Clinical uses of Acute Phase Proteins in Veterinary Diagnostics

Introduction

The use of acute phase proteins (APPs) in veterinary diagnostics has been subjected to much discussion over recent years. The tests are very sensitive, reproducible and cost effective, yet they have failed to become a routine tool in diagnosing and monitoring disease in small animals. In human medicine the C Reactive Protein (CRP) test is one of the most commonly requested assays by physicians, where it is used as a broad spectrum test for inflammation and to monitor if anti-inflammatory drugs are working effectively. Despite CRP playing a similar role in the dog, to date it has not been used widely in veterinary medicine. APPs are highly sensitive indicators of inflammation but they do lack specificity. It is likely that the lack of specificity plus the fact that APP testing has been suggested for a bewildering range of applications has resulted in the tests being underutilised in the veterinary clinic. However, APP testing can be very useful when employed in the right situations. This application note has therefore been prepared to summarise the key areas where the CRP test can offer significant clinical value in canine health.

The Role of CRP in Canine Physiology

CRP is produced in the liver in response to inflammatory stimuli resulting from tissue damage and/or infections. The function of CRP is to bind a range of molecules that are released or present during inflammation, such as cell fragments, bacteria, chromatin and polycations. When the inflammatory cells (e.g. macrophages or granulocytes) are activated by these inflammatory stimuli, the acute phase response is triggered and cytokines e.g. interleukin 6 (IL-6), IL-8, IL-1 and TNF-alpha are released from the inflammatory cells, with IL-6 being the most prominent. These cytokines then induces an enhanced CRP-production in the liver within about 4-6 hours. If the inflammation ceases, the CRP concentrations in the blood peak within 48 hours and then return to normal level within 1-2 weeks.

Any change in CRP indicates a change in the inflammatory burden affecting the subject. CRP is present in the blood at very low concentrations in healthy individuals, often below 5 mg/L, but rises to very high concentrations during ongoing inflammation, even above 600 mg/L, depending on the severity of the inflammatory process, e.g. bacterial infections.
Monitoring Disease

Since CRP levels respond rapidly to inflammatory stimuli, serum concentrations are being used to provide a sensitive measure of disease severity and recovery. Reductions in serum CRP values have therefore been used to indicate that:

- the intensity of the inflammatory disease is decreasing naturally,
- an infection is responding to antibiotic therapy,
- an inflammatory disease is responding to steroid therapy,
- the post-operative condition period is free from complicating infections.

Specific Applications:
Although measurement of CRP and other APPs have been proposed for a wide range of applications in veterinary medicine, there are scenarios where the tests are better suited to clinical evaluation. Some of the most valuable are discussed below.

**Inflammatory Bowel Disease**
Inflammatory Bowel Disease (IBD) occurs when the intestine becomes chronically infiltrated by inflammatory cells (lymphocytes, monocytes and neutrophils). This results in diarrhoea, vomiting and weight loss. IBD can be controlled, but not cured. Control is dependent upon the proper selection of diet and medications, the correct long-term maintenance dosages, careful monitoring by veterinarian and owner, and the absence of other concurrent diseases. Even so, persistence of mild signs, or recurrence of more severe signs may occur.

CRP has consistently been found to be the most useful disease activity marker for IBD in human patients.\(^1,^2\) In humans, serum CRP concentrations correlate with disease activity and histologic inflammation and are useful in predicting relapse of disease. Additionally, it has been shown that a change in serum CRP concentration is useful for assessing the efficacy of drug therapy.\(^2\)

Since the cause of canine IBD remains unknown, it represents a difficult disease to diagnose. In order to provide an objective and quantitative means of disease assessment, the clinical IBD activity index (CIBDAI), was developed and validated.\(^3\) This index uses six prominent GI signs; attitude and activity, appetite, vomiting, stool consistency, stool frequency, and weight loss. These are used to to classify the disease as clinically insignificant, mild, moderate, or severe. A study compared CRP levels with CIBDAI score and histopathologic grade and found that the measurement of serum CRP concentrations correlated with clinical disease activity.\(^4\) Since serum CRP levels are not disease specific, the greatest clinical utility of this marker in dogs with IBD would likely be in monitoring the response to treatment. The reduction in CRP levels during therapy for IBD would therefore indicate treatment efficacy and can also be used as a minimally invasive, sensitive and objective means of monitoring for disease remission and recurrence.

For these reasons, the application of CRP measurement to canine IBD has to date received the most interest in veterinary medicine.

**Monitoring infection treatment and efficacy of antibiotics**
CRP can be used to monitor the efficacy of the antibiotic treatment given for a bacterial infection.\(^5\) By taking sequential CRP measurements, during and after treatment, it is possible to determine if the selected antibiotic is effective in the patient. Failure of CRP
levels to decrease during the first 48 hours of treatment will indicate that an alternative antibiotic should be considered.

Similarly infection by parasitic canine babesiosis, CRP concentrations dropped the day following treatment, and continued to decline to normal concentrations within 1-2 weeks after start of treatment³.

**Pre and Post-operative complications**

Elevated CRP levels in an otherwise healthy dog would indicate and underlying, undetected inflammatory process. This can be due to subclinical infections or developing disease processes. Dogs with pre-operative inflammatory conditions are at greater risk of developing post-operative coagulation problems and even systemic inflammatory response syndrome (SIRS). The inclusion of CRP tests along with a pre-anaesthetic screen can therefore provide valuable information about the potential for post-operative complications. If the post-operative recovery is complicated by infections, CRP concentrations will not start to decrease as expected within three to five days. If an effective antibiotic treatment is started, the CRP concentration should then begin to normalize as the post-operative infection subsides⁷. CRP is therefore a very useful marker to monitor for post-operative complications.

**Sample and Storage Requirements**

The test is performed on serum and only 1 ml of blood taken into a serum gel tube is required.

CRP is stable during storage both in whole blood for a short period and in serum or plasma for longer time. Blood samples containing CRP can be stored overnight at 4°C, serum or plasma samples can be stored more than 2 months at -20°C and several years at -80°C.

**References**


