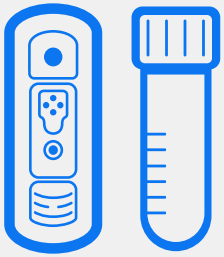
IDEXX

Screening for vector-borne disease

IDEXX 4Dx® Plus Test clinical reference guide



CREATING CLARITY

Every dog, every year

The Companion Animal Parasite Council (CAPC) Guidelines recommend annual comprehensive screening for pathogens transmitted by ticks and mosquitoes.[1] Adding annual cycle of comprehensive testing and year-round prevention to your practice benefits your patients, clients, and practice in 3 important ways:

1. React to changing prevalence
Mosquitoes and ticks are constantly on the move, and annual testing is the most reliable way to determine if new infections are threatening pets in your area. Pets move too, of course; without comprehensive testing, you sacrifice the ability to detect and treat mosquito and tick-borne infections acquired in other locations.

2. Detect and treat coinfection
Comprehensive testing lets you assess a dog's risk of having more than one infection.[2]

3. Measure the effectiveness of prevention protocols
Only comprehensive testing helps you know if your prevention protocols are working. Even a negative result is valuable; it's an opportunity to celebrate the pet owner's role in successfully preventing these infections and keeping their pet healthy.

Know more with every result

With the IDEXX 4Dx® Plus Test, a positive result can also be an indication of ticks and and the pathogens they carry.

When you use the IDEXX 4Dx Plus Test as a screening tool, you may

detect antibodies to these pathogens	carried by these ticks	that may also transmit other pathogens and infections to dogs and people	Geographic tick distribution as of 2021[3]
Ehrlichia ewingii	**Lone star tick** *Amblyomma americanum*	*Ehrlichia chaffeensis* Tularemia Rocky Mountain spotted fever STARI	
Anaplasma phagocytophilum *Borrelia burgdorferi (Lyme disease)*	**Black-legged tick (deer tick)** *Ixodes scapularis* *Ixodes pacificus*	*Bartonella* spp. *Babesia* spp.	
Ehrlichia canis *Anaplasma platys*	**Brown dog tick** *Rhipicephalus sanguineus*	*Babesia* spp. Rocky Mountain spotted fever	
Ehrlichia canis	**American dog tick** *Dermacentor variabilis*	Rocky Mountain spotted fever Tularemia	

Lyme disease

Transmitted by the black-legged tick (deer tick), Lyme disease is caused by the bacterium *Borrelia burgdorferi*. Clinical signs may not appear until several months after infection. Lyme disease has been found throughout North America with cases that have mild to severe disease.

Did you know?

+ Dogs testing positive for antibodies to the C_6 peptide had 43% increased risk of having chronic kidney disease (CKD) compared to seronegative dogs.[4]
+ The C_6 peptide used in the IDEXX 4Dx® Plus Test and Lyme Quant C_6® Antibody Test does not cross-react with the antibody response to commercially available Lyme vaccines.[5]
+ Dogs with seroreactivity to both *B. burgdorferi* and *Anaplasma phagocytophilum* may have two times the risk of developing clinical illness than singularly infected dogs.[2]

Borrelia burgdorferi

Primary vectors

Ixodes scapularis or *Ixodes pacificus*
Black-legged tick (deer tick)

Pathology

+ Localizes in tissues of infected dogs
+ Synovitis (may be subclinical)
+ Lyme nephritis

Clinical presentation

Chronic infection with clinical signs that may present acutely:
+ Fever, anorexia
+ Polyarthritis, lameness
+ Rapidly progressive renal failure
+ Neurologic syndromes

Laboratory abnormalities

+ Elevated C_6 antibody level ≥ 30 U/mL
+ May have proteinuria
+ May have IDEXX SDMA® Test result > 14 µg/dL

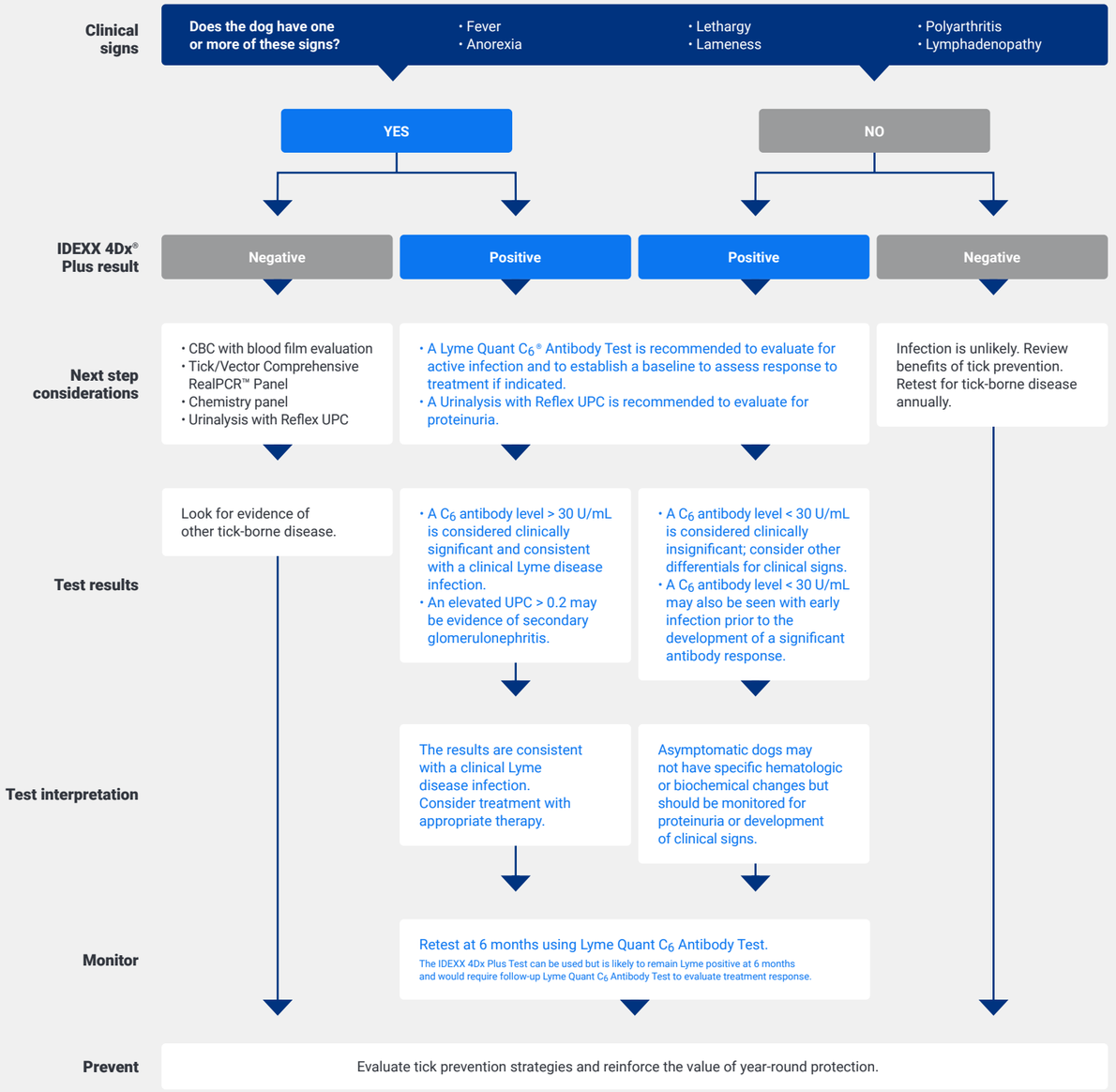
Monitoring considerations

1. If C_6 antibody level drops ≥ 50% from initial level, treatment was successful.
2. If C_6 antibody level drops < 50% from initial titer, differentials include:
   a. Noncompliance with treatment. Consider retreating.
   b. Reinfection. Reevaluate tick control; consider retreating.
   c. Chronic infection.

CKD monitoring

+ Chemistry panel with SDMA
  – Recommended to evaluate for the development of protein-losing kidney disease
+ Urinalysis with Reflex UPC
  – Recommended to evaluate for proteinuria
+ CBC with blood film evaluation
  – Recommended as part of a minimum database

*Serology is typically used to diagnose Lyme disease. *B. burgdorferi* localizes to the tissues and is therefore rarely detectable in the blood by PCR.[6]



Heartworm disease

Dirofilaria immitis, the causative agent of heartworm disease, is transmitted when mosquitoes infected with *D. immitis* larvae feed on (or bite) a healthy dog. Heartworm disease has subtle or mild clinical signs in the early stages, making preventive measures so much more important—especially as advanced infection may result in death.

Did you know?

+ Despite availability of monthly preventives, prevalence rates of canine heartworm have remained consistent nationwide.[7]
+ The American Heartworm Society (AHS) and the Companion Animal Parasite Council (CAPC) recommend testing all dogs for both antigen and microfilariae annually.[7,8]
+ For more information and current recommendations on treating canine heartworm disease, go to **heartwormsociety.org** or **capcvet.org**.

Dirofilaria immitis

Primary vector

Mosquito

Pathology

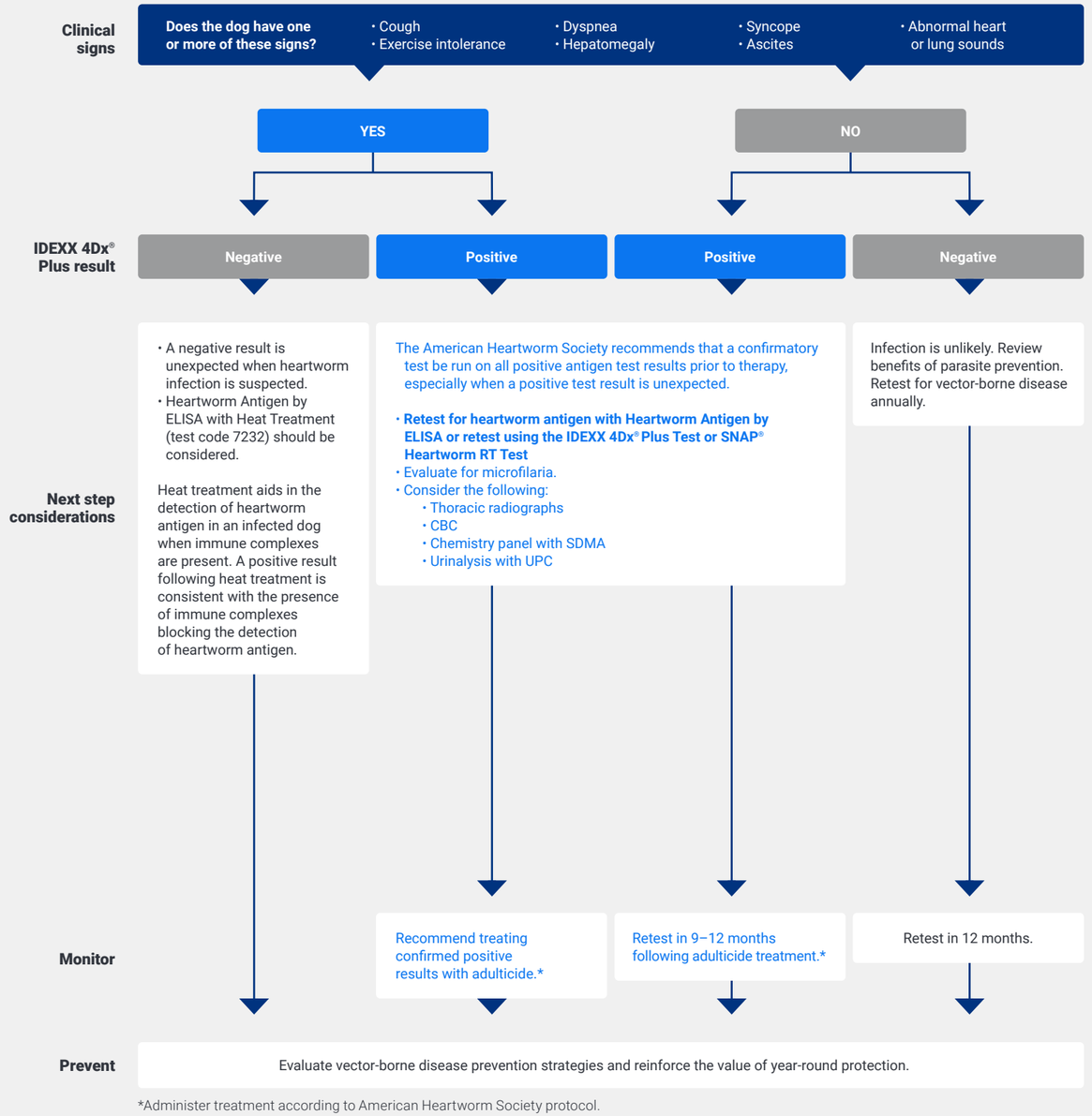
Infective larvae (L3) mature to adult worms in the heart and pulmonary arteries

Clinical presentation

Asymptomatic at first, later developing:
+ Mild, persistent cough
+ Lethargy
+ Exercise intolerance
+ Reduced appetite
+ Weight loss

Laboratory abnormalities that may be seen

+ Eosinophilia
+ Azotemia
+ Increased liver enzymes
+ Proteinuria



*Administer treatment according to American Heartworm Society protocol.

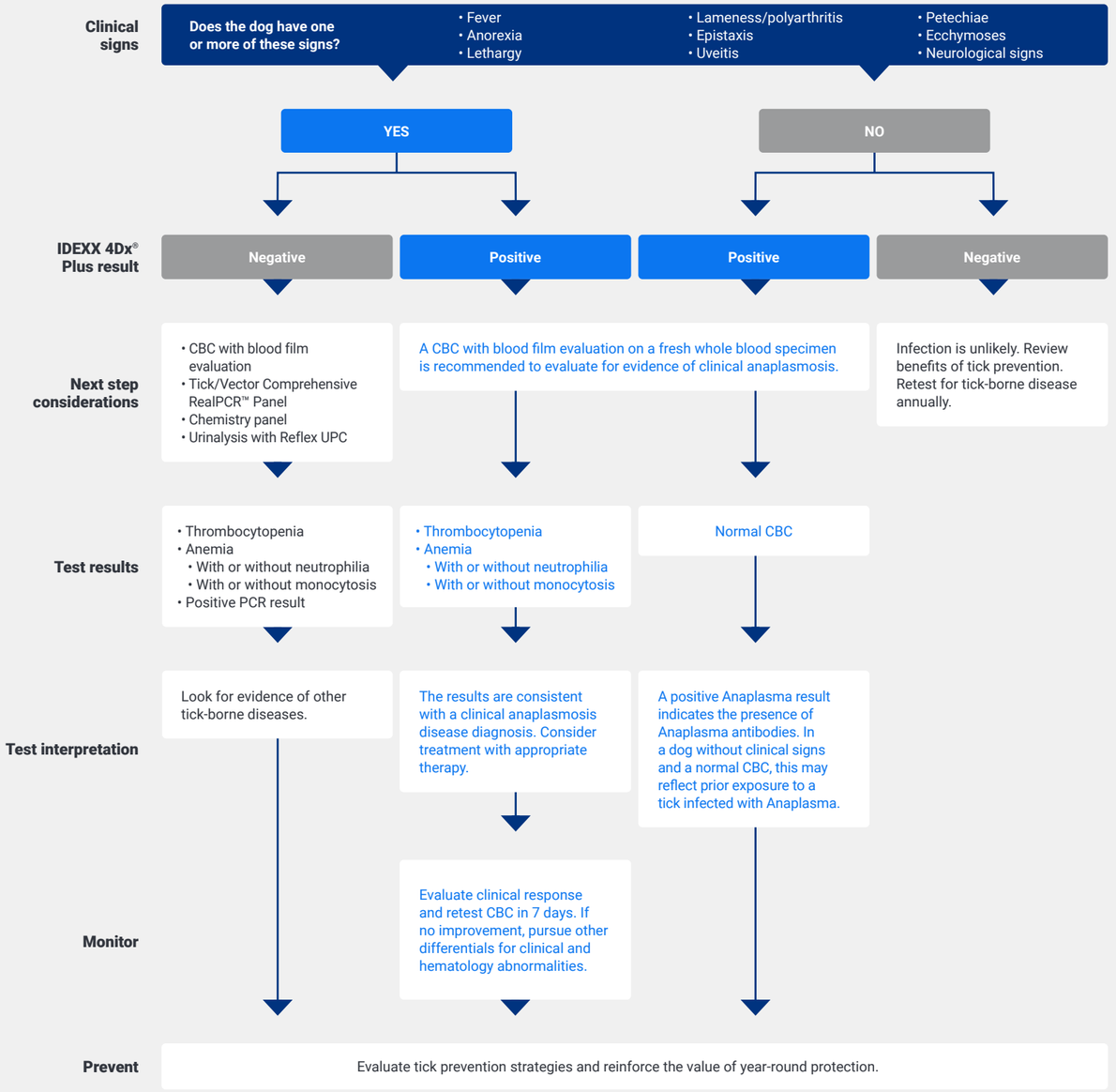
Canine anaplasmosis

Canine granulocytic anaplasmosis is caused by the bacterium *Anaplasma phagocytophilum* (transmitted by the black-legged tick [deer tick]). *Anaplasma platys* (transmitted by the brown dog tick) is the cause of infectious cyclic thrombocytopenia.

Did you know?

+ Many mammalian species, including humans, are susceptible to *A. phagocytophilum* infection.
+ Dogs coinfected with *Anaplasma* and other bacterial pathogens may have more complex disease presentations and respond more slowly to therapy.
+ *A. platys* infects canine platelets and is frequently seen as a coinfection with *Ehrlichia canis*.

Anaplasma phagocytophilum 	***Anaplasma platys*** 
Primary vectors	
Ixodes scapularis *Ixodes pacificus* Black-legged tick (deer tick)	*Rhipicephalus sanguineus* (brown dog tick)
Pathology	
Infects neutrophils	Infects platelets
Clinical presentation	
Can present acutely: + Fever + Anorexia + Lethargy + Polyarthritis, lameness + Neurologic signs	Usually minimal clinical signs, but some dogs may have: + Fever + Uveitis + Petechiae and ecchymoses + Epistaxis
Laboratory abnormalities	
+ Thrombocytopenia + Anemia + Lymphopenia + Increased liver enzymes	Other findings may be seen: + Decreased albumin + Increased globulin + Increased ALP and ALT + Proteinuria + Decreased Urine SG + Increased UPC
Note	
Previous infection may not prevent reinfection and persistent infections are possible.[9,10]	



Canine ehrlichiosis

Canine ehrlichiosis is caused by the bacteria *Ehrlichia canis* (transmitted by the brown dog tick) and *Ehrlichia ewingii* (transmitted by the lone star tick). Canine *Ehrlichia* infections may progress to the subclinical phase or may become chronic infections.

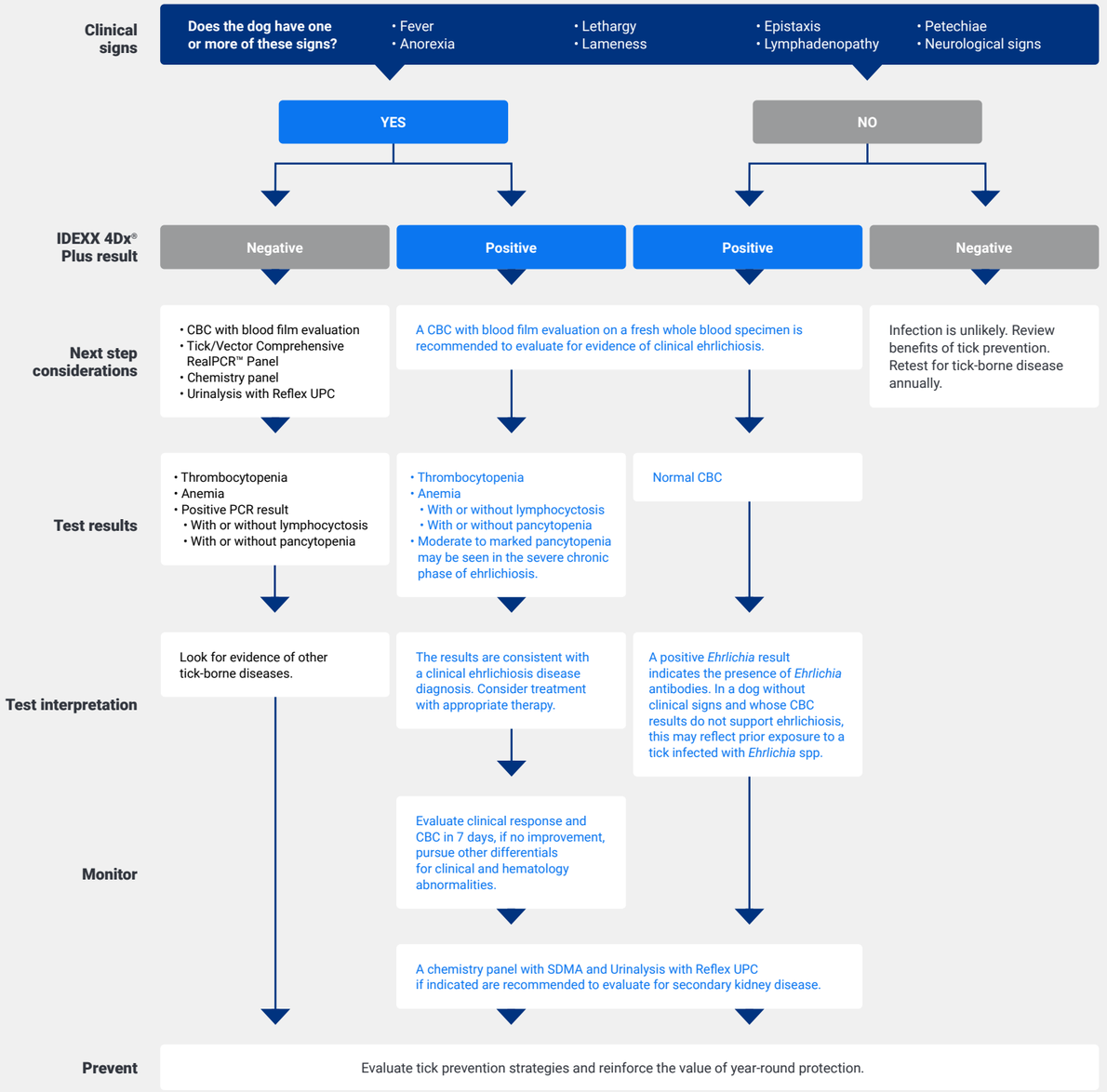
Did you know?

+ Dogs coinfected with *E. canis* and *A. platys* were found to have more severe anemia and thrombocytopenia than dogs with either single infection.[11]
+ In a study of healthy dogs with antibodies to *E. canis*, 39% were thrombocytopenic.[12]
+ Chronic *E. canis* infections, if left untreated, can lead to bone marrow dysfunction or kidney disease.
+ Dogs with *Ehrlichia* antibodies in *E. canis* endemic areas had a 112% increased risk of developing chronic kidney disease (CKD).[13]

CKD monitoring

+ Chemistry panel with SDMA
  - Recommended to evaluate for secondary kidney disease.
+ Urinalysis with UPC
  - Recommended to evaluate for proteinuria
+ CBC with blood film
  - Recommended as part of a minimum database

Ehrlichia canis 	***Ehrlichia ewingii*** 
Primary vector	
Rhipicephalus sanguineus (Brown dog tick)	*Amblyomma americanum* (Lone star tick)
Pathology	
Infects monocytes	Infects granulocytes
Clinical presentation	
+ Fever, anorexia, lethargy + Bleeding disorders + Polyarthritis, lameness + Lymphadenomegaly + Neurologic signs	+ Fever, anorexia, lethargy + Polyarthritis, lameness + Neurologic signs
Laboratory abnormalities	
+ Anemia + Thrombocytopenia + Hyperglobulinemia + Proteinuria	
Other clinical findings may include:	
+ Decreased albumin + Increased globulin + Mild increased ALT and ALP + Increased SDMA + Creatinine + Decreased urine specific gravity, proteinuria + Increased urine protein:creatinine (UPC) ratio.	
Note	
Previous infection may not prevent reinfection, and persistent infections are possible.[12,14]	



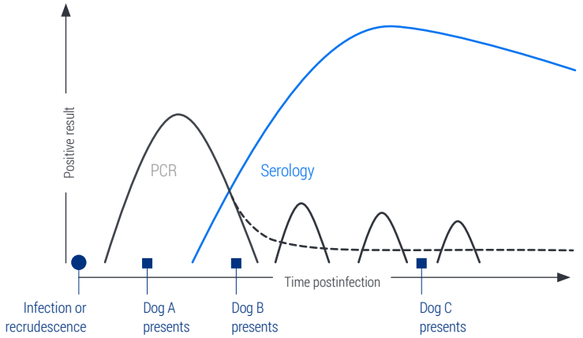
Serology and PCR for sick patients

For dogs presenting with clinical signs consistent with a vector-borne disease, using serology and PCR together improves your ability to make an accurate diagnosis.

Benefits and limitations of each diagnostic method

	Serology	Polymerase chain reaction (PCR)
Measures	Antibody response of host	Nucleic acid (DNA) from pathogen
Benefits	Useful for screening as well as diagnosis of infection	Specifically identifies pathogens indicating active infection
Limitations	Clinical signs may precede a measurable antibody response	A negative PCR result does not necessarily rule out infection

Dogs with ehrlichiosis and anaplasmosis may present with clinical signs at different times after infection. Which sick dog are you dealing with?



When to use the IDEXX vector-borne disease RealPCR™ panels

+ Sick patients with clinical signs and/or laboratory abnormalities consistent with a vector-borne illness
+ Patients with subclinical infections based on history, physical examination, serology, and clinical laboratory findings

"No single test is sufficient for diagnosing an infectious disease in a sick patient."

Edward Breitschwerdt, DVM, DACVIM*
Professor, Internal Medicine
College of Veterinary Medicine,
North Carolina State University

*Dr. Breitschwerdt has a business relationship with IDEXX pursuant to which he receives compensation from IDEXX from time to time. The views expressed in this guide are solely those of Dr. Breitschwerdt.

Depend on the most accurate and comprehensive screen

Available in-clinic or from IDEXX Reference Laboratories

SNAP 4Dx Plus Test

Reference-laboratory quality in the palm of your hand, for superior diagnostic accuracy at the point of care.

Lab 4Dx Plus Test

Available from IDEXX Reference Laboratories as a stand-alone test or as part of a more comprehensive parasite screen with the Fecal Dx Antigen Panel with Lab 4Dx Plus Test-Canine.

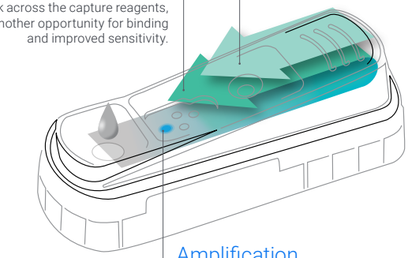
SNAP® technology uses a proprietary three-step process to deliver dependable sensitivity and specificity.

Bidirectional flow

Sample flows across the test and binds with capture reagents. Activating the test unleashes a second flow that drives the sample back across the capture reagents, providing another opportunity for binding and improved sensitivity.

Wash

To enhance specificity, a wash step removes unbound debris that could interfere with results. It also clears the window so you can easily read the result.



Amplification

For maximum sensitivity, a chemical reaction amplifies the signal and generates the SNAP® test's distinctive blue dots, allowing you to see even low-level positives.

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American dog tick (*Dermacentor variabilis*) photographer: Susan E. Ellis, USDA-APHIS-PPQ. Black-legged tick (*Ixodes scapularis*), lone star tick (*Amblyomma americanum*), and brown dog tick (*Rhipicephalus sanguineus*) photographer: James L. Occi.