dibenz [*b*, *f*] oxepine has an appreciably non-planar middle ring. Its overall molecular shape closely resembles that of tricyclic analogues containing 6- and 7-membered rings, viz: phenothiazine, and dibenz [*b*,*f*] azepine.

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The effects of paracetamol on temperature and cardiovascular changes caused by pyrogenic contamination of chronically implanted arterial cannulae in the conscious, renal hypertensive cat

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The use of chronically implanted arterial cannulae to facilitate the recording of arterial pressure in conscious animals is a well established technique. The cannulae are commonly used with an arterial valve (Day & Whiting, 1972) to allow convenient connection to a pressure transducer.

We have used this technique in cats with mild, perinephritic, experimental hypertension (Page, 1939; Poyser, Shorter & Whiting, 1974). Aseptic surgical techniques were employed. PVC cannulae, sterilized overnight in 0·5% alcoholic Hibitane (ICI Ltd.), were inserted in the right carotid artery to the level of the thoracic aorta and were kept patent by injecting 2 ml of sterile heparinized (150 I.U. ml^{-1}, Pularin, Evans Medical), saline (Steriflex No. 1, Allen and Hanburys Ltd.) every second day. Rectal temperature was recorded with an electronic thermometer. A Bell and Howell 4–422–0001 pressure transducer and a Devices M.19 polygraph were used to record arterial pressure. Heart rate was calculated from the pressure trace. Measurements were made at 15 min intervals. During observations the animals were lying unrestrained in their home cages. Ambient temperature was from 21 to 24°.

Pyrogen-like reactions were often observed, beginning 0·75 to 1·0 h after an injection of 2 ml of sterile, heparinized saline, used to clear the arterial cannula at the start of each experiment. Dey, Feldberg & others (1974) have observed a rise in rectal temperature in the cat following intracerebroventricular injection of sterile saline. The effect was prevented by pretreatment with chloramphenicol, suggesting bacterial growth in the cannulae as the source of pyrogen.

In our animals the presence of pyrogens was confirmed by withdrawing 0·5 ml of saline from the arterial cannulae of 5 cats, 18 h after washing through with sterile heparinized saline. These samples were pooled and compared with equivalent volumes of fresh heparinized saline in a standard pyrogen test in groups of 3 rabbits. The sum of the maximum temperature

* Correspondence.

increases of the group which received fresh saline was 0·70°, that of the group which received saline from the cannulae was 3·25°.

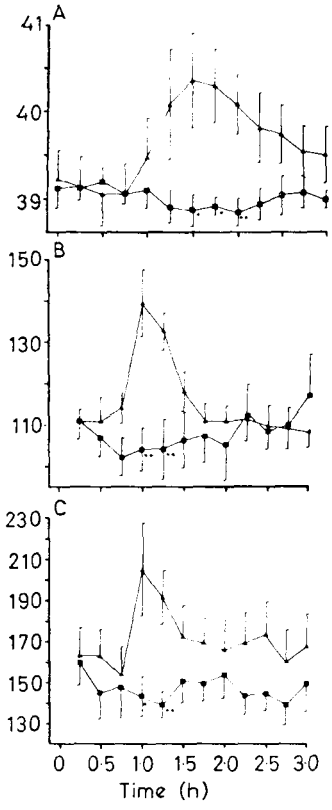

FIG. 1. Records of rectal temperature (°C) (A), mean arterial pressure (mm Hg) (B), and heart rate (beats min^{-1}) (C) from 4 conscious, renal hypertensive cats after injection of 2 ml of sterile, heparinized saline into the arterial cannulae at time 0. Mean values with standard errors of the mean are shown. (▲) Lactose (50 mg kg^{-1}, orally) 45 min before saline injection, (■) paracetamol (50 mg kg^{-1}, orally) 45 min before saline injection. Significance: $*P < 0.05$, $**P < 0.02$ relative to lactose placebo group.

Pyrogen reactions in the cat were characterized by shivering, piloerection and sedation. There were marked increases in rectal temperature, arterial pressure and heart rate. The time courses of these changes are shown in Fig. 1 (placebo group). The maximum increases in heart rate and arterial pressure were reached whilst rectal temperature was only slightly elevated, and preceded the maximum rectal temperature recording by 30 min. The cardiovascular changes returned to baseline values whilst temperature was still maximally elevated. It seems probable that the cardiovascular changes were direct effects of pyrogen and not consequences of the increase in body temperature.

Several drugs which inhibit prostaglandin biosynthesis prevent the increase in rectal temperature which follows intravenous or intracerebroventricular injection of pyrogenic material (Feldberg, Gupta & others, 1973). We have investigated the effects of paracetamol, an antipyretic with some specificity in inhibiting prostaglandin synthetase of brain tissue (Flower & Vane, 1972), on the cardiovascular changes described.

The time courses of the mean temperature, heart rate and arterial pressure changes of 4 cats, pretreated with either lactose placebo (50 mg kg^{-1}, orally) or paracetamol (50 mg kg^{-1}, orally) 45 min before the beginning of the experiment are shown in Fig. 1. The same animals were used in both treatment groups with a minimum of 3 days between treatments. Animals were fasted overnight before use. Paracetamol prevented both cardiovascular and temperature changes associated with the pyrogen reaction, suggesting that increased brain prostaglandin synthesis may be involved in the pyrogen-induced cardiovascular changes in the cat.

It appears, therefore, that the use of indwelling arterial cannulae in the cat may be complicated by contamination of the cannulae with pyrogenic material which produces marked cardiovascular changes. This must be considered when using the technique in assessing the effects of drugs on the cardiovascular system.

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