muscle vessels of the forearm. The drug did not alter the response of hand blood vessels to noradrenaline in the one subject tested.

Clonidine (150 μg) was infused intravenously into four supine subjects at the rate of 25–30 μg/min. There was no pressor response, but all subjects showed a progressive fall in mean arterial pressure. There was, however, an initial increase in hand vascular resistance which was followed by a fall. Intravenous and intra-arterial noradrenaline were given before and after the clonidine, and the effects on arterial blood pressure and hand blood flow measured. The clonidine increased the effects of noradrenaline.

In view of one report of reduced vascular constrictor and dilator responses in cats after chronic clonidine administration, we have studied the vascular and pressor responses to intravenous and intra-arterial noradrenaline before and during oral therapy with clonidine in two hypertensive patients. There was a small increase in the effects of noradrenaline during treatment, but it was less than that seen during bethanidine therapy.

A new method for studying the pharmacology of the superficial veins in conscious man

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A technique has been developed by which it is possible to quantitate the effect of drugs infused directly into the superficial veins of conscious man. Changes in compliance of a dorsal hand vein are estimated by following the size of the vein when it is distended by application of a sphygmomanometer cuff on the upper arm at a standard congesting pressure of 45 mmHg (which gives a pressure of approximately 30 mmHg in the vein). Vein size is measured by a simple optical technique in which a microscope is focused on a skin marker dot over the distended vein and then refocused when the vein has emptied; the distance moved by the microscope is measured on a vernier scale (Nachev, Collier & Robinson, 1970).

Drugs were made up in physiological saline and infused at 0·25 ml/min into the vein approximately 1 cm upstream from the point of measurement. Skin and room temperature were kept constant throughout each experiment.

The venous compliance during infusion of saline alone showed no significant change throughout each experiment and was constant from day to day in any one subject. Noradrenaline produced a dose dependent venoconstriction with a linear log dose-response relationship. The threshold was usually 2–4 ng/min and maximum constriction was produced by 64 ng/min. Adrenaline also produced venoconstriction with similar or slightly less potency. 5-Hydroxytryptamine also caused venoconstriction in a similar dose range but the log dose-response curves tended to be steeper.

Histamine, acetylcholine or isoprenaline produce neither constriction nor dilatation of the resting vein in doses ranging from 2–256 ng/min. However, when the vein was previously constricted by a constant infusion of noradrenaline, each of these drugs produced a dose dependent venodilatation; with the vein 50% constricted the dose required to achieve complete relaxation varied from 32–64 ng/min. The dilator effects of histamine, acetylcholine and isoprenaline could be prevented by prior infusion of mepyramine (5 μg in 10 min), atropine (5 μg in 10 min) or propranolol (10 μg in 10 min) respectively.

The venoconstriction observed with adrenaline, noradrenaline and 5-hydroxytryptamine is consistent with previous studies. Histamine has previously been reported to be a constrictor of limb veins in man (Sharpey-Schafer & Ginsburg, 1962), but we have observed only dilator effects. The dilator effects of isoprenaline indicate the presence of β-adrenoceptors.

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The responses of the isolated perfused spleen of man to sympathetic nerve stimulation, catecholamines and polypeptides

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Little information is available on the smooth muscle responses of the intact human spleen to various stimuli. It has been established in the dog that the spleen has both a resistance and a capacitative function (Davies, Gamble & Withrington, 1968) but indirect evidence suggests that the latter function is lacking in the human. We have successfully perfused, at constant flow, thirteen fresh human spleens with McEwen's (1956) solution equilibrated with 95% O_2 and 5% CO_2. The perfusion pressure was continuously monitored with a Statham transducer (P23Gb) whilst the venous pressure was maintained constant. Changes in perfusion pressure, therefore, reflected alterations in splenic vascular resistance. Volume changes of the spleen were recorded by enclosing it in a plethysmograph containing liquid paraffin at 37° C, but gradual leakages from the splenic capsule made quantitative observations difficult in some experiments. Whenever possible, postganglionic nerves were placed on platinum stimulating electrodes. All drugs were administered by injection into the arterial cannula.

In eight experiments splenic postganglionic nerves were stimulated at frequencies between 0·5 and 30 Hz; graded increases in splenic vascular resistance were observed in all experiments. The threshold frequency appeared to be 3 Hz and maximum increases in vascular tone occurred at 10 Hz. In five of these experiments spleen volume was continuously recorded and in three very small reductions (mean 3 ml) in spleen volume were observed to accompany the nerve stimulation.

Adrenaline and noradrenaline (0·25–25 μg) were administered in twelve experiments and graded increases in splenic vascular resistance were obtained; in five of these experiments spleen volume was continuously monitored and slight reductions (mean 5 ml) in spleen volume were detected. In four experiments the α-adrenoceptor blocking agent phenoxybenzamine (3–10 mg) was administered and the increase in splenic vascular resistance elicited by sympathetic nerve stimulation and the catecholamines was abolished. In two of the experiments the vasoconstrictor action of adrenaline was reversed after phenoxybenzamine to cause vasodilatation. The presence of β-adrenoceptors in the splenic vascular bed is also suggested by the