IDEXX 4Dx Plus Test: Expanded capability, same great performance

Introduction

Vectors and the diseases they transmit have become increasingly prevalent throughout the United States. A recent publication summarizing over 144,000,000 IDEXX 4Dx® Plus Test results from 2013–2019 found that "dogs are commonly infected with vector-borne pathogens, including heartworm and tick-borne disease agents. The geographic distribution of both arthropod vectors and the pathogens they transmit continues to expand."[1] To help veterinarians routinely screen for and more accurately diagnose these vector-borne diseases, IDEXX has improved the IDEXX 4Dx Plus Test by adding new targets to current markers for enhanced detection of antibodies to *Anaplasma* spp. and *Ehrlichia* spp. This enables veterinarians to confidently screen for these tick-borne pathogens. Equally important, the test helps uncover evidence that dogs have been infected with multiple infectious organisms either through bites from multiple tick vectors or coinfections carried by the same vector. This helps in diagnosis, treatment, and awareness of tick-borne diseases.

The IDEXX 4Dx Plus Test—available in-house as the SNAP® 4Dx® Plus Test or from IDEXX Reference Laboratories as the Lab 4Dx® Plus Test—can be used to detect the antigen of *Dirofilaria immitis* and antibodies against *Anaplasma phagocytophilum, Anaplasma platys, Borrelia burgdorferi, Ehrlichia canis*, and *Ehrlichia ewingii* in a single whole blood, plasma, or serum specimen.[2,3]

Same great performance with enhanced detection of *Anaplasma* spp.

The IDEXX 4Dx Plus Test continues to exhibit sensitivity and specificity consistent with the performance shown in numerous peer-reviewed publications.[2,4–7] The additional markers improve the sensitivity and specificity for *Anaplasma* spp. while improving the specificity for *Ehrlichia* spp. detection (see table 1). When the enhancements to *Ehrlichia* spp. and *Anaplasma* spp. detection were evaluated compared to the previous antibody markers on the same sample set (see table 1), the additional antibody markers enabled detection of more positive samples for both *Anaplasma* spp. and *Ehrlichia canis* than previously. In 510 samples evaluated, 21 more antibody-positive samples were detected for *Anaplasma* spp. and 4 more antibody-positive samples were found for *Ehrlichia* spp.

The increased sensitivity of the IDEXX 4Dx Plus Test for detection of *Anaplasma* spp. antibodies is most evident in areas endemic for *A. phagocytophilum*. In a recent serosurvey of almost 20,000 specimens from throughout the US, Wisconsin, Minnesota, New England, and the Middle Atlantic states had the largest percent of positive results. In these endemic regions, the increased sensitivity allows veterinarians to uncover dogs that may have vague or no clinical signs at the time of testing, giving them the opportunity to further evaluate for evidence of clinical anaplasmosis. Accurate diagnosis enables timely treatment in clinically affected dogs and helps support discussions with pet owners on tick control and preventive recommendations. The results in table 2 are by US census region, and the results in figure 1 are by state.

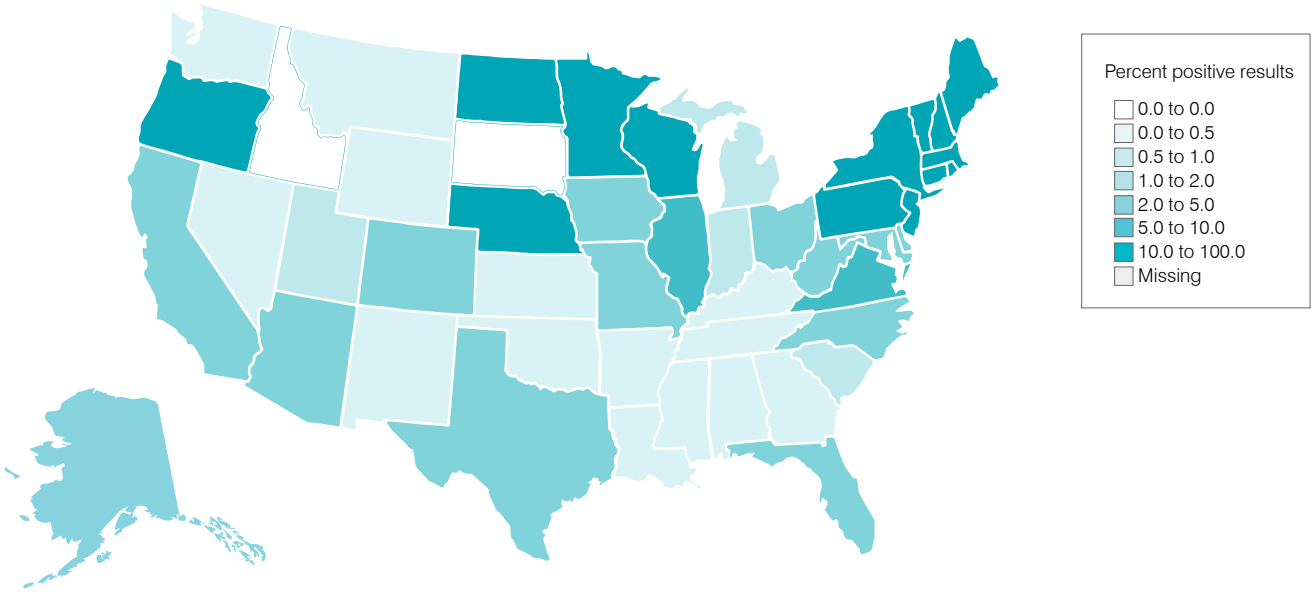


Figure 1. *Anaplasma* percent positive results by state[8]

Additionally, limited experimental infection data has suggested improved alignment with the IDEXX 4Dx Plus Test and PCR-positive dogs at the onset of clinical symptoms for postinfection detection of *E. canis*. Of the 6 dogs experimentally infected with *E. canis*, 3 dogs had detectable antibodies for *E. canis* that correlated with the onset of observable clinical signs and were PCR positive.[8] The remaining 3 dogs were antibody positive within 6 days following onset of clinical signs and PCR-positive results (figure 2). This gives veterinarians the potential for an earlier diagnosis in acutely ill dogs.

Further, the test continues to deliver consistent, accurate detection for *D. immitis* antigen and C_6 antibodies for *B. burgdorferi*, the causative agent for Lyme disease.

Analyte	Reference standard	IDEXX 4Dx Plus Test result		Total	Sensitivity (95% CL)
		+	–		Specificity (95% CL)
Dirofilaria immitis[a]	+	48	1	49	98.0% (89.1%–99.9%)
	–	0	461	461	100.0% (99.2%–100%)
Anaplasma spp.[b]	+	80	5	85	94.1% (86.8%–98.1%)
	–	7	418	425	98.4% (96.6%–99.3%)
Ehrlichia spp.[c]	+	99	7	106	93.4% (86.9%–97.3%)
	–	13	391	404	96.8% (94.6%–98.3%)
Borrelia burgdorferi[d]	+	21	1	22	95.5% (77.2%–99.9%)
	–	3	485	488	99.4% (98.2%–99.9%)

Table 1. Improved IDEXX 4Dx® Plus Test versus reference methods[8]

Reference methods

a. Necropsy or PetChek® Heartworm ELISA positive and PetChek Heartworm ELISA negative

b. *A. phagocytophilum* IFA and *Anaplasma* ELISA

c. *E.canis* IFA and *E. ewingii* ELISA

d. Lyme immunoblot and C_6 ELISA

Census region	Census division	Percent positive results (95% CI)
Midwest	East North Central	4.7% (3.8–5.8)
	Wisconsin	29.6% (22.9–37.1)
	West North Central	4.2% (3.3–5.3)
	Minnesota	19.6% (15–24.7)
Northeast	Middle Atlantic	11.8% (10.5–13.2)
	New England	30.2% (28.7–31.8)
South	East South Central	0.7% (0.3–1.4)
	South Atlantic	2.1% (1.6–2.7)
	West South Central	1.3% (0.8–2)
West	Mountain	1.2% (0.7–1.8)
	Pacific	3.1% (2.5–3.7)

Table 2. *Anaplasma* percent positive results by US census region[8]

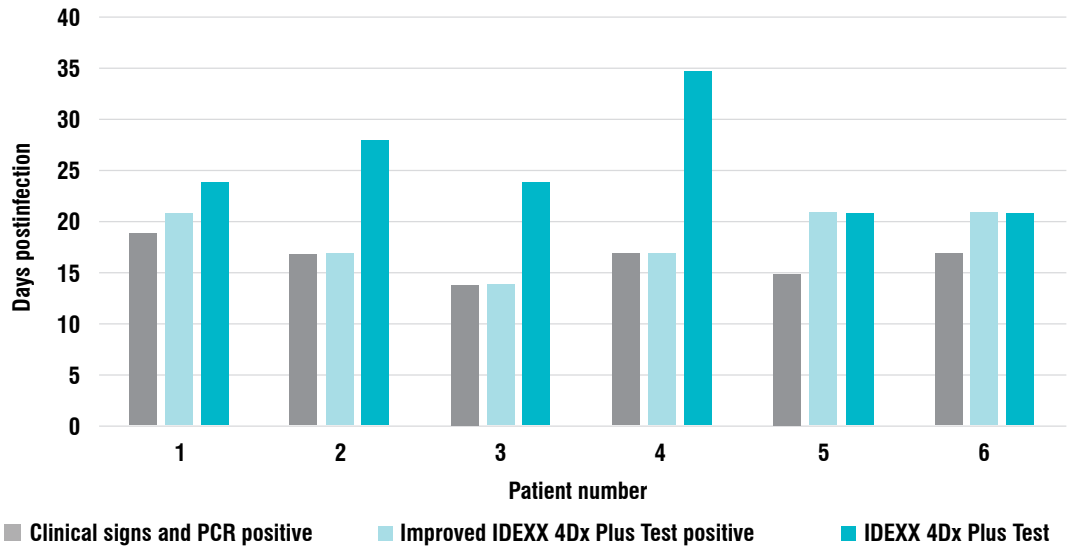
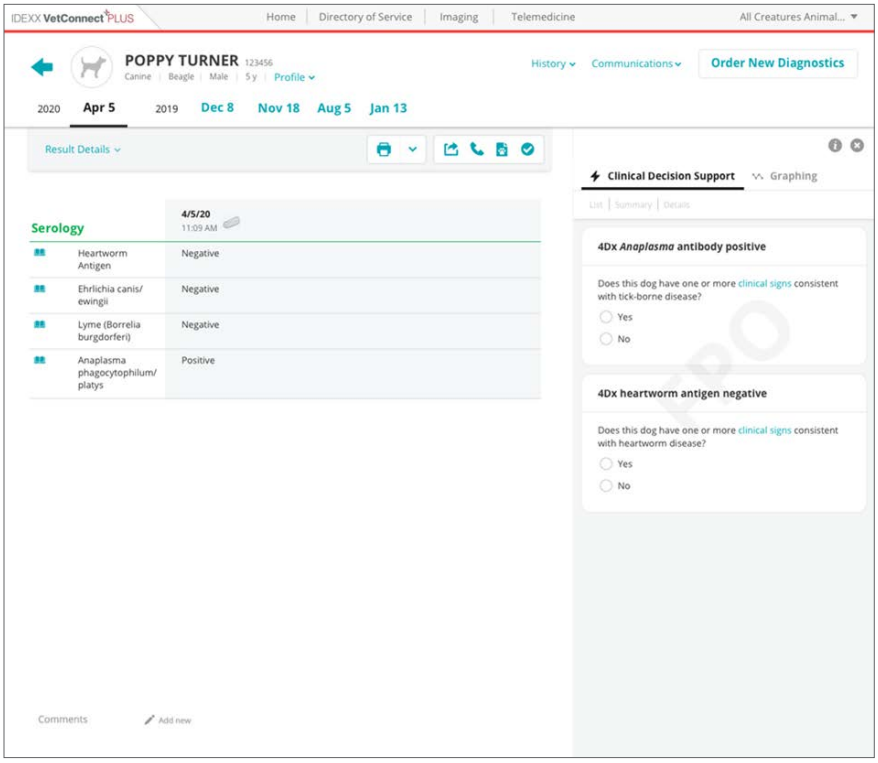
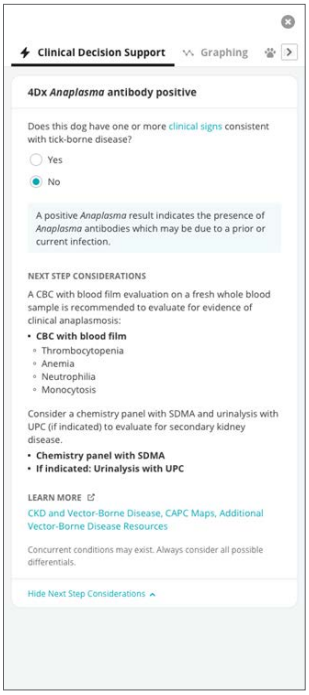


Figure 2. *E. canis* experimental infection—positive result days postinfection[8]

What to do with positive results on the IDEXX 4Dx Plus Test

Using an IDEXX 4Dx® Plus Test for annual vector-borne disease screening provides valuable medical information about the infectious organisms to which dogs in your practice are being exposed. The *IDEXX 4Dx Plus Test Clinical Reference Guide* offers an overview of each organism and associated disease(s), including the vector, clinical signs, and suggested protocols for dogs with a positive serologic result on the IDEXX 4Dx Plus Test. VetConnect® PLUS provides step-by-step results-specific considerations and interpretations aimed at determining if the dog has results consistent with an active infection.





Summary and conclusions

The IDEXX 4Dx® Plus Test delivers comprehensive patient information about vector-borne disease infection, which helps veterinarians better understand vector-borne disease risks in their patient population. The improvements achieved through these additional antibody detection markers increase the sensitivity for *Anaplasma* spp. and specificity for *Ehrlichia canis*, thus enabling confident, timely diagnosis of tick-borne diseases by veterinarians. Specifically, the increased sensitivity for *Anaplasma* spp. antibodies enables veterinarians to uncover dogs that may have vague or no clinical signs at the time of testing, which allows veterinarians to further evaluate for evidence of clinical anaplasmosis. This improved performance, combined with results-specific considerations and interpretations via clinical decision support in VetConnect® PLUS, provides veterinarians confidence and clarity in diagnosis.

References

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