A technique for repeated blood sampling with transfusion in the conscious rat

Agrelo & Dawson (1968) have reported blood pressure measurements in conscious unrestrained rats using cannulation of the caudal artery, with a fine polythene cannula. This technique can also be used for blood sampling, for instance in glucose tolerance tests. This technique has now been improved for the repeated sampling of larger volumes of blood, replacing it with either saline or heparinized blood from a donor. In this way it is possible to study biodegradation of drugs by following the plasma concentrations of a rat over 5 to 6 h.

Blood samples of 1 ml each can be obtained from the caudal artery if the blood volume is replaced. At the end of the experiments the same animal can be anaesthetized and the last blood sample obtained by orbital puncture or from the abdominal aorta.

To demonstrate that the haemodynamics of the rat and the biodegradation of the drug were not significantly altered, we compared rats treated with quinidine sulphate under the stress of artery cannulation, sampling and transfusions, with rats subjected to only one blood extraction, after drug administration.

Male and female Wistar rats (INFyB strain), 100–250 g, were lightly anaesthetized with ether and a 20 s.w.g. needle connected by fine polyethylene tubing (Portex PP 60) was inserted into the ventral caudal artery 2–2·5 cm from the base of the tail and retained in position with a strip of adhesive tape.

With a similar cannula the lateral vein was cannulated approximately 4–6 cm from the tip of the tail. Rigid plastic tube longer than the tail was slid over the two cannulae and anchored by a thread from the adhesive tape holding the cannulae and the tube in place. The rat was placed in a plastic restraining cage.

Over a period of 5–6 h no necrosis of the tail artery occurred and the patency of the cannulae was ensured by using heparinized saline 100 U ml^{-1}.

All the rats received quinidine sulphate, 15 mg kg^{-1} intravenously, and were assigned to the following three groups:

(i) 10 rats with caudal artery cannulae from which 1 ml samples of blood were obtained at 15, 45, 90, 180, 240 min and 24 h (after each extraction the equivalent

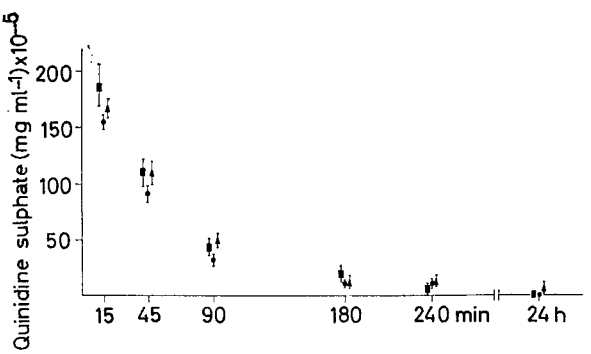

FIG. 1. Rates of elimination of quinidine sulphate given intravenously, 15 mg kg^{-1}, in the three groups of rats. ■ Blood replaced by blood after 6 samples. ▲ Blood replaced by saline after 6 samples. ● Without transfusion after 1 sample.

volume was replaced with heparinized blood from a donor); (ii) 10 rats treated as in (i) but with replacement of blood with saline; (iii) 30 rats without cannulation or transfusion from which only one sample was taken, by abdominal aorta puncture, from groups of five animals at 15, 45, 90, 180, 240 min and 24 h. Quinidine sulphate was determined by a method of Gelfman & Seligson (1961) measuring quinidine fluorescence.

Fig. 1 shows that the half life times are between 34–45 min for the three groups of animals.

Although these results are preliminary we consider the blood concentration pattern acceptable, since the rates of elimination for the three groups do not show significant differences ($P > 0{\cdot}05$).

It is also possible to overcome the limitation of the reduced blood volume (12–15 ml), even in the adult stage, by using this technique.

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Effect of chloroquine on histamine-induced bronchial asthma in the guinea-pig

Chloroquine has direct spasmolytic effects on smooth muscles. Agarwal & Deshmanker (1963) observed that it antagonized the effects of histamine, 5-hydroxytryptamine (5-HT) and acetylcholine on the guinea-pig ileum and tracheal rings. Similar observations were made by Olatunde (1970), who quantitatively showed it to be a more potent antagonist of histamine than of 5-HT and acetylcholine. Chloroquine is concentrated in many tissues, including lung (Berliner, Earle & others, 1948; Grundmann, Virubloresky & Mikutihora, 1970), and since it has been shown to inhibit the catabolic enzyme imidazole *N*-methyl-transferase (Cohn, 1965) we have examined its actions on histamine-induced bronchoconstriction in the guinea-pig.

Bronchoconstriction was induced in guinea-pigs of either sex, 400–900 g, by exposing them to a fine histamine aerosol (1·5% histamine diphosphate solution) in a vapour chamber (Loew, Kaiser & Moore, 1945). One group was pretreated acutely with intraperitoneal injection of chloroquine (20 mg kg^{-1}) 2 h before exposure to histamine aerosol; a second group was pretreated with the same dose daily for 7 days before exposure; a third group was similarly pretreated for 7 days, after which the drug was discontinued for another 7 days before the animals were exposed to histamine. A fourth group formed the controls. A control and a chloroquine pretreated or a control and two pretreated animals were introduced into the vapour chamber together. Time of onset was when the animal showed signs of dyspnoea. Then it was exposed to the aerosol for a further 2 min after which it was removed from the vapour chamber.