**[Ecology of Multi-host Pathogens of Animals](http://www.nature.com/scitable/knowledge/library/ecology-of-multi-host-pathogens-of-animals-105288915)**

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Pathogens are often characterized as specialists or generalists based on the number of different host species they infect, as well as the **phylogenetic relatedness** among hosts. **Host range** can be associated with several factors, including the geographic ranges of pathogens and hosts, host and pathogen phylogeny, and life history traits (Cleaveland *et al.* 2001, Malpica *et al.* 2006). Some studies also point to the influence of mode of transmission in determining the host specificity of different types of pathogens (Pedersen *et al.* 2005). In addition, a pathogen's host range can be specific to a certain strain or subtype of the pathogen, which is the case for various subtypes of influenza A. It is worth noting that the designation of a narrow or wide host range is relative. For example, White Nose Syndrome, a disease caused by a pathogenic fungus infecting several bat species, could be said to have a narrow host range because it only infects one class of animals. One the other hand, it could be considered to have a wide host range compared to a pathogen like *Plasmodium falciparum*, the protozoan that causes malarial illness and only infects humans.

The majority of pathogens of animals are generalists that infect multiple host species, referred to as **multi-host pathogens** or **multi-host parasites**. Some multi-host pathogens are maintained in a **sylvatic**transmission cycle where the pathogen is maintained completely in multiple wildlife species. Among domesticated animal species, roughly 77% of pathogens of livestock and 90% of pathogens of domestic carnivores are known to be multi-host pathogens (Cleaveland *et al*. 2001). Over 60% of all known human pathogens are **zoonotic** (Taylor *et al*. 2001), meaning they originate in animals but can cross-infect humans. In some cases, humans can go on to infect humans or other animals (e.g., plague), while in others (e.g., West Nile Virus) humans are **dead-end hosts**. In the latter case, the pathogen causes disease in an individual human but further transmission to other hosts or vectors does not occur.

**Why and how do pathogens infect multiple host species?**

The ability to infect multiple host species is not limited to pathogens of a specific type (e.g., virus, bacteria, helminth) or pathogens employing a particular mode of transmission (Figure 1). The following are only a small subset of multi-host pathogens (or diseases caused by multi-host pathogens) listed by their mode of transmission:

* Close contact/**direct transmissio**n (including direct contact, airborne, aerosol, bite, or sexual transmission): SARS, rabies, monkeypox, influenza, hantavirus, herpes, SIV (simian immunodeficiency virus)
* Non-close/**indirect transmission** (including fomites, environmental transmission): cholera, avian influenza, anthrax, brucellosis
* Intermediate host: *Schistosomiasis*, *Dicrocoelium dendriticum*
* Vector-borne transmission: West Nile virus, Lyme disease, Chikungunya.

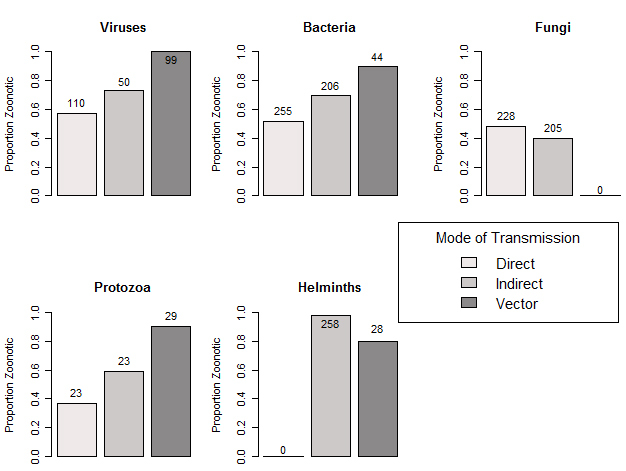


Figure 1: Proportion of pathogens known to be zoonotic, stratified by pathogen class and mode of transmission (adapted from Woolhouse *et al*. 2001).

As demonstrated by this figure, multi-host pathogens (in this case, pathogens that infect at least one non-human animal species in addition to humans), are abundant regardless of the type of pathogen or mode of transmission.

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Depending on the mode of transmission, some pathogens are considered to be obligate multi-host pathogens or parasites; these include parasites with complex life cycles and vector-borne pathogens. Parasites that exhibit a **complex life cycle**require a definitive host for reproduction and one or more intermediate host species for growth and development. Vector-borne pathogens are transmitted between hosts by an intermediate organism, often an arthropod like mosquitoes or ticks, referred to as a **vector**.

Several factors can enable a pathogen to infect multiple host species (e.g., Pulliam & Dushoff 2009). For example, genetic change in the pathogen can occur through selection or through random mutations, allowing the pathogen to become better adapted to infect a new host species (Pepin *et al*. 2010). It is generally believed that the higher a pathogen's mutation rate, the more genetically diverse it will be and therefore the more likely it is that the pathogen is a generalist. For example, RNA viruses mutate about 300 times faster than DNA viruses, and directly transmitted RNA viruses of humans are more likely to be zoonotic than directly transmitted DNA viruses of humans (Drake 1993, Woolhouse *et al*. 2001). Host speciation is another mechanism by which a pathogen that originally infects an ancestral host comes to infect multiple new host species (e.g., Garamszegi 2009). Generally, pathogens tend to infect host species that are phylogenetically similarto each other because these host species share traits (e.g., immunologic, antigenic, or ecological similarities) that make them susceptible to the same pathogens. Conversely, more distantly related host species do not share as many traits, decreasing the chances that they will share pathogen species (Freeland 1983, Davies & Pedersen 2008). Recently speciated hosts share genetic similarities, potentially allowing a pathogen to infect both species. Introductions of non-native hosts and pathogens can also result in the infection of a new host species by providing new opportunities for infectious contact between pathogens and naïve hosts (e.g., Peeler *et al.* 2011).

Infecting a wide range of host species is one way in which a pathogen's chance of persistence is increased. The ability to infect multiple host species is not always adaptive, however, and several ecological trade-offs are associated with the benefit of a broad host range. For example, while single-host pathogens tend to evolve an intermediate level of **virulence** in their host, virulence evolution in multi-host pathogens is more complex. A multi-host pathogen could be highly virulent in one host while exhibiting low virulence in another. The optimal virulence in each host will depend on how each host contributes to pathogen **fitness**(Regoes *et al*. 2000, Gandon 2004, Rigaud *et al*. 2010). Another cost of infecting multiple host species is the degree to which a pathogen can adapt to a host's immune system. If a pathogen only infects one host species, the pathogen can evolve to become highly proficient at evading the immune system of that host. In multi-host pathogens, however, an adaptation in one host species may be maladaptive in another host species (Elena *et al.* 2009). For example, many vector-borne pathogens are viruses, and thus are expected to have a great deal of genetic diversity due to high mutation rates (Cooper & Scott 2001, Ciota *et al*. 2007). However, experimental research (i.e., serial passage experiments involving transmission between an invertebrate vector and a vertebrate host) has shown that viral genetic sequences are largely unchanged after multiple transmissions between very different species. Moreover, viruses that were experimentally allowed to transmit between members of only one species rapidly adapted to that species, with coinciding loss of fitness often observed in the bypassed species (Romanova *et al.* 2007, Coffey *et al.* 2008, Vasilakis *et al*. 2009). This **host alternation** is, therefore, a potential constraint on the genetic diversity of multi-host pathogens.

**Invasion and population dynamics of multi-host pathogens**

The invasion of a naïve population of hosts and subsequent epidemiological dynamics of multi-host pathogens are inherently different from single host systems because multiple host species provide multiple invasion pathways as well as multiple transmission routes. That is, if infection is unsuccessful in one host species, the presence of another host species provides an alternative route for the pathogen to invade a community. Both invasion and persistence are related to a theoretical quantity, ***R0***, referred to as the basic reproductive number and defined as the number of secondary infections resulting from a single primary infection in a completely susceptible population. If *R*0>1, then an introduced pathogen is likely to persist and may cause an epidemic in the host population (Anderson & May 1991). In a community comprised of multiple host species, *R0* may be greater than one for one species, but less than one for another species. In this case, the **community composition** would determine whether or not the pathogen will persist at the community level. The form of transmission (i.e., **density-dependent** versus **frequency-dependent**) also has implications for population dynamics of multi-host pathogens (Dobson 2004). Single-host pathogens that rely on density-dependent transmission rarely drive their host to extinction because the host population will drop below a threshold size such that pathogen transmission can no longer be maintained (Grenfell & Dobson 1995, Hudson *et al*. 2002). Infecting multiple host species, as well as exhibiting frequency-dependent transmission (e.g., sexually transmitted or vector-borne pathogens), increases the chance of pathogen-induced host extinction because the threshold density for pathogen persistence is eliminated (de Castro & Bolker 2005).

In host-pathogen systems with multiple hosts, disease dynamics can also depend on the **competence** of each host species for harboring and transmitting the pathogen, as well as the relative frequency of transmission between host and vector species (LoGuidice *et al.* 2003). Accordingly, the community composition of potential hosts can have a large effect on pathogen dynamics, especially when competencewithin the host community varies substantially (Holt *et al.* 2003, LoGuidice *et al*. 2008). Specifically, theory suggests that, in multi-host vector-borne pathogen systems, more diverse host communities may reduce pathogen transmission by decreasing contacts between infected vectors and highly competent hosts compared with single-species host systems (Schmidt & Ostfeld 2001, Keesing *et al*. 2006). This phenomenon, referred to as the **dilution effect**, has been studied primarily in the Lyme disease system of the Northeast U.S., but has also been demonstrated in other multi-host pathogen systems (Figure 2; Swaddle & Calos 2008, Dizney & Ruedas 2009, Hall *et al*. 2009). Some scientists have argued that while empirical evidence exists for the dilution effect in several multi-host pathogen systems, the mechanism by which disease dilution is occurring is often unknown (e.g., dilution versus density effects; Begon 2008).

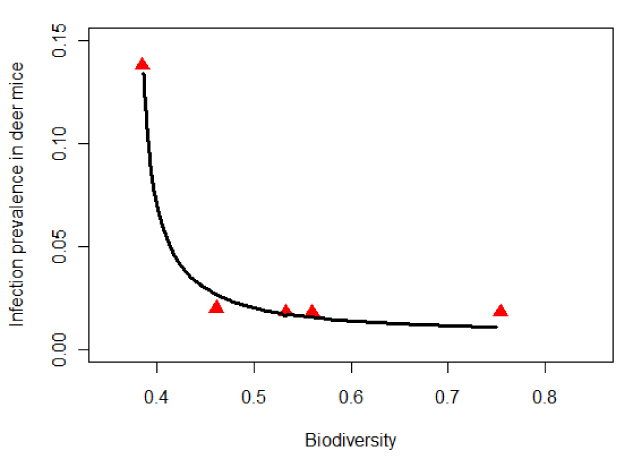


Figure 2: Evidence of the dilution effect, shown here as a decline in prevalence of Sin Nombre virus in deer mice with increasing biodiversity of the surrounding community (adapted from Dizney & Reudas 2009).

Biodiversity was measured using Simpson’s diversity index, which accounts for both species richness (number of species in a community) and species evenness (relative abundance of each species in a community).

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**Multi-host pathogens in a changing climate**

As many pathogens are associated with tropical or equatorial areas of the world, it has been suggested that increased temperatures accompanying climate change will lead to the emergence, re-emergence, or persistence of many more pathogens (Harvell *et al.* 2002). Changes in climate are predicted to lead to range expansion and range shifts of pathogens, their hosts, and their vectors, making precise climate-associated changes in disease dynamics difficult to predict (Lafferty *et al*. 2009, Harvell *et al*. 2009). Adverse effects of climate warming have already been discovered in some multi-host pathogen systems, like chytridiomycosis outbreaks (a fungal infection caused by *Batrachochytrium dendrobatidis*) in amphibian communities. Severe declines in amphibian diversity have been linked to warmer temperatures, which are thought to increase the growth of the fungus (e.g., Bosch *et al.* 2007). Changes in climate are also known to alter certain animal behaviors, like the timing or spatial course of migration, which has the potential to alter multi-host pathogen transmission by changing when and where pathogens and parasites encounter their hosts, affecting both the time and size of disease outbreaks (Altizer *et al*. 2011).

**Why should we study multi-host pathogens?**

Multi-host pathogen systems are intrinsically complex, shaped by pathogen and host dynamics as well as evolutionary, environmental, and climatic interactions. Understanding multi-host pathogens from an ecological perspective provides a variety of potential applications. Multi-host pathogens can, for instance, affect organisms and ecological dynamics far outside their host range. Depending on their effect on a host species (e.g., high virulence/mortality, behavioral modification, reduced fitness/reproduction), multi-host pathogens may regulate not only populations and communities of host species, but also predator, prey, or competitor populations (Hatcher *et al.* 2006). Understanding the ecology and evolution of multi-host pathogens may also be important for species conservation and biodiversity preservation (McCallum & Dobson 1995, Smith *et al*. 2006). Some species that are now declining due at least in part to multi-host pathogens include bird species infected by avian malaria in Hawaii (Van Riper *et al*. 1986) and West Nile Virus in the continental U.S. (LaDeau *et al*. 2007), bat species in the U.S. infected with the pathogenic fungus (*Geomyces destructans*) that causes White-Nose Syndrome (Frick *et al.* 2010), and seals infected with phocine distemper virus in Europe (Swinton *et al*. 1998, Jensen *et al*. 2002). Understanding the ecology of multi-host pathogens, particularly zoonotic multi-host pathogens, can provide information needed for shaping human health policy and may contribute to outbreak detection and other warning systems, or be central to programs aimed at preventing or reducing transmission and human infections by multi-host pathogens.

**Glossary**

**multi-host pathogen:**A pathogen that infects multiple host species

**sylvatic transmission:**Transmission cycle of a pathogen maintained completely in non-human animals

**zoonotic:**Referring to a pathogen that infects humans, but originates from a non-human animal species

**dead-end host:** A host in which a pathogen can cause disease, but not maintain transmission

**phylogenetic relatedness:**Evolutionary distance among species; organisms that share a recent common ancestor and typically have genetic similarities

**host range:**The set of host species that a pathogen or parasite can infect, described by both the number of host species and the phylogenetic relatedness between host species.

**direct transmission:** Occurring from direct or close contact with infectious individuals, including aerosol/airborne transmission, sexual transmission, and transmission via a bite

**indirect transmission:** Occurring from non-close contact with infectious individuals, including fomites and environmental transmission

**complex life cycle:**A parasite life cycle that requires a definitive host for reproduction and one or more intermediate hosts for growth and development

**vector:**Organisms (primarily arthropods like mosquitoes, ticks, and fleas) that transmit a pathogen between host species

**virulence:**Pathogen-induced mortality or other decline in the fitness of a host caused by infection

**fitness:**The potential for an organism to survive and reproduce

**host alternation:** Pathogen transmission between two or more (often disparate) host species, which constrains pathogen adaptation to one host species over another

***R0*:**The basic reproductive number; the number of secondary infections arising from an initial infection in a completely susceptible population

**community composition:**The number and relative abundance of host species in a community

**density-dependent transmission:** Transmission rate that increases with host density

**density-independent transmission:** Transmission rate that functions independent of host density

**competence:**The differential ability of an organism to harbor and transmit a pathogen

**dilution effect:**A net reduction in pathogen transmission from increasing host species diversity

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