comparison to that after procedure II. The total diuretic response in the first 5 h in terms of urine volume and sodium and potassium excretion were similar after oral and intravenous administration, but there were significant decreases in urine volume (28%; $P < 0.01$) and sodium excretion (27%; $P < 0.01$) after oral administration to sodium deprived subjects.

The original observation that, despite a decreased bioavailability of frusemide after oral administration the total diuretic response is similar to that following intravenous administration is confirmed. The response to frusemide is related to drug present in the tissue compartment and can be modified by changes in sodium status.

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Gradients of monoamine levels in guinea-pig isolated ileum

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The function of each region of the gut differs, probably in relation to differences in innervation which have been demonstrated histologically (Maslennikova, 1962; Gillespie & Maxwell, 1971) and pharmacologically (Bennett & Stockley, 1975). Levels of some monoamines which may control gut motility were measured in the present experiments. Adult albino guinea-pigs of either sex (500–850 g body weight) were killed by stunning and bleeding, and the abdomen was opened. The ileal tissue was removed, cleared of fat and mesentery and divided into six approximately equal lengths. They were

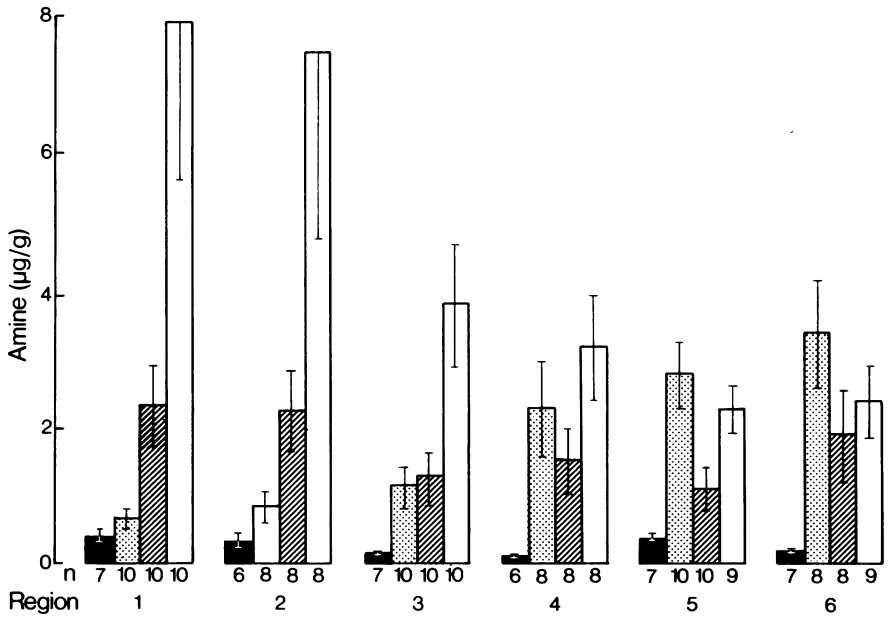

Figure 1 Levels of monoamines in different regions of guinea-pig ileal tissue. The histogram represents levels (µg amine ± s.e. mean/g wet weight) of adrenaline (filled columns), noradrenaline (stippled columns), dopamine (hatched columns) and 5-HT)open columns) in consecutive parts of ileum, each approximately 1/6th of total. Region 1 is proximal, 6 is distal. The number of tissues is shown under each column. Levels of 5-HT decreased down the intestine ($r = 0.974$, $P < 0.001$) and norarenaline increased ($r = 0.924$, $P < 0.01$). Adrenaline and dopamine showed no significant trend ($r = 0.525$ and 0.549 respectively).

opened and the mucosal surface carefully washed with water and blotted. The segments were then immersed in liquid nitrogen, weighed and homogenized in ice-cold acid butanol. Noradrenaline (NA), adrenaline (AD), dopamine (DA), and 5-hydroxytryptamine (5-HT) were extracted, and estimated fluorimetrically after trihydroxyindole formation (Ansell & Beeson, 1968, with the following modification by I.M. Martin, M.R.C. Neuropharmacology Research Unit, Medical School, Birmingham; personal communication). The supernatant from each homogenate was extracted with 10 ml iso-octane and 5 ml water. The aqueous phase (4.5 ml) was removed by a pipette pushed through the upper layer; no material at the interface was removed. This sample was processed as in the original method, but catecholamines were eluted from alumina with phosphate buffer pH 6.5 instead of acetic acid. Trihydroxyindoles were formed using 0.1 ml iodine reagent, 0.2 ml alkaline sulphate and 0.2 ml 6M acetic acid instead of the original quantities. AD was measured by Chang's (1964) method.

5-HT levels decreased aborally whereas NA levels increased (linear correlation coefficient, $P < 0.01$ and 0.001 respectively). DA and AD did not change significantly ($P > 0.1$) (Figure 1). 5-HT stimulates peristalsis in guinea-pig small intestine (Bülbring & Lin, 1958) whereas NA inhibits motility. Although the source of the amines (muscles, mucosa, blood vessels and nerves) is not known, these results are consistent with the finding that intestinal propulsion is more rapid proximally than distally.

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Investigation of the effects of drugs on morphine-induced contractions of the isolated colon of the rat

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Morphine causes some smooth muscle-containing tissue to contract (Weinstock, 1971). Whether or not morphine causes contractions depends on the dose, species and tissue examined (Vaughan Williams, 1954). In dog intestine, morphine produces contractions indirectly by releasing 5-hydroxytryptamine (5-HT) and acetylcholine (ACh) (Burks, 1973). This study sought to determine whether morphine had a similar effect in rat intestine. The effects of morphine were investigated by adding the drug to an organ bath containing 3–4 cm lengths of terminal colon suspended in oxygenated Krebs bicarbonate solution at 37°C. Responses of the colon were recorded isometrically.

Morphine (10^{-5} M) produced an immediate contraction followed at approximately minute intervals by waves of contractions, which gradually decreased in amplitude. When the tissue had ceased responding to the first dose of morphine, addition of a second dose was less effective in causing contractions. Prior addition of naloxone (5×10^{-6} M) to the bath prevented morphine producing contractions but naloxone (5×10^{-6} M) added after rhythmic activity had been initiated by morphine, was less effective in inhibiting the contractions. Morphine-induced contractions were not inhibited by atropine (10^{-4} M), hexamethonium (10^{-4} M) or tubocurarine (10^{-4} M). Indeed, these drugs occasionally potentiated morphine-induced contractions. Unlike in dog intestine, the responses produced by morphine in rat colon were dissimilar from those produced by ACh or 5-HT. The effects of 5-HT antagonists on the morphine-induced contractions were complex. Thus, lysergic acid diethylamide (3×10^{-7} M) did not affect