(4 mg IV). BP increased (+45%) and bradycardia developed (−31%). 48 s after injection peripheral blood flow again showed a biphasic response (FBF +141%; S-CBF +113%); 24 s later FBF had fallen but remained above control (+34%) whereas S-CBF had fallen to below control values (−47%). Thereafter FBF showed a secondary dilator phase (+37%) while S-CBF recovered slowly but remained below control (−16%). A typical response is illustrated in Fig. 1.

Three patients aged 69 to 77 years were given methoxamine (2 mg I.V.). The pattern of response for heart rate, blood pressure and limb blood flow was similar but reduced in magnitude.

The observed biphasic response of FBF to methoxamine in normal limbs is markedly similar to the adrenaline response demonstrated previously by Duff & Swan (1951). For S-CBF the response is similar to that seen during general anaesthesia (Fuzzey, Hope & Payne, 1972) and to the adrenaline response in sympathectomized limbs (Duff & Swan, 1951).

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Double blind controlled trial of indoramin in the treatment of essential hypertension

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Preliminary studies suggest that 3-(2-(4-benzamidopiperid-1-yl) ethyl) indole hydrochloride, indoramin, has a hypotensive action in man (Royds, 1972). Animal studies show that it has cardioinhibitory and α-adrenoceptor blocking action (Alps, Johnson & Wilson, 1970).

Initially, 5 patients with moderate hypertension were studied using divided doses of 60–240 mg daily for 1–10 months. This uncontrolled study did not show a convincing hypotensive effect. Dose dependent sedation was noted by all patients and both men treated experienced failure of ejaculation at the lowest dose of 60 mg daily.

A double blind controlled trial was undertaken in 8 patients with mild or moderate hypertension. On their first out-patient visit on no therapy, the mean arterial pressure of these patients was 196·3/115·0 mmHg. All patients underwent a run-in period on the active drug when increasing doses were administered until either the diastolic blood pressure was 100 mm or lower, or sedation prevented further increase in dosage. The mean daily dose of indoramin was 124 mg (range 60–150 mg). However in 3 patients hydrochlorothiazide 50 mg daily was also administered to bring the diastolic pressure below 105 mmHg, this was continued throughout the trial. There were two 6 week trial periods, one on active drug and

one on placebo tablets of identical appearance. The order of the periods was randomly allocated. During the trial patients attended twice weekly and on each occasion they were interviewed by one observer and then examined by the second observer who remained unaware of their therapy.

TABLE 1. *Mean and* S.E. *of mean of blood pressure and body weight during the trial periods*

	Placebo	Indoramin	Significance (paired *t* test)
Mean systolic B.P. lying (mmHg)	169·3±6·3	161·5±9·2	N.S.
Mean diastolic B.P. lying (mmHg)	104·0±2·2	96·4±3·5	<0·01
Mean systolic B.P. standing (mmHg)	160·1±7·7	156·4±9·3	N.S.
Mean diastolic B.P. standing (mmHg)	104·6±2·2	97·5±2·7	<0·05
Mean weight (kg)	75·7±7·2	77·5±7·0	<0·05

The mean of the 3 observations on each regime (Table 1), shows that indoramin produced a small fall in systolic and diastolic pressure in both the lying and standing positions. There was no postural or exercise induced hypotension. A significant weight gain was noted on the active drug.

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Release of spasmogenic substances induced by vasoactive amines from isolated lungs

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Isolated lungs of rats, guinea-pigs and dogs, perfused with Krebs solution via the pulmonary circulation, release a mixture of spasmogens exhibiting prostaglandin-, slow reacting substance-, and rabbit aorta contracting substance-like activities in response to infusions of 5-hydroxytryptamine, tryptamine, acetylcholine and histamine (0·5–2 μg/ml) through the pulmonary circulation. The release is accompanied by a rise in perfusion pressure representing an increase in vascular resistance (Alabaster & Bakhle, 1970). Specific antagonists of the myotropic action of the amines, e.g. methysergide (100 ng/ml) for the tryptamines and mepyramine (100 ng/ml) for histamine, completely inhibit the induced release of spasmogens and the accompanying rise in perfusion pressure. There is no cross antagonism, i.e. hyoscine will not inhibit tryptamine induced release (Alabaster & Bakhle, 1972).

These findings led to a hypothesis that attacks of migraine may be caused by an analogous release of active substances from the lungs (Sandler, 1972). Following a suggestion contained in this hypothesis we have investigated the effect of ergotamine on release and of tyramine as a releasing agent.