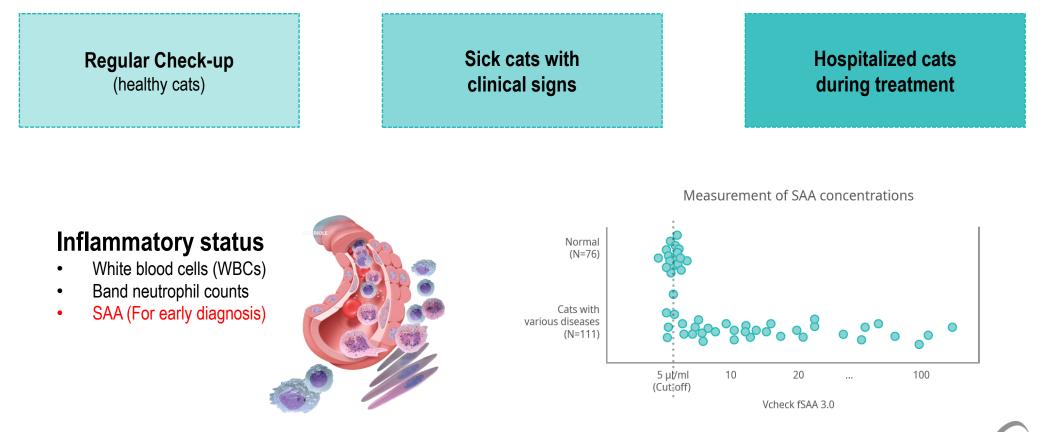
Acute Inflammatory Marker, Serum Amyloid A

BIONOTE Marketing team MARCH 2021



### How to detect inflammatory diseases in cats

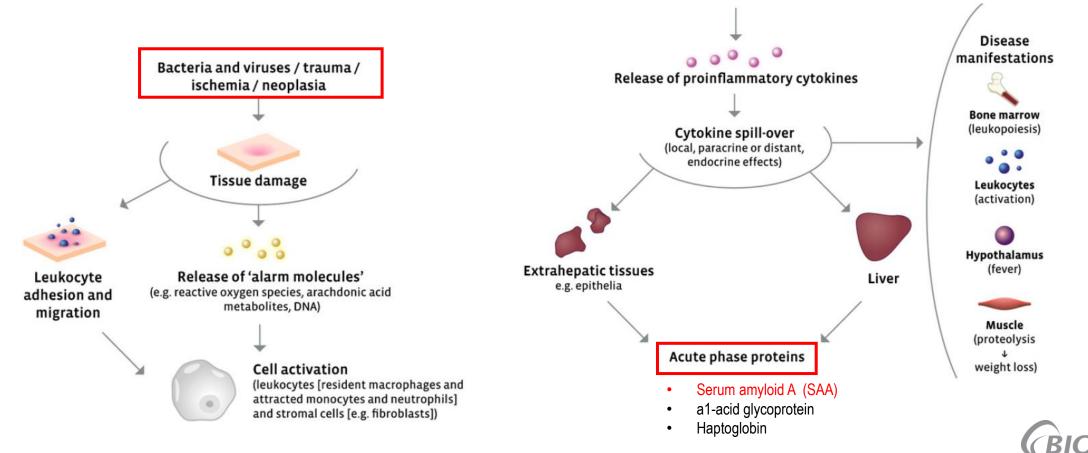




# Serum Amyloid A (SAA)

## What is Serum amyloid A (SAA) ?

• The Acute Phase Response

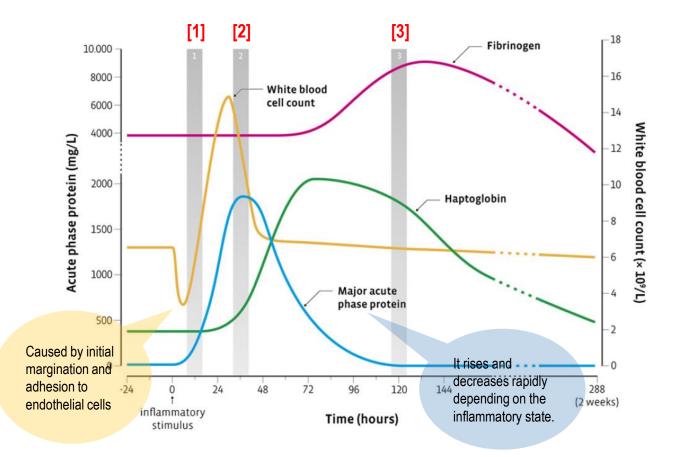


Clin Lab Med. 2011 Mar;31(1):51-70.

# Serum Amyloid A (SAA)

## What is Serum amyloid A (SAA) ?

• The Acute Phase Response



#### Changes of WBC and SAA in diseases cats

#### [1] At the inflammatory stimulus (8~12 hours after)

- WBC counts: decreased, normal or somewhat increased
- SAA: slightly increased

#### [2] 36 hours after

- WBC counts: increased more than the normal range
- SAA: increased more than the normal range

#### [3] 5 days after - After inflammation has been resolved

- WBC counts: return to baseline
- SAA: quickly return to baseline



# Advantages of SAA Testing over WBC counts

## SAA is...

#### 1<sup>st</sup>. More sensitive than WBC (Earlier detection of inflammation)

- Short lag time (6-8 hours) from onset of inflammation to a measurable increase

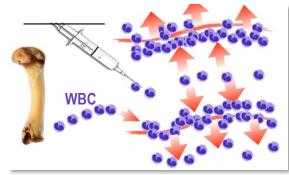
#### 2<sup>nd</sup>. Significantly rises and decreases

- Increases up to 1,000-fold due to inflammatory stimulus
- Prompt decreases after resolution of the stimulus

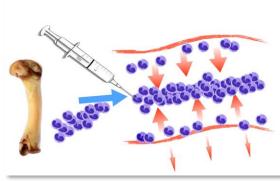
#### 3<sup>rd.</sup> Proportional to the severity of inflammation

- Short half-life (20-24 hours) causing to decrease soon after inflammation has subsided
- $\rightarrow$  Can be used for monitoring response to treatment

#### 4<sup>th</sup>. Not affected by stress, steroids, NSAIDs or antibiotics



▲ Severe inflammation (early phase)



▲ Effect of steroid, epinephrine



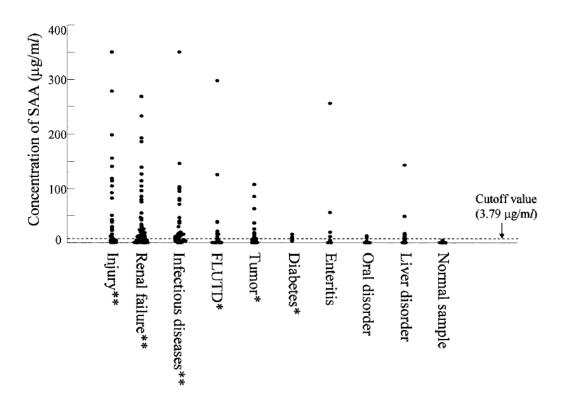
# SAA levels in various diseases

## **Diseases with increased SAA levels**

- Injury
- Infectious disease (bacteria, virus)
- Tumor
- Surgery

#### **Specific diseases**

- Pancreatitis
- Feline infectious peritonitis (FIP)
- Chronic kidney disease (CKD)
- Pyometra
- Cardiomyopathy
- Hepatitis / cholangitis
- Pneumonia / Respiratory tract infections





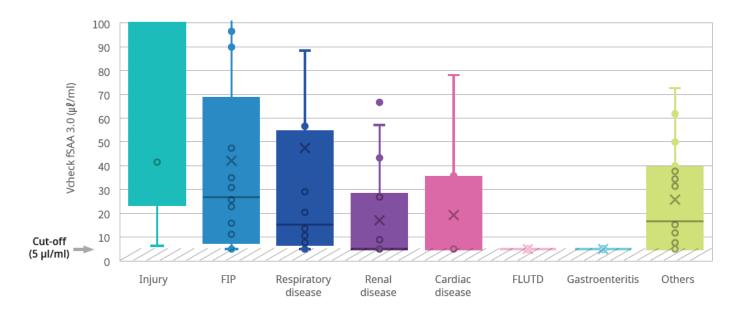
## **Clinical Evaluation - 1**

## High SAA levels in various diseases

- Injury
- Neoplasia
- Feline infectious peritonitis (FIP)
- Chronic kidney disease (CKD)

- Pyometra
- Cardiomyopathy
- Hepatitis / Cholangitis
- Pneumonia / Respiratory tract infections



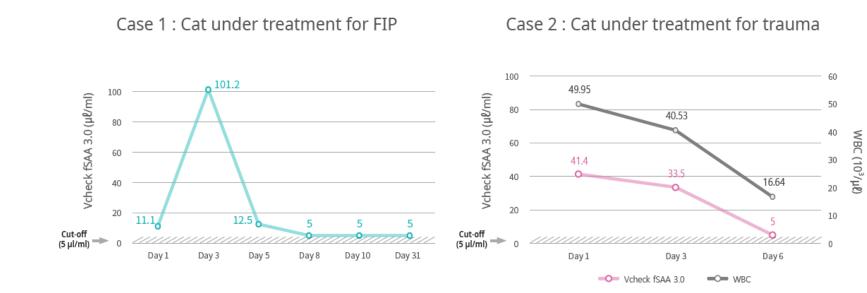




SAA levels in diseased cats (N=111)

# **Clinical Evaluation - 2**

### **Treatment Monitoring of SAA Levels**



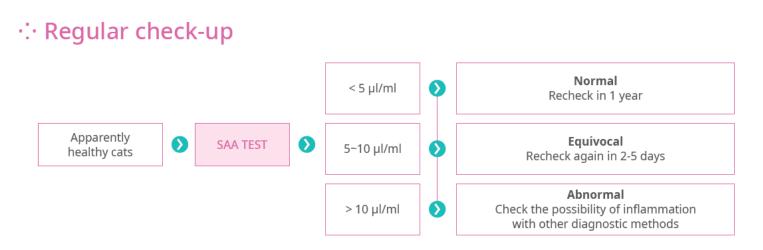
Vcheck Feline SAA 3.0

- High SAA levels in a cat with FIP
- After treatment, SAA levels decreased, reflecting the inflammatory status.

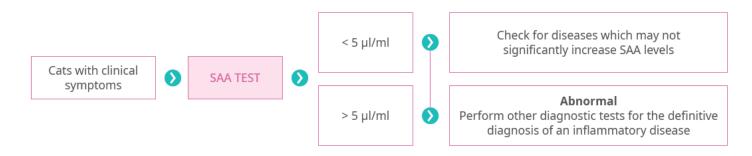
- High SAA & WBC levels indicate presence of infection.
- The concentrations declined rapidly following recovery.



# **Diagnostic Algorithm**



#### ·:· First choice in symptomatic cats







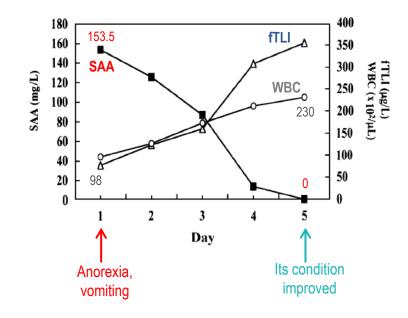
# Case Study

- Case 1 : Pancreatitis
- Case 2 : Chronic kidney disease (CKD)
- Case 3 : Feline infectious peritonitis (FIP)
- Case 4 : Sepsis
- Case 5 : Surgery



### Case 1 : Pancreatitis

- **Patient Information**: 6-year-old, neutered male, domestic shorthair
- **History**: Treated with prednisolone for asthma for 9 months
- Clinical sign: anorexia, vomiting, and fever for 2 days



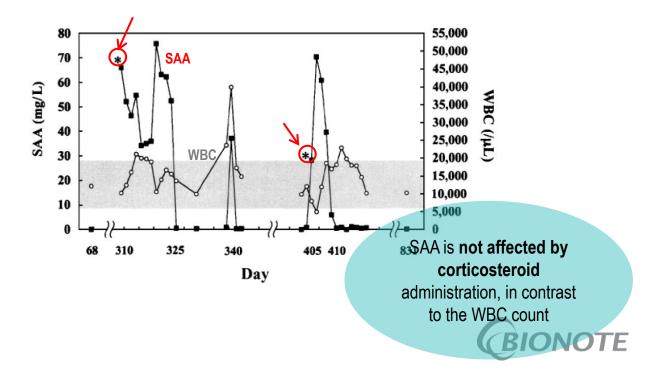
Blood test: normal WBC (9800/uL), abnormal SAA (153.5 ug/ml), azotemia

Veterinary Clinical Pathology, 38(1), 83-86.

• **Ultrasonography**: enlarged pancreas with hypoechoic lesions

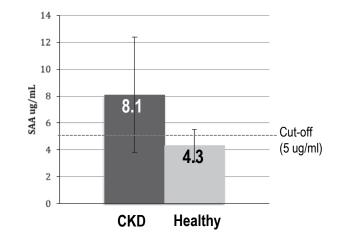
٠

 Histopathology: parenchymal necrosis, leukocyte infiltration with necrosis of the fat tissue → <u>Diagnosis: acute pancreatitis</u>



## Case 2 : Chronic kidney disease (CKD)

- CKD in 15-30% of geriatric cats
  - → An estimated 30–65% of cats with CKD will develop anemia as their renal disease progresses.
- In human patients, chronic inflammation and oxidative stress play key roles in the development and progression of CKD.
  - $\rightarrow$  But, not well characterized in veterinary medicine



High SAA levels in CKD cats (especially, anemic cats)
→ CKD in cats is associated with systemic inflammation.

Table 1. CKD VS. Healthy cats

	Hct (%)	Creatinine (µmol/L)	SAA (µg/mL)	HAP (µg/mL)	Iron (µg/mL)
CKD	29.4 (7.7)	280 (158)	8.1 (6.5)	4.5 (3.3)	85.5 (32.9)
Healthy	41.2 (3.7)	117 (22)	4.3 (1.2)	3.6 (1.6)	100.7 (21.7)
<i>P</i> -value	<.0001	<.0001	.002	.9	.01

Table 2. CKD cats (Anemic VS. Non-anemic cats)

CKD group	Hct (%)	Creatinine (µmol/L)	SAA (µg/mL)	HAP (µg/mL)	Iron (µg/mL)
Anemic	21.9 (5.7)	374 (215)	11.2 (6.8)	5.0 (4.0)	86.3 (40.4)
Nonanemic	33.7 (4.6)	225 (75)	6.3 (5.6)	4.2 (2.9)	84.9 (28.5)
P-value	<0001	.02	.003	.4	.8



J Vet Intern Med. 2017 Mar;31(2):457-464.

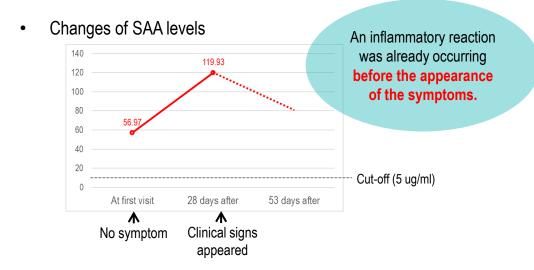
	Not FIP	FIP	
SAA (ug/ml)	<b>10.21</b> ±8.32	82.88±50.23	

The Veterinary Journal 167 (2004) 38-44

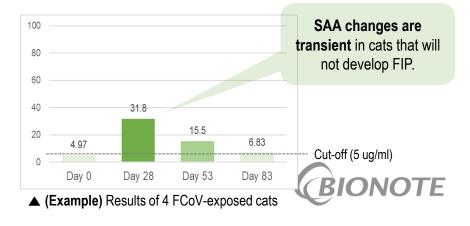
## Case 3 : Feline infectious peritonitis (FIP)

- **Patient Information**: 12 m, female, Persian
- History: no clinical signs, from a cattery which FIP was diagnosed
- 28 days later, it developed a FIP (wet form)
- Blood test
  - FCoV Ab: positive (+)
  - Biochemistry

Unit: g/dL	At first visit (No symptom)	28 days after (symptoms)	53 days after
Total protein	9.1	7.6	9.8
A/G ratio	0.38	0.41	0.38
Albumin	2.5	2.2	2.7
Globulin	6.6	5.4	7.1
SAA (ug/ml)	56.97	119.93	N/A



What if the cat is only exposed to FCoV (Not FIP) ?



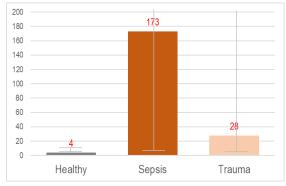
### Case 4 : Feline sepsis

Diagnosis of feline sepsis is still challenging.

- A higher percentage of circulating **band neutrophils** (Leukocytosis with left shift)
- Severe hypoalbuminemia
- Higher frequency of **toxic neutrophil changes** (blood smears)
- High total bilirubin
- High **SAA levels** (> 81 ug/ml: 79.3% sesitivity)
- Leukocyte counts → Not recommended! (Poor diagnostic value)

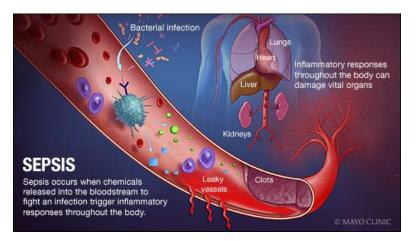
Variable	Controls $(n = 18)$	Sepsis $(n = 29)$	Trauma ( $n = 27$ )	
SAA (mg/L)	4 (1–9)	173 <sup>a</sup> (1–265)	28 <sup>ab</sup> (1–258)	
ALT (U/L)	51 (35-80)	49 (15–3,600)	292 <sup>ab</sup> (70–3,300)	
AST (U/L)	24 (15–36)	130 <sup>a</sup> (20–4,000)	310 <sup>ab</sup> (43–2,500)	
Total bilirubin (µmol/L)	1.7 (1.2–5.8)	$6.8^{a}(1.7-114)$	3.4 <sup>ab</sup> (1.7–32)	
Albumin (g/L)	37 (33–41)	34 <sup>a</sup> (10–41)	28 <sup>ab</sup> (15–38)	
Total protein (g/L)	81 (72–88)	67 <sup>a</sup> (44–107)	59 <sup>ab</sup> (29–83)	
A/G	0.87 (0.63-1.2)	$0.51^{a}(0.25-0.94)$	$0.92^{a} (0.51 - 1.3)$	
Creatinine (µmol/L)	131 (113–169)	98 <sup>a</sup> (45–1,630)	101 <sup>ab</sup> (70–597)	
Glucose (mmol/L)	5.6 (1.8-8.2)	5.8 (0.3–15.0)	$9.3^{ab}(3.1-19.1)$	
Leukocytes (cells $\times 10^9$ /L)	8.4 (2.7–14.9)	$27.0^{a}(0.5-63.6)$	$13.8^{a}$ (4.3–37.9)	
Hematocrit (L/L)	0.41 (0.35–0.47)	$0.33^{a}(0.18-0.50)$	0.31 <sup>a</sup> (0.06–0.42)	

#### ✓ SAA levels





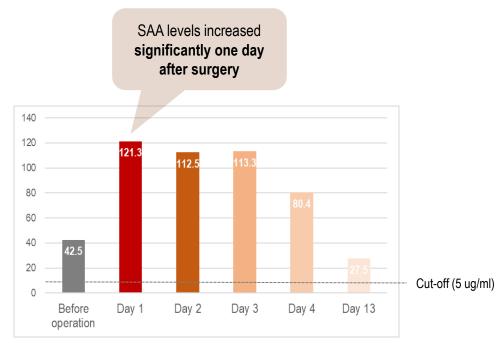
#### J Vet Diagn Invest. 2017 Nov;29(6):856-859.



Vet Immunol Immunopathol. 1999 Mar 29;68(1):91-8.

## Case 5 : Surgery

Feline SAA concentration was found to increase earliest, with other acute phase proteins beginning to increase thereafter.  $\rightarrow$  SAA is an acute phase reactant at the early stage of inflammation.



▲ Changes of SAA levels in cats subjected to surgery for urinary diversion



## **Clinical Application**



#### Monitoring the post-operative effects and recovery

Screening interval (Recommendation)① Before surgery② After surgery③ 2-3 times every 12 hours



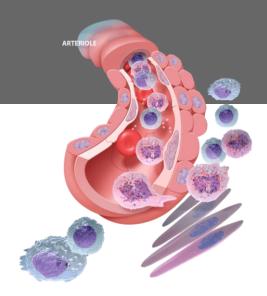
#### Serial monitoring of the response to treatment

Decrease in SAA levels between two consecutive time points could be associated with positive response to treatment.



#### Early detecting the presence of inflammation

SAA increases in the early stage of inflammation, enabling an early detection of inflammation before the presence of clinical symptoms.





#### 1) SAA levels in Chronic inflammation?

Despite the name, they can also change during chronic inflammatory processes.

Chronic inflammation can be perceived as a consecutive series of separate inflammatory stimuli. In such conditions, increased concentrations of APPs are generally observed. However, the increase is lower than during acute episodes of inflammation or infection.

#### 2) SAA levels in Congestive heart failure?

CHF is an inflammatory disorder, and outcome in CHF may be determined by the extent of inflammation.  $\rightarrow$  SAA levels are significantly high in cats with heart failure, but not in cats with preclinical hypertrophy.

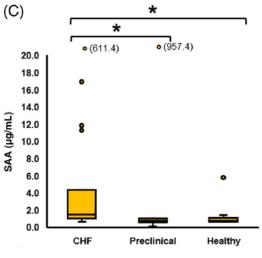
#### 3) Monitoring of SAA or fPL in cats with pancreatitis?

Monitoring using SAA levels is more recommended if there is an economic burden during treatment monitoring.

SAA reflects relatively accurately the severity of pancreatic inflammation compared to fPL enzymes.

 $\rightarrow$  So, patients can be monitored using SAA levels during treatment, and fPL and SAA tests can be evaluated simultaneously after treatment.





<sup>▲</sup> Changes of SAA levels in cats with CHF



# Q & A session

• Acute phase proteins for detecting inflammation



SAA for Cats



CRP for Dogs

BIONOTE Marketing team MARCH 2021

