by a continuous local infusion of either noradrenaline or 5-hydroxytryptamine (Collier, Nachev & Robinson, 1970).

PGB_1 caused venoconstriction when infused over the dose range 100–500 ng/min in three experiments; doses below the constrictor range had no dilator effect when infused into veins preconstricted with noradrenaline (2 expts.). $PGF_{2\alpha}$ caused venoconstriction over the dose range 20–500 ng/min in four experiments; subconstrictor doses had no dilator effect (two expts.).

PGA_2 and PGE_2 had no action on resting veins, but caused vasodilation of veins which had been preconstricted with either noradrenaline or 5-hydroxytryptamine. PGA_2 had a dilator effect over the range 20–400 ng/min in five experiments. PGE_2, at an infusion rate of 100 pg/min, had a marked venodilator effect in all of six experiments; maximum dilatation was usually achieved at a rate of 1 ng/minute. After infusions of PGE_2 at rates of 10 ng/min or more a flare developed in the skin over the veins draining the infusion site. The flare lasted for up to 2 h, and after doses of 100 ng/min was accompanied by burning pain.

Venodilatation in response to PGE_1 and PGA_1, and constriction to $PGF_{2\alpha}$ has previously been reported in dogs (Greenberg & Sparks, 1969; Hedwall, Abdel-Sayed, Schmid & Abboud, 1970; and Mark, Schmid, Eckstein & Wendling, 1971). The observation that PGB_1 and $PGF_{2\alpha}$ constrict the circular muscle of human superficial veins while PGA_2 and PGE_2 cause dilatation provides further evidence that there may be more than one receptor for prostaglandins in a single tissue. Contrary actions of prostaglandins have previously been noted in circular muscle of the gut of man and guinea-pig (Bennett & Posner, 1971), and in circular muscle of human bronchi (Sweatman & Collier, 1968). The development of pain after intravenous PGE_2 has not previously been reported.

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Biphasic response of limb blood flow to intravenous methoxamine in anaesthetized man

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A biphasic response of limb blood flow to intravenous methoxamine was observed in four patients during nitrous oxide-oxygen-halothane anaesthesia. The details of the anaesthetic and experimental methods have been described previously (Fuzzey, Hope & Payne, 1971).

The four patients (ages 46–70 years) developed hypotension with a mean blood pressure of 44 mmHg and a mean heart rate of 66/minute. Forty seconds after the

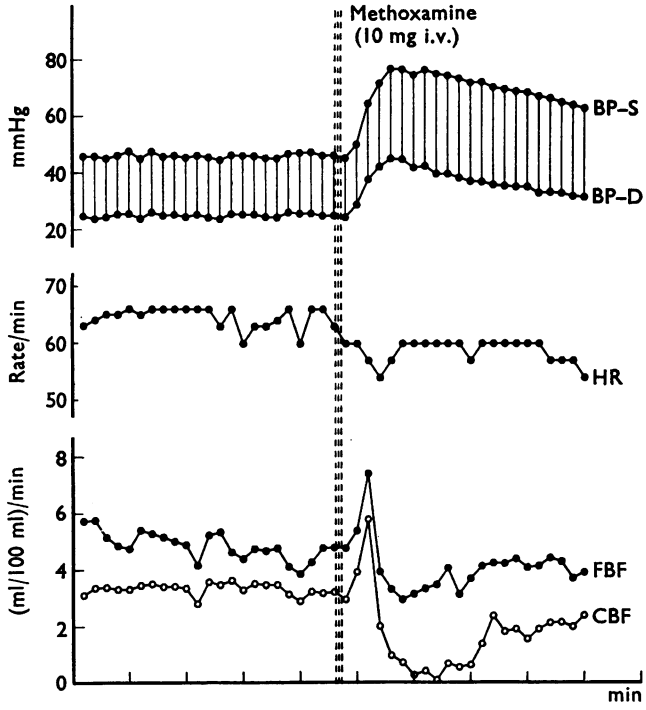

FIG. 1. Response to intravenous methoxamine in a patient anaesthetized with nitrous oxide, oxygen and halothane. Systolic (BP-S) and diastolic (BP-D) blood pressure, heart rate (HR) and forearm (FBF) and calf (CBF) blood flow.

injection of methoxamine (10 mg i.v.) the blood pressure rose to 75 mmHg (+69%) and the heart rate fell to 48/min (−27%). After 6 min the blood pressure was 59 mmHg (+33%) and the heart rate was 54/min (−18%). The peripheral blood flow showed a biphasic response in all patients. Thirty seconds after injection the blood flow rose in both forearm (+44%) and calf (+92%). Thirty seconds later the forearm and calf blood flows had fallen to below the control values (−44% and −83% respectively). Thereafter the blood flows increased slowly but 6 min later the forearm and calf flows were still below control levels (FBF −12%; CBF −22%). In one patient, who required a further injection of 10 mg methoxamine, intravenously 25 min later, the biphasic response was reduced.

A biphasic response to adrenaline has been demonstrated previously (Duff & Swan, 1951; Whelan 1952) and is probably due to a direct peripheral effect (Barcroft, 1963). The observed biphasic response to methoxamine, which is chemically related to adrenaline, is similar.

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