ergic blockade interferes with glycogenolytic and lipolytic actions of catecholamines liberated in response to hypoglycemia thereby counteracting normal homeostatic mechanisms involved in returning blood sugar to normal levels (2,6). Another possibility is that these agents release endogenous insulin as shown by Sussman *et al.* (16) with propranolol in isolated perfused rat pancreas. However, sotalol or propranolol could act synergistically with insulin at its site of action to promote increased glucose uptake by muscle.

That sotalol and propranolol do not alter blood sugar levels *per se* is not surprising since previous work (17) has demonstrated no hypoglycemic effect for sotalol, while the reports on propranolol are conflicting (2–4,6).

The enhancement of insulin by β-adrenergic blocking agents may prove to be a useful effect and perhaps a primary effect of these agents in antagonizing certain of the metabolic actions of catecholamines. However, in view of the clinical results obtained with propranolol (2–4) it is suggested that sotalol be administered with caution to diabetic patients.

Summary. Sotalol and propranolol enhanced insulin-induced hypoglycemia in the rat. Neither agent displayed any significant hypoglycemic activity *per se.*

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Effects of Prostaglandins E_1, A_1 and $F_{2\alpha}$ on the Coronary and Peripheral Circulations* (32898)

JIRO NAKANO
Departments of Pharmacology and of Medicine, University of Oklahoma School of Medicine, Oklahoma City, Oklahoma 73104

Recently, a family of prostaglandins has been identified and their pharmacological properties have been studied in different species of animals (1–3). However, a few studies (4–6) have been made on the cardiovascular effects of prostaglandins E_1 (PGE_1) and $F_{2\alpha}$ ($PGF_{2\alpha}$). It was found that PGE_1 decreases systemic arterial pressure, whereas $PGF_{2\alpha}$ increases it. The present study was undertaken to investigate the effects of PGE_1, prostaglandin A_1 (PGA_1) and $PGF_{2\alpha}$ on the different regional circulations in dogs.

Methods. Thirty dogs weighing between 20 and 28 kg were anesthetized with sodium pentobarbital (30 mg/kg). In all experiments, the hemithorax was opened under artificial respiration. The pericardium was incised and the heart suspended in a pericardial cradle. Sodium heparin (2.5 mg/kg) was given intra-

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venously every half hour. Mean systemic arterial pressure was measured continuously with a Statham pressure transducer (P23AA) connected to a catheter placed in the left subclavian artery through the left mammary artery. Heart rate and myocardial contractile force were measured continuously with an Electronics for Medicine (EFM) tachometer (model TDC-1) and with a Walton-Brodie strain gauge arch (7,8) which was sutured directly to the right ventricular muscle. Blood flow in the left coronary, a common carotid, brachial, femoral, or renal artery was measured continuously with a Shipley-Wilson rotameter (9) as described previously (6, 10–12). All the hemodynamic parameters except heart rate were recorded with an EFM recorder (model DR8). PGE_1, PGA_1, and $PGF_{2\alpha}$ used in this study are crystalline preparations which were dissolved in pure ethanol (1 mg/ml) and diluted further with 0.9% NaCl solution to make a 20 or 40 μg/ml solution.

Each prostaglandin was administered intra-arterially to dogs every 20 min. The amount of the injected prostaglandin solution was always less than 0.1 ml. Peripheral resistance in each artery studied was calculated from the following formula: Peripheral resistance (mm Hg/ml per min) = mean systemic arterial pressure (mm Hg)/regional arterial blood flow (ml/min). The data in this paper were evaluated statistically employing the t test (13).

Results. The results of the intraarterial (ia) injection of PGE_1, PGA_1 and $PGF_{2\alpha}$ on the coronary and peripheral circulations are summarized in Table I. Tracings from representative experiments are illustrated in Fig. 1. As shown in Fig. 1, the ia injection of a single dose (0.1 μg/kg) of PGE_1 increased significantly the femoral arterial blood flow without any significant change in heart rate, mean systemic arterial pressure, and myocardial contractile force. Hence, PGE_1 decreased the femoral peripheral resistance. The effects of the ia administration of the same dose (0.1 μg/kg) of PGE_1 and PGA_1 on the blood flows and peripheral resistances in the coronary, brachial, femoral, carotid, and renal arteries are qualitatively similar to the observation made with PGE_1 in the femoral circulation (Fig. 1, Table I). However, the magnitude and duration of the vasodilator effect of PGE_1 was significantly greater and more prolonged

TABLE I. Summary of the Average Maximum Effects of the ia Administration of 0.1 μg/kg of PGE_1, PGA_1, and $PGF_{2\alpha}$ on Mean Systemic Arterial Pressure (MSAP), and Blood Flows (BF) and Peripheral Resistances (PR) in Coronary, Brachial, Femoral, Carotid, and Renal Arteries in Dogs.[a]

Artery	Parameters	PGE_1	PGA_1	$PGF_{2\alpha}$
Coronary (N = 6)	MSAP (Δ mm Hg)	0 ± 1	0 ± 0	0 ± 0
	BF (Δ %)	+ 73 ± 9[b]	+16 ± 3[b]	− 3 ± 3
	PR (Δ %)	− 58 ± 5[b]	−16 ± 3[b]	+ 5 ± 4
Brachial (N = 6)	MSAP (Δ mm Hg)	− 1 ± 2	− 1 ± 1	+ 1 ± 1
	BF (Δ %)	+108 ± 13[b]	+83 ± 5[b]	−13 ± 2[b]
	PR (Δ %)	− 55 ± 8[b]	−45 ± 4[b]	+16 ± 3[b]
Femoral (N = 6)	MSAP (Δ mm Hg)	− 1 ± 1	0 ± 0	− 1 ± 1
	BF (Δ %)	+111 ± 14[b]	+88 ± 9[b]	−22 ± 4[b]
	PR (Δ %)	− 69 ± 8[b]	−39 ± 9[b]	+28 ± 6[a]
Carotid (N = 6)	MSAP (Δ mm Hg)	− 1 ± 1	− 1 ± 1	—
	BF (Δ %)	+ 87 ± 8[b]	+62 ± 7[b]	—
	PR (Δ %)	− 34 ± 6[b]	−32 ± 8[b]	—
Renal (N = 6)	MSAP (Δ mm Hg)	+ 1 ± 1	− 1 ± 1	0 ± 1
	BF (Δ %)	+ 80 ± 14[b]	+60 ±11[b]	−15 ± 5[b]
	PR (Δ %)	− 42 ± 6[b]	−35 ± 7[b]	+18 ± 5[b]

[a] Results are given as mean ± SE.

[b] $p < 0.05$

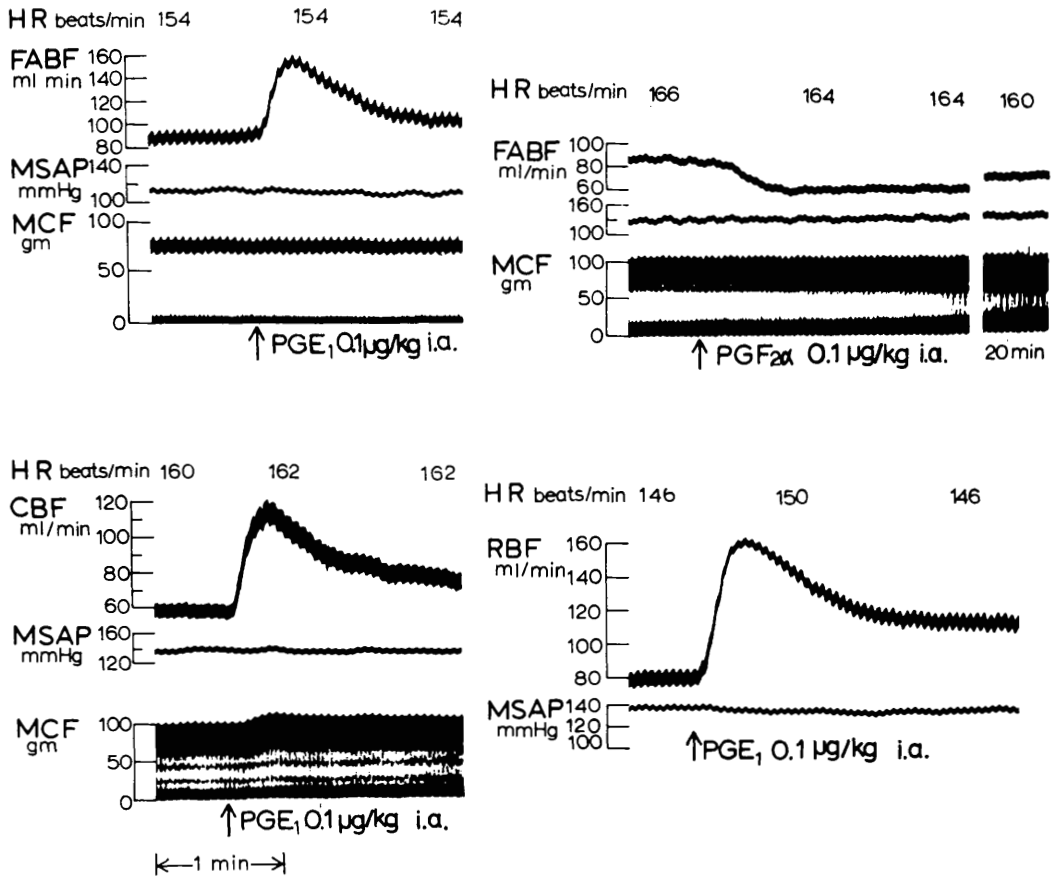

FIG. 1. Effects of the ia administration of a single dose (0.1 μg/kg) of PGE_1 (Upper Left and Lower Tracings) and $PGF_{2\alpha}$ (Upper Right Tracing) on femoral arterial blood flow (FABF), coronary arterial blood flow (CBF) and renal arterial blood flow (RBF) in dogs. HR, MSAP, and MCF denote heart rate, mean systemic arterial pressure, and myocardial contractile force, respectively.

than that of PGA_1. In addition, the intracoronary injection of the same dose of PGE_1 and PGA_1 increased myocardial contractile force significantly. Contrary to the vasodilator effect of PGE_1 and PGA_1, the ia administration of 0.1 μg/kg of $PGF_{2\alpha}$ decreased significantly the femoral arterial blood flow without producing any significant change in heart rate, mean systemic arterial pressure, and myocardial contractile force (Fig. 1 and Table I). Hence, $PGF_{2\alpha}$ increased the peripheral resistance in the femoral artery (Fig. 1 and Table I). The vasoconstrictor effect of $PGF_{2\alpha}$ on the brachial and renal arteries were qualitatively similar to that of $PGF_{2\alpha}$ on the femoral artery. The intracoronary administration of $PGF_{2\alpha}$ did not cause any significant changes in coronary arterial blood flow and myocardial contractile force.

Discussion. From the present study, it is evident that PGE_1 and PGA_1 are potent vasodilators whereas $PGF_{2\alpha}$ is a vasoconstrictor in different regional arteries in dogs. The present observations with PGE_1 and $PGF_{2\alpha}$ are essentially in agreement with those made by previous workers (4–6). They found that PGE_1 is a hypotensive agent in many species of animals, whereas $PGF_{2\alpha}$ is a hypertensive agent in dogs and rats (5,16). In similar preparations in our laboratory, when PGE_1 was compared with other vasodilators, PGE_1 is approximately 5 times more potent as a vasodilator than nitroglycerin, but has only about 1/50 and 1/200 vasodilator

activity of bradykinin and eledoisin, respectively (12,14). The physiological mechanisms of the vasodilator action of PGE_1 and PGA_1, and of the vasoconstrictor action of $PGF_{2\alpha}$ are uncertain from the present study. However, the vasoactivities of these three prostaglandins do not seem to be mediated by the adrenergic, cholinergic, histamine-releasing, or serotonin-releasing mechanism. Recently, in preliminary experiments in this laboratory, the vasodilator effect of the ia administration of 0.1 μg/kg of PGE_1 and PGA_1 was not blocked by the ia injection of atripine (50 μg/kg), propranolol (25 μg/kg) and diphenhydramine (250 μg/kg). Furthermore, the vasoconstrictor action of the ia administration of 0.1 μg/kg of $PGF_{2\alpha}$ was not blocked by the ia injection of phenoxybenzamine (0.5 mg/kg) and methysergide (1 μg/kg). These observations indicate that PGE_1 and PGA_1 dilate and $PGF_{2\alpha}$ constricts directly the regional blood vessels.

Summary. The effects of PGE_1, PGA_1, and $PGF_{2\alpha}$ on the coronary and peripheral circulations were studied in anesthetized dogs. The ia injection of either PGE_1 or PGA_1 increases blood flows and decreases the peripheral resistances in the coronary, brachial, femoral, carotid, and renal arteries. On the other hand, $PGF_{2\alpha}$ decreases blood flows and increases peripheral resistance in the brachial, femoral, and renal arteries. The present study indicates that PGE_1, and PGA_1 dilate and $PGF_{2\alpha}$ constricts directly the regional blood vessels.

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