Letters to the Editor

Reactivity of Wistar rats to dextran

SIR,—The inflammatory anaphylactoid reaction produced in rats by the single intraperitoneal injection of dextran is mediated chiefly through a release of 5-hydroxytryptamine and histamine (Parratt & West, 1957). Recently, Harris & West (1963) found that not all rats of the Wistar strain react to this injection although the concentrations of histamine and 5-hydroxytryptamine in the skin of rats not reacting are similar to the concentrations in the skin of those reacting. Non-reactivity has since been shown to be a genetically-controlled recessive character (Harris, Kalmus & West, 1963). In the present work, we have found that rats obtained from one Wistar colony now contain the non-reactivity gene at a much higher frequency than when it was last reported. The cause of the frequency change has not so far been elucidated.

Wistar albino rats from random-mated stock of the Agricultural Research Council, Compton were injected with dextran (Intradex, Glaxo) according to the method of Harris & West (1963) and divided into two types: those which showed the anaphylactoid reaction consisting of gross oedema of the extremities (hereinafter called Reactors) and those which did not react (called Non-reactors). Although in January 1963 the percentage of non-reactors was similar to that found in the previous 4 years, by April 1963 more than half of the animals tested at each time failed to give the anaphylactoid reaction. The percentage of non-reactors reached above 80% of the total by September 1963 and has since remained at this level. These results are shown in Table 1.

TABLE 1. THE CHANGE IN PERCENTAGE OF NON-REACTOR WISTAR RATS OBTAINED FROM A.R.C., COMPTON, BETWEEN 1962–64

Year	Month	No. of rats tested	Non-reactors	
			No. found	Percentage
1962	Up to Oct.	2,600	573	22
1963	Jan.–Feb.	150	36	24
	April–June	405	206	51
	Sept.–Nov.	179	148	83
1964	Jan.–Feb.	170	136	80
	March–April	214	181	84
	May–June	252	219	87
	July–Sept.	110	90	82
	Oct.–Nov.	500	401	80
Total since September 1963		1,425	1,175	82

To maintain more than a 4 to 1 ratio in favour of non-reactivity which is a recessive character, it can be predicted that most of the reactors now being supplied are heterozygotes and carry the non-reactor gene. By selective breeding, this has proved to be so. Table 2 shows the results of various matings between reactors and non-reactors. The percentages of non-reactors found in the offspring are very close to those expected if the present reactors are mostly heterozygotes. It is hoped that these results will stimulate biologists to check their animal material for reactivity before attempting to determine the anti-inflammatory activity of a new compound by its ability to suppress the dextran anaphylactoid response.

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