# The infectious diseases consequences of monkey business

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Many microorganisms that affect humans have originated in animal species and have subsequently evolved to afflict humans (1). Many factors may contribute to the ability of infectious agents to cross the species barrier and include those related to the host, the pathogen and the host-pathogen environment. The microorganism must be able to establish itself in the new host within an environment that allows transmission to take place. Transmission may be facilitated by proximity, degree of physical contact between animals and humans, and the ability to be inoculated into the new host. Several examples of such pathogens have been recently encountered and include the agents of avian influenza (H5N1 and H9N2), severe acute respiratory syndrome, hantavirus infection and variant Creutzfeldt-Jakob disease. A recent comprehensive literature review (2) identified 1415 species of infectious microorganisms, including 217 viruses and prions, 538 bacteria and rickettsia, 307 fungi, 66 protozoa and 287 helminths, known to infect humans. Of these, almost two of three are zoonotic (ie, capable of being transmitted between humans and animals). Of the 1415 species of infectious microorganisms, 175 are considered to be 'emerging' pathogens (2). Of these, 132 (75%) are zoonotic, with protozoa and viruses considered more likely to be 'emerging' infectious agents than other taxa. Among infectious agents associated with the 'emerging' infectious diseases, RNA viruses are most likely to emerge as the greatest threat. Given the similarity of genetic, physiological and behavioural characteristics of humans and nonhuman primates, the latter are considered high-risk sources of emerging infectious agents with the capacity to infect humans. Primate-to-human cross-species transmission of infectious agents has become a focus of significant scientific interest over the years, given that two simian immunodeficiency viruses (SIV) – SIVcpz from chimpanzees and SIVsm from sooty mangabeys – are the cause of AIDS in humans (3). With increasing human-primate contact being reported in Asia and Africa, both as a result of deforestation and clearing of land for agriculture plus a growing trend toward tourism from European countries, the United States and Canada, to south and southeast Asia and the south Pacific islands, and active marketing of 'monkey temple' tours, the cross-species transmission of infectious agents from nonhuman primates is becoming a significant public health issue.

It is estimated that the number of humans who come into contact with nonhuman primates at monkey temples around the world is probably several million per year; monkey temples are increasingly considered to be a key interface between humans and nonhuman primates (4). Worldwide, monkey temples may account for more human-primate contact than any other activity. Many of the visitors to these monkey temples are foreign tourists, which makes them a potential common source for the global dissemination of emerging infectious agents. Monkey temples can be found throughout south and southeast Asia, and in the south Pacific islands, such as Bali, where the monkeys play a role in Hindu and Buddhist culture (5-8). These temples have become refuges for large populations of nonhuman primates who have readily adapted to humans. Their populations are flourishing with offerings of food and contact with the large numbers of tourists and pilgrims who visit.

On the island of Bali alone, there are more than 40 such temples plus an 'Enchanted Monkey Forest', which are frequented by tourists from around the world (8,9). Approximately 700,000 international tourists visit the island's four main monkey temples every year. Temple workers and people who live near the temples also have a great deal of contact with monkeys. The Buddhist temple of Swayambhunath situated on the top of a hill west of the city of Kathmandu, is one of the most popular and instantly recognizable symbols of Nepal. The temple is colloquially known as the 'monkey temple', and travel brochures often comment on the large tribe of handsome monkeys who guard the hill and amuse visitors and devotees with tricks, including sliding down the banisters of the stairways to the temple. There are also similarly named monkey temples, such as the Lopburi Temple in Thailand (10), a country that is an increasingly popular tourist destination with Canadians.

Extensive, unregulated and often close contact between humans and monkeys occurs at these sites and there is a growing body of evidence documenting extensive human-monkey interactions at monkey temples (5,11). Roving bands of monkeys quickly snatch up any offerings of food made by devotees and tourists, and will also just as quickly grab anything they may be carrying. In addition, the monkeys climb on the heads and shoulders of visitors, which may bring nonhuman primate body fluids into contact with tourists' conjunctiva, nasal and oral mucosa that represent potential portals of entry for infectious agents. Bites and scratches have been reported during encounters between the temple monkeys and their human visitors, resulting in transcutaneous exposure to the body fluids of the temple monkeys, which may carry a host of infectious agents. The monkeys at the temple sites have become a tourist attraction in their own right and, in addition to feeding them, teasing the monkeys is common, which may result in aggressive monkey behaviour. People who live and work in and around temples such as the Swoyambhu temple in Nepal, share common water sources with the rhesus monkey inhabitants of the temple and report that the monkeys frequently invade their homes and gardens in search of food (4).

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The macaque species, principally the rhesus macaque, which is one of the most frequently encountered of the Old World monkeys, are the primates most often associated with temples because they can thrive in human-altered environments (5). Many infectious agents, predominantly viruses, are carried by macaques and with the increasing interactions between humans and macaques in the commercial setting of tourism, several studies (4,11,12) have examined the prevalence of selected enzootic primate-borne viruses in temple-associated or breeding populations of rhesus macaques.

*Herpevirus simiae*, also known as herpes B virus, has been documented in several species of macaques (13), and seroprevalence surveys have demonstrated an antiherpesvirus antibody prevalence of 10% to 80% among wild populations and close to 100% among captive populations (14). Antibody seroprevalence of herpes B virus in samples collected from rhesus macaques at the Swoyambhu temple in Nepal was 64.1% overall, but 100% if only adult macaques were included in the sample (4). The percentage of infected macaques who actively shed herpes B virus at a given time is low, at 1% to 2% (13). Although infection with herpes B virus in macaques is inapparent, herpes B virus infection in humans can cause severe disease with fatal meningoencephalitis and a case-fatality rate of almost 70% (15,16). Several routes of primate-to-human transmission have been implicated, most involving direct exposure to tissue or fluid from an infected macaque. No cases of *H simiae* infection have been reported in persons exposed to wild macaques.

Simian virus 40 (SV40) is a polyomavirus enzootic among species of rhesus macaques of northern India and Nepal, and is excreted in the genitourinary tract of infected macaques (17). Antibody seroprevalence of SV40 in samples collected from rhesus macaques at the Swoyambhu temple in Nepal was 89.7% overall, but 94.7% in adult macaques. (4). Evidence of transmission of SV40 infection to humans has been documented among zoo employees who worked with nonhuman primates, and among workers at monkey export firms in India with seroprevalence rates of 23% and 27%, respectively, among these workers (18,19). SV40 has been found to cause cancer in laboratory rodents, and some investigators have reported detection of SV40 DNA in various human tumours, although the role of SV40 in human malignancies remains controversial (19).

Rhesus cytomegalovirus (RhCMV) is enzootic among rhesus macaques with seroprevalence rates of almost 100% in breeding populations of captive animals and 95% in a sample of temple macaques (4,20). RhCMV infections are inapparent in macaques, but can be fatal in the setting of coinfection with simian type D retrovirus (SRV) and SIV (21). Viral shedding from mucosal surfaces may occur intermittently. To date, no human infection with RhCMV has been reported.

In addition to members of the herpes virus and polyoma virus families, macaques naturally carry several enzootic retroviruses asymptomatically, including simian foamy virus (SFV), SRV and simian T-cell lymphotropic virus type 1 (STLV-1). For example, the seroprevalence of SFV in samples collected from the rhesus macaques at the Swoyambhu Temple in Nepal was 97.4% (4). Although no evidence of STLV-1 infection was found among the latter sample of macaques, other studies have found a STLV-1 prevalence of between 3% and 10% among wild macaques in Indonesia and 100% in a sampling of macaques from Thailand (22,23). SIV has not been detected among Asian macaques but is widely distributed among African nonhuman primates (3). Studies (24) examining monkey temple workers in Indonesia have shown that humans can be infected with SFV and SRV. Research (25-27) on humans exposed to nonhuman primates in the context of laboratory and zoo work exposures has documented SFV seroconversion rates of 1% to 5.3% and an SRV seroconversion rate of 0.9%, respectively. STLV-1 is closely related to human T-cell lymphotropic virus, which is pathogenic to humans. It is hypothesized that human T-cell lymphotropic virus evolved from STLV-1 (28). These enzootic retroviruses are present in multiple body fluids of infected macaques and it is presumed that transmission occurs through bites, scratches and mucosal splashes during contact with humans.

There are several implications for the increased human-macaque interface at monkey temples, other than the play on 'monkey business' to amuse tourists. Physicians who care for sick, returning travellers who have visited monkey temples need to be aware of the potential not only for the usual bacterial infections, but also a host of unique viral infections such as herpes B encephalitis, SFV and STLV-1. It is crucial that physicians have a high index of suspicion for unusual infections in returning travellers to these areas and should inquire about monkey scratches and bites. It is also important to recognize that exposures to macaque body fluids in high-density, relatively uncontrolled settings creates a significantly higher risk for primate-to-human viral transmission than the more controlled environment and limited exposure seen in primate laboratories and zoos, which also routinely use barrier precautions and have postinjury protocols. More importantly, the interaction between temple monkeys and humans may have the potential to create a mixing vessel for cross-species transmission of novel viruses or other microorganisms. With increasing global travel, rapid dispersal of a novel primate-borne pathogen could occur. All physicians must become increasingly aware of the potential of zoonotic transmission and provide sound advice for those travelling to places where close encounters with animal species may occur.

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