Clinical Microbiology Newsletter

Vol. 32, No. 7 **www.cmnewsletter.com** April 1, 2010

Implications of the One Health Paradigm for Clinical Microbiology

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Abstract

Clinical microbiologists have a new and unique opportunity to increase our value to health care by broadening how we think about disease processes and asking ourselves what we can do to help resolve a disease, assist in tracking a cause, or even predict an outbreak before it occurs. Human health, animal health (both wildlife and domestic animals), and environmental health are forever bound together. The convergence of people, animals, and the environment defines the parameters of One Health and directs attention to the impact this overlap has on public health, disease detection, and control. One Health (sometimes referred to as One Medicine) is a concept that promotes, improves, and defends the health and well-being of all species through the integration of the sciences of human medicine, veterinary medicine, and environmental studies. As microbiologists, we need to be aware of this One Health concept and how it can positively impact our profession by allowing us to be more productive members of the health care team. There are several things we can do to get started. We can review organism pathogenicity and evaluate and question test results that may signal an unusual event or process that led to a disease. We can be alert to the epidemiologic potential of organism isolates from patients as they may apply to infection control or community epidemiology. We can become familiar with the zoonotic diseases and recognize the etiologic agents associated with wild and domestic animals and apply that knowledge to our diagnostic skills. As we further understand the "big picture" of One Health, we can ask strategic questions that can lead us to provide further technical assistance to facilitate earlier interventions that lead to positive patient outcomes and ultimately healthier populations. In human medicine, we generally work with one species of animal. Veterinarians work with all the rest. It is time to communicate with and learn from our veterinary clinical microbiology colleagues and begin to understand the critical nature of the human, animal, and environment interface. This is our opportunity to be at the front of this line and not stand on the sidelines watching.

Introduction

At the 2009 American Society for Microbiology General Meeting in Philadelphia, a new concept engaging microbiologists was presented in a symposium entitled "One Health – A New Paradigm for Microbiology and Public Health." The concept of One Health is not new (1,2), but its implementation as an integrated process into our diagnostic work is, and it will take some time for us to learn more about the importance of the concept and truly understand how important the idea really is. Briefly, One Health (sometimes referred to as One Medicine) is a concept that focuses on improving the health of humans and animals through the integration of the sciences of human medicine, veterinary medicine, and environmental studies. These three disciplines are inextricably linked. The convergence of people, animals, and the environment defines the parameters of One Health and directs attention to the impact this overlap has on public health, disease detection, and control. What makes this journey into One Health so intriguing to microbiologists is the absolute need to enhance collaboration between physicians, veterinarians, laboratorians, environmental experts, and public health professionals and to leverage the strengths in leadership and management to achieve the primary goal of One Health: to promote, improve, and defend the health and well-being of all species (3).

On 14 April 2007, the American Veterinary Medical Association Executive Board took official action to establish a One Health Initiative by approving a recommendation to establish a One Health Initiative Task Force (OHITF). The purpose of the task force was to study the feasibility of creating a One

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  0196-4399/00 (see frontmatter)

Health commission that would facilitate cooperation among health science professions, academic institutions, governmental agencies, and private industries to improve the assessment, treatment, and prevention of cross-species disease transmission and mutually prevalent, but non-transmitted, human and animal diseases, and medical conditions (4). The OHITF was asked to define "One Health" and provide approaches that would support and expand the concept across the health professions. Soon after, the American Medical Association House of Delegates also unanimously approved a resolution in support of One Health. The American Society for Microbiology, the Centers for Disease Control and Prevention (CDC), the American Society of Tropical Medicine and Hygiene, the United States Department of Agriculture, the National Park Service, and many other agencies and groups have also endorsed this concept. (Find it on the web at http://www.avma.org/onehealth/.)

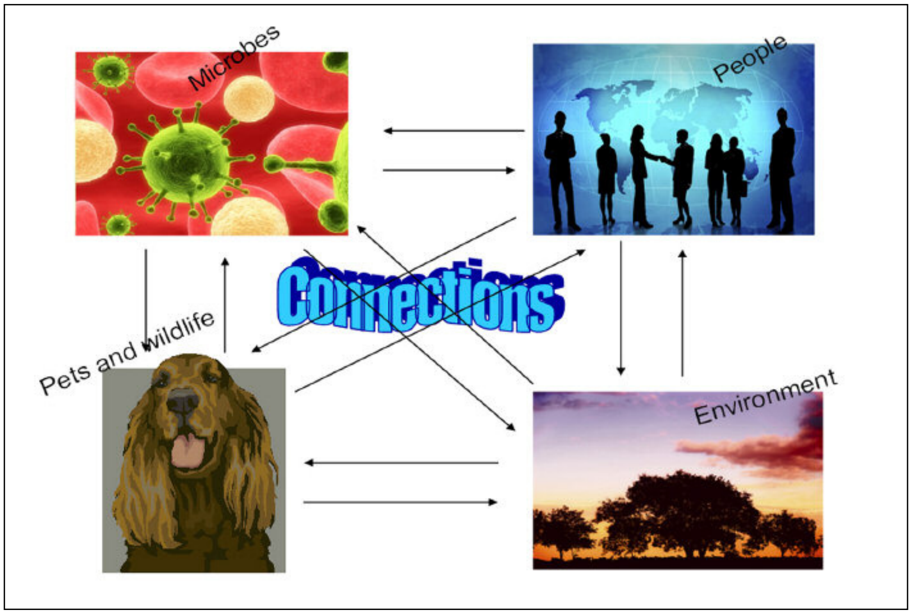

Figure 1. Illustration showing the interconnectedness of humans, animals, and the environment.

Humans and animals have coexisted since their first meeting on the planet, and we have learned that we actually have a lot in common, particularly from a microbiology standpoint: we both have innate immune defenses, and relatively predictable ranges of unique commensal flora, and we both are subject to infectious diseases. Importantly, there are clear differences in pathogenic potential of some microbes between humans and other animals and we can each be susceptible to select microbes from the other. Our intimate relationship with household pets often provides an easy route for cross-species transmission, and some of our close associations with farm animals and food animals provide other novel transmission modes, as does our interaction with wildlife from recreation or encroachment. From wildlife, etiologic agents may be carried to other species by arthropod vectors or even from contaminated skins or meat. Often, it is the environment interacting directly or indirectly with both humans and animals that influences how efficient this transfer of organisms can become. Whether it is climate change, weather anomalies, pollution, habitat alteration, or other environmental influences, the human-animal interface is impacted by the environment in ways that can easily change the "rules of engagement" for disease-producing agents. These agents are much better than humans at surviving adverse conditions, and in the process of survival, it may be the humans and animals that ultimately host the pathogen.

The One Health Concept

The One Health concept is important to microbiologists for a number of reasons. First and foremost, it is clear that our world is interconnected in numerous ways and that the human, animal, and environment interface depends upon equilibrium among all three components (Fig. 1). If one component is altered in any way, the chance for a local, regional, or even global calamity increases. For example, if susceptible individuals are exposed to a pathogen that has mutated due to environmental changes, those individuals may lack natural resistance. Rapid transmission in the naïve human population may lead to a pandemic that could be intensified by concurrent exposure to a susceptible animal species. If an animal species serving as a host to a tick vector has migrated into a new geographic area in response to climate change, a disease may emerge for the first time in this new area as humans or animals fall victim to the etiologic agent not seen before in the new area. It is in effect a cascade of biology that all started with the altering of one component of this triad. In addition, the knowledge that we are in an era of emerging infectious diseases, particularly emerging zoonoses and vector-borne diseases, requires that we act swiftly. Food safety and security are prime concerns of every person on the planet. We are learning more about the impact of climate change on infectious disease and public health and the ensuing consequences. Much of this interaction can be addressed in a new paradigm of infectious disease ecology, i.e., learning more about the susceptibility of certain populations or species to disease, how the disease intensifies in some communities, where the organisms go to survive between disease outbreaks, and how predictable changes, such as rain patterns, temperature fluxes, and removal of vegetation, impact these diseases. The One Health approach involves a shift to understanding and protecting biodiversity and sustainability of the species, as well as a shift from simple problem solving to managing dilemmas, understanding complex problems, and arriving at novel solutions. Hopefully, with commensurate knowledge and skills, we will see a day when predictive analysis will emerge as part of public health science and where the potential for outbreaks can be forecasted before they occur, thereby preventing disease and intervening much further upstream than is now possible. Much like the predictability of hurricanes and other weather disasters, we need to be able to identify the factors needed to predict impending human and animal health disasters. This will allow us to improve health in humans and animals and will give us an appreciation of the continuum of pathogens across species lines.

To evaluate how we are impacted by a One Health approach, consider the following:

- Of the 1,461 diseases of humans, 60% are due to multi-host pathogens that can engage many species (5).
- About 75% of all emerging diseases in humans are zoonotic (6).
- Food and water are essential to life, yet they are incredibly important vectors of disease throughout the world. During 2005 and 2006, a total of 78 waterborne disease outbreaks associated with recreational water (swimming) were reported by 31 states. Illness occurred in 4,412 persons, resulting in 116 hospitalizations and five deaths (7) just from being outdoors and having fun in the water. It is estimated that worldwide about 1.5 million people, mostly children, die each year from diarrheal disease, much of which is food borne or waterborne.
- The initial and ongoing pandemic studies with the H5N1 influenza virus and now the novel H1N1 virus required a huge collaborative effort of human and animal disease specialists working together to confirm the source of the virus and to protect human health through interventions aimed at both the human and animal populations.
- Many of the low-incidence, high-consequence viruses, such as rabies virus, Ebola virus, Marburg virus, and hantaviruses, are known to be animal linked, but the laboratorian is likely not going to have the expertise required to capture, examine, and culture the animal vectors for these etiologic agents or to know their habitats. Also, essentially any disease on our planet is potentially only 1 day away from the U.S. given our global travel capacity. Consider also the risk encountered with legal and illegal importation of animals or reptiles as pets, as they bring along their own microbiota from their countries of origin.
- In 2004, chikungunya re-emerged, causing millions of cases throughout countries in and around the Indian Ocean, resulting in significant morbidity and taxing the health care and public health infrastructure in these regions. Within 3 years, chikungunya had spread into Europe after an infected traveler transmitted the virus to local *Aedes albopictus* mosquitoes, leading to autochthonous transmission in Italy. Over the last 2 years, 56 cases of laboratory-confirmed chikungunya fever were reported in U.S. travelers returning from areas with ongoing disease activity; chikungunya virus was isolated from the blood of many of these patients.

At the CDC, the National Center for Zoonotic, Vector-borne, and Enteric Diseases (NCZVED) was formed in 2005 with the concept of One Health and infectious disease ecology as its theme. Using these concepts, NCZVED has developed a cadre of scientists whose work is aimed at disease prevention and outbreak interventions far sooner than before. To confront infectious diseases in an interconnected world, NCZVED uses a multidisciplinary, collaborative approach to increase efficiency in generating ideas and problem solving and to provide systems analysis approaches leading to upstream solutions, answering not only "What happened?" but "Why did it happen?"

Infectious Disease Ecology

We all recognize that by promoting the health of one species, the health of other species around it improves. The better we understand how this works, the more successful we will be in our goal to identify and control diseases. In human and animal microbiology, we realize that our health status often depends on our body's commensal flora, which includes healthy communities of organisms, not pure cultures of single species, and when these communities are impacted by disease, antimicrobial agents, poor nutrition, or other influences, the balance of health is disrupted and we see the consequences at the laboratory bench and in the patient. For example, a disruption of gastrointestinal flora can result in diarrheal illness; an imbalance in gram-positive vaginal flora leads to vaginosis; a commensal *Staphylococcus aureus* skin organism forced into a superficial puncture wound or trauma site can lead to serious infection; the intrusion of most any agent into a normally sterile body site can usher in a life-threatening illness. This microcosm of activity in the bodies of humans and animals is a picture of the macrocosm of our world of One Health.

Cutting forested areas to allow expansion of human populations or to entice housing complexes exposes humans to the disease vectors that once called that environment their home. The accompanying contamination and pollution impact human and animal health; people living closely with their companion animals or who enjoy the outdoors expose themselves to the zoonotic agents that pets and wildlife may bring into the home; climate change impacts the migration of animals and the arthropod vectors of disease associated with them; rain and temperature impact mosquito populations that can carry West Nile Virus in the U.S. In our daily microbiology work of culturing, recognizing, and reporting microbial agents, we only see the end result of this inextricably linked triad of people, animals, and the environment. However, if we broaden our knowledge to look at the bigger picture of the implications of what we have isolated at the bench, we may be able to contribute to the intervention necessary to prevent subsequent illness. Understanding how the linked triad works and what our role could be will go a long way in broadening our impact on helping to create a healthier world. In One Health, disease may be considered a "symptom" and the root cause will be more elusive than simply knowing the etiologic agent of that symptom. One Health encourages evidence-based analysis much earlier in the disease process than just stopping after isolating the etiologic agent, "fingerprinting" the agent, even finding the host or vector. One Health will look for the root cause(s) that fostered the organism's survival and transmission earliest in the chain of events that finally led to human disease.

To illustrate the concept of the ecology of infectious diseases, one may look at the ecology of Lyme disease in the U.S. and begin to understand the need for multiple skill sets to resolve the root cause of disease. Lyme disease is a tick-borne bacterial disease prevalent in north America caused by *Borrelia burgdorferi*. *B. burgdorferi* and related *Borrelia* species exist in nature in enzootic cycles primarily involving tick vectors, mostly of the *Ixodes ricinus* complex. These ticks have larval, nymphal, and adult stages and feed once during each of the three stages over their 2-year life span, feeding once in late summer, again in early spring as nymphs, and finally in early summer as adults. The risk of infection in humans depends on the population density of these ticks and their vertebrate animal hosts, who remain disease free but are spirochetemic throughout the summer (8). Total populations of the principal reservoir, the white-footed mouse, increase dramatically when their predators and competitors decrease in number, perhaps due to climate change or because of fragmented habitats. Lyme disease incidence increases dramatically as a result. However, in more intact communities with greater biodiversity and less pronounced dominance by white-footed mice, many of the vertebrates are poor reservoirs, meaning that they are less likely to infect ticks that feed on them. Thus, more ticks feed on less competent hosts, disease prevalence decreases, fewer ticks are infected, and disease risk to humans is reduced. In effect, high biodiversity (i.e., healthy natural communities) reduces infection risk. Unfortunately, the white-footed mouse thrives in small forest fragments created by suburban sprawl, so the common desire to live in "the country" or in a wooded setting (which typically consists of small fragments of forest) creates the conditions most likely to increase Lyme disease risk. It takes more than a clinical microbiologist to figure this out!

With more focused research and study in the area of One Health and infectious disease ecology, we can achieve a better understanding of how this interconnectedness leads to more effective health impact and a clearer definition of how the clinical microbiologist can meaningfully contribute more to the interpretive consequences of the organisms isolated at the bench. The impact of climate change on infectious diseases is a good example.

Climate change could facilitate the establishment of new vector-borne diseases imported into the U.S. or alter the geographic ranges of some of these diseases that already exist in this country. Altered weather patterns resulting from climate change could affect the distribution and incidence of food- and water-borne diseases. Changes in precipitation, temperature, humidity, and water salinity have been shown to affect the quality of water used for drinking, recreation, and commercial use. For example, an increase in temperature can lead to outbreaks of *Vibrio* infections following the consumption of seafood and shellfish. Drinking water treatment systems have been overloaded due to heavy rainfall, contributing to illness from *Cryptosporidium* and *Giardia*. Climate's effect on vector-borne diseases, such as plague and tularemia, in the U.S. is clearly documented (9-11). Storm water runoff can also increase fecal bacterial counts in coastal waters, as well as the nutrient load, which, coupled with increased sea surface temperature, can lead to increases in the frequency and range of harmful algal blooms (red tides) and potent marine biotoxins, such as ciguatera fish poisoning. More study is required to fully understand all the implications of ecological variables involved in climate change effects on vector-borne and zoonotic diseases (12).

For infectious diseases impacted by climate and climate change, it is clear that detection, prevention, and response will require a well-integrated human, animal, and environmental health strategy. Rift Valley fever is a vector-borne zoonotic disease that occurs primarily in Africa and infects people, food, animals, and some wildlife. Should this virus enter the U.S., it could potentially cause a devastating epidemic with substantial economic, commercial, and health consequences. Hantavirus diseases, plague, leptospirosis, West Nile virus, Lyme disease, and schistosomiasis, are all directly influenced by changing weather patterns and/or flooding, altered land use, and host-vector interactions. In terms of bio- and agroterrorism, 80% of the recognized select agents, i.e., those of greatest concern for use as bio-and agroterrorism agents, are zoonotic pathogens that may show up just as easily in a veterinary hospital or animal diagnostic laboratory as in a physician's office or a human health laboratory. However, with a few exceptions, we approach these threats as separate and disconnected events, and only now are surveillance systems attempting to integrate information.

One Health Lessons from the Human and Animal Interface

The largest waterborne disease outbreak in U.S. history occurred in 1993 in Milwaukee, WI, when over 400,000 people became ill with diarrhea attributed to the parasite *Cryptosporidium* in the city's drinking water supply (13). This was a perfect example illustrating how the convergent triad played directly into this outbreak. The illness was caused by a zoonotic agent leaching from fields into the water supply. For the laboratorian detecting the organisms microscopically, the story of the role of laboratory medicine was much more than just the recognition of parasite morphology. From the One Health standpoint and using the metaphor of moving solutions upstream to the root problem, one can see that it makes more sense to protect the watershed of the river that supplies drinking water to a town instead of relying only on water treatment plants to kill contaminant organisms. For many human health problems, upstream solutions mean addressing issues related to animal health and the environment.

While the food supply in the U.S. is one of the safest in the world, the CDC estimates that each year 76 million cases of food-borne illness result in the hospitalization of 300,000 persons and the death of 5,000. The source of an Alaska outbreak of *Campylobacter* infection was traced to the consumption of raw peas. It was further determined that the peas became contaminated while they were in the field, not from packaging irregularities. Further tracing showed that the field was directly in the flight path of Sandhill Cranes that left their droppings on the crops, leading to the contaminated product. In this outbreak, 97 people became ill and 54 were culture confirmed. Almost all had diarrhea. Bloody stools were evident in 19% of those infected, and Guillain-Barré syndrome (paralysis) appeared in one person. Isolating the causative organism was only a small part of the process, but understanding that the isolate could be a part of the intestinal flora of these birds helped solve the problem (14).

Contaminated spinach was the vector in another familiar outbreak in the U.S. (15). The animal and environment connection came into play when it was found that wild pigs, not nearby cattle, were able to penetrate the fencing of a farm and wander through the spinach field, leaving their contaminated feces coating the harvested greens. Spinach in the field was harvested by a "lawn mower." Once harvested, the spinach was transferred to a water bath that was contaminated by feces picked up with spinach, thus contaminating an entire day's production of spinach. In this instance, resolution was multifocal. Applying the One Health algorithm, one can see four integrated components:

- Viewed through a public health lens, the focus was on morbidity, mortality, diagnosis, and treatment.
- Viewed through the animal health lens, the organism was found in cattle and wild swine in the spinach-producing region.
- Viewed through the environmental lens, the irrigation system was strained due to weather anomalies.
- The investigation succeeded only when all of this information was integrated through collaboration.

A recent *Salmonella* outbreak was traced to patients who had household dogs. However, the investigators found that the dogs were being fed *Salmonella*-contaminated dog food and they, too, were victims of this food-borne illness; the attribution rested with the manufacturer of the dog food, and the pets were the unwitting vectors. Contamination at the dog food plant showed the true cause, and since this manufacturer packaged the dog food under 20 brand names, the outbreak covered many states and was protracted. Solving these types of problems and developing effective intervention strategies requires a holistic One Health approach where physicians, epidemiologists, veterinarians, and laboratorians all work together to identify an intervention that addresses the root cause, not just the symptom (i.e., the disease).

There are other One Health lessons we have learned from food-borne illness that can be useful. Pathogens from food animal feces can be transmitted to people through contaminated meat, as our continued experience with ground meat and *Escherichia coli* O157 has shown. *Campylobacter* is one of the human pathogens in chicken intestines, and ~50% of retail chicken is contaminated with *Campylobacter.* When chickens are slaughtered, bacteria from their intestines contaminate the water in the processing tank and spread to other chicken carcasses. Improperly cooked chicken may lead to infections in humans.

Use of antimicrobials in animals (an unnatural addition to food) can lead to antimicrobial-resistant infections in humans. In 1986, fluoroquinolones were first marketed. In 1990, the CDC conducted a survey of *Campylobacter* isolates from ill persons and found that none were resistant to fluoroquinolones (ciprofloxacin). Then, in 1995, the FDA approved the addition of a fluoroquinolone to poultry drinking water to treat infections in these chickens, and by 1997, the CDC and the FDA began surveillance for fluoroquinolone resistance in human *Campylobacter* isolates. Two years later, it was determined that persons with fluoroquinolone-resistant *Campylobacter* had diarrhea for longer than persons with fluoroquinolone susceptible *Campylobacter*. This prompted the FDA in 2000 to propose the withdrawal of approval of fluoroquinolones for use in poultry drinking water. In 2005, the FDA withdrew its approval (16,17).

We have learned that pathogens can be transmitted to people when they consume raw produce from a contaminated environment and that wild animals (not just domesticated animals) in the environment can be an ongoing source of pathogens transmitted to people through produce. We know that close contact with farm animals or their environment carries a risk of enteric infections. A contaminated environment in a food-manufacturing facility can lead to contamination of products over years and can lead to human illness by indirect routes. In addition, because they contaminate their environment with pathogens, some animals are not appropriate pets for young children, as evidenced by *Salmonella* infections traced to certain small pet turtles.

The Role of the Clinical Microbiologist in One Health

Clinical microbiologists are an integral part of this holistic approach to a healthy world. Not only do we function in laboratories as diagnosticians, but we also represent the scientists who can determine if a pathogen has changed and become a human pathogen or, in some cases, an animal or plant pathogen due to some genetic or cellular change. Understanding the consequences of what is being isolated and, importantly, what associated information or questions to relay to the attending physician and to the infection control personnel or epidemiologist will lead to the root causes. Of course this is important! Infectious diseases have helped shape the course of human history, and that is likely to continue to some degree. Microbes continue to survive our attempts to control them because of their uncanny ability to survive, adapt, and maintain themselves while being transported through the environment by vectors, only to emerge in susceptible hosts anywhere in the world. During these travels and times of sequestering, microbes have opportunities to create new niches, cross species boundaries to enhance survival, and travel worldwide to establish beachheads in new populations. The emergence of SARS (severe acute respiratory syndrome), hantavirus pulmonary syndrome, and monkey pox in the U.S. should remind us that viruses are as adaptable as bacteria and parasites.

In our role as clinical microbiologists, isolating or detecting *Giardia* should prompt questions about the patient's outdoor activities. Hearing reports about the sudden discovery of dead birds in the area would engage veterinarians, who would alert the laboratory to recommend patient testing for West Nile virus. Knowing a patient's travel history might prompt the laboratory to consider malaria or leptospirosis. Isolating a group C or G betahemolytic streptococcus from the throat of a child might lead to a veterinarian treating a pet or a farm animal for *Streptococcus* carriage. Communicating appropriately that *Salmonella* infections occurred in children who visited a petting zoo might alert veterinarians that the zoo animals may need treatment and that the facility may need to close until the treatment is completed. Finding a specific pathogen in a patient, followed by DNA confirmation of an indistinguishable isolate from cattle near the home, might lead to environmental control of runoff from pastureland.

Understanding these intricacies and how important they are to the health of populations falls directly upon the shoulders of the astute microbiologist. As a profession, no one knows more than we do about these pathogens, how they change and behave in various environments, and what species are susceptible. We have a new and unique opportunity to increase our value to health care and to broaden how we think about disease processes and ask ourselves questions about what we can do to help resolve a disease, assist in tracking a cause, or even predict an outbreak. We can carefully review organism pathogenicity and be prepared to intelligently evaluate and question test results that may signal an unusual event or process. We can be alert to the epidemiologic potential of organism isolates from patients as they may apply to infection control or community epidemiology. We can become familiar with the zoonotic diseases and recognize the etiologic agents associated with wild and domestic animals and apply that knowledge to our diagnostic skills. We can more closely communicate with and learn from our veterinary clinical microbiology colleagues and begin to understand the critical nature of the human, animal, and environment interface.

Using the holistic One Health approach that incorporates human, animal, and environmental health, and with a consideration of climate change, could we as a profession foresee a future where partnering with professionals with unique skill sets, like diagnostic microbiology, human and animal medicine, climatology, epidemiology, mathematical modeling, and sociology, would allow us to actually predict or forecast an outbreak or disease? Can we foresee a time when clinical microbiologists are able to look beyond the diagnostic bench into the universe of One Health and contribute far more than organism names and susceptibility results? This is our opportunity to be at the front of this line and not stand on the sidelines watching.

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