

C-REACTIVE PROTEIN (SEPSIS INDICATOR)

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ABSTRACT

C-reactive proteins are synthesized in the liver and the synthesis is augmented along with a rise in serum concentration in response to burn injuries or infections. The concentration of other acute-phase proteins also rises but the most noticeable increase occurs in c-reactive proteins and serum amyloid A proteins.¹

Many studies have been conducted in patients with major depressive illness, acute pancreatitis, as well as bacterial and viral meningitis. All these studies show direct correlation between sepsis and a rise in c-reactive protein level in serum.² Even Povoia-P, et al concluded that daily measurement of c-reactive protein is more sensitive than the currently used markers such as body temperature (BT) and WBC³ counts, in sepsis detection.

Sepsis is the host response to infection, which imposes another stress to the host in addition to the stress imposed by the trauma alone. This leads to a continuum of responses with increasing severity, e.g. a positive feed back phenomenon. Ultimately the patient either improves and returns to the normal stress response or continues to deteriorate rapidly.

C-REACTIVE PROTEIN

This is so named because it reacts as precipitin with the c-polysaccharide of the pneumococcus. Described originally as occurring in human serum in cases of pneumonia. It is found in any acute-phase response.

THE ACUTE-PHASE RESPONSE

There is an augmented hepatic synthesis of certain proteins and an increase in their plasma concentration, associated with inflammation whether due to burns, other injury or infection. The most startling increase occurs in c-reactive proteins and serum amyloid A protein. Haptoglobin, complement components, ceruloplasmin and fibrinogen are also raised but to a lesser degree.

Distinct and coordinated changes in the concentration of acute-phase proteins occur within 24 hours after injury. The acute-phase proteins maximize

immune responsiveness to the foreign body and repair to damaged tissues. In both non-septic and septic patients during the first 2 to 3 days after injury, there is a rise in c-reactive protein, fibrinogen, alpha-1-antitrypsin and ceruloplasmin concentrations. These concentrations return to normal in non-specific trauma patient, whereas alpha-1-antitrypsin concentration remains high. In contrast the concentrations of acute-phase proteins remain elevated in a septic patient.³⁻⁴

HEPATIC PROTEIN METABOLISM IN SEPSIS

The liver is responsible for production of the acute-phase proteins. The increased hepatic protein synthesis has been suggested to be caused by or dependent upon an increased supply of aminoacids from the peripheral tissues due to proteolysis in skeletal muscles. Despite the accelerated rate of hepatic protein synthesis during inflammation and sepsis, the mechanisms responsible for this stimulation have not only been fully elucidated. The synthesis of specific proteins is probably regulated transcriptionally during inflammation. For example, messenger RNA concentrations for the acute-phase proteins are elevated. Whereas albumin messenger RNA is decreased. The translation phase of protein synthesis pathway is also increased.

Interleukin 6 appears to be responsible for the changes in acute phase messenger RNA levels in trauma and sepsis.

THE C-REACTIVE PROTEIN TO PREALBUMIN RATIO

Pinilla-JC, et al evaluated serum c-reactive protein (CRP) and prealbumin (PALB) in critically ill patients.⁴ The CRP/PALB ratio showed a statistically significant correlation at 48 hours ($r=0.45$, $P<0.01$) and 120 hours ($r=0.53$, $p<0.01$). This ratio showed higher degree of correlation when applied to patient with a diagnosis of sepsis, multiple organ dysfunction or single organ dysfunction. The use of inflammatory markers, CRP and PALB, may be an easy inexpensive method of assessing severity of illness in the critically ill.⁸

C-REACTIVE PROTEIN AND SERUM AMYLOID A PROTEIN AS PROGNOSTIC MARKERS IN THE ELDERLY INPATIENTS.

Nogarth-MB, et al performed a prospective study on geriatric inpatients at Hammersmith Hospital. They found CRP and SAA responses were highly correlated ($r = 0.75$, $P = 0.001$) in infective and inflammatory pathology. They concluded that major elevations of the serum concentrations of CRP and SAA indicated serious disease and predicted poor outcome.⁵

ACUTE – PHASE PROTEINS IN MAJOR DEPRESSIVE ILLNESS.

Major depressive illness is associated with changes in the immune system. Berk-M, Wade AA, Kuschke RH, O'Neil; Kerr-A evaluated levels of complement components C3 and C4, c-reactive proteins and IL-6 in major depressive patients.⁶ The levels of C4, IL-6 and C-reactive proteins were significantly raised.

ACUTE PHASE PROTEINS IN ACUTE PANCREATITIS.

It is important to detect patients with severe form of pancreatitis from the mild form of the disease. Ranson and Imrie scores grade the severity of the disease but they require 48 hours for prognosis to be defined. Dujmovic F evaluated alpha-1-antitrypsin and c-reactive proteins and found an early proportionate rise of c-reactive proteins compared with alpha-1-antitrypsin. He concluded that c-reactive proteins is a good early marker and the high increased levels at the beginning point to a serious course of disease in future.⁷

ACUTE-PHASE PROTEINS IN SERUM AND CEREBROSPINAL FLUID IN THE COURSE OF BACTERIAL MENINGITIS

Paradowski M. et al carried out estimations of c-reactive proteins (CRP) alpha-1-antitrypsin (AAT), alpha-2-ceruloplasmin (CER) and alpha-2-haptoglobin (HPT) in serum and in cerebrospinal fluid (CSF) in patients with bacterial meningitis and viral meningitis. They

showed that AAG and CRP determination in serum and alpha-2-ceruloplasmin in CSF are useful in differentiation between bacterial meningitis and viral meningitis. Determination of AAG, CRP and AAT in serum is a valuable monitoring marker in the course of bacterial meningitis treatment.

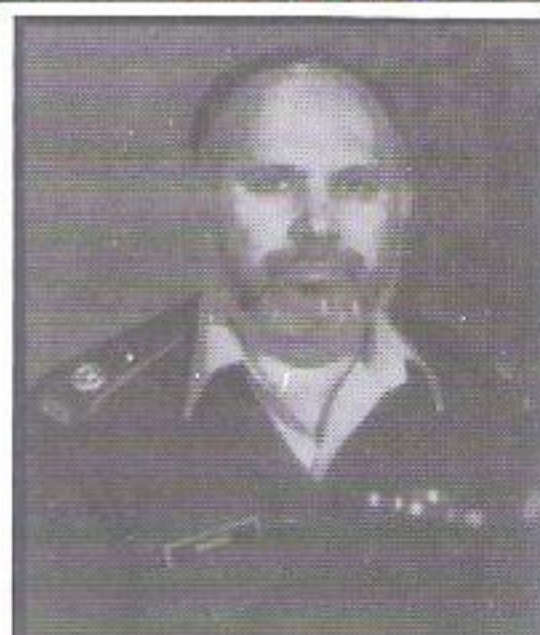
Convenience of serum sampling constitutes an advantage over traditional bacterial meningitis parameters in CSF.

CONCLUSION.

The above discussion clearly shows that CRP is a very sensitive marker of sepsis and its serum levels should be used to monitor the disease process and the effectiveness of its treatment.

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Lt Col Saleem Ahmed graduated from Army Medical College in 1983. He did his grading in anaesthesiology from AFPGMI, Rawalpindi in Sept 1987. He qualified FCPS-I in Mar 1989 and FCPS-II in April 1992. He was sent to UK for OJT in July 2000, where he got training in latest trends in anaesthesiology. He also had a chance to learn about the contemporary practice of pain management and intensive care. He has special interest in intensive care.