Genetic and Phenotypic Aspects of the Interrelationship between Cellular and Humoral Immune Response to Sheep Erythrocytes in Mice

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We showed in an earlier work [2] that when a foreign antigen exerts its action on an organism, the relationship between teo types of immune response and delayed-type hypersensitivity (DTH), on the one hand, and antibody production (ABP), on the other, is determined by genetic factors linked to the major histocompatibility complex in mice (H-2). Two types of immune response are identified: the first type - the prevalence of DTH in mice of the C57Bl/6 strain; and the second type - the prevalence of ABP in mice of the CBA strain. The response in F_1(CBA×C57Bl/6) hybrid mice is of an intermediate type. The difference in the immune response to sheep erythrocytes (SE) is manifested above all in the zone of action of suboptimal doses of the antigen, and is greater in the case of the local than of the overall immune response. The above-metioned conclusions, however, need additional experimental confirmation.

The purpose of the present study was to assess DTH and ABP inb the local and overall immune response to the introduction of a wide range of SE doses into mice of different genotypes.

MATERIALS AND METHODS

Experiments were carried out on 680 mice of different strains: C3H (H-2^k), CC57BR (H-2^b), BALB/c (H-2^d), and DBA/2(H-2^d), and F_1(CBA×C57B1/6) hybrids ((H-2^k×H-2^b), each weighing 18-25 g. The mice were immunized by two means: intraperitoneal injection of SE in doses of 1×10^5 to 1×10^9; and hypodermic injection (into the foot) in doses of 1×10^3 to 1×10^8 SE. After five days the number of antibody-forming cells (AFC) was determined in the spleen (in the case of intraperitoneal immunization) and in the regional (popliteal) lymph node (in the case of hypodermic immunization) by the direct method of local hemolysis [3]. For DTH assessment a resolving dose of antigen (1×10^8 SE) was introduced into the foot one day before the mice were killed. The immune response was assessed by the degree of swelling of the foot (a difference of 0.1 mm was taken as one unit; the occorrence of edema after an initial introduction of 1×10^8 SE was taken as the zero DTH level).

The data obtained were subjected to statistical analysis by Student's *t* test. Only those data were used in which m with respect to M does not exceed 20%.

RESULTS

In the case of intraperitoneal immunization (fig. 1) the antigenic sensitivity threshold for DTH is comparable to that for ABP (the second type of immune response) in mice of the C3H strain, but is lower for DTH by one order of magnotude than for ABP (the first type of immune response) in mice of the CC57BR, BALB/c, and DBA/2 strains. In these

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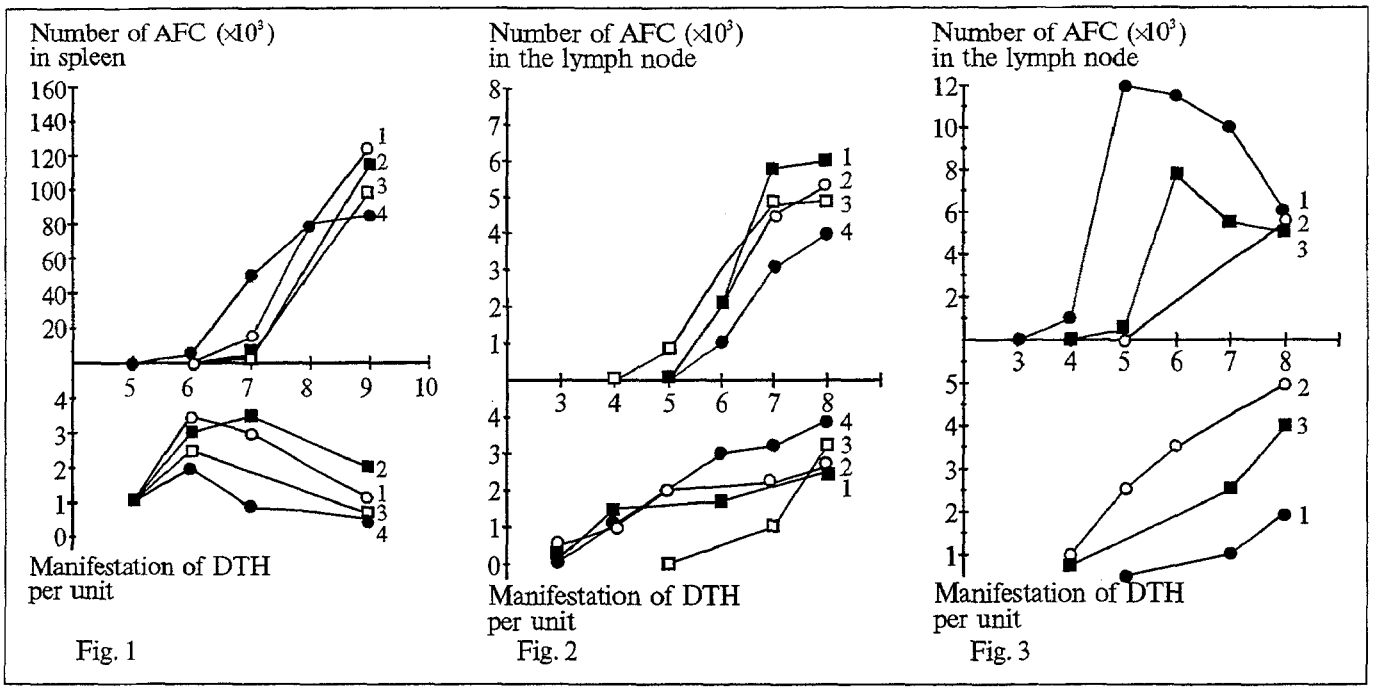

Fig. 1. Relationship between ABP and DTH in mice of the DBA/2 (1), CC57BR (2), BALB/c (3), and C3H (4) straind for intraperitoneal immunization with SE. Abscissa: log of SE dose.

Fig. 2. Relationship between the manifestaion of ABP and DTH in mice of the CC57BR (1), BALB/c (2), C3H (3), and DBA/2 (4) strains for hypodermic immunization with SE. Abscissa: log of SE dose.

Fig. 3. Different versions of the relationship between ABP and DTH in F_1(CBA×C57Bl/6) hybrids for hypodermic immunization with SE. Curves 1, 2, and 3 correspond to different series of experiments. Abscissa: log of SE dose.

mice the antigenic sensitivity threshold for ABP is higher by approximately one order of magnitude than in mice of the C3H strain. In C3H mice, as the dose of antigen introduced intraperitoneally was increased, the DTH level dropped earlier and more markedly, while in mice of the other genotypes the ABP level dradually equalized with the DTH level.

In the case of local immunization (Fig. 2) the antigenic sensitivity threshold differs even more markedly in mice of different strains. It is lower for DTH by approximately two orders of magnitude than for ABP in mice of the C3H strain, but is higher for DTH by approximately two orders of magnitude than for ABP in mice of the other genotypes. As the dose of antigen introduced hypodermically was increased the difference between the first and second type of response gradually leveled out and disappeared completely when the optimal dose (1×10^8 SE) was administered.

In repeated experiments carried out on F_1(CBA×C57Bl/6) male hybrids which were given SE hypodermically, we were able to detect not only the intermediate type of response, but also strongly expressed immune responses of the first and second types (Fig. 3). We were unable to establish experimentally such a pattern in haploid mice, including parents' haplotypes. Furthermore, a distinctive characteristic of the immune response in hybrid mice is the possibility of the prevalence of either ABP or DTH. Evidently, for various reasons that are not yet clear, in such mice there may be a combined influence of both parents' haplotypes or the predominance of one of them. These conclusions conform to a certain extent to the results obtained earlier [1]. The latter indicate that the relationship between ABP and DTH with respect to SE in nonpedigree mice may change, depending on diet and on certain experimental conditions.

Thus, the degree of manifestation and the nature of the immune response are predetermined by both genetic and, at least in some instances, by phenotypic factors. Because of this circumstance, and in view of the possible competitive interrelationship between the cellular and humoral immune response, it is imperative that we approach with greater caution the question of assessing the immune status not only of animals, but also of humans.

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