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Role of Acute Phase Proteins in Animal Disease diagnosis

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Introduction

The acute phase proteins (APP) are a group of plasma proteins, produced in the hepatocyte, the concentration of which varies by 25% or more during the host's response to infection, inflammation or trauma (Baumann and Gauldie, 1994). Therefore, as quantitative markers for disease they can be used for prognosis and monitoring responses to therapy, for general health screening, as well as for diagnosis of disease.

Acute phase proteins (APP) can provide a means to assess the innate immune system's response to disease and in the ability of the APP to provide a "molecular thermometer." As these proteins change their serum concentration in response to inflammation, infection, and trauma, many conditions can cause their elevation or decrease. The APP are highly sensitive for the presence of pathological lesions while having a low specificity for a particular disease. The APP are now recognized as having an important role to play in the diagnosis of diseases in animals.

The production of the acute phase proteins is stimulated by proinflammatory cytokines released into the circulation from the site of infection or inflammation. IL-6, IL-1, IL-11, TNF-α and macrophage inflammatory protein are responsible for stimulating the acute phase response. (Richards *et al.*, 1992).

Classification of APP:

Based on the level of increase or decrease by at least 25% during Acute Phase response (APR) (Eckersall and Bell, 2010)

There are major differences between species in the pathophysiological change in their concentrations during an acute phase reaction.

A) Negative acute phase proteins

Negative acute phase proteins are downregulated, and their concentrations decrease during inflammation. Negative acute phase proteins are those proteins when the level in plasma concentration is decreased lesser than 25% due to response to inflammation. The reduction occurs very fast within 24 hours or may be decreased gradually over a period of days.

Negative acute phase reactants include albumin, prealbumin, transferrin, retinol-binding protein, and antithrombin.

B) Positive acute phase proteins

Positive acute phase proteins are up regulated, and their concentrations increase during inflammation. Positive acute phase proteins are those proteins when the level in plasma concentration is increased more than 25% in response to inflammation usually during 1 to 2 days.

Positive acute phase reactants include procalcitonin, C-reactive protein, ferritin, fibrinogen, hepcidin, and serum amyloid A.

Positive acute phase proteins are again classified as major, moderate and minor depending on their magnitude of increase in the concentration (Tothova et al., 2011)

Major APPs: A major APP has a low concentration in the serum of healthy animals, often at 0.1 µ g/dl (1 µ g/liter) but with the

concentration increasing over 100 or 1000fold on stimulation, reaching a peak 24 to 48 hours after the insult and falling rapidly during recovery.

Moderate APPs: A moderate APP is present in the blood of healthy animals, but on stimulation the concentration will increase 5 to 10fold, reach a peak concentration within 2 to 3 days after stimulation, and decrease more slowly than the major APP.

Minor APPs: A minor APP shows a gradual increase and only increases in concentration by 50% to 100% of the resting level.

It has been established that there is significant variation between species in the acute phase protein profile as not all of the proteins respond in the same way in all species.

Table 1: Expression of APPs in different species of animals

Species	Major APPs	Moderate APPs	Minor APPs	Negative APPs
Dog	CRP, SAA	AGp, Hp, CP, Fb	-	Albumin, transferrin
Cat	AGp, SAA	Hp	-	Albumin, transferrin
Horse	SAA	Hp, Fb	-	Albumin
Cattle	Hp,SAA	AGP, MAP	Fb	Albumin
Sheep	Hp,SAA	AGP	Fb, Cp	Albumin
Goat	Hp,SAA	Fb, ASG	Cp	Albumin
Pigs	Hp,SAA	AGP, CRP	Fb	Albumin
Birds	Hp, SAA, OVT	AGP	MBL	Albumin

CRP: C-reactive protein; SAA: serum amyloid A; AGP: α1-acid glycoprotein; Hp: haptoglobin; Cp: ceruloplasmin; Fb: fibrinogen; ASG: acid soluble glycoprotein. Mannan binding lectin (MBL) ovotransferrin (OVT) (Veas, F, 2011)

Table 2: Acute Phase proteins in different species of Animals associated with some of the diseases (Abdullah, 2021)

Acute Phase Protein	Diseases	Species
Haptoglobin	Pneumonia, Inflammation, Sepsis	Swine
Serum Amyloid A	Pneumonia, Sepsis	Swine
C-reactive protein	Inflammation, Sepsis	Swine
α1-acid glycoprotein	Inflammation	Swine
Ceruloplasmin	Inflammation	Swine
Acid soluble glycoprotein	Inflammation	Swine
Haptoglobin	Infectious Bronchitis	Chickens
Serum Amyloid A	Infectious Bronchitis	Chickens
Lipopoly saccharides binding protein	Mastitis, Respiratory Disease	Cattle
Serum Amyloid A	Mastitis, Respiratory Disease, Amyloidosis	Bovine
Haptoglobin	Mastitis, Respiratory Disease, Amyloidosis	Bovine
α1-acid glycoprotein	Mastitis, Respiratory Disease	Bovine
Haptoglobin	Caseous lymphadenitis, Pulmonary damage	Sheep
Serum Amyloid A	Caseous lymphadenitis	Sheep
Ceruloplasmin	Pulmonary	Sheep

	damage	
Haptoglobin	Inflammation	Goat
Serum Amyloid A	Inflammation	Goat
Acid soluble glycoprotein	Inflammation	Goat

Conclusion

A wide range of diseases affected different farm animals and early diagnosis of these diseases beside the proper way for treatment of disease is essential, therefore APPs with its measurements that are widely used as disease biomarkers and for prognostication in veterinary medicine and are increasingly used in varied areas of research

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