Anaphylactic shock and the blood sugar level

SIR,—Dhar, Sanyal & West (1967) reported that the severity of anaphylactic shock in rats is much altered by varying the level of glucose in the blood. When hypoglycaemia has been induced before challenge, systemic shock is potentiated, whereas shock is delayed when hyperglycaemia is present. We have now found that the severity of systemic anaphylactic shock under these conditions does not always correspond with that of local cutaneous anaphylactic shock.

Groups of 8 Wistar albino rats, 100–150 g, were sensitized by an intraperitoneal injection of horse serum (1 ml) and challenged by an intravenous dose of the same amount of antigen 12 days later (Sanyal & West, 1958). In most of the experiments, *Bordetella pertussis* vaccine (0·25 ml of 80×10^9 organisms/ml) was also injected with the sensitizing dose of antigen. Hypoglycaemia was induced by injecting insulin (5 I.U./kg) intraperitoneally 30 min before challenge whilst experimental diabetes was produced by injecting alloxan (300 mg/kg) subcutaneously into fasted animals 4 days before challenge. Glucose hyperglycaemia was produced by intraperitoneal injections of 5 ml of a 25% (w/v) solution of glucose in water. Mortalities were recorded at 2 and 24 hr respectively after challenge. Other groups of sensitized rats were used to determine the severity at 3 hr after challenge either of intestinal haemorrhage or of the local cutaneous reaction resulting from the subcutaneous injection of antigen (0·1 ml) into one of the paws of rats sensitized 12 days previously and then injected with azovan blue dye (12 mg/kg, intravenously) 30 min before challenge. The intensities of both reactions were recorded on relative scales from 0 to +++. Blood sugar levels were determined using the Folin-Wu method.

The results are in Table 1. Anaphylactic shock without the aid of adjuvant

TABLE 1. EFFECT OF DIFFERENT PRETREATMENTS ON THE MORTALITY OF RATS AND THE EXTENT OF INTESTINAL HAEMORRHAGE AND LOCAL ANAPHYLACTIC REACTION (RECORDED ON A RELATIVE SCALE FROM 0 TO +++) AS A RESULT OF ANAPHYLACTIC SHOCK 12 DAYS AFTER SENSITIZATION WITH HORSE SERUM.
The blood sugar values (mg/100 ml ± s.e.) before challenge are also shown.

Bordetella pertussis vaccine	Pretreatment	Blood sugar	Mortality (out of 8 animals)		Intestinal haemorrhage	Local anaphylactic reaction
			2 hr	24 hr		
Absent	None	98 ± 4·6	0	0	0	++
Present	None	68 ± 10·4	8	8	+++	+++
Absent	Insulin	57 ± 11·0	8	8	+++	++
Present	Alloxan	283 ± 32·6	0	2	+	+++
Present	Glucose	409 ± 31·0	1	8	++	+++
Present	Alloxan + Insulin	101 ± 6·0	0	4	+	+++

was minimal and there were no deaths and no intestinal haemorrhage; nevertheless, the local cutaneous reaction (as measured by the extent and degree of blueing of the paw injected with the specific antigen) was marked. When adjuvant was present, the blood sugar level was statistically significantly reduced and anaphylactic shock was so severe that all 8 animals died within 2 hr with typical extensive haemorrhagic lesions in the intestines; the local response was also intense and greater than that recorded when *B. pertussis* vaccine was absent. Whereas there were no deaths in the group of 8 animals after anaphylactic shock when no vaccine was present, all 8 died within 2 hr when insulin was injected 30 min before challenge; blood sugar levels were about the same as those found

when the vaccine (but no insulin) was injected with the sensitizing dose, and they were significantly lower than the value of non-sensitized control rats (97 $\pm$ 6·8 mg per 100 ml). Typical extensive haemorrhagic lesions were found in the intestines of all of these animals although the intensity of the cutaneous reaction was not different from that found in control animals subjected to anaphylactic shock.

In experimental diabetes, the mean blood sugar level at the time of challenge was over 280 mg/100 ml and only mild anaphylactic shock developed; there were no deaths at 2 hr, but 2 out of 8 animals died overnight with minimal intestinal haemorrhage. Nevertheless, the local cutaneous anaphylactic reaction was intense, the raised blood sugar level failing to modify the severity of the reaction. Similarly, high doses of glucose delayed the time of death (although all 8 animals in the group died within 24 hr), reduced the severity of the haemorrhagic reaction in the intestines, and failed to reduce the local cutaneous response. When insulin was injected into animals made diabetic with alloxan and the blood sugar levels were not statistically significantly different from animals sensitized to the antigen without the aid of adjuvant, there were no deaths 2 hr after challenge and only half of the animals died by 24 hr. Intestinal haemorrhage was minimal and yet the local cutaneous anaphylactic reaction in the paw was intense.

The results show that, during anaphylactic shock in rats, hypoglycaemia greatly increases the severity of intestinal haemorrhage but does not always increase the intensity of the local cutaneous reaction; also, hyperglycaemia markedly reduces the systemic reaction and yet the local cutaneous reaction is not modified. Finally, when insulin is used to reduce the blood sugar level of diabetic rats to control values, systemic anaphylactic shock is reduced but the local cutaneous reaction remains at a maximum.

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