Carbohydrate Metabolism and Anaphylaxis

SIR,—A fundamental approach to an understanding of the mechanisms of anaphylactic reactions is the study of factors that make certain species resistant to the process. The rat is well known to be resistant to anaphylaxis and histamine shock. Several conditions like suprarenalectomy (Dews and Code, 1953), hypophysectomy (Molomut, 1953), pretreatment with *Bordetella pertussis* vaccine (Sanyal and West, 1958), insulin injections before challenge (Sanyal, Spencer and West, 1959), facilitate the production of anaphylactic sensitivity. These conditions also produce hypoglycaemia (Sanyal, 1960). It was of interest, therefore, to discover whether conditions which produced hyperglycaemia had a protective effect against the production of systemic anaphylactic shock, in the rat.

When rats were sensitised 14 days previously by simultaneous injections of horse serum and *Bordetella pertussis* vaccine (Sanyal and West, 1958) the fasting blood sugar level was consistently lower than that seen in untreated animals. When a group of ten sensitised animals was subjected to intravenous challenge with horse serum, severe shock was produced and all animals died within the first 4 hr. Another group of 16 similarly sensitised animals, received subcutaneous injections of 2 per cent aqueous solution of alloxan tetrahydrate (300 mg./kg.), 4 days before challenge. This treatment produced glycoscuria and hyperglycaemia within the next few days. On anaphylactic challenge, the shock produced was mild, and 11 animals recovered. In 5 animals, shock was moderate and these animals died in 12 to 24 hr. after challenge.

In a group of rats similarly sensitised 14 days before, 5 ml. of 25 per cent solution of glucose was injected subcutaneously in each rat, at 0, 1, and $2\frac{1}{2}$ hr. It has been reported before (Adamkiewicz and Adamkiewicz, 1960) and confirmed again that such injections produce hyperglycaemia and glycosuria. Another group of similarly sensitised animals received 5 ml. of 8·46 per cent aqueous solution of sodium chloride at similar time periods, and served as control. The solution of sodium chloride injected was isomolar with 25 per cent glucose solution. Anaphylactic challenge was given intravenously 45 min. after the first injection of glucose or saline. All the animals of the control group receiving saline died of severe anaphylactic shock within first 2 hr.; at autopsy, typical haemorrhagic lesions characteristic of anaphylactic shock in this species were found. In contrast, animals that had received glucose, did not develop signs of anaphylactic shock and could be easily distinguished from animals that had received challenge after hypertonic saline. However these animals also died within 24 hr.; at autopsy, changes in intestines were minimal but subdural haematoma, as has been described to be the effect of over dosage of hypertonic solutions (Selye, 1952), were seen in all rats.

Thus in the rat, the state of blood sugar level influences the development of anaphylactic shock.

An interrelationship of allergic conditions and carbohydrate metabolism has been noticed for man (Van Ufford, 1952) and it has been reported also that nocturnal attacks of asthma may be associated with hypoglycaemia (Abrahamsson, 1941).

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The Action of Inhibitors of Catechol-O-Methyl-Transferase on the Exploratory Activity of Mice

SIR,—In a previous note we reported that pyrogallol enhanced inhibitory learning in rats (Izquierdo, I. and Merlo, 1963), and we considered it likely that this effect was due to a central adrenergic mechanism.

Using an actograph we have studied the exploratory activity in 77 white mice of 12 to 30 g. weight, before and after intraperitoneal injections of pyrogallol (3, 6, 12·5, 50 and 200 mg./kg.) and of 3,4-dihydroxyphenylacetamide (300 mg./kg.). The drugs were dissolved in 0·1 ml./kg. of distilled water just before injection. Control animals were given the water only.

The actographic records were run for 10 min. before, and for 20 min. after the injections. Only the definite suppression of exploratory activity was considered an inhibition. Responses were evaluated as the number of mice showing suppression at each dose of the drugs.

300 mg./kg. of 3,4-dihydroxyphenylacetamide suppressed exploratory activity of 9 out of 10 mice in which it was tested. The results obtained with pyrogallol are plotted in Fig. 1, in which the ordinates correspond to percentage of mice

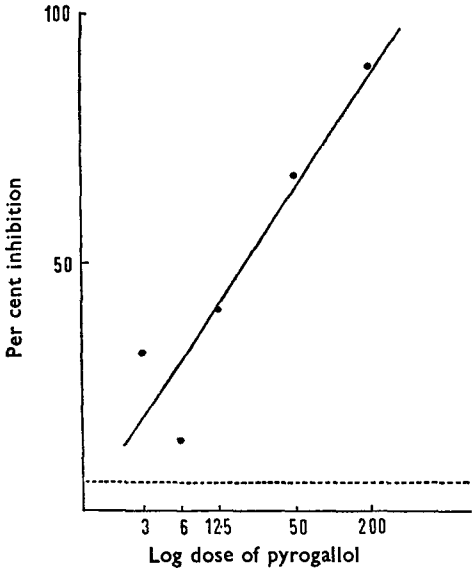

FIG. 1. Inhibition of exploratory activity of mice after pyrogallol. The broken line is the control response.