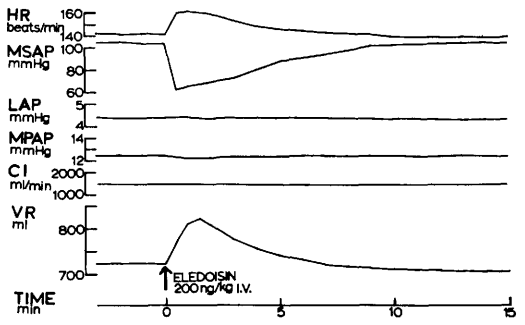

FIG. 3. Effects of eledoisin on heart rate (HR), mean systemic arterial pressure (MSAP), left atrial pressure (LAP), mean pulmonary arterial pressure (MPAP) and blood volume in venous reservoir (VR) in a dog. CI denotes cardiac input.

ing directly catecholamine secretion from the sympathetic post-ganglionic nerve endings and/or adrenals in dogs. Even if eledoisin would stimulate catecholamine secretion directly in dogs, the magnitude of this effect might be much smaller than in chickens or its effect might be overshadowed by the direct vasodilator action, since eledoisin decreases MSAP markedly and increases LAP and MPAP significantly(7). In contrast, it was found in this laboratory that electrical stimulation of cardiac sympathetic nerves or administration of norepinephrine usually increases MSAP and MPAP and decreases LAP. The present study indicates that the rises in LAP and MPAP are due to the increase in SVR by eledoisin. It remains uncertain, however, whether eledoisin decreases the peripheral vascular capacitance by the greater vasodilatation in the postcapillary arterioles(7), or whether eledoisin increases the arteriolovenular communications which exist physiologically in the peripheral vascular beds(8,9).

Summary. The effects of eledoisin on the cardiovascular system were studied in anesthetized dogs. It was found that eledoisin decreased MSAP and increased HR, CO, MPAP, and LAP. In addition, when cardiac input was kept constant by means of a Sigmamotor pump, eledoisin increased the blood level of the venous reservoir, indicating an increase in SVR. The increases in MPAP and LAP observed after eledoisin are most likely due to the increase in SVR.

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Effect of Prostaglandin E$_1$ on Blood Pressure, Heart Rate and Concentration of Free Fatty Acids of Plasma in Man.* (29771)

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The vasodepressor and smooth muscle stimulating activity discovered in extracts from seminal fluid and from male accessory glands(1,2,3,4,5) was named prostaglandin.

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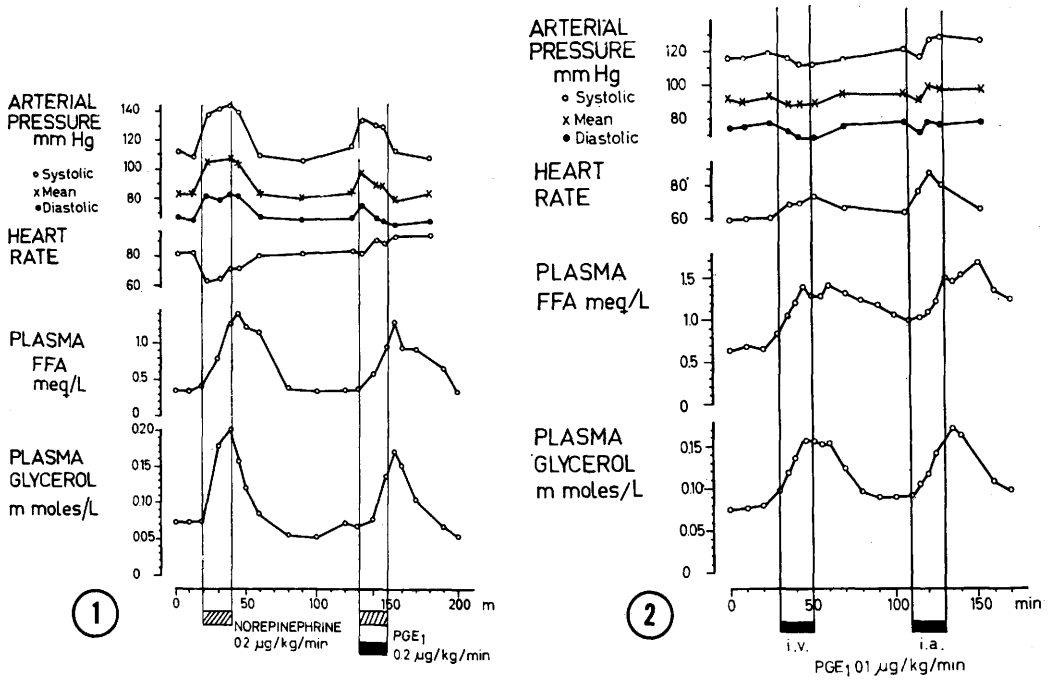

FIG. 1. Blood pressure, heart rate and arterial concentration of FFA and glycerol in plasma during intravenous infusion of norepinephrine and during simultaneous intravenous infusions of norepinephrine and PGE_1 to subject 4.

FIG. 2. Blood pressure, heart rate and arterial concentration of FFA and glycerol in plasma during infusions of PGE_1 to subject 1. The first infusion of PGE_1 was given intravenously, the second intraarterially in the aortic arch.

Recent chemical work has shown that the factor prostaglandin consists of a family of closely related compounds which are called prostanoic acids(6,7,8,9,10). Intravenous injection of prostaglandin into the cat and the rabbit was found to cause a prolonged blood pressure fall(11). Intravenous infusions of prostaglandin E (PGE) to man resulted in tachycardia and slight fall in blood pressure (12). In anesthetized dogs PGE_1, PGE_2 and PGE_3 were found to inhibit the stimulation of the mobilization of the free fatty acids (FFA) of plasma caused by catecholamines (13). Similarly it has been found that PGE_1 *in vitro* inhibits the catecholamine-induced enhancement of FFA mobilization from rat adipose tissue(14).

Data will be reported here on the effect of infusions of PGE_1 into man.

Materials and methods. Five healthy male subjects were studied in the morning after fasting overnight. Intravenous and intra-arterial catheters were inserted into vessels of the arms. Blood samples were taken from the intraarterial catheter into heparinized syringes. The plasma was immediately separated off by centrifugation and processed. FFA was determined titrimetrically(15) and glycerol enzymatically(16). PGE_1 was prepared as described earlier(7).

Results. PGE_1 was infused intravenously into 3 subjects at a rate of 0.1-0.2 µg/kg/min during 20 min (Fig. 1, 2). One subject was also infused intraarterially with PGE_1 as seen in Fig. 2. There were no significant changes in blood pressure during the infusions, while heart rate increased on the average about 20 beats per minute. Concentration of FFA increased in all 3 subjects in response to the infusion of PGE_1. Concentration of glycerol in plasma also increased during the infusion (Fig. 2).

Two subjects were infused first with norepinephrine (0.2 µg/kg/min) for 20 minutes and 90 minutes later simultaneously with norepinephrine (0.2 µg/kg/min) and PGE_1

(0.2 μg/kg/min). The infusion of norepinephrine caused the usual increase in blood pressure and in concentration of FFA and glycerol as well as a bradycardia (Fig. 1). When norepinephrine was infused together with PGE_1 the increase in blood pressure was reduced by about 50% and the bradycardia was completely abolished. The increase in concentration of FFA and glycerol was, however, only slightly reduced by PGE_1. On the other hand, when PGE_1 of the same batch as used in the studies on humans was infused to a dog during infusion of norepinephrine, the FFA level rapidly fell to normal levels in conformity with previous studies(13).

Discussion. The tachycardia observed during the infusion of PGE_1 confirms earlier results in man(12). The increase in concentration of FFA in plasma during the infusion of PGE_1 may be due to increased lipolysis in adipose tissue, since there was at the same time an increase in plasma glycerol level. This finding is surprising as PGE_1 has previously been shown to inhibit the catecholamine induced stimulation of FFA mobilization *in vivo* in dogs(13) as well as *in vitro* from rat adipose tissue(14). PGE_1 also inhibited the basal, nonstimulated release of glycerol from rat adipose tissue *in vitro*(14). Furthermore, when PGE_1 is given to nonanesthetized dogs in large single doses the FFA level in plasma drops considerably(17). If this difference in response to PGE_1 is due to a true species difference with regard either to the direct action of PGE_1 on FFA mobilization or with regard to eventual secondary effects, or whether it is due to differences in experimental design is not known. The present findings during infusions of norepinephrine and PGE_1 are also at variance with our earlier findings in dogs. While there was a significant inhibition of the cardiovascular response to norepinephrine, there was only a slight effect on the changes induced in the levels of FFA and glycerol.

Summary. Infusions of PGE_1 to human subjects caused an increase in heart rate and in concentration of FFA and glycerol in plasma. When PGE_1 was infused intravenously together with norepinephrine the norepinephrine induced increase in blood pressure was reduced and the bradycardia was abolished. The increase in concentration of FFA and glycerol in plasma caused by norepinephrine was, however, only slightly reduced by PGE_1.

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