

CONSULT THE EXPERT

# THE VETERINARY SIGNIFICANCE OF EMERGING INFECTIOUS DISEASES

---

**J. Scott Weese, DVM, DVSc, DACVIM**  
*Ontario Veterinary College*



**E**merging infectious diseases pose a significant threat to humans and animals but are inherently unpredictable. Although historical trends and disease patterns can provide insight, determining which diseases are likely to emerge and the impact they will have on human and animal populations is an educated guess at best. Of additional concern is the estimate that 60% to 80% of emerging diseases are zoonotic,<sup>1</sup> which emphasizes the importance of veterinarians in the identification, prevention, and control of emerging infectious diseases.

An ecosystem approach to health considers disease occurrence to be at the intersection of the microbial agent, the host (human or animal), and the environment.<sup>1</sup> Any alterations in the agent, host, or environment can alter the risk for disease. Thus, new infectious disease threats can emerge from a variety of sources.

### Emergence of New Pathogens

Emergence of new pathogens is uncommon but continues to occur. If highly transmissible, new pathogens can have profound effects, as the worldwide population would be immunologically naïve to the emerging pathogen. For example, the emergence of canine parvovirus in the 1970s<sup>2</sup> became a worldwide epidemic, with rapid international transmission and high morbidity and mortality rates.

Canine influenza is a more recent example of the threats posed by emerging pathogens. The emergence of equine-origin canine influenza H3N8 in the United States in the early 2000s<sup>3</sup> demonstrated the potential impact of antigenic shift of influenza on the canine population. The more recent emergence of avian-origin canine influenza H3N2 caused—and continues to cause—widespread illness and disruption in parts of Asia, the United States, and Canada.<sup>4,5</sup>

---

**If highly transmissible, new pathogens can have profound effects, as the worldwide population would be immunologically naïve to the emerging pathogen.**

### Change in Existing Pathogens

Alterations in existing pathogens can impact a pathogen's virulence (eg, acquisition of new virulence factors) and the ability to treat (eg, acquisition of antimicrobial-resistant genes or antiviral resistance) or prevent disease (eg, alterations in vaccine efficacy, resistance to heartworm prophylaxis). The worldwide epidemic of antimicrobial resistance, particularly methicillin-resistant staphylococci<sup>6</sup> and extended-spectrum  $\beta$ -lactamase production in gram-negative bacteria, has had tremendous impacts on human and animal populations.<sup>7</sup> Multidrug-resistant pathogens cause large numbers of infections every year and can be associated with higher morbidity and mortality rates; the need for more expensive, toxic, or cumbersome treatments; and the risk for transmission to other humans or animals. Economic impacts are similarly profound; the World Bank has estimated that by 2050 the global burden of antimicrobial resistance could surpass that of the 2008 financial crisis.<sup>8</sup> New resistance mechanisms, including resistance to "last-resort" drugs such as colistin,<sup>9</sup> continue to be identified and will continue to pose a problem to the veterinary profession as bacterial evolution outpaces antimicrobial development.

### Development of Virulence

Virulence may develop through an existing but typically nonpathogenic microbe. *Elizabethkingia anophelis* is an example of such virulence development in humans; the risk in animals is unknown. This gram-negative bacterium is widespread in the environment and was considered innocuous until clusters of serious infections were identified in humans, primarily immunocompromised humans in hospitals, in various countries.<sup>10</sup> The reasons for this change are unclear. Although *E anophelis* infection has not been reported in animals, it is possible that there is some degree of risk for infection. Regardless, *E anophelis* highlights the potential for organ-

isms that were previously considered to be ubiquitous and innocuous to cause disease.

### **Change in the Range of Existing Pathogens**

Many pathogens have well defined ranges that may be limited by geography and control measures (eg, rabies), vector ranges (eg, *Borrelia burgdorferi*), reservoir host ranges (eg, *Cytauxzoon felis*), and climate (eg, various parasites). Changes in any of these limiting factors can result in the potential for range expansion. Range expansion can also occur through human activities (eg, international movement of humans and animals) and accidental international transportation of pests and, thus, the pathogens they carry. Although of limited consequence in dogs and cats, introduction of West Nile virus through a route that is still unknown resulted in establishment of this foreign mosquito-borne virus in North America, and the impacts of this disease on humans and some animal populations are ongoing.<sup>11-15</sup>

Expanding ranges of various vector-borne diseases are particularly noteworthy. In North America, tick ranges have been expanding due in part to climate change.<sup>16</sup> When reservoir hosts move in parallel with vectors or when competent hosts are already present in the expansion regions, vector-borne pathogens may spread with the vectors, as shown by the steady movement of Lyme disease into the northern and western United States and into Canada.<sup>17</sup> Such movement highlights the need for predictive modeling to identify new threats and the need for awareness of disease threats in adjacent regions.

### **New Human Encounters in Remote Endemic Ranges**

Various pathogens presumably exist in remote sites where there is little human presence. There are still regions of the world that have had limited human exposure, particu-

## **Apparent emergence of a disease may sometimes simply reflect advances in diagnostic testing.**

larly parts of sub-Saharan Africa and regions of the Amazon basin. With the remarkable biodiversity in these areas, expansion of humans and their animals into these areas may result in exposure to pathogens considered new to the region.

### **Ability to Diagnose**

Apparent emergence of a disease may sometimes simply reflect advances in diagnostic testing. For example, *Bartonella* spp can be difficult to identify. As new methods for detection have become available, members of this genus have been increasingly implicated in a variety of diseases.<sup>18</sup>

Advances in laboratory methods that allow for rapid, cost-effective detection of all microorganisms in a sample, including previously unknown bacteria and viruses, have made it possible to identify unknown microorganisms rapidly and at low cost. This has led to identification of myriad “new” viruses.<sup>19-21</sup> Humans and animals have extensive commensal virome populations, and the ability to identify new viruses currently outpaces the ability to interpret the relevance of these discoveries. A high-profile example is the identification of canine circovirus. After reports of this virus and the subsequent ability to test for it first emerged, there was widespread concern about canine circovirus as a cause of serious enteric disease in dogs; however, proof of its role as a primary pathogen is still

lacking.<sup>22-24</sup> This highlights the potential confusion that can be associated with availability of new diagnostic tests when the clinical relevance of the results is unclear.

### Change in Host Susceptibility

A change in host susceptibility has been exemplified in medicine early in the era of human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS). Before effective HIV management approaches were available, progression to end-stage AIDS resulted in profoundly immunocompromised individuals, which led to identification of a range of previously rare or unknown infectious diseases caused by organisms that were predominantly or only pathogenic in these highly compromised

AIDS = acquired immune deficiency syndrome

HIV = human immunodeficiency virus

hosts (see *Suggested Reading*).<sup>25-29</sup> Such a severely compromising and widespread disease is not currently recognized in animals; however, emergence of new secondary pathogens in humans with AIDS demonstrates the potential for disease caused by a range of novel or overlooked microorganisms associated with the emergence of new, highly susceptible patient populations. It also emphasizes the challenges that might be posed by advances in veterinary care (eg, treatment of cancer or immune-mediated disease) that can prolong the life of patients but increase their risk for infection from existing and emerging pathogens.

### The Future

Logical estimations and models for emergence can be developed, but emergence is ultimately unpredictable. New infectious disease issues will pose threats to animal and, potentially, human populations. Infectious diseases of current significance may not have been recognized or considered important 5 to 10 years ago, and infectious diseases that will be significant 10 years from now may not be currently recognized or considered important, illustrating the dynamic nature of disease. ■

## New infectious disease issues will pose threats to animal and, potentially, human populations.

### References

- Morens DM, Fauci AS. Emerging infectious diseases: threats to human health and global stability. *PLoS Pathog*. 2013;9(7):e1003467.
- Thomson GW, Gagnon AN. Canine gastroenteritis associated with a parvovirus-like agent. *Can Vet J*. 1978;19(12):346.
- Crawford PC, Dubovi EJ, Castleman WL, et al. Transmission of equine influenza virus to dogs. *Science*. 2005;310(5747):482-485.
- Voorhees IEH, Glaser AL, Toohey-Kurth K, et al. Spread of canine influenza A(H3N2) virus, United States. *Emerg Infect Dis*. 2017;23(12):1950-1957.
- Song D, Kang B, Lee C, et al. Transmission of avian influenza virus (H3N2) to dogs. *Emerging Infect Dis*. 2008;14(5):741-746.
- Weese JS, van Duijkeren E. Methicillin-resistant *Staphylococcus aureus* and *Staphylococcus pseudintermedius* in veterinary medicine. *Vet Microbiol*. 2010;140(3-4):418-429.
- Trott D.  $\beta$ -lactam resistance in gram-negative pathogens isolated from animals. *Curr Pharm Des*. 2013;19(2):239-249.
- World Bank Group. Part II. Economic impact of AMR. *Drug-resistant infections: a threat to our economic future*. Washington, DC: World Bank; 2017:19. <http://documents.worldbank.org/curated/en/323311493396993758/pdf/114679-RE-VISED-v2-Drug-Resistant-Infections-Final-Report.pdf>. Accessed May 10, 2018.
- Zhang XF, Doi Y, Huang X, et al. Possible transmission of mcr-1-harboring *Escherichia coli* between companion animals and human. *Emerg Infect Dis*. 2016;22(9):1679-1681.
- Moore LSP, Owens DS, Jepson A, et al. Waterborne *Elizabethkingia meningoseptica* in adult critical care. *Emerg Infect Dis*. 2016;22(1):9-17.
- Gaunt MC, Waldner C, Taylor SM. Serological survey of West Nile virus in pet dogs from Saskatchewan, Canada. *Vector Borne Zoonotic Dis*. 2015;15(12):755-758.
- Morin CW, Comrie AC. Regional and seasonal response of a West Nile virus vector to climate change. *PNAS*. 2013;110(39):15620-15625.
- Centers for Disease Control and Prevention. West Nile virus activity - United States, 2009. *Morbidity and Mortality Weekly Report*. 2010;59(25):769-772.
- Kulasekera VL, Kramer L, Nasci RS, et al. West Nile virus infection in mosquitoes, birds, horses, and humans, Staten Island, New York, 2000. *Emerg Infect Dis*. 2001;7(4):722-725.

**30 mg/mL**

**BRIEF SUMMARY:** Before using this product, please consult the full product insert for more information.

**For oral use in dogs only**

**Appetite Stimulant**

**Caution:** Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

**Description:** ENTYCE® (capromorelin oral solution) is a selective ghrelin receptor agonist that binds to receptors and affects signaling in the hypothalamus to cause appetite stimulation and binds to the growth hormone secretagogue receptor in the pituitary gland to increase growth hormone secretion.

**Indication:** ENTYCE (capromorelin oral solution) is indicated for appetite stimulation in dogs.

**Contraindications:** ENTYCE should not be used in dogs that have a hypersensitivity to capromorelin.

**Warnings:** Not for use in humans. Keep this and all medications out of reach of children and pets. Consult a physician in case of accidental ingestion by humans. **For use in dogs only**

**Precautions:** Use with caution in dogs with hepatic dysfunction. ENTYCE is metabolized by CYP3A4 and CYP3A5 enzymes (See Clinical Pharmacology). Use with caution in dogs with renal insufficiency. ENTYCE is excreted approximately 37% in urine and 62% in feces (See Adverse Reactions and Clinical Pharmacology).

The safe use of ENTYCE has not been evaluated in dogs used for breeding or pregnant or lactating bitches.

**Adverse Reactions:** Field safety was evaluated in 244 dogs. The most common adverse reactions were diarrhea and vomiting. Of the dogs that received ENTYCE (n = 171), 12 experienced diarrhea and 11 experienced vomiting. Of the dogs treated with placebo (n = 73), 5 experienced diarrhea and 4 experienced vomiting.

To report suspected adverse drug events and/or obtain a copy of the Safety Data Sheet (SDS) or for technical assistance, call Aratana Therapeutics at 1-844-640-5500.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at <http://www.fda.gov/AnimalVeterinary/SafetyHealth>

NADA 141-457, Approved by FDA

US Patent: 6,673,929

US Patent: 9,700,591

Made in Canada



Manufactured for:  
Aratana Therapeutics, Inc.  
Leawood, KS 66211

ENTYCE is a trademark of Aratana Therapeutics, Inc.

© Aratana Therapeutics, Inc.

AT2-051-1

February 2018

15. Trock SC, Meade BJ, Glaser AL, et al. West Nile virus outbreak among horses in New York State, 1999 and 2000. *Emerg Infect Dis.* 2001;7(4):745-747.
16. Jaenson TGT, Lindgren E. The range of *Ixodes ricinus* and the risk of contracting Lyme borreliosis will increase northwards when the vegetation period becomes longer. *Ticks Tick Borne Dis.* 2011;2(1):44-49.
17. Bouchard C, Leonard E, Koffi JK, et al. The increasing risk of Lyme disease in Canada. *Can Vet J.* 2015;56(7):693-699.
18. Breitschwerdt EB. Bartonellosis, One Health and all creatures great and small. *Vet Dermatol.* 2017;28(1):96-e21.
19. Carmona-Vicente N, Buesa J, Brown PA, et al. Phylogeny and prevalence of kobuviruses in dogs and cats in the UK. *Vet Microbiol.* 2013;164(3-4):246-252.
20. Li L, Pesavento PA, Shan T, Leutenegger CM, Wang C, Delwart E. Viruses in diarrhoeic dogs include novel kobuviruses and sapoviruses. *J Gen Virol.* 2011;92(11):2534-2541.
21. Kapoor A, Dubovi EJ, Henriquez-Rivera JA, Lipkin WI. Complete genome sequence of the first canine circovirus. *J Virol.* 2012;86(12):7018-7018.
22. Anderson A, Hartmann K, Leutenegger CM, Proksch AL, Mueller RS, Unterer S. Role of canine circovirus in dogs with acute haemorrhagic diarrhoea. *Vet Rec.* 2017;180(22):542-542.
23. Hsu HS, Lin TH, Wu HY, et al. High detection rate of dog circovirus in diarrheal dogs. *BMC Vet Res.* 2016;12:1-6.
24. Zaccaria G, Malatesta D, Scipioni G, et al. Circovirus in domestic and wild carnivores: an important opportunistic agent? *Virology.* 2016;490:69-74.
25. Coelho L, Cardoso SW, Amancio RT, et al. Trends in AIDS-defining opportunistic illnesses incidence over 25 years in Rio de Janeiro, Brazil. *PLoS One.* 2014;9(6):e98666.
26. Mofenson LM, Brady MT, Danner SP, et al. Guidelines for the prevention and treatment of opportunistic infections among HIV-exposed and HIV-infected children: recommendations from CDC, the National Institutes of Health, the HIV Medicine Association of the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the American Academy of Pediatrics. *MMWR Recomm Rep.* 2009;58(RR-11):1-166.
27. Bern C, Kawai V, Vargas D, et al. The epidemiology of intestinal microsporidiosis in patients with HIV/AIDS in Lima, Peru. *J Infect Dis.* 2005;191(10):1658-1664.
28. Viriyavejakul P, Nintasen R, Punsawad C, Chaisri U, Punpoowong B, Riganti M. High prevalence of *Microsporidium* infection in HIV-infected patients. *Southeast Asian J Trop Med Public Health.* 2009;40(2):223-228.
29. Glaser CA, Angulo FJ, Rooney JA. Animal-associated opportunistic infections among persons infected with the human immunodeficiency virus. *Clin Infect Dis.* 1994;18(1):14-24.

**Suggested Reading**

Centers for Disease Control and Prevention. Appendix A: AIDS-defining conditions. *Morbidity and Mortality Weekly Report.* <https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5710a2.htm>. Updated November, 2008. Accessed May 10, 2018.

**LOOK FOR THESE ARTICLES IN FUTURE ISSUES**

- ▶ Vitamin A Deficiency in Insectivorous Lizards
- ▶ Traumatic Fragmented Medial Coronoid Process in a Mature Dog
- ▶ Top 5 Drug Interactions in the Intensive Care Unit
- ▶ Feline Constipation & Megacolon Algorithm
- ▶ Phenylpropanolamine Snapshot