Milne Lecture: Epidemiology

BY NANCY S. LOVING, DVM

"Anecdotal and clinical impressions are appealing but are unreliable sources of information because we often are insufficiently cognizant of the role that chance plays in clinical practice," began Noah Cohen, VMD, MPH, PhD, Dipl. ACVIM, of Texas A&M's College of Veterinary Medicine. He described the importance of integrating the science of epidemiology into equine practice in his delivery of the Milne State-of-the-Art Lecture at the convention. He added, "It is possible to make errors in clinical judgment based on our impressions or the impressions of others. This is because something good or bad can appear to be the effect of some cause (like a treatment) when it is purely due to chance. Moreover, experts are not always correct, and logical reasoning is not always accurate." Thus, veterinarians need to rely on evidence other than just their clinical impressions and the opinions of experts.

Cohen stressed, "As practitioners, we want to be able to rely on the best available clinical evidence, or so-called evidence-based medicine. This integrates the best research evidence with clinical expertise and our patients' unique circumstances. Epidemiology is the fundamental underlying science of evidence-based medicine." He said the best evidence comes from studying patients with naturally occurring disease, noting that experimental disease rarely mimics natural or spontaneous disease. "And, when making medical decisions about horses," he continued, "a laboratory mouse is not equal to a horse."

Periodically, Cohen handed the microphone to his friend and colleague, Bo Brock, DVM, who peppered the talk with allegories that brought home various points. Brock said Cohen's task was daunting: Within a few hours, he had to teach a subject from the beginning, starting with basic terminology. By the session's end, Cohen achieved this goal by weaving the language of probability and epidemiology into the context of real-life clinical situations.

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Dr. Noah Cohen described the practical importance of epidemiology in daily clinical activities. He stressed to a large audience of equine veterinarians that they should not only remain up-to-date on research but also contribute to advancing the profession through conducting evidence-based studies.

The Essentials of Epidemiology

"Why does epidemiology matter to equine practitioners?" asked Cohen. Veterinarians generally provide care to communities and populations of horses. A community might be defined based on location, use, breed, or disease status. Epidemiology is the study of disease (and health) and determinants of disease (and health) in populations. Thus, veterinarians rely on principles of epidemiology when considering "community" health. They also use epidemiology every day when addressing individual patients. "Things learned from other horses are brought to bear on an individual horse, with epidemiology impacting everything we've seen or done before, putting everything into context with experience," said Cohen. For example, if one hears a heart murmur in a horse the interpretation of that murmur is virtually meaningless without the knowledge derived (by oneself and others) from hearing similar murmurs in other horses. Veterinarians in clinical practice also use epidemiology because it is the basis for obtaining and assessing clinical "evidence" from patient-based studies.

Cohen described a proposed hierarchy of clinical evidence: Expert opinions, experimental models, editorials, animal research, or *in vitro* or test tube experiments represent the lowest level of evidence because these are least relevant to patients and might be misleading. Observational studies of patients like case-control studies are in the middle ranks of the hierarchy (e.g., a case-control study of risk factors for pasture-associated laminitis). Randomized controlled trials of patients are the highest form of clinical evidence, as far as individual studies are concerned. The most compelling clinical evidence comes from combining clinical trials for a specific topic in either a systematic review or a meta-analysis (integration of data from a number of independent studies). Because there is a paucity of randomized clinical trials in equine medicine, practitioners must rely heavily on observational epidemiological studies of patients to obtain clinical evidence.

Quantifying: Measuring & Counting

"Epidemiology is a quantitative science for descriptive purposes of counting health outcomes to obtain essential information, or for inferential purposes to measure associations to make inferences about causes," said Cohen.

The NAHMS (National Animal Health Monitoring System) 1998 and 2005 reports outlined statistics of owner-reported data on disease frequency, causes of death, geographic distribution, and management practices. He said these reports provide valuable inferential information. The 2011 equine herpesvirus myeloencephalopathy outbreak further illustrates the value of descriptive epidemiology; providing important information to veterinarians and owners helped control the outbreak.

He defined prevalence and incidence, indicating why this distinction matters: Studies based on prevalent cases are less clear about causation than those based on incidence. Prevalence studies consider factors contributing not only to disease development but also to survival and/or disease duration. Incidence studies examine only factors that contribute to disease development (therefore, causes). For example, if scientists conducting a study of "prevalent laminitis" found an association between grazing muzzles and laminitis, we might conclude that such muzzles cause laminitis. But, horses wearing muzzles might survive longer for detection and study than horses without muzzles; therefore, the association might reflect survival. In contrast, those without muzzles might die of laminitis earlier in the study, and the prevalence association is not so much causal as it is a determinant of survival. In contrast, an association of "incident laminitis cases" with metabolic disease is more likely to reflect endocrine disease as causal.

Clinical scientists use inferential epidemiology to investigate causal association. They use this approach to examine diagnosis, treatment, prognosis, and prevention. While the best answers come from controlled studies of natural disease, Cohen cautioned that "noise" is one disadvantage of these studies. This comes from studying naturally occurring cases in a real-world environment where one cannot control all factors; thus, "noise" from factors other than the determinant of interest influence the association scientists see. For example, while diet might affect colic, other factors (exercise, parasite control, age) might also influence colic development and should be accounted for. "Filtering out this noise is a major challenge," he said.

Exposure refers to a factor shared by a study group, such as treatment, environment (housing, diet, ingested toxins), or attributes (age, gender, or breed). Outcome refers to the endpoint of what is measured, such as a disease, survival, or performance. Inferential epidemiology is used in studies identifying associations between exposures and outcomes—for example, diet is associated with impaction colic, or track surface is associated with musculoskeletal injury.

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The measures of association scientists most commonly use in inferential epidemiological studies are the risk ratio (also called relative risk) and the odds ratio. These are an estimate of how many more times likely a horse is to develop the disease if he's been exposed to a potential causative agent than an unexposed horse.

Confounding

He also pointed out that an apparent association between a given risk factor (such as breed) and a disease (i.e., colic) might be explained by other factors, called confounders, that are associated with both the exposure and disease being studied. In the colic example confounders could include activity level or feeding practices. While there appears to be an association between breed and colic, the apparent association might be because activity level is associated with breed and with colic. Thus, an apparent association between breed and colic might be confounded by activity level.

"A confounder can make an apparent association (harmful or protective) disappear, can mask an existing association (harmful or protective), or can change a harmful effect to a protective effect or vice versa," he said. A confounder might be something investigators have measured and can account for, or it might be an unmeasured factor that cannot be considered. Regardless, "It is safe to assume that there is some degree of confounding in any observational study because it is virtually impossible for any two groups of horses to be identical for all factors except the one of interest."

Positive Predictive Values

Interpreting test results is essential for medical management. High sensitivity (the probability that actual cases will have a positive test result) and high specificity (the probability that horses without the condition will have a negative test result) don't ensure that a test will perform accurately. Positive predictive value refers to the probability that a positive test means a horse truly has disease (i.e., a positive test is truly positive). Conversely, a negative predictive value looks at the probability that a negative test is truly negative.

A practitioner's assessment of the probability of disease before running a test influences how he or she might interpret it. Consider testing for equine protozoal myeloencephalitis (EPM) in a horse with the classical neurologic signs compared to testing for EPM in a horse with bilateral forelimb (both limbs) lameness localized to the heel: There is a very low chance that the heel-sore horse will test positive for EPM, whereas a positive EPM test in the neurologic horse has a high predictive value for EPM. He noted, "If it looks like a duck, is given a duck test, then it's likely to be a duck." It's important to incorporate prior knowledge and subjective impressions into test interpretation: "Problems are often not with the test but rather with human expectations and interpretations."

The Value of Epidemiology

Cohen summarized epidemiology as the fundamental science for clinical research and practice; understanding its principles, methods, strengths, and limitations is essential, since veterinarians use it for all clinical activities. He said professional advances occur through scientific inquiry, with the most relevant research focused on patient-based observations. Cohen urged his audience to strive to continually learn but also to advance the profession by conducting patient-based research.

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