

Diagnostic Guidelines of Pancreatitis

- 4 Steps for diagnosing pancreatitis and assessing the severity -

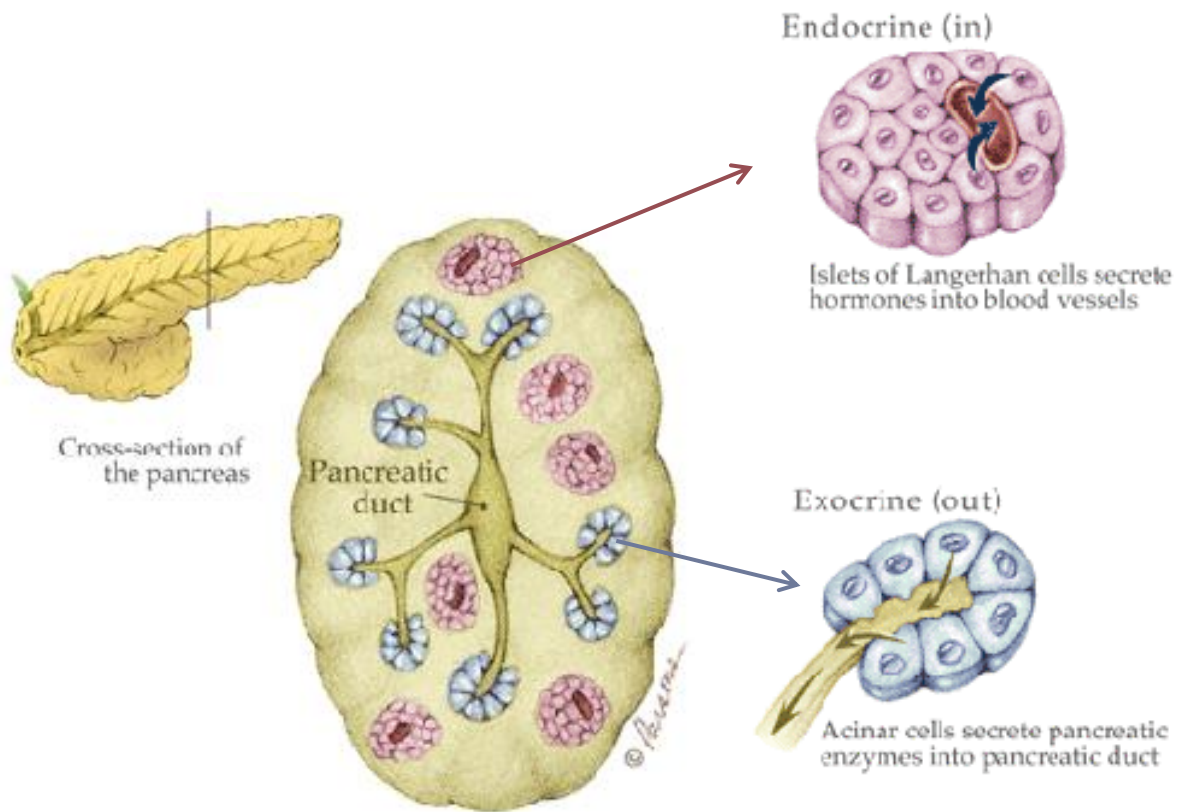
By Angela (D.V.M.)

BIONOTE Marketing team

November 2020



Pancreas Function

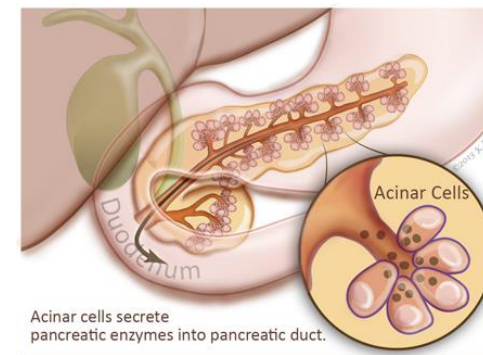


Endocrine parts (Islets of Langerhans)

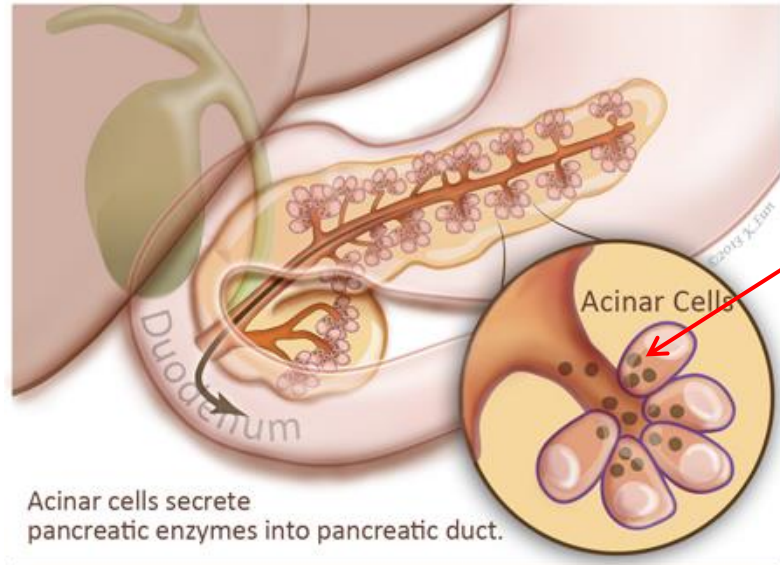
They produce and secrete hormones into the bloodstream;
insulin and glucagon

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

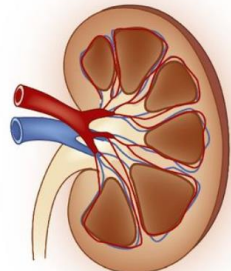
Inflammation stimulates the infiltration of **neutrophils**

- Reactive oxygen species (ROS), cytokines, and nitric oxide (NO)
- **Exacerbates further inflammation**

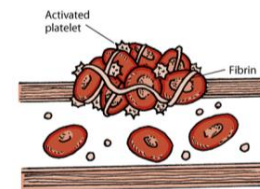
By the way, what is the cause of pancreatitis?

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

Acute kidney injury



Disseminated intravascular coagulation (DIC)

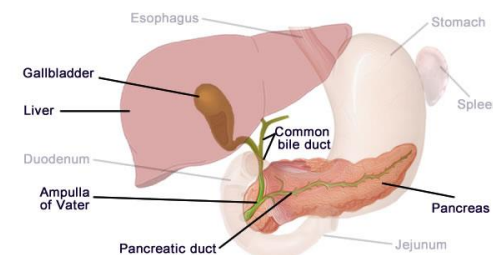
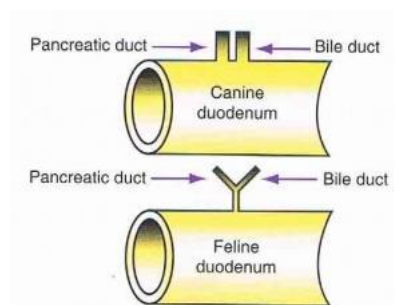
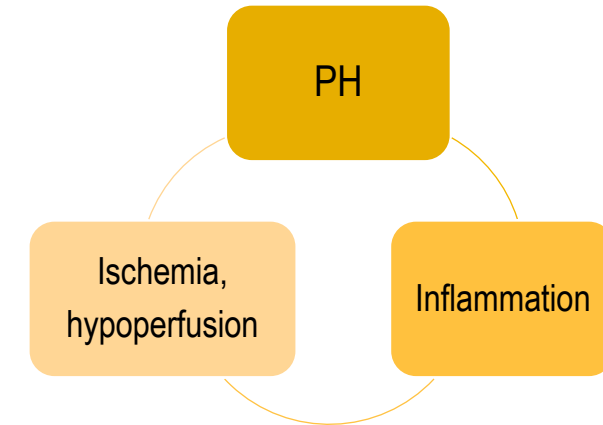


Acute lung injury



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



▲ The relationship between the liver, pancreas, and small intestine in a cat

Triaditis?

A syndrome of concurrent pancreatitis, inflammatory bowel disease (IBD), and cholangitis.

Clinical Signs



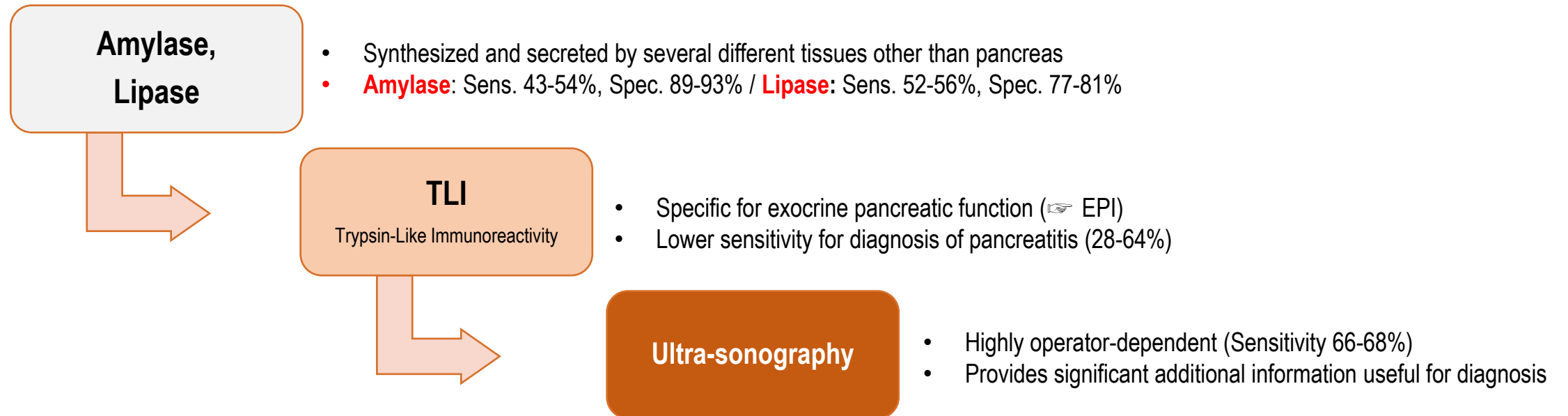
- **Non-specific signs**

Dog: Pancreatitis	
Clinical signs	<ul style="list-style-type: none">• Anorexia (91%)• Vomiting (90%)• Weakness (79%)• Abdominal pain (58%)• Dehydration (46%)• Diarrhea (33%)
<ul style="list-style-type: none">✓ Mild cases: Subclinical (asymptomatic)✓ Severe cases: Systemic clinical signs such as fever or even cardiovascular shock	

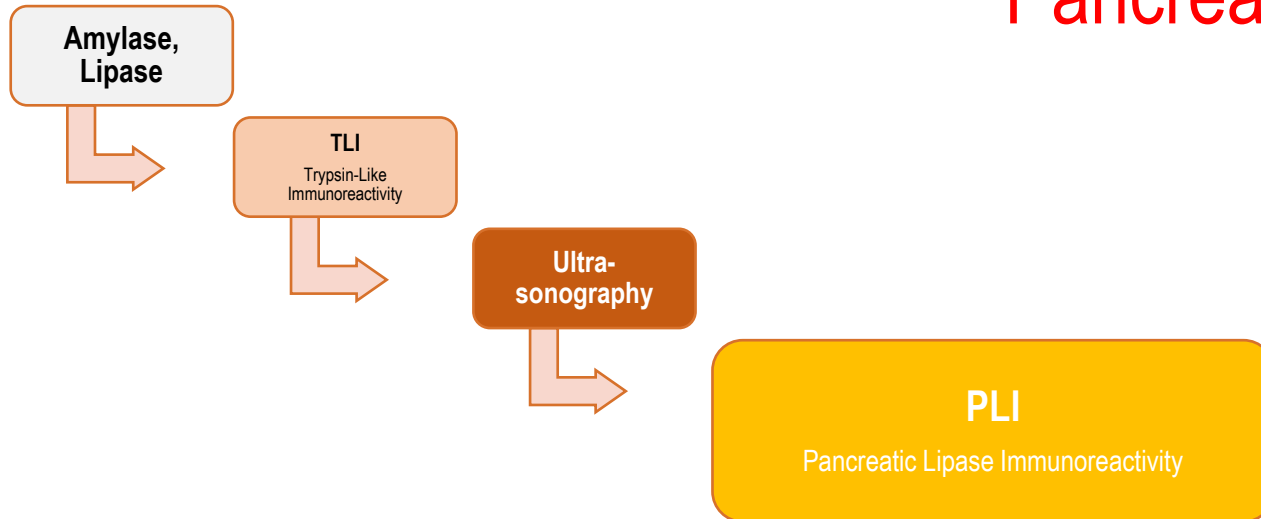
Cat: Pancreatitis	
Clinical signs	<ul style="list-style-type: none">• Lethargy (100%)• Anorexia (97%)• Dehydration (92%)• Hypothermia (68%)• Vomiting (35%)• Abdominal pain (25%)• A palpable abdominal mass (23%)• Dyspnea (20%)• Ataxia (15%)• Diarrhea (15%)
<ul style="list-style-type: none">✓ Less specific clinical signs✓ Low occurrence of vomiting and abdominal pain	

Diagnosis

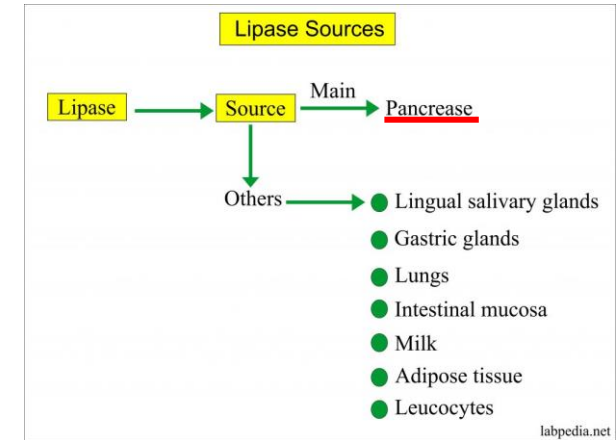
***Histopathology:** Gold standard method for definitive diagnosis of pancreatitis



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

Diagnostic Guidelines

STEP 1. Rule out pancreatitis using a PLI kit

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...](#)



▲ Canine cPL (Vcheck) test

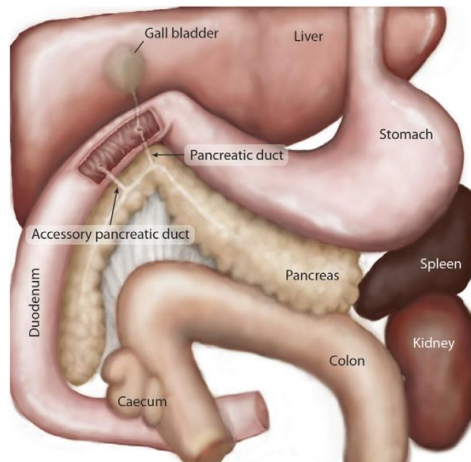
Cut-off of cPL	Sensitivity	Specificity
200 ng/ml	93.6%	77%
400 ng/ml	77.8%	88%

Diagnostic Guidelines

STEP 2. Investigate whether pancreatitis is primary or secondary

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



[The cases that pancreatitis was not the primary cause for presentation]

Dog	SNAP cPL positive	
	Diagnosis	Spec cPL ($\mu\text{g/L}$)
1	Small intestinal foreign body	Insufficient sample
2	Small intestinal foreign body	30
3	Small intestinal foreign body and septic peritonitis	105
4	Small intestinal infarction with bilateral adrenomegaly*	568*
5	Hepatic T-cell lymphoma*	68*
6	Hepatic mass with invasion of the caudal vena cava	404
7	Hepatic masses/septic peritonitis	672
8	Hepatic/splenic masses with hemoperitoneum	720
9	Hepatic abscess	1000
10	Hemoperitoneum/septic peritonitis	550
11	Pyometra and septic peritonitis	30

Diagnostic Guidelines

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**

< 200 ng/ml	200-400 ng/ml	> 400 ng/ml
Pancreatitis very unlikely	Equivocal	Pancreatitis

- Cats**

≤ 3.5 ng/ml	3.6-5.3 ng/ml	≥ 5.4 ng/ml
Pancreatitis very unlikely	Equivocal	Pancreatitis

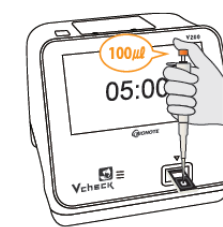
Dilute sample



Mix



Measure



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

Diagnostic Guidelines

For accurate diagnosis of pancreatitis,

① Clinical signs

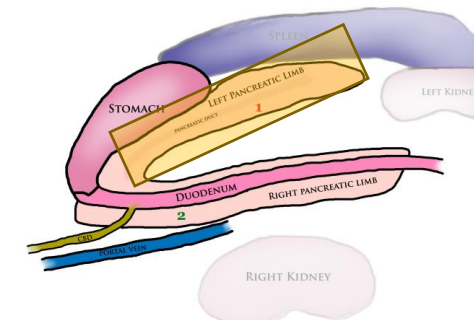
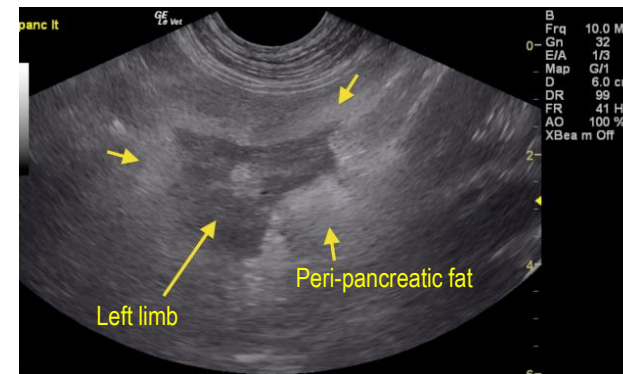
② PLI Testing

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

A dog with acute-on chronic 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**

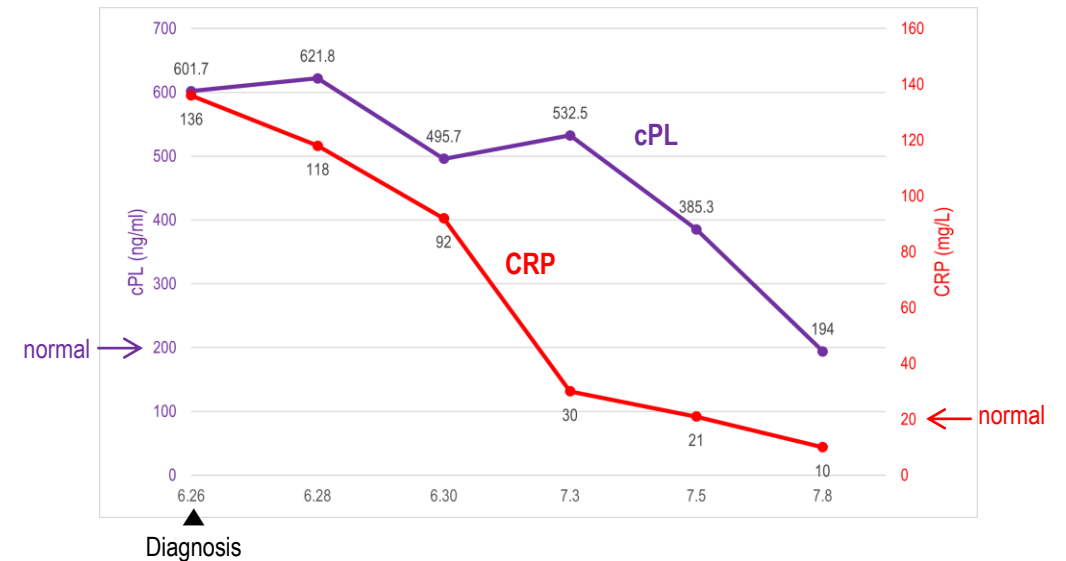
- May be normal, especially in mild cases
- **Increases in liver enzyme: ALKP 2 to 15-fold, ALT 2 to 5-fold**
- **Hyperbilirubinemia: 2 to 5-fold**
- **Increased BUN, CREA: dehydration**
- **Electrolyte: hypochloremia in dogs (81.3%), hypokalemia in cats (56%)**

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

2020/06/26 16:31
SN: VA20B02VA0908
Version: V1.00_R021(0.5)
Operator ID: guest
Patient ID: 
Operator ID: guest
Patient ID:
cPL = 601.7 ng/mL
Procedural Control = Valid
Interpretation: Consistent with
Pancreatitis
<200 ng/ml = Normal



Diagnostic Guidelines

STEP 3. Assess the severity and risk factors

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

System	Criteria	Reference range
Renal	BUN > 84 mg/dl Creatinine > 3.0 mg/dl	BUN 15 ~ 57 mg/dl CREA 0.6 ~ 1.8
Hepatic	Any of ALP, AST or ALT > 3 x upper range	ALKP 47 ~ 254 U/L ALT 17 ~ 78 U/L
Lymphoid	Band neutrophils > 10% or WBC > 24 x 10 ⁹ /L	WBC 4,500~17,000
Endocrine pancreas	Blood glucose > 234 and/or b-OH butyrate > 1 mmol/L	Blood glucose 59~123 b-OH butyrate < 0.6
Acid/base buffering	Bicarbonate < 13 or > 26 and/or anion gap < 15 or > 38 mmol/L	Bicarbonate 15~24 Anion gap 17~35



Replace with CRP
More than 2-fold upper range (> 40 mg/L)

Scientific

A severity score for spontaneous canine acute pancreatitis

CG RUAUX and RB ATWELL
School of Veterinary Science and Animal Production, The University of Queensland, Queensland 4072
Email C.Ruaux@mailbox.uq.edu.au



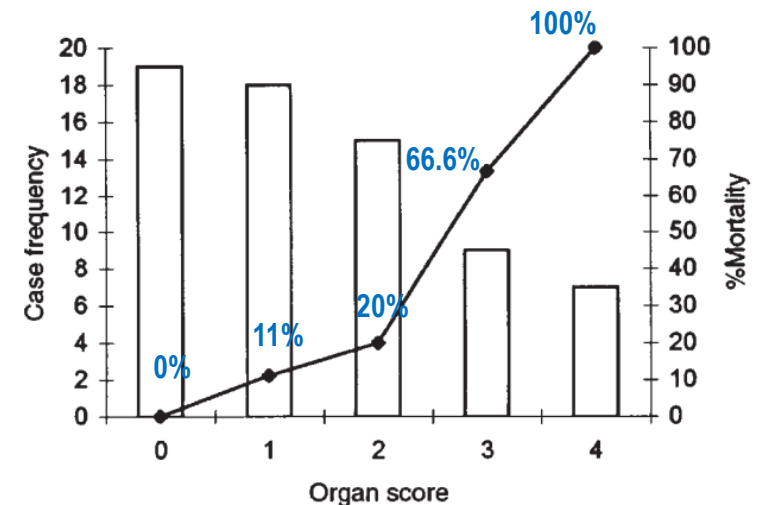
Diagnostic Guidelines

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- **Assess the mortality**

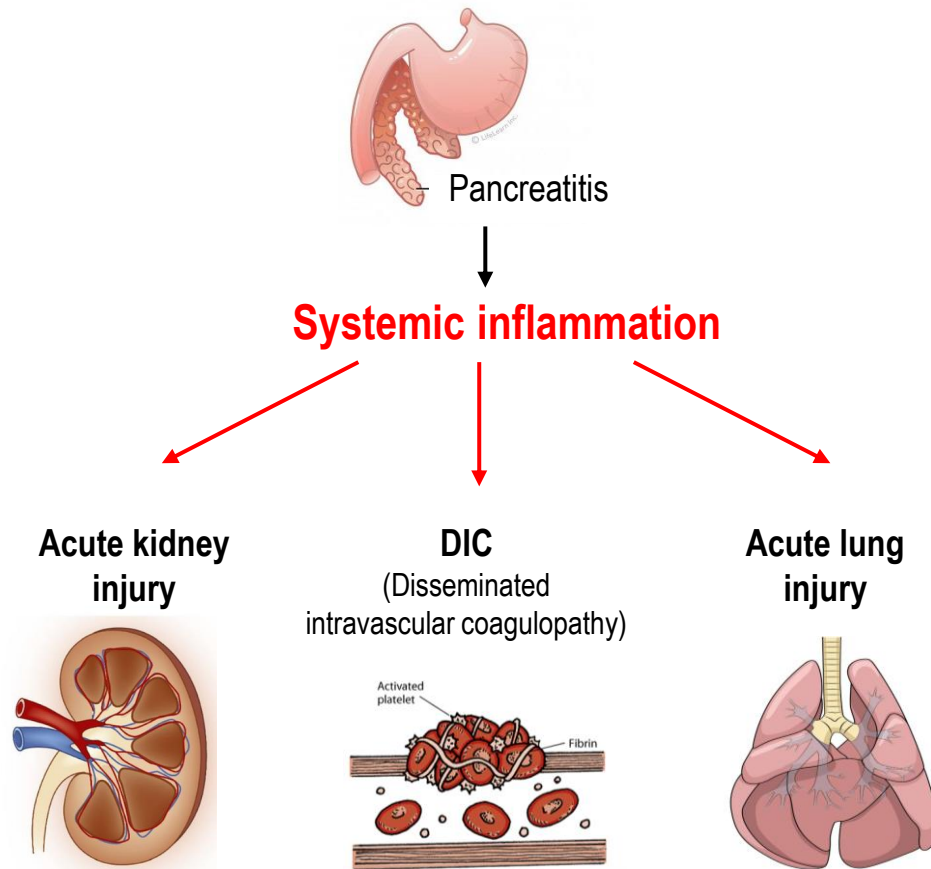


Q. Should I evaluate it with the results at the time of diagnosis?

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**

* PT: Prothrombin time
aPTT: Activated partial thromboplastin time

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) **1 point**
- **Biochemistry:** ALKP 535 (**high**, normal 15-127), ALT 96 (**high**, normal 19-70), **1 point**
 BUN 58 (**high**, normal 8-26), CREA 1.5 (**high**, normal 0.5-1.3), **0 point**
 Glucose 134 (**high**, normal 70-118) **0 point**
- **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

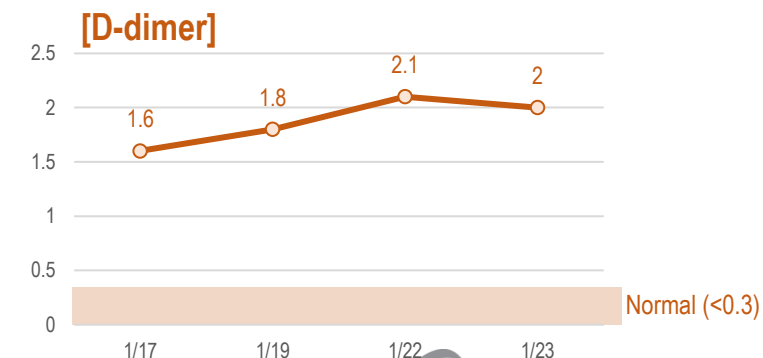
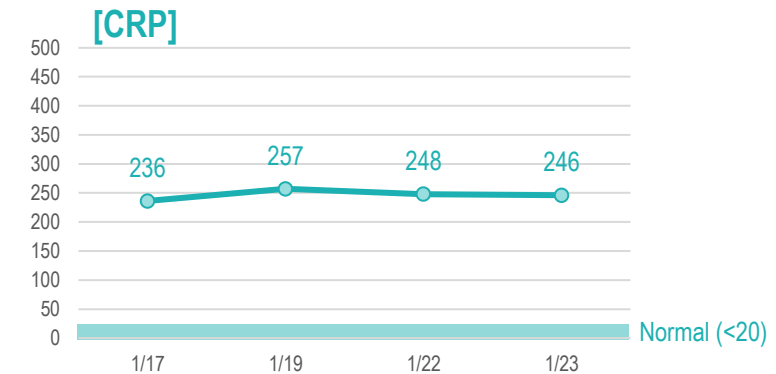
Severity score based upon organ system compromise ⇄ 1 point for each part

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Acid/base buffering	Bicarbonate < 13 or > 26 and/or anion gap < 15 or > 38 mmol/L	Bicarbonate 15-24 Anion gap 17-35

Q. Organ score?

Total 2 point

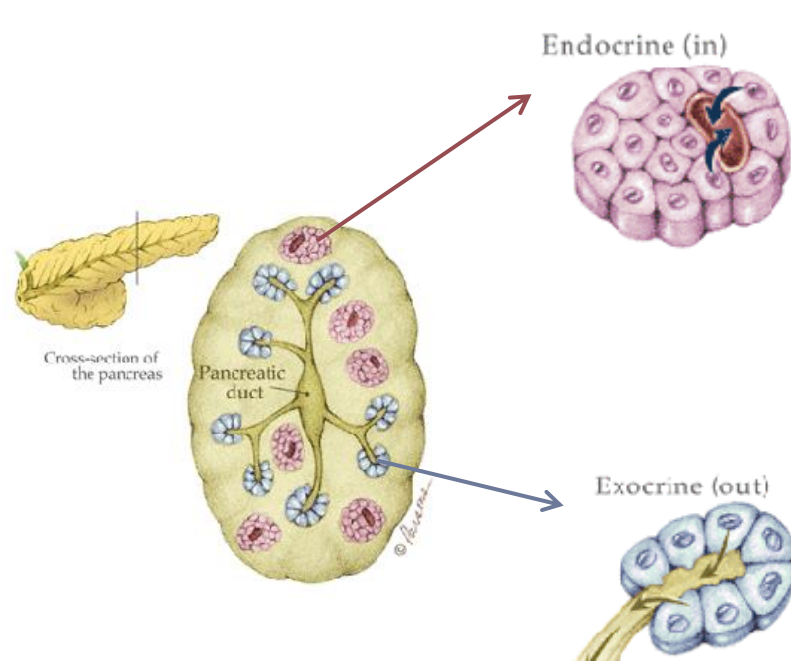
Q. Risk factors?



Diagnostic Guidelines

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]

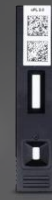
Assess the severity and risk factors

[STEP 4]

(Follow up) Monitor the complications

Q & A session

Pancreatitis



cPL kit

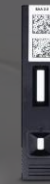


fPL kit

Inflammation



CRP kit



SAA kit

Vcheck analyzers



V200



V2400

DIC, Thrombosis



D-dimer kit

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



<p>Vcheck cPL 2.0</p>	 A black test cassette and a white box labeled 'Vcheck cPL 2.0' with '10 TESTS/KIT' and 'BIONOTE' branding. A yellow circular icon with a thermometer indicates a storage temperature of 1~30°C.	<ul style="list-style-type: none">• Species : Dog• Sample : Serum 25 µl• Testing Time : 5 minutes• Measurement : Quantitative• Measurement Range : 50 – 2,000 ng/ml• Storage Condition : 1 - 30 °C (Room temp.)
<p>Vcheck fPL 2.0</p>	 A black test cassette and a white box labeled 'Vcheck fPL 2.0' with '10 TESTS/KIT' and 'BIONOTE' branding. A yellow circular icon with a thermometer indicates a storage temperature of 1~30°C.	<ul style="list-style-type: none">• Species : Cat• Sample : Whole blood 50 µl, Plasma(EDTA)/Serum 25 µl• Testing Time : 15 minutes• Measurement : Quantitative• Measurement Range : 1 – 50 ng/ml• Storage Condition : 1 - 30 °C (Room temp.)

Vcheck cPL / fPL 2.0 Kit

- Test Procedure & Interpretation



Dilute sample



Mix



Measure

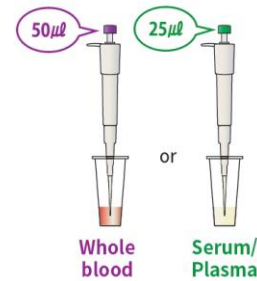


REFERENCE RANGE

< 200 ng/mL	200~400 ng/mL	> 400 ng/mL
Normal	Suspected	Consistent with pancreatitis



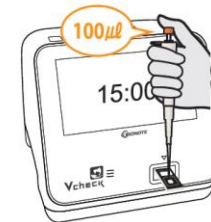
Dilute sample



Mix



Measure



REFERENCE RANGE

Normal	Suspected	Consistent with pancreatitis
≤ 3.5 ng/ml	3.6~5.3 ng/ml	≥ 5.4 ng/ml

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

Reproducibility

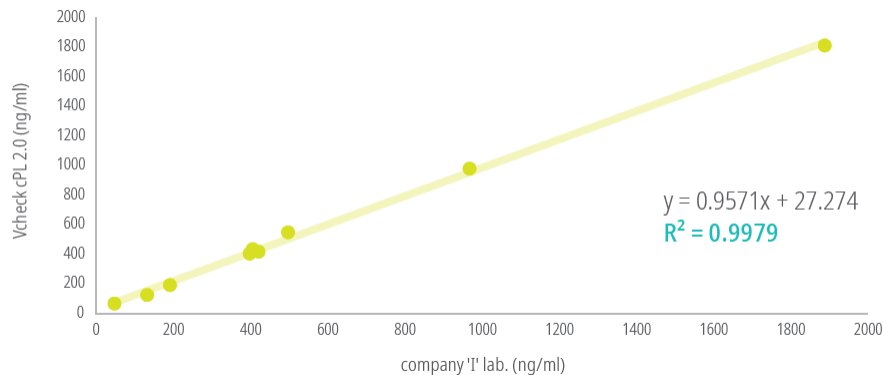
CV < 15%

Accuracy

Bias < 20%

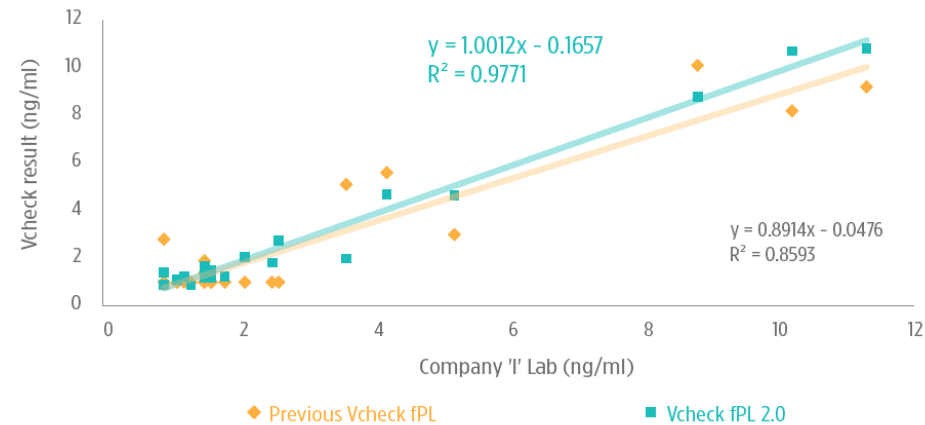
Comparative Evaluation of Vcheck cPL 2.0

- Compared to an ELISA method -



Comparative Evaluation of Vcheck fPL 2.0

- Compared to an ELISA method -



Thank you

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

BIONOTE Marketing team

November 2020

