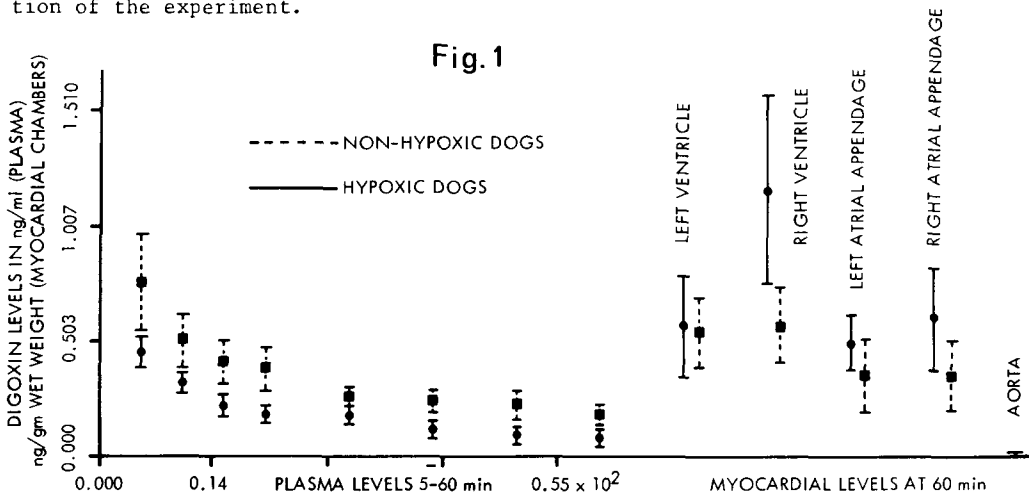


## DIGOXIN PLASMA AND MYOCARDIAL LEVEL CORRELATION IN HYPOXIC DOGS

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The fact that hypoxia may enhance the toxicity of digitalis is well reported (Aronson & Grahame-Smith, 1976). However, few systematic and controlled studies have been carried out to document this hypothesis. A study by Harrison *et al.* (1968) on patients indicated that during hypoxia (average  $\text{PaO}_2 = 44$  mm Hg), 19% less acetylstrophanthidin was required to produce ventricular tachycardia. Doherty *et al.* (1967) reported that in humans there was a constant relationship between plasma and total myocardial digoxin concentration and hence inotropic effect. Against this background an investigation was carried out to observe the effect of hypoxia on plasma and myocardial digoxin levels.

14 greyhounds of either sex were anaesthetized with pentobarbitone sodium (30 mg/kg) and then artificially respired; six with room air ( $\text{PaO}_2 = 90 \pm 3.8$  mm Hg, weight  $22 \pm 2.0$  kg, age  $23 \pm 5.4$  months) and eight with varying  $\text{O}_2/\text{N}_2$  mixtures using a modified Boyles apparatus to produce hypoxia ( $\text{PaO}_2 = 57 \pm 2.1$  mm Hg, weight  $23 \pm 1.4$  kg, age  $25.7 \pm 3.9$  months). Arterial pressure and ECGs on lead II and III were recorded on a Devices M19 recorder and used to indicate the time of peak inotropic effect. Blood gases were recorded on a digital pH/blood gas analyser. Following 90 minutes stabilization in either the hypoxic or non-hypoxic state, digoxin (0.05 mg/kg i.v.) was administered. A full biochemical screening was carried out on blood samples before administration of digoxin and on termination of the experiment.



Plasma samples were taken at 5, 10, 15, 20, 30, 40, 50 and 60 minutes at which time the dog was killed by bleeding from the femoral artery. The heart was removed and samples taken from each chamber; the digoxin was extracted as described by Goltart *et al.* (1974). Plasma and myocardial levels were measured using  $\gamma$ -Lanoxitest radio-immunoassay kit. It was observed that in hypoxia there was a lowering of plasma levels of digoxin and an increase in myocardial levels (Fig. 1). These results infer that the assumption of a constant relationship existing between plasma and total myocardial digoxin is invalid, and digoxin dosage regimens that adjust dosage according to plasma levels, without reference to  $\text{PaO}_2$  levels, may increase the risk of toxicity.

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