Cancer and disease management starts before clinical signs are evident. Routine wellness visits, including appropriate bloodwork, play a vital role in the prevention and early detection of disease.

Once clinical signs appear, quick and effective diagnostic workup requires the right tests for the right decision.

Monitoring patients post treatment is vital to assuring therapeutic effectiveness, surgical completeness, or to gauge disease progression and/or recurrence.
Cancer, Inflammation, and Immunity

A strong relationship exists between cancer, inflammation, and immunity. Effective decision making requires the right data. Choosing the correct blood tests will improve the diagnostic workup and facilitate easier clinical decision making.

Choosing the Right Test

Patients can present either apparently healthy or with clinical signs. VDI offers a family of distinct blood tests for the detection and management of cancer and disease in companion animals. Each test is clinically validated for the specific task it serves.

Specialty Blood Tests

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Screen Pg. 4-5</th>
<th>Diagnose Pg. 6-7</th>
<th>Monitor Pg. 8-9</th>
</tr>
</thead>
<tbody>
<tr>
<td>INCaSe</td>
<td></td>
<td></td>
<td>Pg. 4-5</td>
</tr>
<tr>
<td>TK CANINE CANCER PANEL</td>
<td></td>
<td></td>
<td>Pg. 6-9</td>
</tr>
<tr>
<td>TK FELINE CANCER PANEL</td>
<td></td>
<td></td>
<td>Pg. 6-9</td>
</tr>
<tr>
<td>VITD CANINE</td>
<td></td>
<td></td>
<td>Pg. 12-13</td>
</tr>
<tr>
<td>VITD FELINE</td>
<td></td>
<td></td>
<td>Pg. 12-13</td>
</tr>
<tr>
<td>CRP CANINE</td>
<td></td>
<td></td>
<td>Pg. 10-11</td>
</tr>
<tr>
<td>HPT FELINE</td>
<td></td>
<td></td>
<td>Pg. 10-11</td>
</tr>
</tbody>
</table>
Benefits of cancer screening
Underlying disease can reside in the *apparently healthy* dog. Undiagnosed and unchecked disease can often advance to the stage where options become limited and expensive, and the life of the dog becomes at risk. INCaSe* is a unique blood test that provides advanced notice that hidden disease, including early stages of cancer, may be present. Early warning can lead to early intervention and improved outcomes.

Early detection is challenging
For screening to be effective it must be sensitive, specific, and cost effective. Ultrasonography is costly and lacks specificity for cancer. Palpation finds cases typically in later stages. Biopsy is invasive, costly, and frequently equivocal in early stages. Although these are important tools on the path to diagnosis, they are not particularly effective as screening tools.

Chronic inflammation kills
Chronic inflammation occurs throughout the body when an activated immune system *fails to deactivate* in the normal course. In the absence of any actual pathogens, the immune system starts to attack healthy tissue, which then further activates the immune response. This perpetual cycle continues, wreaking havoc on healthy cells causing widespread damage to tissue and organs. Chronic inflammation can remain hidden for long periods. Undiagnosed and unchecked, this leads to advanced disease, and increased risk of death.

A simple blood test
INCaSe* is a unique blood test that provides advanced notice that hidden disease, including early stages of cancer, may be present. Early warning can lead to early intervention and improved outcomes. Designed to be part of a routine wellness plan, INCaSe* is the most comprehensive single blood test available in monitoring the overall health status in dogs.
Clinical Study

Cancer Detection
In a major clinical study involving the University of Missouri, 360 dogs were collected for analysis and followed for up to 12 months. INCaSe® was able to detect 82% of all cancers 6-months PRIOR TO the onset of visible signs.

INCaSe® is able to detect 100% of all cancers 4-months prior to clinical signs.

Importance of Resolving Inflammation
Dogs with inflammation were associated with a 20% mortality rate vs. 3% mortality rate for those without inflammation. Detectable inflammation, as measured by elevated C-Reactive Protein, was associated with a 7-fold increase in all-cause mortality.

While transient acute inflammation is tightly controlled and part of the healing process, chronic inflammation is the root cause of many illnesses and actually propagates cancer.


How to interpret INCaSe® results

NEGATIVE INCaSe® & inflammation
A “negative” INCaSe® result is a strong indication the dog is healthy and cancer free. Recommended recheck intervals for INCaSe® are every six months or during each wellness visit.

NEGATIVE INCaSe® POSTIVE inflammation
A “positive” finding of inflammation in the absence of proliferation means other potentially serious disorders may exist. Take action to resolve chronic inflammation.

POSITIVE INCaSe®
A “positive” INCaSe® result indicates malignant growth may be present. Additional diagnostic procedures are required for definitive diagnosis.
Diagnose CANINE CANCER PANEL

Diagnose canine cancer

TK CANINE CANCER PANEL has been clinically proven effective on a wide variety of tumor types, both hematological and solid\(^1\). When a suspicious mass is identified, or the dog presents with other indicators common with cancer, TK CANINE CANCER PANEL is used to confirm the presence of neoplastic disease.

**Diagnose CANINE CANCER PANEL**

Dual-biomarker test using proliferation marker Thymidine Kinase (TK) and inflammatory marker C-Reactive Protein (CRP).

TK FELINE CANCER PANEL

Differentiate LSA & IBD

Gastrointestinal disorders such as inflammatory bowel disease (IBD) and intestinal lymphoma are commonly encountered in feline medicine. The challenge with these two similarly presenting diseases is how to quickly distinguish between the two. TK FELINE CANCER PANEL is a blood test to aid in the differential diagnosis of feline IBD and intestinal lymphoma.

**Differentiate feline LSA from IBD using NI.**

Dual-biomarker test using proliferation marker Thymidine Kinase (TK) and inflammatory marker Haptoglobin (Hpt).
Neoplasia Index

The Neoplasia Index (NI) is a dual-biomarker algorithm that combines the dysregulated proliferation marker TK and the systemic inflammatory marker CRP (dogs) or Hpt (cats).

TK is involved in the synthesis of DNA precursors and is only expressed in S-G2 cells (i.e., cell division). TK levels have been shown in numerous studies, both in humans as well as animals, to correlate to the proliferative activity of tumor disease.

CRP/Hpt are major acute phase proteins produced, mainly in the liver, in response to inflammation and the release of cytokines. Serum APP levels correlate to both the severity and duration of the inflammatory stimuli.

These two independent variables – thymidine kinase & acute phase proteins – combine two distinct hallmarks of neoplasia: rapid, dysregulated cell division & systemic inflammation. The algorithm developed to integrate the dual biomarkers, produces the resultant Neoplasia Index.

NI is useful in a wide variety of cancers1-9:

• Lymphoma
• Carcinoma
• Sarcoma
• Hemangiosarcoma
• Histiocytic sarcoma
• Osteosarcoma
• Mast cell tumor (grade II and III)
• Others

8. Selting KA, Ringold, R. Use of thymidine kinase type 1 and C-reactive protein to detect cancer in dogs. Veterinary Cancer Society Abstract 2013.
Postoperative Monitoring

Following surgical procedures, results are used to assess the completeness of excision and monitor disease status:

- Initial postoperative assessment is performed following a 3-week washout period to establish a baseline.
- Measurements are conducted every 4-8 weeks.
- Confirm completeness of excision / disease free interval (left) or tumor recurrence / metastatic disease (right).

Therapeutic Monitoring

For patients undergoing chemotherapy, results can quickly indicate response to the treatment protocol:

- Recommended test intervals are every four (4) weeks for the initial eight week period, then every eight (8) weeks for the duration of the induction therapy.
- Following induction therapy, the cancer panel should be run at each recheck visit.
- Reduced / stable values indicate positive response to treatment (left) while rising levels indicate ineffectiveness of therapy (right).

No Treatment/ Palliative Care

When the nature of the cancer or patient status renders treatment impractical, the cancer panel is used to monitor disease progression:

- In certain cases, the disease may remain in a stable state where the tumor advances slowly even in the absence of treatment (left).
- With other cases, untreated or minimally treated cancer will advance rapidly (right).
**Canine Case Study**

**History:** 11 year old boxer diagnosed with multicentric lymphoma

**Treatment:** 25 week Madison-Wisconsin protocol

**Monitoring:** Upon initiation, both TK & CRP dropped within normal range, indicating a positive response to treatment. Periodic rechecks confirmed status of complete remission during treatment course. Following induction therapy, test monitoring took place every 3 months in unison with recheck exams. The chart records slight variations in TK level, but no steady trend in an upward direction, which often occurs just prior to the patient coming out of remission.

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**Feline Case Study**

**History:** 13 year old DSH diagnosed with multicentric lymphoma

**Treatment:** 25 week Madison-Wisconsin protocol

**Monitoring:** Upon initiation, Hpt (systemic inflammation) dropped notably, indicating a positive response to treatment. Short-term rise in TK (cell proliferation) associated with mass destruction of tumor cells is seen followed by quick decline in TK. Periodic rechecks confirmed status of complete remission during treatment course. Post-treatment, the chart records slight variations in TK level, but no steady trend in an upward direction, which often occurs just prior to the patient coming out of remission.
Inflammation & the Acute Phase Response

The acute phase response is a complex, systemic early-defense system activated by infection, inflammation, trauma and tissue damage or necrosis. Although nonspecific, it serves as a core of the innate immune response. It includes physical and molecular barriers, as well as responses, that serve to prevent infection, clear potential pathogens, and further initiate inflammatory processes, ultimately contributing to resolution and the healing process.

**Triggers:**
- Infection
- Inflammation
- Surgical trauma
- Tissue necrosis

CRP/Hpt: Detect & Monitor Inflammation
As major acute phase proteins, circulating levels of C-Reactive Protein (CRP) in dogs and haptoglobin (Hpt) in cats, rise rapidly upon the onset of inflammatory stimuli. CRP/Hpt levels also fall rapidly as the inflammatory condition is resolved. The concentration of CRP/Hpt correlates to both the severity and duration of the inflammatory stimuli.

Damage Associated with Chronic Inflammation

“Acute Inflammation Defends, Chronic Inflammation Kills”

Acute (short-term) inflammation is a vital life-sustaining function. The complex cascade of events that occurs is needed to initiate a defense against invading bacteria and to repair tissue damage that occurs from trauma, infection, and disease. While acute inflammation is normally tightly controlled and part of the healing process, chronic (long-term) inflammation is both associated with, and the root-cause of disease. Left unchecked, chronic inflammation can lead to disease advancement and even death.
Clinical Application

Pre-anesthesia screen
Dogs in an inflammatory state are at higher risk for post-operative complications due to coagulation compromise and the potential for organ failure. CRP added to the pre-surgical panel can rule-out the presence of sub-clinical disease, including the early stages of cardiac disease.

Detect and Gauge Disease
In situations where the dog presents with non-specific signs such as lethargy, inappetence or weight-loss, CRP can rule-in the presence of underlying disease. CRP levels correlate with disease severity and duration.

Wellness Screen
While APPs are non-specific, they are very sensitive to systemic inflammation. Their non-specificity is a benefit for a general wellness screen as one test covers many diseases. Low levels then become a “rule-out” for serious disorders, and moderate to high levels become a call-to-action for further diagnostic workups.

Monitor Therapy & Recovery
Rapid responding CRP allows for near “real-time” monitoring, used to quickly assess the effectiveness of treatment.

- Treatment independent; unbiased by therapy
- Effectiveness / ineffectiveness indicated in 2-3 days
- Detect relapse during tapering of immunosuppressive therapy

Postoperatively, CRP levels will indicate quickly whether recovery is normal or an infection has set in. CRP is highly responsive in monitoring antibiotic treatment vs the traditional white count (WBC).

Response of WBC Count vs. CRP in Monitoring Recovery from Infection

[Graph illustrating the comparison of CRP and WBC levels over time.]
Vitamin D Sufficiency Important for Cellular Health

Vitamin D is not a simple vitamin but the precursor to the active hormone 1,25VitD. Well understood for its role in calcium homeostasis, vitamin D is recognized for its role in gene regulation and the maintenance of cellular health. Many tissues have vitamin D receptors and will locally convert 25VitD to 1,25VitD. Low stores of vitamin D are associated with a wide range of diseases such as cancer, heart disease, infection, and kidney disease.

Unlike humans, dogs and cats do not produce vitamin D from sunlight; their sole source of vitamin D comes from their diet. Recent studies have shown that vitamin D varies significantly by commercial pet food manufacturer. Further, intestinal absorption varies significantly from dog to dog, and by intact status.

Expanding models of vitamin D have generated new terminology of “Deficiency”, “Insufficiency”, and “Sufficiency” to define the protective effect that increasing stores of vitamin D have against disease.

Testing for 25(OH)D, the primary store of vitamin D, is your best means to objectively measure this important analyte. When found inadequate, dietary supplementation is warranted.
Increased Risk for Disease

Cancer is an **immune dysfunction** disease. Aberrations to the cell’s genes cause uncontrolled growth, and a dysfunction to the immune process prevents the destruction of the aberrant cells. **Inflammation**, both a precursor and a propagator of cancer genesis is, in part, controlled by vitamin D.

Studies have shown that with adequate stores of vitamin D, inflammation is reduced. Further, low stores of vitamin D are associated with a wide range of benign and malignant diseases.

There is a **growing body of evidence** that low stores of vitamin D are associated with a wide range of diseases in dogs and cats:

- **Cancer**
- **Heart disease**
- **Inflammatory bowel disease**
- **Renal disease**
- **Infection**
- **Hyperparathyroidism**
- **Feline tooth resorption**

**Citations:**

VDI Reference Laboratory

Laboratory Services

VDI Laboratory LLC is a specialty diagnostics company that provides veterinary reference laboratory services and in-house diagnostic products. VDI is dedicated to the research and development of innovative biomarkers to assist veterinarians in the diagnostic workup of companion animals.

Our mission is “to provide the highest quality specialty diagnostic services and products for the advancement of care in companion animals.”

Specimen Shipping

VDI provides fast and convenient courier service using FedEx Priority Overnight express on all shipments. VDI provides the veterinarian everything needed for specimen transport in specially designed VDI shipper kits.

VDI Portal

The VDI PORTAL is a web-connected service for VDI clients that gives access to patient reports in a convenient, organized location.

- Quick access to patient reports
- Pull up reports on phones and tablets
- Save and view all reports in one location
- Request literature
- Schedule specimen pickups
- Stay up to date on news from VDI

Consultations

Need help interpreting the results of a test, or have interesting information to share? Call VDI to discuss the case.

- Results interpretation
- Case studies
- Extended applications of the test
- Patient follow-up

VDI continues to pursue new biomarkers to assist the veterinarian. Please stay informed of these developments by visiting us at vdilab.com.
Education

VDI continues to research the use of our laboratory services for expanded application, and is dedicated to the continued development of new biomarkers to aid in the care of companion animals. Stay up-to-date with free education for VDI clients:

The VDI Review
Bi-monthly email containing updates on VDI research, product development, and industry news. review.vdilab.com

Video Website
Short videos examining individual tests and their applications. videos.vdilab.com

Literature Room
Studies, abstracts, and citations are available online through the literature room. litroom.vdilab.com

Support Materials
VDI provides support materials for pet owners. Pet owner brochures for INCaSe®, TK CANINE CANCER PANEL and TK FELINE CANCER PANEL are available at no cost to the clinic.

Health and Cancer Screening
Routine blood tests ensure a healthy dog

Cancer
1 in 3 dogs will develop Cancer

Is cancer the cause of your cat’s GI disorder?
Early detection is key to survival
### Test Services

Contact VDI, or visit us online for details on how to order our test services.

<table>
<thead>
<tr>
<th>Lab Service</th>
<th>Type</th>
<th>Description</th>
<th>Reports Include</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INCaSe</strong></td>
<td>2-Test Panel Canine</td>
<td>To detect occult disease in the apparently healthy dog. The test is able to detect cancer and other serious diseases months in advance of the onset of clinical signs. INCaSe is the most comprehensive single blood test for: • Assuring overall wellness during annual exams • Clinic health screening campaigns</td>
<td>• INCaSe • C-Reactive Protein Note: INCaSe and CRP are qualitative</td>
</tr>
<tr>
<td><strong>INCaSe-D</strong></td>
<td>3-Test Panel Canine</td>
<td>Adding vitamin D testing to INCaSe provides for the assessment of 25(OH)D stores – a risk factor for many serious diseases. Use the test to: • Assure overall wellness during health exams • Assess vitamin D status for adequacy of stores</td>
<td>• INCaSe • C-Reactive Protein • 25(OH)D Note: INCaSe and CRP are qualitative</td>
</tr>
<tr>
<td><strong>TK</strong> CANINE CANCER PANEL</td>
<td>2-Test Panel Canine</td>
<td>For the detection &amp; therapeutic management of cancer in dogs with suspected or confirmed cancer. Use the test to: • Detect initial cancer or recurrence • Monitor treatment effectiveness or surgical completeness</td>
<td>• Thymidine Kinase • C-Reactive Protein Optional VitD add-on</td>
</tr>
<tr>
<td><strong>TK</strong> FELINE CANCER PANEL</td>
<td>2-Test Panel Feline</td>
<td>For the differential diagnosis of intestinal lymphoma and inflammatory bowel disease in cats with gastrointestinal disorder. Use the test to: • Associate root-cause with lymphoma or IBD • Provide a non-invasive alternative or precursor to biopsy</td>
<td>• Thymidine Kinase • Haptoglobin</td>
</tr>
<tr>
<td><strong>HPT</strong> FELINE</td>
<td>Individual Test Feline</td>
<td>For the objective determination of systemic inflammation in cats. Use the test to: • Confirm systemic inflammation / monitor therapy • Pre-anesthesia screening</td>
<td>• Haptoglobin</td>
</tr>
<tr>
<td><strong>CRP</strong> CANINE</td>
<td>Individual Test Canine</td>
<td>For the objective determination of systemic inflammation in dogs. Use the test to: • Confirm systemic inflammation / monitor therapy • Pre-anesthesia screening</td>
<td>• C-Reactive Protein</td>
</tr>
<tr>
<td><strong>VITD</strong> CANINE</td>
<td>Individual Test Canine</td>
<td>For the determination and monitoring of vitamin D [25(OH)D] levels in dogs. Use the test to: • Assess vitamin D status for adequacy of stores • Monitor therapeutic response and maintenance levels</td>
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</table>

### Specimen Requirements

- Serum Specimen
- 1-mL minimum
- Collected using SST, separated and frozen within 45 minutes of draw

### Shipping

All specimen shipments to VDI Laboratory require use of the VDI Shipper Kit pictured here.

All instructions for the collection, handling and transport of the specimen(s) are listed on the inside lid of Shipper Kit. Please take a moment to review them closely prior to drawing blood from the patient.

We utilize FedEx Priority Overnight Express to ensure all specimens are handled with the utmost care.