Radioactive aniline clearance from canine gastric pouches for the measurement of gastric mucosal blood flow

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Clearance of various organic bases by the gastric mucosa was studied by Shore, Brodie & Hogben (1957) who showed that both aminopyrine (pKa 5·0) and aniline (pKa 5·0) are concentrated in the gastric juice. They postulated that these substances were completely removed from the blood flowing through the gastric mucosa. Jacobson, Linford & Grossman (1966) developed the technique of aminopyrine clearance as a measurement of gastric mucosal blood flow. Although aminopyrine clearance is now a widely used method, the estimation of aminopyrine is tedious. We have therefore investigated the possibility of using radioactive aniline instead of aminopyrine.

Commercially available ^{14}C aniline was estimated in plasma and gastric juice by shaking each 1 ml sample in a sealed bottle for 5 min with 10 ml diethyl ether and 0·5 ml M sodium hydroxide. Seven millilitres of the ether phase was then added to 10 ml scintillator and counted in a Packard Tri-Carb liquid scintillation counter.

Aniline clearance was studied in four dogs prepared with separated (Heidenhain) gastric pouches. A loading dose of aniline (10 mg/kg and 10 μCi) followed by a maintenance infusion [(10 mg/kg)/h and 10 μCi/h] was given intravenously. Blood samples were taken at 30 min intervals from another vein or via an indwelling arterial catheter. Gastric juice was collected from the pouch.

This dose of aniline had no effect on the gastric secretion in response to a meal or to histamine infusions. As would be expected there was detectable methaemoglobinaemia. However, the percentage of methaemoglobin, which varied in different dogs from 5 to 11 %, was well below the value of 40 % at which toxic effects are seen (Bodansky, 1951).

Gastric secretion was stimulated by infusing various doses of histamine or pentagastrin intravenously. The clearance of aniline closely followed the acid secretory response.

The theoretical basis of the assumption that aminopyrine clearance measures gastric mucosal blood flow applies equally to aniline clearance. Confirmation that aminopyrine clearance and aniline clearance are the same was obtained in experiments in which the clearances were compared in the same dog and shown to give very similar results. The advantage of aniline clearance is that the use of a radioactive substance simplifies its measurement in body fluids.

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Effect of isoprenaline on histamine induced gastric acid secretion in dogs

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Isoprenaline is a vasodilator substance and would therefore be expected to enhance

the secretory response of the stomach to blood borne stimuli. However, both Harries (1957) using conscious dogs with gastric fistulae and Jacobson, Linford & Grossman (1966) using conscious dogs with separated gastric pouches found that isoprenaline [(0·75–2·75 μg/kg)/min] either decreased histamine induced secretion or had no effect. We have repeated the experiments on dogs with separated gastric pouches and have extended the observations to anaesthetized dogs and by using a wider dose range.

In thirteen experiments on dogs anaesthetized with pentobarbitone, isoprenaline [(0·125–8·0 μg/kg)/min] increased histamine induced gastric acid secretion (HIGAS) on every occasion, although in four of these experiments (in which the gastric secretion was collected through the cannulated pylorus) the increase was apparently preceded by a decrease. The decrease was probably an artefact due to relaxation of the stomach wall which would have produced a temporary change in the drainage of gastric juice.

Two dogs with separated pouches were used. In the first dog isoprenaline [(0·125–4 μg/kg)/min] increased HIGAS in seven experiments. In one experiment with isoprenaline [(4 μg/kg)/min] there was no clear effect. In the second dog increased HIGAS was observed on four occasions with (0·06–0·25 μg isoprenaline/kg)/min and decreased HIGAS on three occasions with (0·5–1 μg isoprenaline/kg)/minute. The inhibitory effect of isoprenaline in this dog was analysed in a further series of experiments. It was not abolished by light pentobarbitone anaesthesia, by pharmacologically effective doses of guanethidine or hexamethonium or by bilateral section of the splanchnic nerves but was abolished both by phentolamine and by propranolol.

We conclude that suitable doses of isoprenaline increase HIGAS in both anaesthetized and conscious dogs. In conscious dogs large doses of isoprenaline decrease the secretory response. The mechanism of this effect is not yet fully understood.

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Explanation for the discrepancy in reported cardiac electrophysiological actions of diphenylhydantoin and lignocaine

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Although diphenylhydantoin (DPH) and lignocaine have now gained widespread acceptance as effective drugs in the therapy of cardiac arrhythmias some controversy has been aroused concerning their fundamental mechanism of action.

In contrast to many other anti-arrhythmic drugs, concentrations of DPH and lignocaine corresponding to therapeutic concentrations in man have recently been reported to cause no significant depression of the maximal rate of depolarization (MRD) of the cardiac action potential (Strauss, Bigger, Bassett & Hoffman, 1968; Bigger, Bassett & Hoffman, 1968; Davis & Temte, 1969; Bigger & Mandel, 1970;