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Simian Spillovers.
Primatology in the Age of Pandemics

For those of us tracking gorillas, chimpanzees, bonobos or orangutans in Africa or Asia, the jungle finally comes home. Because wearing surgical masks and respecting social distancing is what we do for a living – and to save lives...

There is no shortage of diseases that spread from animals to people (zoonoses) or from people to animals (anthroponoses), including virus infections causing dengue, smallpox, rabies or influenza. And by now, we surely can spell "surivanoroc" backwards. Disregarding devastating consequences for a moment, those inter-species jumps are actually a beautiful illustration of how all organisms are linked through evolution – with transmission more likely between those more closely related.

Face-masked primatology in the Congo. (Photo: LuiKotale / Barbara Fruth)

The Human Touch

Thoughts about passing on germs were far from the mind when primatological field work entered into its golden age in the mid-1960s. Front pages of *National Geographic* soon displayed images of Jane Goodall, Diane Fossey and Birutė Galdikas in physical contact with wild chimpanzees, gorillas and orangutans. After all, those were truly mystical moments, when pioneering primatologists made first contact and literally held hands with potentially ferocious relatives. After so much investment of blood, sweat and tears (think treacherous thickets, trails, thorns), what could be more rewarding than hugging and playing with increasingly trustful beautiful beasts? The interspecies affair wasn't one-sided at all – gentle touches or rough-and-tumble were often initiated by the fellow apes themselves.

Alas, those foreign explorers were ignorant that they carried germs against which the tropical inhabitants lacked resistance. Similar to how measles brought by Iberian conquistadores wiped out original populations in the Americas, many non-human apes would die from polio or respiratory infections. (While no consolation to those who passed away, it must be noted that their entire communities would by now have disappeared due to poaching and habitat destruction by humans – had these early primate scientists not soon pushed to create protected areas.)

Spatially distanced observation of apes. (Photo: LuiKotale / Barbara Fruth)

Since those early days, procedures changed drastically. Today, anyone wishing to observe great apes in the wild must be vaccinated to prevent contagion of yellow fever, MMR, polio – you name it. Other rules enforce "social distancing" between human and non-human apes – with 10 meters increasingly recommended. Disposable surgical face masks need to be worn. And upon hearing a "call of nature", you have to bury any tangible outcome. Primatologists like myself who serve the *Primate Specialist Group* (PSG) of the *International Union for the Conservation of Nature* (IUCN) are constantly updating best-practice guidelines.

The youngest members of the study communities might show little respect for our efforts. Since birth, they grew up with the sight of those intriguing bipedal beings, feeling perennially tempted to touch them. We aim to deter such intentions, by ignoring the advances or forcefully stamping the ground. This surely goes against inclination. Because, who wouldn't want to cuddle a fluffy gorilla?

Although field researchers try hard to reduce infections, other humans pose considerable risks. East Africa's mountain gorillas sometimes suffer from mange, mange, caused by parasitic mites spread via domestic animals. In West Africa, apes perish from anthrax, a severe bacterial disease affecting skin and lungs, transmitted by cattle entering forests. Ebola fever has been particularly devastating. An infection kills half of afflicted humans – but three quarters of chimpanzees and 95 percent of gorillas. After an outbreak in jungles of Gabon and the Republic of the Congo, ape populations were practically wiped out.

While the fate of apes generates headlines, succumbing monkeys receive far less attention. Take yellow fever in South-eastern Brazil, which endangers primates in forest islands that remain in a sea of human settlements and land use. Here, because of spatial proximity, more contact occurs – such as when people collect wood for construction or cooking, or when monkeys venture out to feast on crops. Uncounted thousands of marmosets, howler and titi monkeys already died from the mosquito-transmitted virus. Survivors may be persecuted by fearful locals, albeit such revenge killings worsen the situation as hunters are likely to infect themselves.

A bunch of happy bonobos – no humans allowed to join. (Photo: LuiKotale / Barbara Fruth)

Jumping the Lineage

Our field research often pairs up with laboratories. Such "synthetic primatology" is increasingly concerned with diseases. For this, we collect biological samples from animals, both wild and domestic, and local humans alike – including faeces, urine, food remains, soil from forest floors or fields, flies or trapped mosquitoes. These collections are made accessible to leading labs, such as those at the Robert Koch Institute (RKI) in Berlin or the School of Medicine at the University of Pennsylvania.

For example, a recent RKI-led study investigated the evolutionary history of herpesviruses found in hominines – the taxonomic group that includes gorillas, chimpanzees, bonobos and humans. The research utilized 675 faecal samples obtained at 20 sites in 11 sub-Saharan countries, covering all 9 species and subspecies of non-human African apes. Samples included rarely studied types of apes, such as the Nigeria-Cameroon chimpanzee (via the Gashaka Primate Project, directed by myself in North-

eastern Nigeria) or bonobos (via the LuiKotale project in DR Congo, directed by my colleagues Gottfried Hohmann and Barbara Fruth).

Biological samples – such as these faeces of Nigerian chimpanzees – hold clues to virus evolution. Nowadays, DNA can not only be extracted from the dung itself, but also from flies trapped in the surrounding forest. (Photo: Gashaka Primate Project)

Herpesviridae is a family of large double-stranded DNA viruses that infect many vertebrates, causing harmless to fatal diseases from cutaneous lesions, blisters, genital herpes to chickenpox, shingles or Kaposi's sarcoma. Parasites generally don't benefit from killing their hosts, as this disrupts the chain of transmission. However, newly emerging infective agents (such as corona-viruses) haven't learned that yet and often behave like any "young and wild" creature, causing havoc. More "mature" viruses tend

to become less harmful for their hosts, while still ensuring diffusion (think kissing, with lip sores the only punishment).

In fact, most mammalian herpes infections remain asymptomatic – indicative of long-term co-evolution with their host. The affected parties have, so to speak, arrived at a stage of mutually beneficial co-existence. Viruses therefore often become host-specific, mutating "within" their carriers – in a process of co-divergence. With this, cross-species transmission should become rarer and rarer.

To reconstruct the evolutionary history of hominine cytomegaloviruses (CMV) causing herpes, RKI scientists applied a battery of sophisticated methods, including genetic analyses based on PCR (polymerase chain reaction) and probabilistic Bayesian statistics. Results indeed suggest various degrees of co-divergence, but, interestingly, also host switches. Molecular clock computations suggest a transmission of the CMV1 virus type as early as 2.2 mya (million years ago) from gorillas to the lineage of panines (the ancestors of chimpanzees and bonobos). A further transmission of the CMV2 virus type from panines to gorillas likely happened 1.2 mya.

Cross-species transmission requires opportunity. Indeed, chimpanzees and gorillas often lived (and live) in sympatry in rainforests. Thus, groups of both species may forage in the same plant food patch. This allows for viral transmission, whether oral-faecal or via contaminated food items including chewed-up and discarded fruit wedges.

Bonobos, however, occur only South of the Congo river, spatially separated from their close chimpanzee relatives and gorillas. This segregation occurred 0.87 mya – a timeline established by molecular and anatomical comparisons. Interestingly, the data confirm that bonobo and chimpanzee CMV1 and CMV2 virus variants separated in almost perfect synchrony with the divergence of the two ape hosts, at 0.82 mya.

Probing for Cures

We already know of other cross-hominine transmission events, notably of the malaria agent *Plasmodium falciparum* which switched from gorillas to humans, and the HIV-1 agent which switched from chimpanzees to humans. Importantly, while offering fascinating academic insights, such research also holds promise for cures.

Thus, virologists at the University of Pennsylvania studied how human and simian immunodeficiency viruses (HIV/SIVs) use the primary receptor CD4 to enter target cells. Utilizing chimpanzee samples from the Gashaka region in Nigeria and elsewhere, the lab identified coding variants of the receptor that provide antiviral protection – a discovery that may improve treatment. In the same vein, researchers at St. Andrews University

Close relatives in a tangle... Physical contact, such as this interaction with the author, is tabooed in the jungle. However, for orphaned bonobos at the Lola-ya-Bonobo sanctuary, play with humans is a mental life-line. (Photo: Volker Sommer)

aim to understand malaria in humans and chimpanzees inhabiting Nigerian forests – and potentially identify genetic markers associated with increased immunity.

While we are busy in forests and labs, one thing is sure: evolution won't stop. It is only a matter of time, until the next disease agent discovers that its replication is best served by latching on to that perfect host: humans. Not only are humans extremely sociable apes, complete with touchy-feely desires. They also criss-cross the globe, whether driven by famine or war, holidaying or exploration.

Perhaps one day, the vision of the latest *Planet of the Apes* movies will become reality. According to that narrative, a superbug will exterminate humanity, while rendering infected non-human apes more intelligent. Which they won't be for long – unless they become better virologists than we currently are.

Selfie in bonoboland – promising start of an instagram career? (Photo: Volker Sommer)

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