



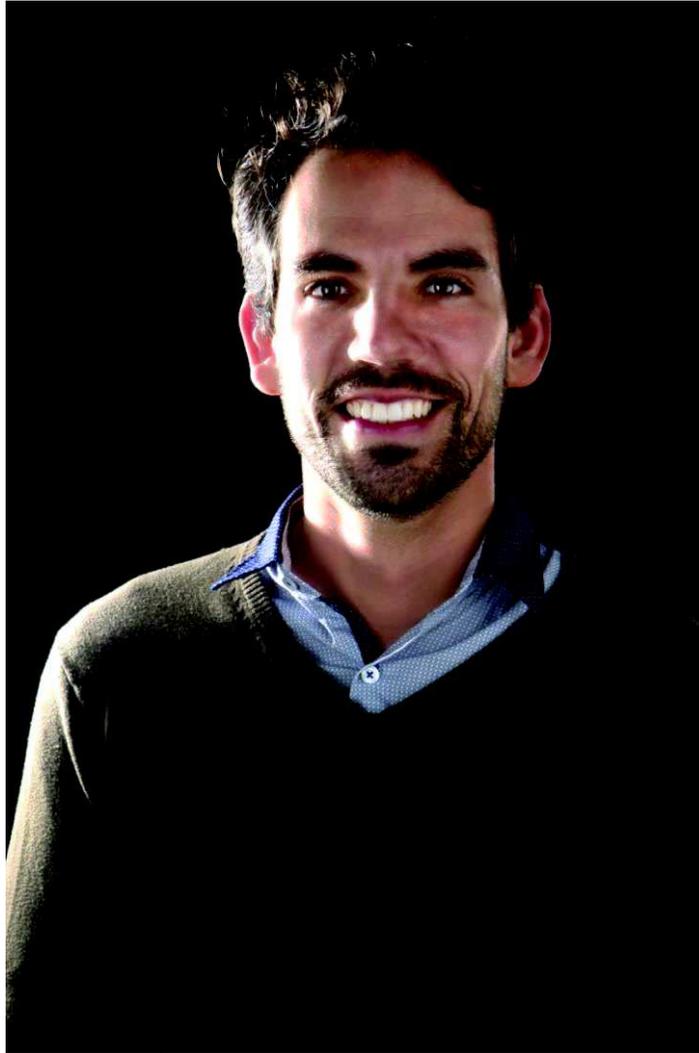
Utilisation du dosage de la Protéine C Réactive (CRP) dans le suivi des processus inflammatoires chez le chien

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Remerciements

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2015-2016
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LinkedIn: <http://ca.linkedin.com/in/remifroment>

PLAN

- Inflammation aigue ?
- La CRP c'est quoi ?
- Comment mesurer la CRP?
- Intérêt clinique de la CRP:
 - Quelques maladies : diagnostic et suivi
- Conclusion
- Références

Concept d'inflammation aigue



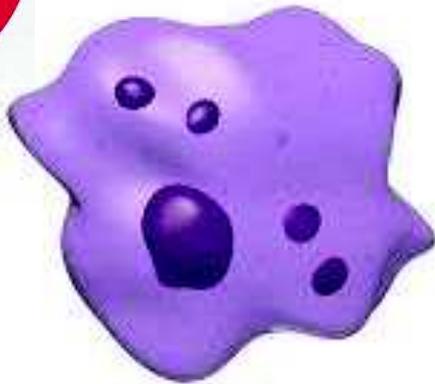
!!! INTRUS !!!

1/Pathogène

**Nombreuses molécules de surface,
ADN, ARN...**

**2/Cellules tumorales / marqueurs de surfaces
"anormaux"**

Concept d'inflammation aigue



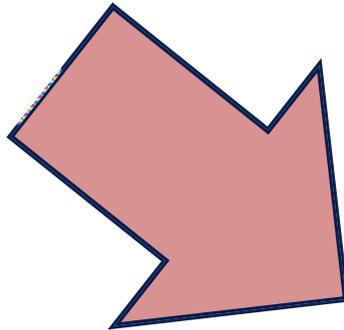
TLR

1/Pathogène

**2/Cellule tumorale /
marqueurs de surfaces**

Immunité innée

Concept d'inflammation aigue

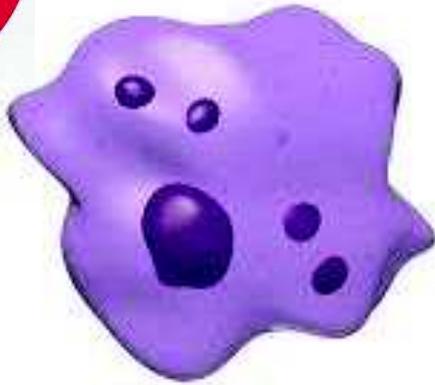


TNF α

IL-1

IL-6

Concept d'inflammation aigue



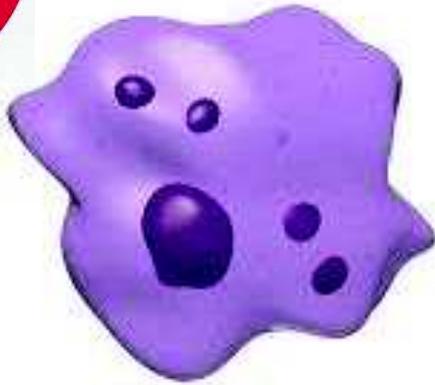
TNF α
IL-1
IL-6
autres

***FOIE**

***MOELLE
OSSEUSE**

***ENDOTHELIUM
VASCULAIRE
*LEUCOCYTES**

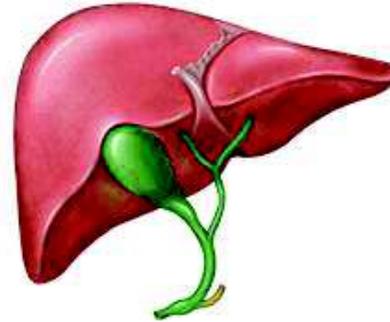
Concept d'inflammation aigue



TNF α

IL-1

IL-6



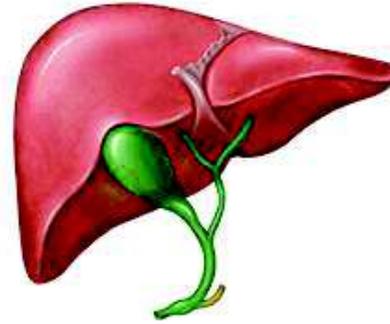
CRP \uparrow

Autres APP \uparrow ou \downarrow

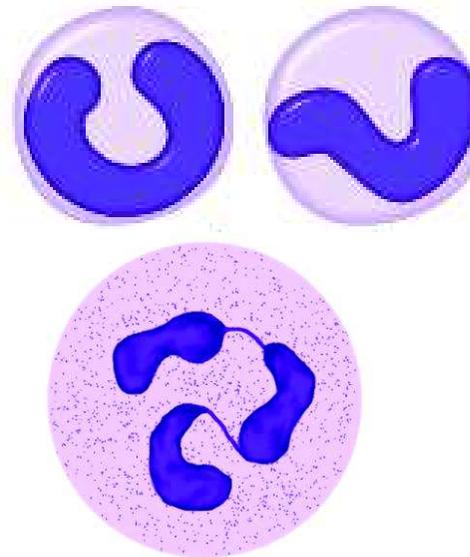
Concept d'inflammation aigue



TNF α
IL-1
IL-6



CRP

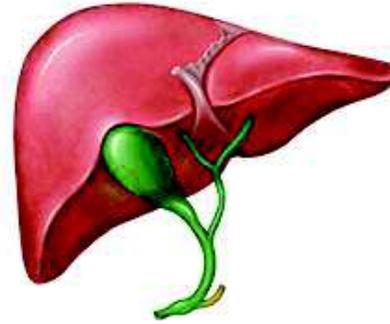


Leucogramme
Neutrophilie
Toxicité
Arneth G
Monocytose
+/- Anémie NR

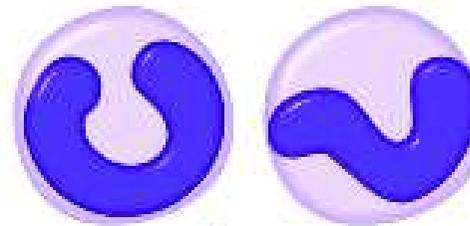
Concept d'inflammation aigue



TNF α
IL-1
IL-6

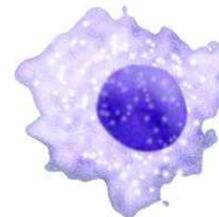
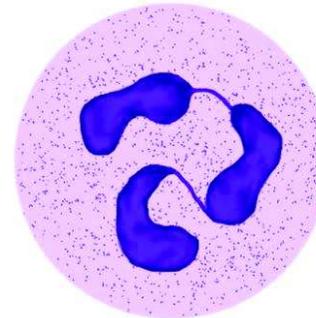


CRP



Leucogramme

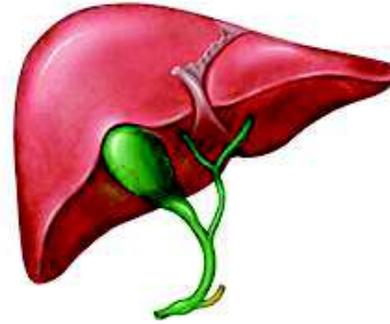
Morphologie frottis



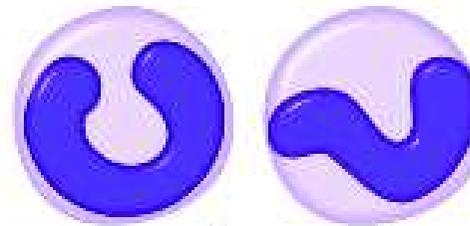
Concept d'inflammation aigue



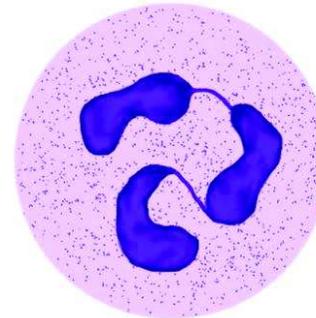
TNF α
IL-1
IL-6



CRP



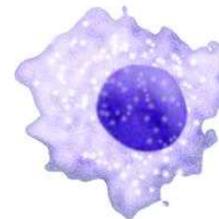
Leucogramme



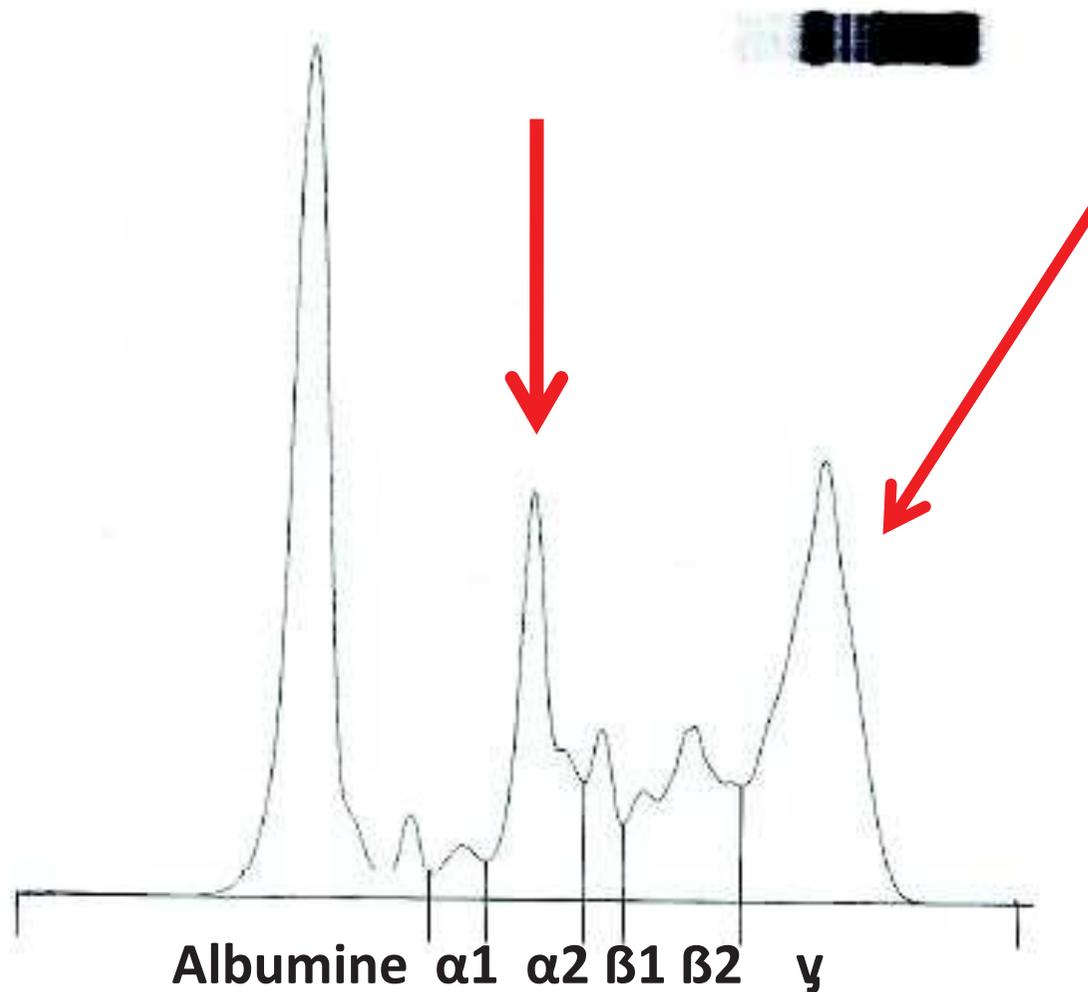
*Migration aux **NL**
(LYMPHOCYTES)

*Pont avec

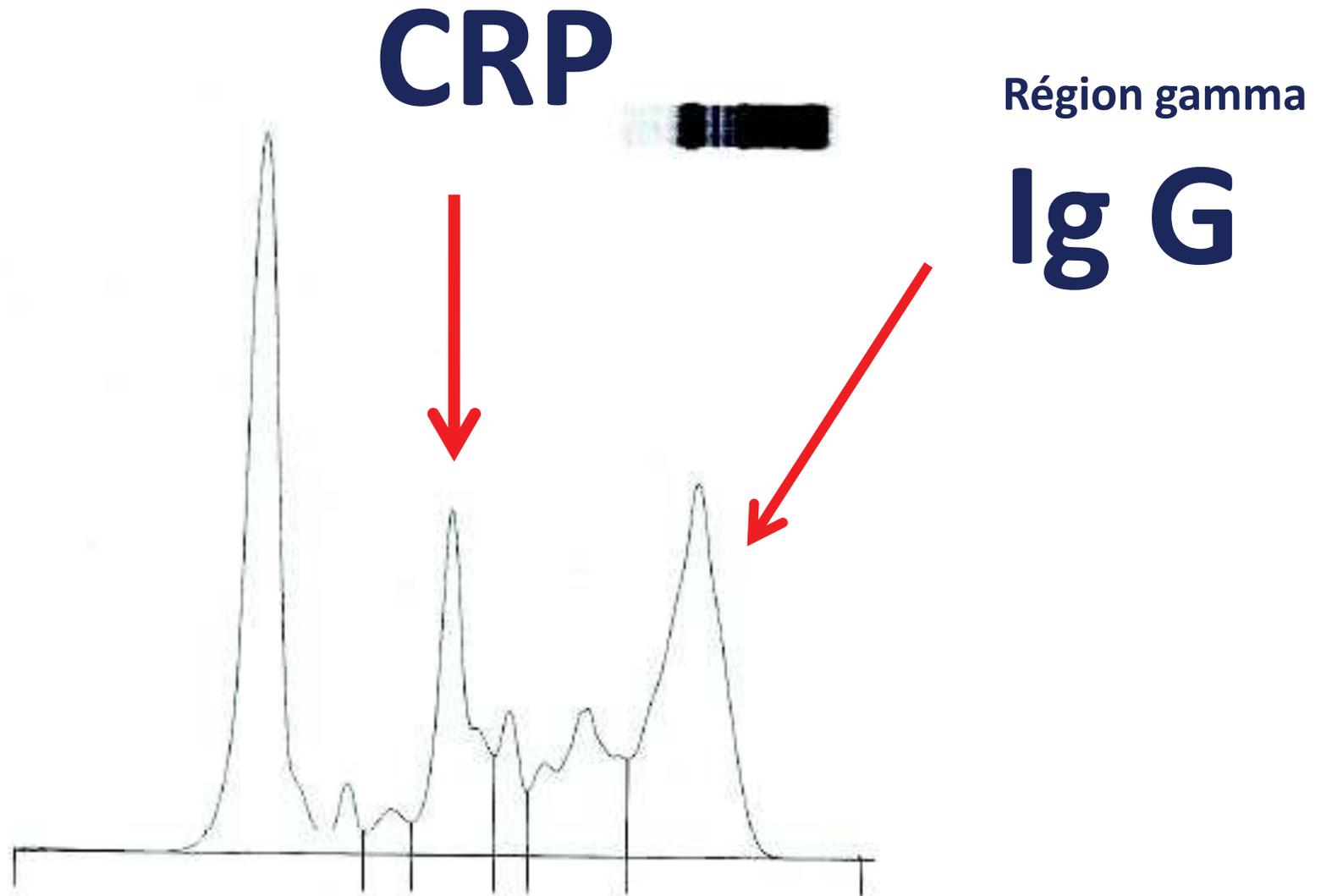
immunité
adaptative



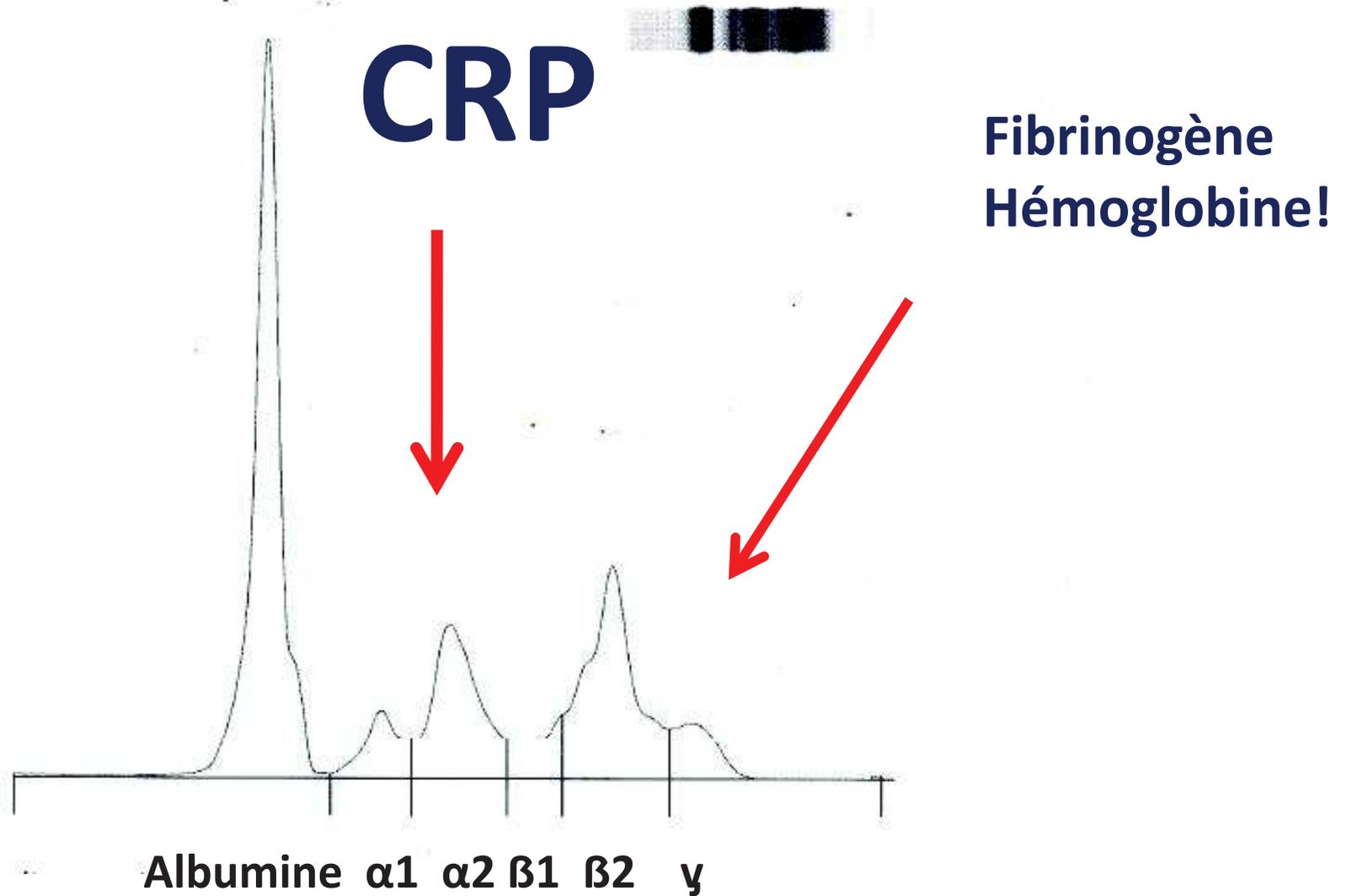
Concept d'inflammation: électrophorèse des protéines



Concept d'inflammation: électrophorèse des protéines



Concept d'inflammation: électrophorèse des protéines



Protéines de l'inflammation

- Majeure, modérée et mineure
 - Variable d'espèce.

Majeur

↑ Jusqu'à
100-1000X

Modérée

↑ 10X

TABLE 5-4 Acute Phase Protein: Major and Moderate Responders in Various Animal Species

Species	Major APP	Moderate APP
Cat	SAA	AGP, Hp
Cow	Hp, SAA	AGP
Dog	CRP, SAA	Hp, AGP, Cp
Horse	SAA	Hp
Mouse	SAA	Hp, AGP
Pig	CRP, MAP	Hp, Cp
Rat	α_2 -macroglobulin	Hp, AGP

Protéines de l'inflammation

- Amplitude de synthèse
 - Variable d'espèce.

CRP

De

IR=0.22-16.4mg/L
(VCP 2005)

À

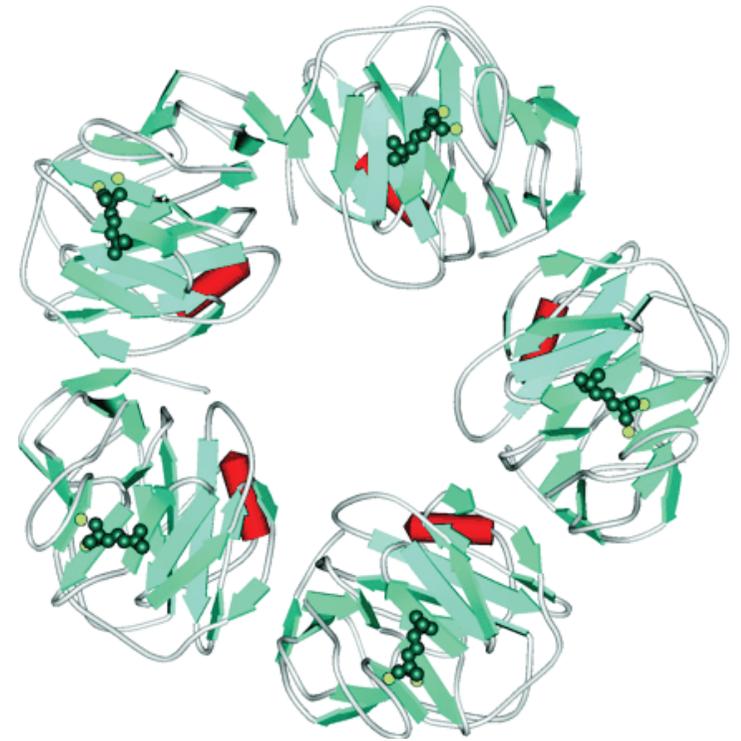
1000 mg/L

TABLE 5-4 Acute Phase Protein: Major and Moderate Responders in Various Animal Species

Species	Major APP	Moderate APP
Cat	SAA	AGP, Hp
Cow	Hp, SAA	AGP
Dog	CRP, SAA	Hp, AGP, Cp
Horse	SAA	Hp
Mouse	SAA	Hp, AGP
Pig	CRP, MAP	Hp, Cp
Rat	α_2 -macroglobulin	Hp, AGP

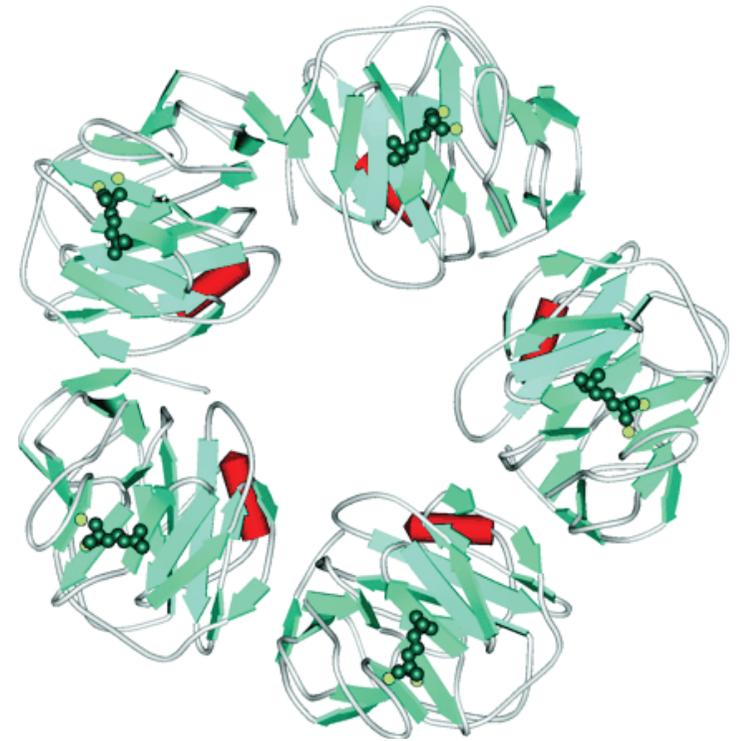
La CRP

- Pentraxine
 - 5 sous-unités
- 1981
 - Découverte
- Liaison
 - Polysaccharide C des bactéries
 - Lipides membranaires / membrane cellulaire altérée
- Active le complément par la voie classique



La CRP

- Augmentation rapide de concentration sérique
 - 4heures
 - Pic 24h : chirurgie
- Modification marquée
 - Jusqu'à 1000X



Dosage de la CRP

- Plusieurs techniques
 - Quantitative
 - Référence: **ELISA**
 - **Laboratoire ORBIO**
 - **Analyseur FUJI**
 - Qualitative/semi-quantitative
 - Peu répandu

Dosage de la CRP

- Plusieurs techniques
 - Quantitative

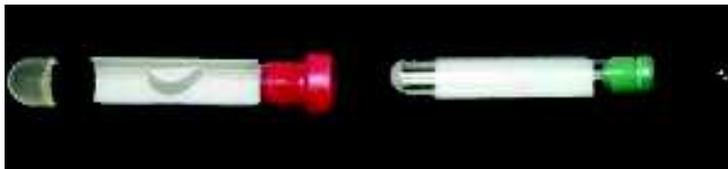
- **Laboratoire ORBIO**

*Kit CRP canin
de Life Assay®*



Dosage de la CRP

- Laboratoire ORBIO



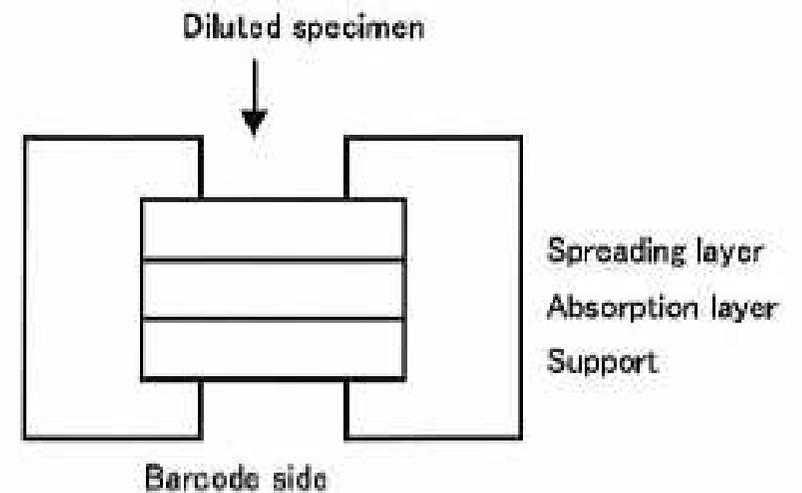
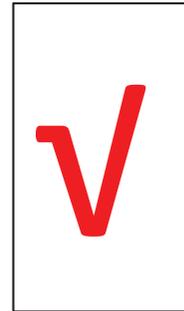
Dosage de la CRP

- Plusieurs techniques
 - Quantitative
- **Analyseur FUJI**
 - Analyseur NX500



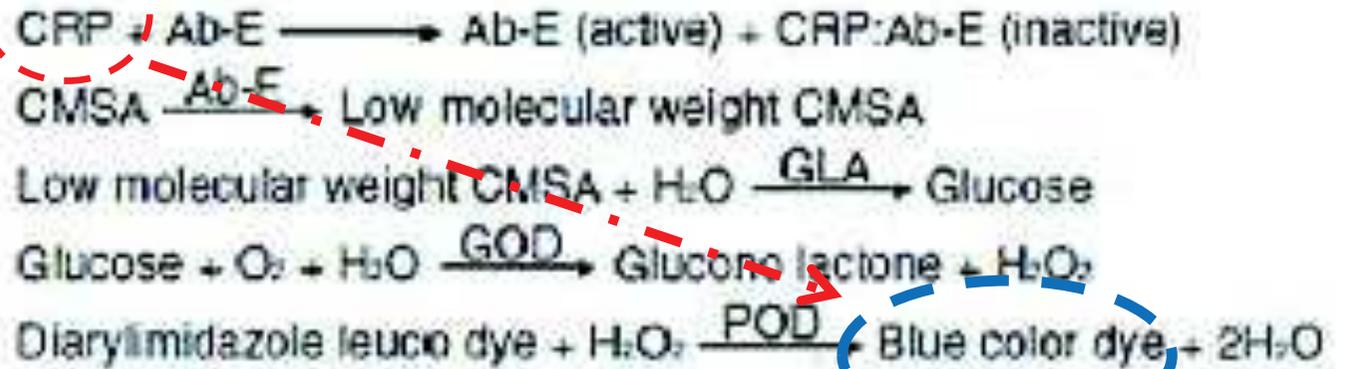
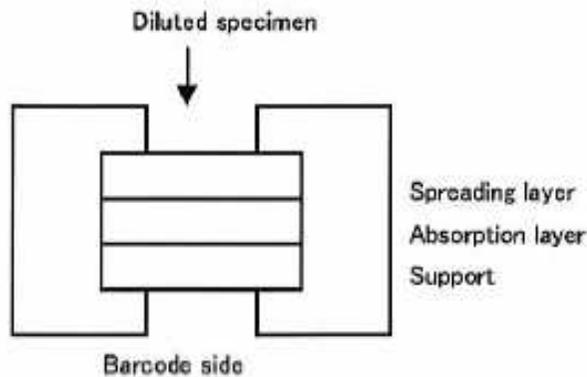
Dosage de la CRP

– Analyseur FUJI



Dosage de la CRP

– Analyseur FUJI



↑↑ absorbance

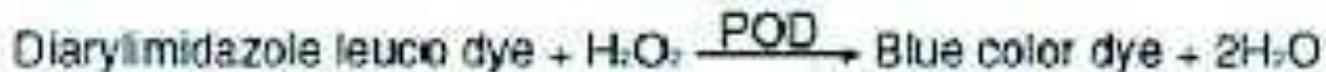
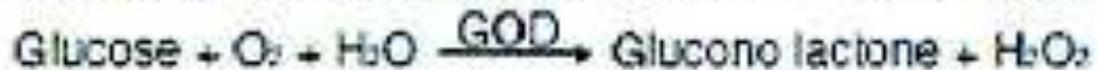
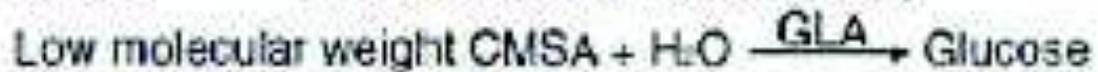
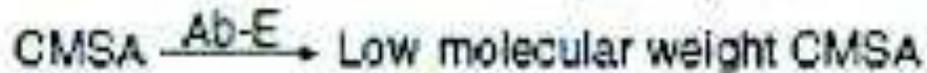
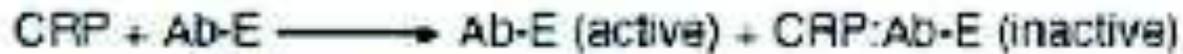
Mesure par spectrophotométrie

Dosage de la CRP

– Analyseur



Patient diabétique !
Glycémie > 3g/L



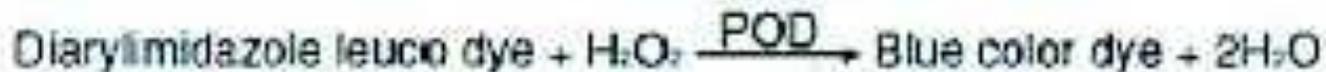
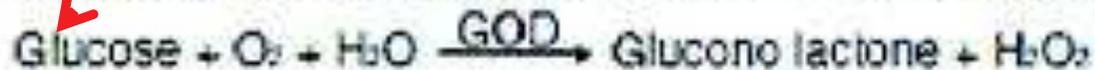
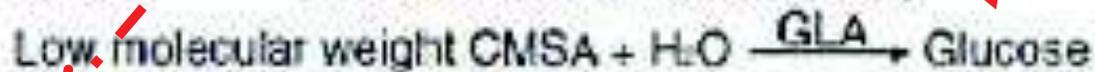
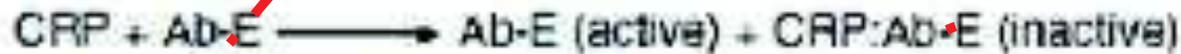
Dosage de la CRP

– FUJI



Patient diabétique !
Glycémie > 3g/L

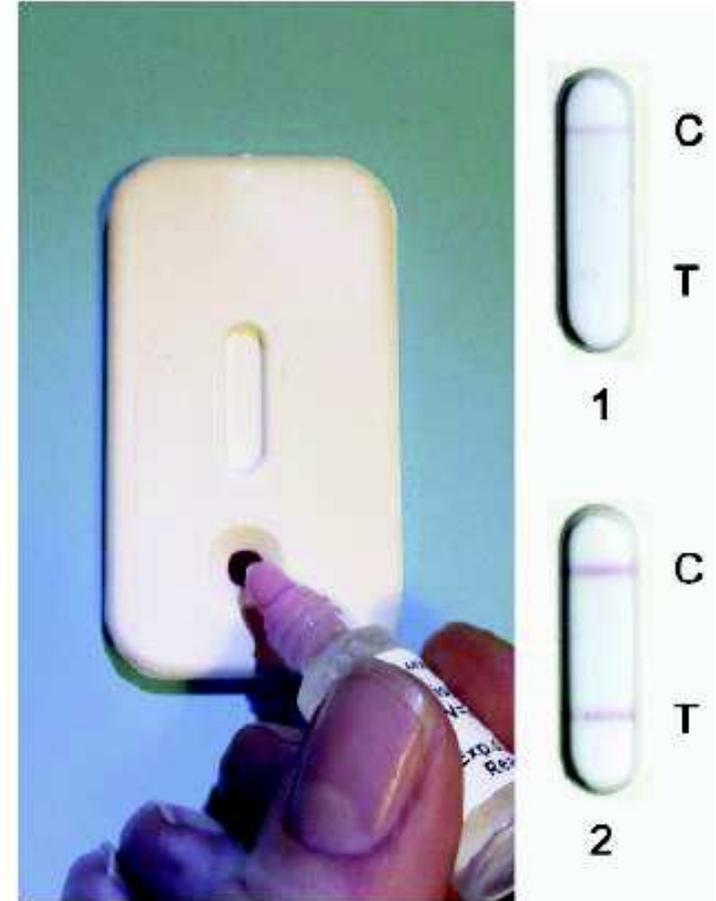
**DILUTION
SUPPLÉMENTAIRE**



Dosage de la CRP

- Plusieurs techniques
 - Qualitative/semi-quantitative
- TECOmedical Dog CRP-visual,
TECOmedical AG, Sissach, Switzerland*
- Rapide
 - Négatif (<5mg/L)
 - Positif

 - Suivi quantitatif impossible



CRP élevée ?

- Des conditions sous-jacentes variées!
 - Nature infectieuse
 - Piroplasmose, Dirofilariose, Démodécie, Leishmaniose, Pyomètre, “sepsis”.
 - Autre
 - Chirurgicale
 - Médiation immunitaire
 - Nature néoplasique

CRP élevée ? Piroplasmose

Veterinary Parasitology 144 (2007) 242–250

Evidence of an acute phase response in dogs naturally infected with *Babesia canis*

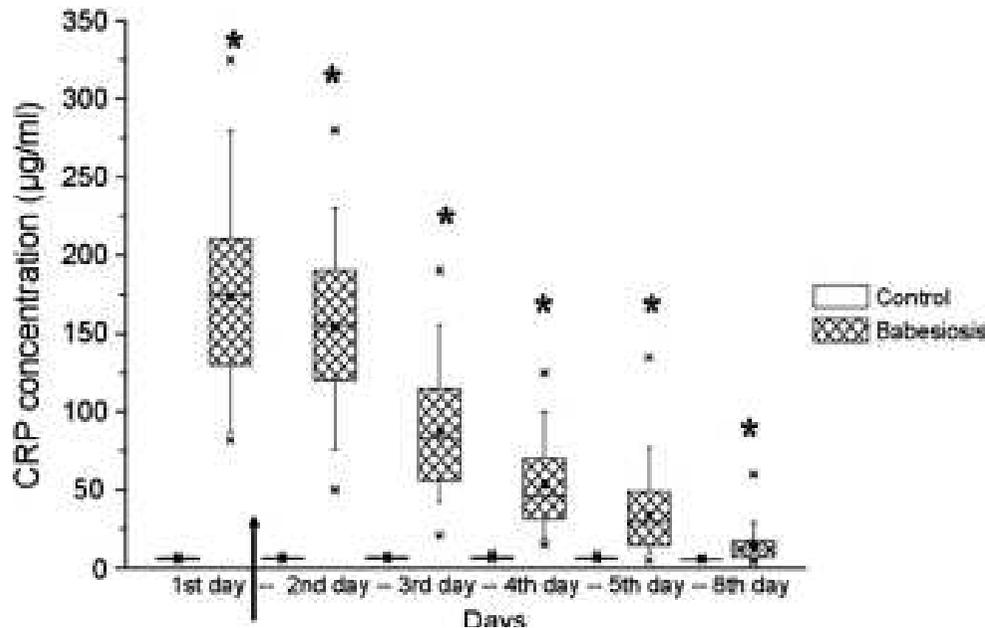
Vesna Matijatko^{a,*}, Vladimir Mrljak^a, Ivana Kiš^a, Nada Kučer^a, Jadranka Foršek^b,
Tanja Živičnjak^c, Željko Romić^d, Zoran Šimec^e, Jose Joaquin Ceron^f

J Vet Intern Med 2013;27:1172–1178

Markers of Coagulation Activation, Endothelial Stimulation, and Inflammation in Dogs with Babesiosis

R. Barić Rafaj, J. Kuleš, J. Selanec, N. Vrkić, V. Zovko, M. Zupančič, A. Trampuš Bakija,
V. Matijatko, M. Crnogaj, and V. Mrljak

Piroplasmose



Vet. Parasitol. 2007

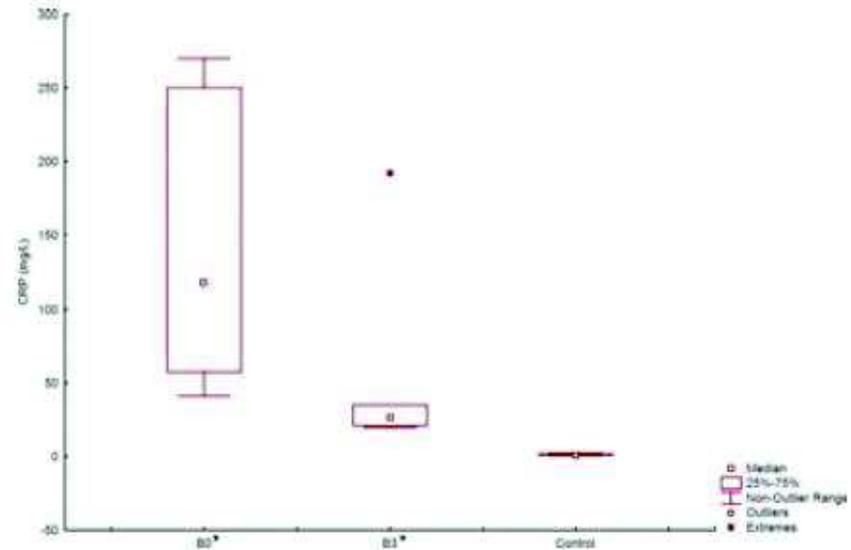


Fig 2. Concentrations of C reactive protein in babesiosis before treatment (B0) and on day 3 after treatment (B3) compared with control, healthy dogs (* $P < .01$).

JVIM 2013

DX: ≥ 150 mg/L

CRP : $\downarrow\downarrow$ après traitement mais reste (très haut) 3 jours

Approchent VR après 8 jours

CRP élevée ? Vers du cœur

Veterinary Parasitology 206 (2014) 48–54

Evaluation of C-reactive protein as a clinical biomarker in naturally heartworm-infected dogs: A field study

Luigi Venco^{a,*}, Walter Bertazzolo^a, Guglielmo Giordano^b, Saverio Paltrinieri^c

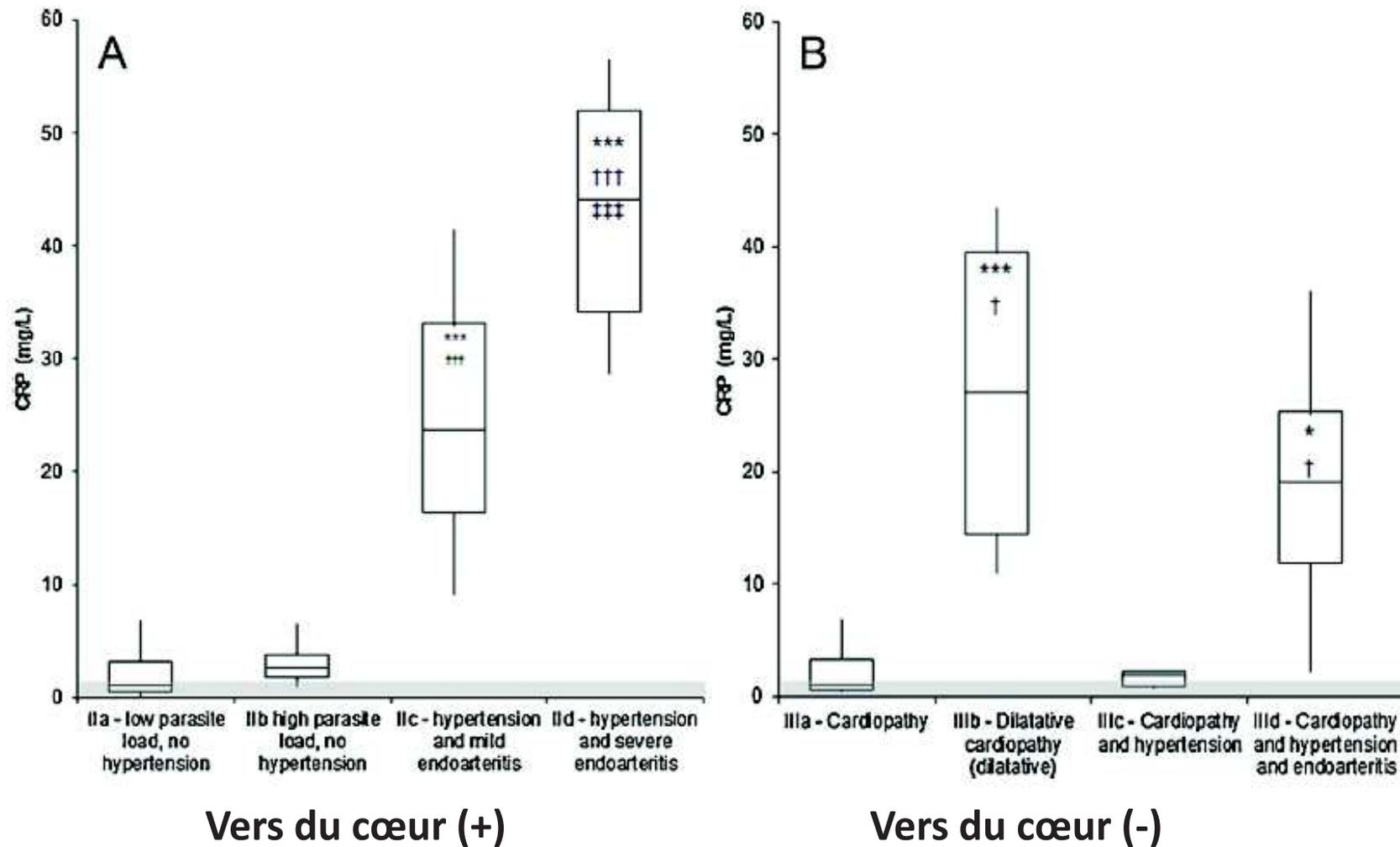
Veterinary Parasitology 209 (2015) 197–201

Acute phase protein response in heartworm-infected dogs after adulticide treatment

J.C. Méndez^a, E. Carretón^a, S. Martínez-Subiela^b, A. Tvarijonaviciute^b, J.J. Cerón^b, J.A. Montoya-Alonso^{a,*}

Dirofilaria

Veterinary Parasitology 206 (2014) 48–54



Dirofilaria

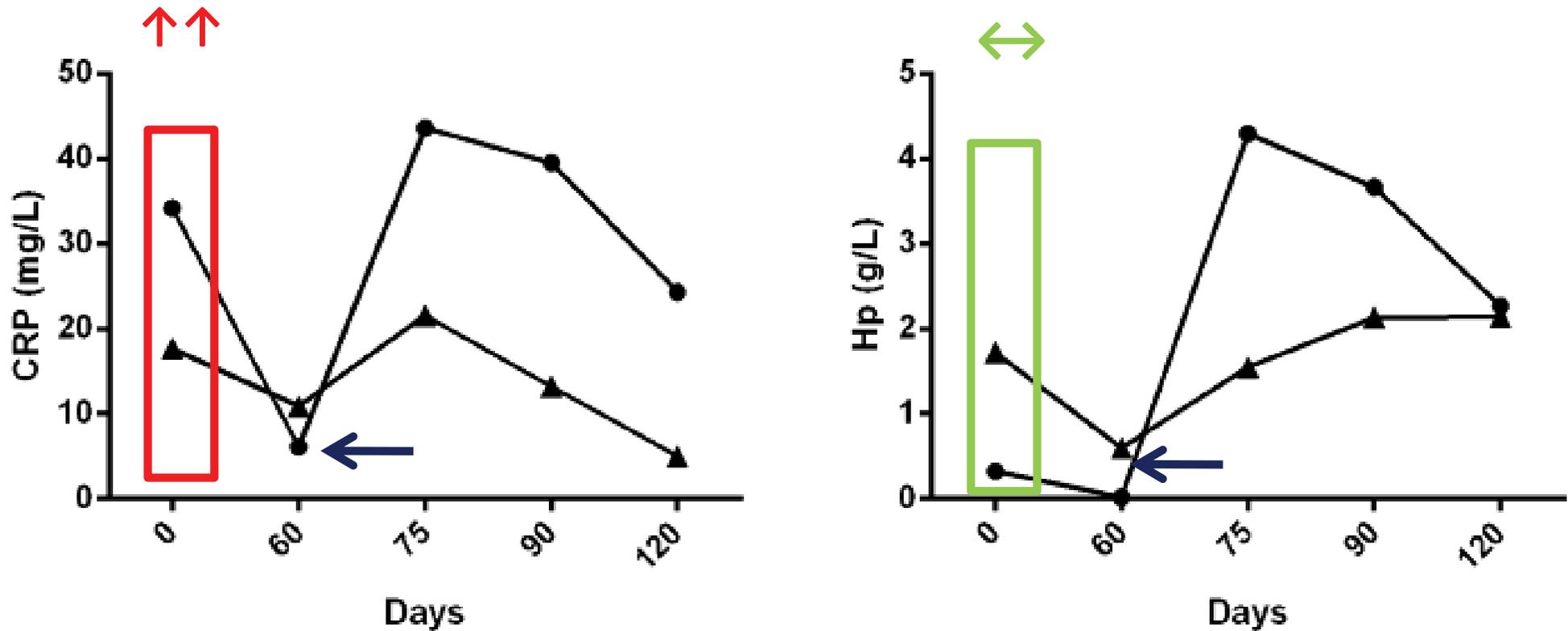


Fig. 2. Median serum C-reactive protein (CRP), haptoglobin (Hp), paraoxonase-1 (PON-1) and albumin in heartworm-infected dogs with low (▲) and high (●) parasite burden during the adulticide treatment.

Au DX: CRP +/- ↑ et Hp "normale"

Dirofilaria

***CRP n'augmente pas "à cause des vers"**

***CRP n'a pas de valeur discriminative sur la charge parasitaire**

***CRP ↑↑ à cause hypertension/artérite
= utilité comme marqueur**

DX: > 40 mg/L: compatible endocardite sévère

***CRP demeure élevée 2 mois post-TT**

Surtout charge forte : >25mg/L

CRP élevée ?

Démodicie

Vet Dermatol 2014; 25: 72–e24

DOI: 10.1111/vde.12108

Canine demodicosis: the relationship between response to treatment of generalised disease and markers for inflammation and oxidative status

Localisée:

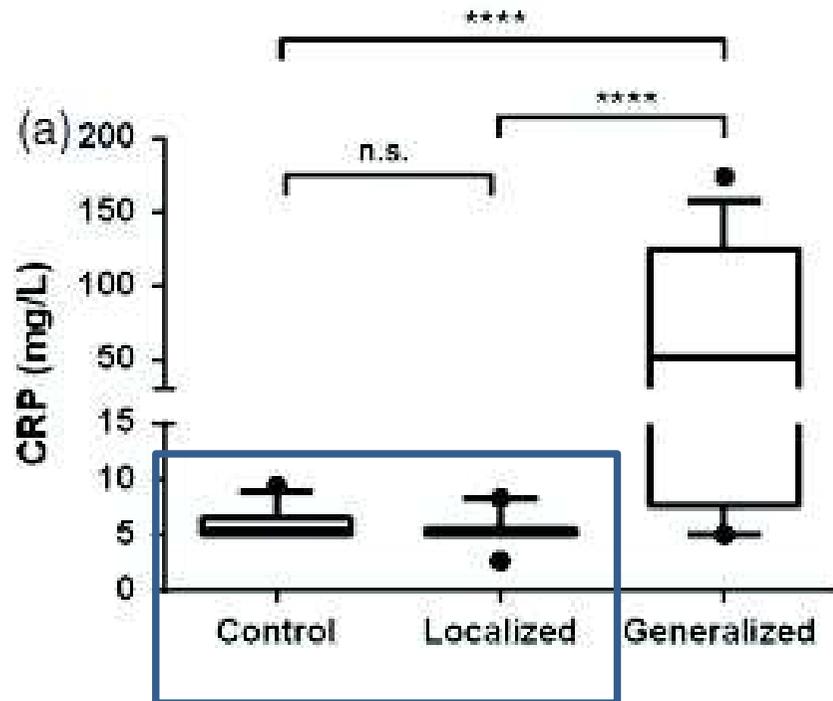
alopécie partielle face/membre; comédons; érythème.

Généralisée:

alopécie multifocale, érythème, hyperpigmentation.

+/- (podo)dermatite-folliculite-furonculose bactérienne

Démodécie



*CRP = probable marqueur utile pour différencier forme localisée vs généralisée

*Valeur élevée compatible avec une forme généralisée

DX généralisé: $\geq 50\text{mg/L}$

CRP élevée ? Leishmaniose

The **Veterinary Record**, February 23, 2002

Serum concentrations of acute phase proteins in dogs with leishmaniasis

S. MARTÍNEZ-SUBIELA, F. TECLES, P. D. ECKERSALL, J. J. CERÓN

Leishmaniose

TABLE 1: Mean (sd) serum concentrations of haptoglobin, C-reactive protein and ceruloplasmin in symptomatic and asymptomatic dogs infected by *Leishmania infantum* and control dogs

	Number tested	Haptoglobin (g/litre) Mean (sd)	N (S)	C-reactive protein (µg/ml) Mean (sd)	N (S)	Ceruloplasmin (mg/dl) Mean (sd)	N (S)
Symptomatic	30	8.8 (5.89)	29 (97)	65.03 (55.06)	28 (93)	19.06 (10.5)	27 (90)
Asymptomatic	55	8.2 (4.94)	49 (89)	30.8 (37.9)	45 (82)	16.9 (13.5)	43 (78)
Control	8	1.95 (0.84)	—	2.52 (2.0)	—	4.93 (0.62)	—

N Number of animals outside control limits (mean [2 sd] of control value), S Sensitivity (%) taking the reference limit as mean (2 sd) of control value

***Possible utilisation "discriminante" de la valeur de la CRP lors de leishmaniose clinique vs asymptomatique.**

Utilité DX pour les formes asymptomatiques

***Intégrer dans une démarche diagnostique complète.**

---> corrélation assez faible CRP vs tracé en gamma au DX.

CRP élevée? Pyomètre

Concentrations of C-reactive protein, serum amyloid A, and haptoglobin in uterine arterial and peripheral blood in bitches with pyometra

Roman Dąbrowski^{a,*}, Krzysztof Kostro^b, Marek Szczubiał^a

APP		Group I	P value (Mann-Whitney U test)	Group IIa	P value (Mann-Whitney U test)	Group IIb
CRP (µg/mL)	Uterine artery	1.19 ± 0.76 ^{a,b,*}	P = 0.00002 (group I vs. group IIa) P = 0.00006 (group I vs. group IIb)	33.53 ± 7.35 ^{aA,++}	P = 0.0007 (group IIa vs. group IIb)	44.95 ± 2.70 ^b
	Vena saphena	1.79 ± 1.39 ^{a,b}	P = 0.00002 (group I vs. group IIa)	32.44 ± 6.27 ^{aA}	P = 0.0007	48.16 ± 3.06 ^b

La valeur moyenne de CRP est différente en fonction du type de pyomètre

↑↑ significative // contrôle sain

Col ouvert: 33 mg/L

Col fermé: 48 mg/L

CRP élevée "SEPSIS"

Journal of Veterinary Emergency and Critical Care 25(5) 2015, pp 611–619

Plasma iron, C-reactive protein, albumin, and plasma fibrinogen concentrations in dogs with systemic inflammatory response syndrome

Carlos Torrente, DVM, MSc, PhD; Edgar G. Manzanilla, DVM, PhD, MPVM, DECPHM;
Luis Bosch, DVM, MSc; Laura Fresno, DVM, PhD; Montserrat Rivera del Alamo, DVM, PhD,
DECAR; Anna Andaluz, DVM, PhD; Yolanda Saco, DVM, PhD and Rafael Ruiz de Gopegui, DVM,
PhD, DECVIM

**Combinaison ↑fer sérique
 ↓CRP**

**= Probables bons marqueurs pronostiques:
à suivre simultanément**

CRP élevée ? Chirurgical _____

REVIEW

Open Access



C-reactive protein: quantitative marker of surgical trauma and post-surgical complications in dogs: a systematic review

Michelle B. Christensen^{1*} , Thomas Eriksen¹ and Mads Kjelgaard-Hansen²

CRP élevée ?

Chirurgical

1. The serum CRP concentration may deviate significantly in dogs with infectious complications post-surgery, when compared to dogs without such complications, but more evidence is needed to confirm these assumptions and to establish criteria for the differentiation of infections from normal post-surgical changes.
2. The serum CRP concentration may reflect the degree of operative trauma following different categories of surgery, but comparable studies based on comparable study designs and comparable assays for CRP measurements are needed to increase the evidence in this field.

CRP élevée ?

Maladie autoimmune

J Vet Intern Med 2014;28:905-911

Serum Biomarkers of Clinical and Cytologic Response in Dogs with Idiopathic Immune-Mediated Polyarthropathy

J.D. Foster, S. Sample, R. Kohler, K. Watson, P. Muir, and L.A. Trepanier

CRP basale des malades = ↑↑ (76.7 -195 mg/L)

↓↓ significative à 2 semaines (<6.3-48 mg/L)

Retour "normal" à 4 semaines (<6.3-24 mg/L)

Très bonne corrélation CRP/comptage cellulaire

CRP élevée ?

Maladies néoplasiques

- CRP augmentée
- Le moins de corrélation DX ou pronostique

CONCLUSION

CRP élevée ?

- Chien malade !
 - **Très sensible**
 - inflammation
 - **Peu spécifique**
 - Processus sous-jacent
 - Interpréter
 - Contexte clinique
 - Tableau biologique
 - Leucogramme
 - EP
 - Autre: sérologie, PCR, ABgramme, etc



Références

- Acute phase proteins in dogs and cats: current knowledge and future perspectives. *Vet. Clin. Path.* (2005)
- Serum concentrations of acute phase proteins in dogs with leishmaniasis. *Vet. Rec.* (2002)
- Evidence of an acute phase response in dogs naturally infected with *Babesia canis*. *Vet. Parasitol.* (2007)
- Markers of Coagulation Activation, Endothelial Stimulation, and Inflammation in Dogs with Babesiosis. *JVIM* (2013)
- Evaluation of C-reactive protein as a clinical biomarker innaturally heartworm-infected dogs: A field study. *Vet. Parasitol.* (2014)
- Acute phase protein response in heartworm-infected dogs after adulticide treatment. *Vet. Parasitol.* (2015)
- Iron status and C-reactive protein in canine leishmaniasis. *JSAP* (2014)
- Canine demodicosis: the relationship between response to treatment of generalised disease and markers for inflammation and oxidative status. *Vet. Dermatol.* (2014)
- Evaluation of a point-of-care test for canine C-reactive protein. *Vet. Clin. Path.* (2011)
- Plasma iron, C-reactive protein, albumin, and plasma fibrinogen concentrations in dogs with systemic inflammatory response syndrome *JVECC*(2015)
- Serum Biomarkers of Clinical and Cytologic Response in Dogs with Idiopathic Immune-Mediated Polyarthropathy. *JVIM* (2015)