



Københavns Universitet



## Gc globulin as a diagnostic and prognostic marker in horses

Pihl, Tina Holberg

*Publication date:*  
2008

*Document Version*  
Publisher's PDF, also known as Version of record

*Citation for published version (APA):*  
Pihl, T. H. (2008). Gc globulin as a diagnostic and prognostic marker in horses: A Ph.d. project. Poster session presented at SHARE Symposium, København, Denmark.



Institut for Produktionsdyr og Heste

# Gc-globulin as a diagnostic and prognostic marker in horses

- A PhD. project

Tina Holberg Pihl<sup>1</sup>, Stine Jacobsen<sup>1</sup>, Gunnar Houen<sup>2</sup>, Pia Haubro Andersen<sup>1</sup>.

<sup>1</sup>Large Animal Surgery, Dep. of Large Animal Sciences, Faculty of Life Sciences, University of Copenhagen,

<sup>2</sup>Department of Research and Development, Statens Serum Institut, Copenhagen

## Resumé

Gc-globulin is a serum protein, which is significantly reduced shortly after tissue injury in humans and laboratory rodents. A low serum concentration of Gc-globulin can therefore be used as a diagnostic and prognostic marker in patients with trauma, sepsis and liver failure. This Ph.D. project will investigate Gc-globulin in horses and evaluate the concentration in horses with acute abdominal pain.

## Introduction

Group specific (Gc) globulin also known as vitamin D-binding protein is part of the extracellular actin-scavenging system that removes actin from the circulation (Lind et al., 1986). Actin is an intracellular structural protein, which is released to blood in patients with tissue injury and cell death. Circulating actin forms filaments, which cause microthrombi and endothelial injury. These effects of circulating actin are extremely harmful, and high levels of free actin are potentially lethal (Haddad et al., 1990; Erukhimov et al., 2000). Gc-globulin binds to actin and removes it from the circulation via the reticuloendothelial system (Figure 1).

Plasma concentrations of Gc-globulin decrease shortly after conditions causing tissue injury and cell death, for example physical trauma (Figure 2) (Dahl et al., 2001), sepsis (Lee et al., 1989), experimentally induced endotoxemia (Watt et al., 1989) or liver failure (Schjødt et al., 2007). In humans, decreases in Gc-globulin levels are observed within 60 minutes after trauma (Dahl et al., 1998).

Studies in humans and laboratory rodents have shown that very low concentration of plasma Gc-globulin are related to an increased risk of developing shock and lethal complications of trauma (Figure 3) (Dahl et al., 1999). Gc-globulin is thus a prognostic marker in intensive care medicine.

It has been suggested that treatment with Gc-globulin to patients with severe tissue injury can prevent development of shock and thereby increase survival chances (Vasconcellos & Lind, 1993). The in vivo toxicity of Gc-globulin infusion is currently being investigated in horses and other species.

Gc-globulin has been demonstrated in horse plasma and its structure closely resembles that of human Gc-globulin (Robinson & Burtneck, 1992). Gc-globulin concentrations in horses under clinical conditions have never previously been investigated.

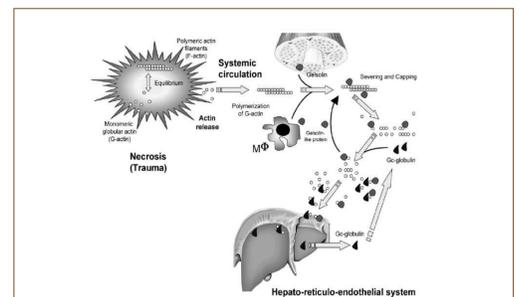


Figure 1. The Actin Scavenging System. Gc-globulin removes actin from the circulation, after cell injury.

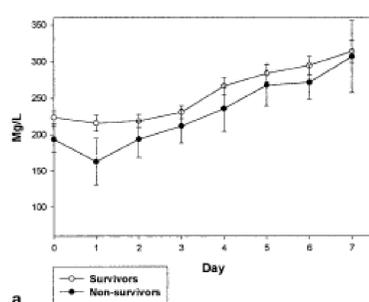


Figure 2. Concentration of Gc-globulin in survivors and non-survivors after severe trauma (Dahl et al., 2001)

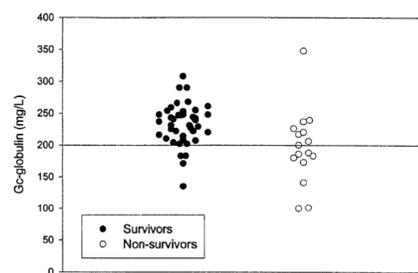


Figure 3. Gc-globulin concentration at admission in 57 multiple trauma patients (Dahl et al 1999).

## Ph.d. project

The Ph.D. project focuses on Gc-globulin as a prognostic marker in horses with acute abdominal pain.

Acute abdominal pain (colic) has a high frequency in horses and is one of the most frequent reasons for a horse to die or be euthanized (Hillyer et al., 2001; Tinker et al., 1997). Impactions and intestinal strangulations are the most common causes of colic. When an intestine is strangulated ischemia of the intestine will develop and the horse needs acute surgery to survive. Many horses do not survive the surgery because they develop shock or sepsis.

### Goal

To assess the usefulness of acute phase proteins (Serum Amyloid A (SAA), haptoglobin, fibrinogen, Intestinal fatty acid binding protein (I-FABP), and Gc-globulin) for predicting the need for surgery and the prognosis of horses with acute abdominal pain.

### Hypothesis

Low Gc-globulin concentration and high SAA, haptoglobin, fibrinogen and I-FABP in plasma and peritoneal fluid correlates with the extent of intestinal ischemia, the need for surgery and survival rate of the horse.

## Methods

1. Development and validation of an assay for measuring equine Gc-globulin.
2. Assessment of Gc-globulin concentration in plasma and peritoneal fluid in healthy horses.
3. Comparison of the acute phase protein concentrations and the need for surgery and survival rate by collection of blood and peritoneal samples of 100 horses with acute abdominal pain referred to the University Hospital for Large Animals (KU-LIFE).
4. Assessment of acute phase protein concentrations and kinetics in plasma and peritoneal fluid in horses with induced intestinal ischemia under general anaesthesia.



## References

- Dahl B, Schjødt FV, Kiær T, Ott P, Bondesen P, Tygstrup N. Serum GC-globulin in the early course of multiple trauma. *Crit Care Med* 1998; (26): 285-289.
- Dahl B, Schjødt FV, Nielsen M, Kiær T, Williams JG, Ott P. Admission level of Gc-globulin predicts outcome after multiple trauma. *Injury*, 1999; (30): 275-281.
- Dahl B, Schjødt FV, Gehrchen PM, Ramlau J, Ott P. Gc-globulin is an acute phase reactant and an indicator of muscle injury after spinal surgery. *Inflamm Res* 2001; (50): 39-43.
- Erukhimov JA, Tang Z, Johnson BA, Donahoe MP, Razzack JA, Gibson KF, Lee WM, Wasserloos KJ, Watkins SA, Pitt BR. Actin-containing sera from patients with adult respiratory distress syndrome are toxic to sheep pulmonary endothelial cells. *Am J Respir Crit Care Med* 2000; (162): 288-294.
- Haddad JG, Harper KD, Gouth M, Pietra GG, Sanger JW: Angiopathic consequences of saturating the plasma scavenger system for actin. *Proc natl acad sci USA* 1990; (87): 1381-1385.
- Hillyer MH, Taylor FGR, French NP, A cross-sectional study of colic in horses on thoroughbred training premises in the british isles in 1997. *Eq vet j*, 2001, (33), 380-385..
- Lee WM, Reines D, Watt GH, Cook JA, Wise WC, Halushka PV, Galbraith RM: Alterations in Gc levels and complexing in septic shock. *Circ shock* 1989; (28): 249-255.
- Lind SE, Smith DB, Janmey PA, Stossel TP. Role of plasma gelsolin and the vitamin d-binding protein in clearing actin from the circulation. *J Clin Invest* 1986; (78): 736-742.
- Robinson RC, Burtneck LD. Stabilization of the structure of horse plasma vitamin D binding protein by disulfide bonds. *Biochem Cell Biol* 1992; (70): 10-15.
- Schjødt FV, Bangert K, Shakil AO, McCashland T, Murray N, Hay JE, Lee WM, predictive value of actin-free Gc-globulin in acute liver failure. *Liver transpl* 2007;(13): 1324-1329.
- Vasconcellos CA & Lind S. Coordinated inhibition of actin-induced platelet aggregation by plasma gelsolin and vitamin d-binding protein. *Blood* 1993; (82): 3648-3657.

