

The inhibitory effect of insulin on pinnal anaphylaxis in the mouse

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Insulin has been reported to increase the severity of systemic anaphylaxis in the rat, mouse and guinea-pig (Dhar, Sanyal & West, 1967a; Adamkiewicz, Sacra & Ventura, 1964), but to have no effect upon a local anaphylactic reaction in the rat paw (Dhar, Sanyal & West, 1967b). The results presented are from experiments undertaken to investigate the effect of insulin upon the development of a local anaphylactic reaction in the mouse pinna.

Male mice were sensitized to horse serum by subcutaneous injection of 0.1 ml of a $\frac{1}{10}$ dilution and 14 days later 0.1 ml of a $\frac{1}{30}$ dilution. Six to eight days after the second dose of horse serum the mice were taken to a warm room (30-32°C) and 1 h later were injected intravenously with Evans blue. Forty minutes later the mice were challenged, under ether anaesthesia, by piercing each ear through a drop of horse serum. A further 30 min later the mice were sacrificed and their ears removed and mounted on cards. The anaphylactic reaction was measured as the area of blueing around the site of challenge.

Insulin (Insulin B.P., Burroughs Wellcome & Co.), given intraperitoneally 40 min before challenge, in the dose range 0.1-20.0 i.u./kg, gave both a dose-related inhibition of the anaphylactic reaction and a dose-related hypoglycaemia. Glibenclamide (2-50 mg/kg p.o.) induced hypoglycaemia and an inhibition of the anaphylactic reaction.

Alloxan (100 mg/kg i.v.) induced severe hyperglycaemia and inhibited the anaphylactic

reaction. Insulin, given to alloxan diabetic mice, produced animals with a normal serum glucose level but in which the anaphylactic reaction was markedly inhibited.

The inhibitory effect of insulin upon the anaphylactic reaction was reduced by surgical adrenalectomy and by the administration of the steroid synthesis inhibitor, metyrapone (2 x 200 mg/kg s.c.). The effect of insulin was unaffected by the α -adrenoreceptor blocking agent, phentolamine (1 or 5 mg/kg i.v.), but was reversed by the β -adrenoreceptor blocking agent, propranolol (25 mg/kg i.p.). With the exception of a slight reductive effect of propranolol, these treatments did not affect the hypoglycaemic response to insulin.

Histamine, 5-hydroxytryptamine and compound 48/80 induced a concentration-related blueing in the pinnae of non-sensitized mice when the ears were stabbed through solutions of these compounds. Pretreatment of the mice with insulin (10 i.u./kg i.p.) reduced the reaction induced by these compounds.

In pinnal anaphylaxis insulin has an inhibitory effect upon the development of the reaction. This effect is independent of its hypoglycaemic effect and appears to be mediated mainly through the adrenal glands.

References

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Muscular work and prostaglandin release

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Exercise is accompanied and followed by an increase in muscle blood flow. The mechanism of

this functional hyperaemia is unclear, although chemical factors seem to be primarily involved (Mellander & Johansson, 1968).

We have measured the output of prostaglandin-like substances (PLS) into the venous blood from hind-legs in 38 vagotomized dogs, anaesthetized with a urethane-chloralose (0.37 g/kg and 75 mg/kg) mixture. PLS activity was measured by the blood-bathed organ technique (Vane, 1964). A rat stomach strip, chick rectum and rat colon were superfused in series at 10 ml/min with re-oxygenated blood from a femoral vein. These tissues