

# Cytokines and the acute phase response in post-treatment reactive encephalopathy of *Trypanosoma brucei brucei* infected mice

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Stimulation of the acute phase response during infection of mice with *Trypanosoma brucei brucei* (*T. b. brucei*) was investigated in an experimental model of the post-treatment reactive encephalopathy (PTRE), a common side-effect of anti-trypanosome therapy. Plasma levels of the acute phase proteins (APP), haptoglobin (Hp) and serum amyloid P (SAP) increased by day 7 post-infection, but by day 20 had fallen to an intermediate level. This was accompanied by induction of the cytokines, interleukin (IL)-6 and tumour necrosis factor- $\alpha$  (TNF $\alpha$ ) in both liver and brain. Treatment of mice on day 21 with a subcurative dose of diminazene aceturate (Berenil®), a procedure known to induce a mild PTRE, cleared the parasite from the circulation with plasma APP and liver expression of mRNA for IL-6 and TNF $\alpha$  returning to the levels in the controls. Cytokine mRNA for both IL-6 and TNF $\alpha$  was detected in the brains of animals with developing PTRE although TNF $\alpha$  was not significantly greater than in the control group. A further subcurative dose of Berenil®, leading to a more severe PTRE, was associated with elevated serum concentrations of Hp and SAP, increased TNF $\alpha$  mRNA in the liver and detectable IL-6 and TNF $\alpha$  mRNA in the brain. mRNA for IL-1 $\beta$  was expressed in brain and liver samples from all animals. A severe PTRE caused a systemic acute phase response which was not apparent with a mild PTRE. The pattern of cytokine mRNA induction was similar following both drug treatments. However, the difference in APP production could be caused by a breakdown in the blood–brain barrier during severe PTRE allowing cytokine synthesised in the brain to enter the circulation and maintain a systemic response.

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