disclosed (fig.). Over a broad dose range from 15 ng to 150 µg Met-enkephalin induces predominantly flexion of the left limb, whereas Leu-enkephalin causes mainly the right limb to flex. The difference in the left/right flexion ratio after administration of Met- and Leu-enkephalin is statistically significant. Moreover, for both enkephalins these values differ significantly from the theoretically random distribution of 50% left flexions to 50% right flexions. These facts suggest that the systems regulating the activity of spinal effector neurons located symmetrically to the sagittal plane may differ in their sensitivity towards Met- and Leu-enkephalin.

Opiate receptors have been found at all levels of the spinal cord in the posterior, lateral and anterior horns and in the intermediate zone of grey matter[11,12]. These receptors may be involved in the regulation of spinal motor reflexes through modulation of the activity of sensory, motor and internuncial neurons. This suggestion is supported by observations that morphine and other opiates affect electrical activity of spinal motoneurons and interneurons[7,13]and force of flexor reflex[14] in intact and spinal animals.

The appearance of hind-limb asymmetry induced by enkephalins in these experiments may indicate an intrinsic asymmetry either in the density or other properties of opiate receptors or in postreceptor elements involved in the enkephalin response. However, since the side on which flexion was induced depended on whether Met-enkephalin or Leu-enkephalin was administered the simplest interpretation is 1. that these receptors are relatively more specific for either of the opiates; and 2. that these receptors are asymmetrically distributed.

Asymmetric reaction and hemispheral asymmetry in the response of the nigro-striatal system to dopaminergic agonists have also been described by Glick et al.[15] These workers found that the left and right striata differ by some 10–15% in dopamine content. Amphetamine administration increased this difference up to 25% and induced rotation of the animal in the direction corresponding to the brain hemisphere with the higher dopamine content[16]. Pentamethylenetetrazol increased the amplitude of wave-spike discharges on the same side of the brain[17]. Our data suggest that in addition to the asymmetry of the dopaminergic system in the brain an asymmetry of the enkephalinergic system in the spinal cord exists.

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Effect of isoprenaline on dopamine receptors in the rabbit isolated renal artery

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Summary. The relaxant effects of isoprenaline on rabbit isolated renal artery and aorta were compared. The results suggest that although isoprenaline acts on β-adrenoceptors in the aorta it stimulates dopamine receptors in the renal artery.

A number of in vivo studies have shown dopamine to be capable of dilating blood vessels in the renal[1-3], mesenteric[4], coronary[5], hindlimb[6] and paw pad[7] vasculatures. More recently, work with mesenteric, renal[8], coronary[9], cerebral[10] and splenic[11] isolated arterial strips, confirming the in vivo observations, has suggested the presence of a dopamine receptor, mediating a type of vasodilation which is unaffected by the presence of β-adrenoceptor antagonists[12].

Earlier studies had indicated that the β-adrenoceptor agonist isoprenaline acted to dilate renal blood vessels by stimulating β-adrenoceptors, since the response was blocked by β-adrenoceptor antagonists[1,2]. However, Bell and Mya[13] have questioned these observations and their in vivo study of the canine renal vasculature has led to the suggestion that isoprenaline induces renal dilatation, at least in part, by interacting with dopamine receptors. The present study seeks to clarify this observation by comparing isoprenaline's relaxant effects on the rabbit isolated renal artery with those on the aorta, where its β-adrenoceptor stimulating properties are well known[14,15].

Methods. Rabbit thoracic aorta and left renal artery were removed immediately after death and placed in Krebs-Henseleit solution, bubbled with a 95% oxygen/5% carbon dioxide gas mixture. The tissues were cut into spiral strips[16] and mounted vertically in 20 ml tissue baths containing oxygenated Krebs-Henseleit solution, maintained at 37 °C. Tissues were stretched under 1–2 g of resting tension for 1 h and then incubated with the α-adrenoceptor antagonist phenoxybenzamine (10 µM) for a further hour before drug-induced tension changes were recorded isometrically. Prostaglandin $F_{2\alpha}$ (3 µM) was used to induce muscle tone and relaxant drugs were administered cumulatively after the

prostaglandin-induced contraction had reached a plateau. In some experiments the antagonist drugs propranolol (1 μM) and haloperidol (1 μM) were incubated with the tissues for 30 min before relaxations were measured.

Results and discussion. The relaxant effects of dopamine and isoprenaline on renal artery and aorta were compared. Prostaglandin $F_{2\alpha}$(3 μM) produced a sustained contraction of 54 ± 8 mg tension in the renal artery and 44 ± 9 mg in the aorta (8 determinations in each case). The EC_{50} values for the dose-response curves of the relaxant effects of dopamine and isoprenaline on each tissue are shown in the table, together with the effects of incubation with the β-adrenoceptor antagonist, propranolol, alone and in combination with haloperidol, a dopamine receptor antagonist. Low figures indicate greater potency for the relaxant drugs, dopamine and isoprenaline.

Isoprenaline was more potent than dopamine in relaxing both tissues but was particularly potent on the aorta. The results show that both dopamine and isoprenaline act on β-adrenoceptors in the aorta, since the relaxation produced by each agent is antagonized by propranolol. However, in the renal artery the relaxations produced by dopamine and isoprenaline were unaffected by the presence of propranolol but inhibited by the dopamine receptor antagonist haloperidol, indicating that both agents induce relaxation in this tissue by stimulation of dopamine receptors. This study confirms the presence of aortic β-adrenoceptors[14,15] and renal dopamine receptors[1,8] but supports the in vivo findings[13] that isoprenaline acts on dopamine receptors in the renal artery.

Effect of propranolol and haloperidol on the relaxant effects of dopamine and isoprenaline on renal artery and aorta

	Aorta	Renal artery
Dopamine	707 ± 63	575 ± 92
Dopamine + propranolol	1096 ± 147*	660 ± 65
Dopamine + propranolol + haloperidol	1112 ± 132*	802 ± 45*
Isoprenaline	8 ± 1	263 ± 28
Isoprenaline + propranolol	208 ± 17**	316 ± 35
Isoprenaline + propranolol + haloperidol	189 ± 41**	360 ± 31*

Mean EC_{50} (μM) values with standard errors for 10 determinations are shown. These values were taken from dose-response curves measuring % relaxation of prostaglandin-induced contractions and control values for each relaxant drug were measured in the absence of antagonist. The significance of differences produced by the presence of antagonists was tested using Student's t-test and 2 levels of significance are shown. * $p < 0.05$ and ** $p < 0.01$.

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Erythrocyte deformability improving action of β-pyridylcarbinol tartrate

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Summary. β-Pyridylcarbinol tartrate was found to prevent the hyperosmotically induced worsening of filterability of rat erythrocytes after in vivo treatments. The effect is attributed to the prevention of the morphological change of the erythrocytes from normal discocytes to echinocytes. The study was made using a scanning electron microscope.

β-Pyridylcarbinol tartrate (β-PC) and its active metabolite, nicotinic acid, are known to decrease the plasma level of low density lipoproteins (LDL) and to increase that of high density lipoproteins (HDL) not only in experimental animals but also in man[2,3]. Such effects of the drugs would be expected to improve erythrocyte deformability; this suggestion is based on the recent evidence that the shape of the erythrocyte may be regulated by both LDL and HDL[4,5]. Therefore, the effects of β-PC and nicotinic acid on both erythrocyte deformability and shape change were examined in the present study.

Materials and methods. Erythrocyte filterability as a measure of erythrocyte deformability was measured in rats, the erythrocytes of which are known to have a similar size and deformability to that of human erythrocytes[6].

In in vitro filterability experiments, packed erythrocytes[7] from male Wistar rats weighing 200–250 g were suspended in an isotonic buffer or a hypertonic buffer. The isotonic buffer contained 145 mM NaCl, 5 mM KCl, 6 mM glucose and 12 mM Tris-HCl buffer, pH 7.4. The concentration of NaCl was doubled in the hypertonic buffer. After incubation at 37 °C for 1 h in the presence or absence of a drug, a 1 ml aliquot was transferred to a glass pipette (⌀3 mm) attached to an stainless steel sieve of 3200 mesh (5 μm) (Fuji Seive, Tokyo) and the filtration time required for the passage of 0.6 ml of erythrocyte suspension was measured. Results were expressed as percentage increase in filtration time of erythrocyte suspension in the hypertonic buffer as compared with that in the isotonic buffer. In ex vivo filterability experiments, rats were orally pretreated with either saline or a drug which was administered in a single dose or repeatedly. 1 h after the (last) administration, the blood collected by cardiac puncture was immediately added to an equal volume of the isotonic buffer or a