The DA agonist bromocriptine did not contract the muscle, but antagonized the responses to both NA and DA. In both cases the antagonism was non-competitive (pD'_2 against NA = 7.62 ± 0.05; pD'_2 against DA = 7.99 ± 0.12). The specificity of this antagonism was determined by observing the effect of bromocriptine on the dose-response curve to carbachol, which was unaltered.

Apomorphine, also considered to be a DA agonist, neither contracted the muscle nor antagonized the responses to NA or DA in low concentrations. However, apomorphine did alter the characteristics of the response to these agonists, producing large oscillations in tone during the contractions.

The results suggest that it is unlikely that specific post-junctional DA receptors exist in the mouse vas deferens. Further, they confirm that the 'DA agonist' bromocriptine is a potent α-adrenoceptor antagonist (Gibson, James, Shaw & Tracey, 1977). The observed differences between bromocriptine and apomorphine on α-adrenoceptor systems may explain some of the differences between these two drugs on CNS activity (Johnson, Loew & Vigouret, 1976).

M.S. is supported by the Ministry of Science and by the University of Azarabadeghan, Iran.

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Vascular effects of bromocriptine in the hindlimb of the dog

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Intra-arterial injection of apomorphine into the canine femoral vasculature produces an immediate and short-lasting vasodilatation (Buylaert, Willems & Bogaert, 1977). This apomorphine effect is mimicked by a number of dopamine receptor agonists and is antagonized by haloperidol and other neuroleptic drugs, suggesting that a dopamine receptor is involved (Buylaert, Willems & Bogaert, 1978). Bromocriptine is an agonist for central dopamine receptors which is used in man. Its effects on the vasculature of the dog hindlimb are reported here.

In mongrel dogs (14–28 kg) anaesthetized with sodium pentobarbitone (30 mg/kg i.v.), blood pressure was measured in the left brachial artery and blood flow was monitored in both femoral arteries (Buylaert *et al.*, 1977). In some animals the sympathetic nerve supply to the right hindlimb was interrupted by transecting the lumbar sympathetic chain (L4–L5). Injections of the drugs were given into the femoral artery through a catheter introduced via the arteria profunda femoris; with the doses chosen, no changes in blood pressure occurred.

Low doses of bromocriptine ($\leq 0.5 \times 10^{-8}$ mol) had no effect on femoral flow when injected into the hindlimb. A higher dose of bromocriptine (4×10^{-8} mol) produced an increase in femoral flow in 26 out of 29 dogs. This increase in flow was slower in onset and of a smaller degree, but longer lasting (>10 min) than the increase seen with apomorphine (0.25×10^{-8} mol); bromocriptine (8×10^{-8} mol) did not further increase the dilatation present after a dose of 4×10^{-8} mol. In 6 dogs, a decrease preceded the increase with 4×10^{-8} mol. In 3 out of 29 animals, only a transient decrease of flow was observed.

Injection of the same dose of bromocriptine (4×10^{-8} mol) into a denervated hindlimb in 5 dogs produced only a transient decrease of femoral flow; this decrease was antagonized by phentolamine (1 mg/kg i.v.; $n = 4$).

Bromocriptine (4×10^{-8} mol) was also injected into the hindlimb 5 to 7 min after local administration of haloperidol (30 μg) or haloperidol (100 μg) (7 animals for each treatment) and the increase in flow was compared to that seen with the same dose of bromocriptine in the contralateral, untreated limb. Haloperidol had no lasting effect on femoral flow and caused a dose-dependent inhibition of the increase in flow by bromocriptine. Lactic acid, the solvent for

haloperidol, did not alter the effect of bromocriptine ($n = 7$).

A cholinoceptive or β-adrenoceptive origin of the increase in flow by bromocriptine was excluded since atropine and propranolol, given in doses that completely blocked the responses to, respectively, acetylcholine and isoprenaline, had no influence on the responses to bromocriptine ($n = 3$). The possibility that bromocriptine increases femoral flow through a partial agonism at postsynaptic α-adrenoceptors is unlikely since even 8×10^{-8} mol bromocriptine injected into the denervated hindlimb did not influence the vasoconstriction produced by locally injected noradrenaline ($n = 5$).

The present experiments suggest that bromocriptine, besides its stimulating effect on postsynaptic α-adrenoceptors, increases femoral flow through stimulation of dopamine receptors presumably located on sympathetic nerve endings, as described for apomorphine (Buylaert *et al.*, 1977). The duration of action of bromocriptine is much longer than with apomorphine as also seen for central dopamine receptors (Corrodi, Fuxe, Hökfelt, Lidbrink & Ungerstedt, 1973).

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Disposition of adrenergic neurotransmitter in saphenous veins of dog and rabbit

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In an earlier paper we reported a difference in sensitivity of saphenous vein segments of dog and rabbit to exogenous noradrenaline, which disappeared after blockade of neuronal uptake by cocaine. No differences between the two species were noted as regards the shape of the frequency-response curve to nerve stimulation (De Mey & Vanhoutte, 1977). The present study was designed to compare, in veins from both animals, the pattern of metabolism of the adrenergic transmitter in basal conditions and during sympathetic nerve activity.

Saphenous veins of dogs and rabbits first were incubated in Krebs–Ringer solution containing 7-[^{3}H]-noradrenaline (3×10^{-7} M; [^{3}H]-NA); they were then mounted for superfusion as previously described (Vanhoutte, Lorenz & Tyce, 1973). The superfusate was collected at given intervals for estimation of total radioactivity ([^{3}H]-efflux) and column chromatographic separation of intact [^{3}H]-NA and its major metabolites (3,4-dihydroxymandelic acid, DOMA; 3,4-dihydroxyphenylglycol, DOPEG; 3-methoxy-4-hydroxyphenylglycol, MOPEG; normentanephrine, NMN; and 3-methoxy-4-hydroxymandelic acid, VMA), as previously described (Verbeuren, Coen & Vanhoutte, 1977).

In basal conditions, the total [^{3}H]-efflux, expressed as d/min per mg wet weight, was significantly greater for veins of the dog than for those of the rabbit. In the dog, the amounts of intact [^{3}H]-NA, and of VMA present in the superfusate were significantly larger than for the rabbit; in the latter, DOPEG and DOMA constituted a significantly larger fraction of the [^{3}H]-efflux than in the dog and MOPEG was the only important O-methylated-deaminated metabolite. In the rabbit the ratio of intact [^{3}H]-NA to the total metabolite fraction was significantly smaller than in the dog.

Electrical stimulation (2 Hz) caused an increase in total [^{3}H]-efflux, which was significantly larger for dogs' veins. This increase consisted mainly of intact [^{3}H]-NA for the dog (56.2 ± 5.4 and $33.8 \pm 5.7\%$ of the total increase in [^{3}H]-efflux for dog and rabbit respectively), and mainly of MOPEG for the rabbit (33.1 ± 1.5 and $42.8 \pm 3.0\%$ for dog and rabbit respectively). As regards the other metabolite fractions, NMN contributed to the increase in [^{3}H]-efflux significantly more in the dog than in the rabbit; the VMA fraction significantly increased in the rabbit and, significantly decreased in the dog veins during electrical stimulation. The changes in the appearance of DOPEG and DOMA with electrical stimulation were comparable in both species.

These results suggest that (a) under basal conditions, intraneuronal leakage of the transmitter and subsequent deamination to DOPEG is more important in rabbit than in dog saphenous veins, (b) the