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Perspective

# Zoonotic Spillover: Transmission of a Pathogen Prevalence

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## DESCRIPTION

Spillover infection occurs when a reservoir population with a high pathogen prevalence comes into contact with a new host population. The pathogen spreads from the reservoir population to the host population, which may or may not be transmitted. The risk of viral spillover is expected to rise dramatically as a result of climate change and land use expansion.

Spillover occurs frequently; in fact, more than two-thirds of human viruses are zoonotic. The majority of spillover events result in self-limited cases with no further human-to-human transmission, such as rabies, anthrax, histoplasmosis, or hidatidosis. Other zoonotic pathogens can be transmitted by humans, resulting in secondary cases and even establishing limited chains of transmission. Ebola and Marburg filoviruses, MERS and SARS coronaviruses, and some avian flu viruses are examples. Finally, a few spillover events can result in the microbe's final adaptation to humans, who become a new stable reservoir, as happened with the HIV virus, resulting in the AIDS epidemic.

Most pathogens that are now only found in humans were most likely transmitted by other animals in the past. If the history of mutual adaptation is long enough, permanent host-microbe associations can be established, resulting in co-evolution and, in the case of endogenous viruses, permanent integration of the microbe genome into the human genome. The closer the two species are in terms of phylogeny, the easier it is for microbes to break through the biological barrier and produce successful spillovers. As a result, other mammals are the primary source of zoonotic agents in humans.

During the late 20$^{th}$ century, zoonotic spillover increased as agriculture's environmental impact encouraged increased land use and deforestation, altering wildlife habitat. The risk of zoonotic spillover is expected to rise significantly as species shift their geographic ranges in response to climate change, particularly in tropical regions experiencing rapid warming.

Spillover transmission is facilitated by subsequent processes that allow an animal pathogen to infect a human. Interactions among several factors, including disease dynamics in the reservoir host, pathogen exposure, and within human factors that affect susceptibility to infections, determine the likelihood of zoonotic spillover. These factors can be divided into three functional phases that describe all major transmission routes.

Pathogen pressure, or the amount of pathogen available to the human host at a given point in space and time, is determined in the first phase by interactions between reservoir host distribution, pathogen prevalence, and pathogen release from the reservoir host, followed by pathogen survival, development, and dissemination outside of the reservoir hosts. Second, pathogen exposure is determined by human and vector behaviour, specifically the likelihood, route, and dose of exposure. Third, the recipient human host's genetic, physiological, and immunological characteristics, as well as the dose and route of exposure, influence the likelihood and severity of infection.

A series of processes link the ecological dynamics of infection in reservoir hosts, the microbiological and vector determinants of survival and dissemination outside of reservoir hosts, the epidemiological and behavioural determinants of exposure, and the within-host biological factors that shape the susceptibility of recipient hosts to determine the risk of spillover. Pathogen pressure is defined as the amount of pathogen available to the recipient host at a given point in space and time, and is determined by the distribution and intensity of infection in reservoir hosts, followed by pathogen release, movement, survival, and possible development to infectious stage.

Pathogen pressure then interacts with the recipient host's (and vector's) behaviour to determine the likelihood, dose, and route of exposure. Following that, a series of within-host barriers determine host susceptibility, and thus the likelihood and severity of infection for a given pathogen dose. Each phase presents multiple barriers to pathogen movement from a reservoir host to a recipient host. Spillover requires the pathogen to pass through each barrier and thus can occur only when gaps align in each successive barrier within an appropriate window in space and time. As a result, zoonotic spillover is a relatively rare event, and while humans are constantly exposed to many potentially infectious pathogens derived from other species, the majority of these microorganisms cannot infect or cause the disease in humans.

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