Animal Reservoirs: Harboring the Next Pandemic

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Animal Reservoirs: Harboring the Next Pandemic

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Recent studies of emerging infectious diseases show most are zoonoses transmitted to humans from domesticated animals and wildlife.

There's a dead blue jay lying on your front doorstep. Outwardly, you see no sign of bodily damage. It could have flown into a window and broken its neck, or, more ominously, it could signal the beginning of the West Nile virus season. West Nile virus, which was unknown in the United States until 1999, is a zoonotic disease—that is, it's carried by animals but transmissible to humans. And you, with the dead bird on your doorstep, have unwittingly become a sentinel in the surveillance system to prevent the spread of zoonoses.

The World Health Organization (WHO) has assumed major international responsibility in the surveillance and prevention of the spread of zoonoses, which it defines, quoting the Pan American Health Organization, as "any disease and/or infection [that] is naturally 'transmissible from vertebrate animals to man.'" Although this definition eliminates vector transmission, a recent review of human infectious diseases that emerged between 1940 and 2004 defines zoonoses more broadly as "those [that] have a nonhuman animal source" (Kate E. Jones et al., 21 February 2008 issue of *Nature*). This characterization includes vector-borne diseases, such as West Nile virus and malaria, and infections that are transmissible through contact with blood or tissue, such as HIV/AIDS. Jones and colleagues noted that, of the 335 emerging infectious diseases they identified, 60.3 percent are zoonotic in origin.

Some of the emerging zoonoses catalogued by Jones and colleagues are familiar. *Escherichia coli* O157:H7, a toxic strain of bacteria first identified in California in 1975, resulted from changes in the food industry. People contract *E. coli* O157 infections from contaminated beef and milk products, and it can also be transmitted from person to person through fecal material. Chikungunya virus, first identified in 1952 in Tanzania and prevalent in the Indian subcontinent, causes an infection similar to dengue fever. Japanese encephalitis virus, first identified in 1989 in Papua New Guinea, is now common throughout eastern and southeastern Asia and the island nations in the western Pacific.

A 2007 literature review of infectious diseases reported for the first time in humans since 1980 excluded arthropod vector-borne diseases (Mark E. J. Woolhouse and Eleanor Gaunt, *Critical Reviews in Microbiology*). Of the 87 new human pathogens catalogued, approximately 80 percent are zoonotic. Zoonotic agents were associated with a range of carriers, from most to least common: ungulates, carnivores, rodents, bats, nonhuman primates, birds, and marsupials. Very few zoonoses were carried by reptiles or amphibians.

Woolhouse and Gaunt point out that very few zoonotics are capable of spreading from human to human, and even fewer are capable of epidemic spread in human populations. Yet there are factors that may lead to increased emergence of zoonotic infections in humans, resulting in the fear that one of these infectious agents could spark epidemics, if not a pandemic. Influenza A H5N1 (avian influenza) is considered one of the zoonoses with pandemic potential. It has been proven to be transmitted from person to person but, as yet, has spawned no epidemics.

"We have met the enemy..."

Zoonoses spread from the interface between humans and domestic animals, livestock, and wildlife. The advent of zoonotic diseases in humans, notes Björn Olsen, an infectious diseases specialist from Uppsala University and Kalmar University in Sweden, results from humans undertaking agriculture. "When we started to live in warm spots and [we] domesticated [animals],...we started to have the transfer of pathogens from domesticated animals." Before that, humans probably were infested with parasites, but human groups were very likely too greatly separated for epidemics to take hold.

This western sandpiper, Calidris mauri*, seen in Lorino, Russia, is typical of the birds that Björn Olsen and his colleagues monitor for strains of avian influenza virus. Photograph: Jonas Bonnedahl.*

As the human population grew, Olsen continues, "due to a series of events and meeting points between wild animals, domesticated animals, and humans,...we had the transfer from [one human] to the next." Now we have reached a point where biodiversity is on the decline and humans are the second most common mammalian species on Earth, after the rat. The most common bird is the chicken, he explains, with more than 20 billion individuals, all raised domestically in monoculture. Bringing the "monoculture" of humans together with domesticated livestock, he says, allows "different microorganisms to make the journey from one organism to another."

According to Olsen, we have only ourselves to blame for the creation of highly pathogenic avian viruses. "This is a result of the domestic animals," he says. The H5N1 strain of avian influenza has a low pathogenic ancestor in the avian community. "When this is meeting poultry,...something happens."

It's not just how we live with domesticated livestock that creates opportunities for zoonotic agents to "host shift," or move from one vertebrate host into another; it's also how we live in our environment. Evolutionary ecologist T. Jonathan Davies, of the National Center for Ecological Analysis at the University of California–Santa Barbara (UCSB), recently coauthored a study on host shift of pathogens between wild primates and humans (*Proceedings of the Royal Society B*, 22 July 2008). Davies points out: "Geography was a predictor where the species shared pathogens. We have moved that geographical barrier between humans and wild primates." This movement, he says, results from a "huge international movement of people invading pristine habitats." He notes that it is very common for colonial powers to come down with new and unusual diseases.

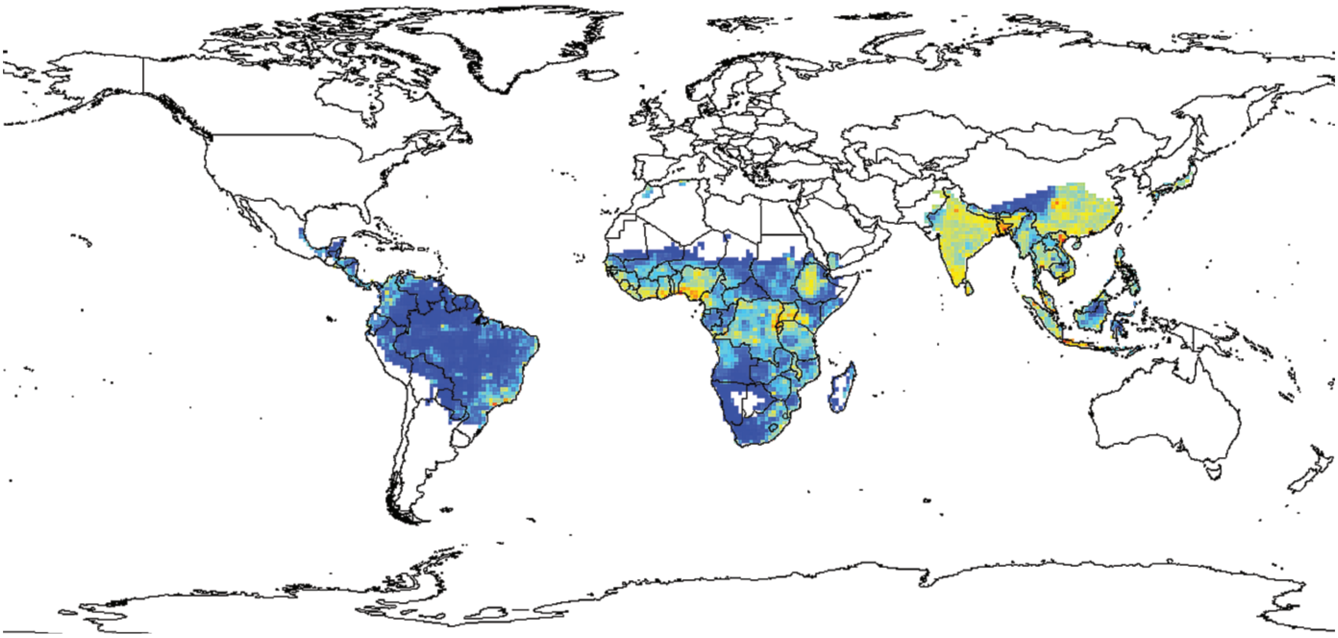
Peter Daszak, director of the Consortium for Conservation Medicine in New York City and a coauthor of the article in *Nature*, gives a concrete example of the human–animal interface. The report in *Nature* identifies hotspots for development of emerging infectious diseases (EIDs) throughout the world. For example, there is a hotspot for EID development in Brazil, where ongoing industrial and agricultural development is destroying the Amazon and creating a new interface between humans and wildlife. But, Daszak points out, "the hotspot is not in the very remotest part of the Amazon. The hotspot is where they're building a road through the Amazon."

Even close to home, the human–wildlife interface is where zoonoses meet the human population. We enjoy venturing into places, such as woodlands, where we're likely to find that interface, says Mary Jane Lis, Connecticut state veterinarian. Daniel Janies of Ohio State University, who applies bioinformatics to infectious diseases, summed up the problem causing transmission of a zoonosis, such as influenza: "People who travel."

UCSB's Davies points out that the 1918 influenza pandemic occurred when there was a large international movement of troops during the First World War. "I would guess that flu jumping between birds and humans and pigs occurred frequently before that time," he says. But with the massive armies in Europe, the time, place, and circumstances were ripe for what became a pandemic. We're probably experiencing similar—or greater—numbers of people moving as in the First World War, he says, and that movement of people moves diseases. International travel was, he explains, "one of the reasons why outbreaks such as HIV may have gone global so quickly." Before this level of human travel, he notes, HIV-1 jumped into the human population from chimpanzees several times. But with international travel, the timing was "right" for an epidemic to begin.

Colin Russell, of the University of Cambridge, and colleagues published a recent report on the global spread of seasonal influenza A viruses (18 April 2008 issue of *Science*). "Anyone with flu who gets on a plane can spread it anywhere," he stated in a press teleconference. And influenza, notes Olsen, is a zoonosis that comes from birds. "All influenza viruses are bird borne," he says.

But it's not just infected humans traveling on planes who create a risk for zoonotic transmission. Infected mosquito vectors also stow away on airplanes and create a risk. Daszak notes that West Nile virus, which landed in the United States in 1999, spread rapidly across the country and now is a potential threat to Hawaii, the Galápagos, and Barbados. As the virus had a devastating effect on passerine bird populations on the US mainland, there is concern that it could infect endangered endemic Hawaiian birds and, on the Galápagos, Darwin's finches. The effect on tourism in both places could be financially devastating.



T. Jonathan Davies tries to anticipate emerging infectious diseases with this map showing the convergence of high human population density and possible risk of pathogens crossing to humans from nonhuman primates. Although the map does not take into account that wild primate population densities are likely to be low where human population density is high, areas of potential for transmission of diseases can be assumed. For example, West and Central Africa stand out as putative hotspots (orange and red), as do parts of Asia, where high human population densities may make the spread of emerging diseases particularly rapid. Courtesy of T. Jonathan Davies, University of California–Santa Barbara.

The Aedes aegypti *mosquito, found in wet tropical and subtropical regions worldwide, is a vector for the viruses that cause yellow fever, dengue fever, and Chikungunya fever. Photograph: US Department of Agriculture.*

What can we do?

Is there any way we can protect the human population from zoonotically derived epidemics? Surveillance of the wild bird population is one thing that can be done. Olsen and his colleagues, based at the Ottenby Bird Observatory on Öland, an island off the southeastern Swedish coast, travel around the world capturing wild birds and taking samples. Depending on the study, they take cloacal swabs or fecal samples, or they remove ticks from birds' bodies. The group's surveillance of wild bird populations, especially duck species, which

*If West Nile virus reaches the Galápagos, the rare and unique Darwin's finches, such as this medium ground finch (*Geospiza fortis*) from Santa Cruz Island, may be vulnerable to infection and death. Photograph: Andrew Hendry.*

The deer tick, Ixodes scapularis*, carries* Borrelia burgdorferi*, the bacteria that cause Lyme disease. As humans move into woodlands, they breach the interface between wildlife—the deer and field mice that harbor* Borrelia *and transmit it to biting ticks—and humans. Photograph: Scott Bauer, US Department of Agriculture.*

frequently harbor influenza A virus subtypes H1 to H12, could provide an early warning that a low pathogenic virus "can make the journey from the wild bird reservoir, through poultry and domestic animals, and eventually end up in humans," he says.

Olsen points out that "high[ly] pathogenic H5N1 virus is best monitored by mortality data in domestic and wild birds." Transportation of poultry and by-products from processing poultry, he explains, is the most effective way of spreading the H5N1 avian virus.

Lis notes that the State of Connecticut has established surveillance programs that look for signs of all avian influenzas in domestic poultry. She says that they have always inspected commercial flocks, but they now "have an inspector going around doing surveillance in backyard flocks." They have also set up a courier service that will pick up dead animals from farmers and veterinarians and take the bodies to the Connecticut Veterinary Medical Diagnostic Laboratory at the University of Connecticut–Storrs. They are looking at animals that showed acute mortality, something highly infectious, neurological symptoms, or cases involving multiple animal deaths. Specifically, they are looking for avian influenza; scrapie in sheep and goats; bovine spongiform encephalopathy, or mad cow disease; and any introductions of foreign animal diseases.

Davies thinks that surveillance for nonhuman primate–carried zoonoses should focus on detecting outbreaks in local human populations in Central and West Africa, where these infectious agents have been evolving in the animal population. But surveillance of human populations differs

Chickens are raised in large facilities housing thousands of birds, leaving them vulnerable to infection if a wild bird (or an insect vector carrying an infectious microbe) comes into contact with them. Photograph: Rob Flynn, US Department of Agriculture.

from surveillance of livestock, Lis notes. People, she explains, can report their symptoms. But livestock owners may not report a sick animal to state authorities "until it causes angst" or hits the owner in the pocketbook. Furthermore, she adds, government authorities "have to build a relationship with the livestock owner."

Predicting and reacting to EIDs

Daszak and colleagues are using mathematical algorithms to predict the likelihood of disease introduction. By understanding the patterns of zoonotic emergence in human populations, they can identify hotspots for the origin of EIDs. However, mapping hotspots of EIDs on the basis of the published literature is apt to be misleading, showing greater numbers of diseases emerging in the eastern United States and Western Europe than in developing nations in southern latitudes. Biodiversity scientist Kate Jones of the Zoological Society of London, who is lead author of the article in *Nature*, says the hotspot map reflects a bias influenced by the place-of-origin reports of these diseases. Published accounts tend to emanate from areas with the technology to identify EIDs and the ready ability to publish results in scientific journals, while the diseases probably originate in tropical areas of Africa, Latin America, and Asia.

But even if researchers can predict the next zoonotically based epidemic, can anything be done to stop it? "Stop eating bushmeat, and [quit] putting animals together in a wild market," recommends Jones. The propinquity of many species of wild animals in markets in southern China allowed the SARS coronavirus to jump from wild bats into another, yet unknown species and then into humans, according to studies of the viral genetic sequences conducted by Janies and colleagues.

We need better regulation of the wildlife pet trade, which goes almost entirely unregulated, say several of the researchers. Daszak explains that in the United States, there is no legislative mandate to inspect any incoming wildlife for unknown pathogens or to test domestic birds for anything other than psittacosis, Newcastle's disease, and avian influenza. After a 30-day quarantine, a bird infected with something that hasn't killed it and for which it has not been tested may be sold in a pet shop. Reptiles aren't quarantined at all, says Daszak. And Lis points out that people are importing exotics, not just for the pet trade, but also for private collections. These animals may pose a health risk to indigenous wildlife if they have contact with native species, such as through a fence or by escaping their enclosures.

A story told by many researchers is that of the alert customs officer in Belgium who confiscated two mountain hawk-eagles, *Spizaetus nipalensis*, that were smuggled in from Thailand for the live animal trade. Both birds were euthanized, and both were infected with highly pathogenic H5N1 avian influenza. These animals, according to Janies, were confiscated two years before H5N1 avian influenza was found in wild birds in Europe.

Others advocate major policy changes. Tracey McNamara, of Western University of Health Sciences in Los Angeles, California, the veterinary pathologist who identified West Nile virus in dead birds at the Bronx Zoo, says: "I think we need to re-create in the United States what the Soviets created at the turn of the century: the Soviet antiplague system." This would require "people with the jurisdiction and legal wherewithal to respond quickly to zoonotic threats in the human and animal populations." McNamara is critical of the inability to respond: "To date, we haven't figured out who's in charge about zoonotic outbreaks." She has doubts about current methods, too. "Looking at all the birds in Mongolia...distracts [us] from the key issues. Even if we know what is going on around the world, what impact does it have on the reality in the United States?" Even if we know what wild birds are carrying, she points out, we can't do anything about it. The best we can do, Olsen and his colleagues warn, is to try to keep wild birds separate from domestic fowl.

McNamara says that borders are porous, and "our ports are wide open." The introduction of West Nile virus into the United States—however it occurred, and there are many hypotheses— along with its rapid dissemination across the contiguous 48 states, could happen again with a different, and potentially more deadly, zoonotic pathogen. Australia and New Zealand have campaigns to look for vectors of disease. But in the United States, she explains, "we wait until we have people in the emergency room."

Lest we think that zoonotic diseases are a threat solely to us as a species, Davies warns that human pathogens pose a threat to wild primates, as well. Ecotours to visit endemic primates may be a means of economic growth, but at the same time, they further threaten already endangered nonhuman primates. "We're getting people from all over the world with entirely new pathogens," says Davies.

"We need an entirely integrated perspective," Jones says. "It's about what the function of the ecosystem is. When you change the composition of the ecosystem, what happens?" To prevent zoonotically based epidemics, we need to change how we think about the environment...and ourselves.

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www.paho.org/english/ad/dpc/cd/cd-unit-page.htm

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