CHAPTER 1

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Review of Ape Disease and Health

Introduction

Ape health is understudied when compared to human health, but it is by no means less complex (see Annex III). Different wild ape species live in a variety of social systems, ranging from semi-solitary orangutans and pair-bonded gibbons to the more gregarious African great apes (see the Apes Overview). The formation of social groups can provide a number of health benefits, from mental and social health to physical health, including via group coordination, increased protection from predators, and enhanced access to grooming partners for the removal of ecto-parasites (Akinyi *et al.*, 2013; Janson and Goldsmith, 1995; Samuni *et al.*, 2018; Wittig *et al.*, 2016). Sociality can also create costs, especially by heightening the risk of exposure to communicable diseases (see Box 1.1).

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Simulation studies comparing disease spread among chimpanzee and orangutan social networks suggest that chimpanzees might generally be more susceptible to the spread of a variety of infectious diseases than orangutans. Accumulated evidence from wild populations, coupled with modeling results, broadly supports the idea that solitary orangutans are less susceptible to communicable diseases, such as ebolaviruses and respiratory diseases, although no systematic comparison of pathogen richness across ape species has yet been undertaken (Carne *et al.*, 2014). Anecdotal reports of mortality associated with disease transmission to orangutans in sanctuaries and zoos are difficult to substantiate and disseminate in the research and ape health practitioner communities. By publishing and documenting cases, practitioners who work in orangutan health can help to fill the knowledge gap concerning the relationship between ape sociality and health.

While sociality can affect disease spread in ape populations, species-specific behaviors can influence exposure to disease. For example, chimpanzees and bonobos (*Pan paniscus*) are known to hunt other mammals, including primates, which can expose them to their prey's pathogens (Leendertz *et al.*, 2011; Samuni, Wegdell and Surbeck, 2020; see Apes Overview). Similarly, apes' settings and degrees of habituation can influence their exposure to pathogens from humans (Grützmacher *et al.*, 2016; Köndgen *et al.*, 2008).

Diseases that can be spread from animals to humans and vice versa are called "zoonoses" (Hubálek, 2003). The past decades have witnessed a rise in emerging zoonotic diseases, the majority of which originate in wildlife (Jones *et al.*, 2008). Disease transmission between species is known as a "spillover event" (Ellwanger and Chies, 2021; see Figure 1.1 and Annex III). As humans' closest living relatives, apes share many of the same genetic, anatomical and physiological features; accordingly, humans and apes tend to be susceptible to similar diseases (Calvignac-Spencer *et al.*, 2021). From a public health perspective, apes are therefore seen as sources or sentinels for human diseases (Calvignac-Spencer *et al.*, 2012). Major human pathogens that originated in apes include the malaria-causing *Plasmodium falciparum* from gorillas and the pandemic HIV-1 group M from chimpanzees (Liu *et al.*, 2010; Sharp and Hahn, 2011). Meanwhile, chimpanzees and gorillas can suffer from diseases that also affect humans, such as yaws and leprosy (Hockings *et al.*, 2021; Mubemba *et al.*, 2020). They have also served as amplifying hosts for ebolaviruses, which has led to several outbreaks in humans (Leroy *et al.*, 2004).

A comprehensive review of the diverse organisms associated with apes would easily fill an entire book and go beyond the scope of this chapter. Rather, the focus here is on health-related issues with available data and a known or likely impact on the conservation or welfare of wild and captive apes. While all apes share certain health issues, those of semi-captive and captive apes largely overlap; the chapter discusses them together to highlight similar challenges as well as management and treatment options. A separate section examines the health of wild apes.

Stakeholders in the fields of public health and conservation usually consider health at the population scale. In contrast, veterinary clinicians, who work mainly in zoos and sanctuaries, focus on individual apes and the groups in their care, with the goal of maximizing animal welfare. This chapter examines aspects of these perspectives for apes in captive and wild settings, based on available data.

Annex III features evidence of confirmed transfers of human pathogens to apes in the wild, excluding anecdotal information. The shortness of this table highlights the critical

FIGURE 1.1

Examples of Pathogen Spillovers between Wildlife and Humans
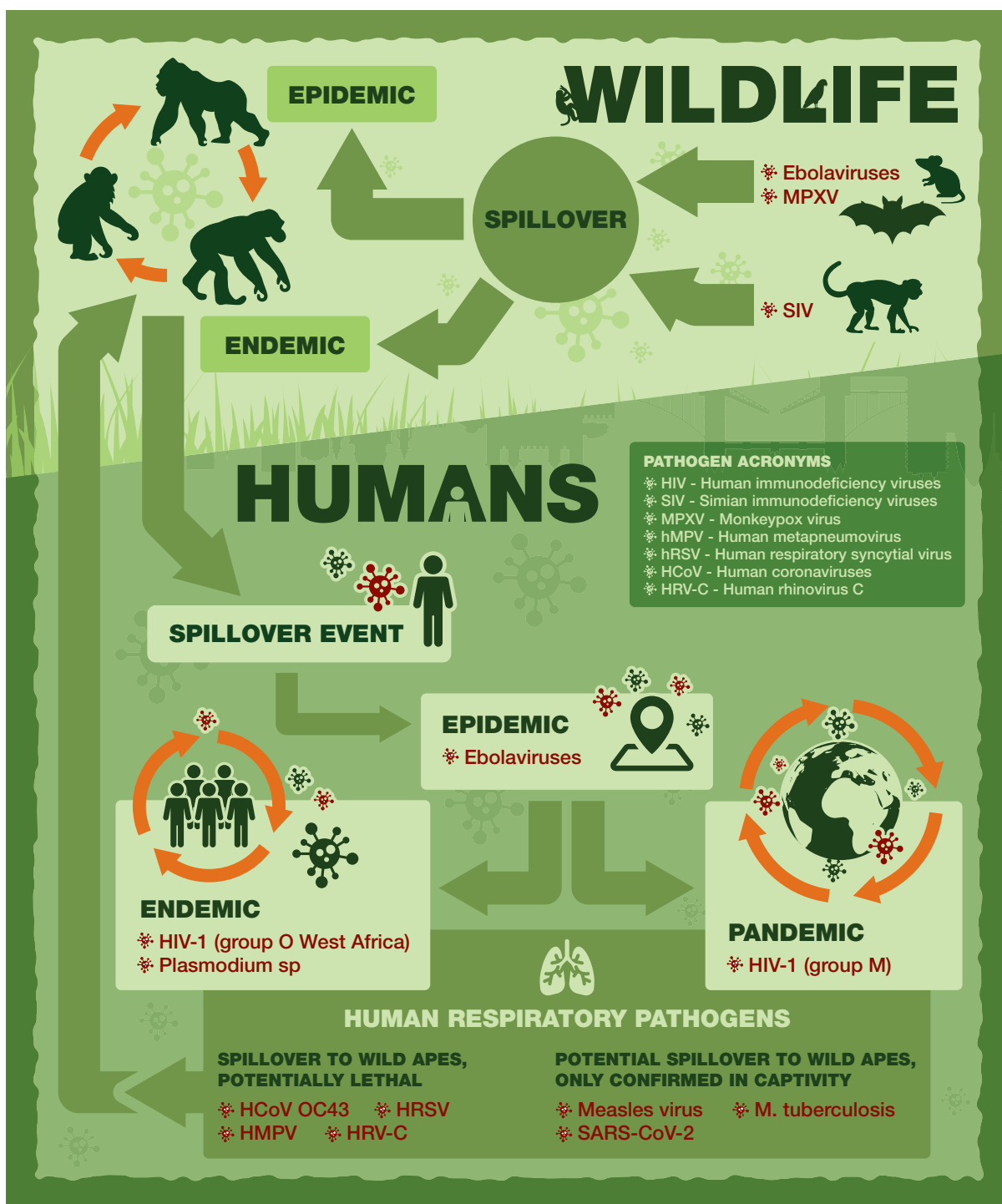
Notes: Arrowheads show directionality of spillover. Potentially lethal pathogens appear in red. Suspected pathogens, which have only been confirmed in captivity, appear in italics. Details and references are available in the main text.

FIGURE 1.2

Properties of Different Settings and Implications for Disease Transmission

WILDLIFE

HUMAN–WILDLIFE CONFLICT
- Destruction of great ape habitats (often for agriculture)
- Shrinking territory lowers food supply
- Food shortages drive apes into villages and farms to "crop raid"
- Creates human-ape conflict with frequent close contact
- Disease transmission in both directions

POACHING
- Illegal hunting of endangered animals
- Close, extended contact with animal body fluids can transmit e.g.: Ebolaviruses, SIV-HIV
- Disease transmission in both directions

RESEARCH AND TOURISM
- Can be a threat to great ape health
- Human respiratory pathogens cause severe disease in great apes
- Can be lethal and affect entire populations
- Hygiene and safety measures important
- IUCN *Best Practice Guidelines for Health Monitoring and Disease Control in Great Ape Populations*

HUMANS

TRADITIONAL MEDICINE AND CONSUMPTION AS FOOD
- Killing and processing of apes
- Sold illegally on wild meat markets
- Direct contact with body fluids during processing and cooking
- Risk of disease transmission for end consumers as well as food processors (e.g. Ebolaviruses, SIV-HIV)

ILLEGAL EXOTIC PET TRADE
- After being poached, apes sold on illegal markets
- Private owners, private zoos
- Prolonged, close contact, high risk for bidirectional disease transmission
- Trade often across contintents
- Potentially spreads pathogens globally

ZOOS AND PRIMATE RESEARCH FACILITIES
- Bidirectional disease transmission possible
- Zoos and research facilities no longer capture apes from the wild
- Nowadays, contact between caretakers/researchers and apes usually rare and limited
- Health and safety measures critical

SANCTUARIES, RESCUE CENTERS AND REHABILITATION CENTERS
- Apes rescued from the illegal exotic pet trade may end up in one of these settings
- Close prolonged contact between caretakers and apes
- Disease transmission in both directions is possible
- Rehabilitation centers may introduce human pathogens to the wild via rehabilitated animals

Note: Details and sources provided in the main text.

need for those working with apes in situ and ex situ to fill the many remaining data gaps on ape diseases. Box 1.2 explores measures, protocols and procedures for the prevention of infectious diseases, as does Chapter 4. Box 1.3 provides an overview of methods used for sample collection from wild and captive apes, which can be used to study different aspects of their health. More information can be found in the relevant literature and through consultation with experts, who can guide the design of prevention strategies, health-monitoring protocols and related systems.

Key findings of the chapter include:

- Apes and humans are susceptible to similar diseases, which allows for spillovers in both directions (see Figure 1.1).
- Health-related risks, challenges and management options vary across wild and captive apes (see Figure 1.2).
- The transmission of respiratory pathogens from humans to apes in both wild and captive settings is common and can cause high morbidity and mortality.
- Infectious diseases are a major conservation threat for wild apes, especially in gregarious species.
- Non-infectious diseases play an important role in the health of captive apes.
- Further research is required to fill knowledge gaps, including with respect to specific diseases, such as myocardial fibrosis, and regarding the relationship between sociality and health.

Wild Apes

Infectious Diseases with a Plausible Effect on Fitness

This section considers several pathogens that have been shown to impact wild ape health or cause mortality. The extreme scarcity of relevant data and observations, however, precludes certainty regarding the extent to which these pathogens affect the survival of ape populations and the frequency with which they cause mortality. More data on the prevalence of these pathogens across ape populations are needed to build a better understanding of their conservation implications.

Monkeypox

Monkeypox is a viral disease that causes smallpox-like symptoms in humans (Bunge *et al.*, 2022). The causative agent of this zoonotic disease was first discovered in a Danish primate laboratory and was therefore named monkeypox virus (MPXV) (von Magnus *et al.*, 1959). Just like great apes and humans, however, monkeys are accidental hosts of the virus, which is thought to have a rodent reservoir (Di Giulio and Eckburg, 2004). MPXV is endemic in West and Central African tropical forested regions, but a recent surge in monkeypox cases across the globe is of grave concern (Zumla *et al.*, 2022).

Today, MPXV is the most relevant *Orthopoxvirus* (family *Poxviridae*) since the eradication of smallpox in 1980 (Di Giulio and Eckburg, 2004; Shchelkunov *et al.*, 2001). The recent marked increase in human monkeypox cases has been attributed to several concurring factors: human encroachment into wildlife habitats, better disease surveillance and declining global smallpox immunity, which previously had a cross-protective effect against MPXV infections.

Clinically, monkeypox and smallpox are hardly distinguishable, although the former has a lower mortality (10%) and human-to-human transmission rate. In humans, the disease starts with fever, malaise and respiratory symptoms, followed by the appearance of a maculo-papular rash; in certain cases, the eyes are affected and severe respiratory distress can occur (Di Giulio and Eckburg, 2004; Sklenovská and Van Ranst,

2018). The ongoing surge in global cases appears to be driven primarily by sexual contact, but in the past MPXV was thought to be transmitted predominantly via direct contact and respiratory droplets (Zumla *et al.*, 2022). While smallpox vaccines provide a partial protection against infection with MPXV, no licensed treatments are currently available (Brown and Leggat, 2016).

In wild primates, MPXV was first detected in 2012 in a sooty mangabey (*Cercocebus atys*), found dead in Taï National Park, Ivory Coast (Radonić *et al.*, 2014). Between 2017 and 2018, three outbreaks occurred in wild chimpanzees inhabiting the same ecosystem. The affected chimpanzees were habituated and followed on a daily basis by the staff of the Taï Chimpanzee Project, which allowed for close observation and sample collection (Patrono *et al.*, 2020). In total, 14 chimpanzees from three neighboring communities developed clinical signs. Four infants had severe illness and exhibited a typical maculo-papular rash, with one fatal case. The other ten chimpanzees showed mild to severe respiratory signs, with no or only a few visible skin lesions. In addition, 11 chimpanzees shed the virus without any clinical signs (Patrono *et al.*, 2020). These findings show that MPXV infections can have diverse clinical manifestations and that they may merit consideration in the differential diagnosis of respiratory infections in African great apes.

Sarcoptic Mange

Sarcoptic mange (also known as scabies) is a highly contagious skin disease caused by the mite *Sarcoptes scabiei*. *Sarcoptes* mites show a certain level of host-specificity but can infect other species under favorable conditions. The human parasite is ubiquitous in tropical Africa and can survive several days in the environment, providing opportunities for indirect transmission, such as through clothing (Arlian, Vyszenski-Moher and Pole, 1989; Browne *et al.*, 2021; Graczyk *et al.*, 2001). *S. scabiei* burrows tunnels into the outer skin layers of its host, causing intense itching and producing red papules that can develop into severe skin alterations, including crusts, hair loss, thickening and inflammation of the skin, as well as secondary infections. Left untreated, scabies can be fatal and have devastating effects on endangered wildlife populations (Pence and Ueckermann, 2002). Pathologies are due to the severe immune response triggered by *S. scabiei,* and disease progression depends on the host's individual health status (Bhat *et al.*, 2017).

While a clear scabies diagnosis requires invasive sampling (skin scrapings), which is problematic with respect to wild apes, the disease can often be recognized based on clinical signs (Engelman *et al.*, 2020). Treatment is relatively simple, usually involving a single dose of Ivermectin administered via darting, complemented with antibiotics in case of secondary bacterial infections (Rowe, Whiteley and Carver, 2019). Given the social nature of apes and the transmissibility of *S. scabiei*, treatment of all cohabiting individuals is advised (Graczyk *et al.*, 2001).

The first *S. scabiei* outbreak among apes was observed in 1996 and involved four habituated mountain gorillas (*Gorilla beringei beringei*) in the Bwindi Impenetrable National Park, Uganda. Three were successfully treated by Ivermectin dart; however, the most affected infant succumbed to the disease and died (Kalema-Zikusoka, Kock and Macfie, 2002). During the second outbreak, five juveniles from two groups were affected and successfully darted (Graczyk *et al.*, 2001). The only observed scabies outbreak among wild chimpanzees took place in 1997, in the Gombe National Park, Tanzania, and resulted in the death of three suckling infants (Dunay *et al.*, 2018; Wallis and Lee, 1999). In view of the high prevalence in surrounding human populations, the contagiousness of the pathogen and the curious

nature of great apes, human-to-ape transmission is the probable source of infection (Kalema-Zikusoka, Kock and Macfie, 2002).

Yaws

Treponema pallidum—the bacterium responsible for venereal syphilis (*Treponema p. pallidum*), bejel (*Treponema p. endemicum*) and yaws (*Treponema p. pertenue*, TPE) in humans—causes a yaws-like disease in primates (Čejková *et al.*, 2012; Centurión-Lara *et al.*, 2006; Marks, Solomon and Mabey, 2014). Since the first mention of the disease in Guinea baboons (*Papio papio*) in the 1960s, the bacterial subspecies TPE has been found to cause necrotizing dermatitis of the face, extremities and anogenital region in various primates across sub-Saharan Africa (Chuma *et al.*, 2019; Fribourg-Blanc and Mollaret, 1969; Fribourg-Blanc, Mollaret and Niel, 1966; Knauf *et al.*, 2018).

TPE infections of wild gorillas and chimpanzees have long been suspected based on clinical signs; they could not be confirmed until recently because of ethical considerations regarding invasive sampling (Harper and Knauf, 2013). The first evidence of TPE infection in great apes was based on the detection of TPE DNA in chimpanzee bones from Ivory Coast and gorilla feces from the Republic of Congo (Chuma *et al.*, 2019; Gogarten *et al.*, 2016). As the samples came from unknown individuals, however, there was no direct link between diagnostics and clinical signs. The link was finally established in 2020, when a wild chimpanzee with yaws-like facial lesions from the Sangaredi area in Guinea was gravely injured by hunters and had to be euthanized by a veterinarian, who was able to perform a necropsy (F. Leendertz, personal observation, 2021). A diagnosis based on these samples provided conclusive evidence that TPE infections had caused yaws-like disease in chimpanzees (Mubemba *et al.*, 2020).

Successful treatment of yaws in sooty mangabeys with long-acting antibiotics has been reported but requires darting (F. Leendertz, personal observation, 2021). Many questions remain regarding TPE transmission in great ape and other primate populations, but direct contact with an unknown animal reservoir or environmental source seems likely (Baylet *et al.*, 1971; Chuma *et al.*, 2018). TPE may also spread within groups via direct contact, sexual transmission or possibly via flies (Gogarten *et al.*, 2019a; Kumm

and Turner, 1936; Satchell and Harrison, 1953). As there is no clear distinction between TPE strains that infect primates and humans, zoonotic transmission could potentially occur, hampering the ongoing World Health Organization campaign to eradicate human yaws (Knauf, Liu and Harper, 2013).

Leprosy

Leprosy is one of the oldest diseases known to humankind, and most people are familiar with its horrifying images of disfigured faces and crippled limbs (Schuenemann *et al.*, 2018). These symptoms are the ultimate consequence of nerve damage caused by the bacterium *Mycobacterium leprae* and occasionally by the more recently discovered *M. lepromatosis* (Han *et al.*, 2008, 2009). Leprosy was long considered a purely human disease, but this notion had to be revised after its detection in nine-banded armadil-

los (*Dasypus novemcinctus*), red squirrels (*Tamiasciurus hudsonicus*) and captive primates, including a chimpanzee (Avanzi *et al.*, 2016; Gormus *et al.*, 1991; Meyers *et al.*, 1985; Suzuki *et al.*, 2011; Truman, 2005; Walker, Withington and Lockwood, 2014). While the infections in armadillos and squirrels are thought to be the results of human-to-animal spillovers, it is unclear whether the captive primates were infected by humans or a different source.

Recent findings of leprosy in wild chimpanzees suggest that a non-human source of *M. leprae* exists (Hockings *et al.*, 2021). Western chimpanzees (*Pan troglodytes verus*) from two wild populations in Cantanhez National Park in Guinea-Bissau and Taï National Park in Ivory Coast presented with leprosy-like lesions, including nodules on the face, hair loss and skin depigmentation, as well as abnormal nail growth and hand deformity. These clinical signs showed a progression over time comparable to advanced leprosy in humans. The *M. leprae* strains detected in fecal and necropsy samples of chimpanzees at the two sites differ from one another, but both are rare and have not been observed in humans from either country. In humans, leprosy is transmitted through direct and prolonged contact, which is extremely unlikely between wild chimpanzees and humans at either site (Hockings *et al.*, 2021). The wild chimpanzees may therefore have been infected with *M. leprae* by an unidentified animal or environmental source.

It remains unknown whether chimpanzee-to-chimpanzee transmission occurs, whether the pathogen is present in other great ape habitats and what impact the disease may have on great ape populations. While treatment with antibiotics is possible in humans and potentially in primates in captive settings, it is not feasible for wild apes because it requires repeated drug administration over a period of several months (CDC, 2017).
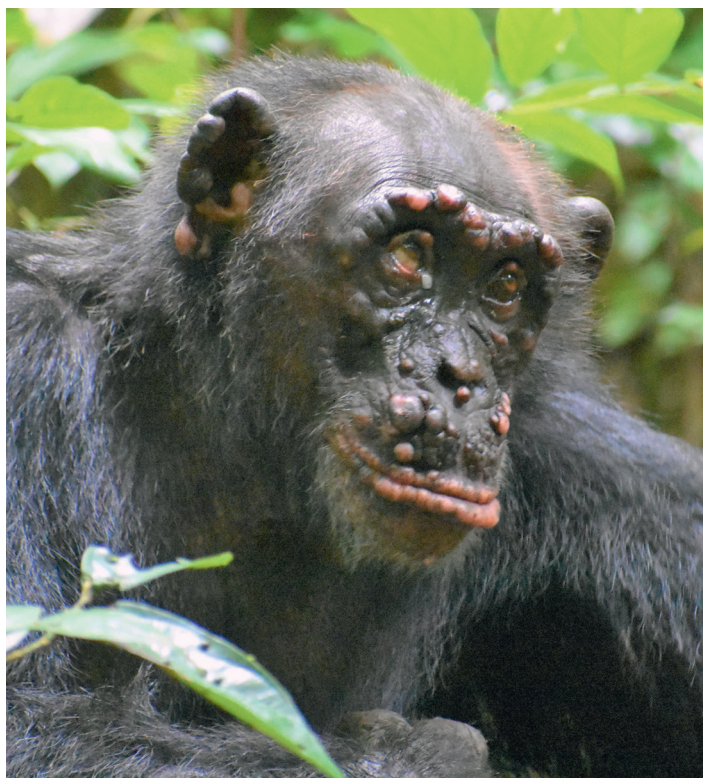
Infectious Diseases with a Measured Effect on Fitness

Research has conclusively demonstrated that certain pathogens have a measurable effect on wild great ape fitness and survival, as well as the potential long-term persistence of impacted populations. This section discusses the effects of four infectious diseases on wild ape populations, highlighting key studies and potential options for prevention and treatment. The last part of this section focuses on respiratory diseases that have had a devastating impact on wild apes. All documented cases involve viruses that are endemic in humans.

Anthrax

Classical anthrax caused by *Bacillus anthracis* is a severe bacterial disease of domestic and wild herbivorous ungulates that sporadically infects humans. Depending on its entry route, the bacterium causes the milder cutaneous form (which has a 20% case fatality rate if untreated) or the often-fatal inhalation or gastrointestinal form (CDC, 2020b). In contrast, sylvatic anthrax is caused by the bacterium *Bacillus cereus* biovar *anthracis*, abbreviated here as Bcbva (Klee *et al.*, 2010). Bcbva was first discovered in Taï National Park in Ivory Coast, where it caused clusters of chimpanzee mortality in 2001 and 2002 (Leendertz *et al.*, 2004). Chimpanzees who appeared healthy hours before were found dead, and post-mortem examination showed internal bleeding. One of the chimpanzees reportedly experienced a sudden onset of unspecific signs, including weakness and vomiting; the individual died within two hours (Leendertz *et al.*, 2004).

Since then, Bcbva was also detected in several chimpanzee carcasses and a gorilla carcass in Cameroon, as well as in the Central African Republic (Antonation *et al.*, 2016; Leendertz *et al.*, 2006a). While the exact geographic and host ranges of Bcbva are unknown, the pathogen was also isolated from a carrion fly in Liberia and a goat in the Democratic Republic of Congo (DRC); moreover, it was found to infect a broad range of other species, including various monkeys, duiker antelopes, mongooses, porcupines and forest elephants (*Loxodonta cyclotis*) (Antonation *et al.*, 2016; Hoffmann *et al.*, 2017). While no Bcbva infections have been reported for bonobos, the infected goat in DRC highlights that the pathogen may be present within the bonobo range (Antonation *et al.*, 2016). It is probably present throughout rainforests in West and Central Africa, but nowhere else is it known to have had as devastating an impact as in Taï National Park (Romero-Alvarez *et al.*, 2020).

In the hyperendemic area of Taï National Park, Bcbva was shown to be the number one mammal killer of infectious origin. It was detected in 40% (81/204) of all wildlife carcasses found between 1996 and 2015 (Hoffmann *et al.*, 2017). Since the start of the veterinary monitoring program in 2001, 38 anthrax-infected chimpanzee carcasses have been detected in the research area of the Taï Chimpanzee Project, which covers the home ranges of four chimpanzee groups (Hoffmann *et al.*, 2017; A. Düx, personal observation, 2022). Given that many chimpanzees disappeared from the habituated groups and their carcasses were never found, the real toll of anthrax on the Taï chimpanzee population is probably higher. Modeling of the long-term survival of Taï National Park chimpanzees has shown that without intervention, Bcbva is likely to lead to their extirpation (Hoffmann *et al.*, 2017).

It is unclear how apes get infected with Bcbva. Classical anthrax is generally considered a point-source infection that occurs in endemic regions (Turner *et al.*, 2014). The bacterium usually does not spread from animal to animal but forms infectious spores that survive for long periods in the environment (Beyer and Turnbull, 2009). Less is

known about Bcbva, but spore-contaminated soil on fruit or plants are considered a likely source of infection (Zimmermann *et al.*, 2017; F. Leendertz, personal observation, 2021). Carrion flies may contribute to the spread by feeding on carcasses and subsequently regurgitating Bcbva-containing material on surrounding vegetation. While viable bacteria could be cultured from flies, it is not clear whether they contain sufficient infectious material to cause disease (Gogarten *et al.*, 2019a; Hoffmann *et al.*, 2017). Observed clusters of anthrax cases support the hypothesis that chimpanzees are infected when feeding from the same contaminated source (Hoffmann *et al.*, 2017; Leendertz *et al.*, 2004; F. Leendertz, personal observation, 2021). For omnivorous chimpanzees, hunting of infected animals could play a role (Leendertz *et al.*, 2004). The risk of within-group transmission is generally low but may be elevated when great apes touch, groom or bite carcasses of their conspecifics (Beyer and Turnbull, 2009; Gonçalves and Carvalho, 2019).

In humans, anthrax can successfully be treated with antibiotics, but due to the rapid progression of the disease in chimpanzees, a timely treatment following the observation of anthrax signs is not feasible (CDC, 2020a). Preventive treatment of individuals who were in close contact with sick and deceased animals might be feasible in some cases and vaccination of animals in hyperendemic regions may become an option in the future.

Ebola

Ebola virus disease (EVD) outbreaks in humans, which occur sporadically in West and Central Africa, have become larger and more frequent over the past decade (CDC, 2022). The disease is often fatal, and symptoms can include fever, vomiting, diarrhea, internal bleeding and multiorgan failure (Jacob *et al.*, 2020). Apes are also susceptible to ebolaviruses, but observations of infected wild apes are rare; recorded signs include lethargy, abnormal behavior and abdominal pain, while post-mortems have shown internal bleeding (Formenty *et al.*, 1999; Georges *et al.*, 1999). Ebolaviruses differ from anthrax, which threatens apes in endemic hotspots, causing isolated cases or mortality clusters infected from the same point source (Hoffmann *et al.*, 2017; Leendertz *et al.*, 2004). In contrast, ebolaviruses are present in unknown animal reservoirs (presumably bats) throughout African range states and can cause large outbreaks among great apes.[1]

Due to the obscure nature of Ebola reservoirs, it can only be speculated how spillover to great apes occurs. If bats are indeed Ebola reservoirs, they could contaminate fruit and leaves with saliva and excretions when roosting in or feeding on trees that great apes frequent (Formenty *et al.*, 1999; Leendertz *et al.*, 2016). Since certain monkeys who hunt and eat bats are themselves prey for chimpanzees, their consumption could be a route of infection (Tapanes, Detwiler and Cords, 2016). Anecdotal reports of great apes catching and playing with bats indicate that direct contact with infected bats could also play a role (M.H. Surbeck, personal communication, 2019).

Irrespective of the route of initial spillover, once a great ape contracts EVD, the disease can spread within and probably between groups (and potentially even species), causing large epidemics (Bermejo *et al.*, 2006; Caillaud *et al.*, 2006). Theoretically, great ape populations' different social structures influence their ability to sustain a large outbreak. At the same time, the effects of an outbreak on different social structures may vary across great ape species (see Box 1.1).

In 1994, *Tai Forest ebolavirus* caused an EVD outbreak among chimpanzees in Taï National Park, killing 25% of the affected social group (Formenty *et al.*, 1999). In Central Africa, *Zaire ebolavirus* caused massive die-offs among chimpanzees and gorillas (Bermejo *et al.*, 2006; Leroy *et al.*, 2004; Walsh *et al.*, 2003). Between 1994 and 2003, the border region between Gabon and the Republic of Congo was hit by several EVD outbreaks in humans, most of which may have been linked to contact with sick or deceased wildlife, in particular chimpanzees and gorillas (Georges *et al.*, 1999; Georges-Courbot *et al.*, 1997; Leroy *et al.*, 2004). During this period almost 200 great ape carcasses were detected in the region and the chimpanzee and gorilla populations shrank considerably (Lahm *et al.*, 2007; Leroy *et al.*, 2004; Rouquet *et al.*, 2005). During just four months in 2002–3, for example, 32 great ape carcasses were detected in the Lossi Gorilla Sanctuary, in the Republic of Congo. Samples from 12 carcasses were analyzed and nine tested positive for *Zaire ebolavirus*. At the same time, 130 of 143 habituated gorillas in the Lossi Sanctuary disappeared (Bermejo *et al.*, 2006).

The total impact EVD has on great apes can only be guessed, as population densities in some remote regions are unknown and veterinary surveillance exists only in a few areas. While no data exist for EVD in bonobos, they are almost certainly at risk as they live in regions of the DRC where EVD outbreaks have occurred. Bonobos are probably susceptible, considering that all other hominins and many other primates can be infected (Inogwabini and Leader-Williams, 2012).

For orangutans, the situation is less clear. Asia is not known to harbor any

human-pathogenic ebolaviruses; however, *Reston ebolavirus*, which circulates in bats in the Philippines, can cause disease in primates (Demetria *et al.*, 2018; Jayme *et al.*, 2015). Other, more distantly related viruses from the same family as ebolaviruses (*Filoviridae*) have been detected in Chinese bats (He *et al.*, 2015; Yang *et al.*, 2017). No filovirus infections in wild or captive orangutans (or gibbons) have been documented. The one publication that suggests there is serologic evidence of exposure is disputed for a few reasons, including the origin of

BOX 1.1

Ebola and the Social Structure of Gorilla Populations

The diversity of great ape social structures suggests that a pathogen may not spread in the same way among bonobos, chimpanzees, gorillas and orangutans (Carne *et al.*, 2014). Similarly, a pathogen's effects on social structures may vary across great ape species. The rarity of observations of naturally occurring infectious agents with a proven pathogenic potential currently precludes a thorough comparison based on real-world data.

Outbreaks of ebola virus disease (EVD) have allowed researchers to study the impact of a lethal disease on social structures in great apes—and, conversely, the influence of social structures on disease risk. Between 2001 and 2005 in the Republic of Congo, multiple EVD outbreaks severely affected populations of western lowland gorilla (*Gorilla gorilla gorilla)* (and, probably to a lesser extent, central chimpanzees (*Pan troglodytes troglodytes*)) (Bermejo *et al.*, 2006; Walsh *et al.*, 2003). The composition and size of gorilla groups can vary markedly, and male gorillas may be solitary. A group may comprise a single male and multiple females, or multiple males and multiple females, or only males. Observations made at the Lokoué site in the Odzala-Kokoua National Park before, during and after an EVD outbreak in 2004 show that individuals living in groups suffered from a higher death rate (97%) than solitary individuals (77%), pinpointing a clear cost of group living (Caillaud *et al.*, 2006). Accordingly, at the population scale, the proportion of gorillas with a solitary lifestyle was markedly higher after the outbreak. Importantly, this risk imbalance resulted in a reversal of the overall sex ratio, as adult females (all living in groups) were more affected than adult males, 8% of whom were solitary (Caillaud *et al.*, 2006).

These changes were not permanent, however. Ten years after the outbreak, both the proportion of solitary gorillas and the overall sex ratio were back to their pre-outbreak values, reflecting transiently altered social dynamics (Genton *et al.*, 2015, 2017). While they may represent an extreme example, EVD outbreaks clearly show the potentially complex interactions of great ape social systems and the pathogens that affect them.
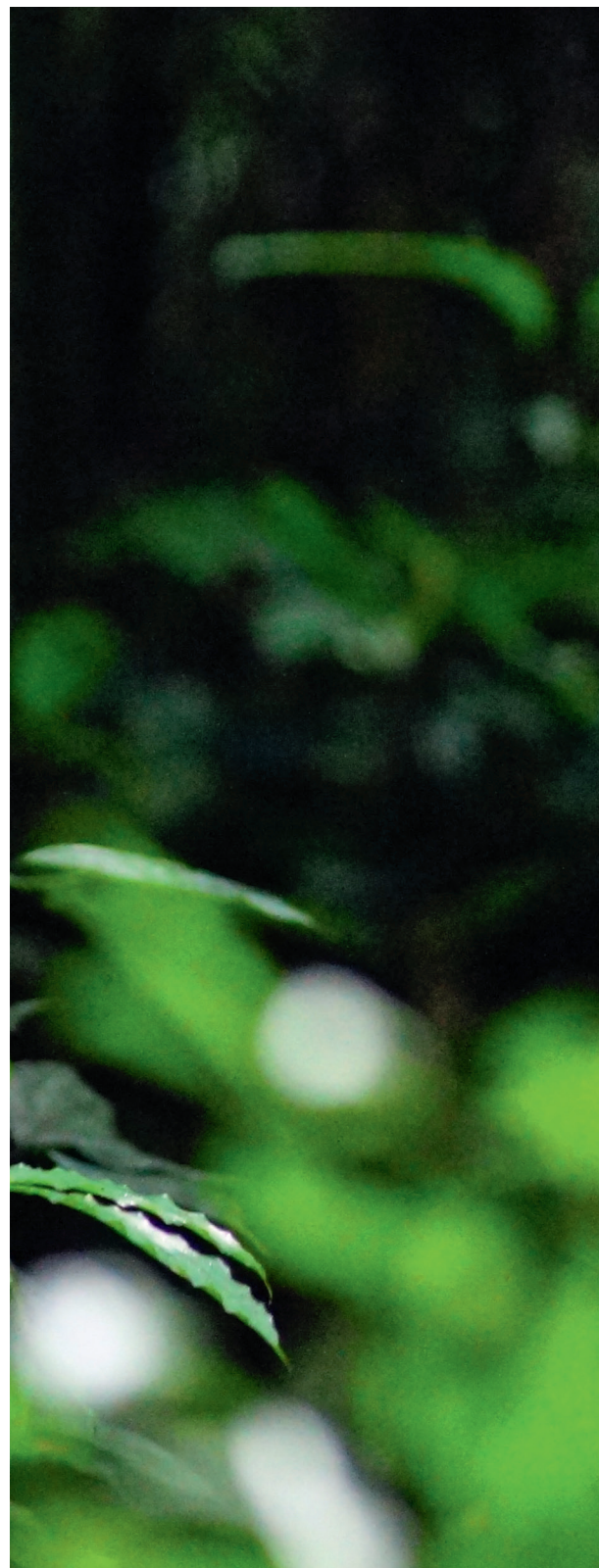
samples and methods; an official "expression of concern" now accompanies this publication (Nidom *et al.*, 2012). The interpretation of serological results requires caution as unspecific reactivity and cross-reactivity are common for the serological ebolavirus assays used (Allela *et al.*, 2005; Natesan *et al.*, 2016). Since orangutans are less gregarious than African great apes, the risk of disease outbreaks of epidemic proportions is probably comparatively low (Carne *et al.*, 2014). The other human-pathogenic African ebolaviruses (*Bundibugyo ebolavirus* and *Sudan ebolavirus*) can also infect primates, but no cases have been observed in the wild (Leendertz *et al.*, 2017).

Since it is not possible to predict where the next Ebola outbreak will occur, management of EVD in great apes is particularly challenging. While no treatment option is available for great apes, different vaccination strategies have been discussed. Even with a safe and effective vaccine, however, the broad-scale vaccination of wild great apes in remote areas would be difficult to accomplish.

Simian Immunodeficiency Virus in Chimpanzees

The simian immunodeficiency virus in chimpanzees (SIVcpz) is a retrovirus that causes an illness similar to the progression of human immunodeficiency virus (HIV) infections in humans (Sharp and Hahn, 2011). The latter stages of infection develop into simian acquired immunodeficiency syndrome, similar to when HIV develops into acquired immune deficiency syndrome, or AIDS (Keele *et al.*, 2009).

Central chimpanzees (*Pan troglodytes troglodytes)* have been identified as the reservoir from which two lineages of HIV-1 independently emerged, the pandemic group M and very rare group N. SIVcpz, the closest relative of HIV-1 group M, is found in multiple sites across the chimpan-

zee range (Sharp and Hahn, 2011). The most recent common ancestor of HIV-1 group M viruses dates back to the late 19th or early 20th century, suggesting that HIV-1 group M passed from chimpanzees into the human population in the region during the colonial period (Gryseels *et al.*, 2019; Keele *et al.*, 2006; Van Heuverswyn *et al.*, 2007). Central chimpanzees transmitted SIVcpz to western lowland gorillas (*Gorilla gorilla gorilla*), giving rise to simian immuno-deficieny virus in gorillas (SIVgor). Gorillas later became the proximal source of two additional HIV-1 lineages, the epidemic group O (mostly restricted to Cameroon) and extremely rare group P (D'arc *et al.*, 2015; Plantier *et al.*, 2009). Chimpanzee and gorilla hunting is the most likely route of SIVcpz and SIVgor transmission to humans (Pepin, 2021).

The evolutionary history of SIVcpz is one of cross-species transmission, which is thought to result from the predatory behavior of chimpanzees, who often prey on monkeys. Male chimpanzees from Taï National Park consume as much as 45 kg of monkey meat per year, yet this behavior has not led to the transmission of the simian immunodeficiency virus that infects the western red colobus (*Piliocolobus badius*) to the chimpanzee population (Gogarten *et al.*, 2014; Leendertz *et al.*, 2011). Chimpanzees may thus be resistant to infection with this SIV strain.

SIVcpz was long thought to be non-pathogenic in its natural hosts, central and eastern chimpanzees (*Pan troglodytes schwein-furthii*). Using a longitudinal study extending over almost a decade, however, Keele *et al.* (2009) show that eastern chimpanzees belonging to two habituated communities in Gombe National Park (Tanzania) incurred an increased likelihood of death and lowered fertility when infected by SIVcpz. The virus also led to clinical manifestations suggestive of AIDS. A subsequent investiga-

tion of the impact of SIVcpz on chimpanzee population dynamics in the same communities and in an additional, non-habituated community suggested that SIVcpz probably played a role in the marked decline of the non-habituated community. While simulations showed that even low SIVcpz prevalence significantly increased the risk of community extinction, female intercommunity migration was found to reduce this risk considerably. These findings indicate that the survival of an infected community can strongly depend on connectivity with other social units (Rudicell *et al.*, 2010).

Respiratory Disease

Respiratory pathogens are recognized as a major cause of mild to severe disease in wild great apes. In the past two decades, continuous veterinary monitoring within conservation programs and the progressive improvement of diagnostic tools applicable to non-invasive samples have allowed for the gathering of solid evidence on the risk of pathogen transmission from humans. Over the same period, common human endemic viruses have been identified across great ape species and habitats. Among the first to be identified in wild human-habituated great apes suffering from severe respiratory disease were viruses of the family *Pneumoviridae*, such as the human metapneumovirus (HMPV) and types A and B of the human orthopneumovirus, previously known as the human respiratory syncytial virus, or HRSV (Köndgen *et al.*, 2008; Rima *et al.*, 2017). Both viruses have been repeatedly detected since. HMPV has been transmitted to western chimpanzees in Ivory Coast, eastern chimpanzees in Tanzania and Uganda, and mountain gorillas (*Gorilla beringei beringei*) in Rwanda (Kaur *et al.*, 2008; Köndgen *et al.*, 2008; Negrey *et al.*, 2019; Palacios *et al.*, 2011). HRSV has been found in western chimpanzees in Ivory Coast, in

western lowland gorillas in the Central African Republic and in bonobos in the DRC (Grützmacher *et al.*, 2016, 2018b; Köndgen *et al.*, 2008, 2017).

More recently, infections with members of other viral families were also reported in wild ape populations. These included the human rhinovirus C (family *Picornaviridae*), the human respirovirus 3 (family *Paramyxoviridae*) in chimpanzees in Uganda and the human coronavirus OC43 (family *Coronaviridae*) in chimpanzees in Ivory Coast (Negrey *et al.*, 2019; Patrono *et al.*, 2018; Scully *et al.*, 2018).

Photo: In assessing how best to manage the health of apes in captive settings, practitioners may opt to vaccinate them, especially against pathogens with a high regional prevalence. Guidelines differ widely but are often based on procedures followed in the country where the apes are kept in captivity. Chimpanzee having an injection. © Justin Taus/ Fauna Foundation

Phylogenetic analyses on the partial or complete viral genome sequences detected in these different outbreaks have consistently confirmed that the strains found in

great apes fall within the diversity of human lineages, clearly indicating human-to-ape spillover. Due to a lack of data on the circulation of these pathogens in local human populations, however, it has not been possible to establish more precise links to the geographical origins of the transmitted strains (Patrono *et al.*, 2022).

The aforementioned outbreaks were associated with mortality events, which contributed significantly to raising awareness on the risks posed by habitat overlap with humans and the need for establishing hygiene rules and surveillance systems within great ape research and tourism projects (Macfie and Williamson, 2010; see Box 1.2). Morbidity varied greatly across outbreaks but was generally high, reaching up to 100% during an HMPV outbreak in western chimpanzees (Köndgen *et al.*, 2010). In contrast, no mortality was associated with the human coronavirus OC43, which caused only mild clinical signs, whereas at least one death occurred in all other cases (Patrono *et al.*, 2018). The highest mortality rates were recorded during outbreaks caused by pneumoviruses, with up to 18% of the population succumbing to infection (Köndgen *et al.*, 2010). The true figure may be even higher given the difficulties in finding carcasses in the rainforest and their rapid decomposition due to environmental conditions, which strongly influences sampling possibilities (Köndgen *et al.*, 2017).

Viral infections often paved the way for secondary bacterial ones, to which mortality was ultimately attributed. Among bacteria, *Streptococcus pneumoniae* (or pneumococcus) has been found in several lethal outbreaks (Chi *et al.*, 2007; Grützmacher *et al.*, 2018b; Köndgen *et al.*, 2017). This opportunistic bacterium is part of the commensal nasal flora and can occasionally become pathogenic, following primary damage of the airway epithelium, which leads to pneumonia (Morris, Cleary and Clarke, 2017). Genomic analyses on some of the pneumococcal strains found in lungs of deceased

BOX 1.2

Prevention of Infectious Diseases

The prevention of infectious diseases encompasses a large range of measures, protocols and procedures to minimize the risk of natural and unintentional infections of humans and animals. Preventive measures work only when there is broad compliance, which requires repeated educational efforts for all involved with ape populations. To be wholly effective, work on preventing infectious diseases requires consultation with appropriate professionals; this chapter is in no way meant to replace such collaboration with experts.

Broadly, disease risk assessments carried out by professionals may help evaluate potential dangers associated with particular situations. When an animal enters a captive setting, a quarantine period allows for the monitoring of behavior and the potential insurgence of clinical signs. During this period, an assessment of the individual's health status is critical to minimizing the risk of novel pathogens entering and spreading in a facility (Gilardi *et al*., 2015; see Chapter 4). Priorities of enclosure design thus include ensuring a physical separation between new animals and the resident population, as well as separate waste disposal and the disinfection of food or enrichment items brought in from outside. Although there is no standard duration, quarantines are typically imposed for 60 to 90 days, depending on diagnostic capacities as well as the ecology and prevalence of pathogens of most concern, as defined in the relevant disease risk assessment. Involving trained professionals in the design and implementation of these procedures can help to safeguard the psychological wellbeing of apes during the period of isolation, as well as during the preceding move between captive settings or from the wild into captivity.

To reduce the risk of infection, a facility can ensure that staff members who attend to captive apes are healthy and vaccinated, limit the number of staff during the quarantine period, and incorporate staffing decisions into its disease risk assessment and disease mitigation strategy. Similarly, it can integrate the use of personal protective equipment into its mitigation strategy. In all captive situations where there is long-term close contact between the (rehabilitant) apes and their caregivers, the use of masks and gloves is advisable during as well as after the quarantine period, especially during periods of high risk, such as flu season (Stevens, 2020; see Chapter 2).

In assessing how best to manage the health of apes in captive settings, practitioners may opt to vaccinate them, especially against pathogens with a high regional prevalence. Guidelines differ widely but are often based on procedures followed in the country where the apes are kept in captivity; detailed guidance may thus need to be requested from the relevant national ministry of health. For all those working with wild ape populations, a key resource on preventive measures overall is the International Union for Conservation of Nature (IUCN) publication *Best Practice Guidelines for Health Monitoring and Disease Control in Great Ape Populations* (Gilardi *et al*., 2015).

chimpanzees co-occurring with HRSV infections revealed a human origin (Köndgen *et al.*, 2017). Human pneumococci were found in both chimpanzees and orangutans living in closer contact with humans, such as in zoos, rehabilitation centers and wild-living populations (Köndgen *et al.*, 2017; Szentiks *et al.*, 2009). Whereas respiratory viral infections are normally cleared and do not persist, pneumococci can become part of the nasopharyngeal flora upon transmission. Once established in an individual, these infections can be transmitted to other group members and can eventually become endemic in a population, potentially influencing the severity of other diseases.

Another bacterium that has been associated with acute lethal pneumonia (co-occurring with HMPV and *S. pneumoniae*) or air sacculitis in wild chimpanzees is *Pasteurella multocida* (Köndgen *et al.*, 2011). The strain's genetic information and phenotype showed no clear evidence of direct acquisition from other animals or humans. Despite the paucity of data available for RNA viruses other than influenza, pneumoviruses have been shown to favor bacterial colonization in the lung through multiple pathways (McCullers, 2014). Based on the evidence gathered thus far, it seems plausible that infections with members of this viral family caused more overt clinical signs and mortality, often due to co-infections, prompting outbreak investigations and opening up the possibility of obtaining a diagnosis. Infections that cause milder clinical

Photo: To reduce the risk of infection, a facility can ensure that staff members who attend to captive apes are healthy and vaccinated and integrate the use of personal protective equipment into its mitigation strategy. © IAR Indonesia (YIARI)/MoEF of Indonesia

signs may be more difficult to observe and diagnose if continuous behavioral observation and routine sampling are not in place.

Infection with *Mycobacterium tuberculosis* has been reported in wild chimpanzees (Coscollá *et al.*, 2013). Bacterial isolation confirmed the initial pathological diagnosis of tuberculosis. Genomic analyses performed on the strain found in a wild chimpanzee revealed a novel *M. tuberculosis* complex isolate, suggesting that a human origin was unlikely.

Thanks to recent advances, diagnostic tools can now be applied to non-invasive samples to determine which types of pathogens are causing disease or death in wild great apes in various settings, including tourism sites, research areas and forests used by local human populations (see Box 1.3). This knowledge can allow for the design of targeted vaccination strategies for people entering great ape habitats, such as local residents, researchers and tourists. Employee health programs—including routine health checks, mandatory vaccinations against pathogens that also have the potential to cause disease in apes, strict hygiene rules and quarantine based on syndromic surveillance—have proven to be effective measures for reducing the risk of disease transmission (Gilardi *et al.*, 2015; Grützmacher *et al.*, 2018a). The presence of asymptomatic carriers within the human population poses a challenge, however.

The establishment of field laboratories to test all staff and visitors entering great ape habitats may represent another step towards improving prevention measures and maximizing the benefits of conservation actions (Grützmacher *et al.*, 2016). Such testing would only cover a part of the human presence in the forest, however. Additional measures for reducing the risk of disease introduction while improving human health include the broadening of vaccination coverage to the population living around the forest. Programs

could make use of commercially available pneumococcal vaccines and, eventually, vaccines against respiratory viral diseases that are currently under development (Leendertz and Kalema-Zikusoka, 2021; see Chapters 2 and 4). This One Health strategy, developed together with local public health authorities, would be an additional way of ensuring direct benefits of conservation activities to local communities (see Chapter 2).

Non-Infectious Causes of Disease

Non-infectious threats to ape health are present both in captive and natural settings. This section discusses some of the human-induced elements that most severely affect ape populations in their natural habitat.

Encroachment into ape habitat by human-caused forest fires, road building, laying of electrical cables, and various farming and mining practices can have immediate effects on animals. These activities can also have long-term impacts on the environment—such as by inducing microclimate change, diminishing food availability and decimating biodiversity—further endangering the survival of great apes (Bettinger *et al.*, 2021; Erb *et al.*, 2018).

Apart from destroying ape habitat, forest fires can cause burns and inhaled smoke can damage the respiratory system, increasing the risk of respiratory infections. These effects can affect many aspects of ape health, as has been documented in humans and orangutans alike (Aguilera *et al.*, 2021; Erb *et al.*, 2018).

Various problems also stem from the construction of roads and associated infrastructure designed to serve the mining or agricultural industries and to connect human settlements. Easier human access to ape environments through roads increases the likelihood of hunting (Laurance *et al.*, 2006). Moreover, roads running through territories directly affect animals by dividing popula-

BOX 1.3

Sample Collection

This box presents sampling options for the study of ape diseases and health. A sample collection approach is best selected based on available methods for subsequent analyses, the markers of health or disease that are being examined, and available resources. The availability of infrastructure—such as liquid nitrogen, a freezer and a refrigerator—may limit the types of samples and storage media, for example. Since methods are continuously improving, it is useful to undertake a careful review of the literature and consultation with experts before developing and following a sampling protocol (Gillespie, Nunn and Leendertz, 2008; Leendertz *et al.*, 2006b; see Chapter 4).

Generally, sampling is either invasive, requiring physical contact with the animals, or non-invasive, in which case it can rely on the collection of samples such as feces, urine, hair or saliva. Many of the techniques for the study of wild animals can also be applied in captivity, but most techniques that are feasible in captivity are not applicable for the study of wild ape health (Gillespie, Nunn and Leendertz, 2008; Leendertz *et al.*, 2006b). This discussion focuses on sample collection in the wild.

Wild apes need chemical immobilization—anesthesia—to allow for invasive sampling. Anesthetizing animals, especially in remote conditions, carries an inherent risk that must be carefully considered against any benefits derived from the procedure (Gillespie, Nunn and Leendertz, 2008; Leendertz *et al.*, 2006b). Non-emergency handling of wild apes is generally considered unethical, so it is only included in management strategies for exceptional circumstances (Gilardi *et al.*, 2015; Gruen, 2018; see Chapter 5). Any proposed invasive sample collection for surveillance purposes needs to go through an extensive review by an ethical committee and secure approval from local and national authorities. To maximize the benefits associated with immobilization, veterinarians can collect a wide range of sample types—including blood, plasma, swabs, biopsies and ectoparasites—for use in a multitude of research programs (Gillespie, Nunn and Leendertz, 2008; Leendertz *et al.*, 2006b).

Post-mortem samples collected after death (during a necropsy) are invaluable for the understanding of disease in wild populations. Since carcasses can contain any number of pathogens that are known (or not yet known) to infect humans, however, the disease risks associated with performing a necropsy are considerable, particularly in remote field settings. Key steps for minimizing risks include restricting post-mortem sampling to veterinarians who have received special training and ensuring procedures are undertaken in consultation with experts and in line with rigorous safety standards (Gillespie, Nunn and Leendertz, 2008; Leendertz *et al.*, 2006b).

Non-invasive sample collection has become an invaluable tool in the diagnosis of disease and the study of behavioral ecology in wild apes. Non-invasively collected samples allow

for repeated collection for longitudinal studies without major disturbance (such as chemical immobilization) of the subject of interest (Behringer and Deschner, 2017; Calvignac-Spencer *et al.*, 2021; Smiley Evans *et al.*, 2015, 2016). Molecular analysis of samples has proven fruitful for understanding the ecology of a diversity of pathogens as well as the apes themselves. Many techniques can be used on non-invasive samples to assess a wide range of factors beyond the animal's own nucleic acids, including infection history (through serology), stress and health status (via hormone analysis) and diet (such as by using metabarcoding or isotope ratios) (Gogarten *et al.*, 2018; Patrono *et al.*, 2022; Samuni *et al.*, 2018). As noted above, collection and preservation strategies are selected based on which analyses are planned (Gillespie, Nunn and Leendertz, 2008; Leendertz *et al.*, 2006b).

If samples are to be obtained from captive apes who cannot be released, operant conditioning can be employed to improve their psychological wellbeing and handleability, which can facilitate both non-invasive and minimally invasive sampling (Rasmussen, Newland and Hemmelman, 2020). Non-invasive sample collection under these conditions does not raise stress hormones in bonobos or orangutans (Behringer *et al.*, 2014). Operant conditioning also facilitates routine imaging techniques, such as radiology and ultrasound, including monitoring of pregnancies (Drews *et al.*, 2011). If there is a need to determine which ape was the source of a fecal sample and it is not possible to observe animals defecating, the animals may be fed inert substances such as indigestible grains, food colorants or colored glitter to aid in stool identification (Fuller, Margulis and Santymire, 2011).

tions, cutting them off from food and water supplies and potential mates, and exposing them to the risk of traffic accidents, which are often fatal. One proposal for reducing the number of road accidents is the construction of artificial canopy bridges that allow for safe animal crossings (Chan *et al.*, 2020).

While the mining and agricultural industries drive road construction and deforestation, they can also impact soil and water supplies by overexploiting and poisoning these resources. Gold ore processing often involves the uncontrolled use of mercury, which can potentially lead to neurological or renal malfunctions and even death in primates (Ontl, 2017). Pesticides from agricultural areas also have the potential to have dire effects on primates (Botha *et al.*, 2015). For example, facial dysplasia has provisionally been attributed to pesticides in wild baboons and chimpanzees in Uganda, where DDT/p,p'-DDE, chlorpyrifos and imidacloprid levels in maize exceeded recommended limits in areas used by chimpanzees. Further studies are needed to confirm that pesticides were related to the observed signs (Krief *et al.*, 2017).

Many anthropogenic disturbances can lead to decreases in the food supply, forcing apes to resort to crop-foraging, which further endangers them in several ways. Exposure to crops that are treated with the above-mentioned chemicals can poison apes, while ongoing, sometimes violent conflict between farmers and apes can lead to lethal physical injuries (Humle and Hill, 2016).

Captive Apes

Captivity significantly alters the environmental conditions for apes and their pathogenic organisms. Enclosure designs thus need to meet physical, social and psychological needs, while also incorporating strategies to reduce infection pressure (see Chapter 8).

In general, population density is higher in captivity than in the wild, as animals are confined to a specified space. Measures are therefore required to minimize the possibility that infectious agents will enter the captive population.

In captive settings, close contact with humans can potentially expose apes to pathogens to which they are susceptible, which can lead to serious outbreaks (Kilbourn *et al.*, 2003; Liptovszky *et al.*, 2019). In addition, stressful situations may create stereotypical behaviors (such as repetitive movements without an apparent function) and other psychopathologies that require managing. Prolonged stress can also impair an ape's immune system and the ability to fight off certain infections or regulate microbiomes. The combination of these factors usually results in a higher disease prevalence under captive conditions (Kilbourn *et al.*, 2003). Particular attention to infectious diseases is needed in rehabilitation centers, especially prior to an animal's release into the wild, to minimize the risk of introducing a novel disease into a wild population (Sherman *et al.*, 2021).

## Diseases with a Likely Effect on Health

Malaria

Malaria is a potentially deadly disease that is caused by *Plasmodium* parasites transmitted through the bites of infected female *Anopheles* mosquitoes. In rescue centers, chimpanzees and orangutans are often diagnosed with *Plasmodium* infections. In most cases, there are no overt clinical signs, or they are mild and transient and do not require treatment. In rehabilitant orangutans, the severity of clinical signs appears to be correlated with increases in parasitemia, especially in individuals with anemia or persistent fever that is unresponsive to acetaminophen or

non-steroidal anti-inflammatory drugs. In these cases, there is some evidence to suggest that antimalarial treatment brings improvement in signs following a treatment-based reduction of parasitemia. The correlation suggests that *Plasmodium* parasites might be clinically relevant and that treatment could be considered when parasitemia is high (J. Philippa, personal observation, 2020).

Altered living conditions in rescue centers could play a part in the ecology of *Plasmodium* infections in orangutans. One set of living conditions relates to population density, which is higher on the ground in captivity than in the more arboreal natural habitat of orangutans. The density of mosquitoes is similarly higher at the ground level than in the canopy. Another set of conditions concerns the proximity to other species, such as humans and wild macaque (*Macaca fascicularis*) populations, which may act as a reservoir or amplifier host of *Plasmodium* parasites (Brant *et al.*, 2016; Siregar *et al.*, 2015). Further studies are needed to elucidate these factors.

Gastrointestinal Parasites

The gastrointestinal tract comprises all the organs of the digestive system, extending from the mouth to the anus. Despite a high prevalence and variety in wild apes, diseases associated with gastrointestinal parasites (protozoa and helminths) are not well documented in the wild (Medkour *et al.*, 2020). In contrast, changes in the gastrointestinal parasite load and clinical disease in captive apes—in both rehabilitation centers and zoos—have been linked to factors such as increased host population density and infection pressure (due to a small living area or substandard hygiene practices), stressful situations and disturbances of the gastrointestinal microbiome, for example due to oral antibiotics (Labes *et al.*, 2010; Maertens *et al.*, 2021; Nurcahyo, Konstanzová and
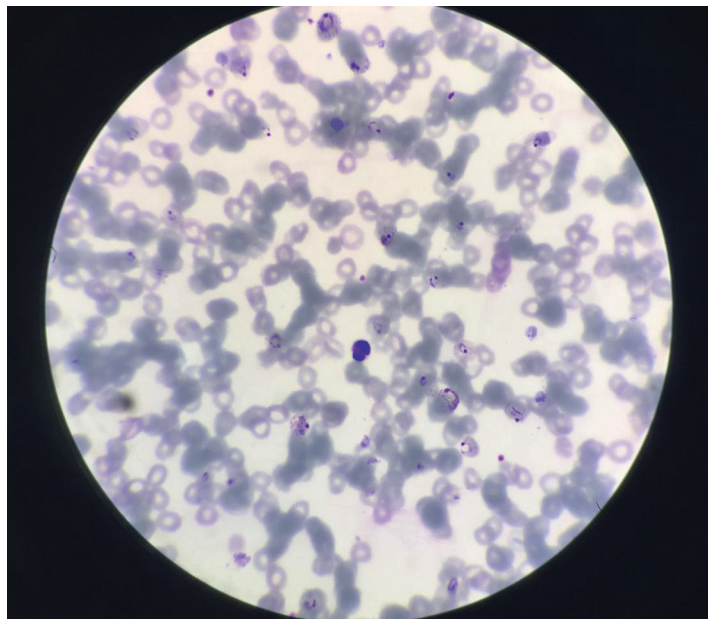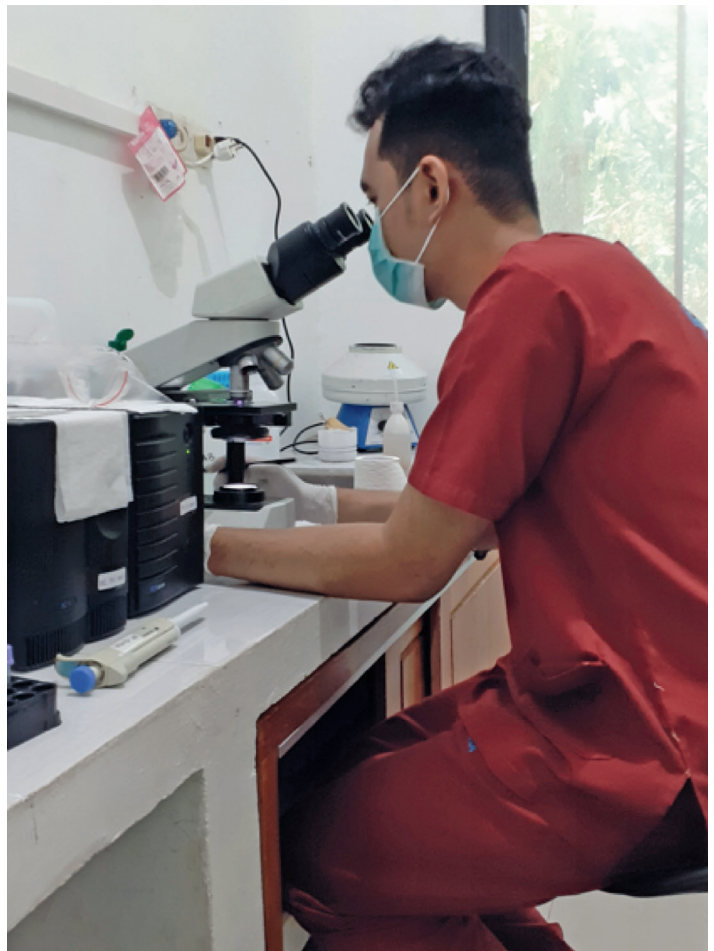
Foitová, 2017). Many captive facilities reduce the severity of parasite infections in the apes by ensuring use of proper biosafety practices and routine anthelmintic treatment (Liptovszky et al., 2019).

Protozoa

Protozoa are single-celled organisms. *Balantidium coli* is a very common commensal infection of wild and captive apes; like other protozoa, it is part of a healthy intestinal microbiome in low to moderate numbers. Its prevalence in captive orangutans is generally higher than in their wild counterparts, however; indeed, observation of clinical disease associated with these infections is restricted to captive animals. Contributing factors to clinical balantidiasis include increased infection pressure in captivity, largely due to higher host population density and stress, and diets rich in easily digestible carbohydrates, or starch (Labes et al., 2010; Schovancová et al., 2013). *Balantidium* infections are usually left untreated in rehabilitation centers and zoos, unless clinical signs accompany increases in numbers. There are case reports of a balantidiasis epidemic in captive western lowland gorillas, including typhlitis requiring surgery and a fatal *B. coli* infection (with a *Salmonella* co-infection) in a captive western lowland gorilla in Cameroon (Lankester et al., 2008; Lee et al., 1990; Teare and Loomis, 1982).

In some situations, other common gastrointestinal protozoa—such as *Cryptosporidium*, *Entamoeba histolytica* and *Giardia*—have caused clinical infections with bloating, cramping or diarrhea in captive apes. In zoos, *Giardia* has been implicated in clinical disease (diarrhea and vomiting). Meanwhile, *Entamoeba* spp. have caused irritable bowel-like signs, ulcerative colitis and diarrhea in gorillas, as well as ulcerative colitis and lung or liver abscesses in chimpanzees. Increased contact with humans has been linked to an increased

prevalence of protozoa such as *Entamoeba histolytica* in rehabilitated orangutans (Stuart et al., 2020).

Balamuthia mandrillaris is a recently described, free-living protozoal organism that has caused fatal acute to subacute necrotizing or granulomatous meningo-encephalitis in humans and captive apes. Isolated cases have been reported in the northern white-cheeked crested gibbon (*Nomascus leucogenys*), western lowland gorilla and orangutan in Australia, Europe and North America.[2] Unvalidated immunofluorescence antibody assays, which permit the identification and highlighting of antibodies in a blood sample, have shown promising results in orangutans. A validated test would be extremely useful for preventive screening of captive apes (Ferris, Ali and West, 2021).

Helminths

The group of worms known as helminths comprises nematodes, cestodes and trematodes. Some of the most common nematodes (roundworms) found in captive apes are *Ancylostoma, Ascaris, Capillaria, Enterobius, Oesophagostomum, Strongyloides* and *Trichuris*.[3] As gastrointestinal commensals they generally do not cause significant morbidity. One important exception is *Strongyloides,* a very common nematode in wild and captive apes (Mul et al., 2007; Nurcahyo, Konstanzová and Foitová, 2017; Penner, 1981; Zulfikri, Ridwan and Cahyaningsih, 2018). Although it is not a clinically important parasite while in the gastrointestinal tract, its larval forms travel widely throughout the body and often result in fulminant, fatal verminous pneumonia and peritonitis, which is commonly fatal in juvenile orangutans housed in zoos (Liptovszky et al., 2019). In rehabilitation centers, young orangutans have been found to be more at risk than older animals (Labes et al., 2010). Fatal strongyloidiasis has been described in a Lar gibbon (*Hylobates lar*) colony as the most

common cause of death, with erosive and ulcerative enteritis, and multifocal-diffuse hemorrhage associated with migrating larvae (DePaoli and Johnsen, 1978). Disseminated infections have been diagnosed ante-mortem in orangutans and are curable (Kleinschmidt, Kinney and Hanley, 2018).

Chimpanzees and orangutans are natural hosts of the *Enterobius* species (Foitová *et al.*, 2008, 2014; Labes *et al.*, 2010). *Enterobius* infections usually cause asymptomatic to mild clinical disease, but there are reports of fatal hemorrhagic colitis in captive chimpanzees, with the parasite maintained in the population for more than 20 years following introduction—despite attempts at treatment (Hasegawa and Udono, 2007; Murata *et al.*, 2002; Yaguchi *et al.*, 2014). Heavy clinical infections have also been recorded in gibbons kept as pets (Smith *et al.*, 1969).

Cestodes, like the other parasites, generally cause low morbidity in their natural ape hosts. *Echinococcus multilocularis*, the fox tapeworm, is widespread in the northern hemisphere and causes alveolar echinococcosis after infection. Captive gorillas seem to be very susceptible, but infected chimpanzees and orangutans have also been reported in European and Japanese zoos (Federer *et al.*, 2016; Wenker *et al.*, 2019). The infection can remain asymptomatic for years, but clinical disease can be (sub)acute and fatal (Wenker *et al.*, 2019).

Other sporadic cases of severe cysticercosis (an infection caused by larval cysts of the tapeworm) in captive apes include a recent case of fatal disseminated *Versteria mustelae* infection in a captive Bornean orangutan (*Pongo pygmaeus* spp.) with a rapid and severe disease progression (Goldberg *et al.*, 2014). Metabarcoding techniques have the potential to standardize helminth taxonomic identification from ape and other primate fecal samples, while simultaneously allowing for descriptions of
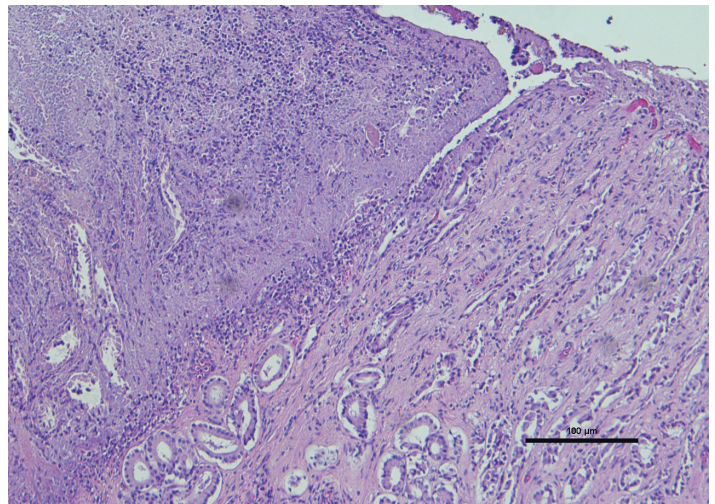
primate-associated parasite communities (Gogarten *et al.*, 2020).

Herpes

Herpes is a group of viral diseases caused by the herpes viruses, which affect the skin (often characterized by blisters or sores) and nervous system. Herpes virus infections have been documented in all apes, and species-specific herpes viruses likely evolved with humans' primate ancestors.[4] Antibodies to human herpes simplex viruses have been reported in rescued gibbons, with a high prevalence likely due to close human contact (Eberle and Jones-Engel, 2017; Sakulwira *et al.*, 2002). Apes are susceptible to other herpes viruses, such as Cytomegalovirus, Epstein-Barr virus and Varicella-zoster (Haberthur and Messaoudi, 2013); mountain gorilla lymphocryptovirus infections have been likened to an Epstein-Barr virus-like epidemiology (Smiley Evans *et al.*, 2017). Manifestation of human herpes simplex virus infections range from stomatitis, or localized signs on the mucous membranes, to systemic infections with encephalitis and fatal outcomes (Gilardi *et al.*, 2014). They have been reported in captive gorilla, orangutan and gibbon populations.[5]

Photo: Inflamed stomach tissue, adult female mountain gorilla, severe acute to subacute ulcerative gastritis. © Gorilla Doctors

Infectious Diseases with a Measured Effect on Health

Candidatus Sarcina troglodytae

Sarcina are bacteria that synthesize and release toxins that cause degeneration in the nervous system (Brown, 2019). Recently, the new, highly virulent *Candidatus Sarcina troglodytae* strain was linked to disease in captive, rehabilitant chimpanzees; the bacteria cause "epizootic neurologic and gastroenteric syndrome," characterized by neurologic and gastrointestinal signs that may result in mortality despite medical treatment (Owens *et al.*, 2021). Further research is warranted to elucidate the exact role of this bacterial strain in the development of the syndrome.

Respiratory Disease

Tuberculosis

Tuberculosis (TB) is the disease caused by infections with *Mycobacterium tuberculosis*, which has a wide host range and is the leading bacterial cause of death for humans worldwide. For these reasons, TB is of specific concern in relation to captive apes. Although prevalence in captive apes is low, an outbreak with environmental shedding could have a disastrous impact considering the large host range and zoonotic aspects (Kock *et al.*, 2021; Lécu and Ball, 2011; Michel *et al.*, 2003; Montali, Mikota and Cheng, 2001). *Mycobacterium tuberculosis* infections have sporadically been reported in captive chimpanzees, orangutans and gibbons in zoos (Michel *et al.*, 2003; Shin *et al.*, 1995; Wilson *et al.*, 1984). Zoo infections are generally thought to have arisen from contact with humans, although animals have been known to carry the mycobacteria into a facility. In one case, an elephant was the source of TB in a chimpanzee and zoo staff (Stephens *et al.*, 2013).

As ape populations are undeniably susceptible to this pathogen, testing for TB is critical before they join captive populations in a rehabilitation center or zoo, especially during the quarantine period (Lécu and Ball, 2011). Orangutan rehabilitation centers appear to be especially vulnerable and affected, as the TB incidence in the human population is very high in range countries where orphaned orangutans are confiscated. Indonesia has a particularly high burden of 312 cases per 100,000 people (WHO, 2020c); Malaysia's TB rate is 92 per 100,000 people (Avoi and Liaw, 2021). Several orangutan centers have had to construct dedicated TB quarantine facilities to house TB-positive animals. These individuals can never be released, as *M. tuberculosis* has never been detected in wild orangutans and the bacteria may be shed years after treatment (Dench *et al.*, 2015). Surveys in wild chimpanzees have not shown the presence of the bacterium (Wolf *et al.*, 2016). Nonetheless, captive, rehabilitant apes cannot be released without a negative TB test and efforts are required to mitigate the risk of transmission from humans and their domestic animals to protect wild populations (Wolf *et al.*, 2014).

Diagnostic challenges may complicate accurate identification of the latent stage of *M. tuberculosis* infection, during which the bacteria remain dormant inside the body, without overt clinical disease or associated shedding of the bacteria. Diagnostics are most accurate when they combine several tests: isolation, culture or molecular detection of the bacteria, chest X-rays and immunological tests that show any previous infection (using antibodies or other immune responses in blood or based on skin tests). Orangutans show a high level of cross-reactivity with non-pathogenic mycobacteria, which can be differentiated by comparative skin tests but may complicate accurate diagnosis (Dench *et al.*, 2015). Furthermore, in its latent stage, TB can remain inside a body for years, capable of escaping stringent therapeutic approaches. These characteristics

highlight the risks associated with introducing TB into a captive facility.

Air sacculitis

Air sacculitis is a common inflammatory condition of air sacs. Connected to the laryngeal tubes of apes (and many other animals), these sacs act as resonating chambers that amplify vocalizations and extend the duration of calls (Hewitt, MacLarnon and Jones, 2002; Riede *et al.*, 2008). Air sacculitis is a condition in which pus accumulates within the air sac, with the potential for serious complications, including fatal bronchopneumonia and sepsis. Of all captive ape species, orangutans appear especially susceptible, although cases in captive chimpanzees and bonobos have also been documented.[6] Sinusitis with concurrent pneumonia may play a role in the way this disease develops (Steinmetz and Zimmermann, 2012).

Bacteria isolated from air sacculitis cases in rescue centers often include intestinal bacteria, whose route of entry into the upper respiratory system is facilitated in captive conditions (Philippa and Dench, 2019). The relatively high incidence in captivity may be driven by other conditions as well. Among rehabilitant orangutans, decreased cage space, overcrowded cages, poor ventilation and environmental factors such as smoke appear to increase incidence (J. Philippa, personal observation, 2020).

Other Viral and Bacterial Respiratory Infections

Reports of respiratory infections in captive and semi-captive great apes are common. Human respiratory pathogens have often been involved in outbreaks of respiratory disease in both categories. Infections caused by human pneumoviruses (HMPV and HRSV), often complicated by secondary infections with *Streptococcus pneumoniae*, have been detected in zoo chimpanzees in Europe and the United States, as well as in
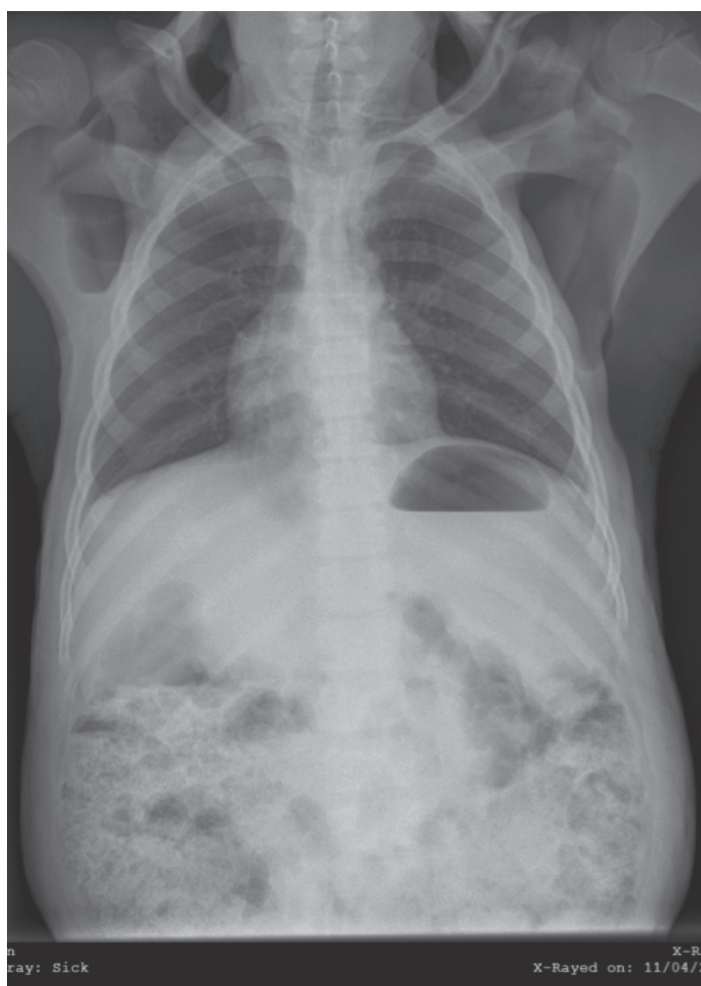
wildlife rescue centers (Köndgen *et al.*, 2017; Slater *et al.*, 2014; Szentiks *et al.*, 2009; Unwin, Chatterton and Chantrey, 2013). Morbidity reached up to 100% and several deaths were reported. Serological investigations have suggested broad exposure to human respiratory pathogens, including influenza A and B viruses of different subtypes (Buitendijk *et al.*, 2014; Kooriyama *et al.*, 2013). These findings were never confirmed by direct pathogen detection methods, however.

The recently emerged severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which caused the COVID-19 pandemic, has been transmitted to gorillas

Photo: Reports of respiratory infections in captive and semi-captive great apes are common. Human respiratory pathogens have often been involved in outbreaks of respiratory disease in both categories. © IAR Indonesia (YIARI)/ MoEF of Indonesia

in zoos in Barcelona, Prague, Rotterdam and San Diego. The spread underscores once more the high risk of transmission of human respiratory pathogens and the importance of observing strict hygiene rules when working in proximity to great apes (Gilardi *et al.*, 2015; Reuters and Gorman, 2021; Reuters Staff, 2021). Although there have been no confirmed cases of SARS-CoV-2 in populations of free-ranging apes, the risk is significant given the high prevalence of the disease in surrounding human populations. Measures to reduce the risk of transmission and the likelihood of outbreaks in wild populations include disease risk analysis of apes to be translocated or reintroduced, as well as enhanced pathogen surveillance (Sherman *et al.*, 2021).

Monkeypox

Shortly after the first identification of MPXV in a macaque colony in a research centre in Denmark in 1958, an outbreak was reported by the Rotterdam Zoo in the Netherlands (von Magnus *et al.*, 1959). Among the affected species, chimpanzees, gorillas and orangutans became ill with different degrees of morbidity and mortality (Peters, 1966). Clinical signs included the typical maculopapular rash and nasal discharge.

Subsequently, in 2014 and 2016, two MPXV outbreaks affected semi-captive chimpanzees in sanctuaries in Cameroon (Devaux *et al.*, 2019; Guagliardo *et al.*, 2020). During the first outbreak, at Sanaga-Yong Sanctuary, six animals fell ill and one succumbed to the infection. In the second outbreak, at the Mefou Primate Sanctuary, one out of the two reported cases had a fatal outcome. A serologic survey of the nearby human population showed that farmers had a higher prevalence of MPXV-specific antibodies than sanctuary workers, indicating that contact with rodents was more likely to cause exposure than contact with apes (Guagliardo *et al.*, 2020).

Melioidosis

Also known as Whitmore's disease, melioidosis is a predominantly tropical infectious disease that can infect humans and animals and has a wide range of both symptoms and severity. Melioidosis is a disease of increasing importance in its endemic region of Southeast Asia and northern Australia. It has caused fatal infections in a zoo-kept gibbon and orangutan, as well as in orangutan rescue centers in Malaysia, gibbons in the Singapore Zoo and, more recently, in rehabilitant orangutans in Indonesia (Nathan *et al.*, 2018; Sim *et al.*, 2018; Sprague and Neubauer, 2004; Testamenti *et al.*, 2020). African apes are also susceptible: in the Singapore Zoo, five gorillas and two chimpanzees have had fatal infections (Sim *et al.*, 2018).

The disease is caused by infections with the bacterium *Burkholderia pseudomallei*, which has a broad host range and can have high case fatality rates in animals and humans. Infections tend to coincide with increased rainfall (Cheng and Currie, 2005). Clinically, signs can range from subclinical to subacute, or wasting with subcutaneous and soft tissue abscesses. Melioidosis can be challenging to diagnose and treat because the organism can remain latent for years and is resistant to many antibiotics.

Non-Infectious Causes of Disease

Malnutrition

Malnutrition refers to the effects of a poorly balanced diet, including obesity, but is more commonly associated with undernutrition and starvation. Best practice guidelines on formulations and target nutrient ranges enable careful management of captive ape diets, based on extensive experience and knowledge (Abelló, Rietkerk and Bemment, 2017; AZA Ape TAG, 2010, 2017; Stevens, 2020). Commercial pellets facilitate a bal-

anced dietary composition for captive apes when supplemented with fresh food items that are closer to the natural diet (Nijboer, 2020). In rescue centers in home range countries, however, commercially produced biscuits or pellets may not be available, such that meeting dietary requirements necessarily involves a careful selection of natural foods, based on calculations of their nutritional values.

Despite this progress, nutritional deficiencies still occur in captive situations where unbalanced diets are provided, or in social groups with fierce competition for food, which can lead to the emaciation of certain individuals. To maintain a healthy nutritional state, ape management can include the monitoring of individual food uptake in social groups and a regular weighing schedule and body scoring to monitor body weights (Abelló, Rietkerk and Bemment, 2017; AZA Ape TAG, 2010, 2017; Stevens, 2020).

Deficiencies and Imbalances

Rickets, osteopenia and metabolic bone disease are well documented in captive apes and other primates. These deficiencies are consequences of dietary calcium–phosphorus imbalances, or insufficient calcium or vitamin D intake (Crissey *et al.*, 1998; Farrell, Rando and Garrod, 2015; Junge *et al.*, 2000). They occur when animals—especially infants but also adult females—are insufficiently exposed to natural ultraviolet light, for example because they are housed indoors (Videan *et al.*, 2007). Zoos in regions farther away from the equator require artificial light to supplement the ultraviolet B rays radiated from the sun, which are insufficient at higher and lower latitudes (Nijboer, 2020).

Vitamin C deficiency causes a disease commonly known as "scurvy," which can occur in all primates, as they are unable to synthesize their own vitamin C. To ensure sufficient uptake, most zoos supplement food with commercial primate biscuits containing stable vitamin C, especially if amounts in green vegetables and fruit are insufficient (Lowenstine, McManamon and Terio, 2018).

Obesity

Obesity is the most common form of nutritional disorder observed in zoo apes; orangutans and gorillas appear to be most affected due to the intake of large amounts of easily processable carbohydrates, while physical exercise is limited (Lowenstine, McManamon and Terio, 2018). Obesity, which is difficult to manage in captivity, inherently predisposes animals to diseases such as diabetes and hypertensive heart disease (Gresl, Baum and Kemnitz, 2000; Lowenstine, McManamon and Terio, 2016). As a reduction of calories in the diet usually results in an immediate decrease in activity, a more effective approach to combating obesity involves ensuring that animals engage in foraging-like "work" to access their food, increasing fiber as well as leaves and branches (known as "browse"), and decreasing sugar in their diet. These practices can reduce the frequency of abnormal regurgitation and re-ingestion, while also reversing pre-diabetes in zoo apes (Cabana, Jasmi and Maguire, 2018; Nash *et al.*, 2021).

Photo: Cardiovascular disease, renal disease and osteoarthritis are the most significant age-related or degenerative diseases among all apes. Heart tissue, adult female mountain gorilla, fibrosing cardiomyopathy.
© Gorilla Doctors

50 µm
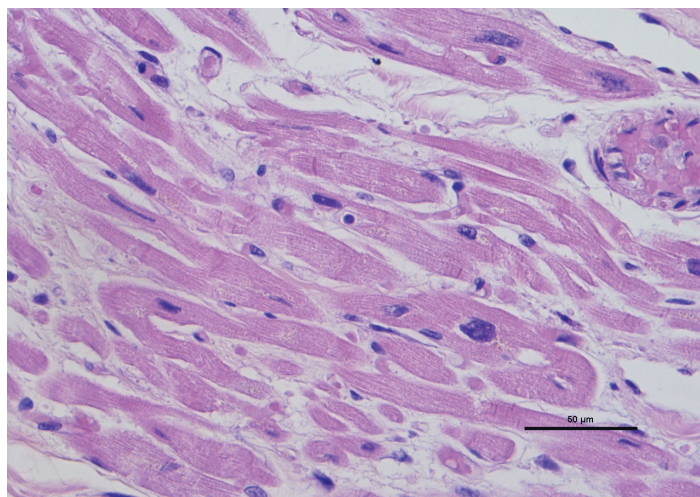
Age-Related Health Issues

Multiple studies examining pathology across captive and free-living apes indicate that cardiovascular disease, renal disease and osteoarthritis are the most significant age-related or degenerative diseases among all apes (Lowenstine, McManamon and Terio, 2018). Other degenerative conditions, including dental disease (dental attrition and tooth loss), ocular conditions (cataracts and retinal disease), and liver disease have also been documented. Pathologic correlates of human brain aging have been reported in chimpanzees, gorillas and orangutans (Lowenstine, McManamon and Terio, 2016). Neoplasms do not seem to be as common in apes as in humans and some other primates, with the exception of benign uterine leiomyomas in female chimpanzees and reproductive malignancies in female lowland gorillas (Brown *et al.*, 2009; Lowenstine, McManamon and Terio, 2016).

Cardiovascular Disease

Cardiovascular disease is an overarching term for conditions that affect the heart and blood vessels. It is a significant contributing factor in the deaths of apes under managed care. Studies indicate that the reported

Photo: Other degenerative conditions include dental disease (dental attrition and tooth loss), ocular conditions (cataracts and retinal disease), and liver disease. © Lwiro Primates Rehabilitation Center

incidence in North American zoos is 45% of bonobos, 41% of western lowland gorillas, 38% of chimpanzees and 29% of orangutans.[7]

Interstitial myocardial fibrosis or fibrosing cardiomyopathy has been the most frequently documented lesion across all great apes, in both zoo and research populations (Munson and Montali, 1990; Schulman *et al.*, 1995). It appears to result in sudden death via malignant arrhythmia or congestive heart failure (Lowenstine, McManamon and Terio, 2016; Murphy *et al.*, 2011). Postmortem data suggest that 41% of gorillas in North America, 81%–100% of chimpanzees living in a research colony and 91% of zoological chimpanzees demonstrate moderate to severe fibrosis (Lammey *et al.*, 2008; Meehan and Lowenstine, 1994; Strong *et al.*, 2018). Left ventricular hypertrophy, combined with coronary arterial arteriosclerosis, is suggestive of systemic hypertension as an underlying pathogenesis (Schulman *et al.*, 1995).

At the time of writing, the only study that had investigated the presence of myocardial fibrosis in sanctuary chimpanzees showed no evidence of the disease in a sample of 23 sanctuary chimpanzees aged 8–27 years (Strong *et al.*, 2020). There are currently no published data examining myocardial fibrosis in sanctuary bonobos, gorillas or orangutans. Further work is required to establish whether myocardial fibrosis presents a similar burden to wild and sanctuary captive apes and, if not, which predisposing factors are responsible for the disease in zoological and research facilities.

Other important cardiovascular lesions among apes are aortic dissection (a major disease in bonobos and lowland gorillas), atherosclerosis and degenerative valvular disease (Lowenstine, McManamon and Terio, 2018). Strokes have been well documented in captive chimpanzees (Jean *et al.*, 2012). Coronary atherosclerosis that was once common in captive apes is now rare, present

only in old apes who previously lived under outdated husbandry conditions (Lowenstine, McManamon and Terio, 2016).

Three ongoing projects are specifically examining great ape cardiac disease:

- the International Primate Heart Project (Cardiff Metropolitan University, n.d.);
- the Great Ape Heart Project (Detroit Zoological Society, n.d.); and
- the Ape Heart Project (Twycross Zoo, n.d.; see Case Study 2.4).

Work from these groups has identified specific cardiac conditions, potential risk factors and early markers of cardiac disease, such as multifocal ventricular ectopy as detected through an electrocardiogram, diabetes, renal disease, obesity, hypertension and metabolic syndrome.[8] In time, comprehensive databases of standardized ante-mortem and post-mortem data generated through these projects are expected to improve the understanding of cardiac disease in these endangered species and may help guide improved husbandry and veterinary practices to mitigate and treat this disease.

Renal Disease

The renal system includes the kidneys, ureters, bladder and urethra, which are responsible for the production and excretion of urine. Renal disease occurs commonly in captive apes. The North American species survival plan ape pathology databases list chronic interstitial nephritis as the most common diagnosis, followed by glomerular lesions (Lowenstine, McManamon and Terio, 2018). Aging, laboratory-housed chimpanzees commonly exhibit evidence of clinically declining renal function (Videan, Fritz and Murphy, 2008). Renal disease was also identified as the cause of death in 26% of orangutans over the age of 40 and 15%–18% of 15–40-year-old orangutans, but it was less common in lowland and mountain goril-

las (Lowenstine *et al.*, 2008; Meehan and Lowenstine, 1994; Nutter *et al.*, 2005). There appears to be a statistical association between cardiac and renal disease in zoo-housed orangutans (Lowenstine *et al.*, 2008).

Osteoarthritis

Osteoarthritis is a condition that results in stiff, painful joints and is commonly reported in captive apes, although the overall prevalence in apes under managed care has not been determined. Ape species survival plan pathology advisors report that osteoarthritis typically occurs on the knees, hips, elbows and lower spine. Lesions have been documented in both captive and free-living individuals (Lowenstine, McManamon and Terio, 2016).

Dental Disease

Enamel hypoplasia (thin or missing tooth enamel) of deciduous and permanent teeth occurs in both wild and captive apes. Enamel formation can be disrupted by external stressors, including rainy seasons in which food

availability is limited (Skinner, 1986). Orangutans are most prone to both linear and localized enamel hypoplasia, which also occurs in chimpanzees and gorillas, while gibbons are seldom affected (Guatelli-Steinberg, 2000; Guatelli-Steinberg, Ferrell and Spence, 2012; Guatelli-Steinberg and Skinner, 2000; Hannibal and Guatelli-Steinberg, 2005).

Psychological Disorders

Psychological disorders are also known as psychiatric disorders or mental health problems. Limited opportunity or ability to conduct natural behavior, physical exercise and—most importantly—mental exercise increases the chances of the development of psychological disorders, including stereotypical behaviors, accompanied by increased levels of stress hormones such as cortisol and catecholamines (Jacobson, Ross and Bloomsmith, 2016; Nash *et al.*, 1999; see Chapter 8). Psychological disorders are more likely to develop in captive apes whose history is not considered. Apes exhibit behavioral disturbances similar to post-traumatic stress disorder (PTSD) following traumatic experiences. Carers are advised to take such signs into consideration, particularly when rescuing orphans, translocating "displaced" apes or confining apes in captivity (Ferdowsian *et al.*, 2011).

Illegal Captivity

Illegal captivity combines multiple health threats resulting from poor husbandry. Illegal captivity generally starts at an early age, when young apes are violently separated from their mothers. They are often kept in deplorable living conditions and generally are not provided with an adequate diet. Illegally kept apes tend to exhibit signs of nutritional deficiencies and PTSD; many are malnourished and emaciated, while a smaller number are obese (Ferdowsian *et al.*, 2011). In the best-case scenario, orphaned babies are intro-

> *Given the myriad threats faced by apes in the wild, understanding what influences their health and fitness may provide critical knowledge for their long-term conservation.*

duced to a proper diet and weaned off any inappropriate food they may have been given previously. Among apes whose illegal captivity lasts longer, physical changes can become irreversible, including metabolic bone disease (Farrell, Rando and Garrod, 2015).

In addition to suffering from psychological disorders and malnourishment, some illegally kept apes are used as photo props or tourist attractions. In Thailand, young gibbons are exhibited at beaches, bars and restaurants, where they are given drugs such as amphetamines to keep them awake at night—and alcohol to "perform" (Gray, 2012). It is thus not uncommon for rescued gibbons to have alcohol or drug dependencies (J. Philippa, personal observation, 2021).

Conclusion

This chapter discusses factors that have major and plausible impacts on the health of wild and captive apes. Far from being an exhaustive review of such factors, it provides a preliminary outline. The expanding body of long-term research is likely to reveal new pathogens and non-infectious factors that influence ape health. From a public health perspective, these ongoing research activities may be able to inform disease risk reduction strategies for humans (Calvignac-Spencer *et al.*, 2012). At the same time, studies of humans' fellow hominins can provide insight into the factors that influenced the health of early human societies and their relationship to the microbial world; these findings could further contribute to improvements in human health (Gogarten *et al.*, 2019b; Moeller, 2017). Given the myriad threats faced by apes in the wild, understanding what influences their health and fitness may provide critical knowledge for their long-term conservation.

As this chapter reveals, only a small proportion of the factors that have a demonstrated or suspected influence on ape health

impact both wild and captive individuals. This finding may be unsurprising, as bacterial and phage communities in captive apes' guts are completely different from those of their wild conspecifics. Indeed, in captive settings, the components of wild apes' microbiomes appear to undergo a complete replacement by human-associated microbes (Campbell *et al.*, 2020; Gogarten *et al.*, 2021). Just as the microbial world facing captive apes is substantially different from that of their wild counterparts, so too are many of the infectious and non-infectious factors affecting their health.

The threat posed by human respiratory pathogens, which have caused significant mortality in both populations, seems to represent the clearest intersection between wild and captive apes. Given ever-increasing rates of anthropogenic disturbance and the resulting increase in human–wildlife contact, the overlap in health threats faced by wild and captive populations is likely to expand. Nevertheless, this overview indicates that targeted strategies are required for the management of both wild and captive ape populations. Closer collaboration among practitioners and researchers working in both in situ and ex situ situations is key to bridging the data gaps and turning anecdotal clinical data into robust peer-reviewed evidence.

Acknowledgments

Endnotes

1   Bermejo *et al.* (2006); Leroy *et al.* (2005); Marí Saéz *et al.* (2015); Olival and Hayman (2014); Pigott *et al.* (2014, 2016).

2   Canfield *et al.* (1997); Gjeltema *et al.* (2016); Hawkins *et al.* (2021); Mätz-Rensing *et al.* (2011); Rideout *et al.* (1997).

3   Labes *et al.* (2011); Mbaya and Udendeye (2011); Mul *et al.* (2007); Panayotova-Pencheva (2013); Tangtrongsup *et al.* (2019); Teo *et al.* (2019); Toft (1982).

4   Eberle, Black Hilliard (1989); Eberle and Jones-Engel (2017); Lavergne *et al.* (2014); Seimon *et al.* (2015); Wertheim *et al.* (2014).

5   Emmons and Lennette (1970); Heldstab *et al.* (1981); Kik *et al.* (2005); Landolfi *et al.* (2005); Mootnick *et al.* (1998); Ramsay *et al.* (1982).

6   Cambre *et al.* (1980); Clifford *et al.* (1977); Kumar *et al.* (2012); Lawson, Garriga and Galdikas (2006); McManamon, Swenson and Lowenstine (1994); Stevens (2020); Zimmermann *et al.* (2011).

7   Gamble *et al.* (2004); Lammey *et al.* (2008); Laurence *et al.* (2017); Lowenstine *et al.* (2008); McManamon and Lowenstine (2012); Meehan and Lowenstine (1994); Seiler *et al.* (2009).

8   Celestino-Soper *et al.* (2018); Doane, Lee and Sleeper (2006); Ely, Zavaskis and Lammey (2013); Lowenstine, McManamon and Terio (2016); Nunamaker, Lee and Lammey (2012); Rosenblum and Coulston (1983); Tong *et al.* (2014).

9   Helmholtz Institute for One Health (www.helmholtz-hzi.de/en) and Robert Koch Institute (www.rki.de).

10 Helmholtz Institute for One Health (www.helmholtz-hzi.de/en) and Robert Koch Institute (www.rki.de).

11 Helmholtz Institute for One Health, Helmholtz-Centre for Infectious Research (www.helmholtz-hzi.de/en), Robert Koch Institute (www.rki.de) and University of Greifswald (zoologie.uni-greifswald.de/en/organization/departments/applied-zoology-and-nature-conservation).

12 Helmholtz Institute for One Health, Helmholtz-Centre for Infectious Research (www.helmholtz-hzi.de/en) and Robert Koch Institute (www.rki.de).

13 Helmholtz Institute for One Health, Helmholtz-Centre for Infectious Research (www.helmholtz-hzi.de/en) and Robert Koch Institute (www.rki.de).

14 At the time of writing: International Animal Rescue (www.internationalanimalrescue.org).

15 Helmholtz Institute for One Health, Helmholtz-Centre for Infectious Research (www.helmholtz-hzi.de/en) and Robert Koch Institute (www.rki.de).

16 International Primate Heart Project, Swansea University (www.swansea.ac.uk and primate-heartproject.co.uk).

17 North Carolina Zoo (www.nczoo.org).

18 Copperbelt University School of Natural Resources (www.cbu.ac.zm/schoolsAndUnits/schoolof-naturalresources).