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CELLULAR AND MOLECULAR GASTROENTEROLOGY AND HEPATOLOGY

COMMENTARY

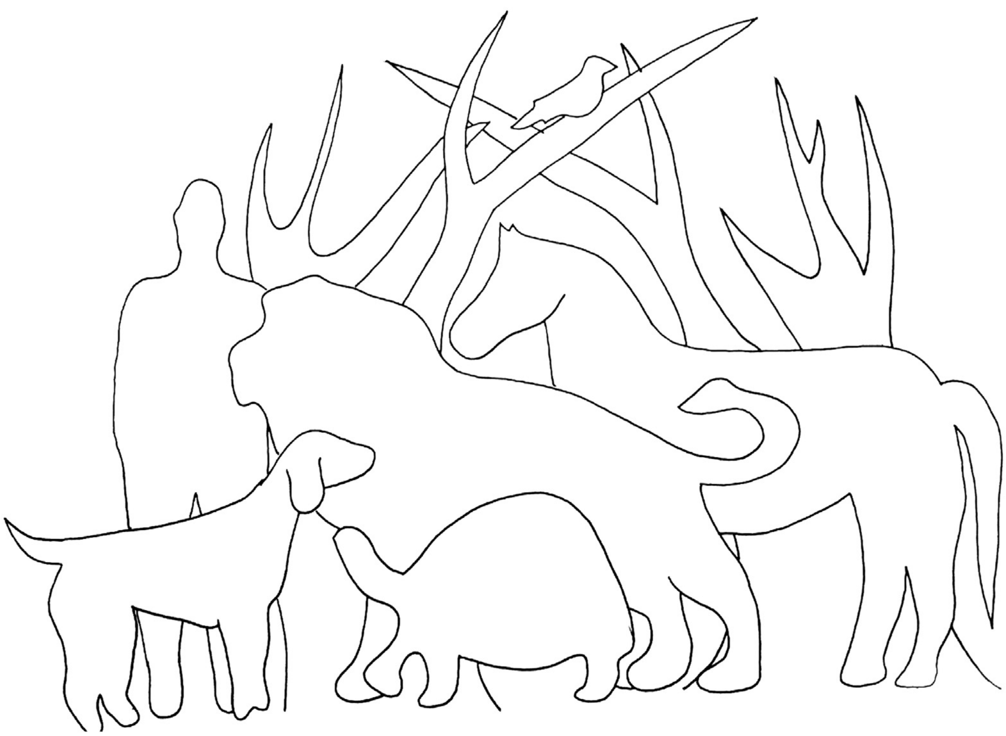
One What? Why GI Researchers Should Know and Care About the One Health Initiative

The One Health Initiative is an international movement that began in 2006 and is supported by, among others, the American Medical Association and the US Centers for Disease Control.[1] Its goal is both laudable and logical: to bring together animal, human, and environmental health practitioners for collaborations that enhance health and well being, broadly and globally. Sadly, although One Health (and the related concept of Zoobiquity[2]) are widely appreciated in the veterinary community, they are generally unknown in the human medical community, especially among subspecialists such as gastroenterologists.[3] I first heard of One Health from a veterinary collaborator a year ago, and an informal survey of colleagues in gastrointestinal (GI) research suggested that most are similarly unaware of One Health.

Veterinarians perform endoscopies and liver biopsies; make use of advanced imaging (computed tomography, magnetic resonance imaging, and positron emission tomography scans) and laboratory tests; use chemotherapy and cutting-edge interventional radiology approaches in pets with luminal, pancreatic, and liver cancers; and manage many diseases such as GI diseases and others on a long-term basis. However, the veterinary and human medical systems largely exist in parallel, with many physicians and nonveterinary school researchers having little appreciation for the breadth of disease in animals or the sophistication involved in modern veterinary care. Gastroenterologists and GI researchers outside of the veterinary community often are unaware of the large number of potentially relevant naturally occurring animal models, many of which are the subject of innovative research into pathophysiology and treatments.

Diseases of cats and dogs with direct relevance to human medicine include inflammatory bowel disease (IBD), pancreatitis, and hepatobiliary disease.[4,5] Both dogs and cats develop a variety of IBD syndromes with similarities to human disease; in particular, cats develop a variant with associated pancreatitis and cholangitis, and some species of dogs (notably German Shepherds) develop a Crohn's disease–like illness with perianal fistulas.[4] Cats can be affected by both primary biliary cholangitis and primary sclerosing cholangitis–like diseases, both of which may shed light on the pathogenesis and treatment of the human equivalents.[4] Companion animal models also may help researchers to understand liver diseases including those associated with copper overload, drug-induced injury, and regeneration.[6] For example, congenital portosystemic shunts with associated liver atrophy are common in dogs, and published and ongoing studies aimed at enhancing regeneration may identify agents that could be useful in human beings.[7,8]

Many vaccines and other therapies originally developed for animals have crossed over to human medicine. This is particularly true for stem cell therapies (which have been



used for, among many diseases, the treatment of canine fistulizing IBD).[9–11] Pet owners increasingly demand state-of-the art care for their animals, and thus there are increasing numbers of veterinary clinical trials that ultimately may have human relevance. Cancers in pets are one of the few large groups of diseases that have caught the attention of the human health system (and the National Institutes of Health). Companion animals develop GI cancers—oral cancers are common in cats; both cats and dogs develop hepatocellular, colorectal, and gastric cancers; and insulinomas are common in ferrets.[12–15] There is increasing use of dogs as part of comparative oncology efforts, particularly the National Cancer Institute Comparative Oncology Program, which is designed to understand tumor biology and test new chemotherapeutic agents and other therapies.[16]

Animals other than pets are also of significant interest to the GI community. GI clinical practitioners are among those on the front lines dealing with the fallout from farming and livestock husbandry practices that lead to food-borne illnesses. Wildlife and livestock can serve as sentinels, key resources in the armamentarium against zoonotic and other infectious diseases, many of which have GI effects; similarly, animals can serve as important indicators of toxic exposures and other environmental disasters. Although this can have immediate relevance as far as preventing human exposures, it also has research relevance. The hedgehog inhibitor cyclopamine, for example, was isolated from the California corn lily *Veratrum californicum* and identified in 1966 after extensive investigations into possible genetic and environmental causes of outbreaks of cyclopia in sheep.[17,18] Similarly, my colleagues and I recently isolated a toxin likely responsible for biliary atresia in livestock.[19]

Perhaps of greatest relevance to the readers of *Cellular and Molecular Gastroenterology and Hepatology* is the concept of One Health in the identification of GI research models. Historically and continuing today, rodents are the primary in vivo animal models used to study GI disease. Although the importance of rodents and particularly genetically altered mice in GI research is dramatic, less well appreciated is the potential utility of large animal models in research. The Online Mendelian Inheritance in Animals database has catalogued more than 1500 potential large animal models of human disease, including those with single-gene defects and those with more complex modes of acquired and inherited disease.[20] Large animals may prove to be superior to rodents as models to study diseases that result from external and environmental stressors, such as those associated with obesity, diabetes, and cancer. Pigs, for example, are particularly useful in studying liver diseases, especially nonalcoholic fatty liver disease.[21] Large animals may better mimic human physiology than rodents and this may, for certain experiments, outweigh the increased cost and other problems in using large animals. Other advantages of large animals include longer life spans than rodents, larger sizes that enable more human-like therapies (and more frequent monitoring of certain side effects), and a greater tolerance for imaging and biopsies.

This issue of *Cellular and Molecular Gastroenterology and Hepatology* includes 2 contributions that highlight the relevance of One Health concepts in GI research. Ziegler et al[22] review the use of large animals, particularly pigs, as physiologically relevant models of luminal GI disease, noting that pigs are in many ways superior to rodents as models to study the intestine. Anwer's[23] Paths and Places column provides practical advice for researchers in veterinary schools and also points out the criticisms veterinary researchers face when trying to obtain funding for projects that link naturally occurring animal models (which often cannot be manipulated genetically) to human diseases. Both articles make clear, as this commentary also has emphasized, that better understanding of the power of animal models and developing and strengthening the links between veterinary and human medicine significantly could benefit human (as well as animal) health. Although One Health envisions broad solutions, often at the policy level, for the treatment and prevention of health problems worldwide, integrated research is an important component and one to which all GI researchers can contribute.

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Conflicts of interest
The author discloses no conflicts.

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