# A Debate Regarding the Usefulness of Cancer Screening Tests in Veterinary Medicine

Written by Maria Vinall

In a point-counterpoint discussion of the merits of cancer screening tests in veterinary medicine, Rance Sellon, DVM, PhD, Washington State University, Pullman, Washington, USA, argued that there is evidence to justify using such tests for diseases such as canine lymphosarcoma (LSA) and for the detection of bladder tumors. Marlene Hauck, DVM, PhD, North Carolina State University, Raleigh, North Carolina, USA, argued that there is not enough evidence to justify using cancer screening tests for these diseases.

Approximately 50% of dogs > 10 years of age will die of neoplastic disease. Noting that several cancer screening tests have come onto the veterinary market in the past few years, Dr. Sellon suggested there is a very large population of animals that might benefit. He asked the group to consider that a principle role of a screening test is to improve care, not by confirming disease but by identifying those who are unlikely to have disease as well as those who could have disease.

Three screening tests are currently available for dogs: the lymphoma blood test (LBT), the bladder tumor antigen (BTA) test, and thymidine kinase 1 (TK1)/canine C-reactive protein (cCRP) test. There is no peer-reviewed information yet available for the LBT; however, Dr. Sellon shared results of studies that evaluated the first-generation Bard BTA and TK1/cCRP tests.

The earliest of the 3 studies to evaluate the Bard BTA test in dogs was a 1999 1-year prospective clinical trial designed to assess the efficacy, sensitivity, and specificity of the test in the diagnosis of canine transitional cell carcinoma (TCC; a disease that carries a poor prognosis that is, in part, due to late disease detection) [Borjesson DL et al. *Vet Clin Pathol* 1999]. Of 65 dogs that were entered in the study, 20 were TCC-confirmed cases, 19 were healthy control cases, and 26 were urologic control cases with various conditions. The Bard BTA was shown to have an overall sensitivity of 90% and specificity of 78% for the detection of the bladder tumor–associated antigen complex in canine TCC. The authors concluded that, in geriatric patients or patients with clinical signs related to the lower urinary tract, diagnosis and screening may be assisted by the BARD BTA test to rule out TCC, and it may be able to provide a diagnosis before the onset of pyuria and hematuria, which could alter the test results. The sensitivity of the BTA test was confirmed in a 2002 study in which it was shown to be effective for differentiating dogs with malignancies of the lower urinary tract from dogs without urinary tract disease, but it could not differentiate dogs with neoplasia from dogs with nonmalignant urinary tract disease [Billet JP et al. *Am J Vet Res* 2002]. One year later, a test sensitivity of 88% for TCC of the lower urinary tract was reported [Henry CJ et al. *Am J Vet Res* 2003].

Three studies have also confirmed the benefit of the TK1/cCRP tests but with varying levels of sensitivity. The first study showed that high plasma TK activity was a sensitive (100%) marker for lymphoma and leukemia in 20 dogs [Nakamura N et al. *J Vet Med Sci* 1997]. A second study [von Euler H et al. *J Vet Intern Med* 2004] reported that a high level of serum TK was a sensitive prognostic marker for survival time in dogs with malignant lymphoma and could identify early signs of progression of disease in treated dogs. In the most recent study, Selting et al. [*Vet Comp Oncol* 2013] reported that serum TK1 and cCRP (when used together as a neoplastic index) are useful in the screening of occult canine cancer.

From these studies, Dr. Sellon concluded that the high sensitivity of BTA and TK1/cCRP screening tools suggest these tests are most useful for identifying patients that do not have cancer, thus having value in small animal practice.

According to Dr. Hauck, a screening test should be inexpensive, acceptable to patients and physicians, and have high predictive value in the population to be screened. The disease in question should be common, serious, treatable, and slow to become symptomatic. Importantly, treatment in

Peer-Reviewed Highlights From the

**American Veterinary Medical Association 2014 Annual Meeting**

July 25–29, 2014
Denver, Colorado

the asymptomatic phase should be superior to treatment after symptoms develop. She also believes that the effectiveness of a screening test depends on its predictive value, which is determined by sensitivity, specificity and, particularly, disease prevalence in the screened population. The lower the prevalence of the disease, the higher the sensitivity and specificity have to be to justify the use of the test.

In diseases with a very low prevalence, even a test with high sensitivity and specificity will produce an unacceptable number of false positives, and the screening may not be defensible because of the high cost of following up all the healthy positives. Screening for disease must be simple, cost-effective, and safe. False positives have the risk of creating psychological damage and increasing the risk and cost of further testing, whereas false negatives may delay diagnosis.

Dr. Hauck noted that, when evaluating the benefit of a screening program, it is important to consider the effects of lead-time, length-of-time, and compliance bias. Lead-time bias is the bias that occurs when 2 tests for a disease are compared and 1 test diagnoses the disease earlier, but has no effect on the outcome of the disease (e.g., it appears to prolong survival when in fact it only resulted in earlier diagnosis when compared with traditional methods). Length-of-time bias is reflected in the overestimation of survival duration among patients whose disease is diagnosed through screening. Since rapidly progressing diseases, which are symptomatic, are more often clinically detected than slowly progressing diseases, a greater proportion of slowly progressing diseases may be detected by screening. Therefore, Dr. Hauck stated that patients diagnosed by screening will, as a group, progress more slowly than those diagnosed by conventional means, even if early treatment has no effect. Compliance bias suggests that individuals who seek screening are more health conscious, more compliant with treatment, and have better outcomes, not because of detection by early screening, but because these individuals assume greater responsibility for their own care.

Dr. Hauck concluded that single and combination diagnostic tests could be wrong. Even correct tests do not replace other clinical information from a history and a physical exam. Identical test results could have entirely different implications for different patients, or in different environments. Highly accurate tests can be clinically useless, or even harmful, for some patients, particularly when the disease is unlikely, or even likely, to be present before the test. Only a test with very high sensitivity can establish a disease absence or presence.

In the end, readers should be aware that there are unknowns regarding the role that cancer screening tests play in clinical veterinary practice. The clinician should carefully consider the question to be answered before using a screening test to make sure that the test result is capable of providing the desired information in any given clinical context.