

to the seventh generations of the two strains. The results were compared with those obtained on renal hypertensive rats.

These substances had about the same effect in rats on normal diet and on high salt diet, but most of them appeared more active in renal hypertensive rats than in rats with hereditary hypertension.

REFERENCES

- DAHL, L. K. & SCHACKOW, E. (1964). Effects of chronic excess salt ingestion: experimental hypertension in the rat. *Can. med. Ass. J.*, **90**, 155–160.
SMIRK, F. H. & HALL, W. H. (1958). Inherited hypertension in rats. *Nature, Lond.*, **182**, 727.

Cardiac effects of thyroxine

A. S. F. ASH, E. LARBI†, LUCIENNE PAPADAKI‡ and ELEANOR ZAIMIS*, *Department of Pharmacology, Royal Free Hospital School of Medicine, London, W.C.1, England*

Recent results suggested that the cardiovascular changes in thyroxine-treated animals may not be the result of an increased sensitivity of the cells to the catecholamines (Zaimis, Metaxas, Harvard & Campbell, 1965; Van der Schoot & Moran, 1965; Buccino, Spann, Pool, Sonnenblick & Braunwald, 1967). In the present study cats were treated with thyroxine, 0.3 mg/day for 12–16 weeks and guinea-pigs with 0.025 mg/day for 7–15 weeks. Guinea-pigs were more affected than cats. The myocardium of the thyroxine-treated animals showed an increase in excitability even before the appearance of tachycardia and an increased sensitivity to vagal stimulation.

Thyroxine treatment produced significant mitochondrial ultrastructural changes; the most striking feature was a mitochondrial pleomorphism (Fig. 1). Many of the mitochondria were enlarged and assumed a variety of abnormal shapes. Measurements of mitochondrial areas showed that there was a 9-fold increase in enlarged mitochondria in the thyroxine-treated cats, and a 7-fold increase in the guinea-pigs.

In heart mitochondria isolated from thyroxine-treated animals, there was an apparent increase in the overall activity of the electron transport chain and the capacity of mitochondria for oxidative phosphorylation. For example, with succinate as substrate, there was an increase in basal rates of respiration as well as in respiration stimulated by adenosine diphosphate. Mitochondrial respiration was measured by means of an oxygen electrode.

It is suggested that in thyroxine-treated animals a cell membrane alteration has taken place, possibly as a result of inhibition of active transport.

† W.H.O. Fellow. ‡ Muscular Dystrophy Fellow.

REFERENCES

- BUCCINO, R. A., SPANN, J. F., JR., POOL, P. E., SONNENBLICK, E. H. & BRAUNWALD, E. (1967). Influence of the thyroid state on the intrinsic contractile properties and energy stores of the myocardium. *J. clin. Invest.*, **46**, 1669–1682.
VAN DER SCHOOT, J. B. & MORAN, N. C. (1965). An experimental evaluation of the reputed influence of thyroxine on the cardiovascular effects of catecholamines. *J. Pharmac. exp. Ther.*, **149**, 336–345.
ZAIMIS, E., METAXAS, N., HARVARD, C. W. H. & CAMPBELL, E. D. R. (1965). Cardiovascular and skeletal muscle changes in cats treated with thyroxine. In *Research in Muscular Dystrophy. Proc. Third Symposium*, ed. Members of the Research Committee of the Muscular Dystrophy Group, pp. 301–311. London: Pitman Medical Publishing Co. Ltd.

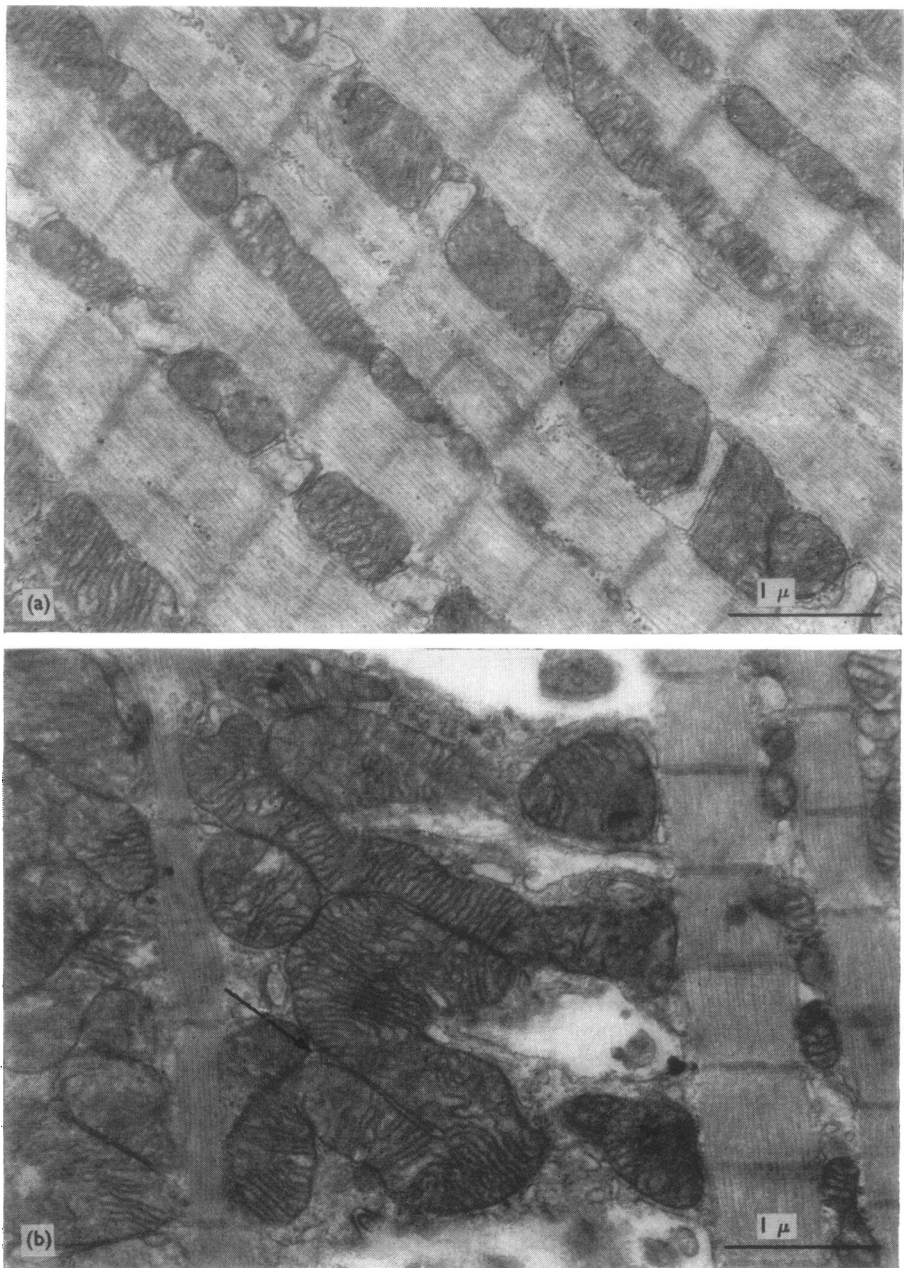


FIG. 1. Sections through the ventricular myocardium of (a) control and (b) thyroxine-treated guinea-pig. In (b) two abnormal mitochondria are seen, one of which is greatly enfolded (arrow).