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.

Ergotamine (650 ng/ml) infused through rat lungs completely prevented the release of spasmogens and the rise in perfusion pressure induced by tryptamine (2 μg/ml), but had little effect on release induced in the same preparation by histamine (2 μg/ml). This action of ergotamine is comparable to that of methysergide and may be similarly related to blockade of tryptamine receptors in smooth muscle. In contrast, diethylcarbamazine (1 mg/ml) and indomethacin (10 μg/ml) are non-specific antagonists, preventing both tryptamine and histamine induced release. Whereas the antagonism by indomethacin persists for at least 1 h after the end of the infusion, that by diethylcarbamazine ceases within 10 min of stopping the infusion.

Tyramine (10–100 μg/ml) does not induce release of spasmogens from the isolated lungs of rat, rabbit or guinea-pig, although in rat and rabbit lungs it increases perfusion pressure. In cat and dog lungs, tyramine (100 μg/ml) induces both release and a rise in pressure. Dopamine (100 μg/ml) induces release in dog but not in rat, guinea-pig or cat lungs.

Tyramine-induced release in cats' lungs is not prevented by mepyramine (100 ng/ml), methysergide (100 ng/ml), propranolol (2 μg/ml), hyoscine (100 ng/ml), phenoxybenzamine (100 ng/ml), ergotamine (6·5 μg/ml) or haloperidol (200 ng/ml). However, it (and histamine induced release) is non-specifically antagonized by diethylcarbamazine and indomethacin, though perfusion pressure still rises.

We conclude from these results that: (1) the ability of agonist amines to induce release of spasmogens from the lung varies markedly between species; (2) the release may be blocked at two distinct points, one at the level of a specific agonist receptor, and the other at a less specific level perhaps subsequent to activation of smooth muscle receptors.

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Anaphylatoxin-induced release of a substance with prostaglandin-like activity in isolated perfused guinea-pig lungs

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A substantial proportion of the mepyramine-resistant bronchoconstrictor and pressor effects of anaphylatoxin (AT) is subject to tachyphylaxis (Sackeyfio, 1971). This suggests a probable involvement of mediators hitherto not implicated in AT activity. This possibility was investigated using the isolated, perfused guinea-pig lung preparation.