Table 1 The transport of cimetidine across rat small intestine *in vitro*

Initial Concentration (μmol/l)	*DNP*	*Serosal Transfer* (nmol/g wet wt/h)	*Serosal/Mucosal Ratio*
40	–	11.9 ± 0.8 (16)**	1.8 ± 0.3 (8)**
40	+	4.1 ± 0.4 (16)**	0.6 ± 0.1 (8)**
200	–	21.2 ± 3.4 (12)*	0.4 ± 0.1 (8)*
200	+	12.0 ± 0.5 (12)*	0.7 ± 0.1 (8)*
400	–	42.9 ± 3.6 (8)	0.6 ± 0.1 (8)
400	+	54.2 ± 7.7 (8)	0.6 ± 0.1 (8)

All values are given as mean ± s.e. mean with the number of determinations in parentheses. * $P < 0.05$, ** $P < 0.001$. Significance values refer to the difference between corresponding results in the presence and absence of DNP using a non-paired *t* test.
Serosal transfer is reported for experiments with cimetidine initially present only on the mucosal side. Serosal/mucosal ratios refer to experiments in which cimetidine was initially present in both solutions.

the same concentrations was present on both the mucosal and serosal sides. 2,4-Dinitrophenol (DNP, 500 μmol/l) was used as an inhibitor of active transport. The sacs were incubated for 1 h at 37°C in an atmosphere of 95% O_2/5% CO_2. Solutions from the mucosal and serosal sides were then extracted and assayed for cimetidine by a high pressure liquid chromatographic method (Randolph, Osborne, Walkenstein & Intoccia, 1977).

At lower concentrations (40 μmol/l and 200 μmol/l), cimetidine transport was inhibited by DNP. DNP also inhibited the transport of [^{14}C]-glucose (400 μmol/l; sp. act. = 248 mCi/mmol) but not of ethanol (4.3 mmol/l), present in the incubations to monitor active and passive transfer respectively. The results in Table 1 indicate an active absorption process for cimetidine observable at lower substrate concentrations which is masked by a diffusion process at higher concentrations (Akedo & Christensen, 1962).

In some experiments cimetidine sulphoxide was detected after incubation and it is possible that this may account for some of the urinary sulphoxide found after oral administration of [^{14}C]-cimetidine (Taylor & Cresswell, 1975).

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The action of dopamine on constrictor responses in the perfused rat mesenteric artery

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Dopamine or apomorphine induced vasodilatation in mesenteric, renal and femoral beds of the anaesthetized dog is mediated by a specific dopamine receptor (Yeh, McNay & Goldberg, 1969; Buylaert, Willems & Bogaert, 1977). Inhibition of stimulation induced noradrenaline overflow by dopamine has been reported for rabbit ear artery (Hope, McCulloch, Rand & Story, 1978), cat spleen and nictitating membrane (Langer, 1973). These and other inhibitory effects of dopamine may be due to an action on an inhibitory presynaptic dopamine receptor (Hope *et*

Table 1 Inhibition by dopamine of nerve mediated constriction of rat mesenteric artery and effects of haloperidol and yohimbine. The magnitude of the effect is expressed as percentage reductions (± s.d.) of the control responses

		Haloperidol		*Yohimbine*
	Control	*0.1 μM*	*0.5 μM*	*10 μM*
Dopamine	*(n-12)*	*(n-6)*	*(n-5)*	*(n-6)*
0.1 μM	17.5 ± 3.6	5.2 ± 3.2	0	—
0.5 μM	31.3 ± 4.7	8.2 ± 2.6	2.8 ± 1.4	29.6 ± 2.7
1 μM	46.6 ± 3.9	11.7 ± 2.8	4.5 ± 1.6	41.9 ± 3.6

al., 1978) or mediated through a prejunctional α-adrenoceptor (Hurst, Marshall & Nasmyth, 1979). We have investigated the effects of dopamine on the vasoconstrictor responses in the perfused rat mesenteric artery preparation (McGregor, 1965). The perfusion fluid contained cocaine (100 μM) and the periarterial nerves were stimulated for 30 s, every 5 min (10 or 20 Hz; 1 ms; 20 V). Doses of noradrenaline (0.1 to 20 μg) were injected into the perfusion.

Infusion of dopamine (0.1–1 μM) resulted in immediate depression of the vasoconstrictor responses to nerve stimulation (Table 1). The results with concentrations of dopamine higher than 1 μM are not included because they inhibited the responses to exogenous noradrenaline, suggesting an additional postsynaptic effect. This inhibition was slow in onset and difficult to wash off.

The dopamine receptor antagonist haloperidol, in concentrations (0.1–0.5 μM) that had no effect on responses to nerve stimulation or to noradrenaline, reduced the depressant effect of dopamine on neuronally mediated vasoconstriction (Table 1).

Yohimbine (10 μM) produced a 10 to 15% increase in the response to nerve stimulation, but did not alter the inhibitory effect of dopamine (Table 1).

It is suggested that dopamine inhibition of vasoconstrictor responses to nerve stimulation in rat mesentric artery may be mediated by a specific inhibitory dopamine receptor and not via presynaptic α-adrenoceptors.

The mechanism of the slow dopamine inhibition of noradrenaline responses has not yet been defined.

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The influence of old age and of renal failure on hepatic glucuronidation in the rat

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There is evidence that the metabolism of some drugs may be altered in old age (Crooks, O'Malley & Stevenson, 1976) and in patients with renal failure (Reidenberg, 1975). The present investigation has examined whether these factors affect glucuronide conjugation in rat liver.

The animals were laboratory bred male Wistar rats of 8 and 30 months age (mean body weights 272 and 549 g respectively). Renal failure was induced by either sub-total nephrectomy (McCance & Morrison, 1956) or ligation of both renal pedicles under halothane anaesthesia. The control animals for the nephrectomized rats were sham-operated and pair-fed. The *in vitro* glucuronidation of 4-nitrophenol and