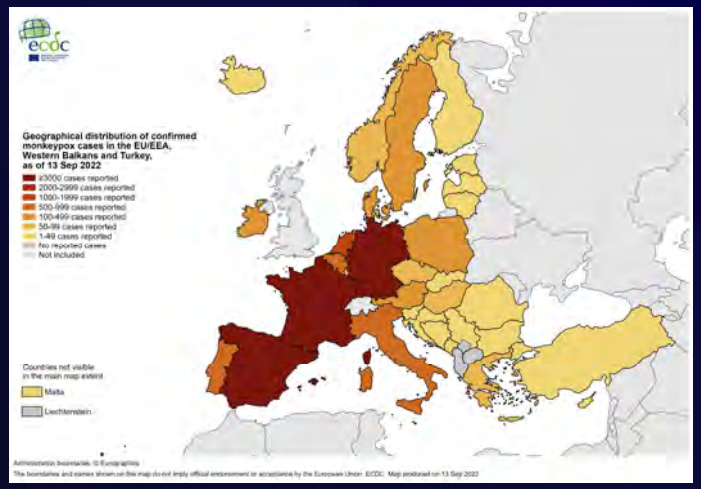
**Table 1. Demographic and Clinical Characteristics of the Persons with Monkeypox.***

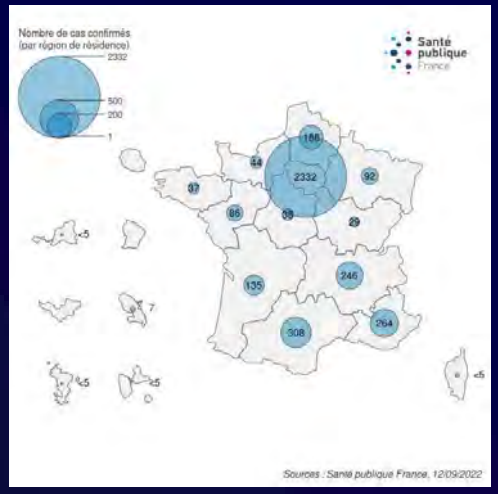
| Characteristic | All Persons (N=528) |
|---|---|
| Median age (range) — yr | 38 (18–68) |
| Sex or gender — no. (%) | |
| Male | 527 (>99) |
| Female | 0 |
| Trans or nonbinary | 1 (<1) |
| Sexual orientation — no. (%)† | |
| Heterosexual | 9 (2) |
| Homosexual | 509 (96) |
| Bisexual | 10 (2) |
| 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) |

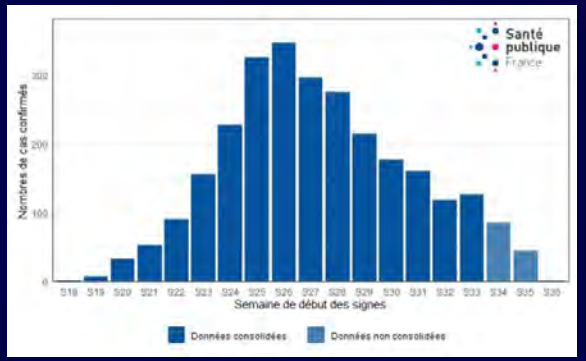
# Epidemiological Data on the 2022 Outbreak of Monkeypox



# 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

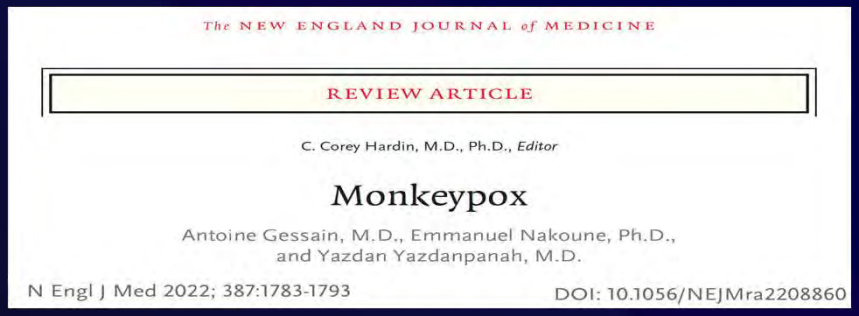
sometimes with only a few painless lesions, but also often in genital, anal and perianal areas (rectitits) and oral lesions (pharyngitis)











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

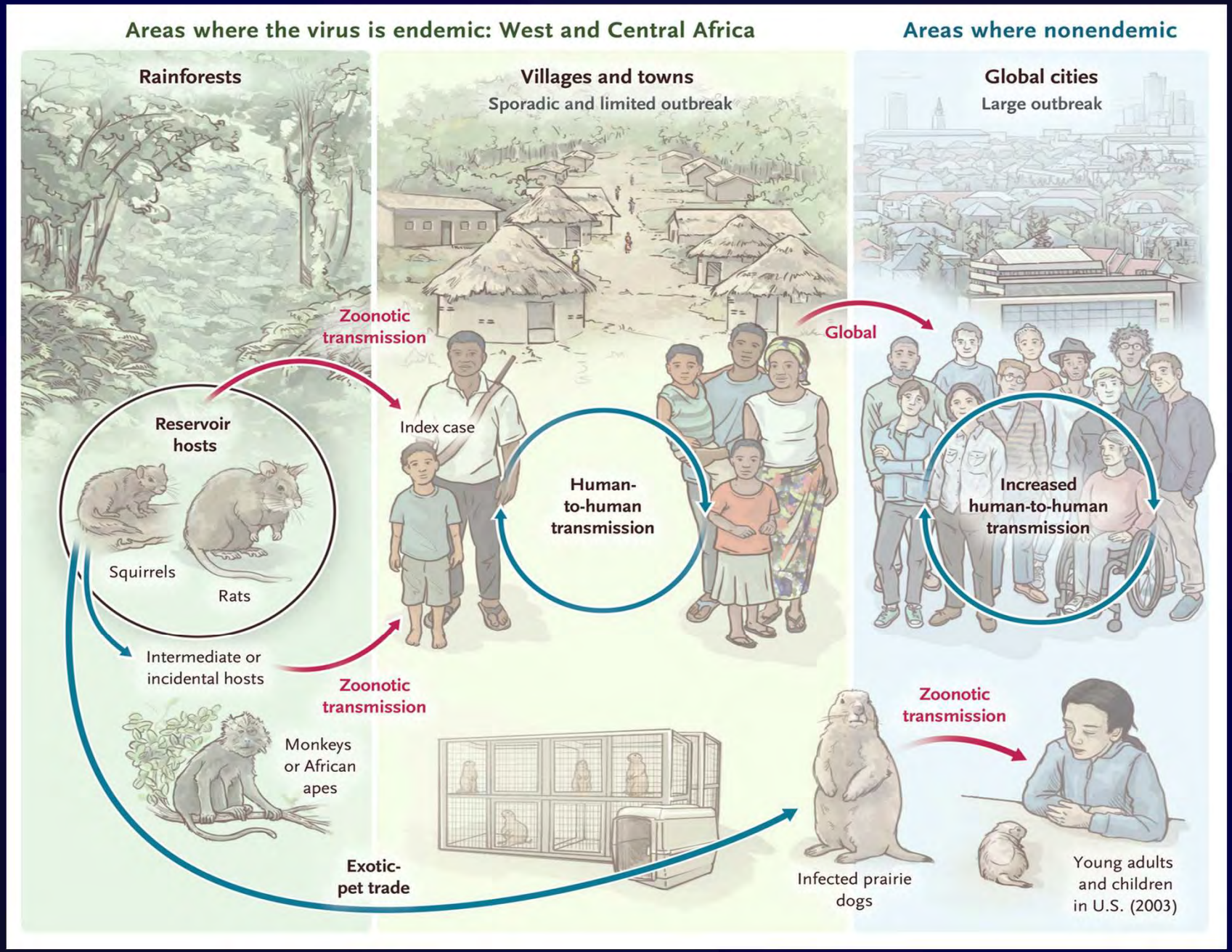
# Comparison of the Classical African and the New Clinico-Epidemiological Form of Monkeypox

**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*

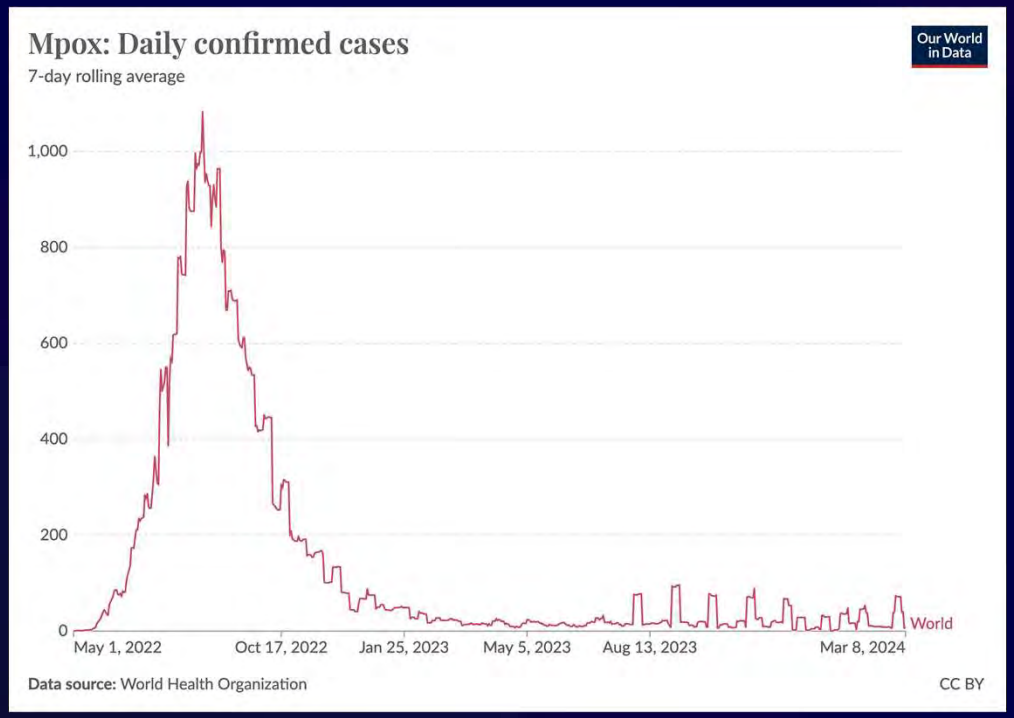
# Natural History of Monkeypox

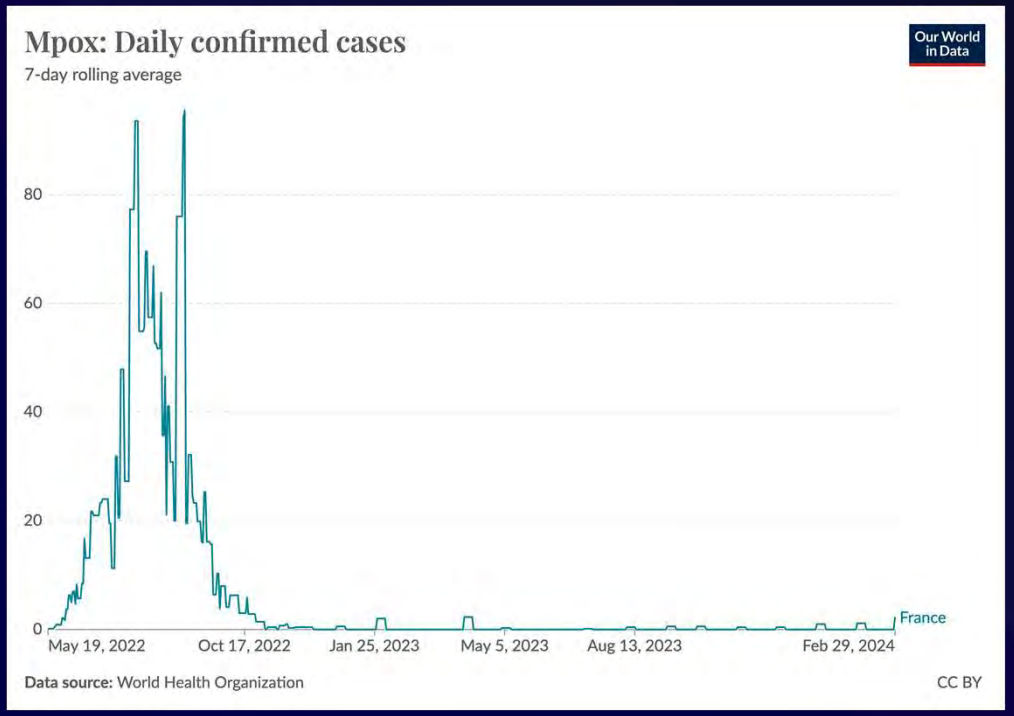



From Gessain et al., NEJM, 2022

# 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

*Disclaimer: Early release articles are not considered as final versions. Any changes will be reflected in the online version in the month the article is officially released.*

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



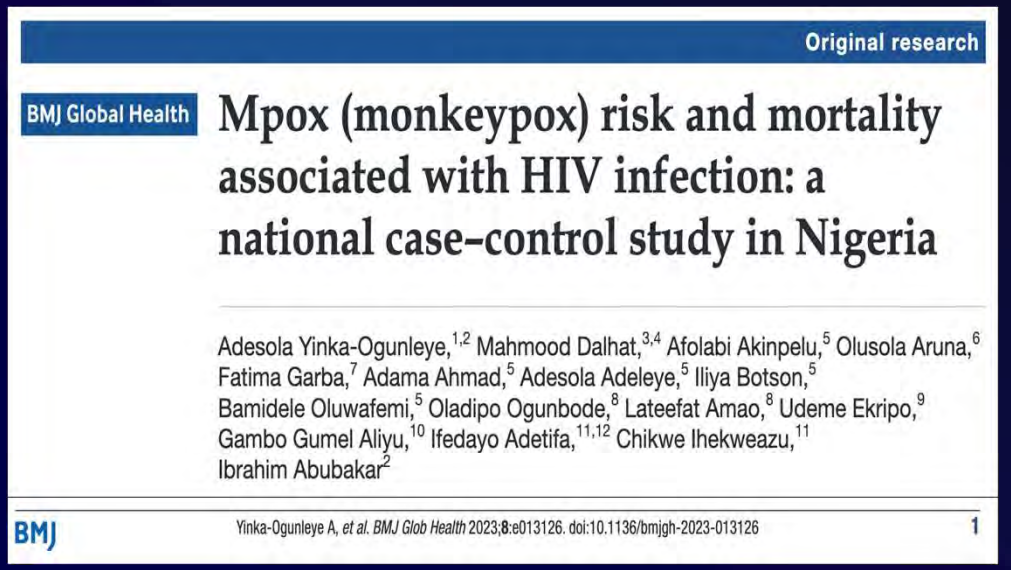
Articles

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

www.thelancet.com Vol 401 March 18, 2023





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]

BMJ Yinka-Ogunleye A, *et al. BMJ Glob Health* 2023;**8**:e013126. doi:10.1136/bmjgh-2023-013126 1

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

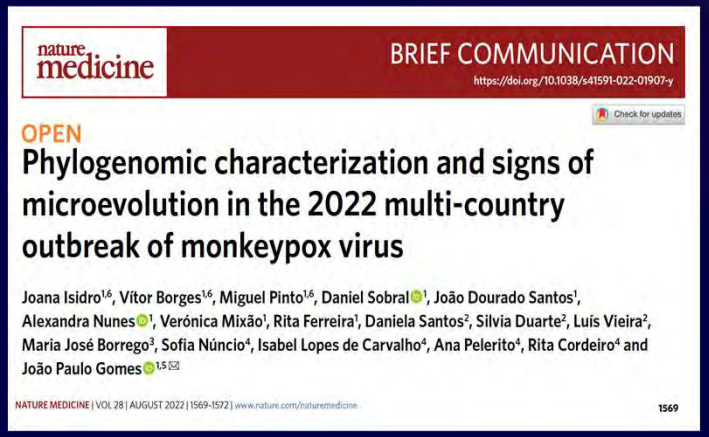
High risk in children dying from Mpox infection irrespective of HIV status

# 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

Check for updates

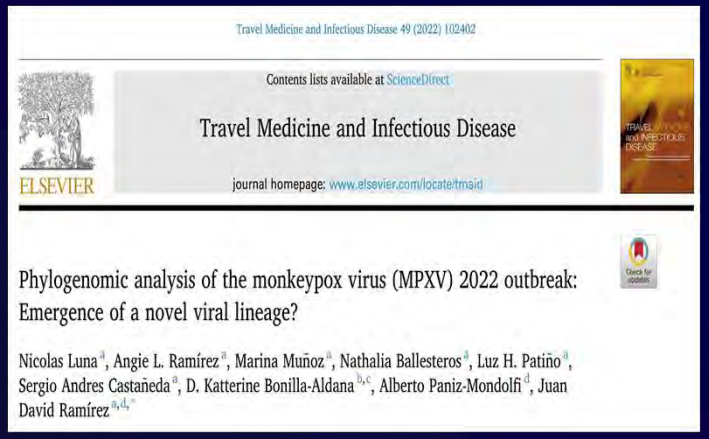
OPEN

**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 1569





Travel Medicine and Infectious Disease 49 (2022) 102402

Contents lists available at ScienceDirect

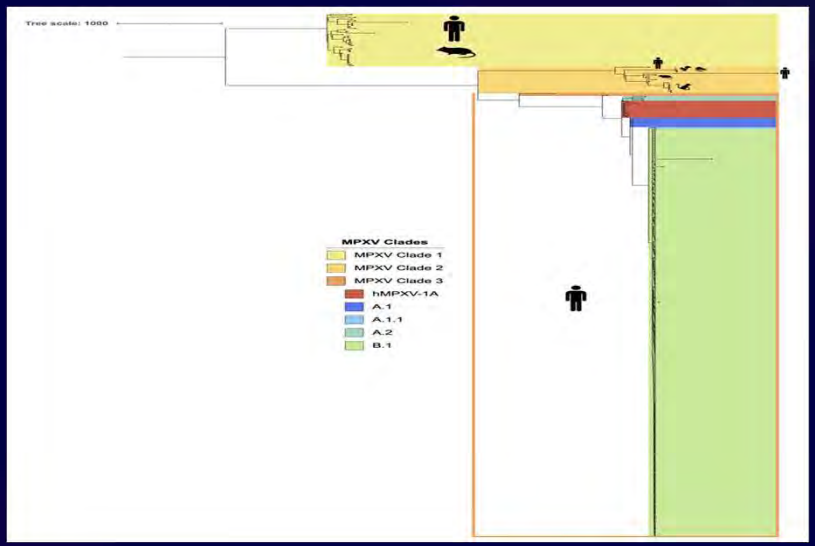
Travel Medicine and Infectious Disease

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

ELSEVIER

**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,*]



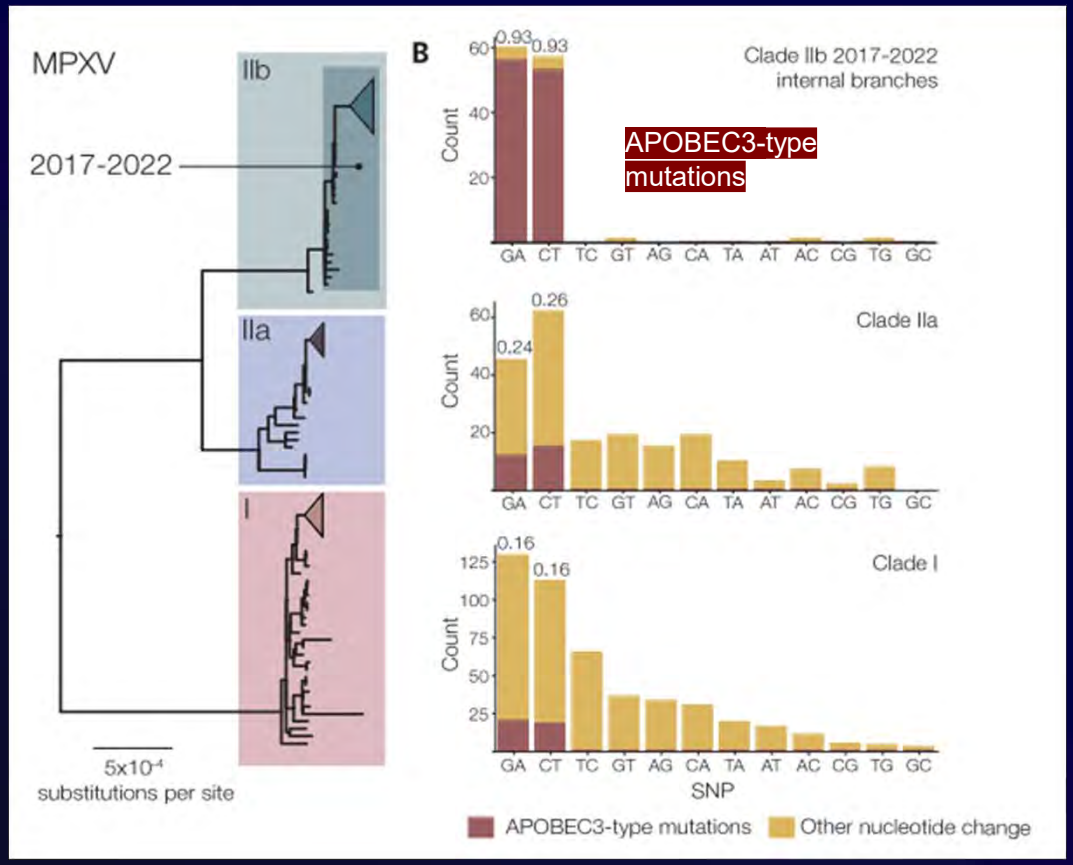
RESEARCH

MPOX

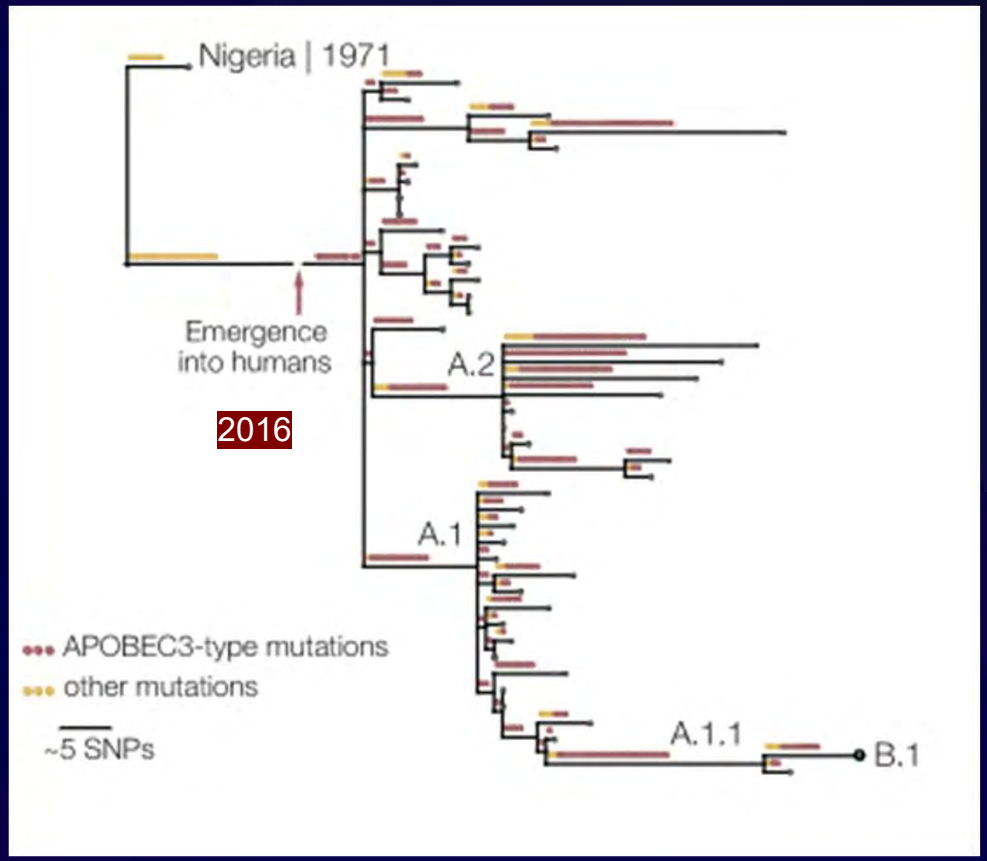
# APOBEC3 deaminase editing in mpox virus as evidence for sustained human transmission since at least 2016

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 (G/A) 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

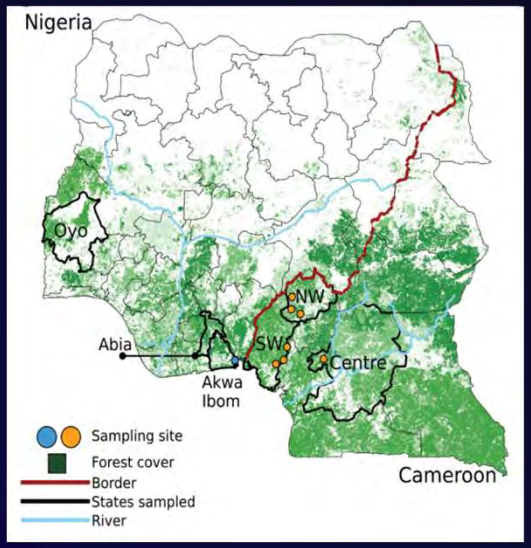
Molecular epidemiology of recurrent zoonotic transmission of mpox virus in West Africa

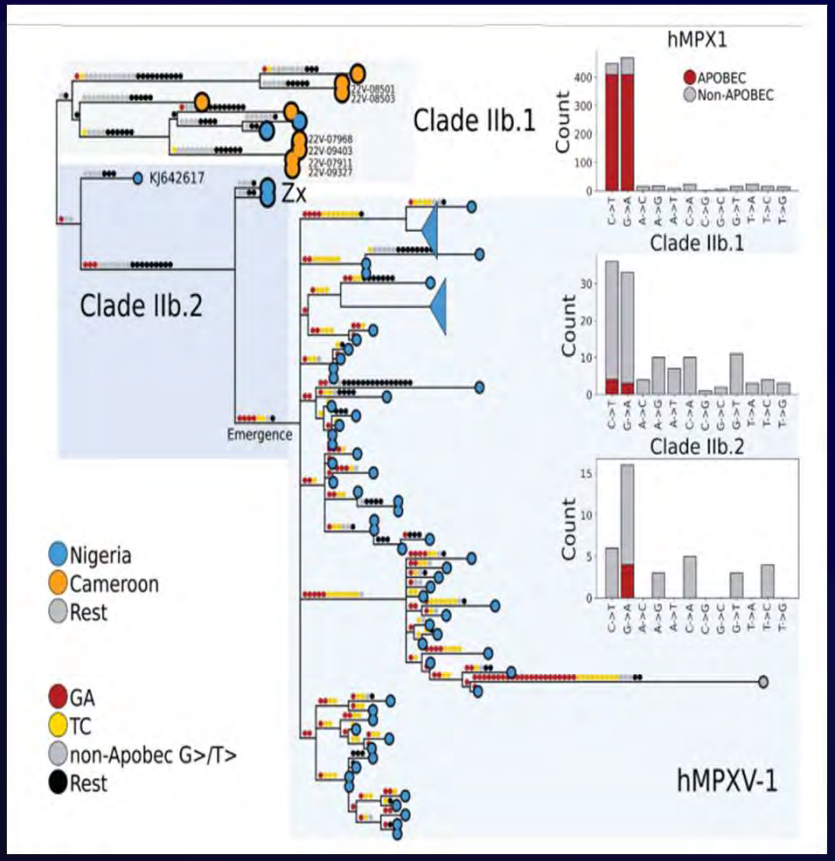
Delia Doreen Djuicy *et al.*

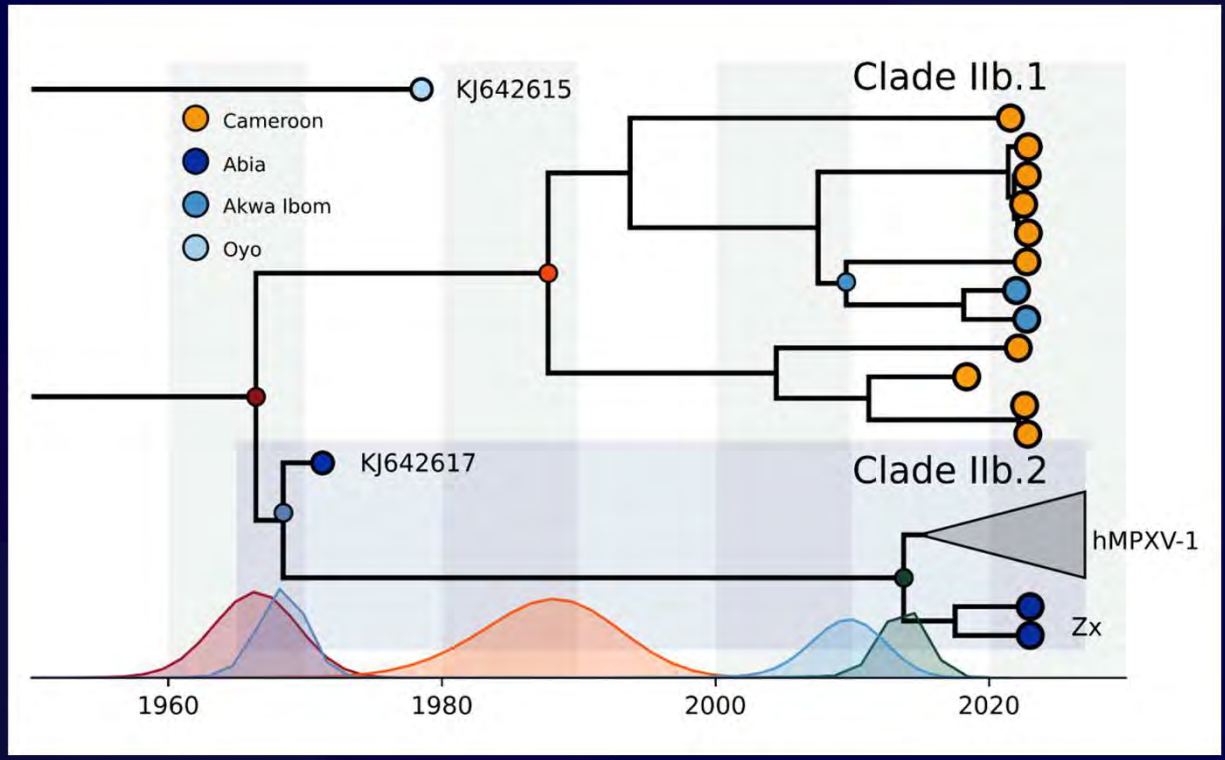
doi: https://doi.org/10.1101/2024.06.18.24309115

# 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 2024/beginning 2023 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.






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



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

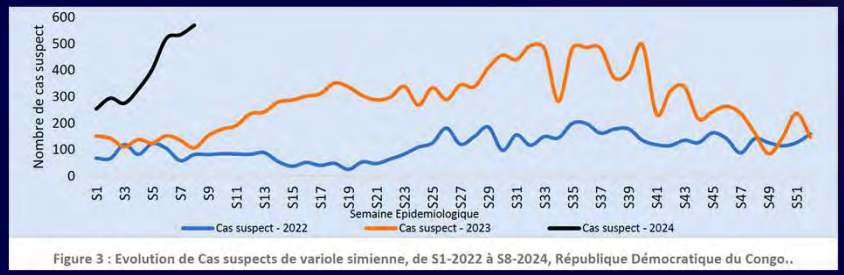


Figure 3 : Evolution de Cas suspects de variole simienne, de S1-2022 à S8-2024, République Démocratique du Congo..

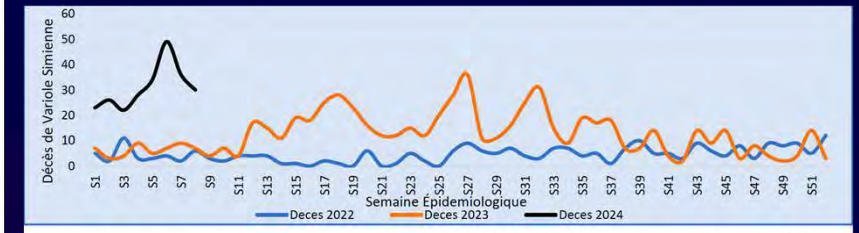


Figure 4: Evolution de décès de variole simienne, de S1-2022 à S8-2024, République Démocratique du Congo.

| 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

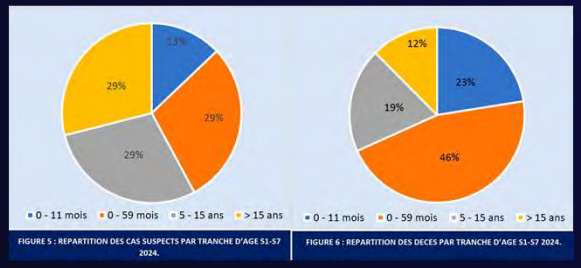


FIGURE 5 : REPARTITION DES CAS SUSPECTS PAR TRANCHE D'AGE S1-S7 2024.
FIGURE 6 : REPARTITION DES DECES PAR TRANCHE D'AGE S1-S7 2024.

| 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% |

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

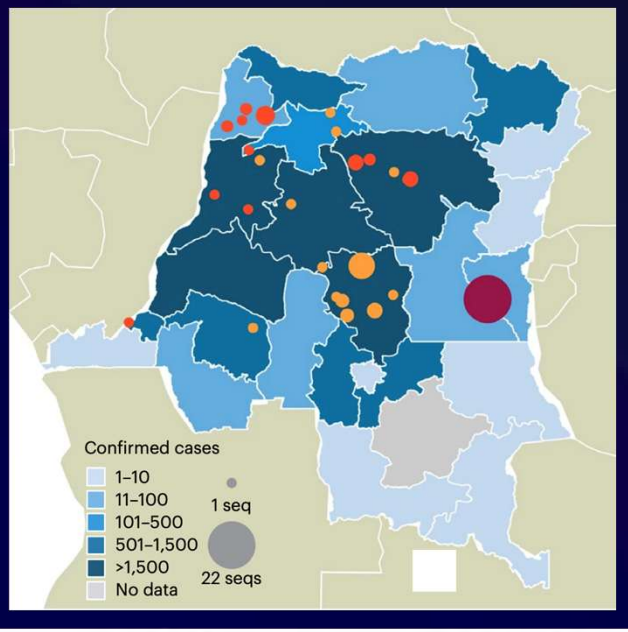
nature medicine

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**

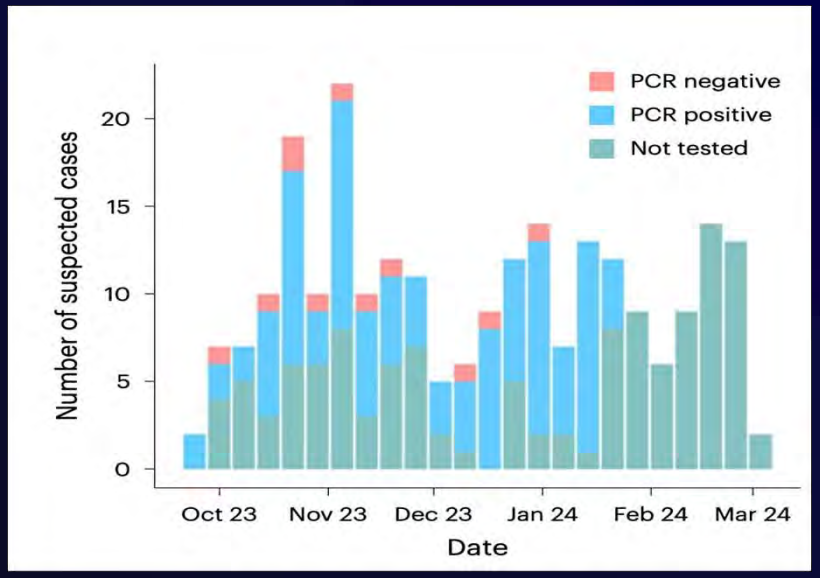
Vakaniaki, E.H., Kacita, C., Kinganda-Lusamaki, E. *et al.*

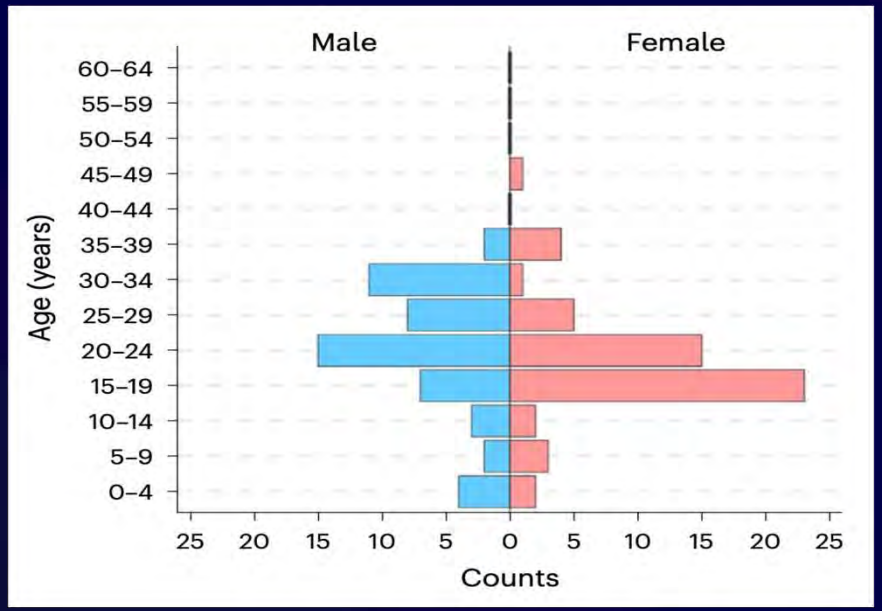
*Nat Med* **30**, 2791–2795 (2024). https://doi.org/10.1038/s41591-024-03130-3




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

241 suspected cases
90% of 119 tested cases MPXV +



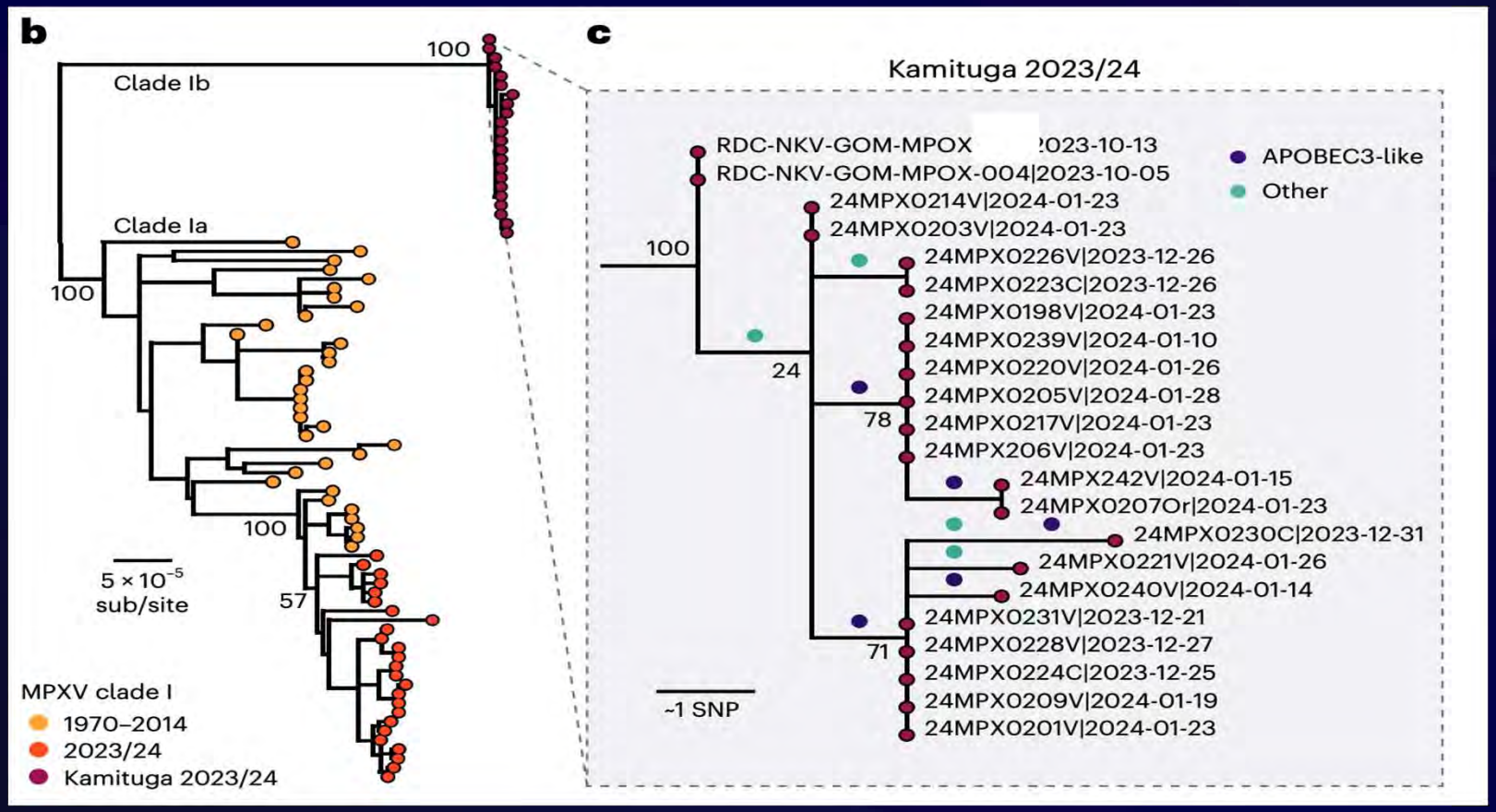

Majority are women

Median age 22 years

Frequent sex workers

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

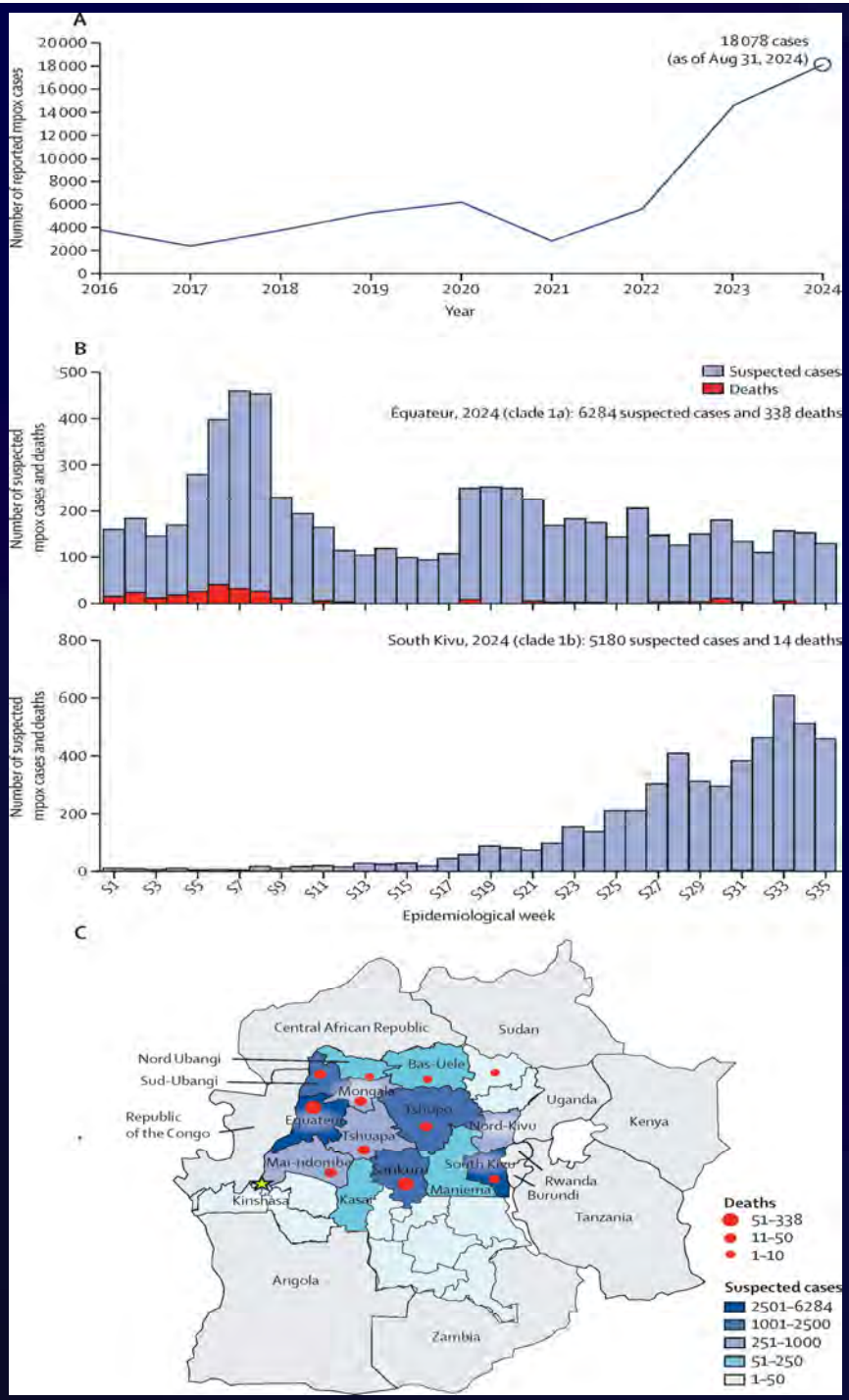
**The predominance of APOBEC3 mutations support that the entire cluster resulted from human to human transmission and the low genetic diversity indicate a recent outbreak**




This new lineage was named clade 1b

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

# Incidence of mpox in DRC




Annual reported cases of mpox in DRC from 2016-2024 with a notable increase in 2023

Epidemic curves by province in 2024 by weeks

Top graph in Équateur province (clade 1a)

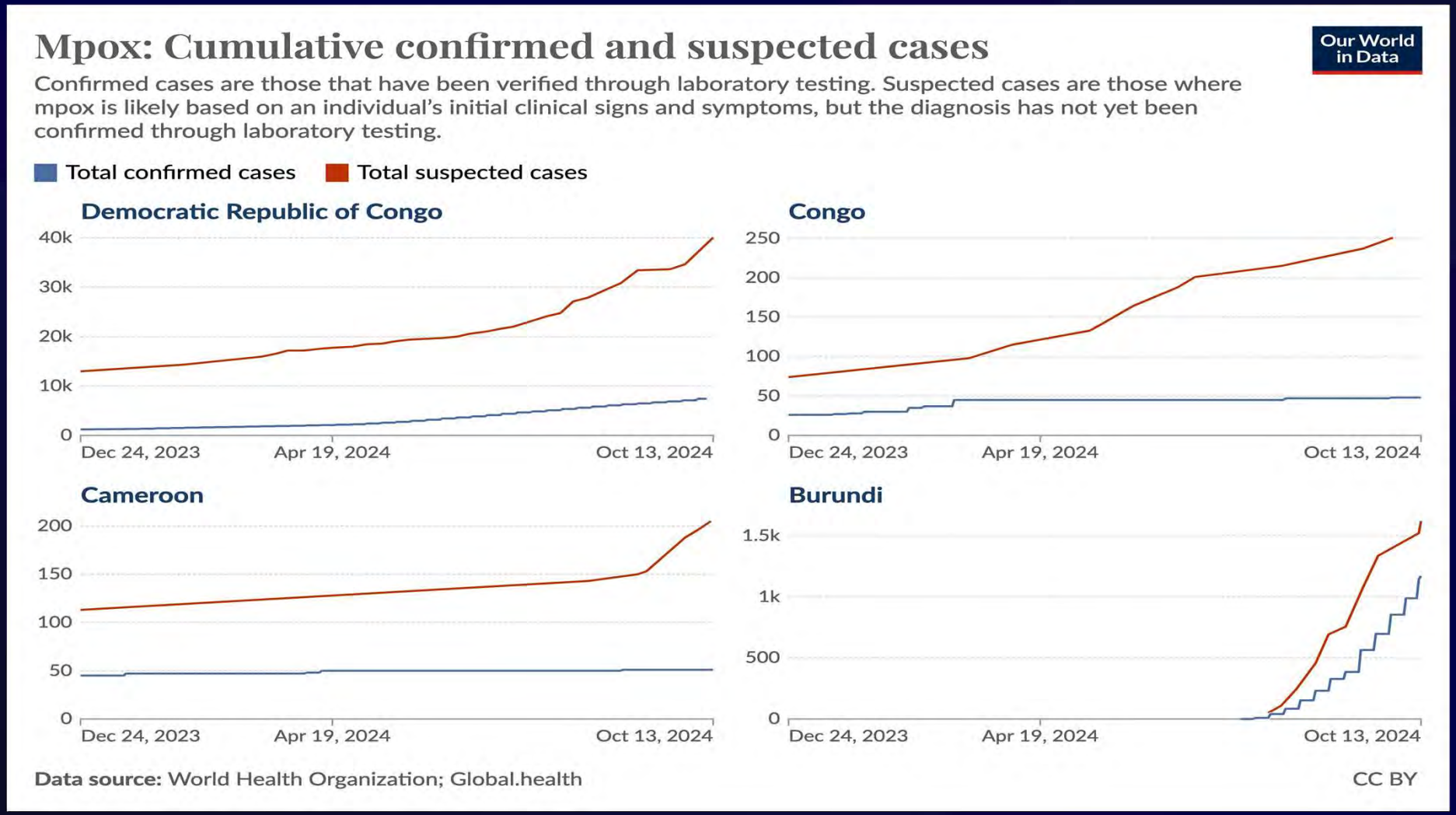
Bottom graph in South Kivu (clade 1b)

Geographical distribution of mpox clades in DRC

Beiras et al. Lancet January 2025

# 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

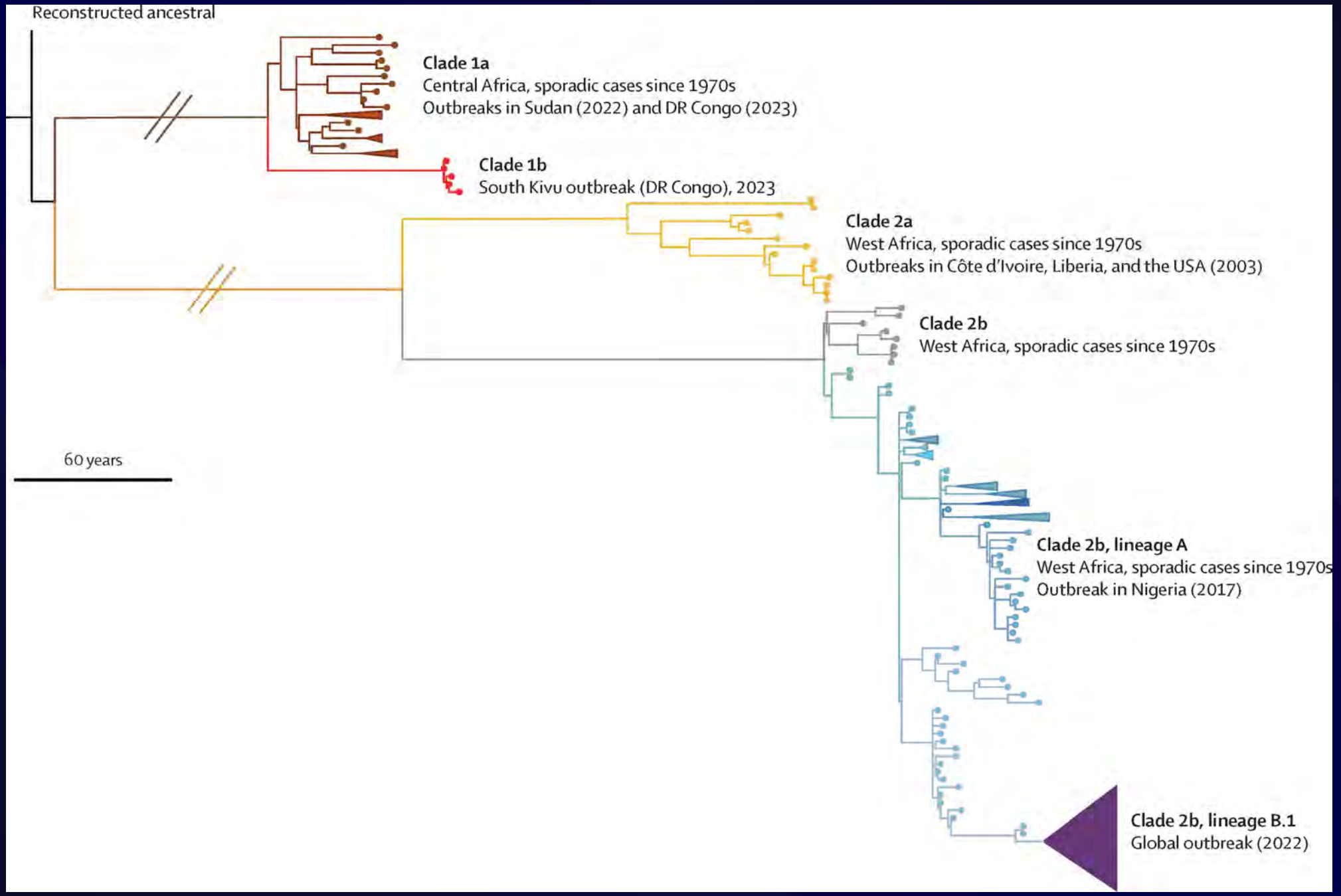
Sweden
Thailand
Germany
USA
UK
France

**Nurses care for mpox patients at a treatment center in Kamituga, a mining town in eastern Democratic Republic of Congo, on September 20, 2024.**



(AFP/WHO)

# Global phylogenetic (with geographical and temporal identification) of mpox clades






Beiras et al. Lancet January 2025

# Epidemiology and Transmission of Monkeypox Virus Clades

| | Clade 1a | Clade 1b | Clade 2a | Clade 2b, lineage A | Clade 2b, lineage B.1 |
|---|---|---|---|---|---|
| Period | 1970–2024 | 2023 | 1970–2018 | 2017–24 | 2022–23 |
| Geographical distribution | Central Africa (west and central Democratic Republic of the Congo) | East Democratic Republic of the Congo, regional spread | West Africa, some international. | Nigerian outbreak 2017–19 | Global since 2022 |
| Transmission dynamics[10,11,13,24,25] | Zoonotic (>70%), little human-to-human spread | Human-to-human spread | Zoonotic (100%) | Zoonotic and widespread human-to-human spread | Sexual contact |
| Historical trends | Low incidence until 2010, then rise | Emerged in 2023, spreading | Sporadic cases and localised outbreaks in west Africa (1970–2018); notable outbreak in the USA in 2003 | 2017 Nigeria outbreak; remains actively spreading | 2022 global outbreak; remains actively spreading |
| Demography | Mostly children | Mostly adults | Adults and children | Mostly adults | Mostly adult men who have sex with men |
| Genomics[4,9,26] | High diversity, multiple zoonotic introductions; infrequent *APOBEC3*-type mutations (8% of all mutations) | Low diversity little spread; substantial mutations observed; frequent *APOBEC3*-type mutations (55% of all mutations) | High diversity, multiple zoonotic introductions; low *APOBEC3* activity (13% of all mutations) | Very frequent APOBEC3-type mutations (90·8% of mutations) | High diversity; frequent *APOBEC3* mutations (84·8% of observed mutations) |

***Table 1:*** **Epidemiology and transmission of monkeypox virus clades**

Beiras et al. Lancet January 2025

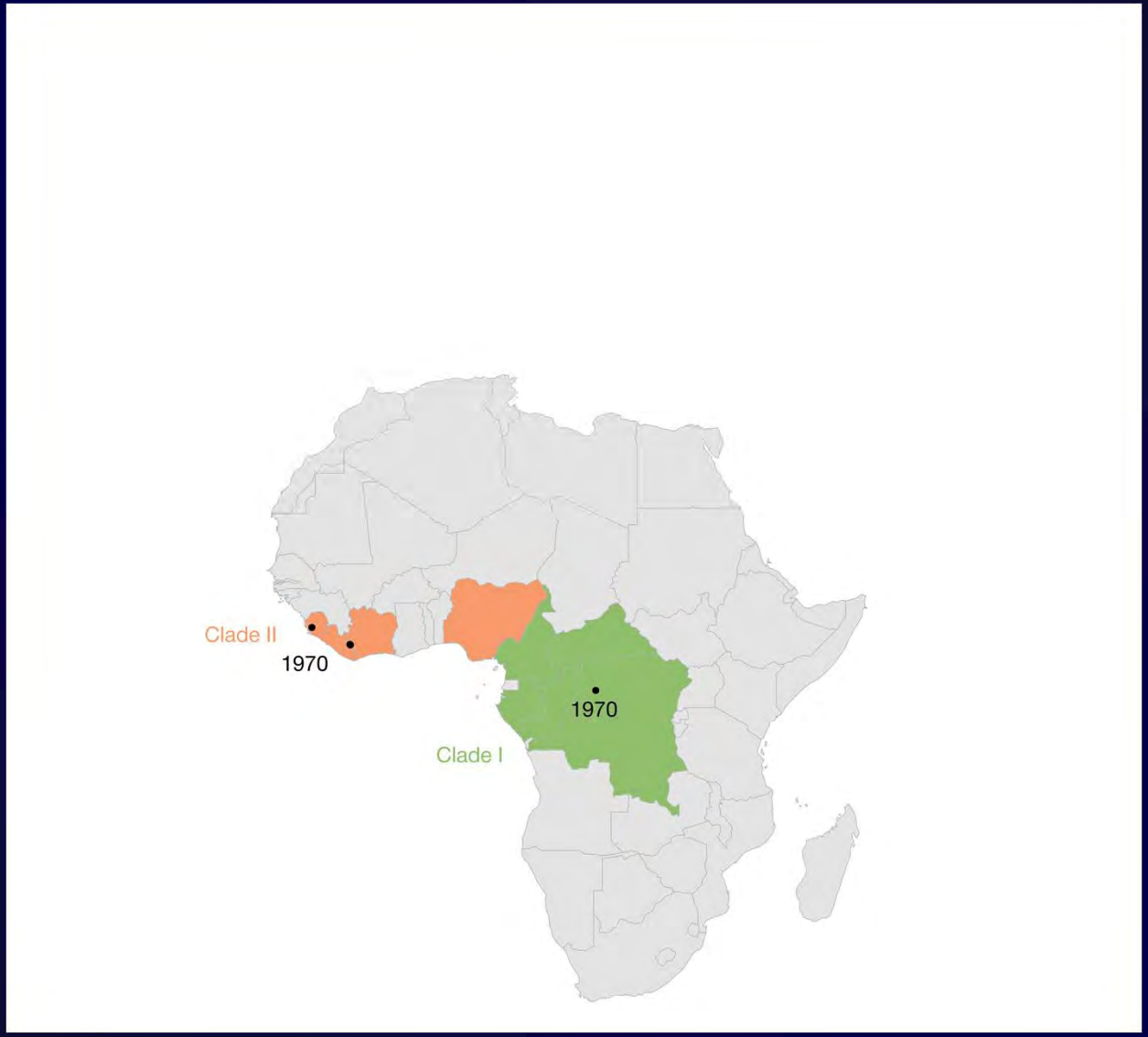
# 1970 DRC



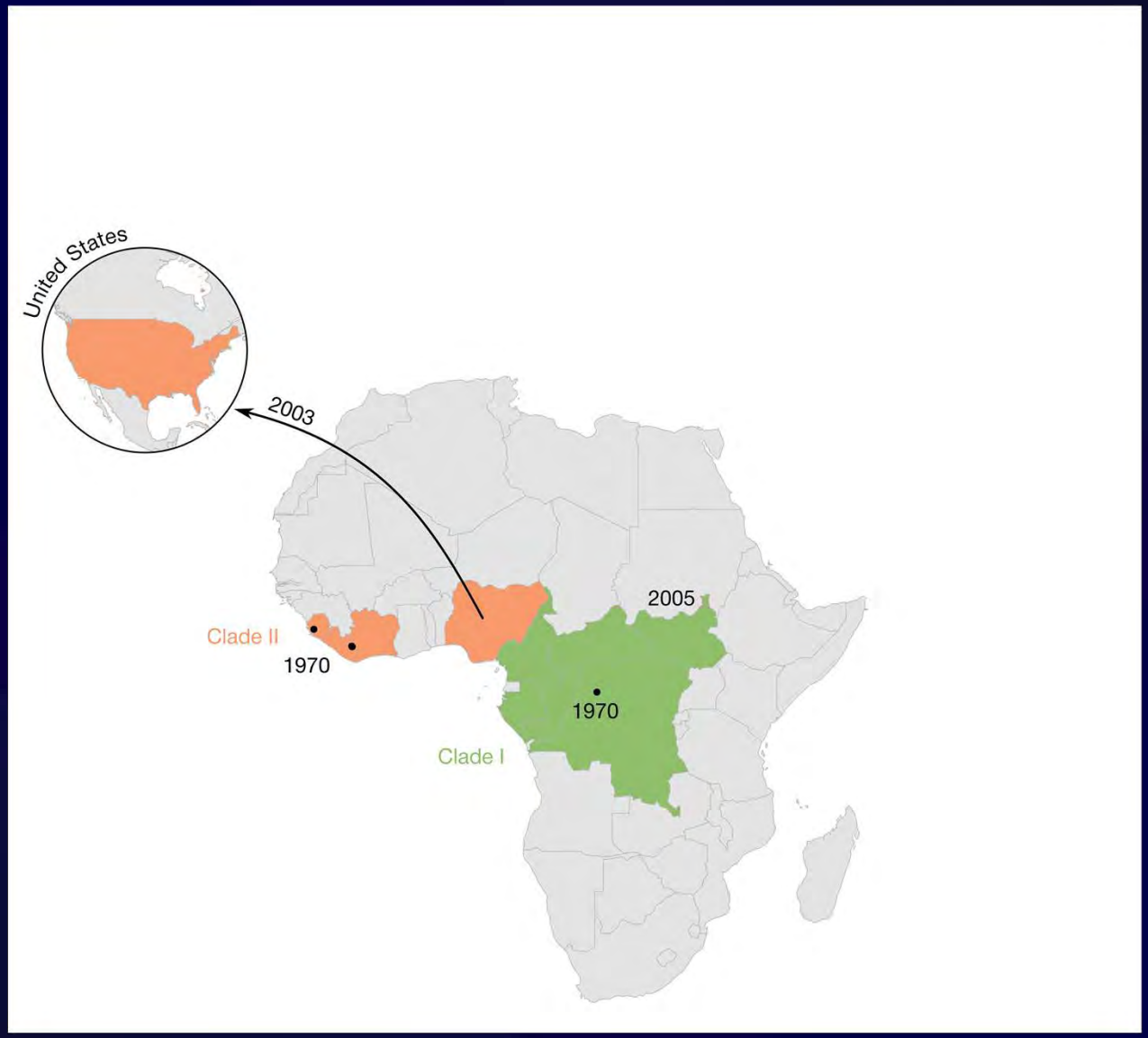
# 1970 DRC and West Africa



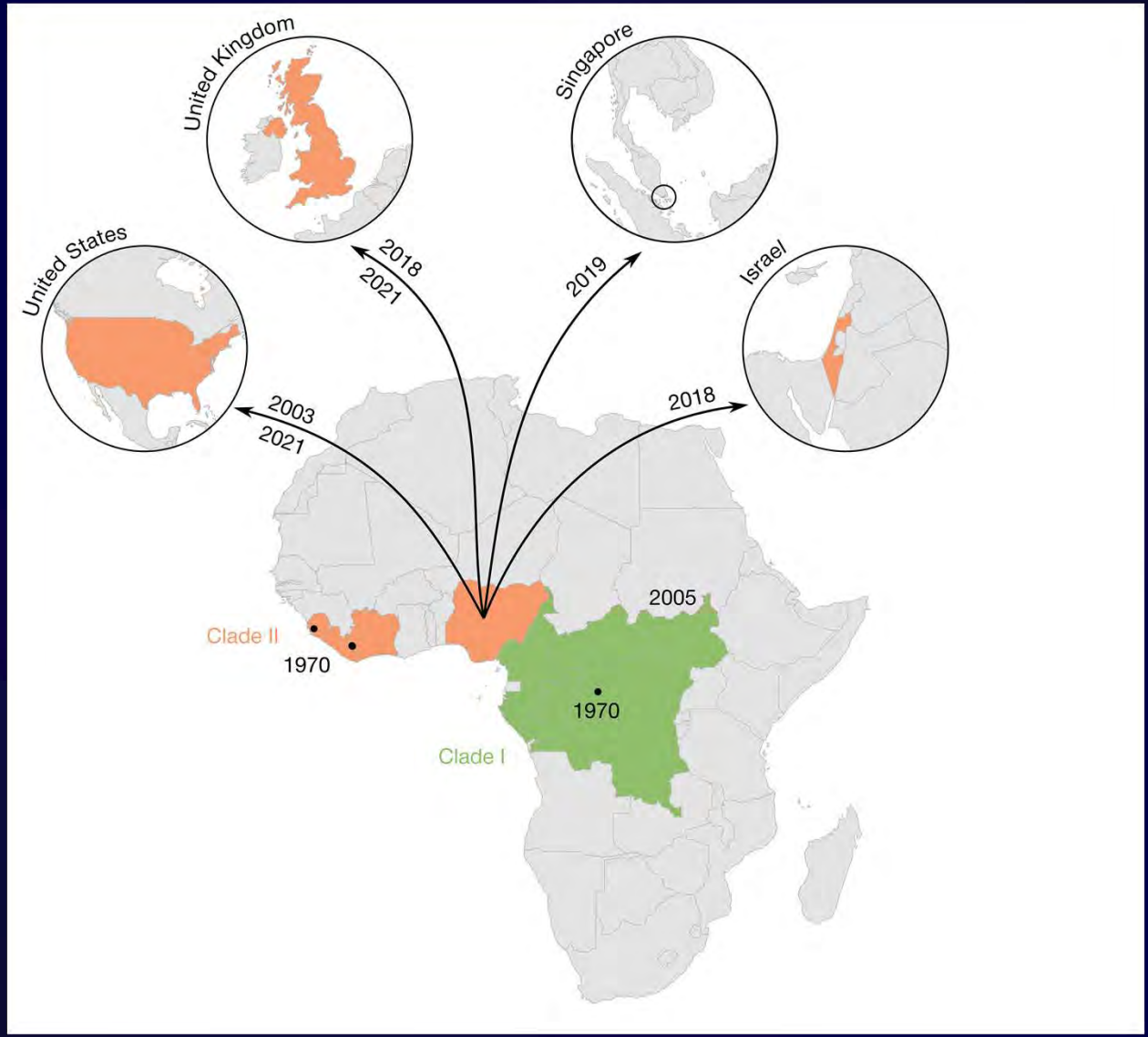
# 1970 DRC and West Africa clade I and clade II



# USA Exportation in 2003 through pets



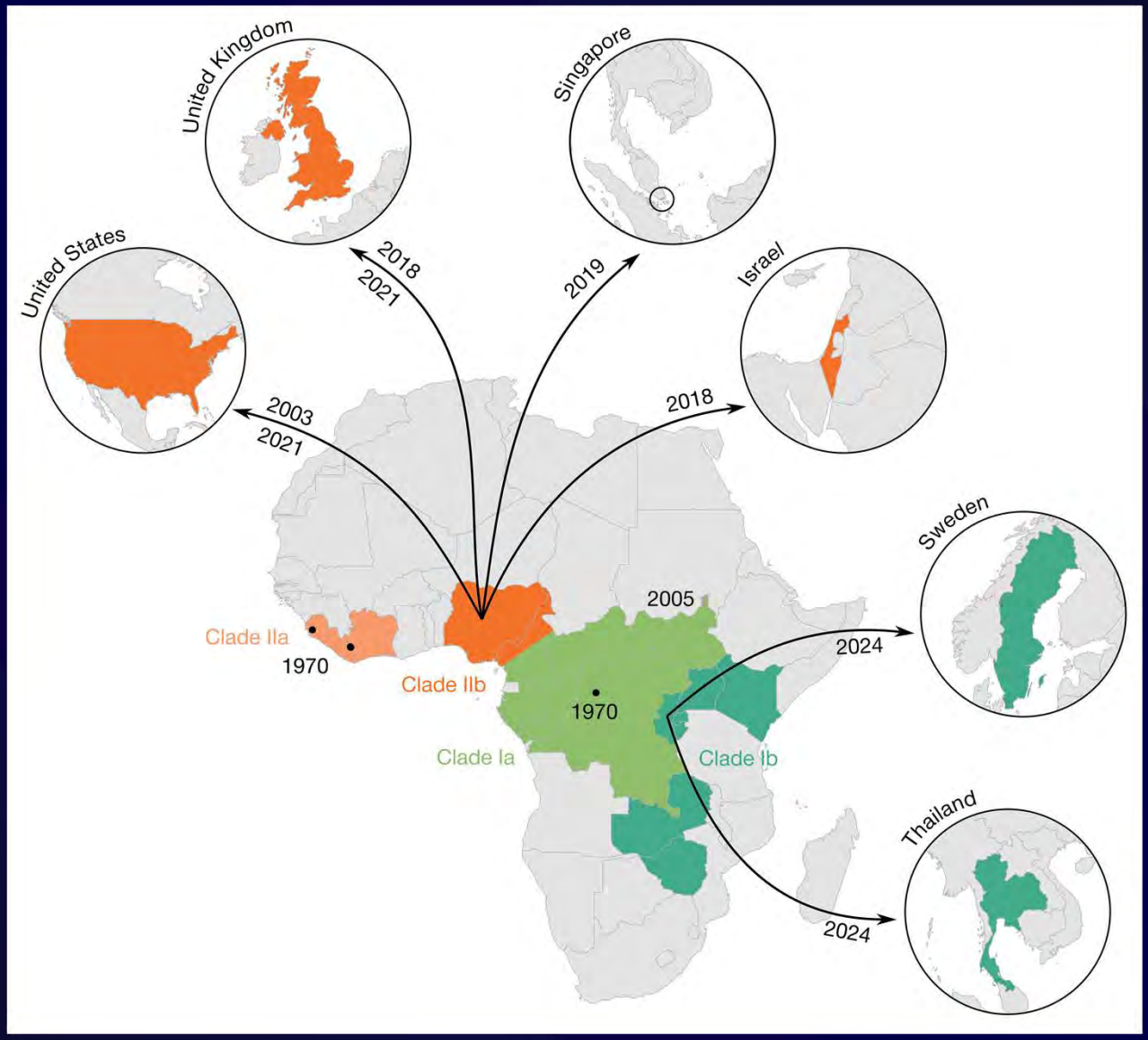
# Out of Africa exportation UK, Singapore, Israel, USA : 2018, 2019, 2021



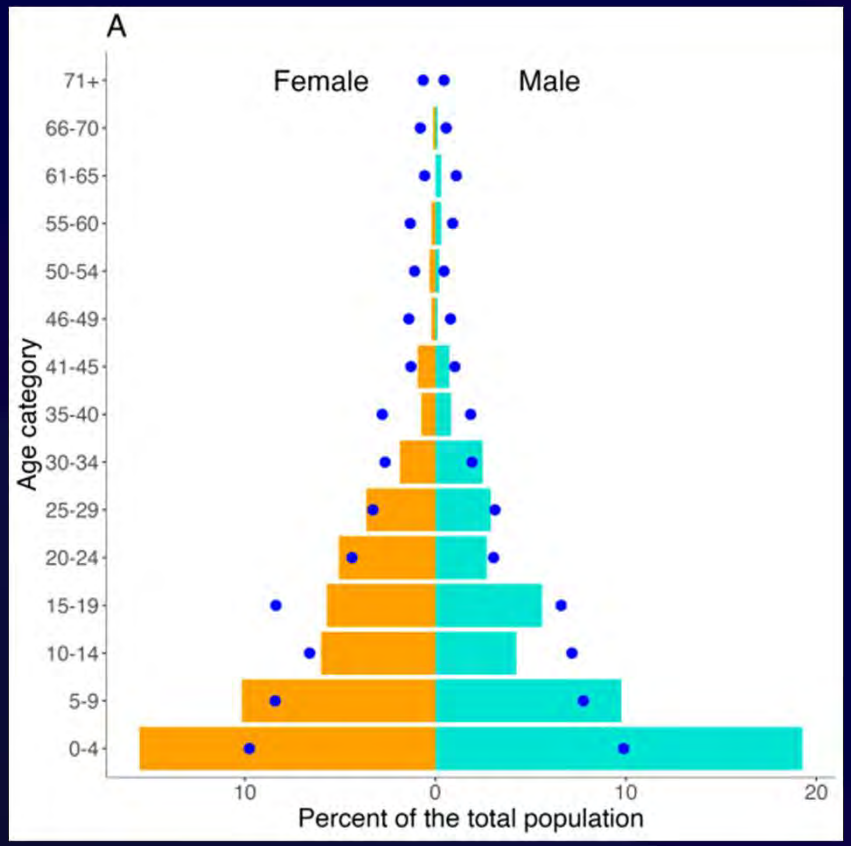
# Emergence of clade Ib in eastern DRC

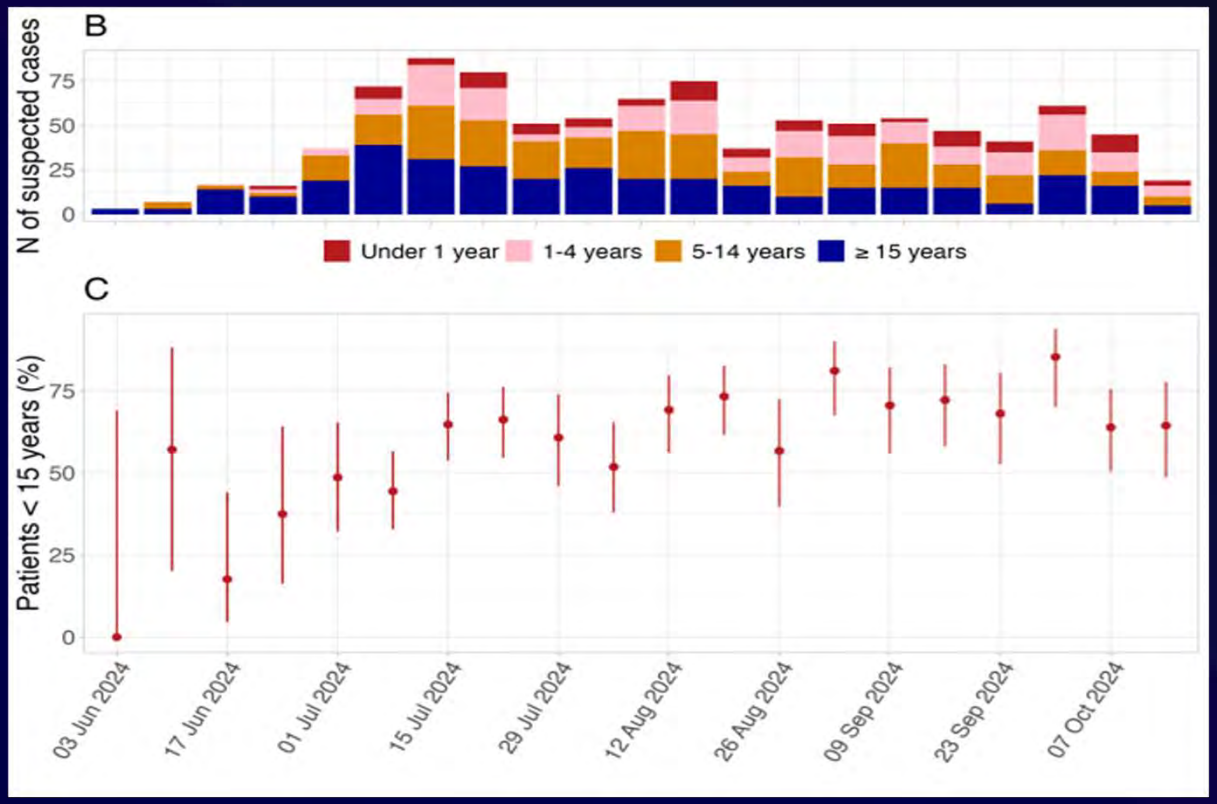


# Expansion of clade Ib in eastern Africa and out of Africa



# *Community transmission of Mpox clade Ib not driven through sexual exposures in Uvira, eastern Democratic Republic of Congo, June – October 2024*




*Description of the mpox epidemic in Uvira.*
*Panel A: Age-sex pyramid of suspected cases and the general population of Uvira, with the bars representing the proportion of men (turquoise) and women (orange) by age group within the study population. The blue dots denote the disaggregation by age and sex from the population estimates based on household composition data from four cross-sectional surveys conducted in Uvira between 2021-2024 (n = 10,604 household members). Panel B: Epidemic curve by age group and week of presentation at the Mpox Treatment Center (MTC).*
*Panel C: Weekly proportion of children under 15 years of age presenting to the MTC.*

# Concurent outbreaks of mpox in Africa

## An update Lancet 4 january 2005

## Disease variability vs. viral strain variability?

The reported clinical presentation of the disease varies substantially between clades. To what extent these differences are influenced by viral clade, patient's immune status, route of exposure, or infectious dose is not entirely clear.

Whether the observed differences in severity of outcomes and CFR of clade 1 and clade 2 monkeypox virus are primarily driven by differences in the virus, population characteristics (eg, age and comorbidities), or access to timely diagnosis and supportive care is not yet fully understood

# Current situation

1) The African Union health agency considers the mpox epidemic still not under control and calls for mobilization.

2) Two concurrent epidemics are raging in Africa: one caused by clade 1a in Central Africa, mainly affecting children, and the other by the new variant, clade 1b, which is affecting adults as well as children in another region, in eastern DRC, and in neighboring countries.

3) The majority of deaths have occurred in the DRC, the epicenter of the epidemic, which launched a vaccination campaign in early October. According to the WHO, more than 700,000 people have so far been vaccinated against Mpox in the DRC and other neigboring countries thanks to donations from the United States and the European Commission.

4) In addition, the WHO and its partners (Africa CDC, the Coalition for Epidemic Preparedness Innovations (CEPI), the Gavi Vaccine Alliance, and UNICEF) have created an access and allocation mechanism. Nearly 3 O00,000 vaccine doses (MVA-BN and LC16m8) have been delivered to 13 countries, and mainly used in DRC.

# Conclusion

The emergence of zoonotic viruses is a permanent phenomenon, without borders, and often unpredictable, in terms of its nature, its target, and its scale.

A never-ending story...?

Preventing viral outbreaks of zoonotic origin is therefore very difficult, but requires:

1) Greater awareness and education among populations, especially at-risk groups, to prevent infection and reduce transmission.

2) The development of rapid and sensitive detection tests to improve diagnosis and, consequently, prevention.

3) Evaluating the effectiveness of treatments and vaccines and improving efforts to make them accessible to all affected groups and regions.

# Acknowledgments


Institut Pasteur de Bangui
Emmanuel Nakouné
Benjamin Selekon
Festus Mbrenga
Christian Malaka
Ella Gonofio
Xavier Konamna

CPC Cameroun
Richard Njouom
Délia Doreen Djuicy

MNHN Paris
Alexandre Hassanin
Manon Curaudeau
Thomas Leflanchec

Institut Pasteur Paris
EPVO unit
Antoine Gessain
Nicolas Berthet
Manon Curaudeau
Thomas Leflanchec
Alexander Tendu

Institut Pasteur Paris
REERI Unit
Jean-Claude Manuguerra
Christophe Batejat
Jessica Vanhomwangen
Valérie Caro

Institut Pasteur Paris
EREEME Unit
Arnaud Fontanet
Camille Besombes
Tamara Gilles-Vernick
Laura Schaeffer

ANRS MIE
Hôpital Bichat
Yazdan Yazdanpanah


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ZOOSURSY

*Epidémiologie et Physiopathologie des Virus Oncogènes*

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