Peripubertal Immune Challenges Attenuate Reproductive Development in Male Siberian Hamsters (Phodopus sungorus)1

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ABSTRACT

Differential allocation of energy to reproduction versus host defense is assumed to drive the seasonal antiphase relation between peak reproductive function and immunocompetence; however, evidence supporting this assumption is only correlational. These experiments tested whether photoperiod affects immune responses to antigens in peripubertal Siberian hamsters, whether such activation of the immune system exerts energetic and reproductive costs, and whether such costs vary seasonally. Male Siberian hamsters were raised from birth in long (LD) or short days (SD), which respectively initiate or inhibit the onset of puberty. To elicit a specific immune response, hamsters were injected with a novel antigen (keyhole limpet hemocyanin [KLH]) as juveniles. Reproductive development was attenuated and body temperature was elevated in LD hamsters relative to saline-injected control animals. In contrast, KLH treatments affected neither thermoregulation nor reproductive development in photoinhibited SD hamsters. In experiment 2, juvenile male hamsters were challenged with bacterial lipopolysaccharide (LPS) in order to elicit an innate immune response. Febrile and anorexic responses to LPS were greater in juvenile LD hamsters relative to photoinhibited SD hamsters. LPS treatments attenuated somatic and testicular development in LD hamsters, but did not significantly affect circulating testosterone concentrations. In contrast, LPS treatments without effect on somatic and reproductive development in SD hamsters. These experiments indicate that photoperiod affects antigen-specific antibody production, febrile responses to LPS, and sickness behaviors in juvenile Siberian hamsters, and that peripubertal activation of the immune system exerts energetic and metabolic costs that can diminish the magnitude of somatic and reproductive maturation in LD. The data also underscore the importance of seasonally dependent life history factors in assessing physiological tradeoffs.

developmental biology, immunology, neuroendocrinology, puberty, testosterone

INTRODUCTION

Seasonal reproduction has evolved in response to annual fluctuations in energy availability [1, 2]. Episodic (noncontinuous) breeding allows non tropical animals to direct energy to reproduction during the time of the year when food is plentiful and ambient temperatures are mild, and toward somatic maintenance and thermoregulation when food is relatively scarce and temperatures are low [1]. Seasonally breeding mammals differentially allocate energy to somatic growth, energy storage, reproduction, and immune function, in addition to other physiological functions, depending on the time of year [3–6]. In addition to thermoregulation, reproduction, and somatic growth, the immune system also requires energy in order to function adequately. Energy demands of the immune system may further increase when the host immune system is challenged [7, 8]. Bacterial infections, which typically elicit both fever (increased thermoregulatory demands) and anorexia (decreased energy intake), also presumably place increased demands on a finite energy budget [9]. From a theoretical perspective [7, 10, 11], processes associated with maintaining and activating the immune system may compete with the processes of somatic growth and reproductive development for access to a finite energy budget. A coincidence between enhanced immune function and inhibited reproductive function in seasonally breeding mammals [e.g., 6, 12, 13] has led to the hypothesis that a physiological tradeoff exists between reproduction and immune function [7, 10, 14, 15]. Mechanistic studies of physiological tradeoffs between reproduction and immunity in invertebrates and nonmammalian vertebrates have received considerable attention [16–19], but comparatively less data are available on the existence and mechanisms of any such tradeoffs in mammals. The present experiments sought to determine the manner by which potential energetic conflicts between reproduction and immune function are physiologically resolved.

Annual changes in day length—invariant from year to year—are predictive of upcoming energy availability and demand and provide the primary external cue by which mammals engage or synchronize seasonal changes in reproductive physiology, energy balance, and immune function [2, 20]. Siberian hamsters (Phodopus sungorus), in common with many nontropical rodents, initiate seasonal transitions in reproductive physiology in response to annual changes in day length. Relatively short (<13 h light/day) day lengths inhibit reproduction [21], and in the wild, hamsters breed only from spring through late summer [22]. The reproductive system of young Siberian hamsters becomes responsive to day length around the time of weaning (~18 days of age) [23], and pups born at opposite ends of the breeding season engage remarkably different life histories. Spring-born pups encounter long days (LDs), immediately initiate puberty, and are fertile by the fifth week of life; pups born during the decreasing days of late summer defer puberty and do not attain adult body size until the following spring [24]. The categorical differences in somatic growth and reproductive development exhibited by juvenile Sibe-
rian hamsters exposed to LDs versus short days (SDs), combined with relatively minor reserves of stored energy (adipose tissue), provide a useful model system for assessing seasonal changes in the extent to which activating the immune system exacts energetic and physiological costs. Moreover, it is not known whether, in common with reproductive function, immune function in juveniles is influenced by photoperiod. Thus, the present experiments 1) tested the hypothesis that photoperiod affects specific and innate immune function in juvenile hamsters, and 2) ascertained costs of immune activation during juvenile growth when energy demand is high and stores are low. In experiment 1, juvenile hamsters were injected with a novel antigen (keyhole limpet hemocyanin [KLH]) that elicits a primary antibody response over the next 2–3 wk; this immunological challenge elicits neither sickness behaviors nor fever and constitutes a relatively moderate energetic challenge [7]. In experiment 2, hamsters were challenged with a single injection of bacterial lipopolysaccharide (LPS), which simulates the initial stages of a bacterial infection, eliciting both fever and anorexia, and thus is considered a more potent energetic challenge. If the generation of either a specific (experiment 1) or an innate (experiment 2) immune response requires energy that would be otherwise allocated to somatic and/or physiological development, we would expect to observe diminished development in hamsters subjected to specific immunological challenges during the peripubertal period.

MATERIALS AND METHODS

Animals

Breeding pairs were composed of adult male and female Siberian hamsters (*P. sungorus*) from a colony maintained in our laboratory. Pairs were housed in polypropylene cages in a room illuminated (400±700 lux) for 16 h/day with incandescent light (LD; lights-on 2300 h, Standard Time). Food (LabDiet 5001; PMI Nutrition, Brentwood, MO) and water were provided ad libitum to breeders. Ambient temperature and relative humidity were held constant at 21°C ± 3°C and 50% ± 10%, respectively. Pairs were inspected daily for the presence of pups, and the day of birth was designated as Day 0. Stud males were removed from the cage on the day of birth, and the dam and pups were either transferred to a short-day photoperiod that provided light 8 h/day (SD; lights-on at 0700 h) or remained in their natal LD photoperiod. In experiment 2, the dam and pups remained together in LD until Day 18, at which time photoperiod treatments began (see below). Pups were weaned, sexed, and individually housed on Day 18 and were provided with a slurry of ground food and water for the first 24 h postweaning. Separate groups of hamsters were used in experiments 1 and 2. All procedures in these experiments were conducted in accordance with the National Institutes of Health guidelines for the use of experimental animals, and the protocols were approved by the local Institutional Animal Care and Use Committee.

Experiment 1: Specific Immunity

On Day 25, hamsters received a single subcutaneous injection of 100 μg of the novel antigen KLH suspended in 0.1 ml sterile saline (LD, n = 7; SD, n = 8); control animals received injections of the saline vehicle alone (LD, n = 6; SD, n = 7). KLH is a respiratory protein of the giant keyhole limpet (*Meagathura crenulata*) and was used because it generates a robust antigenic response in rodents, but does not cause inflammation, fever, or illness [25]. Hamsters, and the contents of their food baskets, were weighed daily (±0.1 g) thereafter to document somatic development and daily food intake, respectively. At 7, 10, and 14 days postimmunization, colonic temperature (Tb) of each hamster was measured in an acoustically isolated room 2–3 h before onset of darkness. These days were chosen to capture peak immunoglobulin production during the course of the immune response [25]. Hamsters were then anesthetized using isoflurane vapor, and the length and width of the left testes were measured (±0.1 mm). The product (testis width^2 * testis length) provided a measure of estimated testis volume (ETV) that is strongly correlated with testis weight (R^2 > 0.9) [26]. A blood sample of 270 μl was also obtained via the orbital sinus from all hamsters at the time of testis measurement. Blood samples were allowed to clot at room temperature for 1 h, the clot was removed, and samples were centrifuged at 2500 × g for 30 min. The supernatant was stored at −70°C until assayed for anti-KLH antibody concentrations by ELISA (see below).

Experiment 2: Innate Immunity

On Day 20 at 1100 h, hamsters received a single s.c. injection of 12.5 μg *Escherichia coli* lipopolysaccharide (LPS; 026:B6; Sigma, St. Louis, MO) in 50 μl sterile saline vehicle (LD, n = 13; SD, n = 12). Control hamsters received s.c. injections of 50 μl vehicle alone (LD, n = 12; SD, n = 12). Tb was measured immediately prior to and 3 h after injection treatments. Daily body mass and food intake were determined as in experiment 1. On Days 18, 25, and 32, hamsters were lightly anesthetized and testis volumes were determined. On Day 32, a blood sample of 270 μl was obtained using heparinized tubes via the retro-orbital sinus. Blood was centrifuged at 2500 × g for 30 min, and the supernatant was stored at −70°C until assayed for testosterone by RIA (see below).

Anti-KLH Immunoglobulin Assay

Serum concentrations of anti-KLH immunoglobulin (IgG) and IgM were determined using an ELISA as described in detail elsewhere [7]. Thawed serum samples from hamsters in experiment 1 were diluted 1:40 with PBS-Tween, and 150 μl of each serum dilution was 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 (from saline-treated hamsters) 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, washed, and then treated with the enzyme substrate (p-nitrophenol 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.

Testosterone Radioimmunoassay

Testosterone was measured using a double-antibody 125I radioimmunoassay kit (DSL-4100; Diagnostic Systems Laboratories, Webster, TX). Cross-reaction of the T antibody to 5α-dihydrotestosterone for this kit is 6% and is supported by the manufacturer, and the upper and lower limits of detectability are 25 and 0.1 ng/ml, respectively. This kit has previously been validated for use in Siberian hamsters [27]. Serum samples were aliquoted in 25-μl amounts into duplicate assay tubes and incubated with 125I radiolabeled tracer and rabbit anti-testosterone antibody for 1 h at 37°C. Pellets were precipitated with goat anti-rabbit gamma globulin serum and polyethylene glycol and were centrifuged at room temperature for 20 min at 1500 × g. The supernatant was then decanted and aspirated, and gamma emissions from each tube were recorded for 1 min using an automated gamma counter (Packard Instrument Company, Meriden, CT). All testosterone values were determined in a single radioimmunoassay for which the intraassay coefficient of variation was 3.7%.

Statistical Analyses

In experiment 1, serum anti-KLH IgM and IgG concentrations were compared using between-subjects ANOVA. Tb values were compared using unpaired t-tests. In experiment 2, changes in Tb after LPS injections were compared using mixed within-subjects factorial ANOVAs, and pairwise comparisons were conducted using Fisher protected least significant difference (PLSD) test. In both experiments, longitudinal changes in food intake, body mass, and testis volumes were compared using a mixed within-subjects factorial ANOVA using treatment (KLH, LPS, or saline) as between-subjects factors and age as a within-subjects factor. Testosterone concentrations were compared using between-subjects ANOVA. Where justified by a significant F-value, between-group means on a given date were compared using PLSD t-tests or unpaired t-tests, where appropriate (ANOVA: Statview 5, SAS Institute, Cary, NC). Observed mean differences were considered significant if P < 0.05.
RESULTS

Experiment 1: Specific (KLH) Immune Responses

KLH antibody production. Hamsters raised from birth in SD exhibited higher primary anti-KLH IgG production 10 days \( (F_{1,13} = 6.2; \ P < 0.05) \) and 14 days \( (F_{1,13} = 5.2; \ P < 0.05) \) after immunization (Fig. 1A); anti-KLH IgM production was significantly lower in SD-exposed hamsters 10 days after antigen presentation \( (F_{1,13} = 5.3; \ P < 0.05) \), but not 14 days postimmunization \( (F_{1,13} = 1.3; \ P > 0.05; \ Fig. 1A) \).

Body temperature. Overall, \( T_b \) of SD hamsters was higher than that of LD hamsters during the interval of 25–39 days of age \( (F_{1,26} = 4.7; \ P < 0.05; \ Fig. 1B) \). Seven days after injections, \( T_b \) of saline-injected control animals were significantly lower than those of hamsters injected with LPS \( (t_{1,11} = 2.9; \ P < 0.05; \ Fig. 1B) \). \( T_b \) of SD hamsters injected with KLH did not differ from those of saline-injected SD hamsters at any time.

Food intake. Between Days 25 and 39, mean daily food intake was significantly lower in SD hamsters relative to LD hamsters \( (F_{1,26} = 101.1; \ P < 0.001; \ Fig. 2A) \). KLH treatments had no effect on food intake during this interval.

Body mass. Body mass increased significantly between Days 25 and 39 \( (F_{20,540} = 322; \ P < 0.001; \ Fig. 2B) \). LD hamsters exhibited significantly higher body mass relative to SD hamsters \( (F_{1,26} = 27.7; \ P < 0.001; \ Fig. 2B) \). KLH treatments had no main effect on changes in or absolute body mass \( (F_{1,26} = 0.002; \ P > 0.05; \ Fig. 2B) \); body mass did not differ as a result of KLH treatment on any day after Day 25 in either photoperiod \( (P > 0.05, \ all \ comparisons) \).

Reproductive physiology. Photoperiod treatments significantly affected reproductive development \( (F_{1,26} = 654; \ P < 0.001; \ Fig. 2C) \), with LD hamsters exhibiting larger testes than SD hamsters on Days 32, 35, and 39 \( (P < 0.05, \ all \ comparisons) \). Photoperiod and KLH treatments interacted to affect reproductive development as measured 7 days (Day 32) after injection treatments \( (F_{2,52} = 6.59; \ P < 0.005; \ Fig. 2C) \). LD hamsters injected with KLH had smaller testes than saline-injected controls on Day 32 \( (P < 0.05) \), whereas KLH treatments had no effect on testis sizes of SD hamsters \( (P > 0.05) \). KLH treatments had no effect on this measure of reproductive physiology in either LD or SD hamsters on Days 35 and 39 \( (P > 0.05, \ all \ comparisons; \ Fig. 2C) \).

Experiment 2: Innate Immune Responses

Febrile responses to LPS. LPS markedly increased body temperature within 3 h of treatment in both LD \( (F_{1,23} = 5.05; \ P < 0.05) \) and SD \( (F_{1,22} = 4.36; \ P < 0.05) \) hamsters (Fig. 3). The magnitude of increase in \( T_b \) subsequent to LPS treatments was significantly greater in LD hamsters as
FIG. 2. Mean ± SEM (A) total daily food intake, (B) body mass, and (C) testis volumes of male Siberian hamsters in experiment 1. Experimental treatments and group abbreviations are as in Figure 1. *P < 0.05 versus SD value at a given age.

FIG. 3. Mean ± SEM colonic temperature (Tb; left panel) and change in colonic temperature (right panel) of male Siberian hamsters in experiment 2. Hamsters were raised from birth in long days (16 h light/day; LD), and at 18 days of age (Day 18) were either transferred to short days (8 h light/day; SD) or remained in LD. On Day 20 hamsters were injected i.p. with bacterial lipopolysaccharide (LPS; 12.5 μg in 0.05 ml saline) or sterile saline, *P < 0.05 versus value of saline-injected hamsters in the same photoperiod at +3 h; #P < 0.05 versus value of LD LPS-injected hamsters.

Compared with SD hamsters (F₁,23 = 6.85; P < 0.05; Fig. 3), food intake. Photoperiod had no main effect on food intake in saline-injected hamsters (F₁,22 = 1.37; P > 0.05; Fig. 4A), although SD hamsters consumed less food than LD hamsters on Days 27 and 29. Food intake measurements were significantly lower on the day following LPS treatment relative to the day following saline treatment (F₁,47 = 7.92; P < 0.01). Moreover, photoperiod affected changes in food intake following LPS treatments. LPS treatments significantly altered food intake over time in LD hamsters (F₁₄,308 = 2.66; P < 0.005), but this effect was not observed in SD hamsters (F₁₄,308 = 0.46; P > 0.05); following LPS treatment food intake was inhibited for two consecutive days in LD hamsters (Day 20, P < 0.0001; Day 21, P < 0.05), whereas food intake of SD hamsters was inhibited only on the day immediately following LPS treatment (Day 20, P < 0.05; Day 21, P > 0.05; Fig. 4A).

Body mass. The pattern of body mass accretion differed significantly between LD and SD hamsters (F₁₄,308 = 11.7; P < 0.0001). SD hamsters weighed less than LD hamsters beginning on Day 29 and continuing thereafter. LD hamsters injected with LPS on Day 20 weighed significantly less than saline-injected controls on the following day and sustained diminished body masses for 7 consecutive days (Fig. 4B). In contrast, LPS injections did not affect body mass of SD hamsters (Fig. 4B).

Reproductive physiology. The rates of reproductive development differed significantly between LD control and SD control hamsters (F₂,44 = 193; P < 0.0001; Fig. 4C). Testis sizes of LD and SD hamsters were comparable on Day 18 (P > 0.05), but LD hamsters had significantly larger testes on Days 25 and 32 (P < 0.05, both comparisons). LPS treatments interacted with photoperiod to affect reproductive development (F₂,90 = 10.5; P < 0.0001). LPS treatments inhibited reproductive development in LD (F₁,23 = 20.1; P < 0.0005), but were without effect in SD (F₁,22 = 0.79; P > 0.05). LPS-injected hamsters housed in LD had significantly smaller testes sizes on Days 25 (P < 0.0005) and 32 (P < 0.0001; Fig. 4C).

Testosterone concentrations. Irrespective of injection-treatment, on Day 32 LD-housed hamsters exhibited significantly higher circulating testosterone concentrations relative to SD-housed hamsters (F₁,43 = 10.2; P < 0.005; Fig. 5). Among saline-treated hamsters, testosterone concentrations were higher in LD relative to SD (P < 0.01), but this relation was not obtained among LPS-treated hamsters (P
> 0.10). However, among LD-housed hamsters, testosterone concentrations of LPS and saline-treated hamsters did not differ ($P > 0.30$), nor did testosterone concentrations differ between treatment groups in SD ($P > 0.70$).

**DISCUSSION**

Photoperiod affected the patterns of IgM and IgG antibody responses to KLH, the magnitude of febrile responses to LPS, and the duration of sickness-induced anorexia in juvenile Siberian hamsters. Peripubertal triggering of either a specific humoral (experiment 1) or a nonspecific innate (experiment 2) immune response was associated with reduced somatic and reproductive development, depending on the type of immune challenge. These metabolic costs (inferred from measures of food intake and $T_b$) were exacerbated when immune challenges were coincident with pubertal development (i.e., in LD hamsters). KLH-treated hamsters undergoing reproductive maturation in LD exhibited elevated $T_b$ and a transient inhibition in reproductive development relative to saline-treated controls. Neither of these effects of antigen treatment was evident in reproductively quiescent hamsters raised in SD. In response to LPS-treatment, both LD and SD hamsters exhibited anorexia and fever; however, fever amplitude and the duration of anorexia were more severe in LD hamsters [cf. 12], and attenuation of somatic growth was evident only in LD hamsters. Furthermore, reproductive organ size was significantly smaller in LD hamsters treated with LPS relative to LD controls. Together, these data identify costs, in terms of increased thermoregulatory demands and deficits in somatic
and reproductive development, associated with activating the immune system early in life. The data are, therefore, consistent with the hypothesis that activating the immune system is subject to tradeoffs against the maintenance of other traits [11, 28]. Decrements in somatic and reproductive development associated with activating a specific immune response were exacerbated in hamsters undergoing more rapid somatic and reproductive development in LD relative to those sustaining reproductive quiescence in SD. This observation suggests that the physiological significance of any tradeoffs associated with mounting an immune response may be conditional (i.e., context-dependent), and, in hamsters of this age, may be evident primarily in individuals undergoing pubertal development or subject to comparable conditions of increased energetic demands [11, 14].

This is the first report to describe effects of photoperiod on functional assays of immunity in juveniles of this species. Thus, in common with the reproductive system [23], the immune system of Siberian hamsters appears modified by photoperiod at an early age. The effect of photoperiod on IgM production in the present report (LD > SD) is consistent with effects of photoperiod on this isotype in adult hamsters [29, 30], but the inhibitory effect of LD relative to SD on IgG production described here is the opposite of that described in adult hamsters [31]. Whether this difference reflects developmental differences in mechanisms responsible for isotype switching or represents a categorically different response in juveniles relative to adults is unknown. Total leukocytes are increased in SD relative to LD male Siberian hamsters at 25 days of age [32], but the cell-specific leukocyte subtypes have not been identified. Although the mechanism(s) remain unknown, the present data suggest that photoperiodic effects on the immune system in juvenile hamsters are functionally significant for antibody production and sickness responses [32].

Experiment 1 identified morphological changes (decreased gonadal development) associated with mounting a specific humoral immune response to KLH. If tradeoffs between somatic and reproductive development versus immune responsiveness indeed exist [11], then the increased energetic demands of mounting an antibody response ought to exact a cost—quantifiable in terms of either diminished somatic or reproductive development, or increased energy intake. However, KLH treatments did not affect food intake or accretion of body mass. In the absence of changes in energy intake, the slight inhibition of gonadal development in LD-housed hamsters may reflect the outcome of competition between the reproductive and immune systems for use of fixed energy resources.

Experiment 2 assessed somatic and reproductive changes associated with responding to a more potent immune challenge. Bacterial LPS induced fever and inhibited food intake in juvenile hamsters regardless of day length; however, the magnitude of the febrile response and the duration of anorexia observed in LD hamsters were approximately twice those exhibited by SD hamsters. Body masses of LD hamsters were lower on the day following LPS treatment and remained lower than those of saline-injected hamsters for the next week. This difference in body mass appears to be largely a consequence of 2 days of reduced feeding, as the body mass growth curves for saline- and LPS-injected hamsters were essentially parallel (slopes of 0.84 and 0.89, respectively) between Days 22 and 32. Testis size, a reliable indicator of testis mass and spermatogenesis in this species [26, 33], was also lower subsequent to LPS treatment in LD pups, and unlike body mass, remained significantly lower on Day 32. In mice and rats, LPS inhibits gonadal steroidogenesis [34–36] with inhibitory intervals ranging from hours [35] to several days [34]; in the present experiment, however, we observed no decrements in testosterone concentrations 12 days after LPS treatment. It is possible that diminished testosterone concentrations may occur shortly following LPS treatments, and more frequent blood sampling would be required to test this conjecture. As with the more modest differences in reproductive morphology observed subsequent to KLH treatment, somatic and reproductive inhibition following LPS treatment was observed only in juveniles exposed to LD after Day 18. Although this photoperiod-specific effect of LPS may simply reflect a “floor effect” (i.e., body masses and testis sizes of SD hamsters could not be further reduced), it nonetheless illustrates a critical role of life history in understanding the costs of immune function in this species [11]. Deficits in somatic and reproductive development associated with peripubertal immune activation were evident only under specific conditions (i.e., in hamsters exposed to a photoperiod that simultaneously induced puberty).

LPS treatment activates the acute phase response (APR) to infection—a coordinated set of behavioral and physiological adaptations (including cytokine secretion, fever, anorexia, diminished activity) that function to contain bacterial infections during their early stages [9]. A nonreplicating pathogen, LPS is a standard immunological tool for assessing innate cell-mediated immune responses, and it elicits an APR similar to that induced by a replicating bacterial infection [37]. Importantly, the APR is an adaptation on the part of the host, not on the part of the infective agent at the cost of the host [9], and therefore reflects efforts on the part of the host to respond to and clear bacterial infection. Any consequences of engaging the APR may thus be viewed as tradeoffs in exchange for the maintenance and deployment of physiological mechanisms that permit adaptive responses to infections [11].

Understanding the conditions under which costs of immune function become apparent provides insight into mechanisms by which underlying tradeoffs may occur. Increased thermoregulatory demands (fever) and decreased energy intake (anorexia) of the APR negatively affect energy balance, but also inhibit bacterial growth during the early stages of an infection [38], and ultimately increase survival [39]. Mounting an immune response to LPS may be particularly demanding on small-bodied juveniles, which
possess substantially smaller reserves of stored energy (white adipose tissue, both in relative and absolute terms) and exhibit higher mass-specific food intake relative to adults [cf. 40; present data]. Such age-dependent changes in energy balance may render adults of this species better suited to contend with a transient energetic challenge—such as that presented by the response to a bacterial infection—without exhibiting significant changes in reproductive morphology [cf. 12, 41]. Converging energetic demands of somatic and reproductive growth during puberty, together with minimal stores of fat, may render peripubertal hamsters exposed to LDs particularly susceptible to the costs of activating an immune response. The present data identify these costs in terms of attenuated somatic and reproductive development. Juveniles not exposed to a productively stimulatory photoperiod manifest a more efficient APR [12] and, by virtue of deferring reproductive development, may be categorically exempt from short-term decrements in reproductive development. In nature, the costs of activating the APR would appear to affect only the cohort of juveniles born and initiating puberty in the spring. Unlike spring-born hamsters, those born after the summer solstice into the shortening days of winter do not initiate puberty in the first 4–5 wk of life, but rather do so after >140 days of age [24], and therefore may incur no developmental costs if challenged with an infection while chronologically young. The mechanisms by which late-summer- and autumn-born hamsters are temporarily spared such costs (i.e., the basis of the observed floor effect in SD hamsters) may arise in part from a coincidence of 1) reduced magnitude and duration, respectively, of febrile and anorectic responses to infection in SD adapted hamsters and 2) a less energetically demanding developmental trajectory associated with delayed puberty [21]. However, exemption from measurable tradeoffs between immune function, somatic maintenance/growth, and reproductive development among hamsters born into shorter day lengths may be only temporary. Ver- nal somatic and reproductive recrudescence [21, 24] may be accompanied by an energetic scenario not unlike that observed in spring-born individuals, wherein activation of the immune system during this interval may incur energetic costs that impinge on development.

In conclusion, the present data document effects of photoperiod on functional measures of immunity, and develop- mental, reproductive, and energetic costs resulting from peripubertal activation of the immune system. Specification of the cellular and molecular mechanisms by which these costs are exacted (e.g., changes in hormone secretion or responsiveness, alterations in energy stores, differential cytokine production) awaits further study. If decrements in development were sufficient to affect the ability to acquire a mate or sire a litter, then the reproductive and somatic effects described here may be of substantial adaptive sig- nificance. Thus, tradeoffs may have evolved to balance the competing costs and fitness benefits of reproduction and robust immune function. The seasonal change in day length—and its consequences with regard to development and life history in photoperiodic mammals—may provide a critical context for assessing the energetic tradeoffs that exist between resistance/responsiveness to disease, somatic growth/maintenance, and reproduction. The present data suggest an important role of life history events in deter- mining whether and when such tradeoffs may occur, and therefore when selection can act on such adaptations. The observation that physiological and morphological costs of immune function are principally evident during an episode of life history when somatic and reproductive development are at their peak, but are not manifest when such develop- mental drives are minimal, provides evidence for the contention that immune function, somatic growth, and re- production may compete for allocation of limited resources.

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