central Illinois. (ii) We recaptured a significantly smaller proportion of the yellow-painted control moths (Table 2). (iii) We found that the control moths were more often and more severely injured than the experimental moths (Fig. 2), and that much of this injury can be attributed to attacks by birds. We believe that the most plausible interpretation of our results is that the black-painted moths were protected by their resemblance to the toxic *B. philenor* and that the yellow-painted moths were more frequently attacked because of their resemblance to the palatable and nonmimetic yellow form of the tiger swallowtail.

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References and Notes

1. G. Mostler, *Z. Morphol. Oekol. Tiere* **29**, 381 (1935); P. J. Darlington, *Trans. R. Entomol. Soc. London* **87**, 681 (1938); J. V. Z. Brower, *Evolution* **12**, 32 (1958); *ibid.*, p. 123; *ibid.*, p. 273; A. P. Platt, R. P. Coppinger, L. P. Brower, *ibid.* **25**, 692 (1971); L. P. Brower, J. V. Z. Brower, P. W. Wescott, *Am. Nat.* **94**, 343 (1960); J. V. Z. Brower and L. P. Brower, *ibid.* **99**, 173 (1965); C. W. Rettenmeyer, *Annu. Rev. Entomol.* **15**, 43 (1970).
2. O. J. Sexton, *Behaviour* **15**, 244 (1960); R. T. Shideler, *ibid.* **47**, 268 (1973); J. Reiskind, *Anim. Behav.* **13**, 466 (1965).
3. F. M. Jones, *Trans. R. Entomol. Soc. London* **80**, 345 (1932).
4. H. B. D. Kettlewell, *Proc. R. Soc. London Ser. B* **145**, 297 (1956); *Annu. Rev. Entomol.* **6**, 245 (1961).
5. L. P. Brower *et al.*, *Science* **144**, 183 (1964).
6. L. P. Brower, L. M. Cook, H. J. Croze, *Evolution* **21**, 11 (1967); L. M. Cook, L. P. Brower, J. Alcock, *ibid.* **23**, 339 (1969).
7. G. P. Waldbauer and J. G. Sternburg, *ibid.* **29**, 650 (1975).
8. W. H. Edwards, *The Butterflies of North America* (Houghton Mifflin, Boston, ser. 2, 1884); L. P. Brower and J. V. Z. Brower, *Ecology* **43**, 154 (1962).
9. Each day before 2:00 p.m., the newly emerged moths were placed in envelopes and stored at 4°C until they were used (within 3 days). Undamaged males were painted on the dorsal surface of the wings with Flopaque paint (Flo-quil Products, Inc., Cobbleskill, N.Y.). An inconspicuous mark on the thorax distinguished each day's release. Painted moths were stored in a cage at 4°C until the next morning. After being allowed to warm up, they were released in the experimental area at the University of Illinois's Robert Allerton Park near Monticello, Illinois. Each trap consisted of a wire box (61 by 71 by 71 cm) with two staggered and inwardly directed funnels on opposite sides of the trap. Each trap contained a small cage baited with at least two pheromone-releasing promethea females. The area within the circle of traps was a mixture of upland and floodplain forest and a small area of prairie. A large and varied population of birds inhabits the area in summer (J. Bursewicz, thesis, University of Illinois, 1961). Unlike the Brower group, we did not release moths again after they had been recaptured.
10. J. V. Z. Brower, *Evolution* **12**, 273 (1958); *Proc. 16th Int. Congr. Entomol.* **4**, 156 (1963); L. P. Brower, J. A. Alcock, J. V. Z. Brower, in *Ecological Genetics and Evolution, Essays in Honour of E. B. Ford*, R. Creed, Ed. (Blackwell, Oxford, 1971), p. 261; A. P. Platt, R. P. Coppinger, L. P. Brower, *Evolution* **25**, 692 (1971); R. T. Shideler, *Behaviour* **47**, 268 (1973).
11. Only two unmarked wild male promethea were captured in the pheromone traps during the entire summer.
12. T. D. Sargent [*J. Lepid. Soc.* **27**, 175 (1972)] presents photogaphs of the damage to moth wings resulting from observed attacks by caged birds.
13. *Callosamia promethea* always rests with the wings held together vertically, and never holds them in the flexed position typical of many moths.
14. To our eyes, the black butterflies and moths are very conspicuous in flight, probably no less conspicuous than the yellow ones.
15. Supported in part by the Graduate Research Board of the University of Illinois at Urbana, and by NIH Biomedical Sciences Support grant RR 07030-09. We thank Dr. W. Keith and F. Turok for making available the natural areas of Robert Allerton Park. We also thank Dr. W. H. Luckmann and the Illinois Natural History Survey for facilities used to rear *Callosamia promethea*.

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Selective Display of Histamine Receptors on Lymphocytes

Abstract. *Histamine, acting on histamine type 2 receptors, increases intracellular cyclic adenosine monophosphate (AMP) and thus modulates the immunologic functions of lymphocytes. Lymphocyte cyclic AMP levels were used to follow the development of histamine receptors. The B lymphocytes have no functional histamine receptors. As T lymphocytes "mature" in immunologic function—from thymocytes to cortisone-resistant thymocytes to splenic T lymphocytes—their response to histamine increases. The response of these subpopulations of lymphocytes to isoproterenol is the inverse of the histamine response. It is suggested that the changing display of histamine receptors plays an important part in the control of immunologic responses.*

Histamine is a low-molecular-weight hormone, widely distributed in mammalian tissues, and is released from storage sites by immunologic and other stimuli (*1, 2*). The activities of histamine are mediated through two specific receptors which can be distinguished by the competitive effects of specific histamine type 1 or histamine type 2 antagonists. Stimulation of histamine type 1 receptors causes a variety of well-recognized "pro"-inflammatory events. At higher concentrations histamine mediates several "anti-inflammatory" effects via histamine type 2 receptors (*2*).

Lymphocytes and other inflammatory cells have specific receptors for a wide variety of hormones (*3*), including histamine. Histamine inhibits the in vitro cytolytic (tumor destroying) activity of alloimmunized effector T spleen cells, and this effect is paralleled by an increase in cyclic adenosine monophosphate (AMP) levels in lymphocytes. Both effects are blocked by the histamine type 2 antagonists burimamide and metiamide, suggesting that histamine acting through specific histamine type 2 receptors activates adenylate cyclase, and that the resulting increase in intracellular cyclic AMP leads to the inhibition of cytotoxic activity (*4*). Histamine can inhibit other lym-

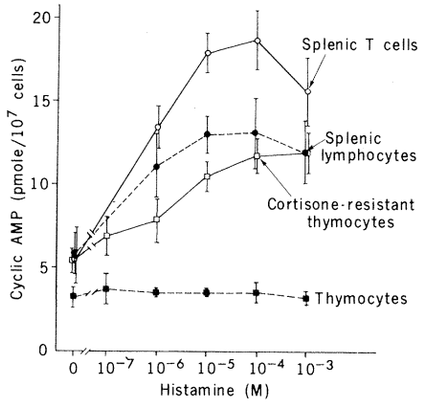

Fig. 1. Young adult age-matched C57B1/6 mice were divided into three groups. For preparation of cortisone-resistant thymocytes, one group of mice received an intraperitoneal injection of 10 mg of cortisone acetate suspension (Merck). Twenty-four hours later, these mice were killed. Thymocytes were also obtained from a second group (untreated mice). The cell yield in cortisone-resistant thymus glands was approximately 1×10^7 (that is, 5 percent of the cell yield in thymuses of untreated mice). A third group of mice was used as a source of spleen cells. The spleen cells were treated with ammonium chloride to remove red blood cells and were then either filtered through glass wool to deplete adherent cells (*14*) (splenic lymphocytes), or filtered through glass wool and then incubated for 45 minutes at 37°C in nylon wool columns (*14*), and the effluent, nonadherent cells were obtained (T cell–enriched splenic lymphocytes, designated "splenic T cells"). All cell preparations were then resuspended to 2×10^7 viable cells per milliliter and incubated for 10 minutes with or without histamine. Intracellular cyclic AMP was assayed as described in the text. The percentage of immunoglobulin (Ig) positive cells (that is, B cells) was estimated by direct immunofluorescence staining by rhodamine-conjugated goat antiserum to mouse Fab fragments. The preparation and properties of this antiserum have been described (*21*). Unfractionated spleen cells contained 55 percent of Ig-positive cells, while T cell–enriched spleen cells contained 19 percent Ig-positive cells. Similar results were obtained in a total of four experiments with cortisone-resistant thymocytes, and in a total of three experiments with spleen cells that were passed through nylon wool. (○) T cell-enriched splenic lymphocytes; (●) splenic lymphocytes; (□) cortisone-resistant thymocytes; (■) thymocytes of normal mice. Each point represents the mean ± standard deviation of quadruplicate determinations.

phocyte functions, such as antibody secretion (*5, 6*) and (via histamine type 2 receptors) MIF (migration inhibition factor) secretion, and antigen- or concanavalin A–induced proliferation (*7, 8*).

The ability of histamine to inhibit cytolysis varies with the time of the primary immune response; that is, inhibition is only 6 percent on day 8 and increases to 45 percent on day 18 (*9*). The progressive increase in inhibition is probably due to the appearance of a subpopulation of effector cells bearing histamine receptors. This suggests the possibility that histamine receptor-bearing cells represent a subpopulation of "more mature" T cells. Using histamine-induced cyclic AMP elevation as a marker for functional histamine receptors, we investigated the relation between these receptors and maturation of T lymphocyte subpopulations. We also examined the differences in responses between T and B lymphocytes (*10*). Our data indicate that T cell–enriched spleen cells and cortisone-resistant thymocytes have histamine receptors, while other thymocytes and splenic B lymphocytes do not.

Young adult male C57B1/6 mice (Jackson Laboratories) were killed by cervical dislocation, and spleen, thymus, and lymph nodes were isolated. Suspensions of single cells were prepared by sieving into minimal Eagle's suspension medium (Grand Island) containing 10 percent fetal calf serum (Microbiological Associates). The spleen cells were treated with NH_4Cl (2 minutes, room temperature) to lyse red blood cells (*11*). Cells (2×10^7) were incubated in 1-ml reaction mixtures with or without histamine (Sigma) or isoproterenol (Sigma) for 10 minutes at 37°C in a mixture of 5 percent CO_2 and 95 percent air. The cell suspensions were centrifuged, and the supernatant was discarded. The cell pellet was suspended in 0.5 ml of 5 percent trichloroacetic acid, and frozen until assayed (*4*). Cyclic AMP was determined by the method of Brown *et al.* as previously modified for lymphocyte preparations (*12*). This is a competitive binding assay, in which ^3H-labeled cyclic AMP (New England Nuclear) and a crude cyclic AMP–binding protein from bovine adrenal gland are used. Histamine and isoproterenol solutions were freshly prepared immediately before use.

The effects of histamine and isoproterenol on the cyclic AMP responsiveness of various lymphoid organs are illustrated in Table 1. The incubation time was 10 minutes, which induces maximal responsiveness in spleen cells. Histamine induces a twofold to fourfold increase in intracellular splenic cyclic AMP (*4, 9*). Lymph node cells have higher basal cyclic AMP levels, but also respond to histamine with a twofold to threefold increase in cyclic AMP. The thymocytes, however, have lower baseline cyclic AMP levels and fail to respond to histamine with a significant increase in cyclic AMP. These cells do, however, have functional adenylate cyclase, since the augmentation of cyclic AMP induced by isoproterenol in thymocytes is greater than that induced by this agonist in spleen cells (Table 1, experiment 1).

Cortisone-resistant thymocytes constitute the most "mature" T cells of this organ in that they can proliferate in response to phytohemagglutinin or serve as helper cells for antibody formation, capabilities which thymocytes as a group lack (*13*). In order to determine whether these cells have histamine receptors, the cyclic AMP responsiveness to histamine of cortisone-resistant (Fig. 1) and control thymocytes were compared. Histamine at concentrations of 10^{-7} to $10^{-3}M$ failed to augment cyclic AMP in thymocytes from untreated mice but induced a significant increase of cyclic AMP in cortisone-resistant thymocytes, with a maximal increase noted at approximately $10^{-5}M$ (Fig. 1).

We next compared the response of the relatively mature cortisone-resistant thymocytes to unfractionated spleen cells (Table 1) and to splenic lympho-

Table 1. Cyclic AMP responsiveness to histamine and isoproterenol of spleen, thymus, and lymph node cells. Single cell suspensions were prepared from spleens; thymus glands; and inguinal, axillary, and submandibular lymph nodes, from groups of at least eight mice. The viable cell yield per spleen was $\simeq 10^8$, per pooled lymph nodes it was $\simeq 10^8$, and per thymus it was $\simeq 2 \times 10^8$. The cell viability in all preparations was 85 to 90 percent, as determined by erythrosin B exclusion. Cells (2×10^7/ml) were incubated for 10 minutes at 37°C with or without drugs, and the cyclic AMP levels were determined. Similar effects were observed in seven other experiments. Results are expressed as the mean ± standard deviation of quadruplicate cultures.

Source of cells	Cyclic AMP (pmole/10^7 cells)				
	No drug	Histamine ($10^{-4}M$)	Ratio*	Isoproterenol ($10^{-5}M$)	Ratio*
		Experiment 1			
Spleen	4.4 ± 0.6	15.4 ± 1.9	3.5	16.5 ± 1.9	3.8
Lymph node	11.5 ± 1.8	27.0 ± 2.0	2.3		
Thymus	2.2 ± 0.3	2.5 ± 1.0	1.1	79.4 ± 14.0	36.1
		Experiment 2			
Spleen	5.8 ± 1.6	13.5 ± 1.9	2.3		
Lymph node	12.8 ± 5.2	21.3 ± 4.0	1.7		
Thymus	3.3 ± 0.8	3.4 ± 0.6	1.0		
		Experiment 3			
Spleen	7.2 ± 1.3	14.2 ± 3.0	2.0		
Lymph node	14.4 ± 2.9	29.1 ± 1.6	2.0		
Thymus	3.3 ± 1.1	3.6 ± 1.6	1.1		

*Ratio of cyclic AMP in cultures containing histamine or isoproterenol to that in drug-free cultures.

Table 2. Effect of antiserum to thy 1.2 antigen, in the presence of complement, on histamine- or isoproterenol-induced increases in cyclic AMP. Groups of ten C57BL/6 mice were killed by cervical dislocation, and spleen cells were obtained. Spleen cell suspensions (2×10^7 cells per milliliter) were incubated with a 1 to 10 dilution of normal mouse serum or antiserum to thy 1.2, and a 1 to 20 dilution of rabbit serum (as a source of complement) for 45 minutes at 37°C. The cells were washed, and their viability was assessed by erythrosin B exclusion. They were then resuspended (2×10^7 viable cells per milliliter) and incubated with or without drug; cyclic AMP was then assayed. The results are expressed as the mean ± standard deviation of quadruplicate cultures. Similar results were obtained in two other experiments.

Drug	Cyclic AMP (pmole/10^7 cells)	
	Normal mouse serum	Antiserum* to thy 1.2
None	4.8 ± 1.9	5.2 ± 1.1
Histamine, $10^{-3}M$	12.3 ± 2.8	4.3 ± 1.7
Histamine, $10^{-4}M$	13.9 ± 4.2	4.9 ± 2.0
Histamine, $10^{-5}M$	11.9 ± 3.6	5.6 ± 2.3
Isoproterenol, $10^{-5}M$	16.5 ± 2.6	14.3 ± 0.5

*Antiserum to thy 1.2 antigen was obtained from Dr. H. Shin (this experiment) and R. C. Kuppers and Dr. C. S. Henney. These antiserums were prepared in AKR mice by immunization with C3H thymuses. The properties of these antiserums have been described (*22*). In our experiment, when 2×10^7 spleen cells were incubated with a 1 to 10 dilution of antiserum to thy 1.2 (in the presence of complement) for 45 minutes at 37°C, 25 to 30 percent of the spleen cells were lysed, as determined both by release of label from ^{51}Cr-labeled spleen cells, and by erythrosin B exclusion.

cytes and splenic T cells (*14*). Whereas the level of cyclic AMP induced by histamine in the total splenic lymphocyte population was slightly greater than that observed in cortisone-resistant thymocytes, the level induced in splenic T cells was much greater (Fig. 1). The shape of the dose-response curve of splenic lymphocytes, T cell–enriched splenic lymphocytes, and cortisone-resistant thymocytes was similar, with maximal augmentation of cyclic AMP at 10^{-5} to $10^{-4}M$ histamine. This response curve is similar to that for histamine type 2 receptor–mediated inhibition of cytotoxic activity of splenic effector T cells (*9*).

The enhanced response to histamine of preparations enriched in T cells suggested that, of the total spleen cell population, only T cells had histamine receptors. This suggestion was confirmed when spleen cells were depleted of T cells by treatment with a mouse antiserum to thy 1.2 antigen (previously called "anti-θ" antiserum) in the presence of rabbit complement. (The remaining cells consisted predominantly of B cells, as well as "null" cells and macrophages.) Histamine did not augment the cyclic AMP of these B cell–enriched (T cell–depleted) populations (Table 2). This unresponsiveness was not due to nonspecific damage by immune complexes or by factors released from the dead cells, for the B cell preparations retained their responsiveness in terms of augmented cyclic AMP on isoproterenol challenge. The responsiveness to histamine and isoproterenol of spleen cells treated with normal mouse serum in the presence of rabbit complement was similar to that of untreated spleen cells (compare Table 2 and Table 1).

Our observations suggest that immature T lymphocytes, thymocytes, and splenic B lymphocytes do not have histamine receptors (*15*). We cannot rule out the possibility, however, that these cells have histamine receptors that fail to activate adenylate cyclase. This possibility can be examined only by direct binding assays, and these, up to now, have been unsuccessful (*16*). Our data are, however, more compatible with the suggestion that as T lymphocytes mature they develop histamine receptors. By direct binding assays with radioactively labeled hormones, other hormone receptors have been shown to develop in vitro during differentiation (*17*). In vivo, insulin receptor density may change, and functional beta-adrenergic receptor activity may disappear during aging (*18*). These observations all suggest that hormone receptors are not randomly distributed on cells.

Fallah *et al.* (*6*) have reported that daily addition of histamine to in vitro primary cultures inhibits IgM plaque-forming cell responses to red cell antigens. It is therefore possible that, in contrast to immature splenic B cells, antigen-stimulated B cells do possess histamine receptors. In support of this Melmon *et al.* (*5*) have reported that plaque formation of spleen cells from immune mice was inhibited by histamine, suggesting that a mature plasma cell possesses histamine receptors that mediate inhibition of antibody secretion. The responsiveness to histamine by B cells from hyperimmune mice remains to be determined (*19*).

It appears that histamine receptor display is associated with the "maturation" of mouse thymus-derived lymphocytes, in that there is a progressive increase in histamine responsiveness from thymocytes to cortisone-resistant thymocytes to splenic T cells. In contrast, isoproterenol induces a greater augmentation of cyclic AMP in thymocytes than in spleen and lymph node T cells, and an intermediate degree of augmentation in cortisone-resistant thymocytes (Tables 1 and 2) (*20*). Our results suggest that differentiation of T cells is accompanied by complex changes in hormone receptor display, with a loss of beta-adrenergic receptors and a parallel appearance of histamine receptors. Since immune events—that is, immediate hypersensitivity reactions—result in release of histamine at concentrations corresponding to the effects we describe, and since histamine has marked modulatory effects on both cell-mediated and humoral immunity, the changes in histamine receptor display with maturation of T cells is of major importance in the attempt to understand the development in vivo of the immune response.

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References and Notes

1. M. A. Beaven, *N. Engl. J. Med.* **294**, 30 and 325 (1976); W. W. Douglas, in *The Pharmacological Basis of Therapeutics*, L. S. Goodman and A. Gilman, Eds. (Macmillan, New York, ed. 5, 1975), p. 590.
2. M. Plaut and L. M. Lichtenstein, in *Handbook of Experimental Pharmacology: Inflammation and Anti-inflammatory Drugs*, S. H. Ferreira and J. R. Vane, Eds. (Springer-Verlag, Berlin, in press); L. M. Lichtenstein, in *Nobel Symposium: Molecular and Biological Aspects of Allergic Processes*, R. Baker, Ed. (Plenum, London, in press).
3. H. R. Bourne, L. M. Lichtenstein, K. L. Melmon, C. S. Henney, Y. Weinstein, G. M. Shearer, *Science* **184**, 19 (1974); P. Cuatrecasas, *Proc. Natl. Acad. Sci. U.S.A.* **63**, 450 (1969); J. P. Hecht, J. A. Dellacha, A. C. Paladini, E. Hurwitz, M. Sela, *FEBS Lett.* **20**, 83 (1972); G. Illiano, G. P. E. Tell, M. I. Siegel, P. Cuatrecasas, *Proc. Natl. Acad. Sci. U.S.A.* **70**, 2443 (1973); J. Holmgren, L. Lindholm, L. Lönnroth, *J. Exp. Med.* **139**, 80 (1974).
4. M. Plaut, L. M. Lichtenstein, E. Gillespie, C. S. Henney, *J. Immunol.* **111**, 389 (1973).
5. K. L. Melmon, H. R. Bourne, Y. Weinstein, G. M. Shearer, J. Kram, S. Bauminger, *J. Clin. Invest.* **53**, 13 (1974).
6. H. A. Fallah, J. L. Maillard, G. A. Voison, *Ann. Immunol. (Paris)* **126C**, 669 (1975).
7. R. E. Rocklin, *J. Clin. Invest.* **57**, 1051 (1976).
8. W. Roszkowski, M. Plaut, L. M. Lichtenstein, in preparation.
9. M. Plaut, L. M. Lichtenstein, C. S. Henney, *Nature (London)* **244**, 284 (1973); *J. Clin. Invest.* **55**, 856 (1975).
10. T (thymus-derived) lymphocytes, which differentiate under the influence of the thymus gland, represent a population distinct from B (bone marrow–derived) lymphocytes. These two cell types differ in surface antigenic markers [for example, mouse T lymphocytes, but not B lymphocytes, have one allele of the thy-1 (previously called "θ") antigen; B lymphocytes, but not T lymphocytes, have readily detectable surface immunoglobulin]; the two types also differ in biologic properties (B lymphocytes differentiate into antibody-secreting plasma cells; T lymphocytes are effector cells in cell-mediated immune reactions, and also may function as helper and suppressor cells) [see M. C. Raff, *Nature (London)* **242**, 19 (1973); J.-C. Cerottini and K. T. Brunner, *Adv. Immunol.* **18**, 67 (1974)].
11. W. Boyle, *Transplantation* **6**, 761 (1968).
12. B. L. Brown, J. D. M. Albano, R. P. Ekins, A. M. Sgherzi, *Biochem. J.* **121**, 561 (1971); C. S. Henney, H. R. Bourne, L. M. Lichtenstein, *J. Immunol.* **108**, 1526 (1972); L. M. Lichtenstein, C. S. Henney, H. R. Bourne, W. B. Greenough III, *J. Clin. Invest.* **52**, 691 (1973).
13. H. Blomgren and B. Andersson, *Exp. Cell Res.* **57**, 185 (1969); *Cell. Immunol.* **1**, 545 (1971); J. J. Cohen, M. Fischbach, H. Claman, *J. Immunol.* **105**, 1146 (1970); J. J. Cohen and H. N. Claman, *J. Exp. Med.* **133**, 1026 (1971); H. Wagner, A. Harris, M. Feldmann, *Cell. Immunol.* **4**, 39 (1972).
14. M. H. Julius, E. Simpson, L. A. Herzenberg, *Eur. J. Immunol.* **3**, 645 (1973).
15. These results confirm reports that the adenylate cyclase activity of several cell types, including rat and mouse thymocytes, did not increase after incubation with histamine. [E. Remold-O'Donnell, *J. Biol. Chem.* **249**, 3615 (1974); M. M. Makman, *Proc. Natl. Acad. Sci. U.S.A.* **68**, 885 (1971)].
16. Because of the low affinity for the histamine–type 2 receptor of the agonists and antagonists available now, it is technically not possible [M. Plaut, L. M. Lichtenstein, C. S. Henney, *Fed. Proc.* **34**, 1004 (Abstr.) (1975); M. Plaut, unpublished].
17. J. Patrick, S. F. Heineman, J. Lindstrom, D. Schubert, J. H. Steinbach, *Proc. Natl. Acad. Sci. U.S.A.* **69**, 2762 (1972); U. Krug, F. Krug, P. Cuatrecasas, *ibid.*, p. 2604.
18. A. L. Rosenbloom, S. Goldstein, C. C. Yip, *Science* **193**, 412 (1976); J. H. Fleisch, K. M. Kent, T. Cooper, in *Asthma: Physiology, Immunopharmacology and Treatment*, K. F. Austen and L. M. Lichtenstein, Eds. (Academic Press, New York, 1973), p. 139.
19. If splenic B cells of normal mice lack histamine receptors, then histamine should not modulate lipopolysaccharide-induced proliferation. In confirmation of this, we have seen only minimal effects of histamine on lipopolysaccharide-induced proliferation (*8*).
20. M. A. Bach, *J. Clin. Invest.* **55**, 1074 (1975).
21. J. J. Cebra and G. Goldstein, *J. Immunol.* **95**, 230 (1965); R. Kamat and J. J. Cebra, in preparation. We thank Dr. Cebra for the serum used in our experiments.
22. A. E. Reif and J. M. V. Allen, *J. Exp. Med.* **120**, 413 (1969); H. S. Shin, M. Hayden, S. Langley, N. Kaliss, M. R. Smith, *J. Immunol.* **114**, 1255 (1975); R. C. Kuppers and C. S. Henney, *ibid.*, in press.
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