

SELECTIVE ROLES OF THYMUS-DERIVED LYMPHOCYTES IN THE ANTIBODY RESPONSE

II. PREFERENTIAL SUPPRESSION OF HIGH-AFFINITY ANTIBODY-FORMING CELLS BY CARRIER-PRIMED SUPPRESSOR T CELLS*

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Our preceding studies indicated that thymus-derived lymphocytes (T cells) primed with a carrier antigen suppressed antibody responses by bone marrow-derived lymphocytes (B cells) against a hapten coupled to the homologous carrier, when they were transferred into immunized recipients (1). The degree of suppression in IgM and IgG antibody responses differed depending primarily on the time when suppressor T cells were transferred to the recipients. Thus, it appeared that susceptibility of B cells to the regulatory influence of T cells is inherently different according to the differentiation stages of B cells following antigenic stimulation. The results are in accordance with the widely noted distinction between IgM and IgG antibody responses with respect to their dependency on T cells (2-4).

Another important facet observed in the above T-cell-mediated suppression of antibody response is the strict specificity of both T and B cells for the immunizing antigen: to elicit effective suppression T cells must be primed by the carrier on which haptens are coupled. These observations suggest that T cells would specifically influence the emergence and selection processes of B cells by antigen, resulting in the observed preferential suppression of certain populations of antibody-forming cells. It has been generally accepted that antihapten antibodies are heterogeneous with respect to their affinity for hapten, which probably reflects the heterogeneity among B cells (5-8). It has also been noted that the intrinsic affinity of IgM antibodies is usually lower than that of IgG antibodies (9-11). In view of these immunochemical bases, the present experiments were undertaken to study what subpopulations of B cells with regards to the affinity of produced antibody are, in fact, selectively suppressed by the carrier-specific T cells.

Materials and Methods

Most essential experimental details have already been described in the preceding paper (1), and only a few points are added here.

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Determination of Relative Avidity for Hapten of the Secreted Antibody by Individual Antibody-Forming Cells.—The relative avidity of the antibody produced by plaque-forming cells (PFC)¹ was determined by the inhibition of plaque formation in the presence of free hapten (8, 12, 13). Direct and indirect PFC were developed in the presence of varying concentrations of ϵ -DNP-L-lysine ranging from 10^{-4} to 10^{-8} M. The percent inhibition by a given concentration of the free hapten was calculated in comparison with the number of PFC obtained without free hapten. The molar concentration of ϵ -DNP-L-lysine resulting in 50% reduction in the number of PFC (I_{50}) was determined by graphic plotting of percent PFC developed in the presence of each concentration of free ligand, and was considered to represent average avidity of the antibody produced by PFC. Since the avidity values thus obtained are influenced by the valency of the antibody molecule, the values for indirect PFC obtained in the presence of direct PFC do not represent the actual binding strength in terms of energetic means. However, they are only operationally used as estimates of relative variables in the binding characteristics of IgG antibody.

In order to learn the distribution of PFC among subpopulations of B cells with respect to their avidity, the absolute frequency of PFC detected in the presence of series of hapten concentrations was determined, and the difference in the number of plaques inhibited by any two ligand concentrations was calculated. This difference represents the number of PFC, in absolute terms, within the given range of avidity. By determining the incremental number of PFC which are inhibited by 10-fold changes in ligand concentration, the avidity distribution of PFC was analyzed (8, 12).

Measurement of Association Constant of Serum Antibody.—When possible, the average association constant (K_0) of serum antibody was determined by the modified Farr test using [³H]-2,4-DNP- ϵ -aminocaproic acid ([³H]DNP-EACA) according to the method described by Stupp et al. (14) The antibody concentration was determined by extrapolation of the value of hapten bound to infinite hapten concentration.

Experimental Design.—Experiments were designed to study the effect of carrier-primed suppressor T cells on the relative avidity of anti-DNP antibodies produced in the primary and secondary antibody responses. In the primary antibody response, 5×10^7 keyhole limpet hemocyanin (KLH)-primed thymocytes or spleen cells were passively transferred into recipient animals that were simultaneously immunized with 100 μ g of DNP-KLH and 10^9 pertussis vaccine. Animals were killed 3 and 6 days after the immunization, at the time points when they were producing maximal direct and indirect PFC in the spleen. The avidity of anti-DNP antibodies produced by these PFC was examined as described above.

The technique of adoptive secondary antibody response was utilized to study the effect of suppressor T cells on the avidity of antibodies produced by secondary immunization so as to avoid possible influence of serum antibodies to the antibody affinity. Donor mice were immunized with 100 μ g of DNP-BGG in complete Freund's adjuvant (CFA). 4 wk later they were sacrificed to obtain DNP-primed spleen cells. 5×10^7 primed spleen cells were adoptively transferred intravenously into lethally (600 R) irradiated syngeneic recipients which were then secondarily immunized with 100 μ g of DNP-KLH and 10^9 pertussis vaccine. The experimental group was further given an intravenous injection of 5×10^7 KLH-primed thymocytes or spleen cells before the secondary immunization. The avidity of anti-DNP antibodies produced by direct and indirect PFC was examined 7 days after the immunization at a time when maximum antibody response was detected.

RESULTS

Suppression of Relative Avidity of PFC for Hapten by Carrier-Primed T Cells in the Primary Antibody Response.—The effect of suppressor T cells on the

¹ Abbreviations used in this paper: BGG, bovine gamma globulin; CFA, complete Freund's adjuvant. [³H]DNP-EACA, [³H]DNP epsilon aminocaproic acid; KLH, keyhole limpet hemocyanin; PFC, plaque-forming cells.

avidity of antibody produced in the primary antibody response was studied by passive administration of 5×10^7 KLH-primed thymocytes or spleen cells into recipient animals that were concomitantly immunized with $100 \mu\text{g}$ of DNP-KLH plus 10^9 pertussis vaccine. A control group of mice was not given KLH-primed cells, but was immunized by the same schedule. The relative avidity of PFC was estimated by the plaque inhibition technique on days 3 and 6 at which animals were producing maximal direct and indirect PFC, respectively.

Fig. 1 represents a plaque inhibition profile of direct PFC of the group given KLH-primed thymocytes in comparison with that of the control group produced by different concentrations of free hapten. The PFC producing high avidity antibody are inhibited from lysing DNP-coupled SRBC by low concentrations

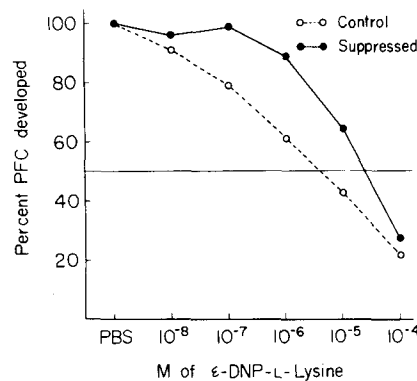


FIG. 1. Inhibition profiles of direct PFC by different concentrations of free hapten in the primary antibody response. The suppressed group was given 5×10^7 KLH-primed thymocytes before immunization with DNP-KLH. Data obtained 3 days after the immunization. Each point is a mean value of six similarly treated mice. The control group was not given suppressor T cells.

of ϵ -DNP-L-lysine, while those producing low avidity antibody require high concentrations of hapten for the inhibition. By comparing the inhibition profiles of PFC, it was noted that a large proportion (about 40%) of direct PFC in the control group was inhibited by relatively low concentrations (less than 10^{-6} M) of ϵ -DNP-L-lysine, while only a small proportion (about 10%) of PFC in the suppressed group was inhibited at these low concentrations of free hapten. The average avidity of antibody-forming cells as expressed by the molar concentration of hapten required for 50% inhibition of PFC (I_{50}) was about ten-fold greater in the suppressed groups than in the control, indicating that suppressor T cells caused a decrease in the relative avidity of the produced IgM anti-DNP antibody at the cellular level.

By a similar procedure, the effect of KLH-primed thymocytes and spleen cells on the avidity of indirect PFC was estimated on day 6 (Table I). The average avidity of indirect PFC was slightly higher than that of direct PFC

TABLE I

Numbers and Average Avidities of DNP-Specific PFC Produced in the Primary Antibody Response in the Mouse Given KLH-Primed Thymocytes and Spleen Cells

Cells* transferred	Anti-DNP response on day 3		Anti-DNP response on day 6			
	Direct PFC		Direct PFC		Indirect PFC	
	Number	I ₅₀ †	Number	I ₅₀ †	Number	I ₅₀ ‡
None	47,400 ×/÷§1.46	5.0 × 10 ⁻⁶	5,150 ×/÷ 1.55	1.4 × 10 ⁻⁶	12,000 ×/÷ 1.40	9.0 × 10 ⁻⁷
KLH-primed Th	26,000 ×/÷ 1.37	2.6 × 10 ⁻⁵	2,100 ×/÷ 1.52	3.6 × 10 ⁻⁶	1,310 ×/÷ 1.42	2.2 × 10 ⁻⁶
KLH-primed Spl	21,300 ×/÷ 1.04	1.0 × 10 ⁻⁵	2,260 ×/÷ 1.78	1.0 × 10 ⁻⁵	1,280 ×/÷ 1.67	3.1 × 10 ⁻⁶

* 5 × 10⁷ thymocytes or spleen cells were passively transferred into recipients simultaneously with the primary immunization with DNP-KLH.

† Molar concentration of ε-DNP-L-lysine required for 50% reduction in the number of PFC.

‡ Standard deviation of the geometric mean—multiply and divide.

in the control group. The passive transfer of KLH-primed thymocytes and spleen cells caused a profound suppressive effect on the average avidity of both direct and indirect PFC. I₅₀ values of the suppressed groups were significantly higher than those of the unsuppressed control group, the difference amounting to one log scale in some cases. It was also shown that although the administration of suppressor T cells on day 0 produced only a slight suppression in the direct PFC numbers, it caused a profound decrease in their avidity, indicating that the changes in avidity are independent variables from those of the number of PFC. The association constant (K₀) of serum anti-DNP antibody was not measurable, because the concentration of antibody at this stage was insufficient for the precise analysis.

Suppression of Relative Avidity of PFC for Hapten by Carrier-Primed T Cells in the Adoptive Secondary Antibody Response.—In the previous paper (1) we reported that carrier-primed T cells can also suppress secondary antihapten antibody response, although the degree of suppression was less than that in the primary antibody response. Since it is predicted that the antibody produced in the secondary antibody response is of high avidity, we studied the effect of suppressor T cells on the avidity of anti-DNP antibody produced by secondary immunization. In order to exclude possible influence of serum antibodies on the antibody avidity of PFC, an adoptive immune response was utilized.

Recipient 600 R-irradiated mice were reconstituted with 5 × 10⁷ spleen cells obtained from syngeneic mice immunized one month before with 100 μg of DNP-BGG in CFA. They were further given a cell transfer of 5 × 10⁷ KLH-primed thymocytes or spleen cells. A control group of irradiated mice were only repopulated with DNP-BGG-primed spleen cells. Within an hour after the cell transfer, all mice were immunized with 100 μg of DNP-KLH together with 10⁹ pertussis vaccine to elicit an adoptive anti-DNP secondary antibody response. The numbers and average avidities of PFC were examined on day 7 at

a time when animals were producing the highest numbers of both direct and indirect PFC.

As can be seen from Table II, the average avidity values of both direct and indirect PFC in the control animals were higher than those in the primary antibody response, indicating that the antibody response had matured both in IgM and IgG classes. KLH-primed thymocytes and spleen cells produced a moderate suppression in the number of both direct and indirect PFC. The average avidity values of the suppressed groups were considerably lower than those of the control group, the difference amounting to nearly one log scale. It is interesting to note that the average avidity of PFC produced under the suppressive influence of carrier-primed T cells was still less than that observed in the normal primary antibody response, indicating that suppressor T cells caused the definite arrest of antibody maturation.

TABLE II
*Anti-DNP Antibody Response in the Adoptive Secondary Antibody Response
Measured 7 Days After the Secondary Immunization*

Cells* transferred	Direct PFC		Indirect PFC		Association constant (K ₀)§
	Number	I ₅₀ †	Number	I ₅₀ †	
None	10,600 ×/÷ 1.46	7.1 × 10 ⁻⁸	46,800 ×/÷ 1.45	2.4 × 10 ⁻⁷	1.8 × 10 ⁶
KLH-primed Th	4,120 ×/÷ 1.39	1.1 × 10 ⁻⁵	9,000 ×/÷ 1.45	2.1 × 10 ⁻⁶	4.0 × 10 ⁵
KLH-primed Spl	1,950 ×/÷ 1.41	1.8 × 10 ⁻⁵	11,300 ×/÷ 2.05	2.0 × 10 ⁻⁶	6.0 × 10 ⁵

* 5 × 10⁷ KLH-primed thymocytes or spleen cells were passively transferred into the recipients that had been X-irradiated and reconstituted with DNP-primed spleen cells.

† Molar concentration of ε-DNP-L-lysine required for 50% reduction in the number of PFC.

§ Measured by modified Farr test using [³H]DNP-EACA of the pooled antiserum.

Figs. 2 and 3 show the representative patterns of inhibition of PFC by different concentrations of free hapten in the control and those given KLH-primed thymocytes. The inhibition profiles of both direct and indirect PFC in the control group exhibited steep slopes in the high concentration range of free hapten, indicating that PFC produced in the secondary antibody response were less heterogeneous with higher avidity than in the primary antibody response. However, the inhibition curves in the suppressed group had shallow slopes that were comparable to those observed in the normal primary PFC response, representing a high degree of heterogeneity of avidities.

The examination of the antibody affinity of the pooled antiserum disclosed a significant decrease in the average association constant (K₀) in groups given KLH-primed thymocytes and spleen cells as compared to the control (Table II). The degree of suppression in K₀ was parallel to that of I₅₀.

Preferential Suppression of High Avidity PFC by Carrier-Primed T Cells in the Primary and Secondary Antibody Responses.—In order to determine the B cell population which was preferentially affected by suppressor T cells absolute frequencies of PFC in various avidity subgroups were determined, and the

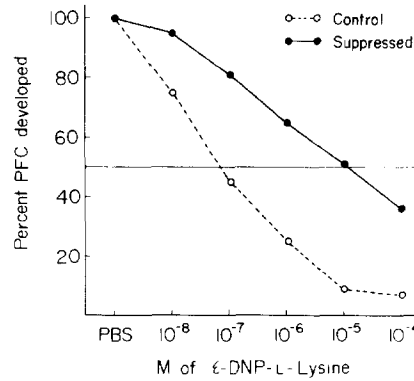


FIG. 2. Inhibition profiles of direct PFC by different concentrations of free hapten in the adoptive secondary antibody response. Irradiated recipients were reconstituted with 5×10^7 DNP-primed spleen cells. The suppressed group was given additional 5×10^7 KLH-primed thymocytes. Data obtained 7 days after the secondary challenge with DNP-KLH. Each point is a mean value of six similarly treated mice.

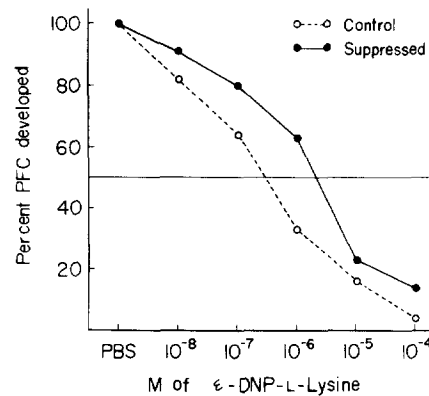


FIG. 3. Inhibition profiles of indirect PFC by different concentrations of free hapten in the adoptive secondary antibody response. Data obtained from the same source of Fig. 2.

values were compared between the control and suppressed groups. This was achieved by determining the incremental number of PFC, which were inhibited by successive 10-fold increases in the concentration of ϵ -DNP-L-lysine, and then calculating the absolute number of PFC in the spleen which are inhibitable by each concentration range of free ligand. The total PFC which had been determined in the slide containing no free hapten was thus divided into five avidity subgroups.

The representative pattern of avidity distribution of direct PFC in the primary antibody response is shown in Fig. 4. In the unsuppressed control group direct PFC on day 3 were distributed among a wide range of avidities, reflecting

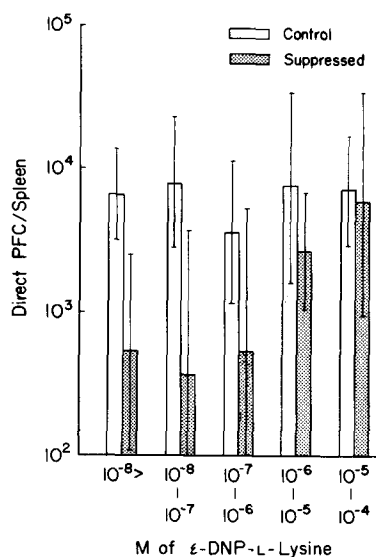


FIG. 4. Avidity distribution of anti-DNP direct PFC produced in the primary antibody response. The suppressed group was given 5×10^7 KLH-primed thymocytes immediately before the primary immunization with DNP-KLH. The control group was not given suppressor T cells. Data obtained 3 days after the immunization. Each column and bracket are the geometric mean and standard deviation calculated from six similarly treated mice.

the high degree of heterogeneity of responding B cells at this early stage. However, it is clearly seen that the frequency of PFC in the suppressed group that had been given KLH-primed thymocytes on day 0 tended to distribute in low avidity groups, indicating that the cells producing high avidity antibody had been preferentially suppressed. An essentially similar pattern of distribution of direct PFC was observed in the group that was given KLH-primed spleen cells. Hence, the decrease in the average avidity of PFC in suppressed groups is considered to be due to the selective loss of PFC with high avidity and the relatively stable level of low avidity PFC. An analysis of avidity distribution of indirect PFC on day 6 was not possible because the level of PFC in the suppressed group was too low.

A similar effect of suppressor T cells on the avidity distribution of direct and indirect PFC was observed in the adoptive secondary antibody response. In this case, calculation of the number of indirect PFC in the presence of various concentrations of ligand was possible. Figs. 5 and 6 depict the data obtained in the groups that were given KLH-primed thymocytes in comparison with those of the control animals. The distribution profiles of both direct and indirect PFC in the control groups show a definite maturation represented by the shift of distribution of PFC frequency into high avidity subgroups. On the other hand, PFC in the suppressed group show a wide distribution among various avidity

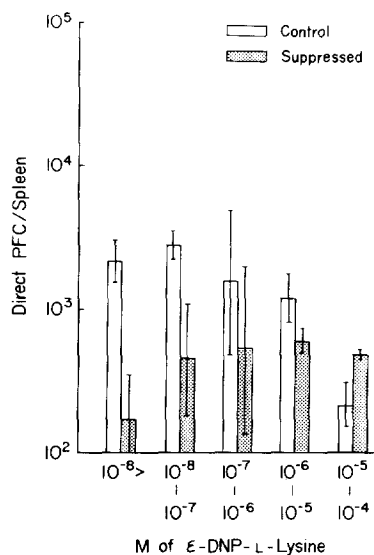


FIG. 5. Avidity distribution of anti-DNP direct PFC produced in the adoptive secondary antibody response. The suppressed group was given 5×10^7 KLH-primed thymocytes before the secondary challenge with DNP-KLH. The control group was not given suppressor T cells. Data obtained 7 days after the secondary immunization. Each column and bracket are the geometric mean and standard deviation calculated from six similarly treated mice.

subgroups, with the lower avidity groups possessing somewhat greater number of PFC. This pattern of distribution is analogous to that observed in the normal primary antibody response. A significant difference in the frequency of PFC, in absolute terms, between suppressed and unsuppressed groups is observed among high avidity subgroups: the absolute numbers of PFC among high avidity subgroups are significantly lower in the suppressed group than in the unsuppressed control group, indicating that the suppressor T cells preferentially affected the cells which had been destined to produce high avidity antibody. Essentially similar results were obtained in groups that were given KLH-primed spleen cells instead of thymocytes. Therefore, low average avidity values observed in suppressed animals are considered to be, in fact, due to the preferential loss of high avidity PFC rather than to the overall decrease in the magnitude of the immune response.

DISCUSSION

The present results clearly point to an important regulatory role of T cells in the maturation of antibody response with regard to emergence or selection of B cells having high affinity receptors for antigen. This was demonstrated by both the decrease in average avidity of PFC and reduction in the absolute number of high avidity PFC in animals given suppressor T cells. Since the affinity of anti-

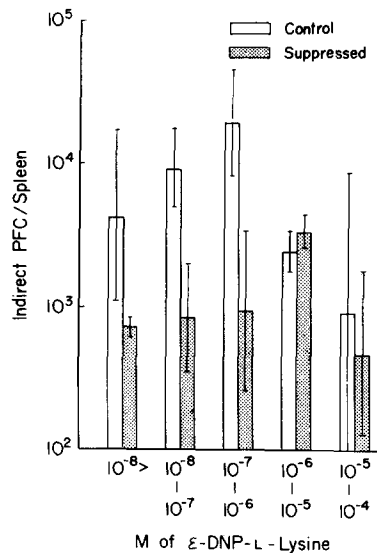


FIG. 6. Avidity distribution of anti-DNP indirect PFC produced in the adoptive secondary antibody response. Data obtained from the same source of Fig. 5.

body produced by a single antibody-forming cell is found to be identical or closely related to that of receptors of precursor B cells,² the decrease in the avidity of antibody produced by PFC should result from selective suppression of B-cell populations possessing high affinity receptors for antigen. The correlation between the changes in average avidity of PFC (I_{50}) and association constant of serum antibody (K_0) in the adoptive secondary antibody response also support this concept.

The observations are consistent with our previous finding that IgG antibody response was more severely suppressed than IgM antibody response by carrier-primed suppressor T cells given simultaneously with primary and secondary immunizations (1), inasmuch as IgG antibody generally possesses a higher affinity for hapten than does IgM antibody (9-11). It has been pointed out that T-cell-independent IgM antibody formation, in general, does not mature even after repeated immunization (15, 16). Thus it is of interest to find that the IgM as well as IgG antibody response in the present system does mature and this maturation has been inhibited by suppressor T cells. These results suggest that the maturation of antibody response is dependent on the function of T cells, and that such a T cell-dependent process in the immune response is strongly affected by suppressor T cells. As the specificity of this T-cell-mediated

² Julius, M. H., and L. A. Herzenberg. 1974. Isolation of antigen-binding cells from unprimed mice: demonstration of antibody-forming cell precursor activity and correlation between precursor and secreted antibody activities. *J. Exp. Med.* Manuscript submitted for publication.

suppression has been firmly established (1), it seems probable that carrier-primed T cells exert selective pressure on the precursor population of hapten-specific antibody forming cells with respect to both the class and affinity of antibodies to be produced by the latter cell type.

It is not known at the present time how such selective pressure is exerted by antigen-stimulated T cells. It is generally held that selection of precursor B cells to differentiate and to synthesize antibody is primarily dependent on the effective concentration of antigen in the micro-environment of B cells, and thus B cells with high affinity for antigen are more easily selected to proliferate and to expand their progeny (5-8). Therefore, the affinity of produced antibody is primarily determined by the thermodynamic relationship between antigen and receptor of precursor B cells. Indeed, Siskind and co-workers (5, 17, 18) and Harel et al. (19) have shown that mere nonspecific modifications of the magnitude of antibody response by adjuvant and immunosuppressants do not significantly alter the affinity of the antibody produced in the rabbit, although a high degree of antigenic competition in guinea pigs does affect profoundly the affinity of the produced antibody (19, 20). However, Taniguchi and Tada (21) reported that affinity of produced antibody in the rabbit is influenced by the carrier-specific T cells. They found that a relative depletion of T cells by surgical or chemical thymectomy caused a marked enhancement of antibody formation accompanied by a striking increase in antibody affinity. Conversely, overstimulation of T cells by pre-immunization with the carrier caused a depressed formation of antihapten antibodies whose affinity was considerably low. They interpreted these phenomena as the consequence of T cells' regulatory function on the selection and emergence of high affinity B cells.

On the other hand, Gershon and Paul (22) have presented evidence using the adoptive cell transfer system that the affinity as well as the amount of antibody depends on the nature of the carrier molecule and on the number of T cells possessed by the immunized animal. They postulated that T cells may function by increasing the rate of antigen-stimulated proliferation of B cells, thus leading to more rapid changes in the population of B cells upon which selective pressure by antigen is being exerted. Therefore, the changes in the affinity in their experiments are largely explained by the increase in the rate of proliferation of B cells in the presence of adequate numbers of T cells.

Perhaps this explanation is also applicable, though inversely, to the present experimental results. If we assume that T cells exert nonspecific inhibitory influence on B cells that are undergoing antigen-stimulated proliferation, such inhibitory effect may preferentially be directed to the cells on which antigen-driven selective pressure is exerted. However, the main difficulty of this explanation lies in the facts that suppressor T cells did not inhibit the proliferation of B cells with low affinity receptors, and that the decrease in average avidity did not always correlate with the reduction of PFC numbers. Also, the nonspecific inhibitory effect has been denied by the fact that T cells primed

with heterologous carrier could not suppress the hapten-specific PFC response even if such T cells were re-stimulated with the corresponding antigen (1).

Another explanation may be derived from the concept of antigen presentation and focussing by T cells (23). It is assumed in this theory that T cells or T-cell products bind antigen and present it to specific B cells. If a larger number of carrier-primed T cells are present, these would deliver a larger amount of effective antigen, that ultimately cause the dose-dependent decrease in the average affinity. It has also been shown that a supraoptimal dose of T-cell product (IgT), that otherwise is capable of stimulating B cells, becomes inhibitory in *in vitro* circumstances especially when macrophages were absent (24).

At the present time, we have no clear evidence to support the above hypotheses. However, recent publications from our laboratory clearly indicated the existence of a subcellular component of carrier-primed T cells that specifically suppresses an ongoing hapten-specific IgE antibody formation in the rat (25, 26). This subcellular component possesses specificity to the carrier determinants of immunizing antigen, and thus is capable of combining the carrier molecule. Although we have no conclusive data as yet on such an antigen-specific inhibitory component in the mouse, it is possible that such inhibitory T-cell component is also involved in the observed suppression of antibody response as well as of antibody maturation: B cells with high affinity receptors may more easily be selected by antigen than those with low affinity receptors, and thus be preferentially affected by the inhibitory T cells or their product which can combine to the carrier determinant of the antigen bound to such selected B cells. However, T-cell-independent subpopulations of B cells, which lack sensitivity to such T cells' influences, would proliferate under the condition where the competitive inhibition by high affinity antibodies is eliminated as the result of the suppression of T-cell-dependent antibody response. Although this explanation is based on the hypothetical existence of the specific suppressor component elaborated by T cells, which has been reported only in the rat (25, 26), some preliminary studies in our laboratory have given affirmative evidence for the presence of the same kind of T cell component (manuscript in preparation).

The above interpretation does not contradict the selectional theory of antibody maturation presented by Siskind and Benacerraf (5), and further allows to explain the conflicting effect of T cells on antibody affinity. It also offers a clue to the understanding of more sophisticated roles of T cells in the regulation of antibody response, namely, the selective pressure of T cells on B-cell response with respect to the 'shift' in the class and affinity of produced antibody in the time course of antibody response. Furthermore, the preferential suppression of high affinity antibody formation caused by suppressor T cells is clearly analogous to the feature in the immunological tolerance produced by high doses of antigen (27-29). In view of the observation made by Gershon and Kondo (30) on the infectiousness of immunological tolerance by T cells, the

attribute of suppressor T cells to the induction of immunological tolerance should await further analysis.

SUMMARY

Passive transfer of thymocytes and spleen cells from donors primed with keyhole limpet hemocyanin (KLH) caused significant decrease in the average avidity of anti-DNP antibodies produced by direct and indirect PFC in the recipients in both primary and adoptive secondary antibody responses against DNP-KLH. The analysis of the avidity distribution of antibodies produced by plaque-forming cells (PFC) indicated that the observed decrease in the average avidity is primarily due to the selective loss of high avidity subpopulation of PFC leaving low avidity subpopulation relatively unaffected. The degree of suppression in antibody avidity did not correlate with the reduction in the number of PFC, and thus causing the "shift" of avidity distribution of PFC to the low avidity end. These results indicate that the "maturation" of antibody in the T-cell-dependent antibody response is influenced by the carrier-specific suppressor T cells with respect to the emergence and selection of B cells having high affinity receptors for hapten. It is suggested that B cells binding antigen with high affinity receptors would be more easily affected than those with low affinity receptors by specific suppressor T cells which are capable of reacting the carrier portion of the same antigen.

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