In most experiments there was an acute fall in arterial blood pressure. This started immediately after forcing in the material, returning to normal in less than 40 s. No consistent changes in central venous pressure, respiratory movements or e.c.g. occurred. However, in occasional experiments the hypotensive effect was more complex, accompanied by a rise in central venous pressure and changes in respiratory rate, and in two experiments the arterial pressure failed to return to its resting level.

Collection of the blood leaving the femoral vein when the material was forced into the medullary cavity did not prevent or reduce the hypotension. These animals were given 100 I.U. heparin/kg I.V. Fat and marrow cells were identified in the femoral venous blood samples. Reinfusion of this blood a few seconds later produced no acute effect, but in one animal there was a protracted fall in arterial pressure and a rise in central venous pressure. It is unlikely that the acute effect is a result of embolism, since it was not modified by delaying the femoral venous return and reinfusion of femoral blood known to contain emboli did not produce an acute response.

These preliminary experiments suggest that the response which normally occurs is produced by a nervous mechanism and that occasionally there is a response of longer duration which might be due to embolic effects.

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## Studies on the mechanism of action of dihydroergotamine (DHE) on the vascular bed of cat skeletal muscle

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In the innervated skeletal muscle vascular bed, DHE elicits a slight dilator effect on the resistance vessels and a constrictor effect on the capacitance vessels (Mellander & Nordenfelt, 1970). The present experiments attempt to elucidate the mechanism by which DHE elicits these effects.

Male cats weighing 2·3–3·4 kg were anaesthetized with chloralose (46 mg/kg) and urethane (464 mg/kg) intramuscularly. The calf muscles (innervated and denervated) were prepared according to the method described by Mellander (1966). The doses of drugs were calculated as their bases.

The results are summarized in Table I. In denervated preparations, the intravenous injection of 15 $\mu$g/kg DHE resulted in constriction of both resistance and capacitance vessels, confirming the findings of Owen and Stuermer (1971). However, in innervated preparations, the dose-related constriction of capacitance vessels in response to DHE (15 $\mu$g/kg and 45 $\mu$g/kg I.V.) was accompanied by a dose-dependent dilatation of the resistance vessels. Phenoxybenzamine (2·5 mg/kg I.V.) abolished the DHE-induced constrictor effect on the capacitance vessels without affecting the dilator response on the resistance vessels. This latter effect was abolished by atropine (2 mg/kg I.V.), revealing a constrictor effect similar in magnitude to that observed in denervated preparations. The intraperitoneal administration of eserine (100 $\mu$g/kg) potentiated the dilator response. Intravenous pretreatment of cats with chlorpheniramine (100 $\mu$g/kg), propranolol (1 mg/kg) and acetylsalicylic acid (200 mg/kg) did not alter the DHE-induced dilatation of the resistance vessels.

It is concluded that the constriction of the capacitance vessels induced by intravenous administration of DHE is mediated peripherally by an action on $\alpha$-adrenoceptors whereas the dilator effect on the resistance vessels appears to be mediated centrally through the release of acetylcholine.

TABLE 1. *The effects of DHE and those after pretreatment with various antagonists on the vascular bed of cat calf muscle. (−): dilatation. Except where indicated all preparations are innervated*

| Drugs | Dose mg/kg I.V. | n | Resistance response (% change) Mean ± S.E. | Capacitance response (ml./100 g tissues) Mean ± S.E. |
|---|---|---|---|---|
| DHE vehicle | — | 13 | 0·46 ± 1·24 | — |
| DHE (denervated muscle) | 0·015 | 5 | 6·40 ± 3·27 | 0·37 ± 0·04 |
| DHE | 0·015 | 6 | −5·21 ± 2·62 | 0·29 ± 0·10 |
| DHE | 0·045 | 8 | −10·75 ± 2·54 | 0·42 ± 0·06 |
| Phenoxybenzamine + DHE | 2·5 + 0·015 | 5 | −17·00 ± 2·13 | 0·06 ± 0·12 |
| Atropine + DHE | 2·0 + 0·015 | 5 | 6·00 ± 2·63 | 0·28 ± 0·01 |
| Eserine + DHE | 0·100 (I.P.) + 0·015 | 6 | −11·17 ± 5·52 | 0·29 ± 0·06 |
| Chlorpheniramine + DHE | 0·100 + 0·015 | 3 | −4·32 ± 4·96 | 0·31 ± 0·03 |
| Propranolol + DHE | 1·0 + 0·015 | 3 | −3·00 ± 2·65 | 0·33 ± 0·24 |
| Acetylsalicylic acid + DHE | 200·0 + 0·15 | 3 | −12·67 ± 5·20 | 0·25 ± 0·14 |

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## The actions of histamine on blood flow and capillary filtration coefficient (C.F.C.) in the cat small intestine

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In 1963, Folkow, Lundgren & Wallentin reported a method for the determination of the functional exchange vessel area in the small intestine of the cat. This plethysmographic method measures the rate of exudation of fluid from the vasculature into the perivascular space that occurs in response to an imposed increment in venous pressure. The rate of the transudation that occurs is dependent upon the tone in the precapillary sphincters, which governs the number of functioning exchange vessels. Capillary filtration coefficient (C.F.C.) is measured as millilitres of fluid (transuded/min)/mm of mercury rise in the venous pressure/100 g of tissue under investigation. The method used in the present study was based on that of Folkow *et al.* (1963).

Nineteen unselected cats weighing between 2·5 and 5·5 kg were anaesthetized with chloralose (70 mg/kg, I.V.) after induction with halothane. Continuous artificial ventilation was employed, using room air supplemented with oxygen to bring the oxygen content of the inspired mixture to approximately 40%. The volume of blood within the external circuit was compensated for with a solution of low molecular weight dextran in 0·9% saline (Rheomacrodex, Pharmacia), and drugs were dissolved in and washed in with 0·9% saline. Histamine acid phosphate administered intravenously in doses of 0·01 to 10·0 (μg/kg)/min regularly produced a fall in C.F.C., indicative of a constriction of precapillary sphincters. The total blood flow increased, usually by about 5–10% over control values. A similar fall in C.F.C. was observed following the infusion of a

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