for 15 min at 4°C. Platelet counts in PRP were determined with the Coulter counter model D using a correction for the haematocrit.

The i.v. administration of aspirin (10 mg/kg), phenylbutazone (10 mg/kg), sulphinpyrazone (50 mg/kg) and indomethacin (1 mg/kg) 1 h before challenge with the antigen (1 mg) resulted in 47% ($P < 0.05$), 56% ($P < 0.05$), 79% ($P < 0.05$) and 86% ($P < 0.02$) inhibition of the thrombocytopenia, respectively.

Dipyridamole (100 mg/kg) given orally was not effective, but oral administration of indomethacin (10 mg/kg) resulted in a 70% ($P < 0.05$) inhibition of the thrombocytopenia.

In view of the known properties of aspirin, phenylbutazone, sulphinpyrazone and indomethacin *in vitro* (Mustard & Packham, 1975; Flower & Vane, 1974) it would appear that the ability of these drugs to inhibit thrombocytopenia in the Arthus reaction is probably a reflection of their inhibitory activity towards the release reaction or prostaglandin synthesis, both of which would be stimulated by the interaction between platelets and antigen/antibody complexes.

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Pharmacokinetics of frusemide related to diuretic response

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Frusemide is a potent short-acting diuretic which inhibits ionic reabsorption from the ascending limb of the loop of Henle. Pharmacokinetic studies suggest that bioavailability of the drug after oral administration is approximately 50% of that after intravenous administration (Calesnich, Christensen & Richter, 1966; Kelly, Cutler, Forrey & Kempel, 1974; Beerman, Dalen, Lindstrom & Rosen, 1975). Despite the relationship between the plasma concentration of frusemide and urine and sodium flow rates (Rupp, 1974), the total diuretic response has been observed to be the same after oral or intravenous administration of equal doses of frusemide to normal subjects (Kelly *et al.*, 1973). This study has attempted to elucidate factors which might account for this observation.

Six healthy males were studied on three separate occasions after administration of frusemide (80 mg intravenously, procedure I), orally unstressed (procedure II) and orally 36 h after frusemide (80 mg orally) followed by a 20 mmol sodium and 160 mmol potassium diet (procedure III). Urine and blood samples were collected at frequent intervals for 5 h together with all urine passed over the subsequent 31 hours. Plasma and urinary frusemide was measured by the methods of Hajdu and Haussler (1964). Urine sodium and potassium were measured by flame photometry.

Following procedure I the plasma concentration of frusemide declined in a biexponential manner. The onset of diuresis was rapid and the half-life of the exponential decline in rate of sodium excretion was similar to that of the late phase of the plasma frusemide concentration curve. Thus there was a plasma concentration-response relationship for this phase. Urine clearance of frusemide was 60% of total clearance. In procedure II the mean peak plasma concentration occurred at 90 min and then declined exponentially. The rise and fall in the rate of sodium excretion paralleled that of plasma frusemide. The plasma concentration-response curve had a parallel shift to the right when the decay phase was compared to the absorption phase. The area under the plasma frusemide concentration-time curve after procedure I was twice that after procedure II. A similar ratio was found when comparing the total recovery of frusemide in the urine. After procedure III the mean peak plasma concentration occurred at 45 minutes. The rate of sodium excretion paralleled plasma concentration of frusemide but the plasma concentration-response curve was significantly shifted to the right in

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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

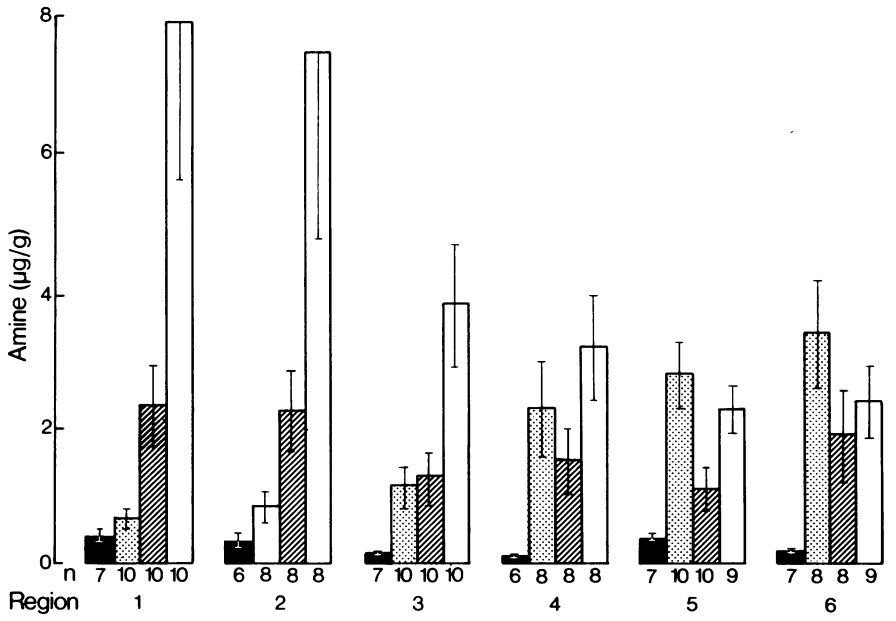

Figure 1 Levels of monoamines in different regions of guinea-pig ileal tissue. The histogram represents levels (µg amine ± s.e. mean/g wet weight) of adrenaline (filled columns), noradrenaline (stippled columns), dopamine (hatched columns) and 5-HT)open columns) in consecutive parts of ileum, each approximately 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).