SERUM CONCENTRATIONS OF TUMOUR NECROSIS FACTOR IN DOGS NATURALLY INFECTED WITH *BABESIA CANIS* AND ITS RELATION TO SEVERITY OF DISEASE

by

Tarquin Vaughan-Scott

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Résumé

Canine babesiosis, caused by the tick-borne protozoan *Babesia canis rossi*, is an economically important and potentially fatal disease of dogs in South Africa. The host's response to many infectious diseases is mediated (at least in part) by intercellular messengers called cytokines. One of the most important cytokines released is tumour necrosis factor (TNF).

A study was designed to measure serum concentrations of TNF in dogs naturally infected with canine babesiosis and to relate TNF concentrations to clinical severity, mortality, rectal temperature and parasitaemia.

There was a statistically significant difference in TNF concentrations between groups of differing disease severity, with a general trend of increasing mean log(TNF) with increasing severity of disease. A noteworthy finding was that dogs with hypoglycaemia had very high TNF (mean 15.03 ng/ml compared to a mean of 2.32 ng/ml for other sick dogs without hypoglycaemia). When TNF values were compared between survival and non-survival groups, there was no significant difference. The rectal temperature of the dogs in this study did not show any statistically significant association with TNF concentrations. When parasitaemia and TNF were examined within groups of infected dogs, there was no significant relationship. However, when the sample size was increased by pooling all infected dogs and treating them as a single group, there was a highly significant positive correlation ($p = 0.003$) between parasitaemia and serum TNF concentrations.

The results of this study were encouraging and indicate that canine babesiosis may share a similar pathophysiology with human malaria in terms of TNF being associated with disease severity. One of the most significant findings in this study was the presence of very high TNF values in two of three dogs with hypoglycaemia. Hypoglycaemia has not been previously recorded in dogs with babesiosis and is a potentially important finding particularly in view of the hypoglycaemia associated with malaria in humans. Malarial hypoglycaemia is correlated with a higher mortality in humans, especially in pregnant women and children. If the findings of this study can be

confirmed and expanded, they may lend further support to the use of canine babesiosis as a model for some of the problems encountered in human malaria research.

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List of Abbreviations

ALP = alkaline phosphatase

ALT = alanine transaminase

ANOVA = analysis of variance

CNS = central nervous system

EDTA = ethylenediaminetetraacetic acid

ELISA = enzyme-linked immunosorbent assay

IFN-γ = interferon-gamma

IL-1 = interleukin-1

IL-6 = interleukin-6

MODS = multiple organ dysfunction syndrome

mRNA = messenger ribose nucleic acid

mTNF = membrane expressed tumor necrosis factor

MTS = 3-[4,5-dimethylthiazole-2-yl]-2,5-diphenyltetrazolium bromide

NCPO = non-cardiogenic pulmonary oedema

NF-κβ = nuclear factor kappa beta

OVAH = Onderstepoort Veterinary Academic Hospital

PaO_2 = partial pressure of oxygen within the pulmonary artery

PAO_2 = partial pressure of oxygen within the alveoli

PO = pulmonary oedema

rcTNF = recombinant canine TNF

SIRS = systemic inflammatory response syndrome

sTNF = soluble tumor necrosis factor

sTNFR = soluble tumor necrosis factor receptors

TNF = tumor necrosis factor

$TNFR_I$ = TNF receptor I

$TNFR_{II}$ = TNF receptor II