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Looking in apes as a source of human pathogens

Mamadou B. Keita, Ibrahim Hamad, Fadi Bittar*

Aix Marseille Université, URMITE, UM63, CNRS 7278, IRD 198, Inserm 1095, 13005 Marseille, France

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ABSTRACT

Because of the close genetic relatedness between apes and humans, apes are susceptible to many human infectious agents and can serve as carriers of these pathogens. Consequently, they present a serious health hazard to humans. Moreover, many emerging infectious diseases originate in wildlife and continue to threaten human populations, especially vector-borne diseases described in great apes, such as malaria and rickettsiosis. These wild primates may be permanent reservoirs and important sources of human pathogens. In this special issue, we report that apes, including chimpanzees (*Pan troglodytes*), bonobos (*Pan paniscus*), gorillas (*Gorilla gorilla* and *Gorilla beringei*), orangutans (*Pongo pygmaeus* and *Pongo abelii*), gibbons (*Hylobates* spp., *Hoolock* spp. and *Nomascus* spp) and siamangs (*Symphalangus syndactylus syndactylus* and *Symphalangus continentis*), have many bacterial, viral, fungal and parasitic species that are capable of infecting humans. Serious measures should be adopted in tropical forests and sub-tropical areas where habitat overlaps are frequent to survey and prevent infectious diseases from spreading from apes to people.

1. Introduction

It is well known that the majority of emerging infectious diseases are of zoonotic origin and are primarily caused by wildlife- or vector-borne pathogens [1]. The increased incidence of zoonoses highlights the critical need for real-time pathogen monitoring in wildlife animals, especially in at-risk regional “hotspots” where new emerging infectious diseases have been reported [1].

Apes (superfamily Hominoidea) include the lesser apes, known as gibbons and siamangs, that are represented by 4 genera (*Hoolock*, *Hylobates*, *Symphalangus* and *Nomascus*) and the great apes that also contain 4 genera (*Homo* (humans), *Pan* (chimpanzees and bonobos), *Gorilla* (gorillas) and *Pongo* (orangutans)) [2]. Because of their high genomic similarity and close evolutionary relationships to human beings, apes share many diseases with humans [3]. These shared infectious diseases may result from pathogens inherited from a common ancestor [4]. However, cross-species transmission between close relatives is also possible. Many factors can create opportunities for pathogen transmission between apes and humans, including their frequent contact during ecotourism, searching for food, research or simply sharing the same ecosystem (i.e., habitat overlap) [5]. The establishment of new infections in humans depends on both the pathogen and human biology (i.e., the capacity of pathogen to expand its host range and become a human pathogen) [5]. Ape pathogens most likely need very few changes, if any, to infect humans. Thus, the absence of appropriate and timely immune responses in the naive humans leads to the emergence and rapid spread of the infectious diseases [5].

Mathematical models showed that a high proportion of pathogens are shared between close relatives such as humans and apes [4–7]. Moreover, recent research has alerted the scientific communities to the emergence of human infections linked to African great apes [8]. Chimpanzees were found to be the natural reservoir of the pandemic and non-pandemic human immunodeficiency virus type 1 (HIV-1) [9], the causative agent of acquired immune deficiency syndrome (AIDS). Moreover, a new *Mycobacterium tuberculosis* strain was recovered from a wild chimpanzee [10], and gorillas were identified as the origin of the human malaria parasite *Plasmodium falciparum* [11]. *Rickettsia felis*, an emerging vector-borne pathogen that causes rickettsioses, was documented in the feces of many species of apes, including gorillas, chimpanzees and bonobos [12]. It is important to note that for AIDS and malaria, African great apes have much more variety of causative related pathogens than those in humans. This difference in pathogen variety suggests that either some specific ape pathogens have not yet been able to infect and spread widely throughout the human population or that cross-infection/adaptation of these species in human beings yet to occur [8].

* Corresponding author. Aix Marseille Université, Faculté de Médecine, URMITE, UM63, CNRS 7278, IRD 198, Inserm 1095, 27 Bd Jean Moulin, 13005 Marseille, France. Tel.: +33 4 91 83 56 49.
E-mail address: fadi.bittar@univ-amu.fr (F. Bittar).

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Unfortunately, the published data regarding pathogens of the apes that live in Asia remain quite poor. Large surveillance efforts in these ape populations are required to document the potential for zoonotic diseases from this continent to spread to humans.

Although the transmission of infectious diseases between apes and humans can occur in both directions, this review focuses on the importance of apes as carriers and possible source of infective organisms that have the potential to become human pathogens.

2. Apes as a reservoir and source of human pathogenic bacteria

Although bacterial and rickettsial diseases represent more than half of the emerging infectious diseases worldwide [1], the literature contains few reports regarding the pathogenic bacteria of apes and no report of transmission to human beings. Enteric bacterial agents such as *Salmonella* spp., *Shigella* spp., *Campylobacter* spp. and *Escherichia coli* can be carried by many species of gorillas [13,14]. Feces of infected animals are the most likely primary sources of these bacteria. Nizeyi et al. reported that the prevalence of isolation for *Campylobacter* spp., *Salmonella* spp., and *Shigella* spp. in mountain gorillas (*Gorilla gorilla beringei*) from Uganda is 19%, 13%, and 6%, respectively, without enteric illness in any observed gorillas [13]. *Salmonella* species and *Shigella* spp. (*Shigella sonnei*, *Shigella boydii*, and *Shigella flexneri*) were isolated principally from subadult and adult gorillas [13]. However, the prevalence of these enteropathogens may have been underestimated due to the low sensitivity of the classical methods used for their detection. The molecular survey conducted recently by Whittier et al. on *G. beringei* using real-time PCR confirmed that the prevalence of *Campylobacter* spp. can reach 85% in mountain gorilla populations [15].

Respiratory bacterial agents have also been recovered in wild great apes (chimpanzees and gorillas) [16–18]. Three bacteria including *Pasteurella multocida*, *Streptococcus pneumoniae* and *Klebsiella pneumoniae,* which are also infectious to humans, have been detected in apes that died from pneumonia. Molecular characterization of these strains indicated the presence of pathogenicity factors such as type 4 fimbriae and superoxide dismutases in *P. multocida* and pneumolysin in *S. pneumonia* that could explain their potential virulence relevance [16,17]. However, in most cases, a viral upper respiratory tract infection by metapneumovirus predisposed these great apes to bacterial infections [16–18].

Several emerging bacteria have been characterized and found to be infective in wild great apes; these bacteria include *Bacillus anthracis* [19] and *M. tuberculosis* [10]. First, two outbreaks of anthrax caused by a variant of *B. anthracis* "*B. cereus* var. *anthracis*" killed at least 6 chimpanzees in Côte d'Ivoire and 3 chimpanzees and one gorilla in Cameroon [19]. Moreover, a recently case of a wild chimpanzee infected with *M. tuberculosis* has been documented in Côte d'Ivoire [10]. The phylogenomic analyses demonstrated that this strain belongs to a new lineage of the *M. tuberculosis* complex, but it is more closely related to lineage 6 that has been described in humans and is known as *Mycobacterium africanum* (West Africa 2) [10].

Finally, *R. felis*, a fastidious intracellular pathogen transmitted to human by ectoparasites and the bites of infected mosquitoes, has also been detected in gorilla, chimpanzee and bonobo feces using molecular methods [12]. In the aforementioned study, the feces of 11% of apes living in the wild (a total of 1028 samples tested) were found to be positive for *R. felis* and *R. felis*-like organisms, thus indicating the importance of apes as potential host or reservoir for this emerging rickettsial bacterium in sub-Saharan Africa where its infection is a common public health problem [12].

3. Apes as a reservoir and source of human pathogenic viruses

There have been various studies demonstrating that apes, especially African great apes, constitute a potential reservoir and source of numerous human pathogenic viruses [20] (Fig. 1). Most species of apes, if not all, can carry retroviruses (family *Retroviridae*) including simian immunodeficiency viruses (SIVs), simian T-cell lymphotropic viruses (STLVs) and simian foamy viruses (SFVs). Thus, considerable research has been conducted to understand the prevalence, genetic diversity, geographic distribution and transmission of these viruses in ape populations [21,22]. It is now well established that the human immunodeficiency viruses HIV-1 groups M and N are very closely related to SIVcpzPtt of chimpanzees (*Pan troglodytes troglodytes*) and thus are of chimpanzee origin, while HIV-1 group P is of western gorilla (*Gorilla gorilla gorilla*) origin [22]. Despite numerous interspecies transfers of the retrovirus from apes to human, only HIV-1 group M originated from chimpanzees in Cameroon and subsequently spread worldwide to become responsible for the pandemic form of AIDS in humans [9,21,22]. Currently, no evidence has been found of SIV infections in Asian apes (orangutans and gibbons) [23]. In contrast to SIVs that are present principally in African gorillas and chimpanzees, STLVs are also retroviruses but are widely distributed among African and Asian apes including gorillas, chimpanzees, orangutans and gibbons [23,24]. In the early 2000s, a serological survey followed by molecular confirmation indicated that a wild-caught gorilla and a wild-caught chimpanzee were infected with STLV-1 strains that were closely related to HTLV-1 strains present in human inhabitants of the same region (south Cameroon); this suggests the possible transmission of STLV-1 to humans from African apes [24]. More recently, phylogenetic studies confirmed this conclusion and showed that STLVs cluster according to geographical origin rather than by host species, leading to the hypothesis that many interspecies transmissions have occurred between primates, including those from apes to humans [21,23].

Ebola virus belongs to the *Filoviridae* family and is a highly virulent virus of humans and nonhuman primates that causes severe hemorrhagic fever and death within few days. This virus has been responsible for outbreaks in several countries of Sub-Saharan Africa, such as the Democratic Republic of Congo, Gabon, Sudan, Ivory Coast, Uganda and, most recently, Guinea [25,26]. Although bats are considered the natural hosts of filoviruses, Ebola virus transmission to humans appear to be linked to direct contact with live or dead apes. Hunters that come into contact with the infected gorilla and chimpanzee carcasses are especially at risk of contracting the disease [25]. Recent surveillance of Asian apes in Indonesia for filoviruses showed that 18.4% of healthy orangutans (*Pongo pygmaeus*) are seropositive for the Ebola virus. This high seroprevalence in asymptomatic orangutans suggests that this ape may serve as carrier or host and thus could present a potential risk for humans living in this region of Asia [27].

The hepatitis B virus (family *Hepadnaviridae*) has also been characterized in apes from both Africa and Asia at high frequencies comparable to those obtained from humans in endemic zones [28]. The presence of cross-species transmission and/or recombination between human and ape hepatitis B virus variants [28] and the close genomic similarity of human and ape hepatitis B viruses [29] calls for extensive phylogenetic investigations to understand the diversity, the evolution and the worldwide spread of this virus.

Other pathogenic viruses, including adenoviruses [30] (family *Adenoviridae*), *Lymphocryptovirus* [31] and cytomegaloviruses [32] (family *Herpesviridae*), metapneumoviruses [16-18] (family *Paramyxoviridae*), polyomaviruses [33] (family *Polyomaviridae*) and enteroviruses [34] (family *Picornaviridae*), are not exclusively

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