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COMMUNICATIONS

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Comparison of a coronary vasodilator drug (carbochromen) and a cardiac stimulant (oxyfedrin) on blood flow and oxygen extraction in experimental myocardial infarcts

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In eighteen dogs, anaesthetized with trichlorethylene, catheters were placed in the coronary sinus, the vein adjacent to the descending branch of the left coronary artery (L.A.D.), the descending aorta and the right atrium. Anaerobic blood samples were taken from each of these sites before, and after, the acute ligation of the L.A.D. A catheter inserted distal to the ligature was used to measure peripheral coronary pressure, peripheral coronary flow (ml/min) and for the injection of ^{133}xenon into the developing infarct. Details of the examination of the clearance curve for the assessment of blood flow, of the techniques of analysis of blood samples for pO_2, pCO_2, pH and oxygen content, and the methods used to measure blood pressure and cardiac output have been previously described (Ledingham, McBride, Parratt & Vance, 1970; Ledingham, Parratt, Smith & Vance, 1971).

In doses (3 mg/kg, i.v.) which increased blood flow in the normal myocardium, carbochromen decreased infarct blood flow (21·4±2·5 to 18·3±1·8 (ml/100 g)/min) and peripheral coronary flow (1·3±0·3 to 1·1±0·1 ml/min) when administered 2–3 h after ligation. The pO_2 of both coronary sinus and coronary venous (infarct) blood was, however, increased (32±2 to 46±3 and 30±2 to 41±5 mmHg respectively), and the extraction of oxygen, both by the normal myocardium and by the ischaemic myocardium, was markedly reduced (51±3 to 29±3% and 54±3 to 35±3% respectively). These effects lasted for 40–75 minutes.

In contrast, oxyfedrin (Kukovetz, 1969), given to eight of these dogs in a dose of 0·5 mg/kg intravenously, 3–5 h after ligation, markedly increased infarct blood flow (13±3 to 22±3 (ml/100 g)/min), peripheral coronary flow (0·7±0·1 to 1·5±0·3 ml/min), heart rate (190±15 to 258±10 beats/min) and cardiac output (1·3±0·2 to 2·6±0·5 l./min). There were decreases in right atrial pressure (from a mean of +3·0 to a mean of +0·6 mmHg) and in peripheral vascular resistance (mean decrease 42%). The extraction of oxygen by the normal myocardium was significantly decreased (62±6 to 47±5%) but that by the ischaemic myocardium was relatively unchanged (58±5 to 53±3%). These effects lasted 30–60 minutes.

These results suggest that vasodilator drugs acting at arteriolar level, such as carbochromen, are unlikely to increase nutritive flow in the early stages of myocardial infarction. Since the pO_2 of blood draining the infarct is increased, however, as is heat clearance from the region (Grayson, Irvine & Parratt, 1969), it suggests that this drug is opening up non-nutritive (shunt) channels. In contrast, oxyfedrin, which increases myocardial contractility and decreases cardiac dimensions (Moore & Parratt, 1972) markedly increases nutritive (capillary) flow through the ischaemic muscle mass. Despite the marked tachycardia, there was electrocardiographic evidence (reduced ST depression) of reduced myocardial ischaemia in two-thirds of the animals given this drug.

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Effects of two hemicholiniums on the concentrations of plasma choline in the rabbit

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The toxicity of hemicholinium No. 3 (HC-3) (Schueler, 1955) is usually ascribed to its property of inhibiting choline entry into tissue and cellular structures. This communication reports the effects of HC-3 and its paraterphenyl analogue (TPHC-3) (Gardiner & Lee, 1969) on the plasma choline concentration of the rabbit.

Rabbits were anaesthetized with pentobarbitone sodium (50 mg/kg, i.v.), and heparin (200 I.U./kg) was administered. Respiration was recorded on smoked paper by a piston recorder connected to the tracheal cannula. Arterial blood pressure was recorded from a common carotid artery. Four control arterial samples (0·5 ml) were withdrawn from a cannula in the fermoral artery at 5 min intervals. The hemicholinium was then injected intravenously and blood samples were taken at 15 min intervals over 3 hours. The free choline concentration in 0·2 plasma was determined by the method of Gardiner & Domer (1968).

In all six animals given HC-3 (350 nmol/kg) and in two of the six given the same dose of TPHC-3, the plasma choline concentrations remained essentially constant over 3 h, like those of the control animals. In the other four animals given TPHC-3 there was a 2–4 fold rise in plasma choline 1–1½ h after injection. The rise occurred only after the animals showed signs of respiratory difficulty, and it declined when respiration improved about 45 min later.