Photoperiod controls the induction, retention, and retrieval of antigen-specific immunological memory

Brian J. Prendergast, Staci D. Bilbo, and Randy J. Nelson

Departments of Psychology and Neuroscience, The Ohio State University, Columbus, Ohio 43210

Submitted 10 July 2003; accepted in final form 1 September 2003

Photoperiod controls the induction, retention, and retrieval of antigen-specific immunological memory. Am J Physiol Regul Integr Comp Physiol 286: R54–R60, 2004. First published September 4, 2003; 10.1152/ajpregu.00381.2003.—Changes in day length affect several measures of immunity in seasonally breeding mammals. In Siberian hamsters (Phodopus sungorus), short day lengths suppress specific secondary antibody responses to the keyhole limpet hemocyanin (KLH) antigen and enhance cutaneous delayed-type hypersensitivity (DTH) responses to dinitrofluorobenzene (DNFB). These experiments tested whether day length affects secondary antibody and DTH responses by altering immune function solely during the interval after the initial exposure to each antigen, solely during the interval after the second exposure, or during both stages of the respective immune responses. Adult male Siberian hamsters were exposed to either a long (16 h light/day; LD) or a short (8 h light/day; SD) photoperiod for 7.5 wk before receiving an initial exposure to each antigen (KLH injection, cutaneous DNFB treatment; separate groups of animals for each antigen). A subset of LD hamsters was transferred to the SD photoperiod, and a subset of SD hamsters was transferred to the LD photoperiod. Other hamsters remained in LD or SD. Eight weeks later, all hamsters were challenged with a second subcutaneous injection of KLH or a second application of DNFB to the ear, and immune responses were measured. Exposure to SD during the primary antibody response did not affect secondary IgG responses, but SD exposure during the secondary response significantly suppressed IgG production independent of day length during the initial KLH treatment. In contrast, exposure to SD during the DNFB challenge enhanced the ensuing DTH response, but this enhancement depended on the photoperiod prevailing during the initial exposure. Exposure to SD during the sensitization stage did not enhance DTH in hamsters subsequently exposed to LD. The data suggest that short photoperiods have enduring effects on immune responsiveness and on the establishment and retention of immunological memory.

seasonality; photoperiodism; delayed-type hypersensitivity; antibody; hamster

ANNUAL FLUCTUATIONS IN FOOD availability, ambient temperature, water, and shelter are some of the challenges with which most mammals must cope to survive and reproduce (3, 22). Seasonal rhythms in the production of offspring are often timed to coincide with energetically favorable phases of the geophysical cycle, and it has been argued that the reproductive cycle is a principal target of natural selection (3, 19). The seasonal change in day length (photoperiod) provides an indication of time of year and functions as a proximate trigger for seasonal adaptations within many physiological systems, including reproduction and metabolism (3, 19). Seasonal changes in the immune system are also evident in many vertebrate species and have been hypothesized to have evolved to facilitate survival in the face of annual cycles in pathogen prevalence and energy availability (7, 15, 16, 21). Recent studies, primarily conducted in seasonally breeding rodents, have documented effects of experimental changes in day length on several in vitro and in vivo measures of immunity (2, 5, 17, 20, 23), supporting the contention that, in nature, seasonal changes in immunocompetence may be driven in part by ambient photoperiod.

In long-day breeding Siberian hamsters (Phodopus sungorus), adaptive cell-mediated immune responses are affected by changes in photoperiod. Adaptation to short day lengths in the laboratory suppresses antigen-induced immunoglobulin concentrations relative to those of hamsters maintained in long photoperiods (8, 23). After initial exposure to some antigens, memory lymphocytes form and survive in the organism for months to years. Immunological memory conferred by these cells allows more rapid and higher antigen-specific immunoglobulin production in response to subsequent encounters with the same antigen (secondary antibody responses; see Ref. 11). In common with primary antibody responses, memory-dependent secondary antibody responses of Siberian hamsters are also inhibited by exposure to short photoperiods (12), suggesting that either the formation, recruitment, or activation of memory T and B cells necessary for the generation of secondary antibody responses is inhibited by exposure to short photoperiods (12). Effects of photoperiod on the formation and/or implementation of immunological memory may not be limited to antibody responses. Delayed-type hypersensitivity (DTH) responses (also termed type IV hypersensitivity reactions), for example, are antigen-specific cell-mediated immune responses that require the formation of memory T cells after initial exposure to an antigen (6); memory T cells potentiate proinflammatory cytokine secretion and accessory cell recruitment upon subsequent exposure to the same antigen. DTH responses play a critical role in organismal resistance to bacterial and viral infections (14). The observation that short photoperiods enhance the magnitude of DTH reactions in Siberian hamsters (1) raises the possibility that short day lengths may potentiate the formation, retention, or activation of immunological memory involved in the generation of DTH responses (1).

Immunological memory is of considerable adaptive significance, as it allows individuals to mount rapid immune responses to familiar antigens, even after long intervals since last exposure to the antigen (11). Antibody production in response to secondary immunization (12) and DTH responses after sensitization (1) each require an initial response to an antigen (i.e., sensitization phase) during which memory lymphocytes are created, and later, a reaction to the eliciting stimulus (challenge or secondary phase) during which the actions of...
memory T and B cells (in the case of antibody production) or memory T cells alone (DTH reactions) augment the response of the immune system to the same antigen. Although day length affects both DTH and secondary antibody production, the stage of each immune response (i.e., during the initial or secondary antigen exposure) during which photoperiod affects the magnitude of the response is not known, as all studies to date have maintained animals in the same fixed (short or long) photoperiod during both initial sensitization and second challenge exposures to the antigen. Thus, in the case of DTH responses, exposure to short days may enhance the DTH response by increasing exposure of dendritic cells to haptons in the skin, by altering antigen presentation in the lymph nodes, or by amplifying clonal expansion of T cells, to name but a few possibilities (all occurring during the sensitization stage). Alternatively, the effect of short days on DTH responses may result from changes in the capacity for inflammatory responses after a second exposure to the antigen (i.e., the result of events occurring during the challenge stage). Analogous enhancing effects of long days on antigen-specific secondary antibody production may be a result of photoperiod effects during the primary antibody response or during the secondary antibody response or may arise from processes occurring during both stages. Because animals in nature likely encounter antigens over the entire course of the year, an important functional question is whether memory-dependent immune responses are influenced only by contemporary or only by antecedent photoperiodic conditions.

The present experiments tested the hypothesis that photoperiod experienced during initial exposure to an antigen exposure affects immune responses after a second exposure to the same antigen. We addressed this question using two distinct antigen-specific cell-mediated immune responses, secondary antibody production in response to inoculation with keyhole limpet hemocyanin (KLH) protein and cutaneous DTH responses to dinitrofluorobenzene (DNFB), both of which share the common feature of immunological memory dependence. Siberian hamsters were used as the experimental model because the effects of photoperiod on each of these immune responses are well established (1, 8, 12).

METHODS

Animals

Experimental animals (n = 104) were male Siberian hamsters (Phodopus sungorus) derived from a colony maintained at the Ohio State University. Hamsters were housed in polypropylene cages (2–3 hamsters/cage) in a room illuminated for 16 h/day with incandescent light (LD; lights on 2300, Eastern Standard Time). Food (LabDiet 5001; PMI Nutrition, Brentwood, MO) and filtered tap water were provided ad libitum. Ambient temperature and relative humidity were held constant at 21 ± 5°C and 50 ± 10%, respectively. Hamsters remained group housed two to three per cage with siblings for the duration of the experiment.

Experiment 1: Effects of Photoperiod During Primary and Secondary Antibody Responses

Photoperiods and experimental protocol. At the beginning of the experiment (week 0), adult (8–10 wk of age) male hamsters (n = 31) were transferred to SD or remained in their natal LD photoperiod (n = 30). On week 7.5, hamsters were sensitized to DNFB on three successive days with 0.5% DNFB (in oil/acetone; see below and Ref. 1). On week 10.5 (21 days after sensitization began), a subset of LD hamsters was sensitized to DNFB on three successive days with 0.5% DNFB (in oil/acetone; see below and Ref. 1). On week 10.5, a subset of SD hamsters was transferred to the LD photoperiod (LD/LD group; n = 31). LD and SD hamsters that were not subjected to photoperiod transfer on week 10.5 remained in LD (LD/LD group; n = 31) and SD (SD/SD group; n = 31), respectively, for the remainder of the experiment. On week 18.5 (8 wk after photoperiod transfer), a blood sample was obtained under light isoflurane anesthesia, and hamsters were inoculated again with KLH (second inoculation 30 μg). Additional blood samples were obtained 3, 7, 10, 14, 21, and 28 days after the second KLH inoculation.

KLH ELISA. Serum concentrations of anti-KLH IgG and IgM were determined using an ELISA, as described in detail elsewhere (4). Thawed serum samples from hamsters in experiments 1 and 2 were diluted 1:300, respectively, with PBS-Tween, and 150 μl of each serum dilution were added in duplicate to the wells of KLH-coated microtiter plates. Positive control (pooled serum from hamsters previously determined to have high levels of anti-KLH antibodies) and negative control (pooled serum from hamsters injected with sterile saline vehicle) samples were also added in duplicate to each plate. The plates were sealed, incubated, and washed before addition of secondary antibody (alkaline phosphatase-conjugated anti-mouse IgG or IgM). Plates were again incubated and washed and then treated with the enzyme substrate (p-nitrophenyl phosphate). After 20 min, the enzyme reaction was stopped, and the optical density (OD) of each well was determined using a plate reader equipped with a 405-nm wavelength filter. Average OD for duplicate wells was expressed as a percentage of its plate-positive control OD value for statistical analyses (8).

Experiment 2: Effects of Photoperiod During Sensitization and Challenge Stages of DTH Responses to DNFB

Photoperiods and experimental protocol. At the beginning of the experiment (week 0), adult (8–10 wk of age) male hamsters (n = 31) were transferred to SD or remained in their natal LD photoperiod (n = 30). On week 7.5, hamsters were sensitized to DNFB on three successive days with 0.5% DNFB (in oil/acetone; see below and Ref. 1). On week 10.5 (21 days after sensitization began), a subset of LD hamsters was transferred to the SD photoperiod (LD/SD group; n = 14), and a subset of SD hamsters was transferred to the LD photoperiod (SD/LD group; n = 15). LD and SD hamsters that were not subjected to photoperiod transfer on week 10.5 remained in LD (LD/LD group; n = 13) and SD (SD/SD group; n = 13), respectively, for the remainder of the experiment. On week 18.5 (8 wk after photoperiod transfer), DTH responses were measured in all hamsters by challenging the right pinna with 20 μl of a 0.2% solution of DNFB.

Induction of DTH. DTH was induced by application of the antigen. DNFB (Sigma), to the pinnae of each hamster after initial immunization (“sensitization”) by application of DNFB to the dorsum (1). Sensitization was induced and DTH elicited as follows: on week 7.5, all hamsters (DNFB naive) were anesthetized with isoflurane, and an area of 2 cm by 3 cm was shaved on the dorsum. Twenty-five microliters of DNFB (0.5% wt/vol in 4:1 acetone-olive oil vehicle) were applied to the shaved dorsal skin on each of three successive days. On week 18.5, baseline thickness of both pinnae was measured in lightly anesthetized hamsters before induction of DTH by using a constant-loading dial micrometer (Mitutoyo, Tokyo). Immediately after induction, the pinnae were washed with 20 μl of 0.2% solution of DNFB.
after baseline pinna measurements were obtained, 20 μl of DNFB [0.2% (wt/vol) in 4:1 acetone-olive oil] were applied to the skin of the dorsal surface of the right pinna (i.e., DNFB “challenge”). Left pinnae were treated with vehicle. Pinna thickness was measured every 24 h for the next 6 days and at less-frequent intervals thereafter. Pinna thickness values obtained on each day after challenge were expressed as a percentage of baseline thickness for statistical calculations. All pinna measurements were obtained between 1400 and 1500, and all measurements were made on the same relative region of the pinna.

Somatic and reproductive measures. In both experiments, somatic and reproductive data were collected at predetermined intervals to verify responsiveness to the photoperiod manipulations. Body masses (±0.1 g) and estimated testes volumes [ETV: calculated as length × width² (in mm) of the left testis; see Ref. 10] were obtained in lightly anesthetized hamsters on weeks 0, 7.5, 10.5, 18.5, and 22.5 (experiment 1) or on weeks 0, 7.5, 10.5, 18.5, and 20.5 (experiment 2). In most Siberian hamster populations, a subset of individuals fails to exhibit the modal reproductive and somatic responses to short days (i.e., gonadal regression, decrease in body weight, pelage molt; see Ref. 18). Hamsters that failed to exhibit a 50% reduction in ETV after 8 wk of exposure to SD (i.e., between weeks 0 and 7.5 or between weeks 10.5 and 18.5) were considered short-day nonresponsive and were excluded from all analyses. These criteria resulted in the removal of two hamsters from experiment 1 and six hamsters from experiment 2.

Statistics. Body masses, testes volumes, changes in pinna thickness, and anti-KLH antibody values were compared using repeated-measures ANOVAs with photoperiod treatment (LD/LD, SD/SD, LD/SD, SD/LD) as a between-subjects factor. Where justified by a significant F-statistic, weekly mean values were compared using Fisher’s protected least-significant difference test or unpaired t-tests, where appropriate (ANOVA; Statview5; SAS Institute, Cary, NC). Observed mean differences were considered significant at P < 0.05.

RESULTS

Experiment 1: Effects of Photoperiod During Primary and Secondary Antibody Responses

Reproductive and somatic measures. Hamsters transferred to SD on week 0 (i.e., SD/SD and SD/LD groups) exhibited gonadal regression over the next 11 wk, in contrast to LD hamsters, which maintained fully developed gonads during this interval (Fig. 1). LD hamsters (LD/LD and LD/SD groups) also increased body mass during this 11-wk interval, whereas SD-housed hamsters did not (Fig. 1). LD/SD and SD/LD hamsters were transferred to SD and LD, respectively, on week 11. Over the next 8 wk, LD/SD hamsters exhibited gonadal regression and decreased body mass, and SD/LD hamsters underwent gonadal regrowth and gained body mass (Fig 1). LD/SD and SD/SD hamsters, which were not subjected to a photoperiod transfer on week 11, did not exhibit significant changes in testis volume or body mass after week 11.

Primary antibody responses. Because all hamsters were exposed only to LD or SD before photoperiod transfer on week 10.5, the data were combined across groups receiving similar photoperiod treatments before week 10.5 (LD/LD and LD/SD; SD/SD and SD/LD) for the purposes of assessing primary antibody responses to KLH. In both LD- and SD-housed hamsters, peak anti-KLH IgG production occurred 21 days after initial inoculation, and peak anti-KLH IgM production occurred 7 days after primary inoculation (Fig. 2). Relative to LD hamsters, hamsters housed in SD for 7.5–10.5 wk had significantly lower anti-KLH IgG concentrations 15 days after initial KLH exposure (P < 0.05) and lower IgM concentrations 21 days after KLH initial inoculation (P < 0.05; Fig. 2).

Anti-KLH IgG and IgM concentrations were assessed again on week 18.5, 8 wk after photoperiod transfers occurred and immediately before the second KLH inoculation. Photoperiod manipulations on week 10.5 did not significantly affect IgM concentrations (Fig. 2). Transfer from LD to SD inhibited IgG production in LD/SD hamsters relative to LD/LD hamsters (P < 0.05), as measured on week 18.5. Conversely, transfer of...
SD/LD hamsters from SD to LD resulted in elevated IgG concentrations relative to SD/SD hamsters ($P < 0.05$; Fig. 2).

**Secondary antibody responses.** Anti-KLH IgM concentrations reached peak values 7 days after the second KLH inoculation (Fig. 3). Neither initial photoperiod nor second photoperiod had a significant main effect on secondary anti-KLH IgM production; however, relative to other groups, SD/SD hamsters exhibited higher IgM values 7 (vs. LD/LD and LD/SD; $P < 0.05$, both comparisons) and 10 (vs. LD/SD; $P < 0.05$) days after the second inoculation.

Peak anti-KLH IgG responses occurred 14 days after the second KLH inoculation (Fig. 3). Factorial ANOVA permitted parsing of effects on secondary antibody production due to photoperiod during weeks 0–10.5 ("initial photoperiod") from those due to photoperiod during weeks 10.5–18.5 ("second photoperiod"). Photoperiod exposure during the primary antibody response did not significantly affect secondary IgG responses [$F(1,46) < 0.01$; $P > 0.90$]; however, second photoperiod had a significant main effect on secondary IgG production [$F(1,46) = 4.07$; $P < 0.05$]. Overall, hamsters exposed to LD during weeks 10.5–18.5 manifested higher secondary anti-KLH IgG values relative to hamsters housed in SD during this interval. Three days after the second inoculation, LD/LD hamsters exhibited higher IgG responses relative to all other groups ($P < 0.05$, all comparisons), which did not differ from one another ($P > 0.20$, all comparisons). Relative to LD/SD hamsters, LD/LD hamsters exhibited higher IgG values 7 and 28 days after the second inoculation.

**Experiment 2: Effects of Photoperiod During Sensitization and Challenge Stages on DTH**

**Reproductive and somatic measures.** Reproductive and somatic responses to photoperiod manipulations in experiment 2 were comparable to those exhibited in response to similar manipulations used in experiment 1. LD/LD and SD/SD hamsters manifested and sustained somatic development and regression, respectively (Fig. 4). LD/SD hamsters initially (weeks 0–11) exhibited somatic growth and sustained full gonadal development; on week 10.5, LD/SD hamsters initiated...
weeks ($P < 0.0001$, all comparisons). Photoperiod exposure during the 7.5-wk before sensitization (weeks 0–7.5) did not significantly affect the magnitude of the DTH inflammatory response exhibited beginning on week 18.5 [$F(1,51) = 3.62; P = 0.06$]; in contrast, photoperiod exposure during the 8 wk preceding DNFB challenge (weeks 10.5–18.5) significantly affected the ensuing DTH response [$F(1,51) = 17.9; P < 0.0001$]. Of the four experimental groups, SD/SD hamsters exhibited the largest and most sustained pinna inflammation (Fig. 5). Between-groups comparisons of within-subjects DTH inflammatory curves indicated that the pattern of inflammation exhibited by SD/SD hamsters differed significantly from that exhibited by all other treatment groups ($P < 0.05$, all comparisons), which did not differ significantly from one another ($P > 0.05$, all comparisons).

**DISCUSSION**

These experiments tested the hypothesis that photoperiod experienced during initial exposure to an antigen (initial inoculation with KLH or sensitization to DNFB) can affect immune responses during subsequent exposure to the same antigen (second KLH inoculation or DNFB challenge), independent of the photoperiod during secondary exposure. The results indicate that photoperiod effects on secondary antibody production and DTH responses differ categorically. Photoperiod during the initial inoculation influences secondary IgM responses, whereas ambient (second) photoperiod overrides the effects of prior (initial) photoperiod exposure on the generation of secondary IgG responses. In contrast, photoperiods occurring during both the sensitization and during the challenge stages interact to affect DTH inflammatory responses.

In experiment 1, photoperiod had no effect on primary anti-KLH IgM responses. Previous reports have described an inhibitory effect of LD on the waning of the primary IgM response; however, these studies (12, 24) used different durations of SD exposure and amounts of antigen during inoculation (12, 24). Moreover, the present data describe a similar

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increase in IgM concentrations in LD relative to SD hamsters (Fig. 2A, cf. Refs. 12 and 24), but after a longer interval had elapsed after primary inoculation. Secondary IgM responses to KLH were also influenced by ambient photoperiod, but in a manner that does not lend itself to straightforward interpretations regarding the relative contributions of initial vs. second photoperiod exposure, or interactions thereof, on IgM production. SD/SD hamsters exhibited secondary IgM responses that exceeded those of LD/SD hamsters 7 and 10 days after second inoculation, suggesting that photoperiod during the initial inoculation may influence secondary responses, given a permissive (i.e., SD) second photoperiod. An enhancing effect of SD/SD relative to LD/LD on secondary responses is not consistent with previous reports (12) of higher secondary antibody responses to KLH in LD (the photoperiodic equivalent of LD/SD) hamsters relative to SD hamsters; however, different inoculation doses and intervals between initial and secondary inoculation (3 vs. 11 wk) preclude direct comparison between this and earlier studies.

Primary anti-KLH IgG production in SD hamsters was suppressed relative to that of hamsters housed in LD (cf. Refs. 8, 12, and 23). Ambient photoperiod during the primary inoculation had no effect on IgG responses elicited by secondary inoculation with KLH. In contrast, SD exposure during the secondary antibody response significantly suppressed IgG production in a manner independent of photoperiod occurring during the primary KLH treatment. After the primary antibody response had peaked (i.e., after week 10.5), transfer of LD/SD hamsters to SD, and of SD/LD hamsters to LD, resulted in decreases and increases, respectively, in anti-KLH IgG concentrations 8 wk later, yielding different baseline anti-KLH IgG concentrations in the circulation on the day of secondary inoculation. This observation suggests that photoperiod alters the retention of immunological memory for prior exposure to the KLH antigen. Together, the data from experiment 1 suggest that photoperiodic effects on antigen-specific primary (8, 23) and secondary (12) antibody production represent photoperiodic effects on immune function occurring during the generation of the specific antibody response itself, rather than a result of enduring effects of photoperiod occurring during the establishment of immunological memory.

In experiment 2, DTH reactions to DNFB challenge on week 18.5 were influenced significantly both by ambient photoperiod (i.e., photoperiod on week 18.5) and by photoperiods that occurred ≥8 wk earlier (i.e., during weeks 0–10.5). Photoperiods during sensitization interacted with those during challenge to affect the magnitude of the final inflammatory response. Irrespective of photoperiod during sensitization to DNFB, hamsters housed in SD during DNFB challenge (LD/SD and SD/SD groups) exhibited larger DTH inflammatory responses relative to hamsters housed in LD during challenge (SD/LD and LD/LD groups). Among the former groups, exposure to SD during sensitization resulted in a significantly larger DTH reaction (i.e., the magnitude of the DTH response in SD/SD hamsters exceeded that of LD/SD hamsters); however, among the latter two groups, this was not the case (i.e., DTH of LD/LD hamsters was comparable to that of SD/LD hamsters). The magnitude of the DTH responses in the present experiment was lower than that observed in previous studies of Siberian hamsters, and the time course of the inflammatory response was relatively protracted; however, this may be related to the long interval between sensitization and challenge in this (11 wk) relative to earlier (7 days) reports (1). Quantitative features notwithstanding, the data are consistent with an earlier report of enhanced DTH responses in SD- relative to LD-housed hamsters (1) and specify that the enhancing effect of SD on this immune response is a consequence of the short photoperiod acting both during the sensitization and during the challenge stages of the response. The present data also permit the inferences that 1) SD exposure during the sensitization stage of the response is neither necessary nor sufficient for photoperiodic enhancement of the DTH response, 2) SD exposure during the challenge stage is necessary but not sufficient for maximal enhancement of the DTH response, and 3) SD exposure during both stages of the DTH response is required for maximal photoperiodic enhancement of this measure of immune function.

DTH responses require the formation of memory T cells after initial exposure to DNFB; antigen-specific lymphocytes formed after sensitization provide long-lasting immunological memory and permit robust responses to subsequent challenges with the same antigen (13). At a formal level of analysis, photoperiod affects both the formation (encoding) and the functional expression (retrieval) of this immunological memory. Thus, in contrast to secondary antibody responses to KLH (experiment 1), upon which antecedent (initial) photoperiods had little bearing, DTH responses appear modified both by contemporary photoperiods and by photoperiods occurring several months earlier.

The mechanisms by which SD enhance skin DTH are not fully understood; however, the present data suggest that SD can act independently during either the sensitization or during the challenge stages of the response. Although the relative numbers of professional antigen-presenting cells in LD and SD are not known, short day-adapted Siberian hamsters have more leukocytes and T lymphocytes in the circulation than do LD hamsters (1). Thus SD exposure may permit greater immunological surveillance during the sensitization stage, which may facilitate formation of immunological memory. Additional mechanisms, occurring after sensitization and before challenge, that would permit retention of immunological memory may also include greater persistence or survival of memory T cells in SD hamsters.

The effect of photoperiod on secondary antibody responses described here confirms a recent report that antigen-specific IgG production is lower in male hamsters housed in SD (12). Siberian hamsters appear capable of modulating the increase in production of antigen-specific immunoglobulins in response to ambient day length. Differing antibody responses to the second KLH inoculation may have resulted from photoperiod-driven changes in either the recruitment or the activation of antigen-specific memory B and T cells present on week 18.5. The observations that, after photoperiod transfer on week 10.5, circulating anti-KLH IgG concentrations declined after transfer to SD and increased after transfer to LD raise the possibility that photoperiod limits the availability of IgG-secreting plasma cells. If this is the case, then it must occur independently of their formation after initial KLH treatment. It is noteworthy that anti-KLH IgG remained elevated (or became elevated) on week 18.5 in hamsters exposed to LD after week 10.5, but IgM was not similarly affected by photoperiod. Paralleling this effect of second photoperiod on the persistence of anti-KLH
IgG production (i.e., on week 18.5) was the observation that second photoperiod significantly affected secondary IgG antibody responses, but secondary IgM responses were largely unaffected by second photoperiod. The mechanism(s) by which IgG 1) remains persistently elevated and 2) is affected by photoperiods occurring long after initial inoculation are presently unknown. The functional significance of such photoperiodic modulation of primary IgG production on secondary IgG responses requires further study.

In summary, these data indicate that day length affects the encoding, retention, and activation of antigen-specific immunological memory. The persistence of KHL-specific immunological memory for the purposes of IgG production is modified by changes in photoperiod, whereas day length affects both the formation and recall of DNF-specific immunological memory for the purposes of mounting DTH responses. DTH responses appear to integrate seasonal information over intervals approaching 6 mo in duration, whereas IgG responses are primarily driven by ambient photoperiod. Inferences regarding any adaptive significance of these differences are not immediately apparent. Differences in the effects of photoperiod history on distinct modes of immunological memory may be related to the types of pathogens encountered at different times of year, although such a conjecture requires more complete field data for this species. At a formal level of analysis, the present data indicate that effects on immune function of antecedent photoperiods extend well beyond the interval during which the photoperiod occurred and that the effects of a prevailing photoperiod are largely unaffected by prior photoperiod exposure.

ACKNOWLEDGMENTS

We thank R. Renstrom for technical assistance and S. Lavelle, M. Hargett, T. Litchfield, and R. Rangel for animal care.

Present address for B. J. Prendergast: Dept. of Psychology, University of Colorado, Boulder, CO 80309.

GRANTS

This investigation was supported by National Institute of Mental Health Grants MH-12875, MH-66144 and MH-57535 and by National Science Foundation Grant IBN 00–0854.

REFERENCES