hyperglycaemic rats and the average number of new lesions produced was reduced from 2·0 to 0·91 per rat. The distribution of the new lesions appeared to be different in the two groups. In normal animals the feet were predominantly affected and in hyperglycaemic animals the tails.

The mechanism of this suppressive effect of hyperglycaemia in allergic and inflammatory conditions is unknown. It has been suggested that hyperglycaemia inhibits, and hypoglycaemia potentiates the antigen-antibody reaction if this reaction involves a carbohydrate moiety (Adamkiewicz, 1963). An example is the tuberculin reaction which high blood sugar levels decrease and low levels increase (Cornforth & Long, 1953). Polysaccharide antigens are known to be involved in this reaction. However, this hypothesis does not take account of how hyperglycaemia inhibits anaphylactoid reactions and suppresses the formation of granulation tissue, processes which do not involve antigen-antibody combination.

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Validity of ptosis as a measure of the central depressant action of reserpine

SIR,—Ptosis is a characteristic feature of the action of reserpine in many animal species and has been used for the bioassay of reserpine-like alkaloids (Rubin, Malone, Waugh & Burke, 1957). It is usually regarded as a sign of the central action of reserpine, and the ability of drugs to prevent reserpine-induced ptosis has been proposed as a test for antidepressants (Chen, 1964). However, ptosis is also produced by adrenergic-neurone blocking agents of the quaternary ammonium or guanidine types (Costa, Kuntzman, Gessa & Brodie, 1962; Fielden & Green, 1965), which do not enter the brain in significant amounts (Boura, Copp, Duncombe, Green & McCoubrey, 1960). Since reserpine causes profound noradrenaline depletion in peripheral adrenergically-innervated tissues, with consequent loss of sympathetic function (Carlsson, Rosengren, Bertler & Nilsson, 1957), it is pertinent to inquire whether reserpine-induced ptosis may not also occur as a result of peripheral sympathetic blockade.

In Table 1, the extent of ptosis, scored on a 0–8 scale (Rubin & others, 1957), is compared with the depletion of heart and brain noradrenaline, or brain 5-hydroxytryptamine (5-HT) 4 hr after subcutaneous injection of various doses of

TABLE 1. EXTENT OF PTOSIS AND DEPLETION OF NORADRENALINE AND 5-HT IN MICE TREATED WITH RESERPINE (R) OR RESERPINE PLUS BRETYLIUM (R + B)

Dose of reserpine (mg/kg)	Ptosis		Noradrenaline depletion (%)				5-HT depletion (%)	
			Heart		Brain		Brain	
	R	R + B	R	R + B	R	R + B	R	R + B
0·025	0	—	40	—	<10	—	—	—
0·05	0	—	65	—	10	—	—	—
0·1	2·0	—	85	—	15	—	—	—
0·3	4·8	0·3	>95	40	35	25	25	30
0·5	5·5	2·0	>95	70	60	65	50	50
1·0	6·3	3·5	>95	85	80	90	70	75

reserpine (Serpasil, Ciba), or reserpine plus bretylium tosylate (20 mg/kg), into groups of 6 mice. The hearts from all 6 mice were pooled, as were the brains from 2 mice in each group. The noradrenaline and 5-HT were extracted with butanol and assayed fluorimetrically (Mead & Finger, 1961; Fielden & Green, 1965). The minimal dose of reserpine producing ptosis was 0·1 mg/kg, which lowered heart noradrenaline by 85% but brain noradrenaline by only 15%. Reserpine is known to deplete noradrenaline more readily from peripheral tissues than from brain (Carlsson & others, 1957), and loss of cardiac responses to sympathetic stimulation has been shown to be detectable after depletion of 85–90% of heart noradrenaline (Gaffney, Chidsey & Braunwald, 1963). More striking evidence that reserpine-induced ptosis is caused primarily by peripheral noradrenaline depletion is the protection afforded by bretylium, a quaternary ammonium compound which does not readily penetrate the brain (Boura & others, 1960). Bretylium alone does not significantly affect mouse-heart noradrenaline although it does produce ptosis which, however, disappears within 4 hr. When it is injected together with reserpine, the reserpine-induced ptosis is markedly decreased as is the fall in heart noradrenaline, but the fall in brain noradrenaline or 5-HT is not. The decrease in ptosis is roughly correlated with the prevention of heart-noradrenaline depletion. This effect is essentially a delay in onset of ptosis, not a reversal, since ptosis was as marked 24 hr after reserpine plus bretylium as after reserpine alone; and if bretylium was given 4 hr after reserpine no diminution in ptosis was seen. Bretylium has previously been shown to protect rats against heart-noradrenaline depletion after giving reserpine (Callingham & Cass, 1962).

Brodie, Spector & Shore (1959) attempted to differentiate between passive eyelid closure due to sympathetic blockade on the one hand, and active eyelid closure due to central parasympathetic stimulation on the other. We have been unable to observe such a distinction, but our experiments do not exclude the possibility that a centrally-produced active eyelid closure may occur with doses of reserpine above 1 mg/kg. It nevertheless seems clear from our results that ptosis after low doses of reserpine is produced by a peripheral rather than a central mechanism. This being so, prevention of reserpine-induced ptosis should be looked at with some caution before it is accepted as a sign of a central antidepressant action.

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Seasonal variation in the resistance of rats

SIR,—For the past three years, the sensitivity of rats to anaphylactic shock has been found to show seasonal variation. It was first thought that the antigen or the adjuvant might have been modified in the summer months but this possibility was finally ruled out by our obtaining similar results with different antigens and different adjuvants. It has since been found that the resistance of the animals varies with the season, as illustrated in Table 1.

TABLE 1. CHANGES IN THE MORTALITY RATE OF WISTAR RATS SUBJECTED TO ANAPHYLACTIC SHOCK AT DIFFERENT TIMES OF THE YEAR 1964

Month	No. of rats tested	No. of deaths	Mortality rate (%)
Jan.–Feb.	45	40	89
April–May	28	20	71
July–Aug.	28	4	14
Nov.–Dec.	36	33	92

Male Wistar albino rats (body weight 150–200 g) obtained from A.R.C., Compton, were sensitised using horse serum (0·5 ml) and *Bordetella pertussis* vaccine (0·25 ml of 80,000 $\times$ 10^6 organisms per ml) intraperitoneally. Ten to twelve days later, they were challenged intravenously with horse serum (1 ml) and deaths were recorded over 24 hr. During the period from June to September, they were relatively insensitive to anaphylactic shock, whereas at other times high mortality rates were obtained. It was possible to reduce the challenging dose to 0·05 ml in the winter and obtain similar high mortality rates. This observation may be of importance to those who are studying the mechanism of anaphylactic shock *in vivo* and that of the antigen-antibody reaction using isolated mast cells.

A similar change in the sensitivity of rats has also been noted after experimental traumatic or tourniquet shock. To produce traumatic shock, anaesthetised male Wistar albino rats were rotated in a revolving drum (40 rotations/min) so that at each rotation they fell 18 inches (the Noble–Collip technique). They were then removed from the drum and their mortality rates were recorded over 24 hr. The results shown in Table 2 indicate that rats in June and July were much more resistant than those in November and needed at least twice as long in the revolving drum to produce similar mortality rates.

To produce tourniquet shock, male Wistar albino rats were restrained and rubber tourniquets were placed high up on the hindlimbs for 4, 5 or 6 hr. They