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LLOYD'S

COMMENTARY

THIS ISSUE of the *Equine Disease Quarterly* features an article by Dr. Noah Cohen addressing the subject of epidemiology. Dr. Cohen skillfully and artfully broached this topic in detail in the Milne Lecture in November at the 57th annual convention of the American Association of Equine Practitioners. As he pointed out, epidemiology is often viewed, much like statistics, in an unfavorable light by students, practitioners, and even academicians. Epidemiology, the study of health and disease events in populations, is often thought of as akin to public health and involving screening, risk factor assessment, and statistical analysis of data with the goal of preventive medicine. In many minds, epidemiology is far removed from day-to-day equine-related practice and activities.

As Dr. Cohen points out in his article in this issue, practitioners are constantly involved in examining and evaluating populations of patients and making judgments on the appropriate course of action based on their own experiences or those of others, all of which culminates in a population-based approach (epidemiology). In fact, when the articles in this issue are evaluated, one finds that each of them is deeply rooted in epidemiology. The parasitology report has its basis in population studies on farms and of groups (ages and uses) of horses. The ever-evolving saga of parasite resistance is best studied and attacked on an epidemiological basis. Also, the current approach to parasite control, which is gaining more attention, is totally based on epidemiology. Parasite control is a population approach of testing and then deworming based on worm burdens instead of simply deworming horses based on the calendar. It is perhaps a more effective means of controlling parasites and mitigating the development of parasite resistance.

Likewise, the article in this issue on conditions affecting the geriatric horse is a population-derived study. A population shift has occurred to include more old horses. With this shift, conditions and diseases affecting geriatric horses have taken on more importance, and it is a priority to develop strategies to approach their health issues. This focus is based on findings in and experiences with this population, so now when we deal with an individual geriatric horse, we employ epidemiological-derived knowledge. Finally, the Fourth Quarter 2011 Report from the International Collating Center and other sources is a pure epidemiological account of disease outbreaks and trends. Its value for the awareness and control of equine diseases cannot be overstated.

So, while we may not always like to think about epidemiology, Dr. Cohen is correct. Epidemiology does not always involve experimental models mired in statistics.However, as every article in this issue confirms, epidemiology often involves studies of our very own patients and populations of those patients in which we constantly utilize population-based knowledge. So the better we understand the principles of epidemiology, the better for the horse.

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INTERNATIONAL

Fourth Quarter 2011*

THE INTERNATIONAL Collating Center, Newmarket, United Kingdom (UK), and other sources reported the following disease outbreaks:

One case of contagious equine metritis (CEM, *Taylorella equigenitalis*) was reported in a non-Thoroughbred stallion in Germany.

A new outbreak of dourine was reported in the Bari Province of Italy involving one mare; the total number of outbreaks confirmed in Italy in 2011 was seven.

Equine influenza was reported from France (four outbreaks), Germany (single case), the UK (five outbreaks), the USA (two outbreaks), and Sweden. Sweden diagnosed the disease in nine of 10 Trotters that were part of a shipment transported to six stables in northern Sweden. Influenza spread to all horses on those premises and to five additional properties. The disease affected 60 Trotters on the 11 premises.

Strangles was reported from Chile, Germany, Ireland, Sweden, the United Arab Emirates (UAE), the UK, and the USA. Chile, Germany, and the UAE diagnosed isolated cases of the disease. Ireland confirmed 37 cases on premises in six counties; Sweden diagnosed strangles in a limited number of young horses and racehorses. The UK reported that the disease was endemic in the country's non-Thoroughbred population. Strangles was confirmed in three states in the USA.

Equine herpesvirus (EHV) respiratory disease was recorded by France, Germany, Japan, and the USA. Most of the outbreaks were caused by EHV-4. Abortion as a sequel to EHV-1 infection was diagnosed in isolated cases in France and Germany; Japan and the USA reported three and four cases respectively. One case of equine herpesvirus myeloencephalopathy was recorded from Germany.

Numerous cases of EHV-2 and/or EHV-5 infection were reported from the USA, some associated with clinical evidence of respiratory disease.

France reported a single case of equine arteritis virus infection; the USA had a small outbreak of equine viral arteritis on a Texas premises involving nine Paint horses.

Equine infectious anemia was confirmed in Germany in isolated cases on two premises.

Equine piroplasmosis (EP) was reported from France, the UAE, and the USA. The disease was considered endemic in France and the UAE. The USA detected a limited number of asymptomatic cases of infection with *Theileria equi*, mostly in Quarter Horse racehorses, a significant percentage of which were imported animals. The number of seropositive EP horses has declined over the past six to nine months of 2011.

Eastern equine encephalomyelitis (EEE) was only reported from the USA in nine animals (a total of 63 for 2011). Over 50% of the cases occurred in Wisconsin (34) with the remainder in six other states.

Italy and the USA reported cases of West Nile encephalitis (WNE). Ninety outbreaks involving 857 horses were confirmed in Italy, of which 189 animals tested positive; 58 displayed clinical signs; and 14 died. The USA reported 49 WNE cases, resulting in a total of 115 cases in 2011.

The third quarter of 2011 saw an increase in Hendra virus activity and distribution in Queensland and New South Wales in Australia. The disease was confirmed on seven properties on the north coast of New South Wales. Queensland reported 13 cases, one west of the Great Dividing Range. Neurologic clinical signs (not respiratory signs) characterized cases of the disease.

Ireland, Switzerland, and the USA reported outbreaks of salmonellosis. Most involved isolated cases caused by *S. typhimurium*, Salmonella Group B, Group C1, or untyped organisms.

A significant number of outbreaks of rotavirus infection were reported from Argentina. Disease of variable clinical severity was diagnosed in foals on eight premises. The USA confirmed two cases of equine clostridial enteritis (*Clostridium perfringens* type A) and a variable number of cases of *Lawsonia intracellularis* enteropathy in foals in two states. Switzerland reported an outbreak of equine atypical myopathy involving three cases; all were fatal. Leptospiral abortion (11 cases) was diagnosed in Kentucky, USA.

** Third quarter report for Australia*

Equine Disease Quarterly

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NATIONAL

Epidemiology in Practice

FOR MANY EQUINE PRACTITIONERS, the topic of epidemiology is an antidote to insomnia. Epidemiology is concerned with understanding the distribution of disease (and health) or the determinants of disease (and health) in populations. Because of the context in which it is often encountered, epidemiology generally is perceived to be about regulatory requirements, food safety, and zoonotic diseases. These areas, though important, hold little appeal for practice-minded veterinarians and students. In fact, the science of epidemiology extends beyond these areas and has direct relevance to all aspects of equine practice. Epidemiology is important to practitioners for at least three reasons.

First, our best source of clinical evidence comes from studies of patients rather than from experimental models of disease (which rarely mimic the complex circumstances and manifestations of naturally-occurring disease) or studies of experimental animals (which also are poor mimics for the target species). Patient-based studies may be observational or experimental; the latter are known as randomized clinical trials. The design, conduct, analysis, and interpretation of patient-based studies are principal activities of modern epidemiology. Thus, epidemiology is a—if not the—basic science of evidence-based equine practice.

Second, equine practitioners or scientists deal with communities or populations of horses on a daily basis. These populations may be defined by their location, such as farms, barns, racetracks, showgrounds or fairgrounds, etc. Communities also may be defined on the basis of breed or activity; for example, we may consider roping horses or Hanoverian horses to be a definable population that experiences health disorders that are particular or particularly common to their group. Finally, we may consider horses with a given disease status to be a community (e.g., horses with recurrent airway obstruction, those with metabolic syndrome, those with degenerative joint disease of the pastern joints, etc.). Thus, a population-based approach is inherent in daily practice.

Third, whenever we treat an individual horse, we apply what we have learned about similar cases from our experiences and from the experiences of others. When I was a student, I remember thinking there was something magical about how my teachers knew that retinal discoloration could indicate a peripheral nerve disorder or that coronitis of all four limbs in a horse with weight loss and soft stool was strongly suggestive of multisystemic eosinophilic epitheliotropic disease. Although I still find diagnostic medicine entrancing, there was nothing supernatural about the knowledge and wisdom of those teachers. Their knowledge was derived from seeing and learning about horses with similar conditions, and their wisdom was manifested by their ability to apply those experiences from the population of similar cases to an individual case. In this way, our interpretations of individuals are always population-based.

Like swords, population-based studies are double-edged. On one side, they are our best sources of clinical evidence because their findings may be directly relevant to horses we treat. On the other side, they are derived from observations in a natural setting in which many other factors that can contribute to disease development are beyond the investigators' control. These uncontrolled factors may lead to systematic error in the design or interpretation of results, known as biases. Much of modern epidemiology is concerned with identifying and accounting for bias. Thus, understanding principles of epidemiology is a useful investment of time to make us better interpreters of clinical evidence and thereby better practitioners. So next time you are doing some reading, consider reviewing a little epidemiology—maybe just before bedtime....

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Evolution in Equine Parasite Control

WHILE INFORMATION on anthelmintic resistance in equine parasites has been available for a long time, the equine industry has been very slow to acknowledge or respond to it. Numerous studies have documented the increasing prevalence of resistance to the different commercially available drug classes. Not surprisingly, parasitologists have strongly recommended reducing treatment intensity by moving away from the traditional calendar-based treatment protocols, which are based upon anthelmintic treatment of all horses at regular intervals year-round. Current recommendations involve regular analysis of fecal samples for the presence of parasite eggs before decisions on treatment are made. Several questionnaire-type surveys have revealed that despite these recommendations, horse owners in many countries still rely on frequent, regular anthelmintic treatments without any consideration of the parasite species that may be involved and the efficacy of anthelmintic drugs used against those parasites.

Several possible reasons may account for this approach: 1) parasitologists lack effective channels of communication to convey their message; 2) the anthelmintic resistance has not yet reached a level that represents a threat to equine health; 3) the calendar-based approach has been much easier to follow than the more complicated treatment strategies based on testing fecal samples; and 4) in many countries, cheap anthelmintic drugs have been available over the counter, so horse owners have not had to retain the services of a veterinarian, thereby lessening the expense. Singly or collectively, the foregoing factors have made it very difficult to change old habits when it comes to parasite management on horse farms.

However significant these obstacles, major changes in parasite management on farms have been observed in recent years. Awareness of anthelmintic resistance among equine veterinarians and their clients appears to be increasing. As a result, testing for parasite eggs in fecal samples is becoming more and more common. Several reasons have been put forward to account for this change. Several European countries have now implemented prescription-only restrictions on anthelmintic drug formulations, and these restrictions have led to a much greater degree of veterinary involvement in the treatment decision process. Under prescription-only conditions, veterinarians are expected to perform parasite surveillance and prescribe appropriate anthelmintics. As a result, the intensity of treatment has decreased considerably. Even in countries without this legislation, substantial changes have been observed. Many veterinary practitioners in the USA have adopted fecal testing, and several laboratories now offer egg counts and advice on a larger scale.

Apart from legislation in Europe, the most important factor that has promoted change is likely the influence of the Internet. In the past decade, several equine news media have established efficient portals for dissemination of knowledge to horse owners. Online broadcast of news, blogs, webinars, questions and answers, etc. has helped make new information more accessible and the average horse owner more aware of equine health issues than he or she was a decade or two ago.

As a result, veterinarians and horse owners worldwide are now realizing the problems resulting from following the traditional calendar-based deworming protocols for controlling strongyles and ascarids, which is generating many queries and challenges for parasitologists. Included are questions on how to interpret current diagnostic tests, the need for new diagnostic techniques, assessment of the impact of parasitism on equine health, equine performance under different deworming regimens, understanding modes of drug resistance, etc. The challenges confronting parasitologists, veterinarians, and members of the horse industry are many, and the need for research in equine parasitology is greater than ever.

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The 'Older' Horse: An Immunological Perspective

IN RECENT YEARS there has been a shift in the U.S. horse population, with aged horses (≥ 15 years) an increasing percentage (20-30%). Many of these older horses remain actively involved in equestrian sport competitions, are still being bred, or serve as companion animals. Thus, further understanding of how the biology of aging affects the older horse has become increasingly important and valid, given the greater demand for veterinary care and management of these animals. Unfortunately, as with elderly people, old horses suffer from age-related diseases, such as arthritis, congestive heart failure, Cushing's syndrome, and cancer. They also experience age-related changes in immune function.

A decline in the function and regulation of the immune system is a hallmark of aging, termed "immunosenescence." It greatly affects the ability of this aged population to resist infection and respond effectively to vaccination. In fact, it has been shown that like elderly humans, geriatric horses are susceptible to influenza virus infection despite pre-existing immunity to the virus. With age, all components of immunity are affected. These components include innate and adaptive responses to prevent infection and respond satisfactorily to vaccination. This process is very complex; however, changes in T lymphocyte function underlie much of the age-related decline in the protective immune response. Proper T-cell function is crucial in combating invading organisms and maintaining a pool of memory cells to handle future encounters with the same antigen. The exact causes of immunosenescence are not clear, although it is becoming more evident that this process is multifactorial and correlates with universally observed processes across species, including the following: thymic involution (attributing to a decreased pool of naïve T-cells capable of responding to new pathogens), chronic antigenic stimulation due to persistent infections (predominantly causing clonal exhaustion of memory T-cells), and signal transduction changes in immune cells. Collectively, these alterations contribute to the diminished ability of the immune system to respond to vaccination, enhancing susceptibility of this age group to infectious disease.

It's important that vaccines and vaccination strategies are developed that keep pace with the changing risk profile of an aging horse population. Vaccines are only effective, however, if the immune system is capable of responding to them. Research efforts are being directed at furthering our understanding of how different formulations of vaccines may overcome immunosenescence in the aged horse.

It is also important to recognize how different vaccine constructs stimulate the immune system. Inactivated or "killed" vaccines are processed and recognized by the immune system as exogenous antigens; they induce primarily an antibody response but poor cell-mediated immune (CMI) responses. "Live" vaccines are processed by the immune system as endogenous antigen, which mimics how a natural viral infection is processed; these antigens elicit both antibody and strong CMI responses. Indeed, it has been shown that older horses are capable of responding to a vectored, or live, influenza vaccine. Further research is needed to improve our understanding of vaccine effectiveness in aged horses. Areas of current investigation

(The 'Older' Horse continued from page 5)

include using high-dose vaccines, multiple administration of vaccines, DNA vaccines with immunostimulatory properties, and vaccines containing new adjuvants. It is also important to recognize that other factors, such as chronic diseases, age-associated inflammation ("inflamm-aging"), frailty, stress, and nutritional status likely contribute to impaired immune responses to infectious agents and vaccinations with age. These types of studies will help provide a platform on which to further investigate mechanisms responsible for a decline in immune responses with advancing age.

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