LETTERS TO THE EDITOR

Mouse Strain Difference in Response to Antihistamine Drugs

SIR,—It may appear as a truism to state that the species of animal sensitive to histamine challenge respond more readily to the protective action of antihistamines but differences in the responses of mouse strains serve to illustrate that such diversity may be of genetic origin.

Mice from five strains (one random bred, LAC greys, two inbred, C57BR/cd and CBA, and their reciprocal crosses) were sensitised to histamine with pertussis vaccine. The controls were challenged directly with histamine acid phosphate while the test mice first received a subcutaneous dose of one of three antihistamine compounds and were subsequently challenged. Adult mice between six and eight weeks old were used, and where available were distributed in equal numbers of the sexes and equal numbers of control and test mice. The differences between the numbers of mice surviving in the test groups and in the control groups were calculated as mice surviving due to the action of the antihistamine drug.

Results in Table I are in the order of strain sensitivity to histamine that had been previously determined (Brown 1959) and the challenge dose of histamine used for each strain was at least 2·5 times the approximate average lethal dose. The absolute histamine sensitivity for each strain varies with the sensitisation response to histamine produced by the batch of pertussis vaccine used. The hybrid strains and the LAC greys have an average lethal dose to histamine of about 100 mg./kg. body weight. To a larger dose of histamine, 250 mg./kg. mouse, the LAC greys are slightly less sensitive than the hybrid strains and the effect of antihistamine, particularly that of the larger doses, upon the responses, is perhaps not so marked and thus in accordance with the known effects in other species.

TABLE I

THE EFFECT OF ANTIHISTAMINE DRUGS GIVEN SUBCUTANEOUSLY TO MICE 20 MIN. BEFORE CHALLENGE WITH HISTAMINE ACID PHOSPHATE

Strain	Histamine acid phosphate mg./kg. mouse	No. of mice per group	Surviving control mice		Mice surviving as a result of antihistamine dose in in mg. per mouse											
					Tripelennamine				Chlorpheniramine				Diphenhydramine			
					0·08		0·40		0·02		0·10		0·08		0·40	
			Nos.	per cent	Nos.	per cent	Nos.	per cent	Nos.	per cent	Nos.	per cent	Nos.	per cent	Nos.	per cent
C57BR/cd	100	21	1	5	11	52	19	91	1	5	18	86	8	38	20	95
$BRCF_1$	250	38	4	11	16	42	33	87	19	50	33	87	24	63	34	90
$CBRF_1$	250	41	5	12	23	56	33	81	17	42	33	81	21	51	35	85
LAC greys	250	37	10	27	18	49	28	76	15	41	26	70	17	46	28	76
CBA	800	44	21	48	5	11	3	7	5	11	15	34	2	5	6	14

A consideration of the inbred strains and their genetically similar reciprocal crosses, shows that the insensitive strain CBA is little protected against histamine by any antihistamine drug, while the other strains are in the main well protected. An exception is shown by the C57BR/cd mice against the lower dose of chlorpheniramine. A five-fold increase in the concentration of this drug results in a seventeenfold increase in response. Such a demonstration of precision suggests that chlorpheniramine action is specific against histamine, and that C57BR/cd mice would be exceptionally valuable for its assay.

Several deductions may be made from the general responses to antihistamine of drugs of the inbred strains and their hybrids. First, the unresponsiveness of the CBA strain and the responsiveness of the hybrids and C57BR/cd strain indicate that this reaction is controlled by an incompletely dominant trait. Non-response, as it is confined to one parent and does not appear in the progeny, may be controlled by a recessive gene in the same way as non-anaphylactoid reaction (Harris and West, 1961). Second, the same pattern of response occurs in all species; those animals easily sensitised to histamine are well protected by antihistamine. Finally, the differentiation between antihistamines by the homozygous C57BR/cd strain may point to a relation between homozygosity and specificity, suggesting that at some point in this particular reaction a single gene may be involved.

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REFERENCES

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Harris, J. M. and West, G. B. (1961). *Nature (Lond.)*, **191**, 399–400.

Gamma Irradiation of *Bacillus subtilis* Spores

SIR,—When aqueous suspensions of *Bacillus subtilis* spores were exposed to gamma irradiation from a Cobalt-60 source and subsequently stored at 0° and 20° more survived at 20° than at 0°.

Also the slopes of the lines relating dose to numbers of survivors were not parallel, but converged at approximately total survival at no dose of radiation. Thus spores subsequently stored at 20° survived larger doses of gamma radiation than the spores subsequently stored at 0°.

These results are summarised in Table I.

TABLE I

DIFFERENCE IN SLOPES OF LOG PER CENT SURVIVOR/DOSE REGRESSIONS AFTER STORAGE FOR ONE MONTH AT 0–4° AND 20–26°

Temperature	Correlation coefficient	Regression coefficient (rad. 10^{-5}	'D' value (rad. 10^5)
0–4°	−0·9841	−0·5425	1·83
20–26°	−0·9950	−0·4493	2·23

('D' value = decimal reduction factor)
Calculated 'd' (Bailey, 1959) = 2·284
Tabulated 't' (P = 0·05) = 2·228
There is therefore a significant difference in slope.

When an aqueous suspension of *B. subtilis* spores is heated at 60° for 3 min., or 60° for 15 min., or 90° for 5 min., there is a progressive increase in the number of spores which produce colonies on agar plates. But if a second sample of the spore suspension was first irradiated and then heated in the same way, there was a decrease in the number of spores producing colonies on agar plates (Table II.)

It is well-known that heating at sub-lethal temperatures causes dormant spores to germinate with a resultant increase in viable count (Desrosier and Heiligman, 1956; Curran and Evans, 1945 and 1947). This response varies