

Characteristics of fertile menstrual cycles

by Donna Day Baird, PhD¹

Baird DD. Characteristics of fertile menstrual cycles. *Scand J Work Environ Health* 1999;25 suppl 1:20–22.

Key terms conception, estrogen, fecundability, hormones, luteinizing hormone, progesterone.

Hormonal changes during the menstrual cycle have been described well, and marked differences from the norm, such as very low luteal progesterone found during lactation, are associated with low fecundability. The extent to which less marked variability in hormonal patterns affects female fecundability is not known because the normal variation in the hormonal characteristics of conception cycles has not been described adequately. Most data comparing hormones in conceptive and nonconceptive cycles come from infertility patients taking drugs to stimulate follicular development and ovulation. Few data are available for unstimulated cycles from women with no fertility problems. Such studies are difficult because they require recruitment of women trying to conceive and longitudinal study of their hormones so that data can be collected for both conceptive and nonconceptive menstrual cycles.

The North Carolina Early Pregnancy Study (1) enrolled 221 women at the time they began trying to become pregnant. Participation continued through the 8th week of clinical pregnancy or until 6 months had elapsed with no clinically recognized conception. During their participation, the women collected first-morning urine specimens daily. The specimens were used to analyze estrogen and progesterone metabolites, luteinizing hormone (LH), and the pregnancy hormone human chorionic gonadotropin.

In the Early Pregnancy Study we used 2 approaches to examine hormonal factors associated with fecundability. First, we examined paired conception and nonconception cycles from a sample of 32 women (2). In this analysis we analyzed the difference in hormone levels between the clinical conception cycle and a selected nonconception cycle of each woman. The appropriate timing for sexual intercourse, a prerequisite for conception, was controlled in this analysis by selecting only those nonconception cycles that had well-timed sexual

intercourse. In our 2nd approach we used all available menstrual cycles, including 189 conception cycles. We conducted a fecundability analysis (unpublished results: "Preimplantation Urinary Hormone Profiles and the Probability of Conception in Normal Women" by Baird et al) in which the cycle-by-cycle probability of conception was modeled as a function of hormonal pattern variables (analogous to a time-to-pregnancy analysis with hormone variables regarded as exposure variables). Only cycles with intercourse in a previously-defined 6-day fertile window were included. The frequency and timing of intercourse within that fertile window were adjusted for in the multivariate model (3).

Figure 1 shows estrogen and progesterone metabolite profiles from the 1st approach. Hormonal variables found to be associated with failure to conceive in this analysis were (i) a slow luteal rise in progesterone and (ii) lower midluteal estrogen and progesterone (defined as the mean of luteal days 5 and 6). Figure 2 shows estrogen, progesterone, and LH data for the 2nd approach. Hormonal variables associated with failure to conceive in this analysis were (i) low midluteal progesterone, (ii) lower LH, and (iii) higher follicular progesterone.

The majority of previously published data on hormonal profiles in conception cycles from women with no known fertility problems come from 2 studies. Stewart et al (4) reported plasma estrogen, progesterone, and LH patterns for 14 conceptive cycles. They found lower midluteal estrogen and progesterone associated with failure to conceive. Lipson & Ellison (5) reported on salivary estrogen and progesterone for 17 conception cycles. In their analysis lower estrogen, especially during midfollicular days, was associated with failure to conceive.

Clinical conditions in infertility patients also provide information on hormonal characteristics associated with reduced fecundability (6). Premature ovarian failure is characterized by high basal LH and follicle-stimulating

¹ National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, United States.

Reprint requests to: Dr DD Baird, National Institute of Environmental Health Sciences, Epidemiology Branch A3–05, PO box 12233, Research Triangle Park, NC 27709, USA. [E-mail: BAIRD@NIEH.NIH.GOV]

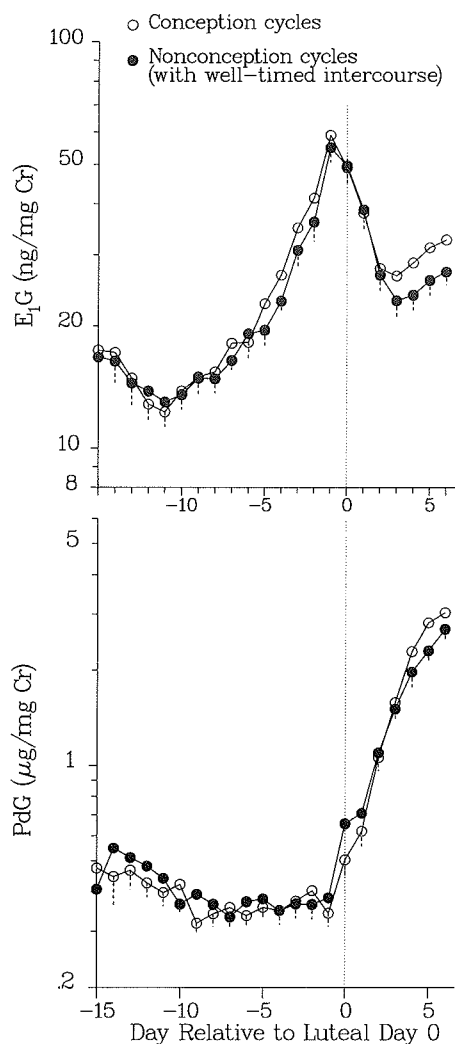


Figure 1. Daily geometric means of the urinary estrogen [estrone 1-glucuronide (E₁G)] (top panel) and progesterone [pregnanediol glucuronide (PdG)] (lower panel) metabolites for the paired conception (open circles) and nonconception cycles (dark circles) of 32 women whose nonconception cycles had well-timed sexual intercourse. Data are centered on luteal-day 0, the estimated day of ovulation (vertical dotted line). The standard errors (shown by a single dotted line for each day) are based on within-woman differences between the 2 cycles, that is, the difference between the corresponding daily values in the 2 cycles for each woman is calculated, the differences being averaged across women and the standard error of the resultant mean difference being determined.

hormone (FSH). Polycystic ovary disease is associated with high basal LH levels, and inadequate luteal phase involves low luteal progesterone. The consistencies and inconsistencies among the various findings summarized in this report are discussed.

Hormonal correlates of fecundability may provide new directions for research on environmental and occupational determinates of fecundability. The hormonal patterns associated with environmental and occupational risk factors can be studied as end points in themselves. For example, hormonal studies could be conducted of

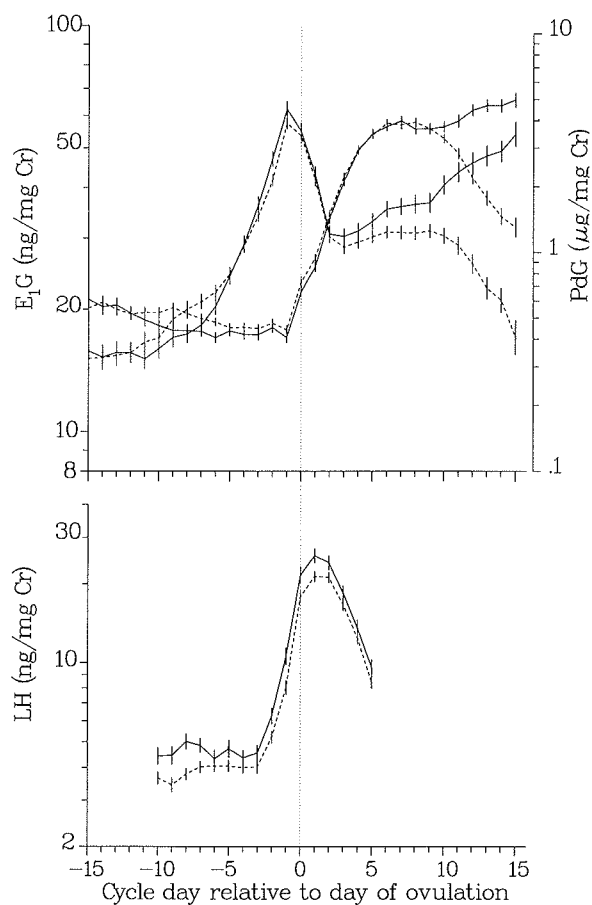


Figure 2. Daily geometric means of urinary hormone data for conception cycles (solid lines) and nonconception cycles (dotted lines) shown on a log scale. The standard error for each day is shown by vertical lines. The top panel shows urinary estrogen [estrone 1-glucuronide (E₁G)] and progesterone [pregnanediol glucuronide (PdG)] metabolites, and the lower panel shows urinary luteinizing hormone (LH). The data are centered on luteal-day 0, the estimated day of ovulation (vertical dotted line).

cycling women with chronic exposure to nitrous oxide, an occupational exposure that has been associated with reduced fecundability (7). If hormonal differences that have been associated with reduced fecundability are seen in the exposed women, the case for a causal role of the exposure would be strengthened. For some exposures, experimental studies could actually be designed. For example, an experimental approach could be used to study potential dietary or metabolic effects on fecundability.

References

1. Wilcox AJ, Weinberg CR, O'Connor JF, Baird DD, Schlatterer JP, Canfield RE, et al. Incidence of early loss of pregnancy. *N Engl J Med* 1988;319:189-94.
2. Baird DD, Wilcox AJ, Weinberg CR, Kamel F, McConaughy DR, Musey PI, et al. Preimplantation hormonal differences between the conception and non-conception menstrual cycles of 32 normal women. *Hum Reprod* 1997;12:2607-13.

3. Zhou H, Weinberg CR. Modeling conception as an aggregated Bernoulli outcome with latent variables, via the EM algorithm. *Biometrics* 1996;52:945—54.
4. Stewart RD, Overstreet JW, Nakajima, ST, Lasley BL. Enhanced ovarian steroid secretion before implantation in early human pregnancy. *J Clin Endocrinol Metab* 1993;76:1470—6.
5. Lipson SF, Ellison PT. Comparison of salivary steroid profiles in naturally occurring conception and non-conception cycles. *Hum Reprod* 1996;11:2090—6.
6. Yen SSC, Jaffe RB. *Reproductive endocrinology*. Philadelphia (PA): Saunders, 1986.
7. Rowland AS, Baird DD, Weinberg CR, Shore DL, Shy CM, Wilcox AJ. Reduced fertility among women employed as dental assistants exposed to high levels of nitrous oxide. *N Engl J Med* 1992;327:993—7.