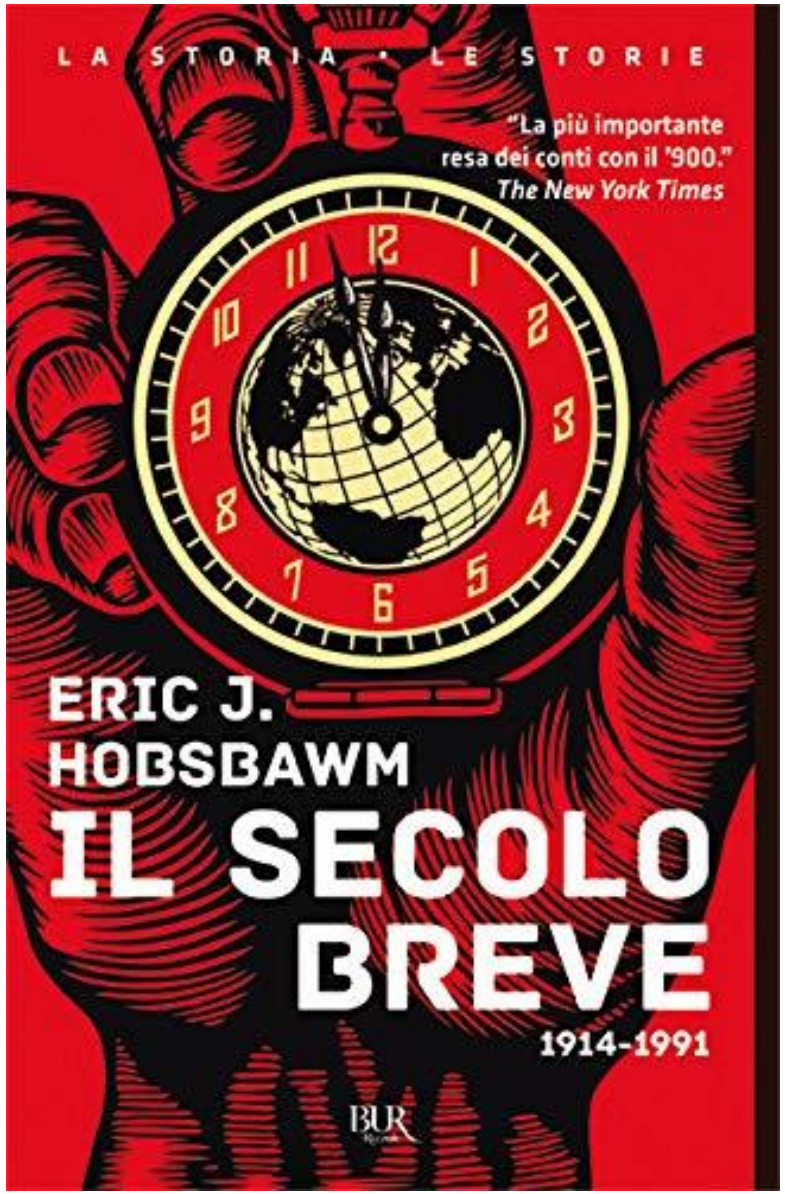
UNIVERSITÀ DEGLI STUDI DI MILANO

DIPARTIMENTO DI SCIENZE BIOMEDICHE E CLINICHE

# *Spillover: dal secolo breve agli anni 2000*

**Spinello Antinori**


**Milano 12 ottobre 2023**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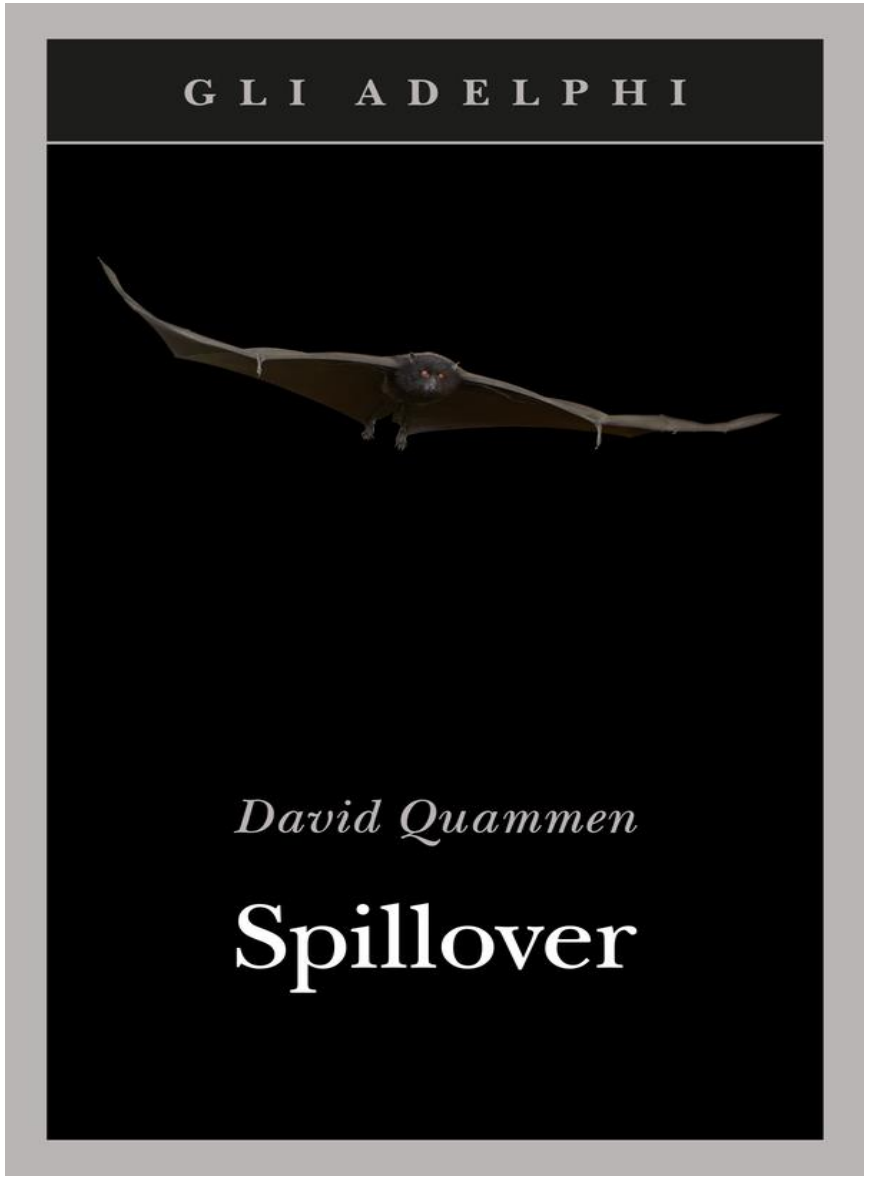
GLI ADELPHI
David Quammen
Spillover

Environmental Research 233 (2023) 116416

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Environmental Research

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# Environmental spillover of emerging viruses: Is it true?

Laurent Gavotte [a], Cédric Gaucherel [b], Roger Frutos [c,*]

This increased contacts between wild life and humans leads to a higher probability of transmission to humans. However, the exact process by which this transmission occurs is not clearly established yet. The concept most often used both in the scientific literature and general news to characterize the mechanism of emerging diseases is the "spillover". This concept has been used for the last two decades and even more so since the emergence of COVID-19. Many scientific articles refer to this term giving it a recognized status of key and central mechanism in the process of disease emergence. However, although widely used and accepted by the scientific community and the public, there is no reference publication describing clearly, unambiguously and rigorously a mechanism of spillover. Furthermore, an explicit definition or a reference to a pioneer article explaining the term is rarely given in recent articles. The risk is not only that of misleading jargon but also that of considering as a solid scientific concept something lacking clear definition and demonstration. This permanent reference to an uncharacterized process of "spillover" is blurring the whole image and is masking the true nature of interactions between humans and the environment. It

**Table 1**
List of source articles for the ten definitions identified for spillover.

| Article title | Authors | Def | Year | cited* |
|---|---|---|---|---|
| *Emerging infectious diseases of wildlife-threats to biodiversity and human health.* | Daszak et al. | 1 | 2000 | 18 |
| *Pathogen spillover in disease epidemics* | Power & Mitchell | 2<br>3 | 2004<br>2004 | 20<br>37 |
| *Host range, amplification and arboviral disease emergence* | Weaver | 4 | 2005 | 20 |
| *Pre-spillover prevention of emerging zoonotic diseases: What are the targets and what are the tools?* | Childs | 5 | 2007 | 23 |
| *Cholera-modern pandemic disease of ancient lineage* | Morris | 6 | 2011 | 5 |
| *Modeling of wildlife-associated zoonoses: applications and caveats* | Alexander et al. | 7 | 2012 | 2 |
| *Presence of vaccine-derived Newcastle disease viruses in wild birds* | Ayala et al. | 8 | 2016 | 3 |
| *National safety survey of animal-use commercial probiotics and their spillover effects from farm to Humans: An emerging threat to public health* | Fu et al. | 9 | 2020 | 1 |
| *Responsible biosecurity and risk mitigation for laboratory research on emerging pathogens of amphibians* | Woodhams et al. | 10 | 2021 | 0 |

# Role of Spillover and Spillback in SARS-CoV-2 Transmission and the Importance of One Health in Understanding the Dynamics of the COVID-19 Pandemic

McKenzie N. Sparrer,[a] Natasha F. Hodges,[a] Tyler Sherman,[a] Susan VandeWoude,[c] Angela M. Bosco-Lauth,[b] Christie E. Mayo[c]

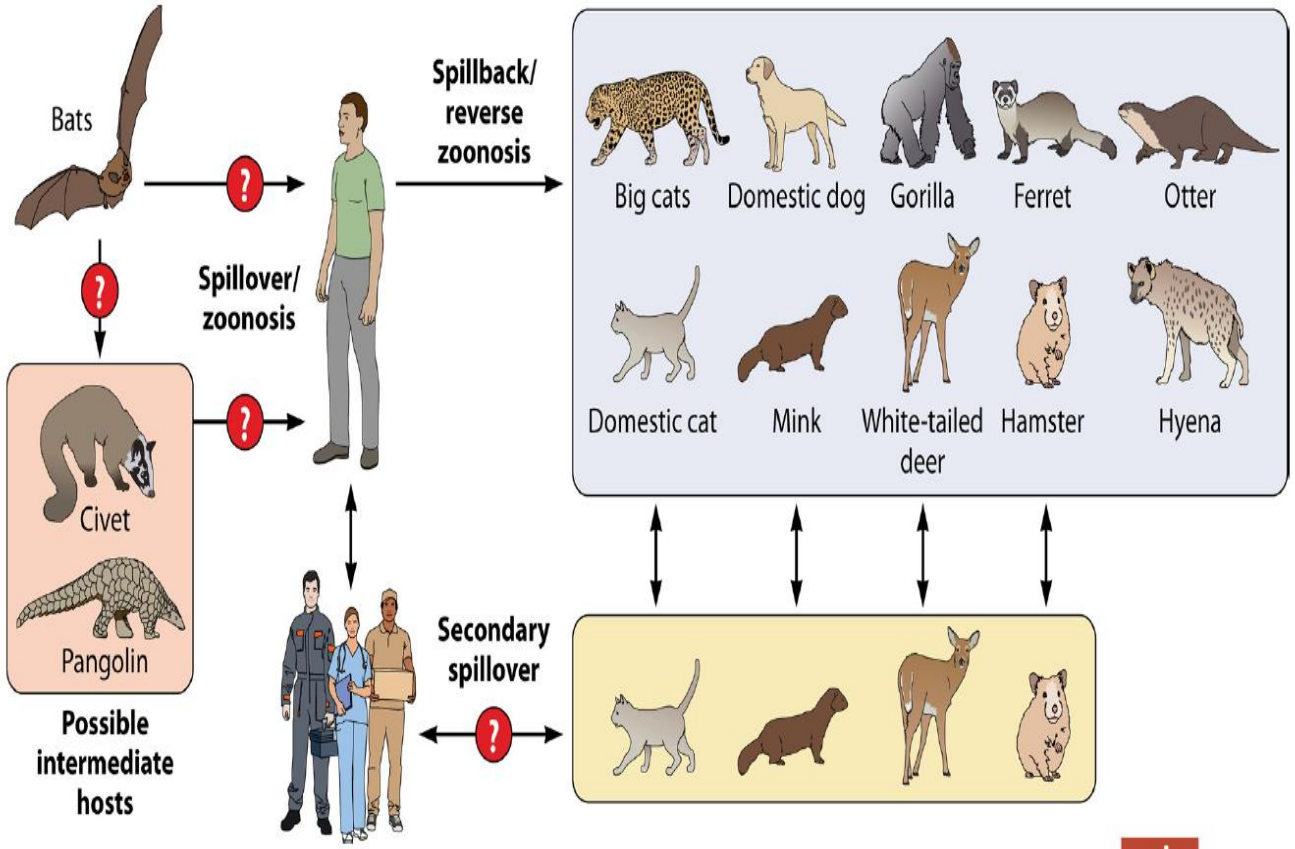


**FIG 1** Transmission pathways of SARS-CoV-2 and examples of natural infection of animal species.

**TABLE 1** Glossary of terms referenced in this review

| Term | Definition with relevant example |
|---|---|
| Zoonosis | An infectious disease that is transmitted from animals to humans. E.g., influenza virus, ebolavirus, SARS viruses. |
| Reverse zoonosis | An event in which a previously zoonotic pathogen has undergone spillover into humans begins to infect novel, nonhuman animals. E.g., transmission of SARS-CoV-2 from humans into white-tailed deer. |
| Spillover | An event in which a species-specific pathogen establishes infection in a novel susceptible host. E.g., transmission of Nipah virus from bats into pigs. |
| Spillback | A specific instance of spillover that occurs when a pathogen is transmitted from a novel host back into an origin host. E.g., transmission of SARS-CoV-2 from humans into wild-caught bats. |
| Secondary spillover | A specific instance of spillover that occurs when a previously zoonotic pathogen that has undergone spillover into humans infects novel, susceptible animals that in turn infect naïve or previously-exposed humans. E.g., transmission of SARS-CoV-2 from humans into white-tailed deer and then back into humans. |

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# Mapping Global Bushmeat Activities to Improve Zoonotic Spillover Surveillance by Using Geospatial Modeling

Soushieta Jagadesh, Cheng Zhao, Ranya Mulchandani, Thomas P. Van Boeckel

Human populations that hunt, butcher, and sell bushmeat (bushmeat activities) are at increased risk for zoonotic pathogen spillover. Despite associations with global epidemics of severe illnesses, such as Ebola and mpox, quantitative assessments of bushmeat activities are lacking. However, such assessments could help prioritize pandemic prevention and preparedness efforts. We used geospatial models that combined published data on bushmeat activities and ecologic and demographic drivers to map the distribution of bushmeat activities in rural regions globally. The resulting map had high predictive capacity for bushmeat activities (true skill statistic = 0.94). The model showed that mammal species richness and deforestation were principal drivers of the geographic distribution of bushmeat activities and that countries in West and Central Africa had the highest proportion of land area associated with bushmeat activities. These findings could help prioritize future surveillance of bushmeat activities and forecast emerging zoonoses at a global scale.

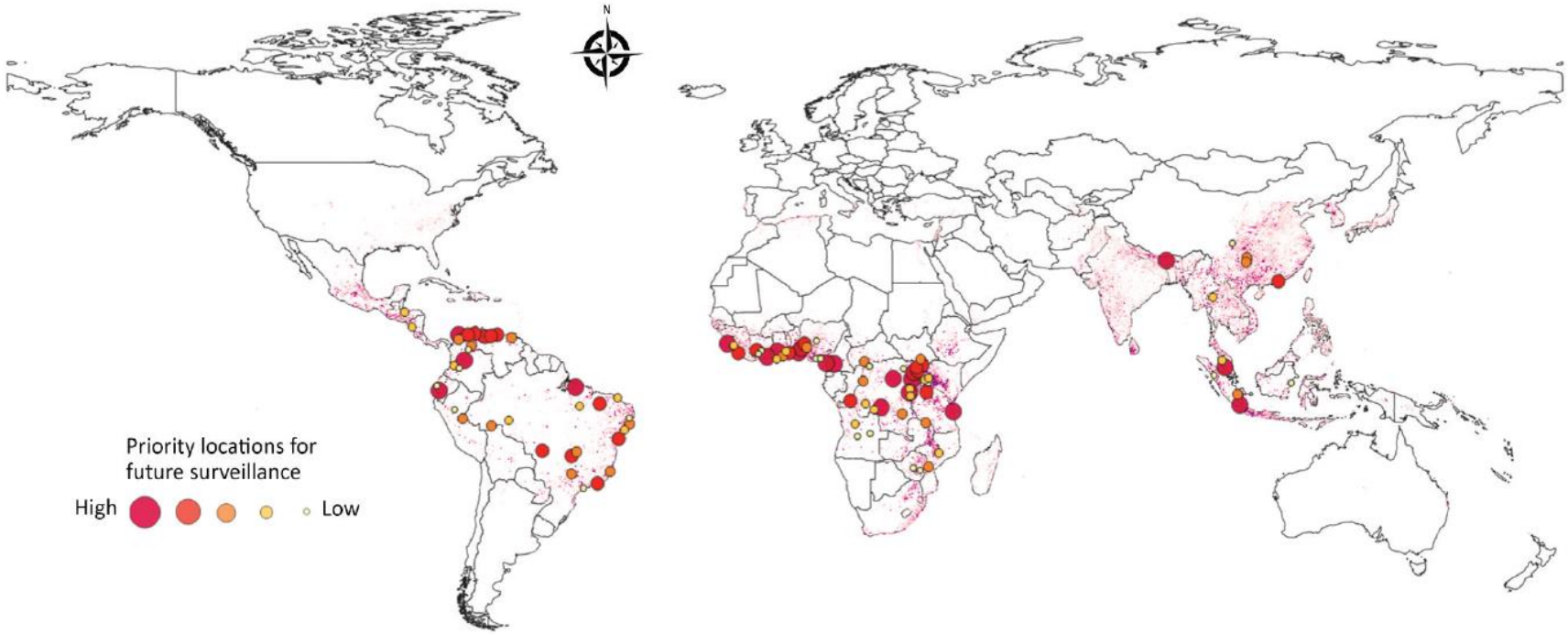


**Figure 3.** Predicted priority regions for future survey efforts in urban areas as determined by a model of global bushmeat activities (hunting, preparing, and selling bushmeat) to improve zoonotic spillover surveillance. The 100 priority locations identified are indicated by the necessity for surveillance, a previously described measure (*30*). Color and size of dots indicate high to low priority of needed surveillance efforts.

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Original article

# Psittacosis contagion in 1930: an old story in a new era of zoonotic disease

Kathryn M. Weston [a, *], Adam Polkinghorne [b, c], James M. Branley [b, c]

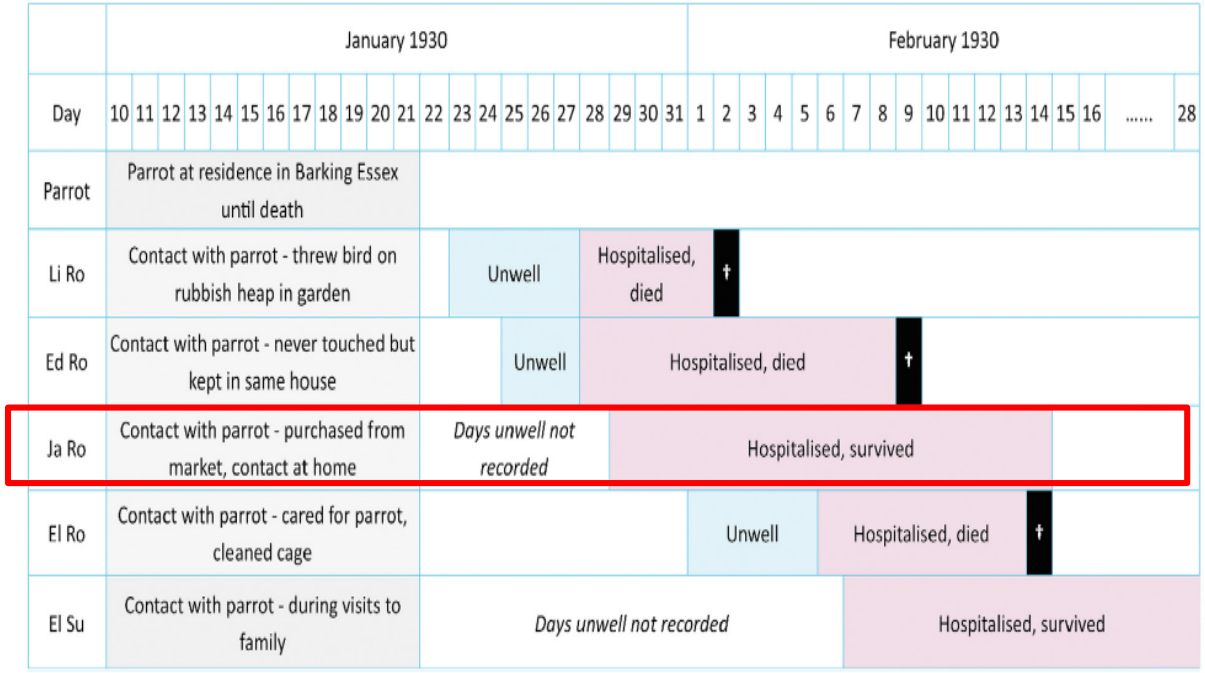


**Fig. 1.** Timeline of illness for psittacosis cases 1930. Note, a further case (H Ve), who worked in the Ro family house, was reported with three days illness, diagnosed as psi during the same period.

# The great parrot fever pandemic

The psittacosis cluster described in this report was one of similar outbreaks reported in the period 1929–30 on four continents, namely Europe (Germany, Switzerland, France, Denmark, Holland), Africa (Egypt, Algeria), North America (USA) and South America (Argentina) [1]. The mortality rate in the Essex cluster reviewed here was fifty percent. These results were similar to those reported from twenty cases of psittacosis documented in Hamburg in 1929, where the case fatality rate was thirty-five percent [17].

**Table 1**
Clinical features reported in hospital notes for individuals diagnosed with psittacosis and associated with the Essex psittacosis cluster in January-February 1930.

| Symptom | Li Ro | Ed Ro | El Ro |
|---|---|---|---|
| Fever (max) | 106°F (41.1°C) | 104°F (40°C) | 103.5°F (39.7°C) |
| Headache | Yes | Yes | Yes |
| Photophobia | Yes | Yes | Yes |
| Cough | Yes | Yes | Yes |
| Muco-purulent sputum | No | Yes | Yes |
| Increased respiration | Yes | Yes | Not recorded |
| Lung sounds | Yes | Yes | Yes |
| Other | Sweating, nausea, vomiting, cyanosis | Collapse, severe epistaxis, increased pulse rate, bloody sputum, delirious, bleeding gums | Bronchitis, cyanosis, dyspnoea |
| Duration of symptoms prior to death | 11 days | 16 days | 14 days |
| Cause of death | Heart failure. Haemorrhagic pneumonia. Septicaemia. Psittacosis. | Pneumonia. Septicaemia. Psittacosis. | Haemorrhagic pneumonia. Septicaemia. Psittacosis. |

Surviving cases: Ja Ro was reported to have had a temperature of 102°F (38.9°C) and 17 days of illness; H Ve was reported to have had a temperature of 103°F (39.4°C) and three days of illness. No other symptoms were noted for these two cases. No case notes for El Su were located; however she was hospitalised for a lengthy period.

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Volume 305 DECEMBER 10, 1981 Number 24

# *PNEUMOCYSTIS CARINII* PNEUMONIA AND MUCOSAL CANDIDIASIS IN PREVIOUSLY HEALTHY HOMOSEXUAL MEN

## Evidence of a New Acquired Cellular Immunodeficiency

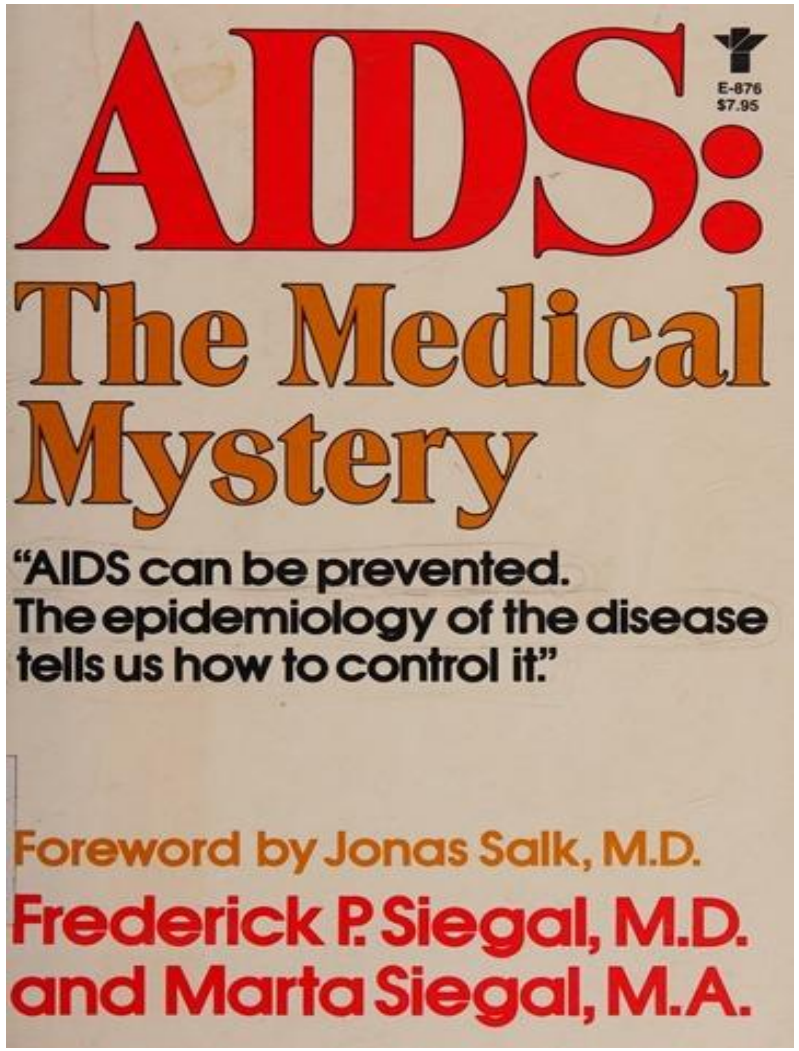
MICHAEL S. GOTTLIEB, M.D., ROBERT SCHROFF, PH.D., HOWARD M. SCHANKER, M.D., JOEL D. WEISMAN, D.O., PENG THIM FAN, M.D., ROBERT A. WOLF, M.D., AND ANDREW SAXON, M.D.

**Abstract** Four previously healthy homosexual men contracted *Pneumocystis carinii* pneumonia, extensive mucosal candidiasis, and multiple viral infections. In three of the patients these infections followed prolonged fevers of unknown origin. In all four cytomegalovirus was recovered from secretions. Kaposi's sarcoma developed in one patient eight months after he presented with esophageal candidiasis. All patients were anergic and lymphopenic; they had no lymphocyte proliferative responses to soluble antigens, and their responses to phytohemagglutinin were markedly reduced. Monoclonal-antibody analysis of peripheral-blood T-cell subpopulations revealed virtual elimination of the Leu-3+ helper/inducer subset, an increased percentage of the Leu-2+ suppressor/cytotoxic subset, and an increased percentage of cells bearing the thymocyte-associated antigen T10. The inversion of the T helper to suppressor/cytotoxic ratio suggested that cytomegalovirus infection was an important factor in the pathogenesis of the immunodeficient state. A high level of exposure of male homosexuals to cytomegalovirus-infected secretions may account for the occurrence of this immune deficiency. (N Engl J Med. 1981; 305:1425-31.)

# AN OUTBREAK OF COMMUNITY-ACQUIRED *PNEUMOCYSTIS CARINII* PNEUMONIA

## Initial Manifestation of Cellular Immune Dysfunction

HENRY MASUR, M.D., MARY ANN MICHELIS, M.D., JEFFREY B. GREENE, M.D., IDA ONORATO, M.D., ROBERT A. VANDE STOUWE, M.D., PH.D., ROBERT S. HOLZMAN, M.D., GARY WORMSER, M.D., LEE BRETTMAN, M.D., MICHAEL LANGE, M.D., HENRY W. MURRAY, M.D., AND SUSANNA CUNNINGHAM-RUNDLES, PH.D.




1983

When, in the fall of 1980, a young man called Joey appeared for a consultation at the clinical immunology service of our medical center, he had already become the despair of several New York internists.

Although Joey wasn't aware of it, we had seen within the previous few months, in the same medical center, four other young men with a similar story: horrendous infections with no predisposing history of congenital immune problems of deliberate immunosuppression. Their only common denominator was homosexual activity



**SEVERE ACQUIRED IMMUNODEFICIENCY IN MALE HOMOSEXUALS, MANIFESTED BY CHRONIC PERIANAL ULCERATIVE HERPES SIMPLEX LESIONS**

FREDERICK P. SIEGAL, M.D., CARLOS LOPEZ, PH.D., GLENN S. HAMMER, M.D., ARTHUR E. BROWN, M.D., STEPHEN J. KORNFELD, M.D., JONATHAN GOLD, M.D., JOSEPH HASSETT, M.D., SHALOM Z. HIRSCHMAN, M.D., CHARLOTTE CUNNINGHAM-RUNDLES, M.D., PH.D., BERNARD R. ADELSBERG, M.D., DAVID M. PARHAM, M.D., MARTA SIEGAL, M.A., SUSANNA CUNNINGHAM-RUNDLES, PH.D., AND DONALD ARMSTRONG, M.D.

**Abstract** Four homosexual men presented with gradually enlarging perianal ulcers, from which herpes simplex virus was cultured. Each patient had a prolonged course characterized by weight loss, fever, and evidence of infection by other opportunistic microorganisms including cytomegalovirus, *Pneumocystis carinii*, and *Candida albicans*. Three patients died; Kaposi's sarcoma developed in the fourth. All were found to have depressed cell-mediated immunity, as evidenced by skin anergy, lymphopenia, and poor or absent responses to plant lectins and antigens in vitro. Natural-killer-cell activity directed against target cells infected with herpes simplex virus was depressed in all patients. The absence of a history of recurrent infections or of histologic evidence of lymphoproliferative or other neoplastic diseases suggests that the immune defects were acquired. (N Engl J Med. 1981; 305:1439-44.)

Brief Communication

A. Lazzarin, M. Galli, D. Geroldi, A. Zanetti, P. Crocchiolo, F. Aiuti, M. Moroni

# Epidemic of LAV/HTLV III Infection in Drug Addicts in Milan: Serological Survey and Clinical Follow-up

**Summary:** A clinico-epidemiological study is reported concerning a group of 306 parenteral drug addicts (PDAs), 71 of whom were affected with the lymphadenopathy syndrome (LAS); all were followed-up between 1981 and 1984. Although full-blown acquired immune deficiency syndrome (AIDS) was observed only in one case, none of the other patients examined have undergone complete recovery so far. The results of our study point to a wide circulation of LAV/HTLV III among our group of PDAs, starting at least as early as 1981 and preceding by a few months the development of clinical signs and symptoms of LAS. A peak incidence of the latter was observed during the winter of 1983/1984, running parallel with a marked increase in seropositives for LAV/HTLV III antibody. Drug addiction, sexual promiscuity and a low standard of living all seem to play a decisive role in the spread of the infection and, consequently, of the diseases related to it (LAS, AIDS-related complex and AIDS). In fact, PDAs appear to represent the major source of the disease in Italy.

**Zusammenfassung:** *Epidemie von LAV/HTLV III-Infektion bei Drogenabhängigen in Mailand: Serologische Untersuchungen und klinische Verlaufsbeobachtung.* Eine klinisch-epidemiologische Studie wurde bei einer Gruppe von 306 Rauschgiftsüchtigen durchgeführt, von denen 71 an generalisierter Lymphadenopathie (LAS) leiden; sie wurden zwischen 1981 und 1984 kontinuierlich betreut. Obwohl nur in einem einzigen Falle die Entwicklung eines vollständigen erworbenen Immundefizienz-Syndroms (AIDS) beobachtet wurde, wurde andererseits bisher bei keinem der anderen Patienten eine eindeutige Heilung nachgewiesen. Die Ergebnisse unserer Untersuchung weisen auf eine ausgebreitete Zirkulation des Virus in unserer Drogensüchtigen-Gruppe mindestens seit 1981 hin, ein Phänomen, welches klinischen Lymphadenopathie-Zeichen und Symptomen um einige Monate vorausging. Eine auffällig hohe Inzidenz dieser Krankheit wurde während des Winters 1983/1984 parallel zu einem steilen Anstieg der LAV/HTLV III-Seropositivität beobachtet. Rauschgiftsucht, geschlechtliche Promiskuität und niedriges Lebensniveau scheinen eine entscheidende Rolle in der Ausbreitung der Infektion und der mit ihr assoziierten Krankheitsbilder (LAS, AIDS related complex, AIDS) zu spielen. Drogensüchtige scheinen die größte Infektionsquelle in Italien darzustellen.

## Introduction

In March 1983, an outbreak of lymphadenopathy syndrome (LAS) was observed in a group of heroin abusers living in the same suburb of Milan (1). Most of the affected subjects were subsequently assigned to methadone maintenance treatment at the Drug Addicts' Assistance Centre of the L. Sacco Hospital in Milan.

During the following 18 months, an increasing number of LAS cases was observed among this group.

An epidemiological assessment regarding this outbreak and other clinical data collected during the follow-up period are reported here.

It is now well documented that closely related lymphotropic retroviruses (LAV, HTLV III, ARV) represent the aetiological agent of LAS and AIDS (2–4). For this reason we are also reporting a study concerning the retrospective tracing of the LAV/HTLV III antibody in the same group of patients.

## Patients and Methods

The present investigation was performed on a group of parenteral drug addicts (PDA) attending the Drug Addicts' Assistance Centre at the L. Sacco Hospital in Milan during the years 1981 to 1984. The total number of cases followed-up at the Centre was 85 (71 males, 14 females) in the first semester of 1981, 116 (94 M., 22 F.) in the second semester of 1981, 158 (131 M., 27 F.) in the first semester of 1982, 190 (159 M., 31 F.) in the second semester of 1982, 208 (176 M., 32 F.) in the first semester of 1983, 240 (197 M., 43 F.) in the second semester of 1983, 253 (205 M., 48 F.) in the first semester of 1984 and 306 (251 M., 55 F.) in the second semester of 1984. In the second semester of 1982, four patients (all males) developed clinical signs and symptoms of LAS. In the first and second semesters of 1983, 16 (14 M., 2 F.) and 36 (26 M., 10 F.) patients, respectively, and in the first and second semesters of 1984, 65 and 71 patients, respectively, developed these signs and symptoms (Figure 1).

The diagnosis of LAS was made according to the criteria established by the Centers for Disease Control (CDC) (5) in patients complaining of lymphadenopathy involving two or more extrainguinal sites and lasting for at least six months and of two or more of the following symptoms: intermittent fever, fatigue, night sweats, non-intentional weight loss and hepatosplenomegaly.

The patients were all tested for LAV/HTLV III antibodies. In

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*A. Lazzarin*, M.D., *M. Galli*, M.D., *P. Crocchiolo*, M.D., *M. Moroni*, M.D., Clinica delle Malattie Infettive, Università di Milano, Ospedale L. Sacco, I-20157 Milano;
*D. Geroldi*, M.D., Clinica Medica, Università di Pavia, I-Pavia;
*A. Zanetti*, M.D., Istituto di Virologia, Università di Milano, I-Milano;
*F. Aiuti*, M.D., Cattedra d'Immunologia Clinica, Università di Roma, I-Roma.

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## *Lymph Node Finding in Drug Abusers*

*To the Editor*—We read with interest the report by Drs. Guarda and associates[2] concerning the histologic features of lymph nodes in homosexual men, and the more recent article by Drs. Domingo and associates[3] on the pathology of unexplained lymphadenopathy in subjects at risk for the acquired immunodeficiency syndrome (AIDS). Over the last three years, however, many studies of homosexual men have suggested that the ratio between immunoregulatory subsets of T-helper and T-suppressor circulating cell populations is inverted in most of the patients with idiopathic lymphadenopathy syndrome (ILS).[4] Furthermore, a particular form of lymphadenitis associated with Kaposi's sarcoma[4] recently has been described in homosexuals and in hemophiliacs with acquired immunodeficiency-like syndrome.[5,6] The most striking observation in these cases is the presence of many Leu-2a suppressor-cytotoxic phenotypes in the follicular centers of lymph nodes, even though the predominant T-cells in lymphatic follicles normally have OKT 4+/Leu-3a phenotypes.[7]

In our hospital we have observed 11 cases of drug addicts with generalized lymphadenopathy whose histologic features, as described by Guarda and associates and by Domingo and associates, are characterized by follicular hyperplasia with preserved and dilated sinuses. All of the patients had had the typical symptoms of ILS (according to the criteria of Nicholson and associates, 1984) for at least three months before the biopsy was performed. All of the patients had a history of two or more years of drug abuse, with two or more intravenous injections daily. Frozen sections of the lymph nodes were studied with various commercially available antisera: OKT 3, OKT 4, OKT 8 (Ortho Diagnostic Systems, Inc., Raritan, NJ); Leu-1, Leu-2a, Leu-3a, Leu-7 (Becton–Dickinson Laboratory Systems, Mechelen, Belgium); anti-human IgD (Dakopatts A/S, Copenhagen, Denmark); Vectastain ABC Kit® (Vector Laboratories, Inc., Burlingame, CA).

The most interesting feature of our cases is the presence of numerous OKT 8+/Leu-2a+ phenotypes bearing cells in follicular centers and mantle zones (Fig. 1), with a slight reduction in the number of OKT 4+/Leu-2a+ phenotypes and without particular involvement of Leu-7+ (NK) positive cells (fig. 2) whose number and location appeared to be normal. In conclusion, we have observed lymphadenitis with the same immunohistochemical pattern seen in patients with immunodeficiency-like syndrome (so far described only in homosexuals or hemophiliacs) in 11 cases of drug abusers without any evidence of homosexuality or viral infections in course. In all our cases, however, the distribution of the Leu-7+ cells was normal. This report may support the hypothesis that this immunologic impairment may be correlated with some etiologic factor introduced intravenously, perhaps acting over a long period of time. As the follow-up of all our patients ranges from six months to one year, we have no data about the possible evolution of our cases to AIDS. Additional data may be available in the future.

CARLO L. PARRAVICINI, M.D.
ADRIANO LAZZARIN, M.D.
MASSIMO GALLI, M.D.
EMILIO BERTI, M.D.
ROBERTO ZERBONI, M.D.
GIULIO C. COSTANZI, M.D.
*Institutes of Morbid Anatomy, of Infectious Diseases, and of Dermatology*
*University of Milan*
*Milan, Italy*

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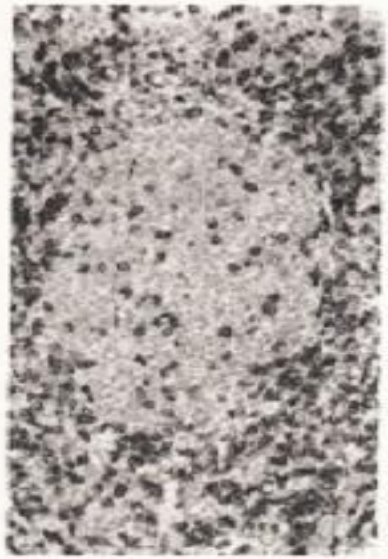
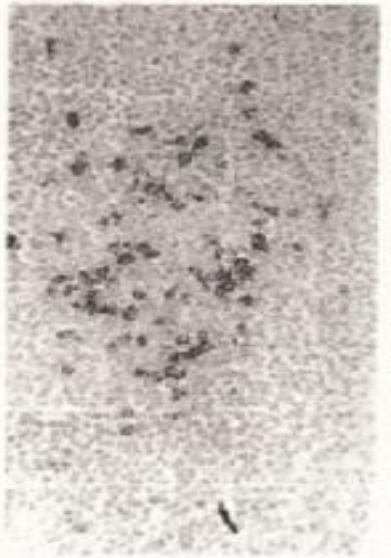
1. Domingo J, Chin NW: Lymphadenopathy in a heterogeneous population at risk for the acquired immunodeficiency







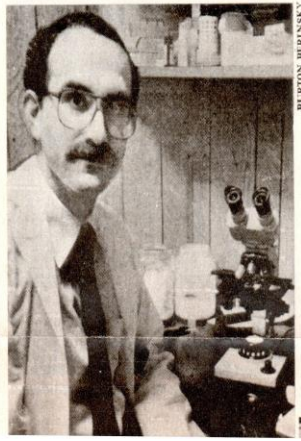
MEDICINA/NUOVE MALATTIE

# Per soli gay

*Una strana epidemia sta mietendo vittime tra gli omosessuali Usa. Si manifesta sotto forma di infezioni intestinali, polmoniti e perfino un raro tipo di tumore. E i casi mortali sono sempre più numerosi.*

Gli specialisti sanno bene che gli omosessuali maschi alla continua ricerca di nuovi partner si ammalano abbastanza facilmente di epatite, sifilide e blenorragia. Ma, recentemente, almeno negli Stati Uniti, le comunità gay delle principali città sono state colpite da una strana e allarmante forma di epidemia, spesso mortale. La causa è ancora ignota, ma i modi in cui si manifesta sono almeno tre: infezioni intestinali normalmente osservate solo ai tropici, una polmonite molto violenta e un tipo di cancro – il sarcoma di Kaposi – caratteristico dell'Africa equatoriale.

Questa strana epidemia sembra risparmiare le lesbiche e gli eterosessuali (i pochi pazienti segnalati sarebbero stati contagiati da bisex).



BURTON BERINSKY

ridurre drasticamente le difese naturali dell'organismo. Del piccolo gruppo di malati osservati da Gottlieb tre oggi sono morti.

Il sarcoma di Kaposi si manifesta con protuberanze violacee nelle gambe, e finora era stato considerato caratteristico dei discendenti anziani di emigrati italiani o ebrei, nei quali però aveva un'evoluzione estremamente lenta. Una variante molto più letale, che invade rapidamente numerosi organi e può uccidere nel giro di pochi mesi, era stata osservata solo in bambini o adolescenti africani. Il primo caso diagnosticato negli Stati Uniti risale al 1979, e riguardava un omosessuale.

**Finora le autorità** sanitarie americane hanno potuto contare 75 polmoniti interstiziali, 77 sarcomi di Kaposi e 18 casi nei quali ambedue le malattie erano, o sono, presenti. Conoscono anche altri 13 tipi di infezioni poco comuni (una riguarda un'ulcera anale – quattro

*A sinistra, il dottor Daniel William e, sotto, una piscina californiana*

# AIDS as a Zoonosis: Scientific and Public Health Implications

Beatrice H. Hahn,[1]* George M. Shaw,[1,2] Kevin M. De Cock,[3] Paul M. Sharp[4]

The «cut hunter»



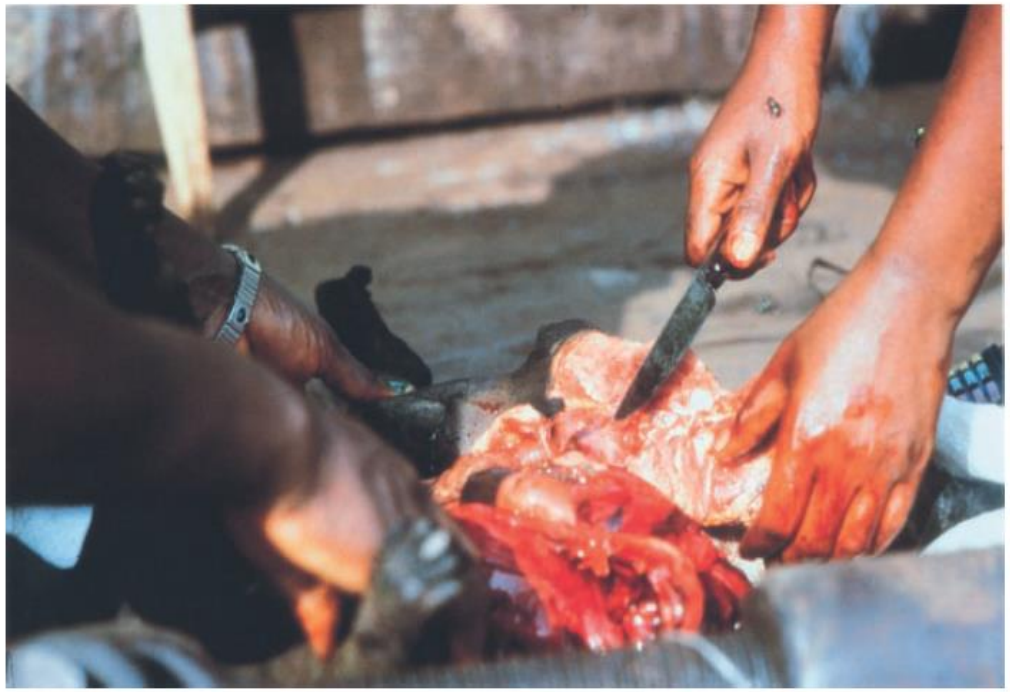


**Fig. 4.** Human exposure to primate blood during food preparation. [Photograph courtesy of Karl Ammann]

**Fig. 6.** Bushmeat market in west central Africa. A chimpanzee (separated into skull, rib cage, limbs, and various internal organs) is shown in the middle of the photo, along with other smoked or fresh meat, including two blue duikers and a spot-nosed guenon in the upper right corner. [Photograph courtesy of Karl Ammann]

# Origins of HIV and the AIDS Pandemic

Paul M. Sharp[1] and Beatrice H. Hahn[2]

*Cold Spring Harb Perspect Med* 2011;1:a006841

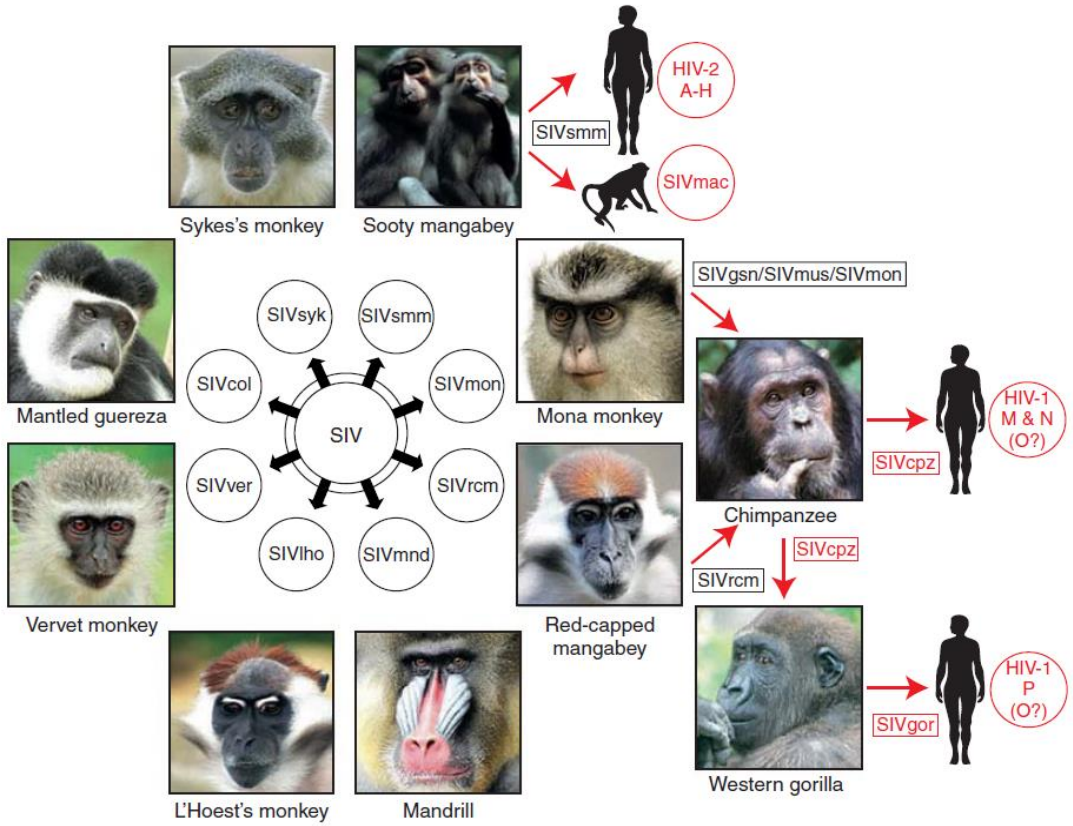
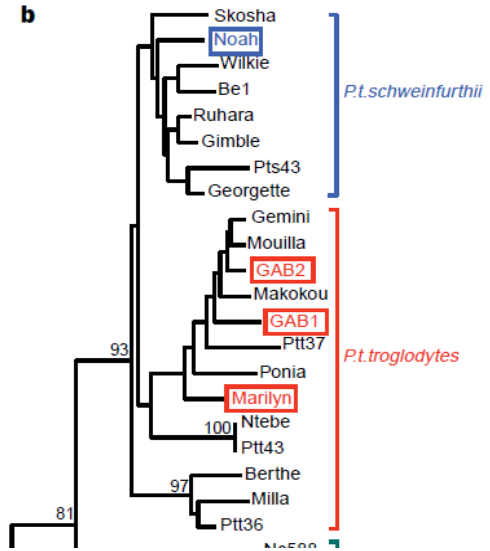
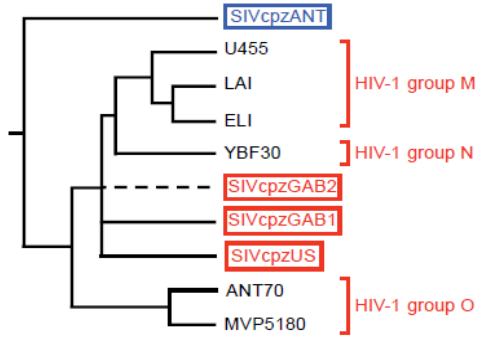



Figure 1. Origins of human AIDS viruses. Old World monkeys are naturally infected with more than 40 different lentiviruses, termed simian immunodeficiency viruses (SIVs) with a suffix to denote their primate species of origin (e.g., SIVsmm from sooty mangabeys). Several of these SIVs have crossed the species barrier to great apes and humans, generating new pathogens (see text for details). Known examples of cross-species transmissions, as well as the resulting viruses, are highlighted in red.

# Origin of HIV-1 in the chimpanzee *Pan troglodytes troglodytes*

Feng Gao*, Elizabeth Bailes†, David L. Robertson‡, Yalu Chen*, Cynthia M. Rodenburg*, Scott F. Michael*§, Larry B. Cummins‖, Larry O. Arthur¶, Martine Peeters#, George M. Shaw*☆, Paul M. Sharp† & Beatrice H. Hahn*




NATURE | VOL 397 | 4 FEBRUARY 1999 | www.nature.com

# Chimpanzee Reservoirs of Pandemic and Nonpandemic HIV-1

Brandon F. Keele,[1] Fran Van Heuverswyn,[2] Yingying Li,[1] Elizabeth Bailes,[3] Jun Takehisa,[1] Mario L. Santiago,[1*] Frederic Bibollet-Ruche,[1] Yalu Chen,[1] Louise V. Wain,[3] Florian Liegeois,[2] Severin Loul,[4] Eitel Mpoudi Ngole,[4] Yanga Bienvenue,[4] Eric Delaporte,[2] John F. Y. Brookfield,[3] Paul M. Sharp,[3] George M. Shaw,[1,5] Martine Peeters,[2] Beatrice H. Hahn[1]†

Human immunodeficiency virus type 1 (HIV-1), the cause of human acquired immunodeficiency syndrome (AIDS), is a zoonotic infection of staggering proportions and social impact. Yet uncertainty persists regarding its natural reservoir. The virus most closely related to HIV-1 is a simian immunodeficiency virus (SIV) thus far identified only in captive members of the chimpanzee subspecies *Pan troglodytes troglodytes*. Here we report the detection of SIVcpz antibodies and nucleic acids in fecal samples from wild-living *P. t. troglodytes* apes in southern Cameroon, where prevalence rates in some communities reached 29 to 35%. By sequence analysis of endemic SIVcpz strains, we could trace the origins of pandemic (group M) and nonpandemic (group N) HIV-1 to distinct, geographically isolated chimpanzee communities. These findings establish *P. t. troglodytes* as a natural reservoir of HIV-1.

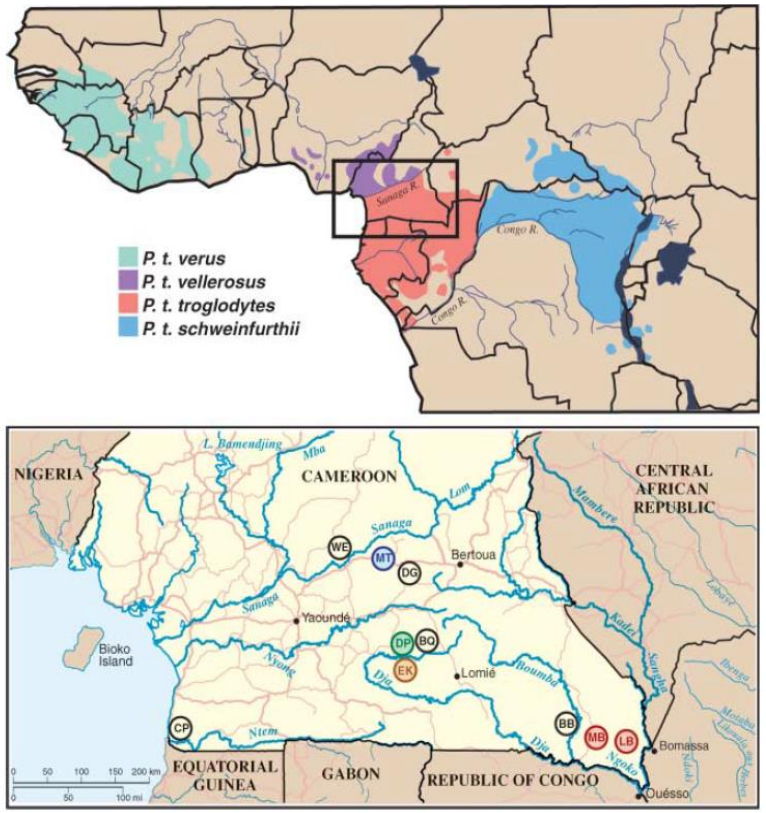



**Fig. 1.** Natural ranges of the four chimpanzee subspecies (top) and locations of wild chimpanzee study sites WE, MT, DG, DP, BQ, EK, CP, BB, MB, and LB in southern Cameroon (inset and bottom). Field sites with endemic SIVcpz*Ptt* infection are color-coded to correspond with the SIVcpz*Ptt* lineages shown in Figs. 3 and 4.

# Host and viral traits predict zoonotic spillover from mammals

Kevin J. Olival[1], Parviez R. Hosseini[1], Carlos Zambrana-Torrelio[1], Noam Ross[1], Tiffany L. Bogich[1] & Peter Daszak[1]

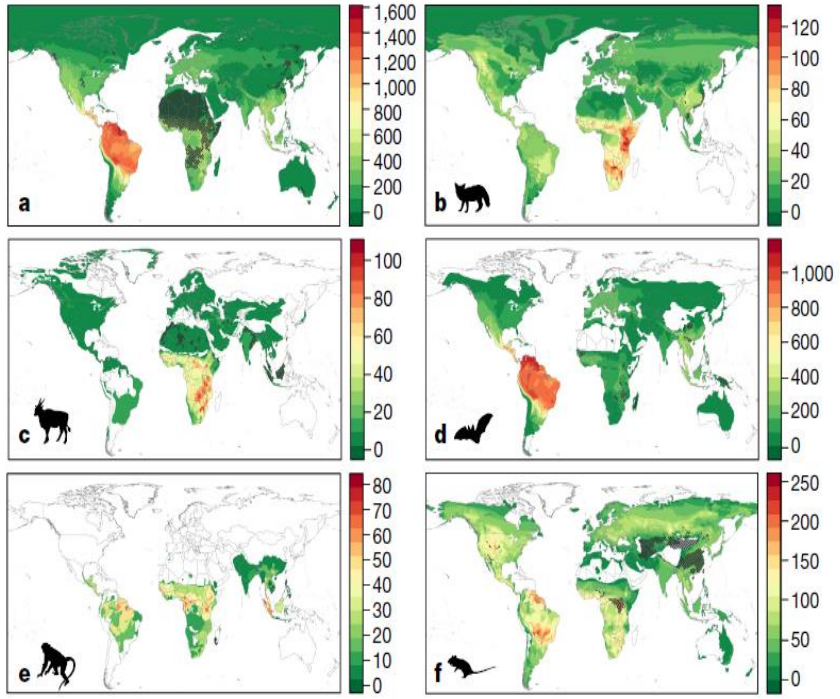



**Figure 3 | Global distribution of the predicted number of 'missing zoonoses' by order.** Warmer colours highlight areas predicted to be of greatest value for discovering novel zoonotic viruses. **a**, All wild mammals ($n = 584$ spp. included in the best-fit model). **b**, Carnivores (order Carnivora, $n = 55$). **c**, Even-toed ungulates (order Cetartiodactyla, $n = 70$). **d**, Bats (order Chiroptera, $n = 157$). **e**, Primates (order Primates, $n = 7$: **f**, Rodents (order Rodentia, $n = 183$). Hatched regions represent areas where model predictions deviate systematically for the assemblage of species in that grid cell (approximately 18 km × 18 km, see Methods). Animal silhouettes from PhyloPic.

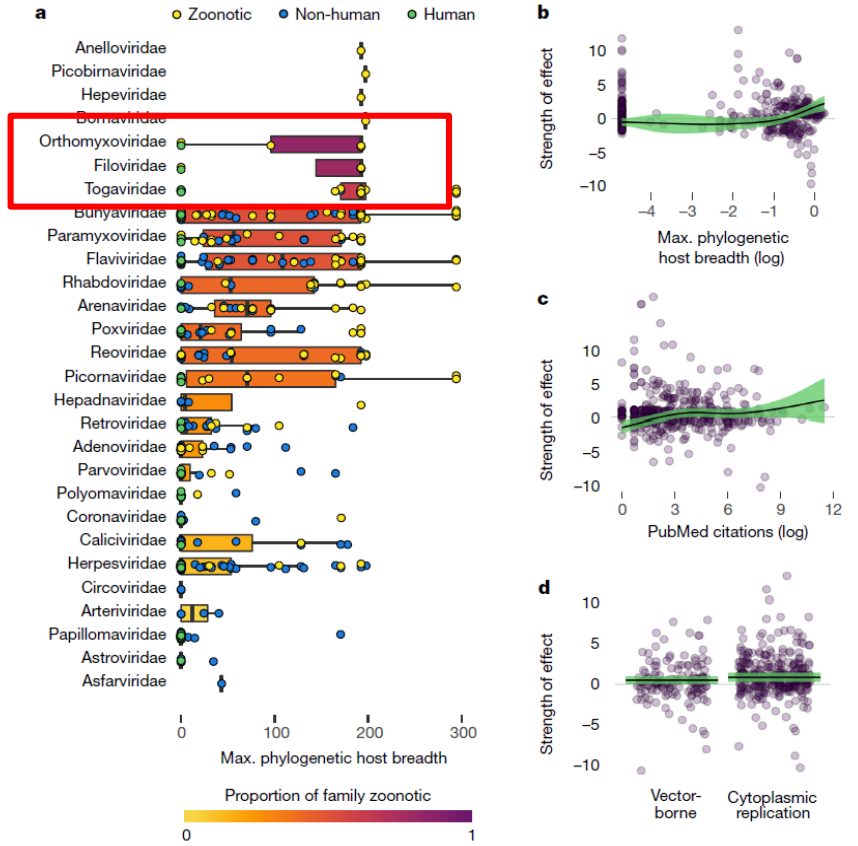


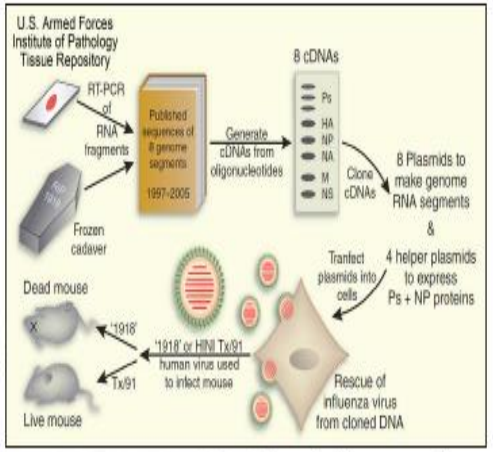

**Figure 4 | Traits that predict zoonotic potential of a virus.** **a**, Box plot of maximum phylogenetic host breadth per virus (PHB, see methods) for each of 586 mammalian viruses, aggregated by 28 viral families. Individual points represent viral species, colour-coded by zoonotic status. Box plots coloured and sorted by the proportion of zoonoses in each viral family. **b–d**, Partial effect plots for the best-fit GAM to predict the zoonotic potential of a virus. **b**, Maximum PHB. Viruses that infect a phylogenetically broader range of hosts are more likely to be zoonotic. **c**, Research effort (log, number of PubMed citations per viral species). **d**, Whether or not a virus replicates in the cytoplasm or is vector-borne. Viral genome length and whether or not a virus is enveloped improved the overall predictive power but were non-significant and are not shown (see Extended Data Table 1).

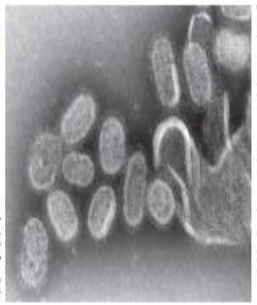
Jeffery K. Taubenberger

Terrence M. Tumpey

Peter Palese

Adolfo Garcia-Sastre



Reconstructed 1918 influenza virus, negative contrast electron microscopy
Cynthia Goldsmith, CDC

Beginning in 1995, Jeffery Taubenberger and his colleagues at the Armed Forces Institute of Pathology obtained gene sequences of the 1918 influenza virus from formalin-fixed lung autopsy materials and from frozen lung tissues from an Alaskan influenza victim buried in permafrost in 1918. Painstakingly, over ten years the eight viral RNA genome segments were reconstructed by plasmid-based reverse genetics; that is, viral RNA was isolated (from fragments under 200 nucleotides in length), then each fragment was reverse transcribed into cDNA and amplified by RT-PCR. The cDNAs were inserted into plasmids and amplified in bacteria and then sequenced and assembled for infection of cells in culture. When the reconstructed virus obtained from the cell cultures was analyzed, it was found that all eight genome segments were of avian derivation and all differed in important ways from all other human viruses. When the reconstructed virus was used to infect mice it was extremely virulent – it replicated to very high titer and was much more lethal than contemporary viruses. Reassortant viruses containing mixtures of genes from the 1918 virus and other virus strains indicated that virulence was largely based in the hemagglutinin gene, but was polygenic. Some researchers had predicted that the 1918 virus would not be more pathogenic than other human influenza viruses, that its massive human toll in 1918 was the result of secondary bacterial pneumonias and the absence of antibiotics, perhaps along with the stress from World War I. The death of mice by the reconstructed 1918 virus makes that scenario less likely.

**The nucleotide sequence of the eight RNA segments was obtained using random primers, reverse transcriptase and PCR. cDNAs were constructed from synthetic oligonucleotides and the cDNAs cloned in plasmids. Cells were transfected with the plasmids plus four helper plasmids and influenza virus was rescued and used to infect mice.**


Taubenberger JK, Reid AH, Krafft AE, Bijwaard KE, Fanning TG. Initial genetic characterization of the 1918 "Spanish" influenza virus. Science 1997;275:1793-1796.

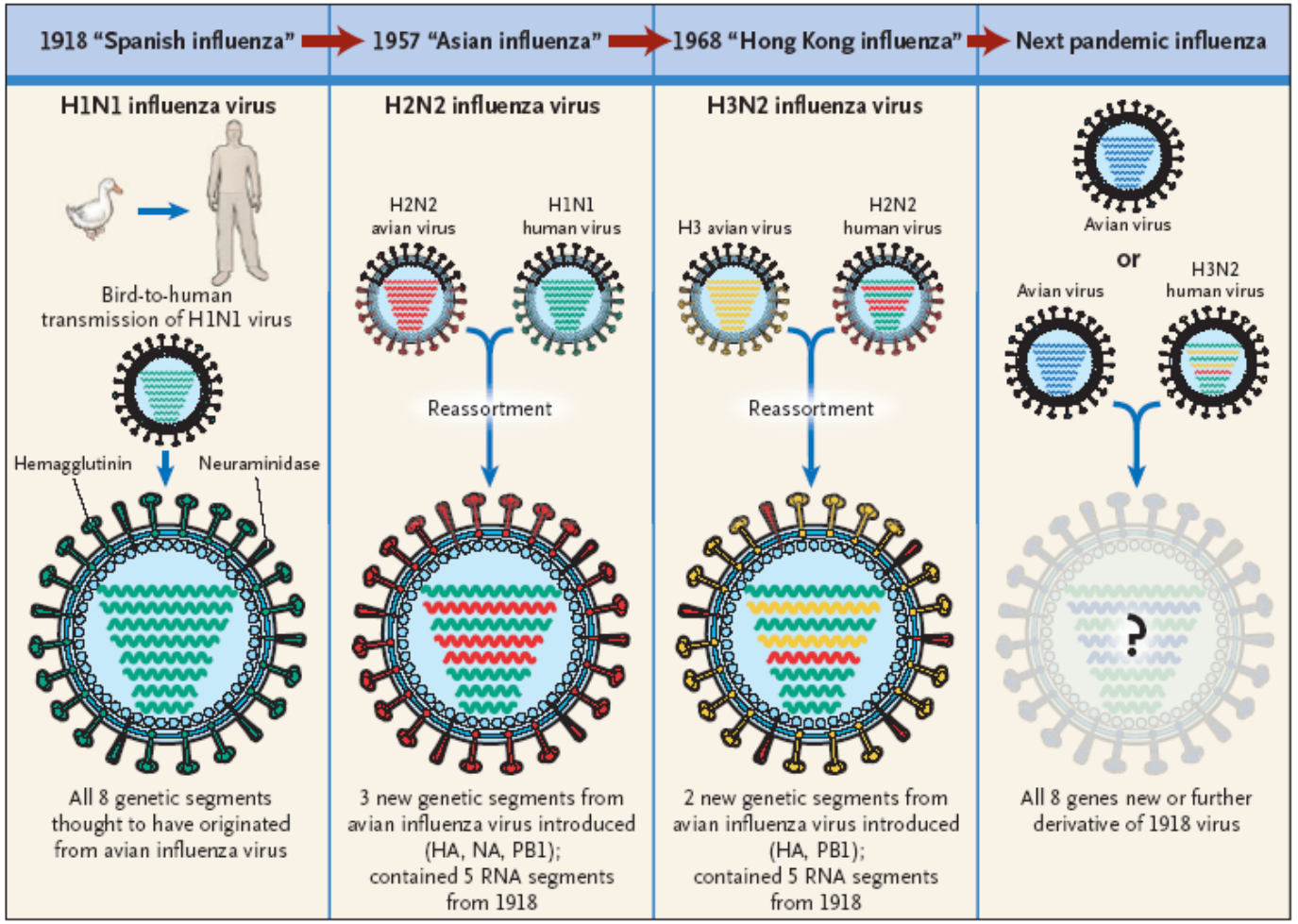
Reid AH, Taubenberger JK, Fanning TG. Evidence of an absence: the genetic origins of the 1918 pandemic influenza virus. Nat Rev Microbiol. 2004;2:909-914.

Tumpey TM, García-Sastre A, Taubenberger JK, Palese P, Swayne DE, Basler CF. Pathogenicity and immunogenicity of influenza viruses with genes from the 1918 pandemic virus. Proc Natl Acad Sci USA. 2004;101:3166-3171.

Tumpey TM, Basler CF, Aguilar PV, Zeng H, Solórzano A, Swayne DE, Cox NJ, Katz JM, Taubenberger JK, Palese P, García-Sastre A. Characterization of the reconstructed 1918 Spanish influenza pandemic virus. Science 2005;310:77-80.


2005 • Jeffery Taubenberger, Terrence Tumpey, others • 1918 influenza virus sequenced and virus reconstructed






## Taubenberger, Nature 2005

# Alarming situation of emerging H5 and H7 avian influenza and effective control strategies

Jianzhong Shi [a,b], Xianying Zeng[b], Pengfei Cui[b], Cheng Yan[b] and Hualan Chen [a,b]

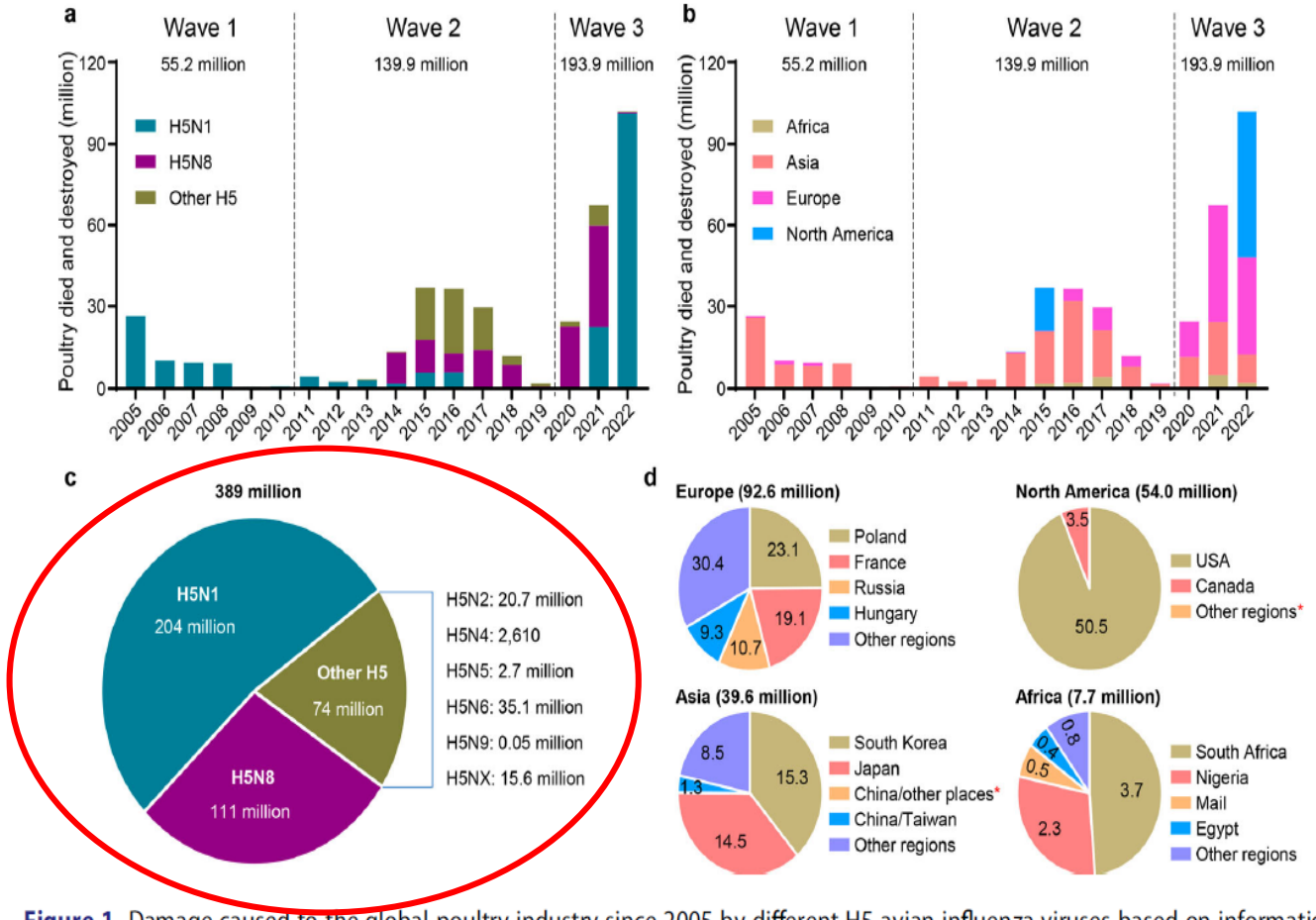



**Figure 1.** Damage caused to the global poultry industry since 2005 by different H5 avian influenza viruses based on information reported in the OIE-World Animal Health Information System. The number of poultry that died or were destroyed during outbreaks caused by different subtypes of H5 influenza viruses (a, c) in different continents (b), and (d) the number of poultry that died or were destroyed in different countries or regions since 2020. *, fewer than 10,000 birds died or were destroyed in the indicated country or regions.

**Table 2.** Human infections caused by H5 viruses around the world from January 2003 to April 2022*.

| | Case information | | | | |
|---|---|---|---|---|---|
| Country | Total Number | Year | Virus subtype | Number infected | Number of fatalities |
| Azerbaijan | 8 | 2006 | H5N1 | 8 | 5 |
| Bangladesh | 8 | 2008, 2011–2013, 2015 | H5N1 | 8 | 1 |
| Cambodia | 56 | 2005–2014 | H5N1 | 56 | 37 |
| Canada | 1 | 2013 | H5N1 | 1 | 1 |
| China | 127 | 2003, 2005–2015 | H5N1 | 53 | 31 |
| | | 2014–2022 | H5N6 | 74** | 32 |
| Djibouti | 1 | 2006 | H5N1 | 1 | 0 |
| Egypt | 359 | 2006–2017 | H5N1 | 359 | 120 |
| India | 1 | 2021 | H5N1 | 1 | 1 |
| Indonesia | 200 | 2005–2015, 2017 | H5N1 | 200 | 168 |
| Iraq | 3 | 2006 | H5N1 | 3 | 2 |
| Lao | 4 | 2007, 2020 | H5N1 | 3 | 2 |
| | | 2021 | H5N6 | 1 | 0 |
| Myanmar | 1 | 2007 | H5N1 | 1 | 0 |
| Nepal | 1 | 2019 | H5N1 | 1 | 1 |
| Nigeria | 1 | 2007 | H5N1 | 1 | 1 |
| Pakistan | 3 | 2007 | H5N1 | 3 | 1 |
| Russia | 7 | 2020 | H5N8 | 7 | 0 |
| Thailand | 25 | 2004–2006 | H5N1 | 25 | 17 |
| Turkey | 12 | 2006 | H5N1 | 12 | 4 |
| UK | 1 | 2021 | H5N1 | 1 | 0 |
| US | 1 | 2022 | H5N1 | 1 | 0 |
| Viet Nam | 127 | 2003–2005, 2007–2010, 2012–2014 | H5N1 | 127 | 64 |
| Total | 947 | / | / | 947 | 488 |

*Data obtained from the WHO website.
**Forty-nine of the 75 human cases infected with H5N6 virus have occurred since January 2021.



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https://doi.org/10.1080/22221751.2022.2155072

Travel Medicine and Infectious Disease 55 (2023) 102638

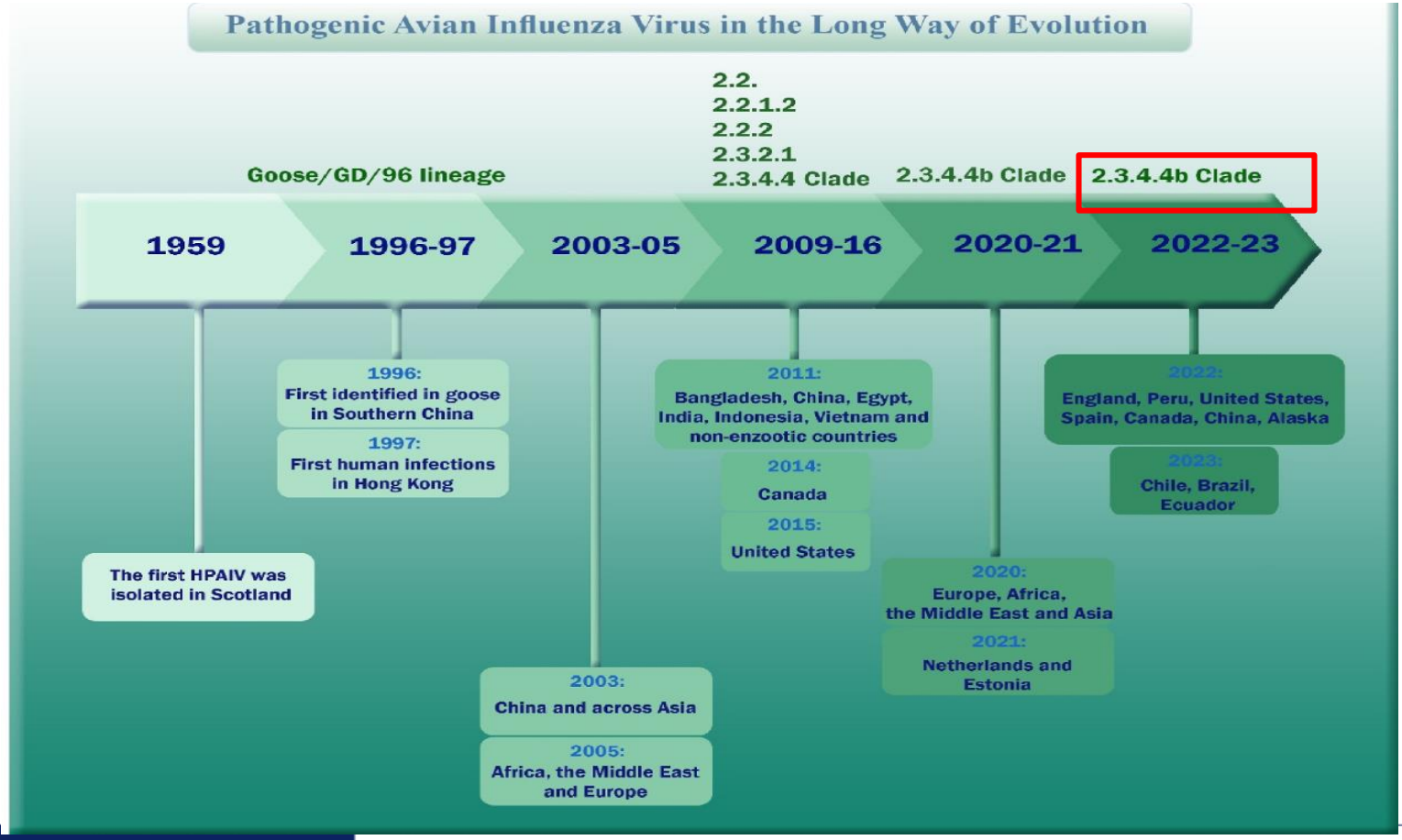
Contents lists available at ScienceDirect

Travel Medicine and Infectious Disease

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

# A comprehensive review of highly pathogenic avian influenza (HPAI) H5N1: An imminent threat at doorstep

Javad Charostad [a], Mohammad Rezaei Zadeh Rukerd [b,c], Shahab Mahmoudvand [d,e], Davood Bashash [f], Seyed Mohammad Ali Hashemi [g], Mohsen Nakhaie [b,*], Keivan Zandi [h,i,**]



Travel Medicine and Infectious Disease 55 (2023) 102634

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Travel Medicine and Infectious Disease

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Avian influenza spillover to humans: Are we prepared to deal with another potential pandemic?

The world is going through its largest-ever recorded outbreak of avian flu, tearing through the poultry and wild bird populations (Fig. 1). The endemic is the largest on record in Europe, North America and Japan and is driven mainly by the H5N1 avian flu virus, clade 2.3.4.4b. In 2022, HPAI infections with H5N1 viruses from clade 2.3.4.4b resulted in the loss of an excess of 131 million poultry across 67 countries. The disease has spread rapidly in 2023, and infections have been reported in 14 additional countries [1]. As of 12 July 2023, an excess of 58 million poultry birds are diagnosed with HPAI resulting from infections with H5N1 viruses from clade 2.3.4.4, in addition to a little more than 7000 wild birds, in the United States alone [2].

Of note, while the risk of avian flu infection was previously thought to be the highest during the active spring migration from autumn to summer, experts now believe that its presence in multiple wild bird species has elevated the risk levels through all the seasons. Unfortunately, this means that the outbreaks may not soon abate in poultry birds. In these last, density of birds was related with high risk of outbreak in Lombardy regions (Italy) when regions with higher bird density >10,000 birds/km$^2$ have high probability of outbreak event (67%), and outbreak were more frequent in provinces where had any previous outbreak [10].

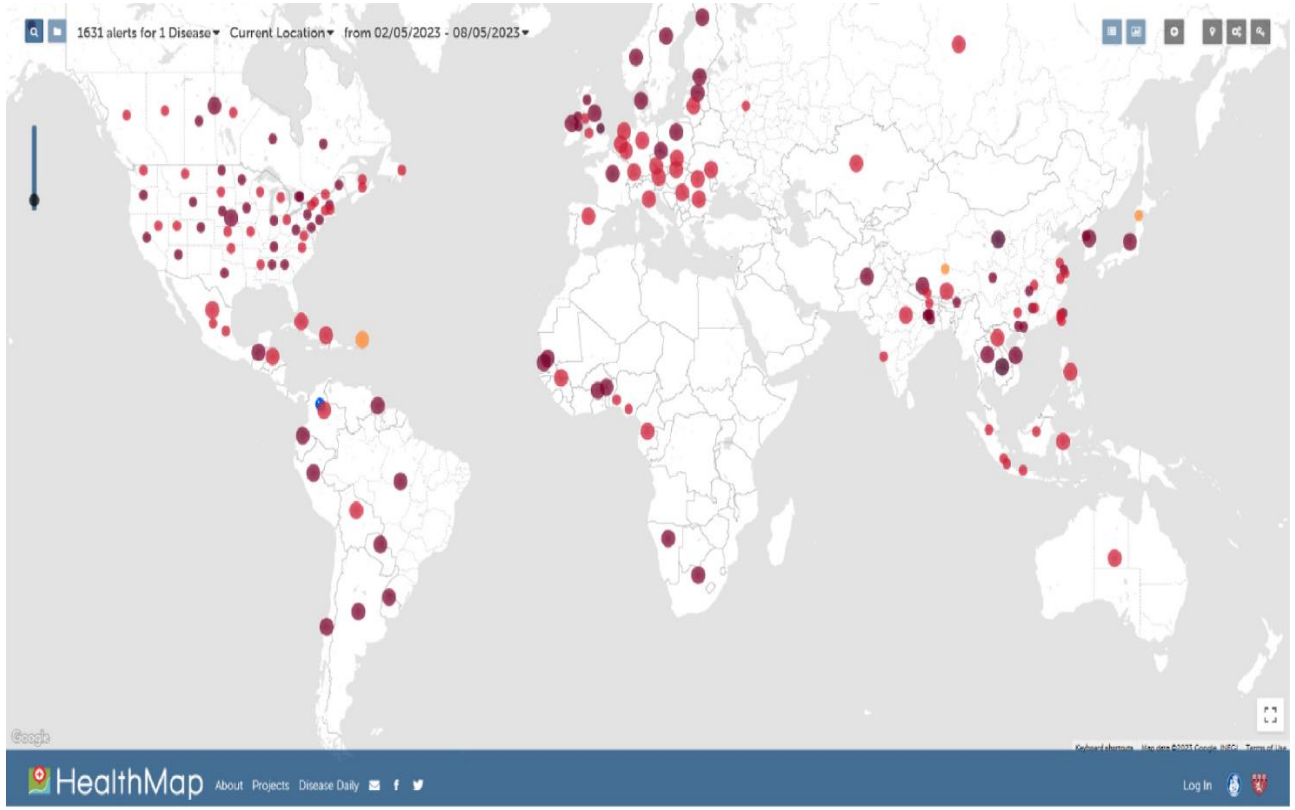


Fig. 1. Global alerts on avian influenza at HealthMap during the last six months (February–August, 2023).

# Alarming situation of emerging H5 and H7 avian influenza and effective control strategies

Jianzhong Shi [a,b], Xianying Zeng[b], Pengfei Cui[b], Cheng Yan[b] and Hualan Chen [a,b]

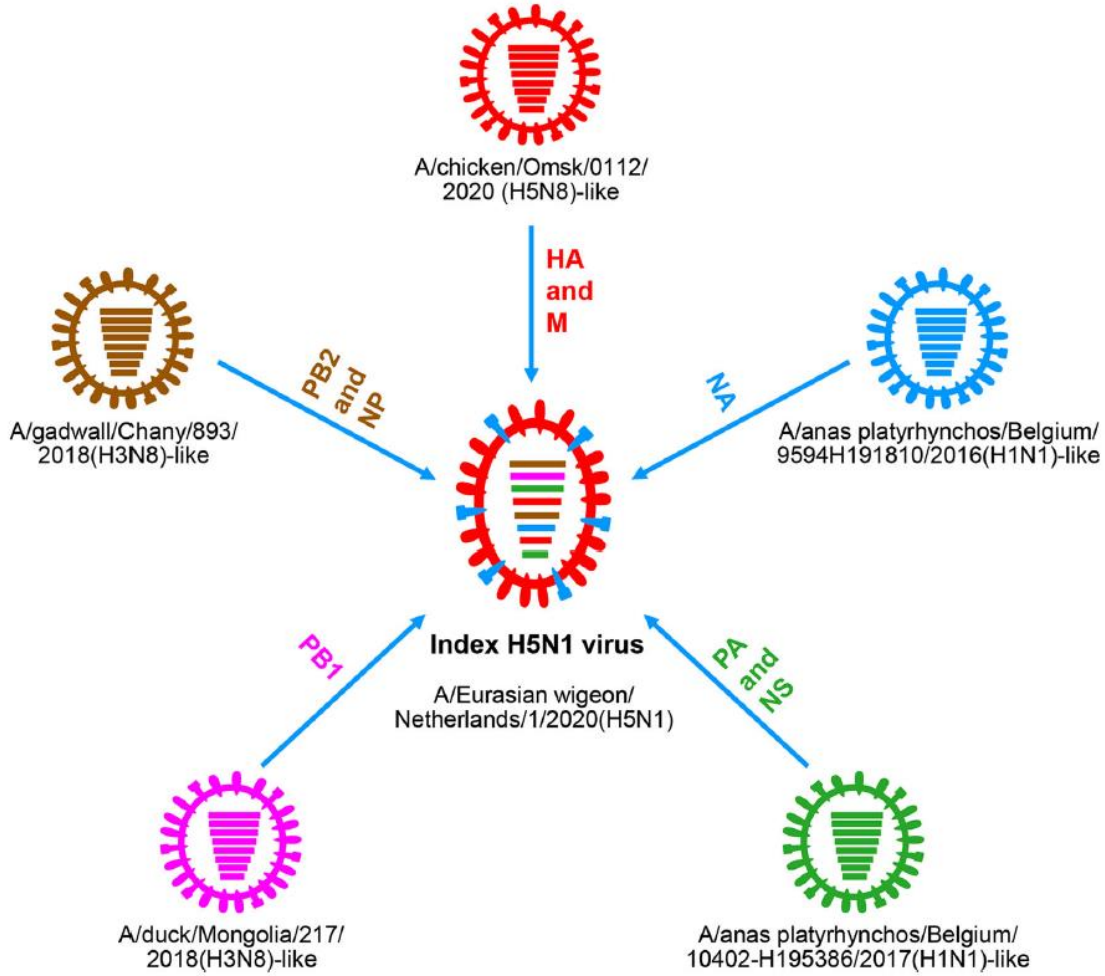


**Figure 2.** Formation of the index H5N1 virus bearing the 2.3.4.4b HA gene in 2020. The eight bars represent the eight gene segments (from top to bottom: PB2, PB1, PA, HA, NP, NA, M, and NS), and the colour of the bar indicates the closest donor strain of the gene segment.



Emerging Microbes & Infections
2023, VOL. 12, e2155072 (12 pages)
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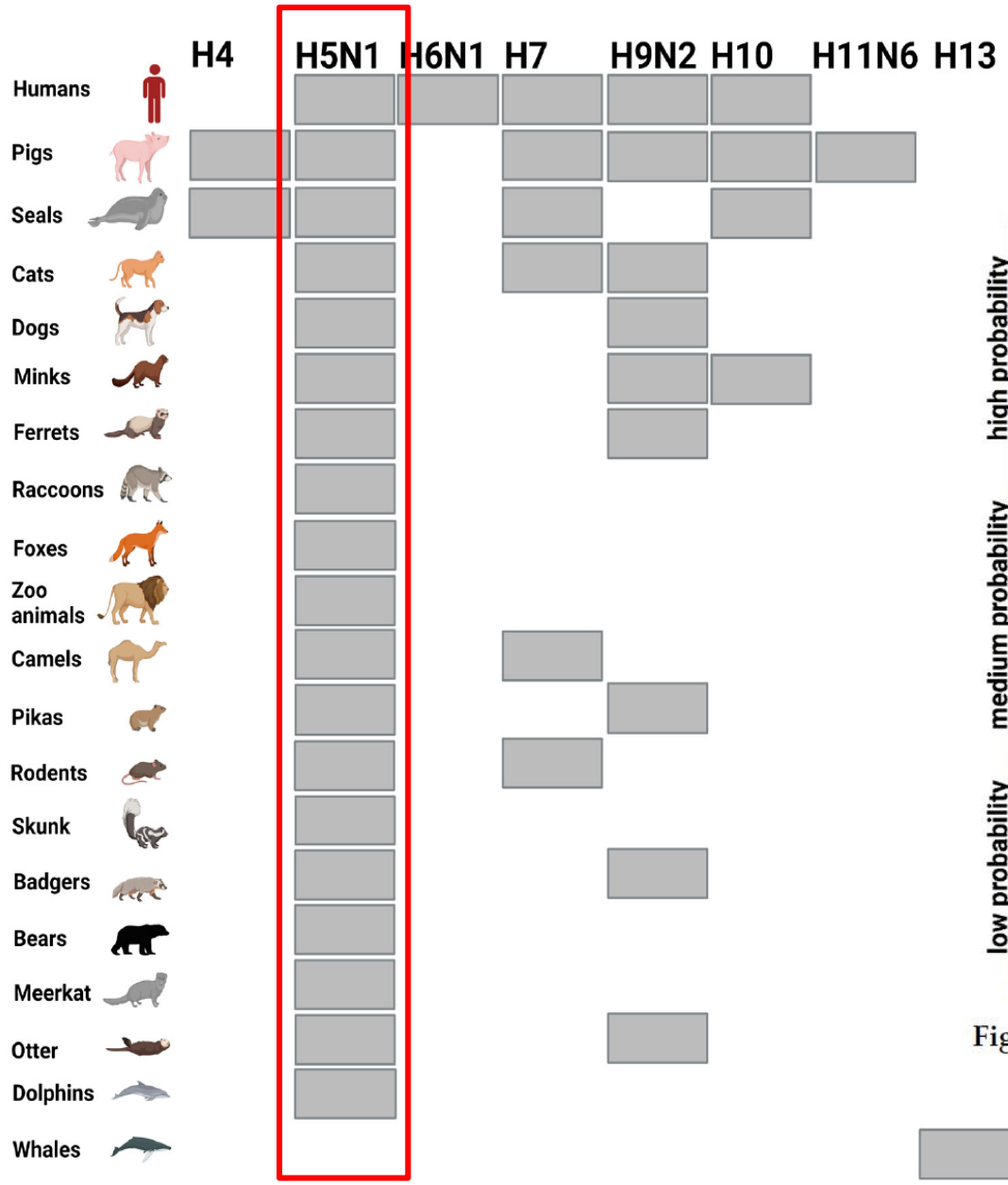



*Review*

# Zoonotic Animal Influenza Virus and Potential Mixing Vessel Hosts

Elsayed M. Abdelwhab [1,*] and Thomas C. Mettenleiter [2,*]


**Figure 3.** Potential "mixing vessel" hosts for the generation of zoonotic animal influenza viruses.



*Viruses* **2023**, *15*, 980. https://doi.org/10.3390/v15040980


What is ‘Disease X’?
BBC NEWS

# Highly Pathogenic Avian Influenza A(H5N1) Clade 2.3.4.4b Virus in Wild Birds, Chile

Naomi Ariyama,[1] Catalina Pardo-Roa,[1] Gabriela Muñoz, Carolina Aguayo, Claudia Ávila, Christian Mathieu, Leonardo I. Almonacid, Rafael A. Medina, Barbara Brito, Magdalena Johow, Victor Neira

# Outbreak of highly pathogenic avian influenza A(H5N1) clade 2.3.4.4b virus in cats, Poland, June to July 2023

Katarzyna Domańska-Blicharz[1], Edyta Świętoń[2], Agnieszka Świątalska[3], Isabella Monne[4], Alice Fusaro[4], Karolina Tarasiuk[1], Krzysztof Wyrostek[1], Natalia Styś-Fijoł[1], Aleksandra Giza[2], Marta Pietruk[2], Bianca Zechchin[4], Ambra Pastori[4], Łukasz Adaszek[5], Małgorzata Pomorska-Mól[6], Grzegorz Tomczyk[1], Calogero Terregino[4], Stanisław Winiarczyk[5,7]

RAPID COMMUNICATION

# Asymptomatic infection with clade 2.3.4.4b highly pathogenic avian influenza A(H5N1) in carnivore pets, Italy, April 2023

Ana Moreno[1], Francesco Bonfante[2], Alessio Bortolami[2], Irene Cassaniti[3,4], Anna Caruana[8], Vincenzo Cottini[7], Danilo Cereda[5], Marco Farioli[5], Alice Fusaro[2], Antonio Lavazza[1], Pierdavide Lecchini[6], Davide Lelli[1], Andrea Maroni Ponti[6], Claudia Nassuato[7], Ambra Pastori[2], Francesca Rovida[3,4], Luigi Ruocco[6], Marco Sordilli[6], Fausto Baldanti[3,4,*], Calogero Terregino[2,*]

# Highly pathogenic avian influenza A(H5N1) virus infection on multiple fur farms in the South and Central Ostrobothnia regions of Finland, July 2023

Erika Lindh[1,*], Hanna Lounela[2,*], Niina Ikonen[1], Tuija Kantala[2], Carita Savolainen-Kopra[1], Ari Kauppinen[2], Pamela Österlund[1], Lauri Kareinen[2], Anna Katz[1], Tiina Nokireki[2], Jari Jalava[1], Laura London[2], Marjaana Pitkäpaasi[1], Jaana Vuolle[2], Anna-Liisa Punto-Luoma[1], Riikka Kaarto[3], Liina Voutilainen[1], Riikka Holopainen[2], Laura Kalin-Mänttäri[1], Terhi Laaksonen[2], Hannu Kiviranta[1], Aino Pennanen[1], Otto Helve[1], Ilona Laamanen[2], Merit Melin[1], Niina Tammiranta[2], Ruska Rimhanen-Finne[1], Tuija Gadd[2], Mika Salminen[1]

# Highly Pathogenic Avian Influenza A(H5N1) Clade 2.3.4.4b Virus in Domestic Cat, France, 2022

François-Xavier Briand, Florent Souchaud, Isabelle Pierre, Véronique Beven, Edouard Hirchaud, Fabrice Hérault, René Planel, Angélina Rigaudeau, Sibylle Bernard-Stoecklin, Sylvie Van der Werf, Bruno Lina, Guillaume Gerbier, Nicolas Eterradossi, Audrey Schmitz, Eric Niqueux, Béatrice Grasland

# Risk for Infection in Humans after Exposure to Birds Infected with Highly Pathogenic Avian Influenza A(H5N1) Virus, United States, 2022

Krista Kniss,[1] Kelsey M. Sumner,[1] Katie J. Tastad, Nathaniel M. Lewis, Lauren Jansen, Derek Julian, Mike Reh, Emily Carlson, Robin Williams, Samir Koirala, Bryan Buss, Matthew Donahue, Jennifer Palm, Leslie Kollmann, Stacy Holzbauer, Min Z. Levine, Todd Davis, John R. Barnes, Brendan Flannery, Lynnette Brammer, Alicia Fry

Commentary

BMJ Global Health

2023;8:e013146

# We are underestimating, again, the true burden of H5N1 in humans

Mokhtar Gomaa,[1] Yassmin Moatasim,[1] Ahmed El Taweel,[1] Sara H Mahmoud,[1] Amira S El Rifay,[1] Ahmed Kandeil,[1,2] Pamela P McKenzie,[2] Richard J Webby,[2] Rabeh El-Shesheny ,[1] Mohamed Ahmed Ali,[1] Ghazi Kayali [3]

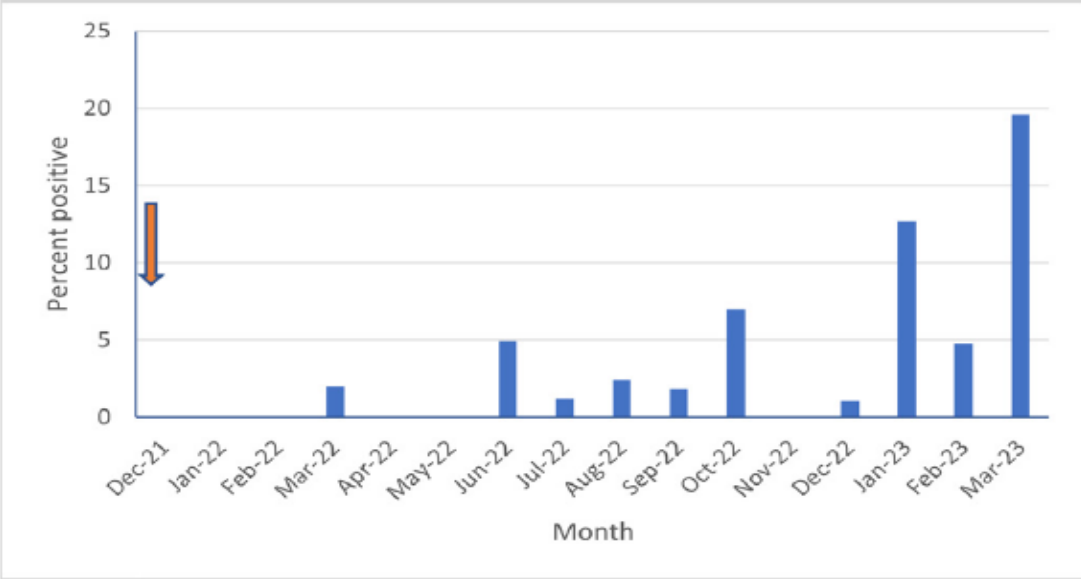



**Figure 2** Percentage of sera positive for anti-H5N1 antibodies by month. Arrow indicates detection of H5N1 in domestic and wild birds in the markets.

**SUMMARY BOX**

⇒ From mid-2021, a dramatic increase in activity and geographical distribution of clade 2.3.4.4b H5N1 viruses in animals occurred.

⇒ The extent of clade 2.3.4.4b human infections is unknown, but almost certainly more than the reported number, especially as this virus has shown an ability to infect several non-human mammals on a large scale.

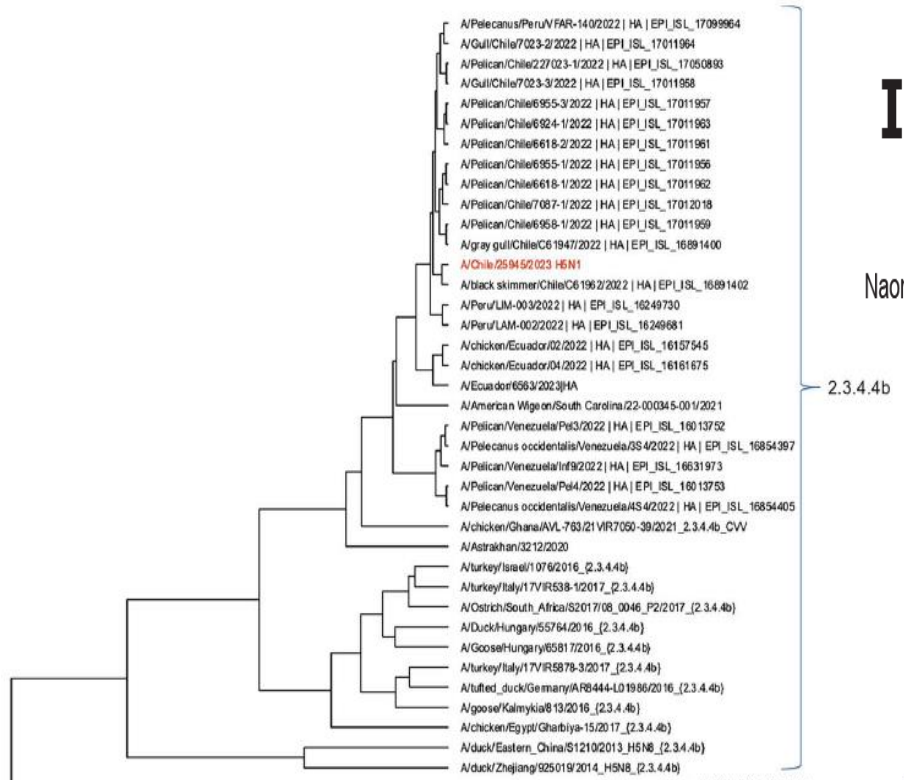
⇒ Our study in five live bird markets showed that human seropositivity appeared to follow virus detection in wild and domestic birds sold live in the markets suggesting this as source of virus exposure.

⇒ Our estimate of 4.6% clade 2.3.4.4b H5N1 seroprevalence is more than double that of our earlier clade 2.2 seroprevalence estimate suggesting that the currently circulating viruses are more infectious to mammalian hosts.

⇒ The scale, geographical scope and increasing list of infected species with clade 2.3.4.4b viruses urge the conduct of additional seroprevalence studies.

# The first reported case of human infection with H5N1 avian Influenza A virus in Chile

Andrés Castillo, PhD[1,*], Rodrigo Fasce, BSc[2,*], Barbara Parra, MSc[1], Winston Andrade, PhD[2], Paulo Covarrubias, PhD[1], Andrea Hueche, BSc[2], Constanza Campano, BSc[1], Carolina Tambley, BSc[2], Marcelo Rojas, BSc[1], Maykol Araya, MT[3], Felipe Hernández, BSc[2], Patricia Bustos, MSc[2] and Jorge Fernández, PhD[1,*]




# Highly Pathogenic Avian Influenza A(H5N1) Clade 2.3.4.4b Virus in Wild Birds, Chile

Naomi Ariyama,[1] Catalina Pardo-Roa,[1] Gabriela Muñoz, Carolina Aguayo, Claudia Ávila, Christian Mathieu, Leonardo I. Almonacid, Rafael A. Medina, Barbara Brito, Magdalena Johow, Victor Neira

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 29, No. 9, September 2023

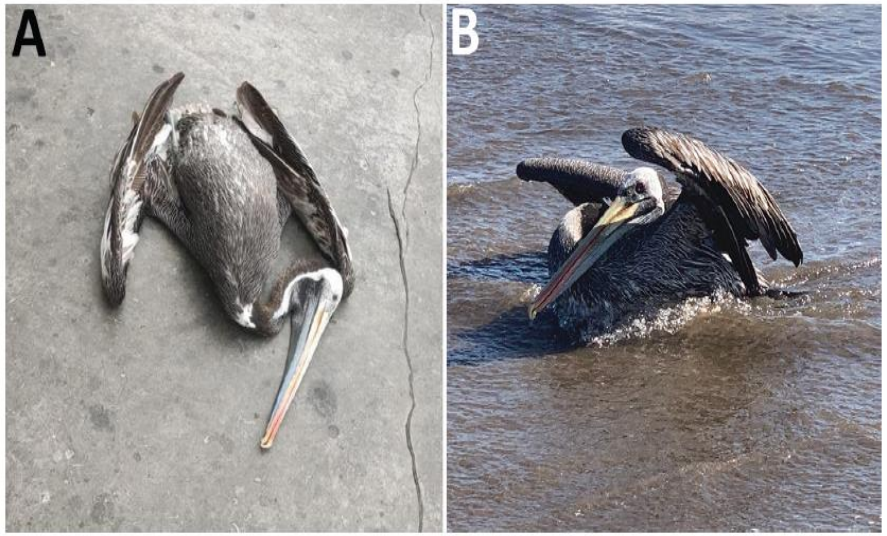
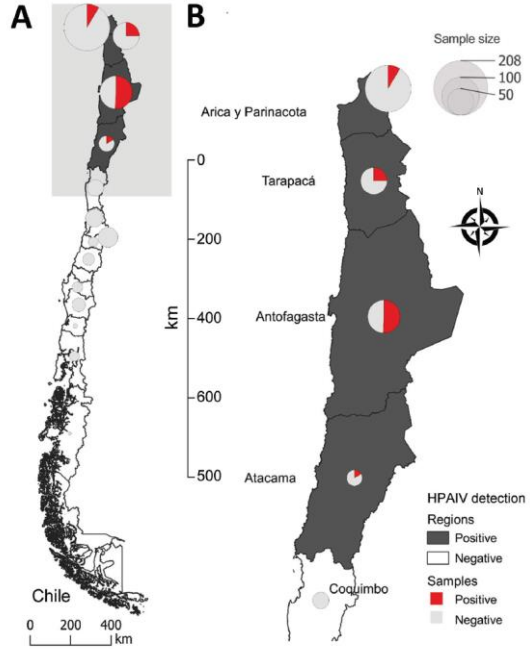



**Figure 2.** Images of Peruvian pelicans (*Pelecanus thagus*) collected and sampled for highly pathogenic avian influenza virus H5N1 clade 2.3.4.4b, Chile. A) Dead pelican found on land near shoreline; B) ill pelican in water near shoreline.

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*Journal of Travel Medicine*, 2023, 1–3
https://doi.org/10.1093/jtm/taad083
Research Letter

# First case of human infection with highly pathogenic H5 avian Influenza A virus in South America: A new zoonotic pandemic threat for 2023?

**Alfredo Bruno, MSc, PhD (c)[1,2,3,†,*], Alonzo Alfaro-Núñez , PhD[4,5,†], Doménica de Mora, MSc[1,†], Rubén Armas, MSc, PhD (c)[1,6], Maritza Olmedo, BSc[1], Jimmy Garcés, Vet[1] and Miguel Angel Garcia-Bereguiain, PhD[7,*]**

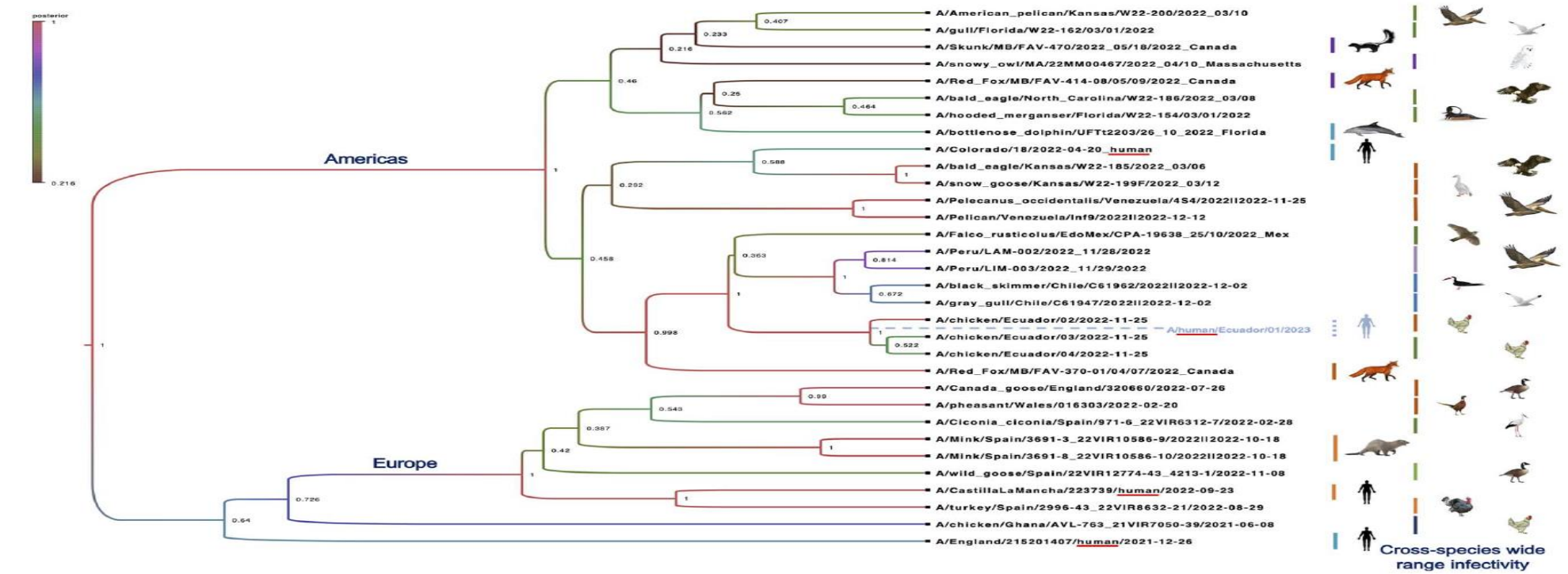



**Figure 1.** Phylogenetic analysis based on the sequences for hemagglutinin (HA) gene. The H5N1 strain circulating in Ecuador belongs to the clade 2.3.4.4b responsible for the current avian flu outbreaks in Europe and the Americas in 2020-2023. The diagram shows the wide range of cross-species transmission of the clade 2.3.4.4b, including in various occasions human and other mammal species hosts (the sequences for the suggested origin "outgroup" from Ghana and England in 2021 are included in the analysis; the dotted line shows the human case from Ecuador assuming the same viral strain detected in poultry).



*Journal of Travel Medicine*, 2023, 1–3
https://doi.org/10.1093/jtm/taad032

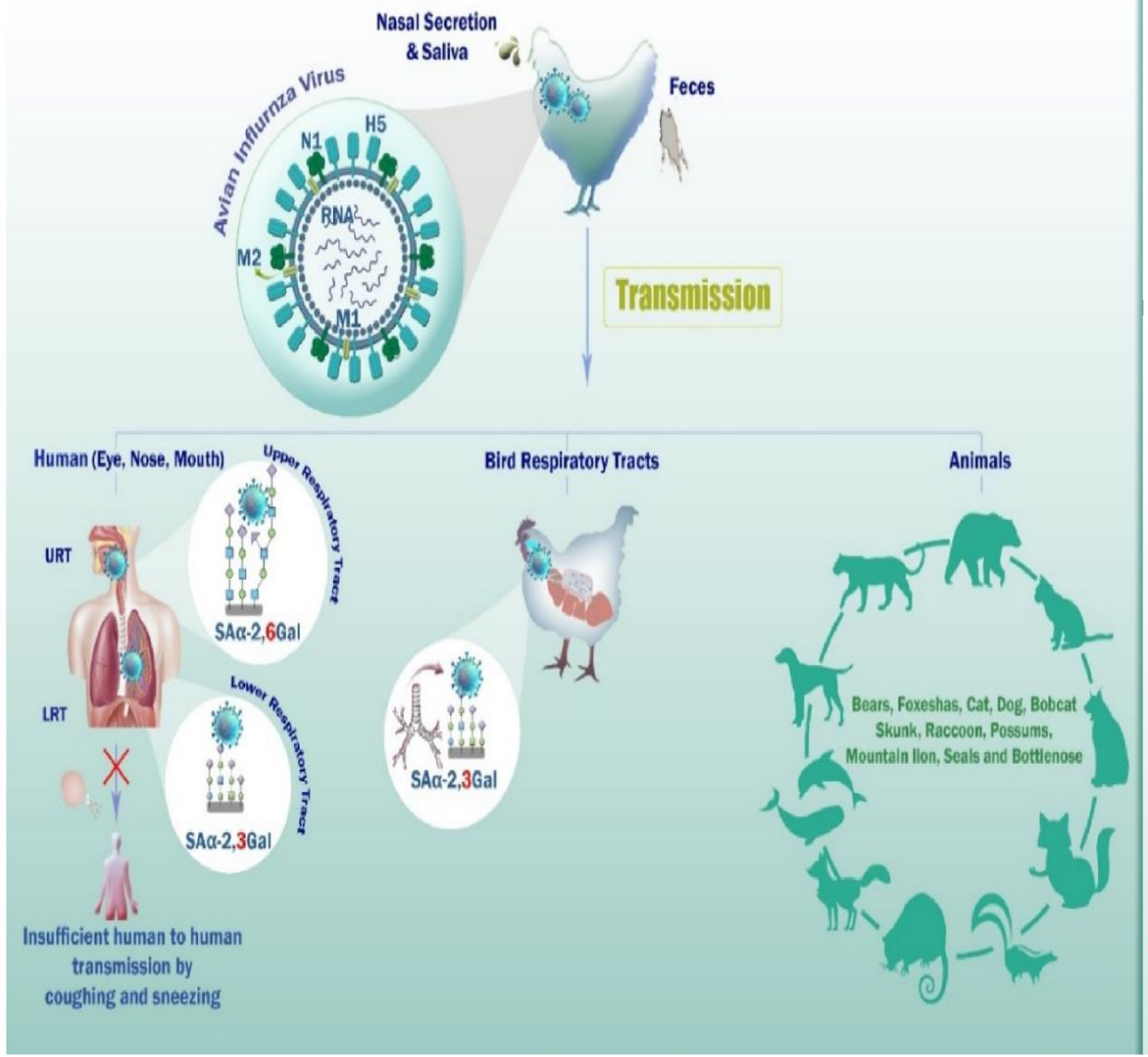
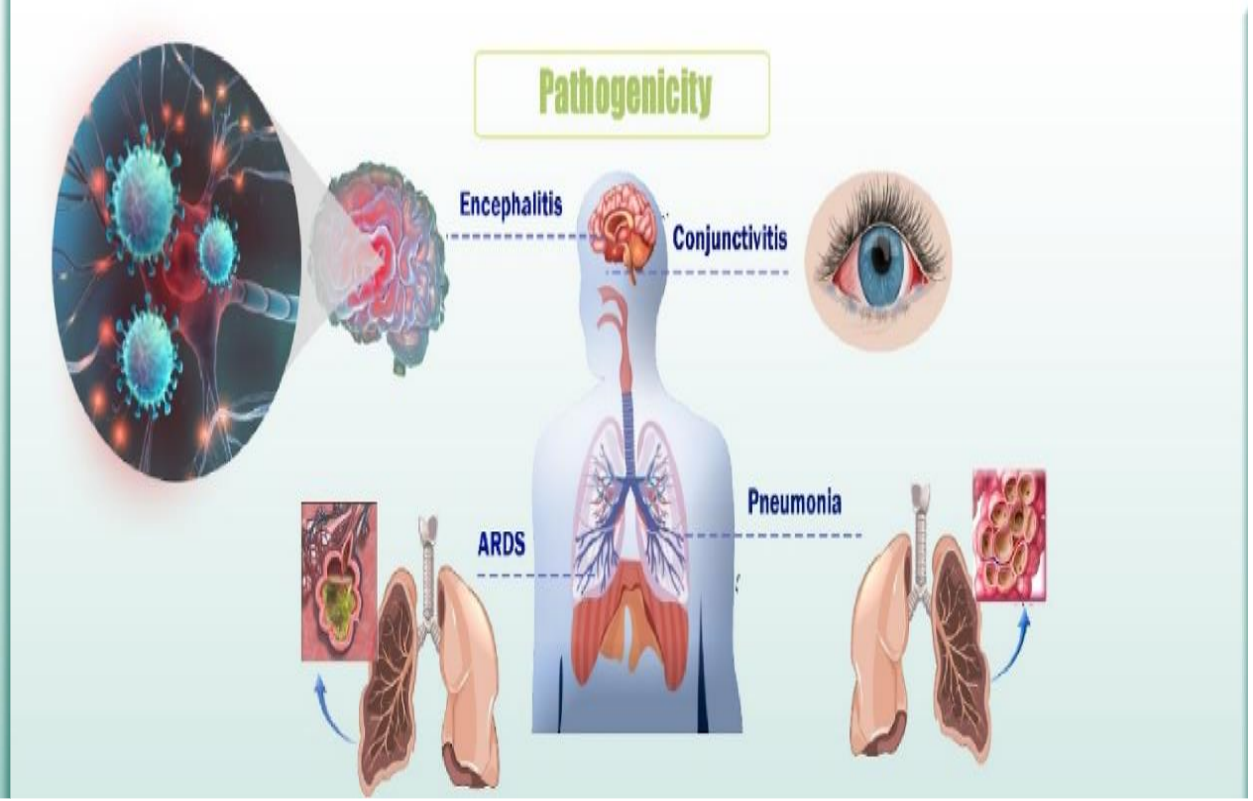


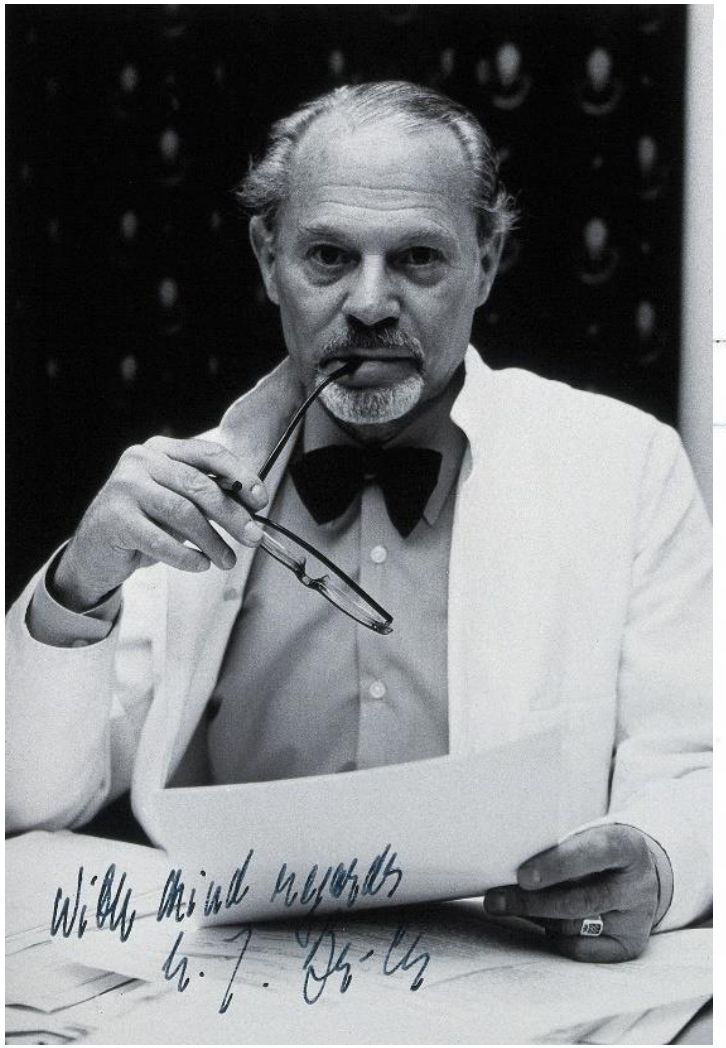

**Table 2**
Distribution of confirmed HPAI H5N1 cases and associated fatalities by Country in 2022 and 2023.

| Country | 2022 Case (Death) | 2023 Case (Death) | Total Case (Death) |
|---|---|---|---|
| Cambodia | 0 (0) | 2 (1) | 2 (1) |
| Chile | 0 (0) | 1 (0) | 1 (0) |
| China | 1 (1) | 1 (0) | 2 (1) |
| Ecuador | 1 (0) | 0 (0) | 1 (0) |
| Spain | 2 (0) | 0 (0) | 2 (0) |
| United Kingdom of Great Britain and Northern Ireland | 0 (0) | 4 (0) | 4 (0) |
| United States of America | 1 (0) | 0 (0) | 1 (0) |
| Vietnam | 1 (0) | 0 (0) | 1 (0) |
| Total | 6 (1) | 8 (1) | 14 (2) |






Charostad J et al. Travel Med Infect Dis 2023;55: 102638



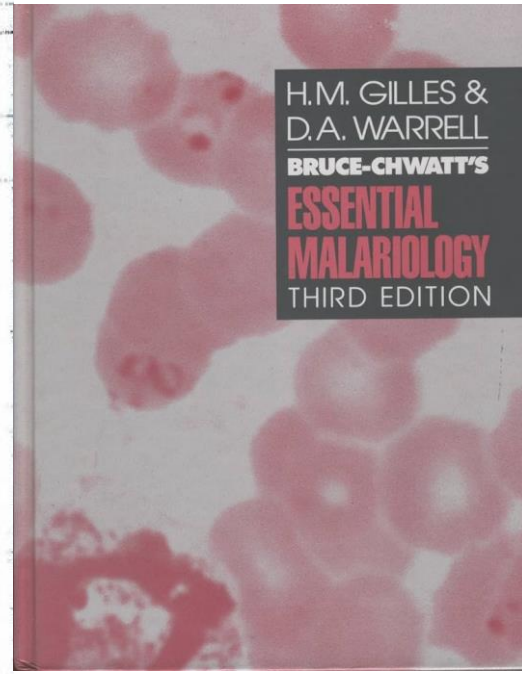


# MALARIA ZOONOSIS IN RELATION TO MALARIA ERADICATION

L. J. BRUCE-CHWATT*
*World Health Organization, Geneva, Switzerland*
Received October 13th, 1967

## INTRODUCTION

The term "zoonosis" expresses generally the concept of a disease of animals that can affect the human species. VIRCHOW who coined this term used it to separate the infections of animals from those of humans. Over the past 50 years there have been many attempts to give this comprehensive term some precision or to introduce various other terms (anthropozoonoses, zooanthroponoses, amphixenoses, cyclozoonoses, etc.) to distinguish diseases acquired by animals from man, to indicate some special epidemiological features or to separate the diseases produced by an infective agent from those due to toxins and poisons. These problems have been outlined by MAYER[1] (1942), by GARNHAM[2–6] (1952, 1963), by HEISCH[7] (1956), AUDY[8,9] (1954, 1958), ABDUSSALAM[10] (1959), NELSON[11] (1960), HOARE[12] (1962), PAVLOVSKY[13] (1964), SCHWABE[14] (1964), FIENNES[15] (1967) and others.



# A large focus of naturally acquired *Plasmodium knowlesi* infections in human beings

*Balbir Singh, Lee Kim Sung, Asmad Matusop, Anand Radhakrishnan, Sunita S G Shamsul, Janet Cox-Singh, Alan Thomas, David J Conway*


**Findings** All DNA sequences were phylogenetically indistinguishable from those of *P knowlesi*, a malaria parasite of long-tailed macaque monkeys, but were significantly different from other malaria parasite species. By PCR assay, 120 (58%) of 208 people with malaria tested positive for *P knowlesi*, whereas none was positive for *P malariae*. *P knowlesi* parasites in human erythrocytes were difficult to distinguish from *P malariae* by microscopy. Most of the *P knowlesi* infections were in adults and we did not note any clustering of cases within communities. *P knowlesi* infections were successfully treated with chloroquine and primaquine.

**Interpretation** Naturally acquired *P knowlesi* infections, misdiagnosed by microscopy mainly as *P malariae*, accounted for over half of all malaria cases in our study. Morphological similarities between *P knowlesi* and *P malariae* necessitate the use of molecular methods for correct identification. Further work is needed to determine whether human *P knowlesi* infections in the Kapit division are acquired from macaque monkeys or whether a host switch to human beings has occurred.

*Lancet* 2004; **363:** 1017–24



Lancet 2004; 363:1017-24

# The vectors of *Plasmodium knowlesi* and other simian malarias Southeast Asia: challenges in malaria elimination

Indra Vythilingam[a,*], Tock Hing Chua[b,*], Jonathan Wee Kent Liew[a,c], Benny O. Manin[b], and Heather M. Ferguson[d]

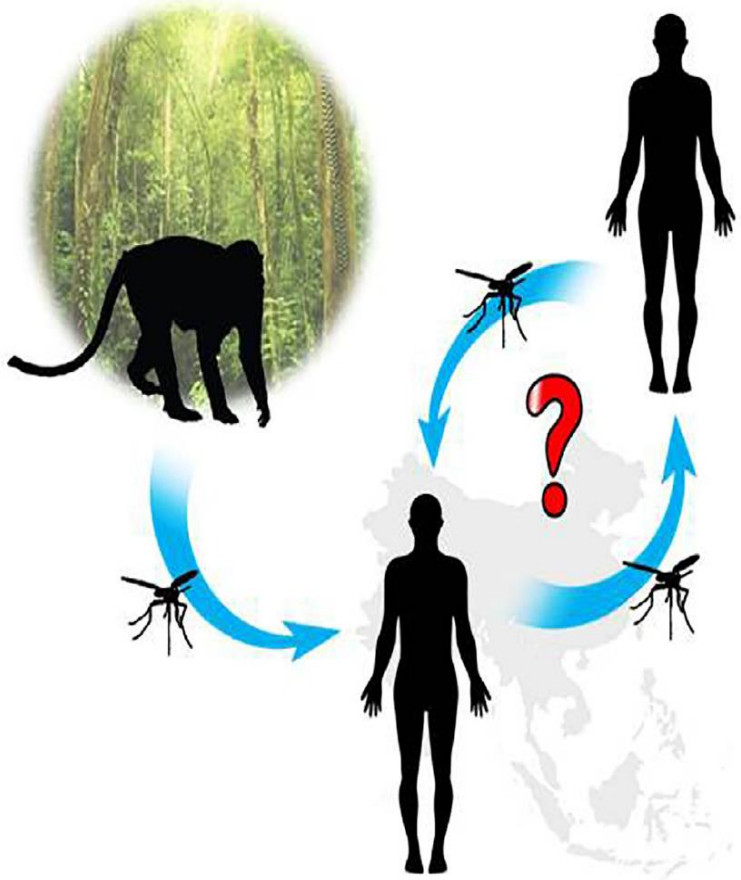


**Fig. 3** Diagram depicting the current transmission of *P. knowlesi* from macaques to humans by vector mosquitoes in Southeast Asia. Whether human to human transmission is occurring is not conclusive yet.

# Primate malaria: An emerging challenge of zoonotic malaria in Indonesia

Meyby Eka Putri Lempang [a], Farahana Kresno Dewayanti [b], Lepa Syahrani [b], Dendi Hadi Permana [b], Ratmawati Malaka [c], Puji Budi Setia Asih [b], Din Syafruddin [b,d,*]

Table 1

*Plasmodium* species that infect human and non-human primate worldwide [43].

| | Vivax-type parasites | Ovale-type parasites | Malariae-type parasites | Falciparium-type parasites | Other-type parasites |
|---|---|---|---|---|---|
| Human | *P. vivax* | *P.ovale* | *P. malariae* | *P. falciparum* | *P. knowlesi* |
| Macaque | *P. cynomolgi* | *P. fieldi* | *P. inui* | *P. coatneyi* | |
| | | *P. simiovale* | | *P. fragile* | |
| Gibbon | *P. eylesi* | | | | |
| | *P. hylobati* | | | | |
| | *Pithecophaga jefferyi* | | | | |
| | *P. youngi* | | | | |
| Orangutan | *P. pitheci* | | | | |
| Chimpanzee | *P. schwetzi* | | *Prosevania rodhaini* | | |
| Cacajao | | | *P. brasilianum* | | |
| Howler monkey | *P.simium* | | | | |
| Mangabey | *P. gonderi* | | | | |
| Erythrocytic cycle parasite invasion | 48 h (Tertian) | 48 h (Tertian) | 72 (Quartan) | 48 h (Tertian) | 24 h (Quotidian) |

One Health 14 (2022) 100389

Permana *et al. Parasites & Vectors* (2023) 16:267
https://doi.org/10.1186/s13071-023-05880-4

Parasites & Vectors

RESEARCH Open Access

# The potential for zoonotic malaria transmission in five areas of Indonesia inhabited by non-human primates

Dendi Hadi Permana[1,2], Hasmiwati[3], Dwi Anita Suryandari[4†], Ismail Ekoprayitno Rozi[2,5], Lepa Syahrani[2,6], Wuryantari Setiadi[2], Nuzulia Irawati[3], Rizaldi[3], Suradi Wangsamuda[7], Yenni Yusuf[7], Irdayanti[7], Hijral Aswad[7], Puji Budi Setia Asih[2†] and Din Syafruddin[2,7*]

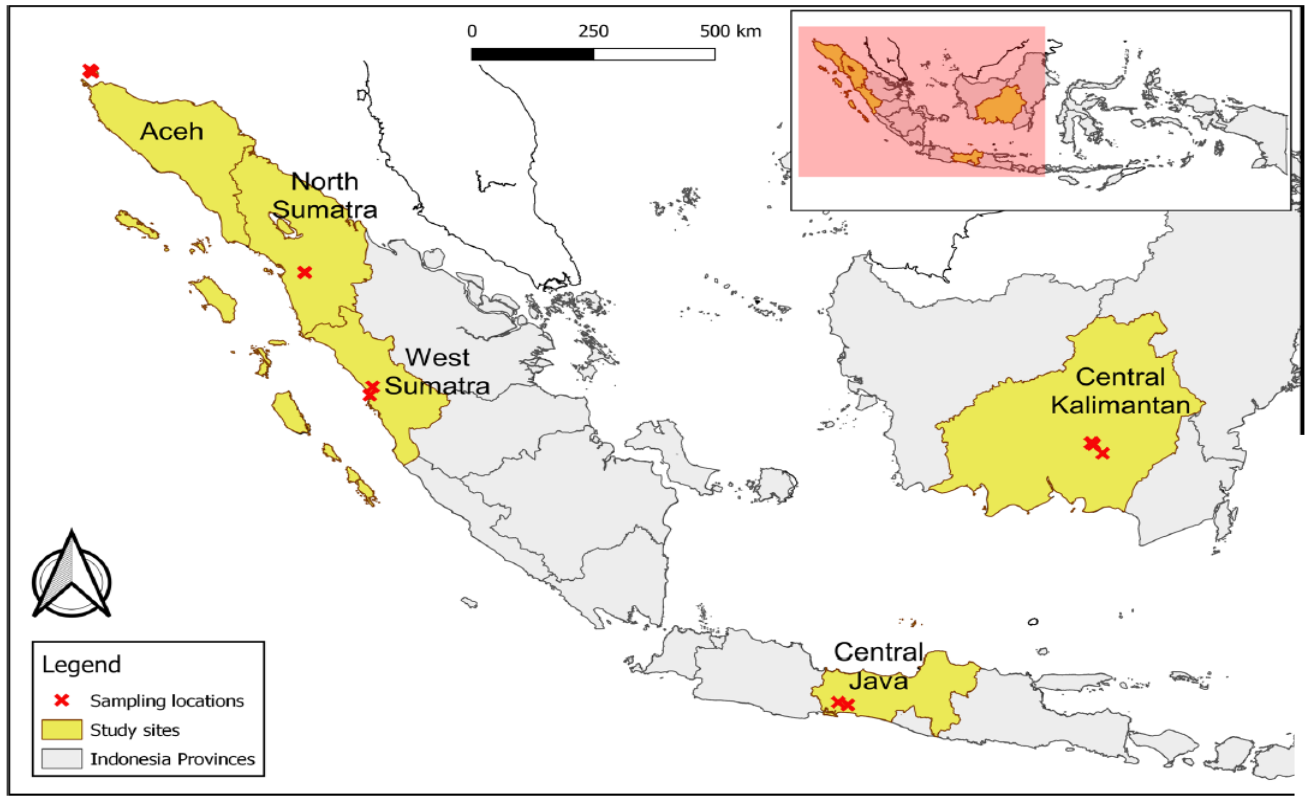



**Fig. 1** Location of the sampling sites (red crosses) near the boundaries of five provinces of Indonesia


**Fig. 5** Types of mosquito breeding sites. **a** Artificial water container; **b** coconut shell, leaf, tree hole; **c** ditch; **d** hoof print; **e** man-made pond; **f** mangrove; **g** natural pond; **h** paddy field; **i** puddle; **j** spring; **k** stream margin; **l** swamp; **m** tire track; **n** well

**Table 4** *Plasmodium* species identified in endemic malaria-positive NHPs from the five provinces

| Location | *Plasmodium coatneyi* | *Plasmodium cynomolgi* | *Plasmodium inui* | *Plasmodium knowlesi* | *Plasmodium* sp. | Total |
|---|---|---|---|---|---|---|
| Central Java | – | – | 2 | 2 | 8 | 12 |
| North Sumatra | – | – | – | – | 2 | 2 |
| West Sumatra | – | 1 | 9 | 5 | – | 15 |
| Aceh | 1 | 9 | 7 | – | – | 17 |
| Central Kalimantan | – | – | 1 | 2 | 6 | 9 |
| Total | 1 | 10 | 19 | 9 | 16 | 55 |

# *Plasmodium cynomolgi* as Cause of Malaria in Tourist to Southeast Asia, 2018

Gitte N. Hartmeyer, Christen R. Stensvold, Thilde Fabricius, Ea S. Marmolin, Silje V. Hoegh, Henrik V. Nielsen, Michael Kemp, Lasse S. Vestergaard

We report human infection with simian *Plasmodium cynomolgi* in a tourist from Denmark who had visited forested areas in peninsular Malaysia and Thailand in August and September 2018. Because *P. cynomolgi* may go unnoticed by standard malaria diagnostics, this malaria species may be more common in humans than was previously thought.

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 25, No. 10, October 2019

# Naturally Acquired Human *Plasmodium cynomolgi* and *P. knowlesi* Infections, Malaysian Borneo

Thamayanthi Nada Raja, Ting Huey Hu, Khamisah Abdul Kadir, Dayang Shuaisah Awang Mohamad, Nawal Rosli, Lolita Lin Wong, King Ching Hii, Paul Cliff Simon Divis, Balbir Singh

2017. Using nested PCR assays, we found 845 (80.6%) patients had either *P. knowlesi* monoinfection (n = 815) or co-infection with other *Plasmodium* species (n = 30). We noted the annual number of these zoonotic infections increased greatly in 2017 (n = 284). We identified 6 patients, 17–65 years of age, with *P. cynomolgi* and *P. knowlesi* co-infections, confirmed by phylogenetic analyses of the *Plasmodium* cytochrome c oxidase subunit 1 gene sequences. *P. knowlesi* continues to be a public health concern in the Kapit Division of Sarawak, Malaysian Borneo. In addition, another simian malaria parasite, *P. cynomolgi*, also is an emerging cause of malaria in humans.

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 26, No. 8, August 2020

# *Plasmodium cynomolgi* Co-infections among Symptomatic Malaria Patients, Thailand

Chaturong Putaporntip, Napaporn Kuamsab, Urassaya Pattanawong, Surasuk Yanmanee, Sunee Seethamchai, Somchai Jongwutiwes

**Table 2.** Demographic and parasitologic features of *Plasmodium cynomolgi*–co-infected patients among febrile patients who sought treatment at malaria clinics or local hospitals in 5 provinces, Thailand

| Patient* | Age, y/sex | Province | Month | Season | Monkey in proximity | Microscopy diagnosis | Parasites/μL‡ | PCR diagnosis |
|---|---|---|---|---|---|---|---|---|
| TSY1522 | 38/M | Tak | 2007 Nov | Dry | No | *P. vivax* | 12,160 | *P. vivax*, *P. cynomolgi* |
| CT606† | 30/M | Chanthaburi | 2009 Oct | Rainy | Yes | *P. vivax* | 86,535 | *P. vivax*, *P. cynomolgi* |
| UBY120 | 32/M | Ubon Ratchathani | 2015 Aug | Rainy | Yes | *P. vivax* | 570 | *P. vivax*, *P. cynomolgi* |
| NR105 | 53/M | Narathiwat | 2008 Jul | Rainy | Yes | *P. vivax* | 4,620 | *P. vivax*, *P. cynomolgi* |
| YL3179 | 15/M | Yala | 2016 Apr | Dry | Yes | *P. vivax* | 1,140 | *P. vivax*, *P. knowlesi* *P. cynomolgi* |
| YL3634 | 40/F | Yala | 2016 Dec | Rainy | Yes | *P. falciparum* | 60 | *P. falciparum*, *P. cynomolgi* |
| YL3680 | 49/M | Yala | 2016 Dec | Rainy | Yes | *P. vivax* | 3,720 | *P. vivax*, *P. cynomolgi* |
| YL3685 | 18/M | Yala | 2016 Dec | Rainy | Yes | *P. vivax* | 4,680 | *P. vivax*, *P. cynomolgi* |
| YL4278 | 21/M | Yala | 2017 Oct | Rainy | Yes | *P. vivax* | 7,440 | *P. vivax*, *P. cynomolgi* |

*Alphanumeric designations represent provinces and serial number of blood samples.
†Patient from Cambodia, but had lived in Thailand for 1 year just prior to illness, with no history of travel outside of the country.
‡All species of malaria parasites (all stages) were determined from ≥200 leukocytes on Giemsa-stained thick blood films.



# Natural Human Infections with *Plasmodium cynomolgi*, *P. inui*, and 4 other Simian Malaria Parasites, Malaysia

Nan Jiun Yap,[1] Hanisah Hossain,[1] Thamayanthi Nada-Raja, Romano Ngui, Azdayanti Muslim, Boon-Peng Hoh, Loke Tim Khaw, Khamisah Abdul Kadir, Paul Cliff Simon Divis, Indra Vythilingam, Balbir Singh, Yvonne Ai-Lian Lim

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 27, No. 8, August 2021

We detected the simian malaria parasites *Plasmodium knowlesi*, *P. cynomolgi*, *P. inui*, *P. coatneyi*, *P. inui*–like, and *P. simiovale* among forest fringe–living indigenous communities from various locations in Malaysia. Our findings underscore the importance of using molecular tools to identify newly emergent malaria parasites in humans.

# Monkeypox virus history

1959: Monkeypox virus (MPXV) isolated initially in Copenhagen from imported chimpanzees (*Cynomolgus* spp.) affected by a pox-like disease[1]

In 1970 first identification of a human case of Monkeypox (9-months old child admitted to the Basankusu hospital, Democratic Republic of Congo with a smallpox-like disease)[2]

The animal reservoir has not yet been identified. MPXV has been isolated twice from wild animals:in 1985 from a simptomatic squirrel (*Funisciurus anerythrus*) in DRC[3] and in 2012 from a sooty mangabey (*Cercocebus atys*) in Ivory Coast.[4]


1. Von Magnus, P.; Andersen, E.K.; Petersen, K.B.; Birch-Andersen, A. A Pox-like Disease in Cynomolgus Monkeys. Acta Pathol. Microbiol. Scand. **1959**, 46, 156–176.
2. Ladnyj, I.D.; Ziegler, P.; Kima, E. A human infection caused by monkeypox virus in Basankusu Territory, Democratic Republic of the Congo. Bull. World Health Organ. **1972**, 46, 593–597.
3. Khodekevich L, Jezek Z, Kinzanzka K. isolation of monkeypox virus from wild squirrel infected in nature. Lancet **1986**;1:98-99.
4.Radonic A et al. Fatal monkeypox in wild-living sooty mangabey, Cote d'Ivoire, **2012**. Emerg Infect Dis 2014;20:1009-1011

Table 1. Orthopox Viruses That Infect Humans

| Virus | Human-to-human transmission | Animal-to-human transmission | Major animal host |
|---|---|---|---|
| Variola (smallpox) | Yes | No | None |
| Monkeypox | Yes | Yes | Rodents |
| Vaccinia | Yes | Yes | Cattle |
| Cowpox | Yes | Yes | Cats, rodents, cattle |
| Buffalopox | Yes | Yes | Cattle |
| Akhmeta virus | No | Yes | Small mammals, cattle |
| Alaskapox | No | Yes | Small mammals |
| Camelpox | No | Yes | Camels |
| Horsepox | No | Yes | Horses, cattle |



Billioux BJ et al. JAMA Neurol, Sept 20, 2022

*Bulletin of the World Health Organization*, **66** (6): 747–752 (1988)


# Monkeypox virus: ecology and public health significance

L. KHODAKEVICH,[1] Z. JEŽEK,[2] & D. MESSINGER[3]

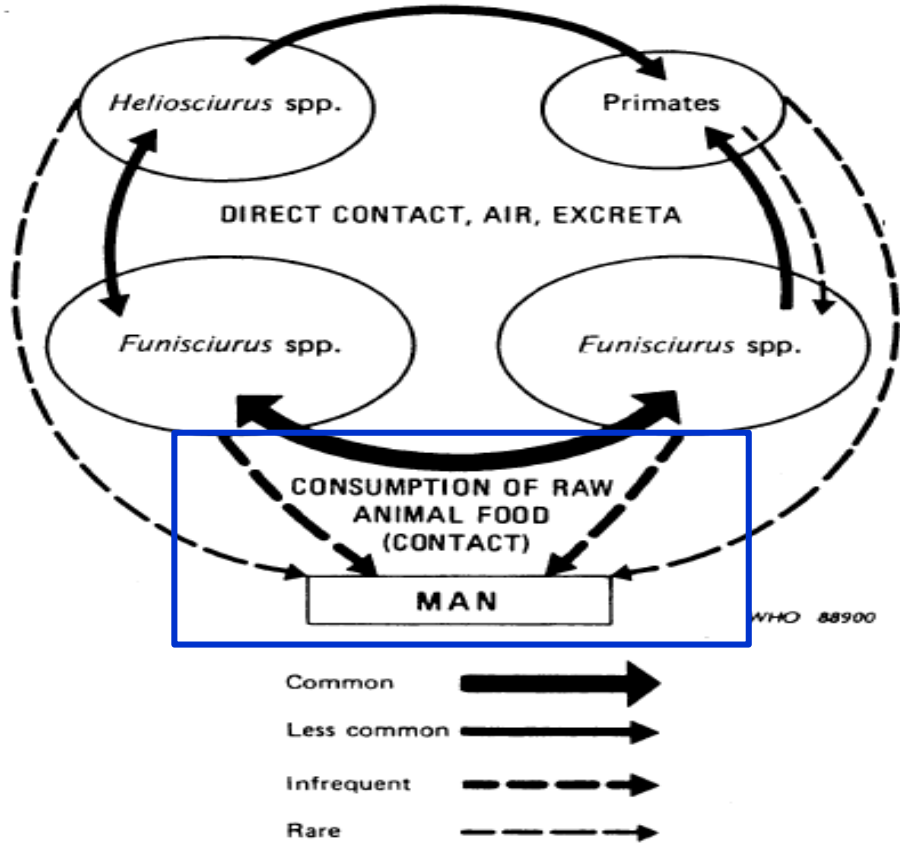



Fig. 2. Diagram to illustrate the transmission of monkeypox virus in nature and from animals to man.

Table 2. Estimated incidence of monkeypox virus infection among various animals and human beings[a]

| | Antibody prevalence rates (*P*) | Lifespan (*t*) (years) | Incidence (*I*) (cases/year/ 1000 individuals) |
|---|---|---|---|
| *Funisciurus* spp. | 0.24 | 2 | 240 |
| *Heliosciurus* spp. | 0.15 | 4 | 75 |
| Non-human primates | 0.08 | 7 | 23 |
| Human beings | 0.01 | 50 | 0.04 |

[a] The calculation of the incidence rates is based on the following formula adapted from Freeman & Hutchison (*24*): $I = P/(t/2) \times 1000$.

**Table 1. Outbreaks of Monkeypox: 1970–2021**

| Decade | 1970–1979 | 1980–1989 | 1990–1999 | 2000–2009 | 2010–2019 | 2020–2021 | | | |
|---|---|---|---|---|---|---|---|---|---|
| Endemic Countries | Number of Cases Reported* by Decade | | | | | | Total Cases | Deaths | References |
| Cameroon[a] | 1 | 1 | —[b] | — | 16 | — | 18 | N/A | [28–32] |
| Central African Republic | — | 8 | — | — | 61 | — | 69 | 0 | [7, 21, 33–38] |
| Côte d'Ivoire | 1 | — | — | — | — | — | 2 | 0 | [4, 39] |
| DRC* | 38 | 343 | 511 | 10 027 | 18 788 | 7374 | 37 081 | N/A | [4, 18, 22, 39–50] |
| Gabon | — | 4 | 9 | — | — | — | 13 | N/A | [51–53] |
| Liberia | 4 | — | — | — | 6 | — | 10 | N/A | [54, 55] |
| Nigeria | 4 | — | — | — | 228 | 42 | 274 | N/A | [6, 56, 57] |
| Republic of the Congo | — | — | — | 73 | 24 | — | 97 | N/A | [58–60] |
| Sierra Leone | 1 | — | — | — | 2 | — | 3 | 0 | [61–64] |
| South Sudan | — | — | — | — | 19 | — | 19 | 0 | [65] |
| Nonendemic Countries | | | | | | | | | |
| Israel | — | — | — | — | 1 | — | 1 | 0 | [66] |
| Singapore | — | — | — | — | 1 | — | 1 | 0 | [67] |
| United Kingdom | — | — | — | — | 4 | — | 4 | 0 | [68, 69] |
| United States | — | — | — | 47 | — | 2 | 49 | 0 | [5, 19, 70, 71] |

Abbreviations: DRC, Democratic Republic of the Congo; N/A, data not available or unclear.

*Reported cases include confirmed, probable, and/or suspected. All DRC cases from 2000 to 2009 and 2010 to 2019 were suspected cases. .

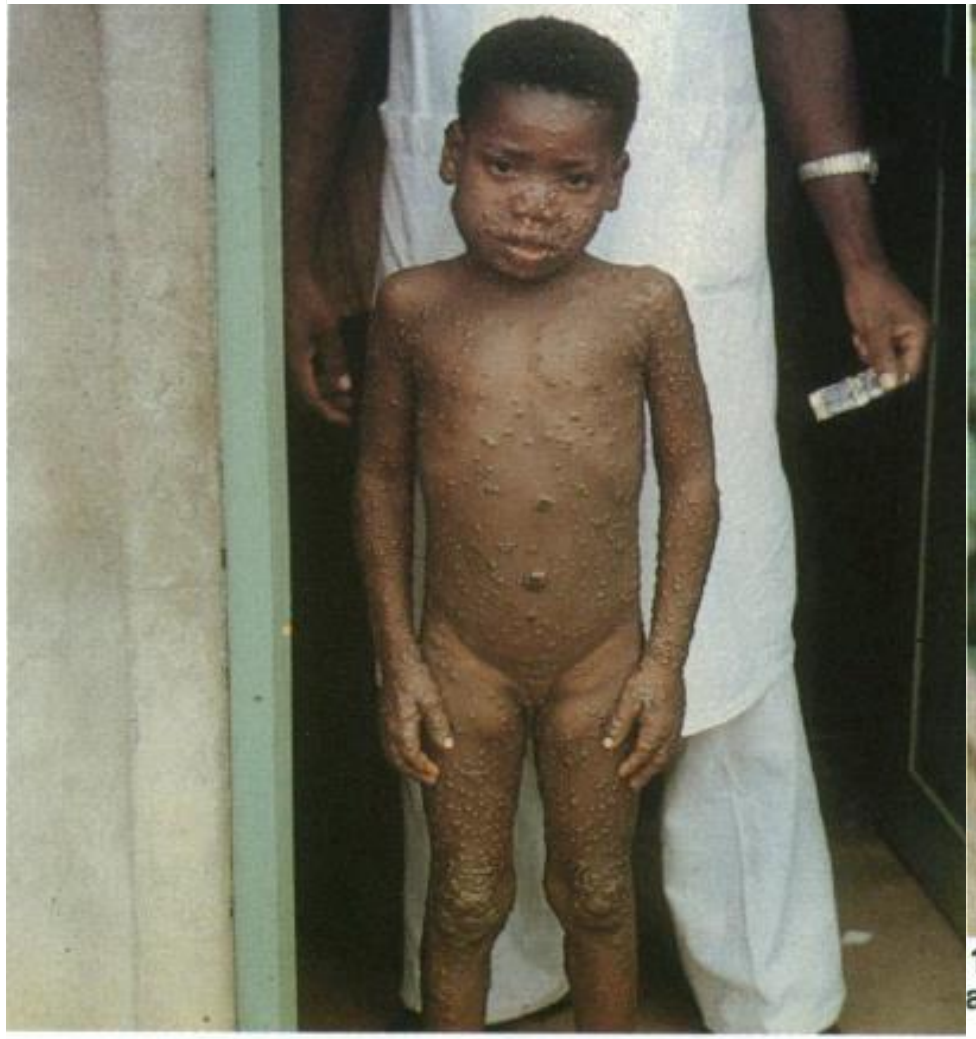
[a]Cameroon is the only country where both viral clades have been reported in humans.

[b]Dash denotes a period without reported outbreaks.

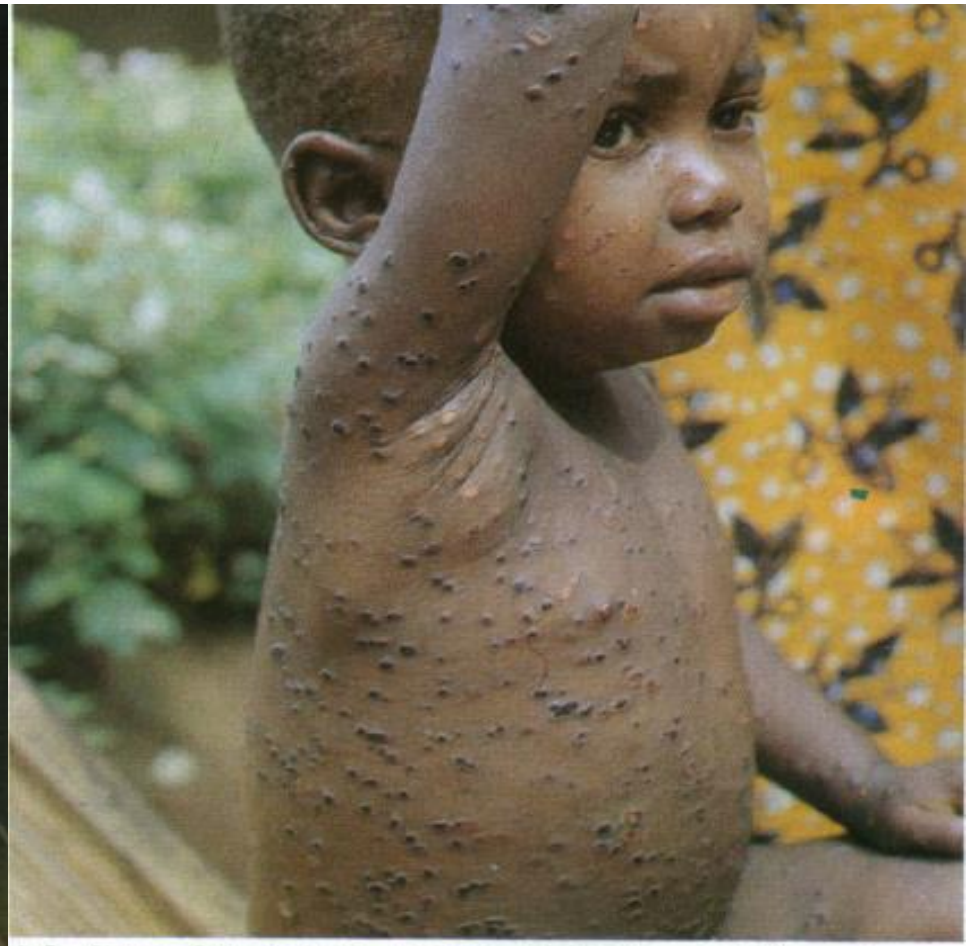
*Bulletin of the World Health Organization*, 62 (5): 703 – 713 (1984)



# The current status of human monkeypox: Memorandum from a WHO Meeting*



1.1. Case 25, age 7 years. Day 7 of rash in the acute stage. Note distinct bilateral inguinal lymphaden–opathy. There is also submaxillar lymphadenopathy on the right side.



1.3 Case 81, age 3 years. Rash in scabbing stage, approximately day 12. Note lymphadenopathy in armpit.

*Bulletin of the World Health Organization*, **58** (2): 165-182 (1980)

# Human monkeypox, 1970–79*

J. G. BREMAN,[1] KALISA-RUTI,[2] M. V. STENIOWSKI,[3] E. ZANOTTO,[3]
A. I. GROMYKO,[1] & I. ARITA[1]

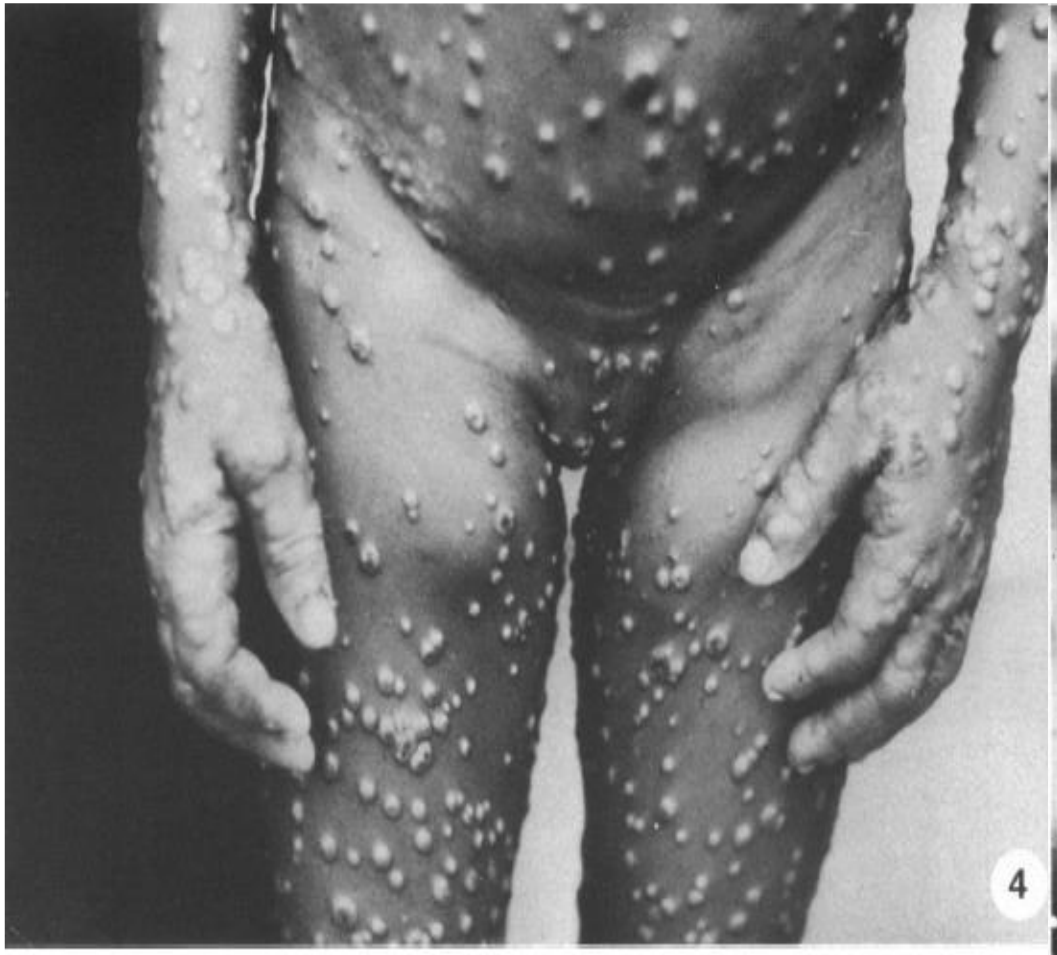
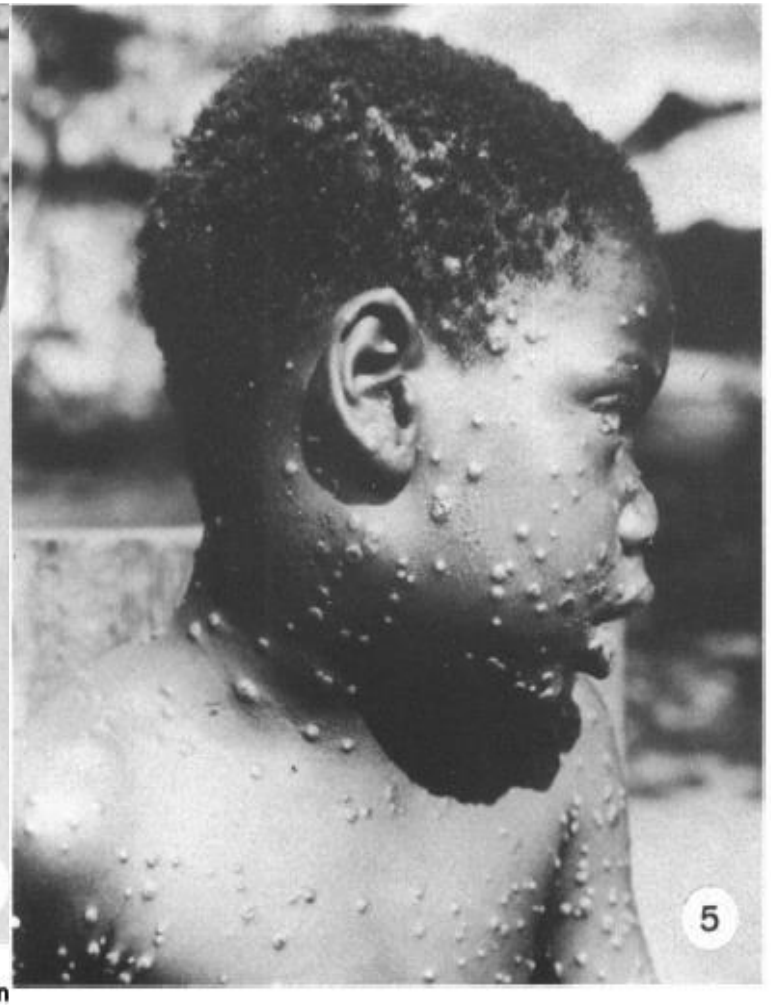


Fig. 4. Heavy concentration of lesions on the hands, inguinal lymphadenopathy, and pustules on genitalia.



Swollen lower face and neck due to cervical and submandibular lymphadenopathy.

# 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

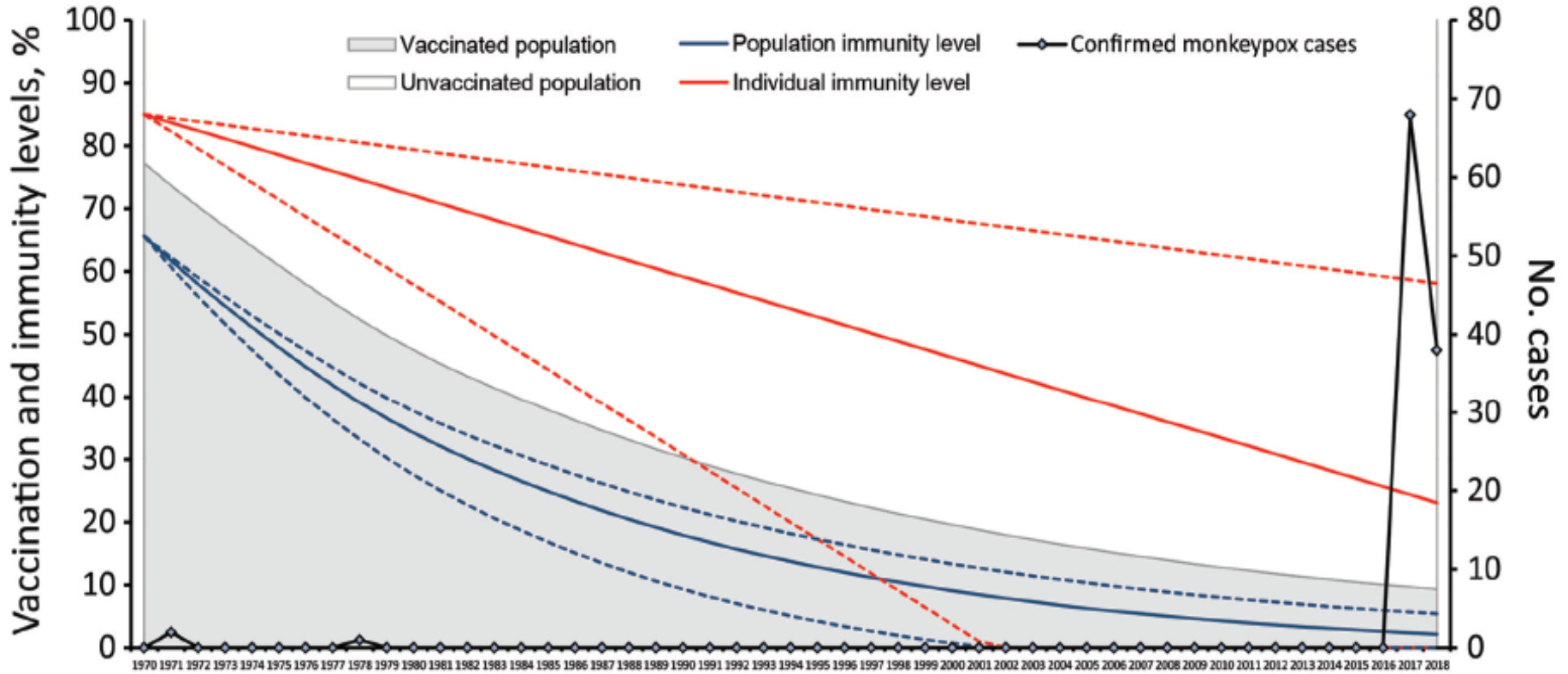



**Figure 1.** Relationship between population- and individual-level smallpox vaccination and immunity rates and resurgence of monkeypox cases in Nigeria, 1970–2018.

# 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]

Table 2. Average annual incidence of human monkeypox by age group and vaccination status, in health zones with active disease surveillance, Sankuru District, Democratic Republic of the Congo: 2006–2007

| | Unvaccinated* | | | Vaccinated | | | Unvaccinated vs. vaccinated | | |
|---|---|---|---|---|---|---|---|---|---|
| Age group | MPX† cases | Incidence‡ | 95% CI§ | MPX cases | Incidence‡ | 95% CI§ | Incidence ratio¶ | 95% CI§ | *P* values |
| >0–4 | 185 | 8.87 | 7.68–10.24 | — | — | — | — | — | — |
| 5–9 | 167 | 7.06 | 6.07–8.22 | — | — | — | — | — | — |
| 10–14 | 185 | 9.35 | 8.10–10.80 | — | — | — | — | — | — |
| 15–19 | 96 | 7.03 | 5.75–8.58 | — | — | — | — | — | — |
| 20–24 | 52 | 4.16 | 3.18–5.46 | 2‖ | 5.91 | 0.72–21.50 | 0.70 | 0.17–2.89 | 0.627 |
| 25–29 | 29 | 4.58 | 3.19–6.58 | 6 | 2.87 | 1.06–6.29 | 1.59 | 0.66–3.84 | 0.298 |
| 30+ | 17 | 6.35 | 3.97–10.17 | 21 | 0.59 | 0.39–0.91 | 10.77 | 5.68–20.41 | <0.001 |
| Total | 731 | 7.35 | 6.84–7.90 | 29 | 0.76 | 0.53–1.10 | 9.64 | 6.65–13.97 | <0.001 |
| *b.* > *1980* | 695 | 7.36 | 6.83–7.92 | 3 | 4.50 | 0.93–13.16 | 1.63 | 0.52–5.07 | 0.307 |
| *b.* ≤ *1980* | 36 | 4.05 | 2.92–5.60 | 26 | 0.78 | 0.53–1.14 | 5.21 | 3.14–8.62 | <0.001 |

*Bulletin of the World Health Organization*, 66 (4): 459–464 (1988)


# Clinico-epidemiological features of monkeypox patients with an animal or human source of infection

Z. JEŽEK,[1] B. GRAB,[1] M. SZCZENIOWSKI,[2] K. M. PALUKU,[2] & M. MUTOMBO[2]

Table 2. Distribution of the main characteristics of the exanthem in unvaccinated monkeypox patients, by presumed source of infection

| Characteristics | Infection from animal source | Infection from human source |
|---|---|---|
| Occurrence: | | |
| Monomorphic[a] | 176 (79.3)[b] | 57 (78.1) |
| Pleomorphic[a] | 46 (20.7) | 16 (21.9) |
| Total observed | 222 | 73 |
| Lesions: | | |
| Discrete | 124 (55.9) | 48 (65.8) |
| Semiconfluent | 70 (31.5) | 23 (31.5) |
| Confluent | 28 (12.6) | 2 (2.7) |
| Haemorrhagic | 0 (0) | 0 (0) |
| Total observed | 222 | 73 |
| Body distribution: | | |
| Centrifugal | 192 (86.5) | 54 (74.0) |
| Centripetal | 8 (3.6) | 5 (6.8) |
| Indefinite | 22 (9.9) | 14 (19.2) |
| Total observed | 222 | 73 |
| Presence of pocks: | | |
| Facial | 196 (88.3) | 60 (82.2) |
| Palmar | 157 (70.7) | 49 (67.1) |
| Plantar | 156 (70.3) | 40 (54.8) |

[a] Monomorphic = all lesions at the same stage; pleomorphic = more than one crop of lesions.
[b] Figures in parentheses are percentages.

Table 3. Frequency of lesions on mucous membranes and of tonsillitis in unvaccinated monkeypox patients, by presumed source of infection

| | Infection from animal source | Infection from human source |
|---|---|---|
| Total observed | 222 | 73 |
| Lesions on mucous membranes:[a] | 175 (78.8)[b] | 50 (68.5) |
| Oral | 166 (74.8) | 41 (56.2) |
| Conjunctival | 45 (20.3) | 12 (16.4) |
| Genital | 74 (33.3) | 14 (19.2) |
| Absent | 47 (21.2) | 23 (31.5) |
| Tonsillitis: | | |
| Present | 119 (53.6) | 29 (39.7) |
| Absent | 103 (46.4) | 44 (60.3) |

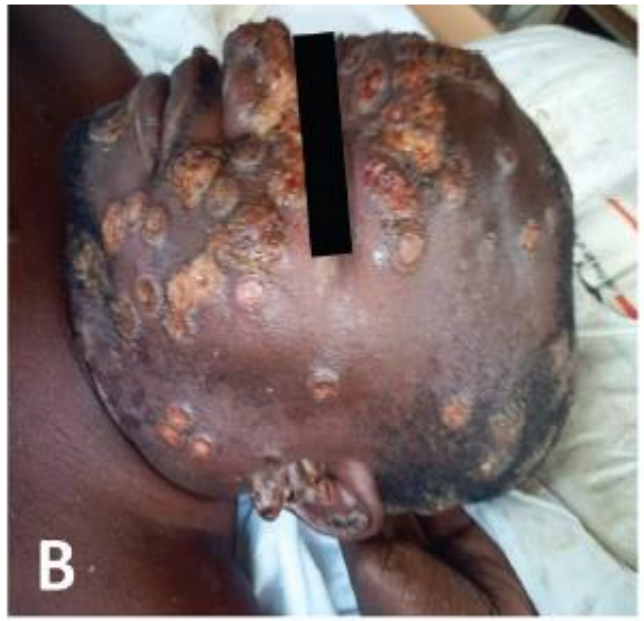
[a] For several patients more than one site was affected.
[b] Figures in parentheses are percentages.

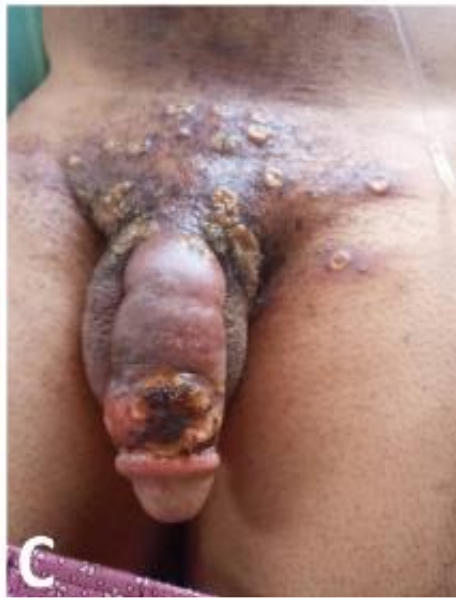
*Clinical Infectious Diseases*

BRIEF REPORT

# Clinical Course and Outcome of Human Monkeypox in Nigeria

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



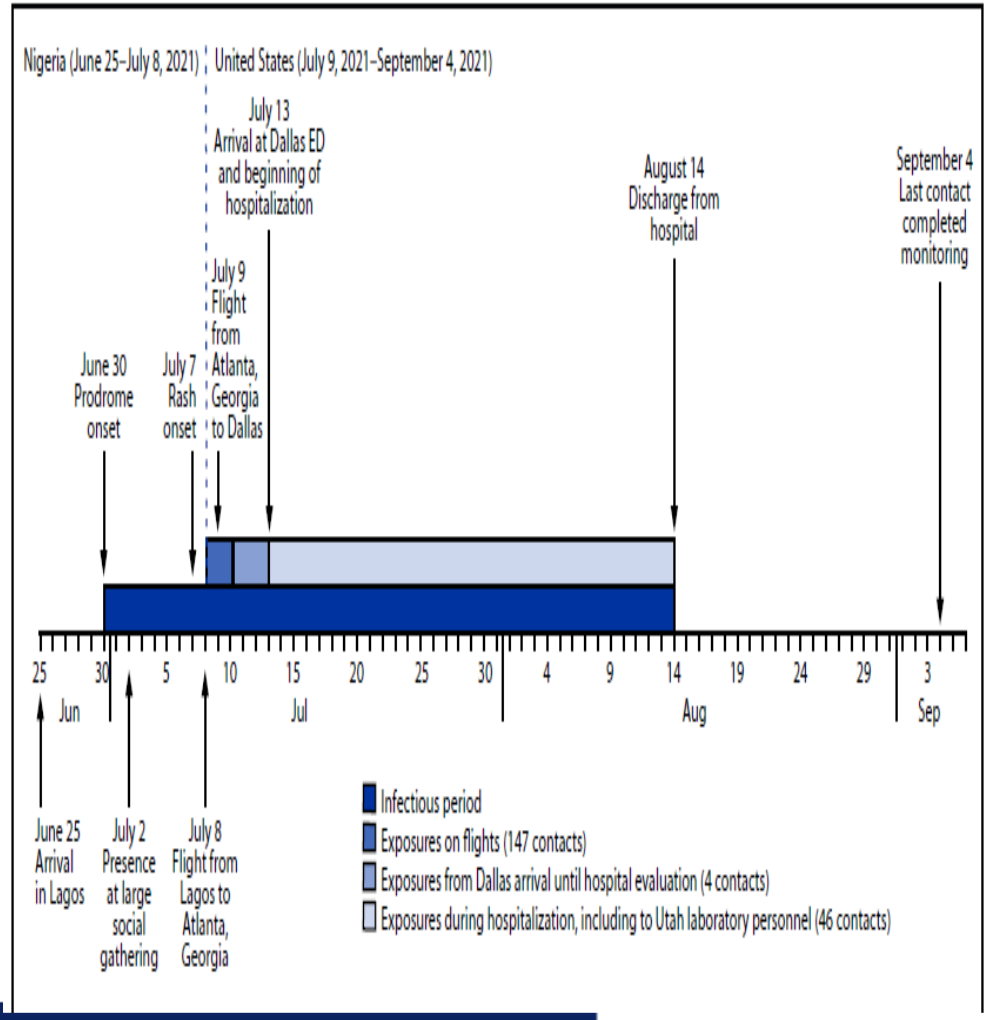

The demographic and clinical characteristics of the 40 cases in relation to their HIV status are summarized in Table 1. The cases were 28 days to 54 years of age (median, 32 years) and the majority (77.5%) were male.

The following clinical features were observed: skin rash (n = 40), fever (n = 36), lymphadenopathy (n = 35), genital ulcer (n = 25), body aches (n = 25), headache (n = 19), sore throat (n = 18), pruritus (n = 15), and conjunctivitis and photophobia (n = 9). Nasal congestion, cough, skin ulcers, and hemorrhagic skin lesions were observed in 5 cases each. Other less common features were nausea and vomiting (n = 3), hepatomegaly (n = 3), and scrotal edema (n = 2).

Of 35 cases who gave details of their first symptom, 23 (65.7%) had rash as the first symptom, while 12 (34.3%) had fever as first symptom. In 2 patients, genital rash associated with ulcer was the first symptom. Skin rashes were observed on the following sites: face (97.5%), trunk (92.5%), arms (87.5%), legs (85%), genitalia (67.5%), scalp (62.5%), palms (55%), soles (50%), mouth (37.5%), and eyes (25%).

# Monkeypox in a Traveler Returning from Nigeria — Dallas, Texas, July 2021

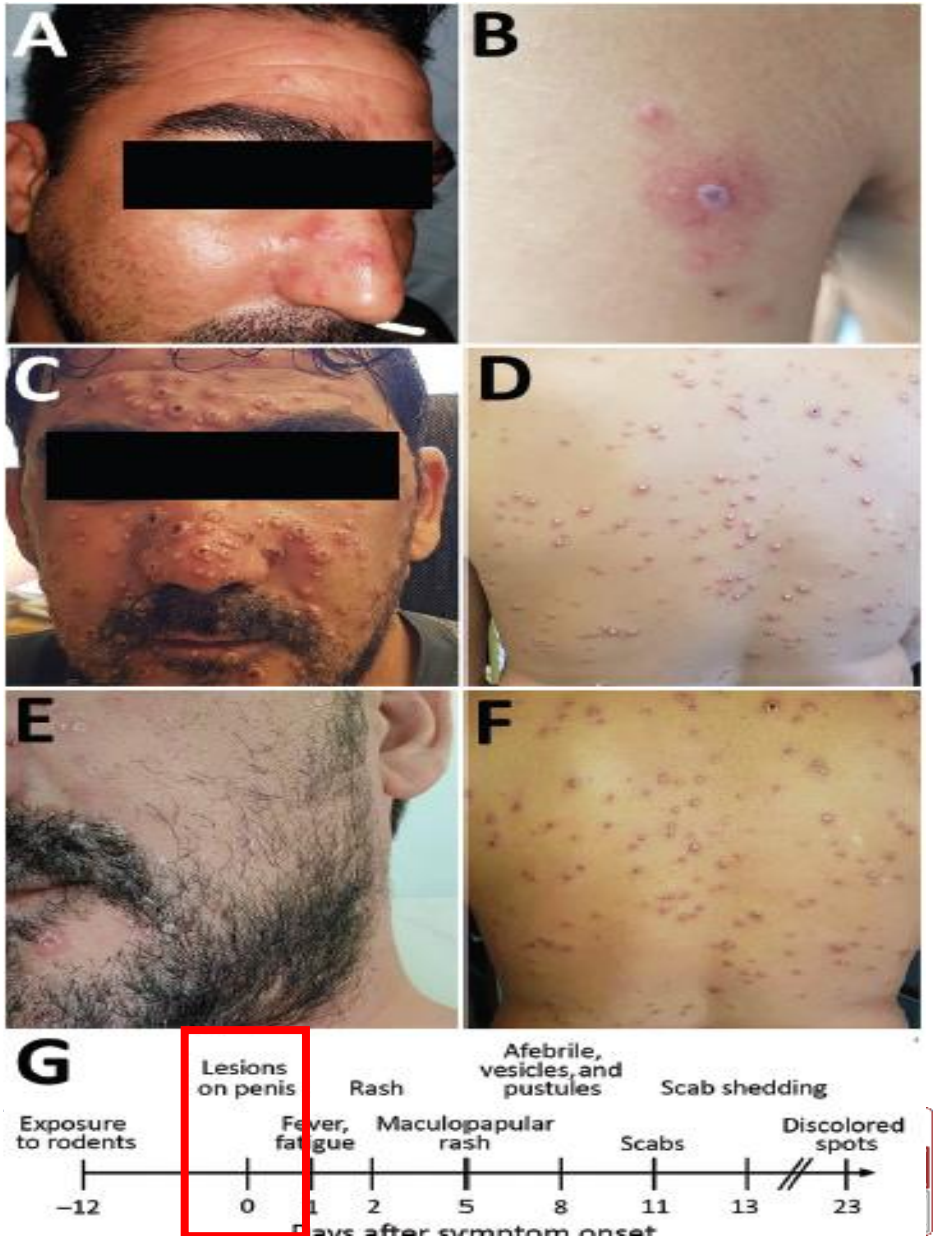
FIGURE. Time line of patient activities and potential exposures to *Monkeypox virus* from patient's arrival in Lagos, Nigeria to completion of monitoring for the last exposed known contact — Dallas, Texas, June–September 2021




# Diagnosis of Imported Monkeypox, Israel, 2018

Noam Erez,[1]

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 25, No. 5, May 2019



# Ongoing Monkeypox outbreak outside Africa


## Event background

On 7 May 2022, the United Kingdom (UK) reported an imported case of monkeypox (MPX) in a person travelling from Nigeria. The case reported developing a rash-like illness on 29 April 2022 and travelled from Lagos to London on 3-4 May. The diagnosis was confirmed by monkeypox virus (MPXV) PCR on a vesicular swab on 6 May by the UK Health Security Agency (UKHSA) Rare and Imported Pathogens Laboratory.

On 13 May 2022, the UK reported two further cases of MPX who are part of the same family and not linked to the single imported case from Nigeria which was notified on 7 May. The cases were confirmed by PCR testing on vesicle swabs. A third family member had previously developed a rash but recovered fully. None of the individuals in this cluster had travelled or had contact with anyone with a relevant travel history [1].

On 15 May 2022, the UK reported four additional cases of MPX, confirmed by PCR. None of these cases have known epidemiological links to the imported case from Nigeria (notified on 7 May) or to the family cluster (notified on 13 May). The four cases were men who have sex with men (MSM) and presented with a vesicular rash-like illness. They were identified through attendance at genitourinary medicine (GUM) clinics. The cases are being managed in high consequence infectious diseases units in the UK [1].

On 18 May 2022, two additional cases (also MSM) were reported, one in London and one in the South-East of England[1].

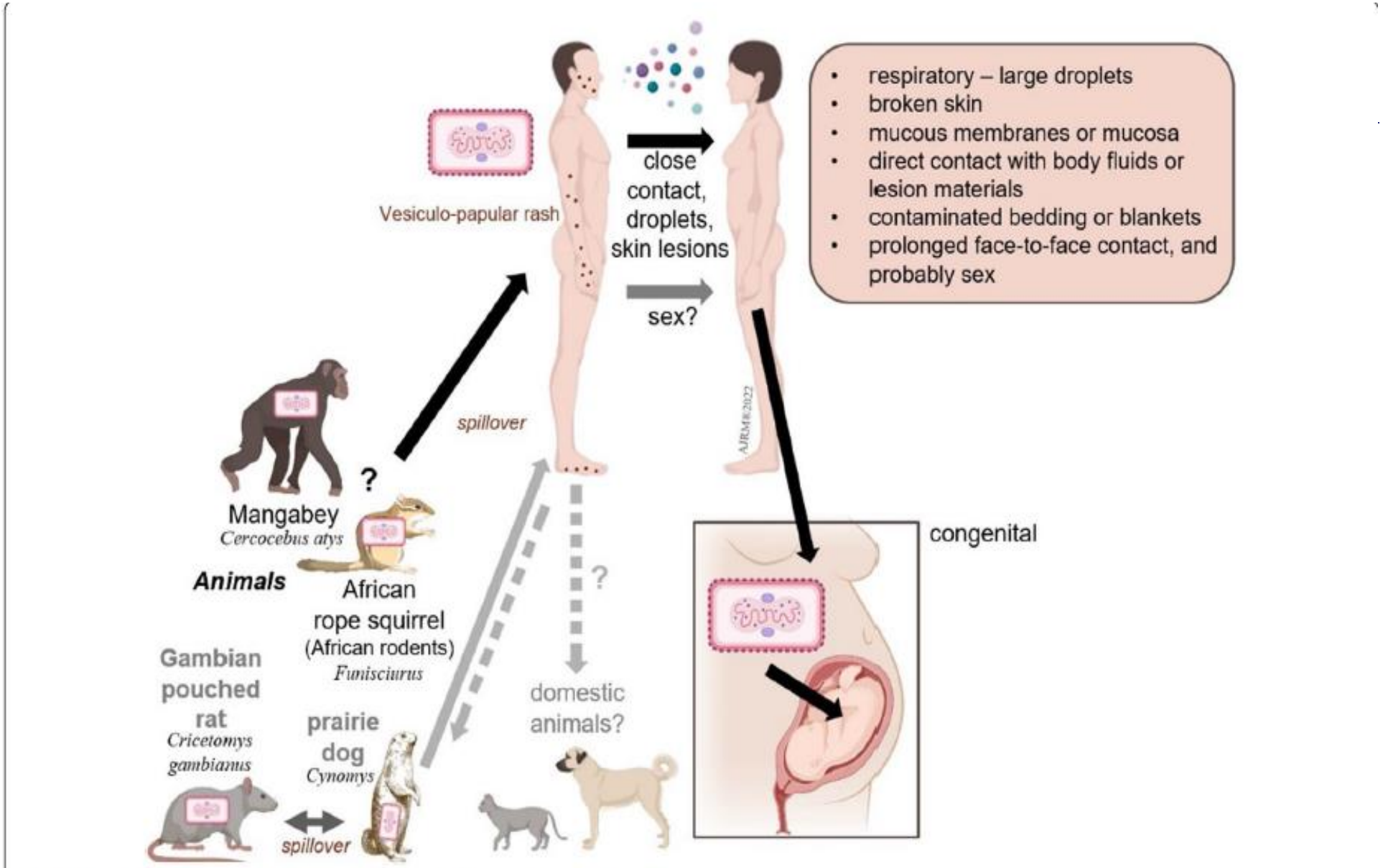
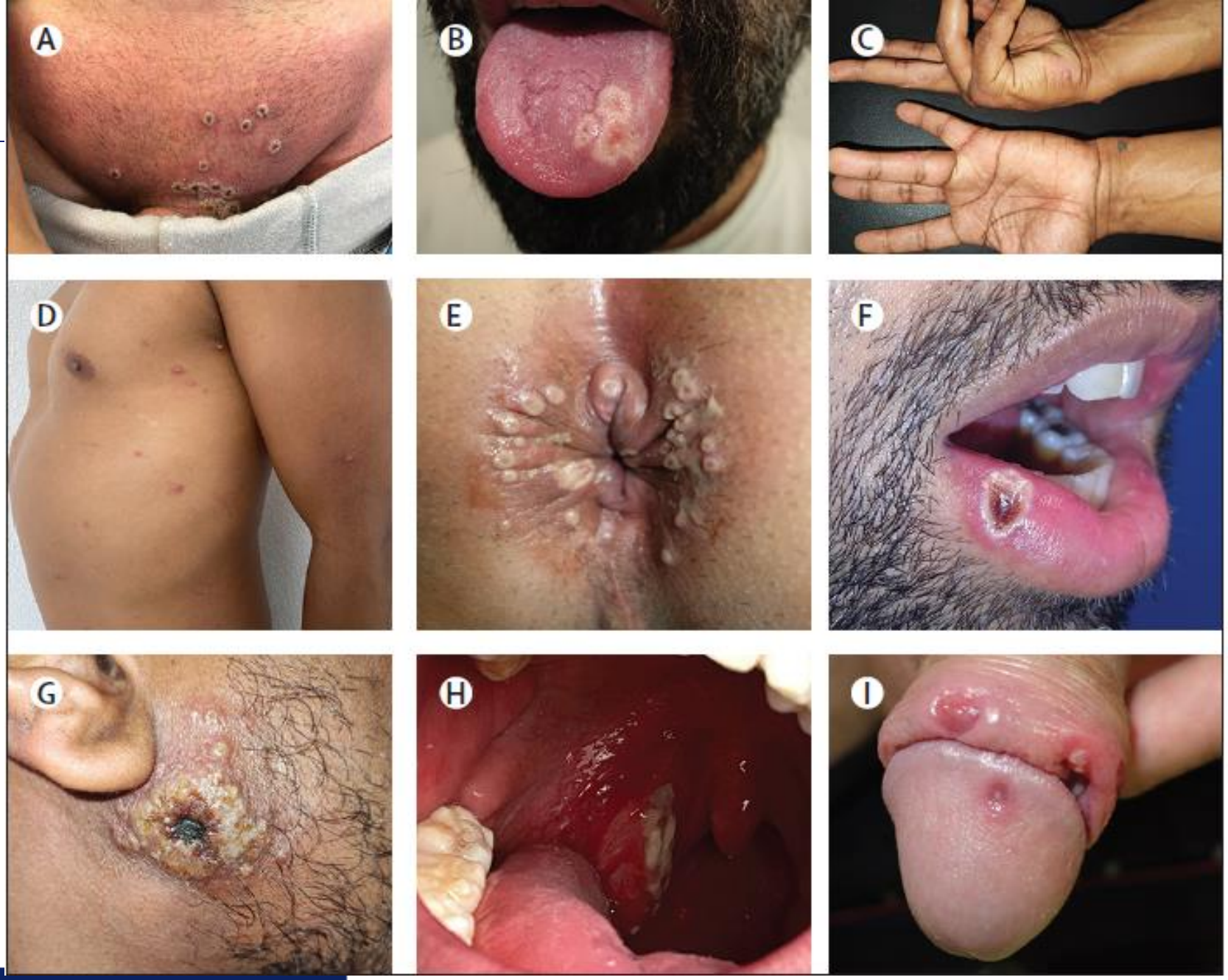



**Fig. 1** Transmission routes associated with monkeypox infection






Tarin-Vicente EJ et al. Lancet, August 8, 2022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