Onset and Characteristics of the Midcycle Surge in Bioactive and Immunoactive Luteinizing Hormone Secretion in Normal Women: Influence of Physiological Variations in Periovulatory Ovarian Steroid Hormone Secretion

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ABSTRACT

Limited studies in nonhuman primates suggest that the midcycle LH surge is characterized by distinctly different patterns of bioactive (LH-BIO) and immunoactive (LH-RIA) LH secretion. To further examine the patterns of midcycle LH-BIO and LH-RIA secretion and explore the influence of physiological variations in steroid hormone feedback on LH surge dimensions, we studied seven normal ovulatory women over the periovulatory interval. In each, blood samples were obtained every 3 h and transvaginal ultrasonography was performed every 12 h over a 6-7 day interval at midcycle. Serum levels of LH-RIA, FSH, estradiol (E2), progesterone (P4), and 17-hydroxyprogesterone were determined by RIA; LH-BIO was estimated using a mouse Leydig-cell bioassay. Hormone data were standardized to the time of surge onset in LH-RIA (time zero), defined as a 100% increase above a 6-point running mean baseline value; surge cessation was defined as a decline to below baseline concentration.

Mean LH-RIA surge duration was 54.0±4.0 h. LH-BIO surge onset was simultaneous with that of LH-RIA and coincident with the peak in E2 levels (mean data). Mean P4 and 17-hydroxyprogesterone rose in a parallel, phasic manner, an abrupt increase in slope occurred between -6 h and +30 h but an acute rise in P4 was not consistently observed among individuals. The surge onset to follicle rupture interval (mean 37.6±4.2 h) positively correlated with peak LH-RIA (r=0.76, P<0.05), surge amplitude (r=0.74, P<0.05) and surge onset to peak interval (r=0.87, P<0.05). There were no significant relationships between E2 or P4 (mean, peak, integrated, slope) and onset to peak interval (LH-RIA, LH-BIO, FSH).

These data suggest that in women, 1) onset of the midcycle surge in LH-RIA and LH-BIO is simultaneous, and 2) surge characteristics are not influenced by physiological variations in steroid hormone secretion that occur beyond the thresholds required for surge initiation. (J Clin Endocrinol Metab 75: 489-497, 1992)

THE MIDCYCLE gonadotropin surge is the most dramatic endocrinological event in the normal menstrual cycle and is responsible for initiation of the complex sequence of secondary events that culminates in ovulation. The dynamics of the spontaneous immunoactive LH (LH-RIA) surge are well described (1-3), but data regarding the pattern of bioactive LH (LH-BIO) secretion at midcycle are quite limited (4, 5). Evidence from earlier nonhuman primate studies suggests that the patterns of midcycle LH-RIA and LH-BIO secretion are temporally, quantitatively and/or qualitatively distinct (4); comparable human data are lacking.

Numerous studies have helped to define the complex hypothalamic-pituitary-ovarian feedback interactions that combine to induce the midcycle gonadotropin surge (6-12); both estradiol (E2) and progesterone (P4) play an important role. Whereas the obligatory stimulus is clearly the rapid rise in E2 levels that accompanies the latter stages of preovulatory follicular maturation, periovulatory P4 influences both the time of onset and ultimate magnitude of the surge. Both the minimum strength/duration requirements for effective estrogen positive feedback (6-8) and the manner in which P4 influences the timing and dimensions of the surge (8-12) are established. However, whether the timing, composition, and/or magnitude of the surge are influenced by the wide range of physiological variations in midcycle steroid hormone secretion is not clear.

The design of a previous study (3) in which we obtained frequent blood samples throughout the immediate periovulatory interval in a group of normal cycling women afforded us the opportunity to reexamine certain aspects of the endocrine dynamics that surround the midcycle gonadotropin surge and ovulation. Specifically, in the current study we sought to examine: 1) the relative patterns of LH-RIA and LH-BIO secretion during the periovulatory interval. 2) the

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we examined appeared to be influenced by the wide range of physiological variations in ovarian steroid secretion observed among subjects. Neither the pattern nor level of E2 or P4 secretion was related to the timing, composition, or magnitude of the midcycle gonadotropin surge. These data suggest that once minimum threshold requirements for induction of a normal gonadotropin surge are met, surge characteristics are not further influenced by physiological variations in steroid hormone secretion.

Previous studies have suggested that the periovulatory rise in P4 may trigger an LH surge firing mechanism that is first cocked by an interval of incremental E2 exposure (2). We did observe a phase rise in mean periovulatory P4 and 17OHP levels that closely approximates the pattern previously described (2), but the putative acute preovulatory increase in P4 did not occur in all individuals. Only three subjects experienced a sudden increment in serum P4; a less striking increase was detected in a pair of others, but the rise in P4 was only very gradual in the remaining two subjects.

Correlations between the surge onset to follicle rupture interval and LH-RIA peak, surge amplitude, and surge onset to peak interval are of interest. However, follicle rupture was arbitrarily defined as occurring at the time of that sonogram demonstrating follicular collapse when, in fact, it may have occurred at any time in the preceding 12-h interval. Any conclusions regarding the influence of surge dimensions on the time of ovum release must take into account the interval between scans. Nevertheless, our data suggest that a more abrupt LH surge may accelerate follicle rupture and imply that initiation of the ovulatory sequence may require a threshold level of LH.

In summary, frequent blood sampling throughout the periovulatory phase demonstrated a simultaneous onset of the midcycle surge in LH-BIO and LH-RIA that occurred coincident with the peak in preovulatory E2 concentrations. Onset and dimensions of the LH surge did not correlate with the patterns or levels of midcycle steroid hormone secretion but did relate to the time of follicle rupture. These data contrast with earlier observations in the nonhuman primate and suggest that characteristics of the midcycle gonadotropin surge are not sensitive to physiological variations in steroid hormone feedback but may influence the ovulatory sequence within the follicle.

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