TABLE 2. THE RESULTS OF VARIOUS MATINGS TO SHOW THAT THE REACTORS ARE PREDOMINANTLY HETEROZYGOTES

Mating	Litters	Offspring (F_1 generation)	Non-reactors		
			No. found	Percentage	% expected*
Reactor x Reactor	10	123	26	21	25
Reactor x Non-reactor	4	45	24	53	50
Non-reactor x Non-reactor ..	4	37	37	100	100

* % expected is the maximum number of non-reactors expected if the parent reactor is a heterozygote.

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Sympathomimetic amines and vascular permeability

SIR,—Both dextran and egg-white increase vascular permeability when injected intradermally into rats and produce oedema when given subcutaneously into the plantar region of the foot. These reactions are prevented when large doses of adrenaline and noradrenaline are injected intravenously a short time before the dextran and egg-white (Parratt & West, 1958). A study has now been made of the relative activities of some sympathomimetic amines given *intradermally* in inhibiting these changes in vascular permeability.

Male Wistar albino rats obtained from Bengers Ltd., Holmes Chapel, were injected intravenously with azovan blue dye (7 mg/kg) and then given dextran (Intradex, Glaxo) intradermally into the ventral abdominal skin (100 μg/0·1 ml) and subcutaneously into one hind paw (6 mg/kg). In other areas of the abdominal skin, the dextran, mixed with varying amounts of the isomers of adrenaline, noradrenaline and isoprenaline, was injected in volumes of 0·1 ml whilst the other hind paw received dextran and one of the amines. (–)-Adrenaline was effective in doses of 1 μg intradermally and 5 μg subcutaneously. The relative activities of the other amines are shown in Table 1. Inhibition of the egg-white responses was also tested and found to be similar to that of dextran.

As (–)-noradrenaline is much less active than (–)-adrenaline, vasoconstriction does not appear to play an important role in these vascular permeability changes. The effect on carbohydrate metabolism is more likely since the relative activities of the amines are related to their ability to produce hyperglycaemia; in addition, exogenous glucose prevented both the dextran and egg-white responses. Bradykinin release may also be involved in these responses, and when the action of

bradykinin was tested the relative inhibitory activities of the sympathomimetic amines were similar to those recorded in Table 1. However, the doses used

TABLE 1. INHIBITION OF THE DEXTRAN RESPONSE IN RATS BY SYMPATHOMIMETIC AMINES

Route of injection of dextran	Dose of amine producing inhibition ((−)-adrenaline = 1)			
	(+)-adrenaline	(−)-noradrenaline	(+)-noradrenaline	(±)-isoprenaline
Intradermal	10	9	90	490
Subcutaneous.. ..	9	10	95	500

were much smaller; for example, 0·1 μg adrenaline was effective when given with or 10 min before the bradykinin dose (0·1 μg). In contrast, exogenous glucose exerted only a feeble inhibitory action on the bradykinin response.

Recently, Aschheim & Zweifach (1964) showed that intradermal adrenaline followed by the external application of xylene rendered rat skin resistant 24 hr later to intradermal injections of histamine liberators such as compound 48/80. They considered that the adrenaline-xylene treatment was both efficient and reliable as a method for depleting the skin of vasodilator amines. This is unlikely as we have found little release of histamine from the skin under this treatment. Moreover, when similar experiments were made with other sympathomimetic amines, the relative activities were very close to those shown in Table 1. Noradrenaline was much less active than adrenaline (minimum dose used was 0·1 μg), and isoprenaline was almost without effect. As with the bradykinin response, exogenous glucose had only a feeble action on the adrenaline-xylene treatment. It is possible that xylene inhibits the formation of bradykinin and adrenaline inhibits the action of free bradykinin, or that the adrenaline-xylene treatment fixes the tissue mast cells for a period of time.

Finally, we have evidence that adrenaline is more active than noradrenaline, and much more active than isoprenaline, in preventing the effects of thermal injury in rats (45° for 30 min). In these experiments, the sympathomimetic amines were given in divided doses to maintain suitable tissue levels and so prevent the effects of the bradykinin which is known to be released when hind paws of rats are kept at this temperature.

These experiments illustrate that adrenaline and possibly noradrenaline are likely to act as local anti-inflammatory hormones in the tissues, thereby controlling the development of inflammation resulting from injury.

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