HOMOCYTOTROPIC IgG_1 AND IgE ANTIBODIES AND PASSIVE CUTANEOUS ANAPHYLAXIS IN MICE OF VARIOUS STRAINS

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Experiments on mice of nine strains with different H-2 genotypes showed that a predisposition to anaphylaxis at the stage of formation of IgG_1 and IgE antibodies and sensitivity of the skin to passive anaphylaxis and to histamine are independent characters, interaction between which and with other factors form the overall predisposition to immediate allergy.

KEY WORDS: *reagins; passive cutaneous anaphylaxis; histamine; genotype.*

Ability to respond immunologically to various synthetic and native antigens is determined by immune response (Ir) genes which, in mice, are linked with the basic H-2 histocompatibility complex [1, 3, 13]. Investigations have shown that animals of different strains are unequally sensitive to passive cutaneous anaphylaxis (PCA) induced by IgG_1 and IgE antibodies [4, 8].

The object of this investigation was to study the ability of mice of different strains to produce homocytotropic antibodies of the IgG_1 and IgE classes against a particular antigen and the sensitivity of the animals of these strains to PCA induced by IgG_1 and IgE antibodies. Together with determination of the sensitivity of the animals to PCA, cutaneous sensitivity also was determined to histamine, one of the mediators of anaphylaxis.

TABLE 1. Sensitivity of Mice to Histamine and PCA Induced by IgG_1 or IgE Antibodies (M ± m, n = 5).

Strain of mice and H-2 type	PCA				Intensity of cutaneous reaction to histamine
	$\log_2 \frac{1}{T}$		$\frac{1}{T_i} : \frac{1}{T_n}$		
	IgG_1—ПКА	IgE—ПКА	IgG_1—ПКА	IgE—ПКА	
Noninbred	9,3±0,3	8,3±0,3	—	—	
AKR (H-2^k)	7,1±0,4**	8,5±0,2	1 : 4	1 : 1	
BALB/c (H-2^d)	9,3±0	4,3±0***	1 : 1	1 : 16	0,43±0,009
CBA (H-2^k)	7,1±0,2***	7,1±0,2**	1 : 4	1 : 2	0,39±0,012
CC57BR (H-2^b)	6,3±0,3***	4,3±0***	1 : 8	1 : 16	0,52±0,015
CC57W (H-2^b)	7,3±0,3**	7,3±0,3*	1 : 4	1 : 2	
C57BL/6 (H-2^b)	6,3±0***	6,3±0***	1 : 8	1 : 4	0,34±0,013
DBA/2 (H-2^d)	10,3±0,3*	2,5±0,2***	2 : 1	1 : 64	0,28±0,008
SWR (H-2^q)	10,5±0,2*	8,7±0,2	2 : 1	1 : 1	
129 (H-2^{bc})	8,3±0*	3,5±0,2***	1 : 2	1 : 32	

Legend: 1. T) Titer of PCA; T_i and T_n) titers obtained in inbred and noninbred mice, respectively. 2. *) $P < 0.05$, **) $P < 0.01$, ***) $P < 0.001$ compared with results obtained in noninbred mice. 3. Intensity of skin reaction to histamine expressed as amount of Evans' blue dye (in μg) extracted from two areas of skin in the same animal, into each of which 0.01 μg histamine was injected.

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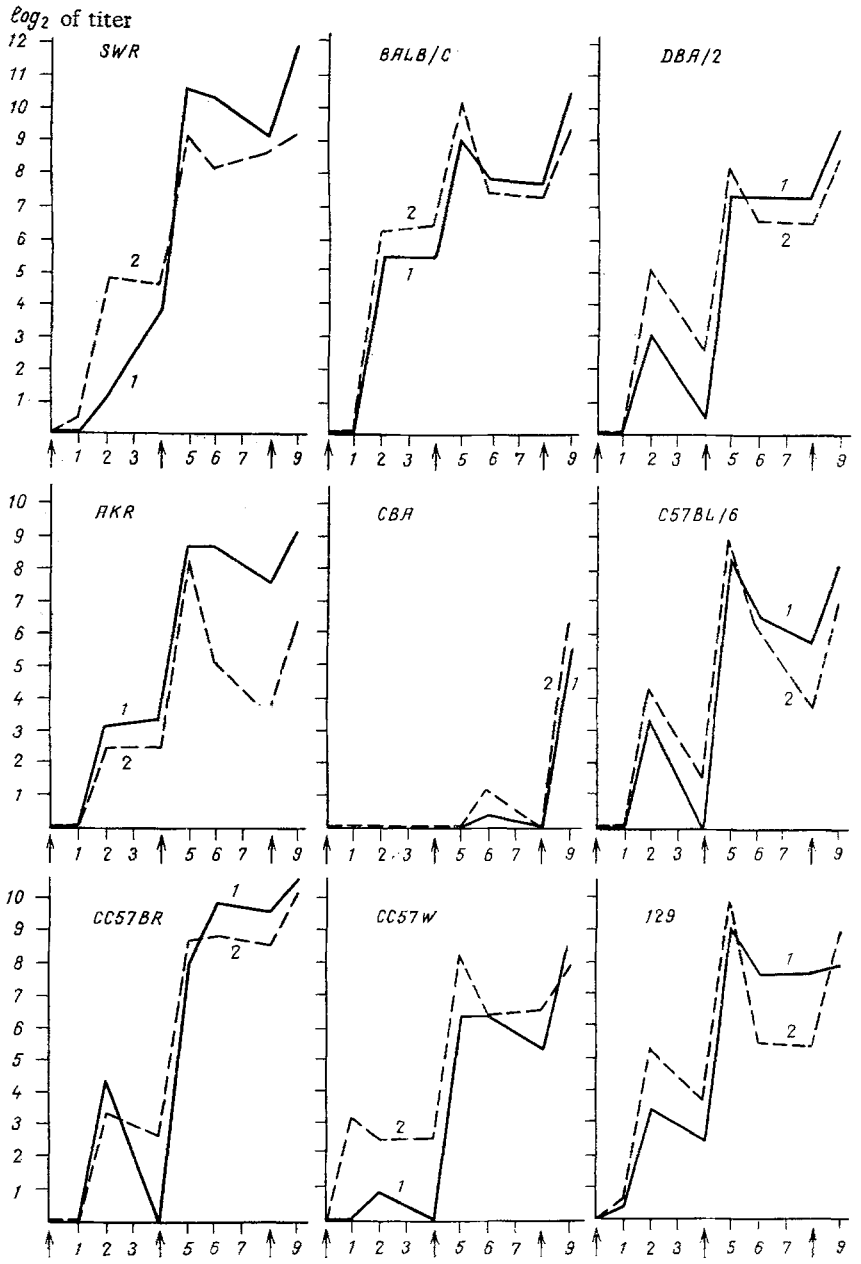

Fig. 1. Dynamics of formation of antibodies of classes IgG_1 (1) and IgE (2) during immunization with ovalbumin (0.5 μg per mouse). Arrows indicate times of injection of ovalbumin. Curves plotted from mean values, each obtained from five recipients. Strains of mice in which antibody formation was detected are indicated in the figure. Abscissa, duration of observation (in weeks); ordinate, log 1/T, where T is the antibody titer.

EXPERIMENTAL METHOD

Mice of strains AKR, BALB/c, CBA, CC57W, CC57BR, 129, C57BL/6, DBA/2, and SWR were used. Two schemes of immunization were adopted: 1) A single intraperitoneal injection of 150 g ovalbumin with 5 mg $Al(OH)_3$ in 0.5 ml physiological saline was given; 2) 3 injections each of 0.5 μg ovalbumin with 0.5 mg $Al(OH)_3$ in 0.5 ml physiological saline were given intraperitoneally at intervals of 4 weeks. The titers of the IgG_1 and IgE antibodies were determined and assessed by the method described earlier [5] in the PCA test on uninbred albino mice in individual sera obtained from five animals of each strain 1, 2, 4, 5, 6, 8, and 9 weeks after the beginning of immunization. The sensitivity of the inbred mice to PCA induced by homocytotropic IgG_1 and IgE antibodies was determined by sensitizing the animals with one

standard serum against ovalbumin of BALB/c mice. The sensitivity of the BALB/c, C57BL/6, CC57BR, and DBA/2 mice to histamine was assessed from the degree of staining of the skin after intradermal injection of 0.001, 0.01, and 0.1 μg histamine in 30 μl physiological saline after intravenous injection of a solution of Evans' blue dye (0.2 ml of a 0.5% solution). The intensity of staining was determined spectrophotometrically from the amount of dye extracted from the skin with formamide [6].

EXPERIMENTAL RESULTS

A single injection of a "high" dose (150 μg) of ovalbumin caused the formation of IgG_1 and IgE antibodies by the 7th day of immunization in the mice of all strains tested. Their titers were 1:20-1:80, except in C57BL/6 mice, in which they did not exceed 1:10. In all mice except DBA/2 the titers of IgE antibodies at this time were rather higher than those of the IgG_1 antibodies. Later, in all the mice the titers of IgG_1 antibodies increased and remained high throughout the period of observation, whereas the titers of IgE antibodies fell after the second to fourth weeks of immunization, and in the mice of strains CC57W, C57BL/6, and 129 they actually fell below 1:5.

By fractional immunization with low doses (0.5 μg) of ovalbumin it was possible to prolong the formation of IgE antibodies and to obtain an increase in their titers after each antigenic stimulation (Fig. 1). Strain CBA (genotype $H\text{-}2^K$) differed from all the other strains studied in that marked formation of IgG_1 and IgE antibodies took place only after the third immunization. If a "high" dose of the antigen was used no differences could be detected.

The results are thus in good agreement with those obtained by other workers who studied the effect of dose of antigen and method of immunization on the intensity of reagin formation [5, 10, 12-14] and the way in which the character of the immune response depends on inherited factors [9, 12, 13].

Determination of the sensitivity of the inbred mice to PCA induced by IgG_1 and IgE antibodies revealed differences in that sensitivity depending on the strain of the animal (Table 1). Sensitivity to anaphylaxis induced by antibodies of these classes was not necessarily parallel. No connection was found between sensitivity to PCA and the character of the immune response. The unequal sensitivity of the mice to PCA may have been due to a variety of factors [2, 7, 8, 11], one of which is possibly sensitivity of the skin to histamine, the mediator of anaphylaxis. The CC57BR mice were found to be most sensitive to histamine, followed in descending order by BALB/c, CBA, C57BL/6, and DBA/2 mice (Table 1). Comparison of sensitivity to histamine with sensitivity to PCA showed that histamine sensitivity is linked neither with ability to be sensitized by IgG_1 antibodies nor with sensitivity to anaphylaxis due to IgE antibodies.

The results are evidence that a predisposition toward anaphylaxis at the stage of formation of allergic antibodies, sensitization of target cells by homocytotropic antibodies of the IgG_1 and IgE classes, and sensitivity to histamine, the mediator of anaphylaxis, are independent characters, interaction between which and with other factors forms the overall predisposition toward the development of immediate allergy.

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