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.

We are grateful to the Scottish Hospital Endowment Research Trust for financial support and to Dr. J. Domenet for a gift of oxyfedrin.

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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 Four control arterial samples (0·5 ml) were withdrawn from a cannula in the fermoral artery at 5 min intervals.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.

With higher doses (HC-3 1400 nmol/kg or TPHC-3 700 nmol/kg) there was little change in the plasma choline concentration or in the respiration within the first hour. About 60 min after a repeated dose of either drug the animals began to show signs of progressive respiratory distress, which was followed by a continuous rise in plasma choline concentration. The terminal choline concentration was from 8–10 times greater than basal values (about 12 nmol/ml). The increase in choline concentration was greatest in those animals whose respiration was most severely affected.

Since the rise in plasma choline was always secondary to respiratory difficulty it appears that it was a consequence of hypoxia rather than the result of a primary effect of the hemicholinium on the entry of choline into tissues.

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Effect of hydrocortisone and indomethacin on changes in LDH isoenzymes in skin after thermal injury

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After a mild thermal injury of 60° C for 1 min to one hind limb of cats and rabbits there are changes in the total lactic dehydrogenase (LDH) activity and in the proportion of LDH-1 in the skin of the injured limb (Lewis, Lowe, White & Worthington 1970; Lewis, Peters & White 1971). At 2 h the concentration of total LDH activity is significantly below control level whereas 6 h after the injury the activity is significantly raised. At 2 h the proportion of isoenzyme LDH-1 activity expressed as a percentage of total LDH activity is significantly raised to 181% of normal but returns to normal during the following 12–24 hours.

In the present experiments the anti-inflammatory drugs hydrocortisone (100 mg, 10 mg and 1 mg) and indomethacin (50 mg, 5 mg and 1 mg) were administered by close arterial injection over a 30 min period immediately after the injury. Although the fall in the concentration of total LDH activity 2 h after injury was not affected even by the highest doses of the anti-inflammatory agents, the increase in total LDH at 6 h, and the increase in the proportion of LDH-1, were significantly reduced. Thus the increase in total LDH activity to 126% of control level as a result of injury was significantly inhibited by all doses of hydrocortisone and by indomethacin (5 mg and 1 mg). The rise in the percentage of LDH-1 to 181% 2 h after injury was inhibited by all doses of both anti-inflammatory drugs.

Although it is not yet clear what role these enzyme changes play in the inflammatory process, the present findings indicate that the inhibition of increased LDH activity and particularly of the change in isoenzyme pattern in the skin might constitute an important aspect of the action of steroid and non-steroid anti-inflammatory agents.

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