minced rat lung incubated under oxygen with compound 48/80.

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PHARMACOLOGY

Analysis of the Vasodilator Effect of Adrenaline on the Skeletal Muscle Vessels of Man

INTRA-ARTERIAL infusions of small amounts of adrenaline cause a marked but transient increase in the flow of blood in the calf of the leg; this is followed by a return to the base-line or even by a decrease in flow of blood, although the infusion continues[1]. The biphasic effect of adrenaline may be explained by interaction with the different adrenergic receptors[2], the primary vasodilatation being mediated by the β-receptors and the secondary vasoconstriction being brought about by action on the α-receptors. Supporting such an explanation is the observation that the decrease in flow of blood in the muscles of the fore-arm due to adrenaline can be abolished by an intra-arterial infusion of dibenyline which is known to inhibit the action of adrenaline on the α-receptors[3]. Proof of the existence of β-receptors in blood vessels of man has so far not been reported.

In order to elucidate the increase in flow of blood in muscle due to intra-arterially administered adrenaline in man, we used the dichloro analogue of isoproterenol (*DCI*, Lilly Compound 20522) which in experiments on animals was found to abolish almost exclusively the action of adrenaline on the β-receptors[4]. This compound, therefore, can be considered a useful tool for the qualitative separation of α- and β-adrenergic receptors. Measurements of flow of blood were made in the calves of healthy male volunteers, 20–25 years of age, using the venous occlusion plethysmography[5]. All substances were subjected to infusions in the femoral artery by means of an electrically driven infusion pump. The transient vasodilatation in the calf caused by a 3 min. infusion of 1·76 μgm./min. l(−)adrenaline, which is easily reproducible in intervals of 3–8 min., could be abolished by a preceding infusion of *DCI*.

Fig. 1 shows a typical experiment. After a dose of 22 mgm. *DCI* within 5½ min., which produced some vasodilatation, the increase in flow of blood due to adrenaline was not diminished, but modified so that a secondary vasoconstriction followed (cf. A_1 and A_2, Fig. 1). After a further dose of 20 mgm. *DCI* within 2 min., however, no increase in flow of blood was observed during the following infusion of adrenaline (A_3); a decrease appeared instead. A small vasodilator effect was produced by adrenaline again 9 min.

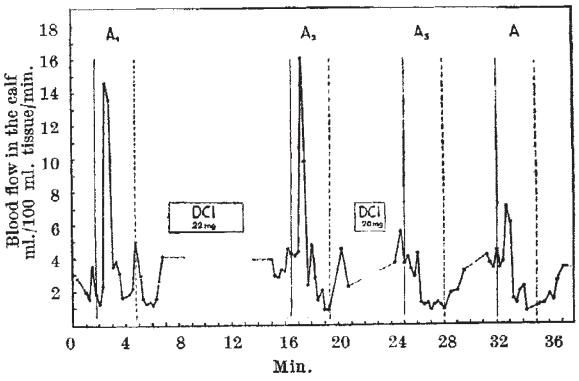

Fig. 1. A_1, A_4, A_2 and A_4, intra-arterial infusion of 1·76 μgm./min. l(−)adrenaline. *DCI*, 22 mgm.; intra-arterial infusion of 4 mgm. *DCI*/min. for 5·5 min. *DCI*, 20 mgm.; intra-arterial infusion of 10 mgm. *DCI*/min. for 2 min.

later, which was followed by a vasoconstrictor action (A_4).

The transient vasodilator effect of 0·8 μgm./min. isoproterenol (isopropyl-noradrenaline) (3 min. infusion time) on skeletal muscle vessels, which is similar to that of adrenaline[6], was also blocked by 37·5–62·5 mgm. *DCI*. The increase of flow of blood in the calf due to synthetic bradykinin[7], however, was not influenced by *DCI*.

It can be concluded from these experiments that the transient increase in flow of blood in the skeletal muscle vessels of man caused by adrenaline (and isoproterenol) is mediated by an interaction with the adrenergic β-receptors. If these are blocked by *DCI*, an increase in flow of blood does not occur, and sometimes even a decrease could be observed during the infusion of adrenaline. This vasoconstrictor effect may be explained by unmasking the action of adrenaline on the adrenergic alpha receptors.

Note added in proof. Similar findings have been reported by U. R. Bharadwaj and R. G. Shanks (*J. Physiol.*, **160**, 5*P*; 1961) on the human fore-arm.

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Effect of 'Busulphan' ('Myleran') on the Spermatogenic Cell Population of the Rat Testis

THE ability of alkylating agents to produce selective effects on spermatogenesis and sperm in rodents has been reported in several publications[1–3]. A comparison of the timing of sterile periods after treatment with the accepted duration of spermatogenic events in the testis has enabled the phase of spermatogenesis affected by particular compounds to be located.

Following the intraperitoneal administration of 'Busulphan' (10 mgm./kgm. in arachis oil) normal fertility is retained for about 50 days, after which sterility soon develops associated with oligo- or

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