Diagnostic Guidelines of Pancreatitis

- 4 Steps for diagnosing pancreatitis and assessing the severity -

By Angela (D.V.M.)

BIONOTE Marketing team
November 2020
Pancreas Function

**Endocrine parts**  
(Islets of Langerhans)  
They produce and secrete hormones into the bloodstream; insulin and glucagon

**Exocrine parts**  
(Acinar cells)  
They produce and transport enzymes that will exit the body through the digestive system;
What is Pancreatitis?

Inactivated pancreatic enzymes stored in the pancreas are released into the intestines

Premature Activation of the Enzymes
- Pancreatic autodigestion
- Pancreatitis

Inflammation stimulates the infiltration of neutrophils
- Reactive oxygen species (ROS), cytokines, and nitric oxide (NO)
- Exacerbates further inflammation

Acute kidney injury
Disseminated intravascular coagulopathy (DIC)
Acute lung injury

By the way, what is the cause of pancreatitis?

So, other diseases should be monitored in a patient with acute severe pancreatitis.
Causes

- Most commonly idiopathic (90%)

- May occur secondary to a range of conditions
  - Dietary indiscretion: High-fat diet, obesity
  - Breed: Miniature schnauzers, terriers, miniature poodles
  - Drug therapy: Azathioprine, Thiazide, Furosemide…(Not steroid)
  - Co-existing disease: Feline triaditis
  - Hyperadrenocorticism and hyperlipidemia
  - Ischemia: Trauma, surgery, and shock
  - Infectious diseases: Toxoplasma gondii, FCV, FIP, FHV

Image courtesy of veterinary technical specialist Sarah Collins.

Triaditis?
A syndrome of concurrent pancreatitis, inflammatory bowel disease (IBD), and cholangitis.
**Clinical Signs**

- **Non-specific signs**

<table>
<thead>
<tr>
<th>Dog: Pancreatitis</th>
<th>Cat: Pancreatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical signs</strong></td>
<td><strong>Clinical signs</strong></td>
</tr>
<tr>
<td>- Anorexia (91%)</td>
<td>- Lethargy (100%)</td>
</tr>
<tr>
<td>- Vomiting (90%)</td>
<td>- Anorexia (97%)</td>
</tr>
<tr>
<td>- Weakness (79%)</td>
<td>- Dehydration (92%)</td>
</tr>
<tr>
<td>- Abdominal pain (58%)</td>
<td>- Hypothermia (68%)</td>
</tr>
<tr>
<td>- Dehydration (46%)</td>
<td>- Vomiting (35%)</td>
</tr>
<tr>
<td>- Diarrhea (33%)</td>
<td>- Abdominal pain (25%)</td>
</tr>
</tbody>
</table>

✓ **Mild cases**: Subclinical (asymptomatic)
✓ **Severe cases**: Systemic clinical signs such as fever or even cardiovascular shock

✓ Less specific clinical signs
✓ Low occurrence of vomiting and abdominal pain

By Jörg M. Steiner, med.vet., Dr.med.vet., PhD, DACVIM, DECVIM-CA, AGAF
Diagnosis

Amylase, Lipase
- Synthesized and secreted by several different tissues other than pancreas
- Amylase: Sens. 43-54%, Spec. 89-93% / Lipase: Sens. 52-56%, Spec. 77-81%

TLI
Trypsin-Like Immunoreactivity
- Specific for exocrine pancreatic function (☞ EPI)
- Lower sensitivity for diagnosis of pancreatitis (28-64%)

Ultra-sonography
- Highly operator-dependent (Sensitivity 66-68%)
- Provides significant additional information useful for diagnosis

*Histopathology: Gold standard method for definitive diagnosis of pancreatitis
Diagnosis

“Pancreas-specific lipase”

- Detection of pancreatic lipase by the use of specific antibody
- Measuring pancreatic lipase exclusively (Sens. 86.5-93.6%, Spec. 66.3-77.0%)
- Screening test ⇔ Rule out pancreatitis
- Consider the possibilities of false positive / negative results
Diagnostic Guidelines

[STEP 1] Rule out pancreatitis using a PLI kit

[STEP 2] Investigate whether pancreatitis is primary or secondary

[STEP 3] Assess the severity and risk factors

[STEP 4] (Follow up) Monitor the complications
Dogs suspected with pancreatitis ➔ Quantitative PLI testing ➔

< 200 ng/ml: Rule out pancreatitis

200 ~ 400 ng/ml: Diagnose pancreatitis with moderate accuracy
☞ Consider the false positive possibilities…

> 400 ng/ml: Diagnose pancreatitis with high accuracy
☞ Consider the false positive possibilities…

<table>
<thead>
<tr>
<th>Cut-off of cPL</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>200 ng/ml</td>
<td>93.6%</td>
<td>77%</td>
</tr>
<tr>
<td>400 ng/ml</td>
<td>77.8%</td>
<td>88%</td>
</tr>
</tbody>
</table>

STEP 1. Rule out pancreatitis using a PLI kit
cPL: False positive results

- Pancreatic inflammation is not the primary cause.
- Possible factors causing pancreatic inflammation:
  - Diffuse abdominal inflammation (septic peritonitis)
  - Any condition that causes hypoperfusion, or ischemia

<table>
<thead>
<tr>
<th>Dog</th>
<th>Diagnosis</th>
<th>Spec cPL (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Small intestinal foreign body</td>
<td>Insufficient sample</td>
</tr>
<tr>
<td>2</td>
<td>Small intestinal foreign body</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>Small intestinal foreign body and septic peritonitis</td>
<td>105</td>
</tr>
<tr>
<td>4</td>
<td>Small intestinal infarction with bilateral adrenomegaly*</td>
<td>568*</td>
</tr>
<tr>
<td>5</td>
<td>Hepatic T-cell lymphoma*</td>
<td>68*</td>
</tr>
<tr>
<td>6</td>
<td>Hepatic mass with invasion of the caudal vena cava</td>
<td>404</td>
</tr>
<tr>
<td>7</td>
<td>Hepatic masses/septic peritonitis</td>
<td>672</td>
</tr>
<tr>
<td>8</td>
<td>Hepatic/splenic masses with hemoperitoneum</td>
<td>720</td>
</tr>
<tr>
<td>9</td>
<td>Hepatic abscess</td>
<td>1000</td>
</tr>
<tr>
<td>10</td>
<td>Hemoperitoneum/septic peritonitis</td>
<td>550</td>
</tr>
<tr>
<td>11</td>
<td>Pyometra and septic peritonitis</td>
<td>30</td>
</tr>
</tbody>
</table>

[The cases that pancreatitis was not the primary cause for presentation]
For accurate diagnosis of pancreatitis,

① Clinical signs  ② PLI Testing  ③ Ultrasonography  ④ Laboratory tests

“These tests should always be performed in animals with suspected pancreatitis because they are useful for the diagnosis or exclusion of other diseases.”
Diagnostic Guidelines

For accurate diagnosis of pancreatitis,

1. Clinical signs
2. PLI Testing
3. Ultrasonography
4. Laboratory tests

- Dogs
  - Digestive symptoms: Vomiting (90%), Abdominal pain (58%), Diarrhea (33%)
  - Non-specific signs: Anorexia (91%), Weakness (79%), Dehydration (46%)

- Cats
  - Non-specific signs: Lethargy (100%), Anorexia (97%), Dehydration (92%), Hypothermia (68%)
Diagnostic Guidelines

For accurate diagnosis of pancreatitis,

① Clinical signs
② PLI Testing
③ Ultrasonography
④ Laboratory tests

- Dogs

<table>
<thead>
<tr>
<th>PLI Level (ng/ml)</th>
<th>Pancreatitis</th>
<th>Equivocal</th>
<th>Unlikely</th>
</tr>
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<tbody>
<tr>
<td>&lt; 200</td>
<td>Very unlikely</td>
<td></td>
<td></td>
</tr>
<tr>
<td>200-400</td>
<td>Equivocal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 400</td>
<td>Pancreatitis</td>
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- Cats

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<tr>
<td>≤ 3.5</td>
<td>Very unlikely</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.6-5.3</td>
<td>Equivocal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 5.4</td>
<td>Pancreatitis</td>
<td></td>
<td></td>
</tr>
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</table>

Sample type: Serum / plasma / whole blood
Quantitative result within 5-15 minutes
**Diagnostic Guidelines**

For accurate diagnosis of pancreatitis,

1. **Clinical signs**
2. **PLI Testing**
3. **Ultrasonography**
4. **Laboratory tests**

- Low sensitivity (68%), but very high specificity. Good tool to confirm or deny the presence of pancreatitis.
- US Diagnosis:
  - Pancreas: hypoechoic, mottled, thickening / irregular margin
  - Peri-pancreatic fat: hyperechoic (due to fat saponification, inflammation)
  - ± duodenal change
  - ± biliary change
  - ± peritoneal fluid

Image courtesy of Andi Parkinson Intrapet Imaging, Baltimore, MD, USA. Remo Lobetti et al. Pancreatic Ultrasound in 54 Dogs with Acute Pancreatitis
Diagnostic Guidelines

For accurate diagnosis of pancreatitis,

1. Clinical signs
2. PLI Testing
3. Ultrasonography
4. Laboratory tests

- **CBC**
  - May be normal, especially in mild cases
  - Leukocytosis, neutrophilia with a degenerative left shift
  - Anemia and thrombocytopenia: early indications of DIC

- **Serum biochemistry**
  - May be normal, especially in mild cases
  - Increases in liver enzyme: ALKP 2 to 15-fold, ALT 2 to 5-fold
  - Hyperbilirubinemia: 2 to 5-fold
  - Increased BUN, CREA: dehydration
  - Electrolyte: hypochloremia in dogs (81.3%), hypokalemia in cats (56%)
DIAGNOSTIC GUIDELINES

Case Study #1

- **Signalment:** Maltese, 7 yrs, NM
- **History:** Vomiting, anorexia for 2 days
- **PE:** abdominal pain
- **Testing**
  - **CBC:** WBC 25,100 (high), neutrophil (high)
  - **Biochemistry:** ALKP 315 (high), ALT 91 (high), BUN 51.2 (high), CREA 1.6 (high)
  - **Vcheck cPL:** 601.7 ng/ml (abnormal; normal < 200)
  - **Vcheck CRP:** 136 mg/L (abnormal; normal < 20)
  - **Ultrasonography:** necrotizing pancreatic changes

- **Diagnosis:** Acute pancreatitis
### Diagnostic Guidelines

**STEP 3.** Assess the severity and risk factors

- **Severity score** based upon organ system compromise
  - 1 point for each part

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<thead>
<tr>
<th>System</th>
<th>Criteria</th>
<th>Reference range</th>
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<tbody>
<tr>
<td>Renal</td>
<td>BUN &gt; 84 mg/dl, Creatinine &gt; 3.0 mg/dl</td>
<td>BUN 15 ~ 57 mg/dl, CREA 0.6 ~ 1.8</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Any of ALP, AST or ALT &gt; 3 x upper range</td>
<td>ALKP 47 ~ 254 U/L, ALT 17 ~ 78 U/L</td>
</tr>
<tr>
<td>Lymphoid</td>
<td>Band neutrophils &gt; 10% or WBC &gt; 24 x 10⁹/L</td>
<td>WBC 4,500~17,000</td>
</tr>
<tr>
<td>Endocrine pancreas</td>
<td>Blood glucose &gt; 234 and/or b-OH butyrate &gt; 1 mmol/L</td>
<td>Blood glucose 59~123 b-OH butyrate &lt; 0.6</td>
</tr>
<tr>
<td>Acid/base buffering</td>
<td>Bicarbonate &lt; 13 or &gt; 26 and/or anion gap &lt; 15 or &gt; 38 mmol/L</td>
<td>Bicarbonate 15<del>24 Anion gap 17</del>35</td>
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Replace with CRP
More than 2-fold upper range (> 40 mg/L)
STEP 3. Assess the severity and risk factors

- **Severity score** based upon organ system compromise ➔ 1 point for each part

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Q. Should I evaluate it with the results at the time of diagnosis?

A. No, It is important to check these factors for a week (at least 4 days).
Diagnostic Guidelines

STEP 3. Assess the severity and risk factors

In patients with severe acute pancreatitis,

- **Acute kidney injury (AKI)**
  - Due to hypovolemia, cytokine-induced ischemia, inflammation
  - Monitor the BUN, Creatinine or SDMA (for early detection of renal dysfunction)

- **DIC** *(Disseminated intravascular coagulation)*
  - The coagulation cascade can be activated, resulting in DIC*.
    (*DIC occur in patients with severe pancreatitis and other serious systemic diseases, such as sepsis due to peritonitis or neoplasia.)*
  - DIC: thrombocytopenia, prolonged PT/APTT, decreased antithrombin III, and increased D-dimer

- **Acute lung injury**
Diagnostic Guidelines

Case Study #2

- **Signalment:** 3 yr / Poodle / Neutered male
- **History:** Decreased energy, vomiting three days ago
- **PE:** abdominal distention
- **Testing**
  - CBC: WBC 26,710 (high, normal 5,000-16,000), neutrophil 18,000 (high, normal 3,000-11,000)
  - Biochemistry: ALKP 535 (high, normal 15-127), ALT 96 (high, normal 19-70), BUN 58 (high, normal 8-26), CREA 1.5 (high, normal 0.5-1.3), Glucose 134 (high, normal 70-118)
  - Vcheck cPL: 936.7 ng/ml (abnormal; normal < 200)
  - Vcheck CRP: 236 mg/L (abnormal; normal < 20)
  - Vcheck D-dimer: 1.6 mg/dL (abnormal; normal < 0.3)
  - Ultrasonography: Acute pancreatitis lesion

- **Diagnosis:** Acute pancreatitis

**Q. Organ score?**

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<tr>
<td>Acidbase buffering</td>
<td>Bicarbonate &lt; 13 or &gt; 20 and/or anion gap &lt; 15 or &gt; 36 mmol/L</td>
<td>Bicarbonate 15-24, anion gap 17-20</td>
</tr>
</tbody>
</table>

1 point for each part

**Q. Risk factors?**

1 point

0 point

0 point

0 point

Total 2 point

**[CRP]**

- Normal (<20)

<table>
<thead>
<tr>
<th>Date</th>
<th>CRP Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/17</td>
<td>236</td>
</tr>
<tr>
<td>1/19</td>
<td>257</td>
</tr>
<tr>
<td>1/22</td>
<td>248</td>
</tr>
<tr>
<td>1/23</td>
<td>246</td>
</tr>
</tbody>
</table>

**[D-dimer]**

- Normal (<0.3)

<table>
<thead>
<tr>
<th>Date</th>
<th>D-dimer Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/17</td>
<td>1.6</td>
</tr>
<tr>
<td>1/19</td>
<td>1.8</td>
</tr>
<tr>
<td>1/22</td>
<td>2.1</td>
</tr>
<tr>
<td>1/23</td>
<td>2</td>
</tr>
</tbody>
</table>
STEP 4. (Follow up) Monitor the complications

Chronic pancreatitis can lead to **progressive destruction of the pancreas.**

**Diabetes mellitus**
- A syndrome that is characterized by hyperglycemia due to the loss of insulin production
  - 30-40% of dogs with diabetes have pancreatitis
  - Pancreatitis may also be common (51%) in diabetic cats

**EPI (Exocrine Pancreatic Insufficiency)**
- A syndrome that is characterized by a lack of effective pancreatic exocrine secretion in the small intestine
  - Due to pancreatic acinar atrophy (PAA)
  - From chronic pancreatitis (in 50% dogs, 100% cats with EPI)

Diagnostic Guidelines

[STEP 1] Rule out pancreatitis using a PLI kit

[STEP 2] Investigate whether pancreatitis is primary or secondary

[STEP 3] Assess the severity and risk factors

[STEP 4] (Follow up) Monitor the complications
Q & A session

Pancreatitis
- cPL kit
- fPL kit

Inflammation
- CRP kit
- SAA kit

DIC, Thrombosis
- D-dimer kit

Vcheck analyzers
- V200
- V2400
Product Introduction

Vcheck cPL 2.0 & fPL 2.0

✓ Specifications
✓ Test Procedure / Result Interpretation
✓ Performance
### Vcheck cPL / fPL 2.0 Kit

**Specifications**

- Vcheck series for diagnosis of pancreatitis in dogs and cats

<table>
<thead>
<tr>
<th>Vcheck cPL 2.0</th>
<th>Vcheck fPL 2.0</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Species</strong></td>
<td>Species</td>
</tr>
<tr>
<td>Dog</td>
<td>Cat</td>
</tr>
<tr>
<td><strong>Sample</strong></td>
<td>Sample</td>
</tr>
<tr>
<td>Serum 25 μl</td>
<td>Whole blood 50 μl, Plasma(EDTA)/Serum 25 μl</td>
</tr>
<tr>
<td><strong>Testing Time</strong></td>
<td>Testing Time</td>
</tr>
<tr>
<td>5 minutes</td>
<td>15 minutes</td>
</tr>
<tr>
<td><strong>Measurement</strong></td>
<td>Measurement</td>
</tr>
<tr>
<td>Quantitative</td>
<td>Quantitative</td>
</tr>
<tr>
<td><strong>Measurement Range</strong></td>
<td>Measurement Range</td>
</tr>
<tr>
<td>50 – 2,000 ng/ml</td>
<td>1 – 50 ng/ml</td>
</tr>
<tr>
<td><strong>Storage Condition</strong></td>
<td>Storage Condition</td>
</tr>
<tr>
<td>1 - 30 °C (Room temp.)</td>
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</tr>
</tbody>
</table>
Vcheck cPL / fPL 2.0 Kit

- Test Procedure & Interpretation

**REFERENCE RANGE**

<table>
<thead>
<tr>
<th></th>
<th>&lt; 200 ng/mL</th>
<th>200-400 ng/mL</th>
<th>&gt; 400 ng/mL</th>
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<tbody>
<tr>
<td>Normal</td>
<td>Suspected</td>
<td>Consistent with pancreatitis</td>
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<th>Normal</th>
<th>Suspected</th>
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</thead>
<tbody>
<tr>
<td>≤ 3.5 ng/ml</td>
<td>3.6-5.3 ng/ml</td>
<td>≥ 5.4 ng/ml</td>
</tr>
</tbody>
</table>

- Dilute sample
- Mix
- Measure

1-30°C

Whole blood
Serum/Plasma

25μL
100μL
Vcheck cPL / fPL 2.0 Kit

• Performance

  Strong correlation with an ELISA method from laboratories
  - Vcheck cPL 2.0: $R^2=0.998$; slope 0.96
  - Vcheck fPL 2.0: $R^2=0.977$; slope 1.00

Comparative Evaluation of Vcheck cPL 2.0
- Compared to an ELISA method -

\[ y = 0.9571x + 27.274 \]
\[ R^2 = 0.9979 \]

Comparative Evaluation of Vcheck fPL 2.0
- Compared to an ELISA method -

\[ y = 1.0012x - 0.3657 \]
\[ R^2 = 0.9771 \]

\[ y = 0.8994x - 0.0436 \]
\[ R^2 = 0.0595 \]
Thank you

If you have any questions, please do not hesitate to contact our regional managers.

BIONOTE Marketing team
November 2020