Human Ovarian Function and Reproductive Ecology: New Hypotheses

A series of eight hypotheses is presented, based on the results of current research, concerning the responsiveness of the human ovary to constitutional and environmental variables. These hypotheses are motivated by a theoretical position that seeks to understand human reproductive physiology as the product of natural selection. The hypotheses are: (1) Ovarian responsiveness occurs along a graded continuum. (2) The graded continuum of response forms a final common pathway for various "stresses." (3) Ovarian function tracks energy balance, not simply nutritional status. (4) Ovarian function tracks aerobic activity independently of energy balance. (5) Additive interactions characterize the interaction of constitutional and environmental factors modulating ovarian function. (6) Reproductive maturation is synchronized with skeletal maturation, especially of the pelvis. (7) Peak ovarian function is not ordinarily achieved until the early twenties. (8) Late reproductive maturation is associated with a slower rise in indices of ovarian function with age, and a lower level of ovarian function in adulthood. Together, these hypotheses provide for two, non-exclusive theories of facultative modulation of female reproductive effort. One theory views ovarian function as responsive to the prospects for positive reproductive outcome as these may be affected by maternal age, maturation, energy balance, and activity level. The second theory views ovarian function as responsive in a similar way to the need to maintain long-term maternal energy balance.

It has been twenty years since Frisch and Revelle first published their controversial hypothesis linking menarche to nutritional status in human females (Frisch and Revelle 1970, 1971). The debate touched off by this hypothesis and its successors has continued into the present, encompassing criticisms and responses on many levels, ranging from data analysis and interpretation (Johnston, Malina, and Galbraith 1971; Frisch, Revelle, and Cook 1971; Johnston et al. 1975; Billewicz, Fellowes, and Hytten 1976; Frisch 1976; Cameron 1976; Trussell 1978; Frisch 1978; Reeves 1979; Trussell 1980; Ellison 1981a, 1982) to health policy and international development (Scott and Johnston 1985; Ellison 1991). Both because and in spite of this debate, interest in the ecological responsiveness of the human reproductive system has grown among anthropologists, human biologists, demographers, and physiologists, each group initiating data collection and hypothesis testing by the methods of their respective disciplines. Demographic approaches have been particularly important in shaping current understanding of human fertility regulation in natural fertility populations (Henry 1961; Bongaarts and Potter 1983; Wood and Weinstein 1988). Yet one of the most important advances in this area, the recognition of the importance of the temporal pattern of nursing behavior in regulating natural birth intervals, was achieved by integrating an understanding of reproductive physiology into demographic research (Delvoye et al. 1977; Konner and Worthman 1980; Short 1983). As a result, the role of lactation as a natural birth-spacing mechanism, at first the subject of cautious speculation by both demographers (Henry 1961) and clini-
cians (Udesky 1950; Gioiosa 1955), has now virtually achieved the status of a principle of human population biology (Howie and McNeilly 1982; Short 1987) and public health policy (WHO/NRC 1983; Kennedy, Rivera, and McNeilly 1989).

During the same two decades, a wealth of information has also been accumulated concerning biological constraints on human ovarian function other than those associated with breastfeeding. Significant nonpathological variation in ovarian function has now been associated with age, nutritional status, energy balance, diet, and exercise. Much of this information has come from clinical and physiological studies, although potential applications to a broader understanding of human ecology have not been lost to anthropologists (Bentley 1985; Peacock 1986, 1990). On the basis of this information it is now possible to formulate more sophisticated hypotheses than those originally advanced by Frisch and Revelle, which help to synthesize our current understanding, expose its weaknesses, and identify promising areas of future research.

This article provides such a set of hypotheses with a specific focus on the ecological responsiveness of human ovarian function to factors other than lactation. My emphasis is on physiological studies that pertain specifically to ovarian function, and not on demographic data that provide for second-order inferences only. This approach is a reflection both of a theoretical perspective and of more practical considerations. The theoretical perspective is evolutionary; that is, it is assumed that human reproductive physiology as it now exists is the product of natural selection, encumbered, as always, with historical and design constraints. From this perspective, variation in ovarian function may represent adaptive flexibility or responsiveness to conditions, rather than pathological dysfunction. Additionally, from this perspective one assumes that modern human environments have changed faster than our endowed physiology. Thus, the mechanisms modulating human ovarian physiology may still be true to their original design, even though patterns of fertility may be the product of historically novel situations.

As a more practical matter, many of the results of demographic studies are still at variance with the results of physiological studies concerning the ecological regulation of human ovarian function. A reconciliation of these approaches is certainly still possible, even inevitable, and indeed has begun to be realized in some quarters (Campbell and Wood 1988; Ford and Huffman 1988; Leslie and Fry 1989; Ellison, Peacock, and Lager 1989). My goal in this article, however, is not to forge such a reconciliation prematurely. As study of the demographic importance of the physiology of lactation has taught us, it may be valuable to push both forms of inquiry forward without ceding ascendancy to either, in the expectation of benefiting from the dialectic that emerges.

I will first present a series of eight hypotheses concerning ovarian function as an element of human ecology, based on recent research results. These hypotheses are presented largely in descriptive terms as an attempt to summarize and codify current information. Yet they are still clearly hypotheses, some more strongly supported than others. As a group, the hypotheses also provide a basis for initial steps toward a more synthetic theory of the ecology of ovarian physiology in the second part of this article. Functional interpretations of the patterns described in the eight hypotheses are presented, for the most part, in the context of that discussion. An ecological theory of ovarian function, as part of a broader theory of human reproductive ecology, will have immense value, not only to human biologists, but to students of human culture as well. Indeed, few areas of inquiry have greater claim to the common ground that still exists among the various subfields of anthropology than that which has as its center the phenomenon of human reproduction.

The Hypotheses

Hypothesis 1. Ovarian function shows a graded response continuum to important ecological, behavioral, and constitutional variables. Early studies of age, lactational, nutritional, and exercise effects on female reproductive physiology stressed the onset and maintenance of regular menstruation. It is now apparent that disruptions in menstrual function represent only
the extreme end of a graded continuum of ovarian response to these variables (Figure 1).

Between the extremes of a fully fecund ovarian cycle and the interruption of menstrual
function are more subtle degrees of variation in ovarian function. The mildest form of
ovarian suppression involves a lower profile of progesterone secretion in the post-ovula-
tory, luteal phase of the cycle. A sufficiently suppressed luteal phase is termed “luteal
insufficiency” or “luteal inadequacy,” referring to the compromised ability of the corpus
luteum to provide hormonal support to the endometrium during implantation and early
pregnancy (Riddick et al. 1983; McNeely and Soules 1988; Stouffer 1988). Suppression
of follicular development in the first half of the cycle may occur as well, and indeed is
often a precursor of luteal suppression in the same cycle (DiZerega and Hodgen 1981).

Ovulatory failure, which may occur without noticeable changes in menstrual pattern
(Poindexter and Ritter 1983), represents a yet more profound suppression of ovarian
function, necessarily dropping the probability of conception for that month to zero.

These various forms of ovarian suppression are not independent conditions, but occur
along an ordered gradient reflecting etiology. Mild luteal suppression may occur in iso-
lation, but more profound luteal suppression is ordinarily a consequence of prior follic-
ular suppression (DiZerega and Hodgen 1981). Follicular suppression, if profound

enough, can lead to ovulatory failure (Yoshimura and Wallach 1987). Continued
suppression can lead to menstrual irregularity, oligomenorrhea, and, if the suppression
is both profound and sustained, amenorrhea (Poindexter and Ritter 1983). When ovarian
suppression occurs in association with environmental, behavioral, or constitutional
“stresses,” the degree of suppression along this gradient ordinarily correlates with the
intensity of the stress. While extreme thinness (Frisch and McArthur 1974), rapid or ex-
treme weight loss (Graham, Grimes, and Campbell 1979; Pirke et al. 1985), heavy ex-
ercise (Bullen et al. 1985), early adolescence (Apter and Vihko 1983), and frequent, in-
tense nursing characteristic of the early postpartum period (McNeilly et al. 1982; Howie
et al. 1982) are all associated with irregular or absent menstrual cycles, moderate thinness
(Bates, Bates, and Whitworth 1982), moderate weight loss (Lager and Ellison 1990),
moderate exercise (Ellison and Lager 1986), late adolescence/early adulthood (Ellison,
Lager, and Calfee 1987), and less intense nursing characteristic of the period of supple-
mented breastfeeding (Howie et al. 1981, 1982) are all associated with reduced ovulatory
frequency and luteal suppression, even though menses may be regular. Movement across
the gradient of response within the lifespan of a woman can be observed in all these cases:
toward diminished ovarian function with progressive weight loss (Ellison, Peacock, and
Lager 1989), extended exercise (Bullen et al. 1985), or increasing age after 35 years (Dor-
ing 1969); and toward augmented ovarian function with increasing age during adoles-
cence (Apter and Vihko 1983; Read et al. 1984; Ellison, Lager, and Calfee 1987), weight

Figure 1
The graded continuum of ovarian response to certain ecological, behavioral, and consti-
gain or stabilization (Bates, Bates, and Whitworth 1982; Lager and Ellison 1990), or declining nursing intensity postpartum (Howie et al. 1981, 1982).

Ordinarily, only the extreme end of this gradient—that which involves disruptions of menstrual function—lies above the clinical horizon, obvious to a woman or apparent to her physician from a menstrual history. Detection of moderate suppression of ovarian function requires more sophisticated and often more invasive procedures, and conditions in this range often go unnoticed by both women and their physicians. Subtle expression does not, however, imply benign effect. Luteal suppression of progesterone production, for instance, is associated with failure of conception and repeated abortion (Lenton et al. 1988; McNeely and Soules 1988), and follicular suppression of estradiol with ova of diminished fertilizability (Yoshimura and Wallach 1987). More important, there is no instance yet reported of an ecological variable associated with disrupted menstrual function that has not also been associated, at a more moderate level, with these more subtle changes in ovarian function. Thus, a corollary of this first hypothesis would be that there is no discrete, “one-zero” modulation of ovarian function short of pathology. Ovarian function is on a “rheostat,” not an “on/off switch.”

Hypothesis 2. The graded continuum of ovarian suppression forms a “final common pathway” through which various ecological, behavioral, and constitutional variables affect female fecundity. The points at which weight loss, exercise, youth, age, and lactation intersect with the hypothalamic-pituitary-ovarian (HPO) axis may vary, and any given variable may have more than one point of intersection. Elevated prolactin levels associated with lactation have been shown both to be associated with altered hypothalamic regulation of pituitary gonadotropin release (Baird et al. 1979) and to inhibit gonadal steroid production (McNatty et al. 1979). Intense exercise disrupts the hypothalamic-pituitary axis (Cumming et al. 1985), possibly through increased levels of endogenous opioids (Howlett et al. 1984; Yen 1984), though testosterone and prolactin levels are raised acutely as well (Shangold, Gatz, and Thyssen 1981). Weight loss is associated with decreased production of extragonadal estrogens (Siiteri, Williams, and Takaki 1976; Pintor et al. 1980; Ellison 1984) and hypothalamic dysfunction (Warren et al. 1975; Vigersky et al. 1977). Adolescent cycles are characterized by elevated androgen to estrogen ratios (Apter, Viinkka, and Viikko 1978), strong circadian variation in pituitary activity (Boyar et al. 1974), and a reduced capacity for steroid production (Apter et al. 1987).

Despite this diversity of intersection points with the reproductive endocrine axis, the final impact of all these variables on female reproductive capacity is mediated by the gradient of ovarian response described above. That is, changes in the activity of the HPO axis take on functional significance primarily insofar as they affect the production of ova, their fertilizability, or the ability of fertilized zygotes to implant and survive early gestation, ovarian function being the principal determinant of each of these. The gradient of ovarian response thus serves as a “final common pathway” linking a broad array of ecological, environmental, and constitutional factors to human fecundity. Changes “above” the level of the ovary in the HPO axis express themselves functionally in changes in the production of ova and their quality (Stanger and Yovich 1984; Yoshimura and Wallach 1987; Eissa et al. 1987), which in turn are conditioned by and/or expressed as changes in ovarian steroids, while many important events “below” the level of the ovary, such as implantation and early gestation, are guided and regulated by ovarian steroid production (Stouffer 1988; Fritz 1988; Eisenberg 1988). Ovarian function thus becomes the “linchpin” of the female reproductive system, with steroid levels being the most useful, readily detectable reflection of ovarian function.

This hypothesis proves to be an asset to many research tasks of interest to anthropologists, since ovarian activity, reflected in patterns of steroid production, is much easier to monitor under field conditions than hypothalamic or pituitary activity (Ellison 1988). Indeed, even if it were a simple matter to monitor the hypothalamic-pituitary axis, it would still be necessary to infer the impact of changes at this level on ovarian function in order to interpret their significance for human fecundity. For instance, it seems likely that
aerobic exercise suppresses female reproductive function by disrupting the pattern of hypothalamic secretion of gonadotropin-releasing hormone, possibly as a consequence of altering endogenous opioid production within the central nervous system (as noted above). Yet it is not necessary for an anthropologist, interested in the question of whether women’s workloads in a given society affect their reproductive physiology, to attempt to assay hypothalamic activity. Changes at this level would only have significance for female fecundity if they are sufficient to suppress ovarian activity to an appreciable degree. A corollary, however, is that ovarian function integrates the effects of a potentially diverse array of factors affecting female reproductive physiology, and in so doing loses the power of discrimination. Our imaginary anthropologist may, for example, find that high workloads in his or her society are associated with significantly suppressed ovarian function, and yet be unable to say whether that suppression is analogous in its mechanisms to the suppression associated with aerobic exercise.

**Hypothesis 3. Ovarian function reflects trends in energy balance, not simply nutritional status.** Even women of normal weight for height show evidence of luteal suppression and ovulatory failure when losing weight (Bates, Bates, and Whitworth 1982; Pirke et al. 1985; Pirke et al. 1989; Lager and Ellison 1990). The more precipitous the weight loss, the more severe the ovarian suppression. Stabilization or reversal of the energy balance leads to a reversal of the direction of progress through the gradient of ovarian suppression. In addition, a lag time is observable between a period of weight loss and the full expression of ovarian suppression (Lager and Ellison 1990). As a result, the cumulative effect of moderate weight loss over an extended period can be comparable to that of a shorter period of more precipitous weight loss. We observed ovarian suppression to intensify among a group of horticulturalist women in the Ituri Forest of Zaire over a four-month period of gradual weight loss (Ellison, Peacock, and Lager 1989), and to be most severe just after the peak of a period of seasonal food shortage (Ellison, Peacock, and Lager 1986; Peacock and Ellison 1984). This pattern of response has the effect of rendering the ovary more sensitive to medium to long-term trends in energy balance—that is, those that extend for several months or more—while responses to short-term variations may be somewhat buffered by the graded nature of ovarian response and the lag time in its expression.

This hypothesis stands in contrast to the various versions of the hypothesis originally advanced by Frisch and Revelle (1970, 1971), which have all stressed nutritional status rather than energy balance. In its most recent form (Frisch 1987), the Frisch hypothesis holds that a minimum percentage of body fat by weight is ordinarily required for the maintenance or restoration of menstrual cycles in a mature woman, with a different level of fatness required for the initial onset of menstrual cycles in adolescent girls. Considerable evidence supports the notion that extremes of underweight are associated with disruptions of hypothalamic-pituitary activity (e.g., Warren et al. 1975; Vigersky et al. 1977), but it is not clear from the research protocols whether those conditions of extreme underweight are themselves associated with persistent negative energy balance. Similar disruptions are in fact observable in association with simple weight loss as well (Graham, Grimes, and Campbell 1979). Within the normal weight range, however, there is no evidence of variation in ovarian function that is associated with indices of nutritional status, as opposed to measures of change in nutritional status (Ellison 1984; Ellison, Lager, and Calfee 1987; Lager and Ellison 1990).

**Hypothesis 4. Ovarian function reflects aerobic activity independently of energy balance.** A substantial literature now documents the association of various forms of aerobic exercise with suppressed ovarian function (cf. Howlett 1987; Cumming 1990; Warren 1990). This literature has drawn the attention of anthropologists interested in the potential impact of physical activity on female reproductive function (Bentley 1985; Peacock 1986). Yet questions have also been raised concerning the degree to which exercise-associated suppression of ovarian activity is independent of other, potentially confounding variables, such as nutritional status/body composition and other constitutional factors (Frisch, Wyshak, and Vincent 1980; Frisch et al. 1981; Malina 1983). Frisch (1987) has suggested
that reproductive suppression in female athletes may be mediated by altered fat/lean ratios of body composition, while Malina (1983) has suggested that female athletes may represent a biased sample of the female population selected for constitutional or developmental attributes—for example, high androgen profiles or late maturation—which might be correlated independently with suppressed ovarian function.

By subjecting untrained women to rather vigorous exercise regimes while supplying some with sufficient calories to maintain their weight, Bullen et al. (1985) were able to show that exercise suppresses ovarian function independently of weight loss and of other attributes self-selected in successful female athletes. Catherine Lager and I (Ellison and Lager 1985, 1986) observed milder suppression of ovarian function in association with moderate recreational running and stable weight in women of normal weight for height. In addition to confirming that exercise-associated ovarian suppression is not limited to trained or excessively lean athletes, this study also indicated that aerobic activity need not be at an extreme level to measurably affect ovarian function, since the average running distance was only 12.5 miles per week. Moderate exercise of an hour or more a day has also been linked to a 4.7-fold increase in the risk of infertility among nulligravid women (Green et al. 1986), indicating that changes in ovarian function of this kind and magnitude can have a significant effect on reproductive performance.

An important caution must be entered here, however, for those interested in the potential applicability of this hypothesis to other forms of physical activity, including those more typical of the workloads and activity patterns of women in traditional societies. The data on exercise and female reproductive function derive almost exclusively from studies of periodic, aerobic activities, such as running, gymnastics, swimming, dancing, and rowing. There are few if any data linking patterns of low-level, chronic activity—such as walking, carrying children, and cultivating gardens—with changes in ovarian activity. Several ongoing field studies were designed specifically to address this question. Until results of these or similar studies are in, however, one must be careful not to extend this hypothesis beyond the limits of the data that give rise to it.

Hypothesis 5. Additive interaction characterizes the combined effects of ecological, behavioral, and constitutional variables on ovarian function. When two or more of the factors capable of suppressing ovarian function are present simultaneously, they often interact additively, increasing the resulting degree of ovarian suppression. Lunn et al. (1980; Lunn, Austin, and Whitehead 1984) have shown that prolactin levels (ordinarily strongly correlated with the degree of ovarian suppression) of nursing mothers in The Gambia vary with food availability and can be lowered by dietary supplementation. Bullen et al. (1985) have shown that the combined effects of heavy exercise and weight loss produce more severe ovarian suppression than exercise alone (Figure 2). Schweiger et al. (1987) have shown that the degree of ovarian suppression associated with weight loss depends on age, being greater in late adolescent/young adult women.

The catalog of possible interaction effects is by no means completely studied even for dyadic combinations, much less for more complex suites of variables. Yet it is just such combinations of factors that are likely to be encountered in many natural fertility populations: high workload in combination with poor energy balance, poor energy balance in combination with intense and prolonged lactation, and so on. Particularly under-studied at this point are interactions between age and lactation, although demographic data have long led to speculation that lactational suppression of ovarian function is more profound in older mothers (Henry 1961; Potter et al. 1965; Goldman, Westhoff, and Paul 1987). It would be equally interesting to investigate further the interaction between energy balance and age implied by the work of Schweiger et al. (1987). If it is true that young women are particularly sensitive to the effects of energy balance, then the practice of feeding girls in conjunction with puberty ceremonies, which has a relatively wide cross-cultural distribution, may take on new meaning as a cultural attempt to manipulate the fecundability of newly marriageable females.
Comparison of the effects of exercise alone with those of exercise and weight loss combined in inducing suppression of ovarian function in previously untrained women (data from Bullen et al. 1985).

Hypothesis 6. Female reproductive maturation is synchronized with skeletal maturation, especially of the pelvis. During our evolutionary history the female pelvis has been subjected to two contrasting sets of selection pressures: those concerning bipedal locomotion, favoring narrower pelves, and those concerning parturition, favoring a more ample birth canal. As a consequence, the size and maturity of the pelvis act as important constraints on successful reproduction. In the life cycle of an individual female, these mechanical constraints must first be overcome before energetic constraints on reproduction become predominant. As a result, the milestones of female reproductive maturation show a clear and close relationship to the progress of skeletal maturation (Shuttleworth 1937; Tanner 1962; Marshall 1974; Marshall and Limongi 1976), and pelvic maturation in particular (Moerman 1982; Ellison 1982). The relationship between menarcheal age and skeletal/pelvic maturation is stronger than that between menarcheal age and relative weight or fatness, which are themselves correlated with skeletal maturation (Ellison 1981a, 1982), and holds both within and between populations (Ellison 1982).

This hypothesis, like hypothesis 3, stands in contrast to the original Frisch-Revelle hypothesis and its successors. The original Frisch-Revelle hypothesis (1970, 1971)—that menarche was associated with the attainment of a “critical weight”—was plagued by faulty statistical analyses, and despite extended critique in the literature (Johnston, Malina, and Galbraith 1971; Frisch, Revelle, and Cook 1971; Johnston et al. 1975; Billewicz, Fellowes, and Hyttten 1976; Frisch 1976; Cameron 1976; Trussell 1978; Frisch 1978; Reeves 1979; Trussell 1980; Bongaarts 1980; Menken, Trussell, and Watkins 1981; Ellison 1981a, 1981b, 1982; Frisch 1982) these failings continue to be underappreciated. Part of the confusion stems from the publication of the original analyses in two journals, one of which—Science—is widely available and often cited, the other of which—Archives of Disease in Childhood—is less available and less frequently cited. Yet it is in the second journal that the most telling feature of the analysis, a plot of the data for weight and age at menarche that gave rise to the hypothesis, is featured (Frisch and Revelle 1971). As that plot makes abundantly clear, the relationship between weight at menarche and age at menarche is a virtual textbook example of a zero correlation. For example, using data from the Berkeley Growth Study (Tuddenham and Snyder 1954)—the largest of the three longitudinal growth studies used by Frisch and Revelle—virtually the same relationship can be demonstrated between menarcheal age and the ordinal position of the 67 female sub-
jects in the published version of the data as between menarcheal age and menarcheal weight (Figure 3). Rather than use a correlational analysis, however, Frisch and Revelle subjected the data to an analysis of variance—an unnecessary and inappropriate analysis for examining the relationship between two continuous measurement variables—concluding that the mean weight at menarche does not change across arbitrary menarcheal age groups. It is this analysis that is summarized, without a figure, in Science (Frisch and Revelle 1970).

In fact, menarcheal age and menarcheal weight are as unrelated as two variables that are both reflections of overall development can be. This point was belabored by early critics of the hypothesis, who framed it in terms of the enormous variance about the mean menarcheal weight in each menarcheal age class (Johnston, Malina, and Galbraith 1971). Subsequent amendments to the original hypothesis were essentially attempts to escape from this trenchant criticism. For example, the reduction in the residual variance, which at first seemed to be achieved by the introduction of estimates of percent body fat (Frisch, Revelle, and Cook 1973), was later shown to be an ephemeral artifact of neglecting the error term in the regression equations used to form the estimates (Reeves 1979). Finally, the notion of an average weight or fatness at menarche was dropped altogether in favor of the notion of a minimum fatness required (Frisch and McArthur 1974). Yet even this concept is poorly supported by the data on menarche, since crossing the minimum threshold of fatness does nothing to change the probability of experiencing menarche in the next interval of time (Billewicz, Fellowes, and Hyttten 1976; Trussell 1978, 1980; Ellison 1981a, 1982), a fact that is reflected in the persistent enormous variance in the fatness at which menarche actually occurs. One might as well propose a minimum shoe size as necessary for the attainment of menarche on the basis of some empirical value below which few if any women are observed to menstruate.

Skeletal maturation and pelvic size do meet the criteria of a functional minimum that fatness and weight fail to meet (Ellison 1981a, 1981b, 1982), and therefore provide a more credible working hypothesis. One can even question the Frisch hypothesis on theoretical grounds and ask: Why, if fatness is the governing constraint on reproductive maturation, do girls bother to grow “up”? Why not simply stop growing at an earlier age and gain weight? At least part of the answer is simple: mechanical constraints on reproduction exist prior to energetic constraints. Until a woman has achieved the physical capacity for

Figure 3
Comparison of the relationship between menarcheal age and menarcheal weight among subjects in the Berkeley Growth Study with the relationship between menarcheal age and the ordinal position of those same subjects in the published tabulation of the Berkeley Growth Study data (Tuddenham and Snyder 1954).
successful reproduction—at least partially a function of size and scale—energetic capacity is irrelevant.

If the pelvic size hypothesis is at this stage more credible, it is by no means confirmed; more data are surely needed. There are, however, two problems in particular contributing to confusion in this area that ought to be appreciated. First is simply the highly correlated nature of all physical measurements during maturation (Ellison 1981a, 1982); one variable (e.g., weight) may appear to bear a significant relationship to reproductive maturation, which it in fact gains through its correlation with another variable (e.g., pelvic size). Second is the developmental sequence in which limiting constraints may be arranged. That is, for example, pelvic constraints on successful reproduction may exist prior to energetic constraints developmentally, and yet those energetic constraints may be very real once the pelvic constraints have been overcome. Anorectic adolescents may pass the pelvic threshold and yet be under an energetic threshold, obscuring the relevance of the prior constraint. For this reason it is, I think, necessary to keep hypotheses concerning ecological influences on reproductive maturation (e.g., this hypothesis) distinct from hypotheses concerning ecological influences on adult reproductive function (e.g., hypothesis 3), and not be tempted to confl ate them into two manifestations of the same hypothesis, as Frisch and McArthur (1974) have done.

Hypothesis 7. Peak ovarian function is not ordinarily achieved until the early twenties. During the first years after menarche, menstrual cycles are characterized by a high frequency of ovulatory failure and luteal phase defects (Apter, Viinikka, and Vihko 1978; Vihko and Apter 1984; Venturoli et al. 1987). Significant suppression of ovarian function is still observable in women aged 18 to 22 years relative to women 23–35 years, after controlling the potentially confounding factors of exercise and energetic balance (Doring 1969; Ellison, Lager, and Calfee 1987). This extended process of ovarian maturation is parallel to the final stages of skeletal maturation and pelvic remodeling, which are not ordinarily complete until the late teens/early twenties (Moerman 1982). The probability of success and the quality of pregnancy outcome are both lower in women who are postmenarchial but still adolescent (Liestol 1980; Wyshak 1983), possibly reflecting the combined effects of ovarian immaturity and nutritional competition between the fetus and its still growing mother.

A notion of “adolescent sterility” has long maintained a place in the literature on the fertility of young women (Montagu 1946). More recently the concept has been revised into a more sophisticated notion of “adolescent subfecundity,” but empirical attempts to measure its potency from demographic data are problematic (Foster et al. 1986). It is probably best to recognize that several different factors may be contributing to patterns of fertility in this age range, including psychosocial factors as well as biological ones, and to attempt to understand each separately. In addition, any attempt to model evolutionary influences on human sexual behavior and mating patterns based on assumptions about the age-specific fecundability of females depends on an adequate understanding of age variation in ovarian function.

In this context it is notable that accurate information on changes in ovarian function with increasing age is presently inadequate for the formulation of a specific hypothesis. If anything, the data support a decline in fecundity after age 35 without becoming precipitous until after age 40 (Doring 1969; Federation CECOS, Schwartz, and Mayaux 1982; Menken 1985; Menken, Trussell, and Larsen 1986), but it is difficult as yet to be sure how significant this decline is, or the extent to which it represents ongoing attrition through menopause versus declining ovarian function prior to menopause. It should soon be possible, however, to generate a specific hypothesis about aging and ovarian function to complement the picture in adolescence and young adulthood.

Hypothesis 8. Late reproductive maturation is associated with a slower rise in indices of ovarian function with age, and a lower level of ovarian function in adulthood. The principal evidence for this hypothesis comes from the work of Apter and Vihko (Apter and Vihko 1983; Vihko and Apter 1984), although the hypothesis itself was foreshadowed by Frisch on the basis
of historical data (Frisch 1978). In studying the menstrual cycles of adolescent girls, Apter and Vihko (1983) found that ovarian function increased with age at an absolutely faster rate among girls with an earlier menarcheal age than among those with a later menarcheal age. Girls who reached menarche at or before age 12 years, for example, achieved a 50% ovulatory rate within 1 year after menarche, while girls who did not reach menarche until age 13 years or older took 4.5 years to reach the same ovulatory frequency. The evidence is equivocal over the question of when, if ever, late maturers catch up to early maturers in ovarian function (cf. Apter and Vihko 1983; Vihko and Apter 1984). Venturoli et al. (1987) have also found that an earlier establishment of regular cycles in adolescence is associated with an earlier attainment of adult endocrine profiles of ovarian function. In their study, persistently irregular but ovulatory cycles in adolescence are associated with slower progress in ovarian function with age, though the trajectory eventually catches up with that associated with early establishment of regular cycles. Persistent anovulatory cycles, they suggest, may represent a basic physiological defect that often continues into adulthood. To this may be added data from studies of linkages within the gynecological histories of individual women (Gardner 1983; Gardner and Valadian 1983), which indicate that late maturers continue to have higher incidences of oligomenorrhea and dysmenorrhea than early maturers well into their reproductive prime.

A good body of cross-cultural data does not yet exist to test whether the relationship between tempo of growth and level of adult ovarian function also holds between populations. It is perhaps noteworthy that among the Lese of Zaire, where menarche does not ordinarily occur until roughly age 16 years, the trajectory of ovulatory frequency by age parallels that found among Boston women, but at a significantly lower level (Figure 4). Nor can that difference in level be accounted for entirely by the suppressive effects of weight loss and nutritional stress (Ellison, Peacock, and Lager 1989). It is important, however, to remember that in any population variation in menarcheal age has both heritable and environmental components (Johnston 1974). We do not yet know whether variation in the level of adult ovarian function is correlated with one or both of these sources

![Figure 4](image-url)

**Figure 4**
Ovulatory frequency by age for Lese and Boston women (Ellison, Peacock, and Lager 1989).
of variance in menarcheal age. If the correlation holds for one but not the other of these sources of variance, the potential exists for empirical studies to contradict each other depending on the relative weight given to environmental versus genetic variance in menarcheal age by different research designs.

This hypothesis is perhaps the most controversial of the set. Much of the research in this area is not motivated by any concern to understand age-specific patterns of female fecundity, but rather to understand an apparent association between early menarcheal age and increased risk of breast cancer. Furthermore, contradictory data exist, particularly from earlier studies. For example, MacMahon et al. (1982) found no significant relationship between menarcheal age and ovulatory frequency after controlling for years since menarche. Their study, however, was based on urinary pregnanediol measurements of samples originally collected for other purposes by a variety of protocols and representing a heterogeneous group of subject populations. These methodological problems make their data difficult to interpret.

Although the precise form of the relationship may yet be unclear, the bulk of evidence to date supports the notion that "defects" of ovarian function in adolescence are associated to a significant degree with similar "defects" later in adulthood. The thrust of this hypothesis is to question the assumption of pathology that is often attached to patterns of ovarian function that depart from the textbook typology of "normal" and to substitute more neutral descriptive language based on the continuum of ovarian function described in hypothesis 1. The introduction of such neutral language then opens the way for functional, as opposed to dysfunctional, interpretations of the patterns and autocorrelative relationships in ovarian function across the lifespan of individual women that are so often observed. Such a functional interpretation will be introduced in the discussion of an ecological theory of ovarian function, below.

### Toward an Ecological Theory of Human Ovarian Function

Frisch (1984, 1988) took the first steps toward an ecological theory of human ovarian function by suggesting that the purported relationship between fatness and fecundity had evolved to prevent wasteful attempts at reproduction when a woman's energetic reserves were inadequate to provide for a very high probability of success. Perhaps it has been the power of this functional interpretation of variation in menstrual function that has sustained the Frisch hypothesis in the face of overwhelming empirical critique. Nor should the value of this contribution be minimized; it has, in fact, transformed most subsequent discussions of human reproductive maturation and adult reproductive function and injected a healthy respect for normal variation and its functional significance into the overly typological realm of clinical research. I believe, in fact, that it will be this theoretical contribution that will eventually remain as Frisch's enduring intellectual legacy.

The hypotheses reviewed here support two somewhat different theoretical positions, not necessarily mutually exclusive, concerning the ecological responsiveness of human ovarian function. One perspective views the pattern of ovarian responsiveness as an evolved mechanism to optimize the probability of a successful reproductive outcome in any individual instance of reproductive effort. The other perspective views the same pattern as a mechanism for ensuring long-term energy balance in reproducing females and avoiding a downward spiral of physical depletion brought on by successive cycles of pregnancy and lactation.

Although many of the details of the empirical relationships between ecological, behavioral, and constitutional variables on the one hand and ovarian function on the other differ from those specified in her hypotheses, it is possible to carry over Frisch's theoretical position in altered form. That is, the hypotheses enunciated here can still be incorporated into a theory stipulating that ovarian responsiveness has evolved to reduce investment of reproductive effort when the probability of successful outcome is sufficiently low. The constraints on the probability of successful reproductive outcome are different,
however. In adolescence, as discussed in detail above, physical constraints associated with pelvic size are more predictive of a successful reproductive outcome than are energetic constraints. In adulthood, energetic constraints appear to become effective, but more in terms of energy balance than in terms of stored energy supplies. Such an interpretation would depend on other linkages being in place, many of which have empirical support. For instance, infant mortality risk is highly associated with low birth weight (Shapiro, Schlesinger, and Nesbitt 1968). Full-term birth weight is associated with maternal pregnancy weight and pregnancy weight gain (Eastman and Jackson 1968). If negative energy balance results in lower prepregnancy weights and lower weight gains in pregnancy, then it could in fact be predictive of a poor reproductive outcome. Conversely, positive energy balance would be predictive of a more positive reproductive outcome. The fact that ovarian function appears more responsive to periods of negative energy balance that extend over more than one month supports this view. Especially under marginal nutritional conditions, weight gain in early pregnancy may provide a crucial supply of stored energy for the demands of later pregnancy and lactation (Prentice and Whitehead 1987). The pattern of ovarian responsiveness to weight loss may have been designed to minimize the probability of initiating a pregnancy in a state of negative energy balance when the potential for this first trimester fat accumulation is compromised. From this perspective the responsiveness of ovarian function to energy balance may be interpreted as a mechanism to modulate reproductive effort in accord with its expected returns (i.e., the probability of a successful pregnancy). If the costs of a given level of reproductive effort are fixed, in terms of the mortality risk incurred by the mother, and the other opportunities for reproduction foregone, then adjusting reproductive effort on the basis of its probability of successful outcome would be favored by natural selection.

The effect of aerobic exercise on ovarian function can be incorporated into this theoretical framework if its anabolic consequences are taken into account. That is, regular exercise shifts individual metabolism in favor of protein anabolism as part of a suite of physiological adjustments to what is perceived by the body as a new chronic level of physical demand. These changes increase the metabolic requirements of the individual woman even if her weight remains stable, effectively reducing the fraction of her energy intake available for reproduction. From the point of view of the potential for gaining weight in early pregnancy, this situation may simulate negative energy balance to a certain degree.

The most likely functional interpretation of hypothesis 8 in this context is that slow physical development and reproductive maturation provide a kind of “bioassay” of chronic qualities of the environment, particularly energy availability. Late maturation relative to genetic potential indicates a chronically poor nutritional environment and early development a chronically rich one. The correlation between adult ovarian function and age at reproductive maturation suggests that the baseline for adult ovarian function may be established in accordance with this assay of chronic environmental quality. One can question, however, the wisdom of curtailing reproductive effort if there is little likelihood that currently unfavorable circumstances will soon improve. That is, a strategy to avoid the costs of reproducing under conditions of poor energy balance only works if those conditions can, in fact, be avoided. Shouldn’t a woman living under chronically stressed conditions set her baseline for ovarian function at the same level as a woman living under chronically better conditions, while retaining the ability to make facultative adjustments in ovarian function as environmental conditions fluctuate about their average levels? To the extent that prepregnancy weight and pregnancy weight gain are independent correlates of reproductive outcome, the answer to this question may be “no.” The time available for weight gain in pregnancy is fixed, so that a lower level of ovarian function prior to conception does not alter the potential for first trimester weight gain. It does, however, extend the opportunity for prepregnancy weight gain, an opportunity that may be particularly important if the previous sequence of pregnancy and lactation has resulted in a net energy drain on the mother.
The consideration of long-term energy balance in reproducing women is central to the second theoretical perspective that can be supported by the hypotheses reviewed here. It is necessary, however, to shift one's thinking to a longer time frame: rather than consider the effect of patterns of ovarian function on immediate reproductive outcomes, this perspective considers the effect on maternal morbidity and mortality, with benefits and costs measured in terms of changes in net reproductive success over a woman's lifetime. According to this view, importance is attached to the maintenance of a long-term energy balance in reproducing women (Prentice et al. 1981; Adair 1984; Whitehead, Paul, and Ahmed 1986; Prentice and Whitehead 1987). Each period of pregnancy and lactation constitutes an elevated energy demand over the nonpregnant, nonlactating state; under marginal nutritional circumstances these states can even constitute a net energy drain, which must be balanced by a net positive energy balance during the waiting time to conception separating periods of lactational amenorrhea and pregnancy in natural fertility populations.

Short (1983) has emphasized the relative rarity of menstrual cycles in the reproductive history of noncontracepting women. The majority of women's reproductive lives under conditions of natural fertility are spent pregnant or lactating, with only a handful of menstrual cycles experienced as waiting time to conception every two to four years. Recent models of proximate determinants of human fertility have also suggested that the variance in interbirth intervals attributable to variation in waiting time is only minimal to moderate, and certainly far less than that attributable to variation in the length of lactational amenorrhea (Bongaarts and Potter 1983; Wood and Weinstein 1988). However, the period of menstrual cycling during the waiting time to conception may constitute the only opportunity for recouping maternal condition and achieving a net energy balance over a woman's reproductive lifetime. The functional significance of this period increases as chronic energy availability decreases and other opportunities to meet the increased energetic demands of reproduction dwindle. Thus, the functional importance of the length of the waiting time to conception may not lie in its effect on interbirth intervals, but in its effect on maternal morbidity and mortality.

The hypotheses reviewed in this paper are compatible with this theoretical view as well. Negative energy balance, aerobic exercise as indicative of both increased energy expenditure and an adjusted internal energy budget, and slow physical and reproductive maturation as indicative of chronically poor energy availability all decrease a woman's ability to recoup her physical condition and reestablish a long-term energy balance. Suppressed ovarian function under these circumstances increases the waiting time to conception and hence the time available to achieve these goals. Although superficially similar to the first theoretical perspective, this perspective views the pattern of variation in ovarian function as adjusting reproductive effort in accordance with its costs, rather than in accordance with its expected returns. While the first view focuses on the rate of production of offspring, the second focuses on the morbidity and mortality probabilities faced by the mother. There are practical implications as well. Adjustments in waiting time to conception may have only a moderate impact on interbirth intervals, and thus not figure strongly in analyses that use total fertility rate—the average number of offspring ever born to post-reproductive women (Bongaarts and Potter 1983; Campbell and Wood 1988). If the major effects of facultative changes in waiting time to conception are on maternal mortality, then an analysis using net fertility rate—average offspring ever born to a woman, including allowance for reproduction lost through increased mortality—would be called for. It is perhaps paradoxical that the functional significance of facultative variation in ovarian function might lie in its impact not on fertility, but on mortality.

These two theoretical perspectives are, of course, not mutually exclusive. The patterns of variation in ovarian function summarized in the eight hypotheses presented here may simultaneously meet two selective pressures and hence have dual functional significance. A more robust theory will only evolve as the hypotheses themselves are confirmed, adjusted, or replaced. In the meantime, however, such a nascent theory can itself suggest
further hypotheses to be considered. In particular, one area of potential importance in the ecology of ovarian physiology is still largely unexplored, that being the relationship between chronic disease burden and ovarian function. Many specific diseases can, of course, have tremendous impact on fecundity, though they may not affect ovarian function in particular. Examples would include venereal diseases, which may cause lesions of the reproductive tract, and malaria, which may compromise placental oxygen transport. McFalls and McFalls (1984) provide a useful review of the catalog of such specific diseases and their effects on reproduction. Little is known, however, about the impact of chronic disease morbidity per se on ovarian function. To the extent that high disease burdens may divert metabolic energy to support immune function, tissue repair, and other responses, the energy available for reproduction may be reduced. Hence one might predict that ovarian function should vary inversely with disease burden by analogy with the effects of weight loss and exercise. Another clear implication of these initial theoretical formulations is the importance of a life-historical perspective on human reproductive function. A new emphasis will have to be placed on long-term, prospective studies that follow individual women through adolescence and reproductive maturity into old age in order to properly understand the longitudinal relationships that probably obtain among aspects of growth and maintenance, morbidity, and fecundity. Such an undertaking, akin to the establishment of longitudinal growth studies in the early part of this century, requires vision on the part of funding agencies and patience and persistence on the part of researchers, yet promises returns well worth the investment.

Most important, however, a theoretical perspective of this kind allows for a broader view of human reproductive physiology than the overly eidetic view of most clinical textbooks. As with other areas of human biology, ovarian function demonstrates a considerable range of variability. Attempting to force that variability into a dichotomous framework of health and pathology obscures more than it enlightens our understanding. To the extent that we are able to discover functional significance in the variability we observe, we improve our ability to incorporate human reproductive ecology into the broader context of human evolution.

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