## **SUMMARY OF THESIS\***

TEIXEIRA Jr., Antônio Lúcio – Desnervação autonômica cardíaca na tripanosomíase americana experimental em ratos: resposta funcional a neurotoxinas. Belo Horizonte, 2000. (Dissertação de mestrado – Instituto de Ciências Biológicas da Universidade Federal de Minas Gerais)

## AUTONOMIC DENERVATION IN THE EXPERIMENTAL AMERICAN TRYPANOSOMIASIS IN RATS: FUNCTIONAL RESPONSE TO NEUROTOXINS

A well documented feature of Chagas disease is an extensive reduction in number of neuronal cell bodies in cardiac parasympathethic ganglia, and oesophageal and colonic myenteric plexus. This autonomic denervation has been suggested to play a role in the development of the late manifestations of Chagas disease, i.e. dilated cardiomyopathy, megacolon and megaoesophagus. Severe cardiac autonomic denervation also occurs in the acute experimental American trypanosomiasis in rats. The present study aims at verifying whether this denervation, as demonstrated histochemically, was accompanied by impairment of heart function, as assessed by the chronotropic response to the scorpionic (*Tityus serrulatus*) crude venom in the isolated rat heart preparation.

The venom extracted from the scorpion *Tityus serrulatus* contains potent neurotoxins that activate sodium channels in neuronal terminals leading to the release of the mediators acetylcholine and noradrenaline. We have shown that activation of isolated heart preparation (Langendorff's) with *T. serrulatus* venom induces a marked rhythm alteration characterised by significant early bradycardia followed by tachycardia which were blocked by muscarinic and  $\beta_1$ -adrenoceptor antagonists, respectively. Thus, *T. serrulatus* venom is a useful tool to evaluate chronotropic response of adrenergic and cholinergic nerve terminals in isolated rat heart preparation.

In control hearts, the venom induced significant bradycardia (73% decrease in heart rate) followed by tachycardia (10% increase in heart rate). In infected animals, despite the severe (sympathetic) or moderate (parasympathetic) cardiac denervation, the venom provoked similar bradycardia (63% decrease), but the tachycardia was higher (50% increase). The basal heart rate of infected animals (164  $\pm$  15 bpm, beats per minute) was significantly lower compared to control rats (213  $\pm$  13 bpm). Atropine prevented this lower rate in infected animals. Our results demonstrated minor cardiac sympathetic dysfunction with sparing of the parasympathetic function.

Altogether, our present and previous studies in rats, and the evidence of progressive autonomic denervation in chronic chagasic cardiomyopathy favour the notion that autonomic denervation may be a consequence and not the cause of the chronic Chagas heart disease.

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