The Dynamic Nature of Canine and Feline Infectious Disease Risks in the Twenty-first Century

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- Driver • Infection • Climate • Surveillance • Emerging • Resistance • Virulence
- Travel

KEY POINTS
- Numerous factors influence the frequency, location, and emergence of canine and feline infectious diseases.
- Exploring each of these drivers assists in evaluating their impact on canine and feline health and potentially identifying modifiable components.
- Large data gaps exist (most importantly, reliable estimates of disease occurrence, by location and time) that currently prevent an in-depth evaluation and ranking of the relative importance of each driver.
- There is a need for a robust and dependable surveillance system for canine and feline infectious diseases to provide the data needed to model disease drivers and help anticipate the introduction of future pathogens and their emergence and spread and strengthen control measures.
INTRODUCTION

Infectious diseases of dogs and cats seem to be in a state of rapid change, including changes in overall prevalence of established pathogens, geographic or spatial changes in disease incidence, inherent changes in the pathogenicity or virulence of known pathogens, and the emergence of newly identified pathogens. The proposed drivers for disease change in human populations are an area of great interest and research attention. Although many such drivers are likely similar for dog and cat populations, these groups differ from people to some extent. Exploring the dynamic nature of canine and feline infectious diseases and the likely drivers of current and future shifts may help the veterinary community prepare for change and potentially modify those drivers determined to be most influential. From a public health standpoint, many pathogens affecting dogs and cats also are zoonotic; thus, changes in pathogen frequency in dog and cat populations can have important human health implications. Dogs and cats may be effective sentinels of exposure or disease for some human pathogens, based on factors, such as their susceptibility to disease, likelihood of exposure, and routine diagnostic testing (eg, tick-borne pathogen exposure as part of routine heartworm testing). Because it has been estimated that 60% to 80% of emerging diseases are zoonotic, the veterinary community plays a pivotal role in the identification, prevention, and control of emerging infectious diseases.2

An ecosystem approach to health, often referred to as the epidemiologic triad, considers disease occurrence to be at the intersection of the agent/pathogen, host (in this case, the dog or cat), and environment. Any shift in the interplay of the pathogen–host–environment characteristics can alter the risk of disease.3 Thus, drivers of disease change come from an extensive list of factors involving 1 or more of these areas. The multitude of pathogen sources involved in feline and canine infections adds additional complexity. Wildlife, other companion animals, people, and vectors (eg, fleas and ticks) all serve as possible pathogen sources for dogs and cats, creating a web of infectious disease drivers (Table 1). In this article, these various theorized drivers of canine and feline infectious diseases are reviewed and explored to gain a better understanding of the challenges facing disease forecasting and to propose steps to provide improved disease monitoring in dog and cat populations. This will contribute to an improved understanding of, and means of modifying, disease drivers, to control and prevent infectious diseases in dogs and cats.

DRIVERS FOR CANINE AND FELINE INFECTIOUS DISEASE EMERGENCE AND CHANGE

Emergence of New Pathogens

In all biologic systems, existing members evolve and new pathogens emerge. Although less common than other mechanisms of disease change, novel feline and canine pathogens continue to be identified. This phenomenon has been most recently demonstrated with the emergence and rapid dissemination of novel influenza A viruses in dogs. In the early 2000s, a novel canine influenza virus (CIV) emerged from an established equine influenza virus (H3N8).4 This canine-adapted variant, H3N8 CIV, first became established in racing greyhounds (presumably due to shared contact surfaces and close proximity to infected horses) and then rapidly spread into other dog groups (eg, shelters, kennels, and companion dogs), causing sporadic outbreaks with high canine morbidity throughout parts of the United States.4–6 The more recent emergence of an avian-origin CIV (H3N2) has resulted in canine illness in parts of Asia, the United States, and Canada.7,8
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Abbreviations: CIRDC, canine infectious respiratory disease complex; MRSA, methicillin-resistant Staphylococcus aureus.

<sup>a</sup> Examples purposely not exhaustive and should be considered illustrative. More than 1 driver may be involved in changes in a given pathogen.

Change in Existing Pathogens

Alterations in an existing pathogen can influence its pathogenicity, virulence, and resistance to treatment or prevention measures. Pathogens can develop novel traits while circulating in a host population, allowing the pathogen to unlock host resources that otherwise would remain unavailable, thereby improving the fitness of the pathogen. An example of altered pathogen virulence is the hypervirulent feline calicivirus (FSV) associated with virulent systemic disease (VSD). Although a common cause of generally mild upper respiratory disease in cats, FCV mutants have been observed that result in a hypervirulent, systemic form of the disease, resulting in high mortality (22%–75%). To date, several FCV-associated VSD outbreaks have been observed, identified in several geographically distinct locations.

A prime example of pathogen resistance to treatment is highlighted by the antimicrobial resistance (AMR) epidemic currently affecting all species globally, including dogs and cats. The rapid emergence and spread of methicillin-resistant staphylococci and multidrug-resistant (MDR) Escherichia coli, including extended-spectrum β-lactamase (ESBL) producers, are at the forefront of concern for AMR in dogs and cats. Methicillin-resistant Staphylococcus pseudintermedius (MRSP) has rapidly spread in canine populations and to a lesser extent in feline populations. This pathogen is a common cause of bacterial folliculitis, otitis, and surgical site infections, and treatment can be complicated because of high levels of resistance. Although β-lactamase-producing bacterial isolates have been common for some time, there has been a recent emergence of ESBL producers, which are resultantly resistant to numerous β-lactam antimicrobials, including cephalosporins. Drivers for AMR are complex; however, recent antimicrobial administration seems important in the development of MRSP and MDR E. coli colonization and infections. Prudent antimicrobial use as a component of sound antimicrobial stewardship practices in all health care fields is desperately needed to reduce AMR and preserve the utility of existing and future antimicrobial drugs.

Change in the Range of Existing Pathogens

Many pathogens have well-defined ranges that are restricted by factors, such as geography, weather, and the presence of pathogen reservoirs or vectors. Drivers that change these limiting factors can have profound impacts on local and global canine and feline disease incidence.

Land-use changes and changes in climate and weather that have an impact on host and vector habitats or pathogen survival may drive pathogen range expansion or contraction. Expanding ranges of various vector-borne diseases are particularly noteworthy. The influence of weather and climate on arthropod diseases are particularly well-described. Examples include warming global temperatures that allow ticks and tick-borne diseases to move poleward, with range expansion into higher altitudes. Additionally, such changes may increase the length of the transmission season, resulting in an increase in local vector-borne canine and feline disease. Similar trends are predicted to occur with canine and feline heartworm; the range of the parasite is likely to expand as warmer temperatures increase the heartworm development units (heat requirement for heartworms to complete incubation to the infective stage) past the minimum threshold in colder climates. Conversely, elevated temperatures are expected to create environments not favorable for the development or survival of some tick species in locations, such as South Africa.
Accompanying tick range expansion are a multitude of tick-borne pathogens that have demonstrated an ability to reproduce and be transmitted in novel areas. This is particularly well illustrated by the tick vector *Ixodes scapularis* and the pathogen *Borrelia burgdorferi*, the causative agent of canine borreliosis (Lyme disease), as noted by the steady movement of canine borreliosis within the United States and into Canada.\(^{19}\) Between 1996 and 2016, the number of United States counties in which *I scapularis* or *I pacificus* was established doubled to 45% of all counties.\(^{20}\) A similar range expansion has been documented with *I ricinus* in parts of Europe, including Sweden, the United Kingdom, and Russia.\(^{21}\) A combination of changes in climate, agriculture, and land use is likely involved in these vector and pathogen extensions.\(^{3}\)

Geographic jumps by pathogens often are facilitated by travel and trade, serving to connect distant landscapes and their respective host, vector, and pathogen communities. Such movements may be limited (ie, neighboring jurisdictions or within the same country) or extensive (ie, international or intercontinental). As an example, the pathogen *Brucella canis* is a troubling pathogen given its health impact on breeding dogs (eg, infertility, abortions, and other health manifestations), subclinical yet infectious period, and zoonotic potential. Among the factors linked to canine *B canis* outbreaks in the United States is intrastate and interstate movement of dogs. For instance, in Michigan over a 10-year period, most canine cases and human *B canis* exposures were associated with an influx of dogs from commercial dog production facilities where *B canis* was endemic (seropositivity 9%–83%). This included the movement of infected dogs from 22 Michigan counties and 11 states.\(^{22}\) The concern for the spread of *B canis* is so great that some investigators have argued for mandatory testing of dogs before interjurisdictional or international movement.\(^{23}\)

A similar situation has occurred with H3N2 CIV. This virus seemed to have been circulating in dogs in Asia for several years,\(^ {24}\) before first entering the United States in 2015, likely through international dog importation.\(^ {8}\) Additional introductions of infectious dogs from abroad, with resulting outbreaks, are suspected to have occurred into the United States and Canada, based on phylogenic analysis of virus isolates.\(^ {8}\) The consequences of this geographic movement are evident in the estimated tens of thousands of dogs that have been infected across the United States and Canada. Dog and cat importation has been involved or suspected to be involved in several other pathogen introductions\(^ {25}\) and is likely to increase in frequency, given the high mobility of these species through owner travel, rescue organizations, and distributors.

Geographic jumps also can occur with vectors. If imported vectors and their associated pathogens are introduced into a hospitable environment, or competent vectors are introduced into an environment where the pathogen already exists, novel pathogen transmission can occur. As an example, Public Health England established a tick surveillance program in part to track ticks entering the country on recently traveled or imported animals. Between 2005 and 2016, 10 tick species representing 6 genera were identified entering the United Kingdom from 15 countries. More than half of all identifications from animals with a history of travel were tick species non-native to England, illustrating the risks to dog, cat, and human health.\(^ {26}\)

Sometimes, unexpected changes in ranges occur. For example, West Nile virus emerged in North America in 1999, with tremendous long-lasting animal and human health consequences. This marked change in range could have occurred through intentional (legal or otherwise) movement of an infected reservoir host (eg, bird) or inadvertent movement of the infected mosquito vector. Although of minimal concern to canine and feline health, this highlights the potential severe consequences of pathogen movement.
Anthropogenic changes to the environment are well-described contributors to changes in the presence and frequency of human infectious diseases, including zoonotic diseases.27 Such changes may include or result in animal habitat fragmentation, habitat destruction, and urbanization. Each of these may alter wildlife population structures and increase emerging infectious diseases within wildlife.1 For example, human density within a species’ range is positively associated with zoonotic pathogen richness in mammals, which influences disease emergence.28 Additionally, environmental changes often increase the frequency and magnitude of contact between wildlife species and domestic species, including dogs and cats, thereby increasing disease transmission risks.3,29 Canine leptospirosis is an example of such canine-wildlife interface dynamics. Multiple wildlife species, including racoons, rodents, and opossums, carry distinct *Leptospira* serovars, which are shed in urine, and contact with infectious urine can result in canine disease. Over recent years, there has been an increase in the perceived incidence of canine leptospirosis, with reported outbreaks of unprecedented size and location. Studies suggest an important driver for this perceived increase in canine disease is increased direct and indirect contact between dogs and *Leptospira*-shedding wildlife, including the interactions of these species in urban locations.30–32

Dogs and cats themselves, along with other domestic animal species, also are involved in changes in canine and feline infectious disease spread, because changes in the frequency or intensity of contact with infectious animals drive disease dynamics. Shelter animals and free-roaming animals are important pathogen sources within their own populations but also drive pathogen spread into populations of owned dogs and cats that have direct or indirect contact with free-roaming animals or those recently adopted from a shelter. The impact of these populations on overall canine and feline infectious disease dynamics is difficult to quantify. Several examples are readily available, including the role free-roaming dogs likely serve as a reservoir for canine transmissible venereal tumor in many countries33 and as a reservoir for rabies virus in Africa, Asia, and Central/South America.33,34 In addition, shelter animals are considered a likely source for *B canis* transmission to the general canine population in certain areas; for instance, in Mississippi shelters where *B canis* was present, the mean modeled seroprevalence was high (18%).35 Additionally, evaluation of H3N8 CIV transmission in the United States revealed that animal shelters likely served as important persistent sources for the virus. CIV had a high reproductive potential in these facilities (mean R₀ of 3.9), and these locations served as refugia from the sparsely connected majority of the dog population (for which R₀ was estimated to be close to 1, a level at which infection ceases to transmit in a population), allowing the virus to continue circulating.36

Close contact between pet dogs or cats also can drive infectious disease occurrence. Group settings, where many dogs or cats have direct or indirect contact, are becoming increasing popular. Such activities or environments include daycare facilities, boarding facilities, training classes, dog parks, shows, and sporting events. Veterinary clinics also can contribute to infectious disease spread if there is poor implementation of and compliance with infection control practices.37 This is perhaps of greatest concern when group settings take place within veterinary clinics or during other opportunities for spread between clinics and group settings (eg, shared staff, kennels, and buildings). Disease transmission in these scenarios may result in an outbreak within a facility and/or spread into the general dog/cat populations once infected animals return home.38,39 In many situations, animals may come...
from distant locations (nationally or internationally) and thus spread pathogens to

distant locations on returning home. It is likely that canine group settings played a
critical role in intensifying and spreading H3N2 CIV through the United States dog
population.8

As highlighted previously, several of the pathogens infecting dogs and cats are zoo-
notic. Some of these organisms predominantly circulate between people, with spill-
over infections in dogs and cats. Once these pathogens have colonized or infected
an individual dog or cat, further transmission often is possible to other dogs or

cats or back to people. This phenomenon is particularly well described with Staphy-

lococcus aureus.40 Therefore, alterations in the frequency and intimacy of contact be-
tween infectious people and dogs/cats can further drive canine and feline infectious
diseases. Although every person is likely infectious with some organism at any given
time, this risk is greatly magnified in human health care settings. Dogs and cats
frequently visit or even reside in many human health care facilities as part of animal-
assisted therapy (or similar) programs often allowing for close interactions between
these animals and patients. Anecdotally, this practice seems to be increasing in fre-
cquency. Despite guidelines aimed at reducing pathogen transmission to and from an-
imals in these settings, many gaps are reported,41,42 with pathogen transmission
documented between the groups.43,44 Although the frequency of transmission of
pathogens to dogs/cats in these environments has been described, the risk and inci-
dence of subsequent transmission to humans and other animal populations are un-
known but certainly likely to occur.

Change in Host Susceptibility

Immune function is a key determinant of pathogen infectivity, pathogenicity, and viru-
ulence. Animals that are immunosuppressed often are at an increased risk for infection
and generally experience more severe disease, disease of longer duration, or more
severe or unexpected complications than others that are immunocompetent. Immu-
nosuppression arises from many sources or reasons, including genetic/primary
causes, infection with immunosuppressive pathogens, chemotherapy or immunosup-
pressive medical therapies, pregnancy, asplenia, and extremes of age. For example,
immunosuppression can increase risk for clinical (especially severe) canine papilloma
virus infection,45 and feline leukemia virus (FeLV)-induced immunosuppression can be
associated with several secondary infections (eg, coccidiosis and upper respiratory in-
fections).46 Some causes of immunosuppression seem stable or decreasing in fre-
cquency, such as FeLV infection in some regions,47 whereas some advances in
veterinary medical care (eg, cancer treatment) that result in immunosuppression,
and thus increase infection risk, are increasing.

Change in Prevention Measures

Medical advances constantly are being made to prevent infectious disease trans-
mision. Canine and feline vaccines against emerging and endemic pathogens
continue to be developed and improved (eg, canine leishmaniasis, canine leptospi-
rosis, and canine influenza). Advances in tick and flea prevention technologies have
resulted in products with increased effectiveness and longer duration of effect, theo-
retically reducing vector-borne disease risks. Safe and effective environmental dis-
infectants are increasingly available. All these factors likely have contributed to
reducing canine and feline infectious disease risk. Uptake of products resulting
from such advances, however, may be hampered by factors, such as financial con-
straints, availability, or perceived need. Due to few data, the magnitude of such im-
pacts are unknown.
Change in Ability to Detect

The perceived emergence of a disease sometimes may simply reflect advances in diagnostic testing, in particular the identification of viruses previously difficult to identify or classify. Differentiating new pathogens from new recognition of existing commensals can be a challenge. For example, feline morbillivirus is a novel paramyxovirus that has been identified in domestic cats in several countries.\(^48,49\) Infection with the virus is suspected to be chronic and associated with feline renal diseases.\(^48,49\) New diagnostic methods\(^50\) undoubtedly have assisted in the recent identification of this apparently common, persistent, globally distributed pathogen that has likely been present in cats for some time.

Surveillance programs, whereby specific infectious diseases or conditions are tracked, allow for early recognition of changes in disease occurrence and outbreaks. Such surveillance efforts can have important impacts on the perceived prevalence of canine and feline pathogens. For instance, efforts to systematically diagnose and record clinical cases of feline sporotrichosis were dramatically increased during a cat-associated human sporotrichosis outbreak.\(^51\) A large, unprecedented epidemic of feline sporotrichosis was identified in Brazil, with more than 4000 cats diagnosed with sporotrichosis in Rio de Janeiro between 1998 and 2015, with an accompanying 4188 cat-associated human cases over a similar timeframe.\(^51\) Without such human disease impacts, efforts and resources directed toward characterizing feline cases likely would have been limited and the extent of this outbreak underappreciated.

Currently, most countries have limited surveillance systems dedicated to canine and feline diseases. The paucity of canine and feline disease data is illustrated in the examples (discussed previously) for each driver. Disease outbreaks or unusual disease occurrences (eg, changes in pathogen virulence, emergence, and introduction through transport/travel) constitute the overwhelming majority of reports of disease occurrence in companion animals. There is limited information on changes in frequency or location of established, common pathogens. In comparison with human and livestock diseases, none of the international health agencies is mandated to coordinate surveillance of diseases in companion animals (with the possible exception of rabies).\(^52\)

To address the gap in canine and feline surveillance data, several groups have independently initiated surveillance programs, through partnerships with wide-scale corporate laboratory testing (eg, Companion Animal Parasite Council in the United States and Canada) or private practice sentinel clinics (eg, Computer-based Investigation of Companion Animal Disease Awareness in the United Kingdom). Mining direct-feed, real-time data from private practices also recently has been used to investigate specific canine and feline health outcomes, although to date minimally used to investigate infectious diseases.\(^53\) Although they are useful initiatives, these programs generally are inadequate for tracking disease trends, because they are fragmented and findings generally cannot be compared across programs/jurisdictions due to a lack of standardization of nomenclature, disease definitions, and means of diagnosis.\(^52\)

NEXT STEPS

Dedicating additional resources to better tracking of canine and feline infectious diseases is needed to help inform prevention and control measures. Some of the drivers of disease, such as climate change, are likely to be critically important, but solutions to address/reduce its progression are complex and long term. Other drivers, such as pathogen introduction through travel and trade, probably are comparatively simple...
to address (eg, through control measures, such as quarantine and veterinarian pre/post-travel evaluation) and could have rapid, critical, and measurable impacts on the occurrence of canine and feline disease. Despite having identified several likely drivers of current and future canine and feline infectious diseases, however, the specific impacts of these drivers are poorly understood. This limited understanding challenges the ability to best direct resources to controlling canine and feline infectious disease spread and emergence.

In comparison, significant progress has been made in untangling these drivers in human infectious diseases. Between 2008 and 2013, 116 human infectious disease threat events were detected by the European Centre for Disease Prevention and Control. In analyzing these events, researchers identified 17 unique drivers, with 2 or more drivers likely responsible for most of the events. The top 5 contributing drivers were (in descending order based on overall frequency ranking of all events) (1) travel and tourism, (2) food and water quality, (3) natural environment, (4) global trade, and (5) climate. A hierarchical cluster analysis revealed travel and tourism to be separate from all the other drivers, suggesting that this driver should be considered distinct and that specific measures should be dedicated to addressing it.

Improving monitoring for canine and feline infectious diseases is a critically important step to facilitate the evaluation of changes in frequency, location, and impact of disease. Furthermore, such data would lend itself to modeling disease drivers to help prioritize risk-based surveillance actions; anticipate future pathogen introductions, emergence, and spread; and strengthen control measures. The most cost-effective strategy to address changes in infectious diseases in dogs and cats, as in other species, is to directly tackle the underlying infectious disease drivers rather than individual pathogens, diseases, and transmission events, whenever possible.

SUMMARY

Canine and feline infectious diseases are constantly changing in nature, frequency, and location. Due to limited surveillance efforts, the extent of these changes for the most part is unknown. Based on assumptions from human health data and documented outbreaks or other high-profile events, several drivers of these changes are suspected. There is a strong and immediate need for improved surveillance systems to reliably track feline and canine infectious diseases, both within and across political boundaries. Such data will allow for disease drivers to be further explored and ranked. Modifiable drivers should be prioritized and targeted to assist in preventing disease spread.

REFERENCES


