Screening for vector-borne disease

SNAP® 4Dx® Plus Test clinical reference guide
The Companion Animal Parasite Council (CAPC) Guidelines recommend annual comprehensive screening for pathogens transmitted by ticks and mosquitoes. Adding an 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.

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 SNAP® 4Dx® Plus Test, a positive result can also be an indication of ticks and other pathogens in your area.

When you use the SNAP® 4Dx® Plus Test as a screening tool, you may detect antibodies to these pathogens carried by these ticks that may also transmit other infections to dogs and people

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Ticks carried by ticks</th>
<th>Other infections transmitted to dogs and people</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaplasma phagocytophilum</td>
<td>Deer tick or black-legged tick</td>
<td>Ehrlichia chaffeensis, Tularemia, Rocky Mountain spotted fever (STARI)</td>
</tr>
<tr>
<td>Ehrlichia ewingi</td>
<td>Lone star tick</td>
<td>Ehrlichia chaffeensis, Tularemia</td>
</tr>
<tr>
<td>Ehrlichia canis</td>
<td>Brown dog tick</td>
<td>Babesia spp.</td>
</tr>
<tr>
<td>Anaplasma platys</td>
<td>Brown dog tick</td>
<td>Babesia spp.</td>
</tr>
<tr>
<td>Ehrlichia canis</td>
<td>American dog tick</td>
<td>Rocky Mountain spotted fever, Tularemia</td>
</tr>
</tbody>
</table>

Geographic tick distribution as of 2015

- **Lone star tick**
- **Deer tick or black-legged tick**
- **American dog tick**
- **Rocky Mountain spotted fever**
- **Tularemia**
Lyme disease

Transmitted by the deer tick or black-legged 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 ranging from mild to severe.

**What to do with your SNAP® test result**

<table>
<thead>
<tr>
<th>Positive result indicates infection</th>
<th>Negative result infection is unlikely</th>
</tr>
</thead>
<tbody>
<tr>
<td>Determine C6 antibody level with the Lyme Quant C6® Test</td>
<td>Performed minimum database, including:</td>
</tr>
<tr>
<td>Clinical signs and laboratory findings DO support Lyme disease (C6 antibody level &gt;30 U/mL)</td>
<td>Complete chemistry panel with the IDEXX SDMA® Test to evaluate for kidney disease</td>
</tr>
<tr>
<td>Review benefits of tick prevention</td>
<td>Complete urinalysis to evaluate for proteinuria</td>
</tr>
</tbody>
</table>

**Diagnose**

- Clinical signs and/or laboratory findings DO support Lyme disease (C6 antibody level >30 U/mL)
- Complete chemistry panel with the IDEXX SDMA® Test, CBC, and complete urinalysis

**Treat**

- Doxycycline/tetracycline

**Monitor**

- Monitor for clinical signs, retest C6 antibody level to confirm success of treatment and/or inform re-exposure to infected ticks

**Prevent**

- Evaluate tick prevention strategies and reinforce value of year-round protection

**Did you know?**

- Dogs testing positive for antibodies to the C6 peptide had 43% increased risk of having chronic kidney disease compared to seronegative dogs.
- The C6 peptide used in the SNAP® 4DX® Plus Test and Lyme Quant C6® Test does not cross-react with the antibody response to commercially available Lyme vaccines.
- Dogs with seroreactivity to both *B. burgdorferi* and Anaplasma phagocytophilum may have two times the risk of developing clinical illness than singularly infected dogs.

**Borrelia burgdorferi**

- Primary vectors: *Ixodes scapularis* or *Ixodes pacificus* (dor tick and black-legged tick)
- Pathology: Localizes in tissues of infected dogs
- Clinical presentation: Chronic infection with clinical signs that may persist acutely:
  - Fever, anorexia
  - Polyneuritis, lameness
  - Rapidly progressive renal failure
  - Neurologic syndromes
- Laboratory abnormalities:
  - Elevated C6 antibody level ≥30 U/mL
  - Proteinuria
  - IDEXX SDMA® Test >14 µg/dL

**Heartworm disease**

- *Dirofilaria immitis*, the causative agent of heartworm disease, is transmitted by infected mosquitoes when *D. immitis* larvae are transferred to a healthy dog. Heartworm disease has no obvious clinical signs in the early stages, making preventive measures so much more important—especially as advanced infection may result in death.

**What to do with your SNAP® test result**

<table>
<thead>
<tr>
<th>Positive result</th>
<th>Negative result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirm with relast®*</td>
<td>Evaluate for microfilaria</td>
</tr>
</tbody>
</table>

**Diagnose**

- Radiographs
- CBC/chemistry panel
- Complete urinalysis
- Other tests as appropriate

**Treat**

- Treatment depends on supplemental test results

**Monitor**

- Retest in 6–12 months

**Prevent**

- Prescribe year-round heartworm prevention as recommended by AHS and CAPC guidelines

**Did you know?**

- Despite availability of monthly preventives, prevalence rates of canine heartworm have remained consistent nationwide.
- The American Heartworm Society (AHS) and the Companion Animal Parasite Council (CAPC) recommend testing all dogs for both antigen and microfilaria at least annually.
- For more information and current recommendations on treating canine heartworm disease, go to heartwormsociety.org or capsvet.org

**Dirofilaria immitis**

- Primary vector: Mosquito
- Pathology: Infective larva (L3) matures to adult worms in the heart and pulmonary arteries
- Clinical presentation: Asymptomatic at first, symptoms developing:
  - MEd, persistant cough
  - Lethargy
  - Exercise intolerance
  - Polyneuropathy
- Laboratory abnormalities:
  - Weight loss
  - Eosinophilia
  - Anemia
  - Increased liver enzymes
  - Proteinuria

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

*A heartworm antigen test by ELISA at a reference laboratory is recommended as the confirmatory test.*
**Canine anaplasmosis**

Canine anaplasmosis is caused by the bacterium *Anaplasma phagocytophilum* (transmitted by the deer tick or black-legged 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
- **Primary vectors**: *Ixodes scapularis* (deer tick or black-legged tick), *Ixodes pacificus*
- **Pathology**: Infects neutrophils
- **Clinical presentation**: Can present acutely:
  - Fever
  - Anorexia
  - Lethargy
  - Polyarthritis, lameness
  - Neurologic signs
- **Laboratory abnormalities**:  
  - Thrombocytopenia
  - Lymphopenia
  - Increased liver enzymes

### Anaplasma platys
- **Primary vectors**: Most likely *Rhipicephalus sanguineus* (brown dog tick)
- **Pathology**: Infects platelets
- **Clinical presentation**: Usually minimal clinical signs, but some dogs may have:
  - Fever
  - Uveitis
  - Petechia and ecchymoses
  - Epistaxis
- **Laboratory abnormalities**:  
  - Thrombocytopenia
  - Thrombocytopения

**Note**

Previous infection may not prevent reinfection and persistent infections are possible.9,10

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**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, lasting days, months, or years.

**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

### Ehrlichia canis
- **Primary vector**: *Rhipicephalus sanguineus* (brown dog tick)
- **Pathology**: Infects monocytes
- **Clinical presentation**:  
  - Fever, anorexia, lethargy
  - Polyarthritis, lameness
  - Neurological signs
- **Laboratory abnormalities**:  
  - Anemia
  - Thrombocytopenia
  - Hyperglobulinemia
  - Proteinuria
  - IDEXX SDMA Test >14 µg/dL

**Note**

Previous infection may not prevent reinfection, and persistent infections are possible.11,12

### Ehrlichia ewingii
- **Primary vector**: *Amblyomma americanum* (lone star tick)
- **Pathology**: Infects granulocytes
- **Clinical presentation**:  
  - Fever, anemia, lethargy
  - Bleding disorders
  - Polyarthritis, lameness
  - Neurological signs

**Note**

Previous infection may not prevent reinfection, and persistent infections are possible.11,12

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### What to do with your SNAP® Anaplasma and Ehrlichia test results

<table>
<thead>
<tr>
<th>Positive result</th>
<th>Negative result Exposure is unlikely</th>
</tr>
</thead>
<tbody>
<tr>
<td>The dog has been exposed and may be infected</td>
<td></td>
</tr>
</tbody>
</table>

**What to do next?**

- **Check for hematologic abnormalities (CBC with or without blood film evaluation) and changes in serum biomarkers**
- **Perform a complete chemistry panel with the IDEXX SDMA® Test and complete urinalysis**

**Diagnosis**

- Clinical signs and/or laboratory findings DO support anaplasmosis/ehrlichiosis
- Clinical signs and/or laboratory findings DO NOT support anaplasmosis/ehrlichiosis

**Treat**

- Doxycycline/tetracycline
- Not generally recommended

**Monitor**

- Evaluate clinical response and CBC in 1 week; if no improvement, pursue other diagnoses
- Perform annual minimum database, including complete chemistry panel with the IDEXX SDMA® Test, CBC, and complete urinalysis

**Prevent**

- Evaluate tick prevention strategies and reinforce value of year-round protection

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*Additional diagnostics may be beneficial. See the “Serology and PCR for sick patients” section of this guide for more information.*
For sick dogs presenting with clinical signs consistent with a vector-borne disease, using serology and PCR together improves your ability to make a complete and accurate diagnosis.

**Benefits and limitations of each diagnostic method**

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

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

<table>
<thead>
<tr>
<th>Positive result</th>
<th>Infection or recrudescence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog A</td>
<td>presents</td>
</tr>
<tr>
<td>Dog B</td>
<td>presents</td>
</tr>
<tr>
<td>Dog C</td>
<td>presents</td>
</tr>
</tbody>
</table>

**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 finding
- Monitoring response to therapy—a negative PCR result indicates a reduction in pathogen load

*Edward Breitschwerdt, DVM, DACVIM*

Professor, Internal Medicine
College of Veterinary Medicine, North Carolina State University

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

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*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.*
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.

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

Depend on the most accurate and comprehensive screen

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