



Menstrual Cycle Mapping in Dried Urine

Dried urine testing provides a simple and convenient way to assess fluctuations in daily hormone levels over an entire month, known as menstrual cycle mapping. This allows women with irregular cycles, cyclic hormone-related symptoms such as pre-menstrual syndrome (PMS) or headaches, infertility, or luteal phase defects to determine the source of their problems.

By collecting symptom information on each day of collections, the practitioner can combine test results with their patient's symptoms to determine the cause of the hormone imbalance or the observed symptom profile.

Hormones During the Menstrual Cycle

Estradiol and progesterone regulate reproductive function in women. Cyclical hormonal fluctuations help define key events during the menstrual cycle. In the beginning of the follicular phase at the start of the cycle, estradiol levels increase, curbing menstruation and thickening the uterine lining while follicles begin to mature in the ovaries. The follicular phase culminates in a peak in estradiol levels, which in turn stimulates the pituitary to produce a mid-cycle surge in luteinizing hormone (LH) that triggers ovulation. Thus, ovulation is defined by high estradiol levels together with high LH levels. After ovulation, the dominant follicle that released the egg transforms into the corpus luteum, which secretes large amounts of progesterone and smaller amounts of estradiol. This is the luteal phase during which progesterone initiates the secretory changes in the uterine lining, preparing it for reception of a fertilized egg, should fertilization take place. In the luteal phase LH production is suppressed and will stay low until the following cycle's ovulatory phase. Estradiol levels rise again during the luteal phase but to a smaller extent than in the follicular phase. Progesterone levels peak during this phase and then fall towards the end of the menstrual cycle, unless fertilization of the egg has occurred. In the event of fertilization of the egg, the corpus luteum continues to secrete progesterone which maintains the thickened uterine lining during pregnancy.

Available Tests

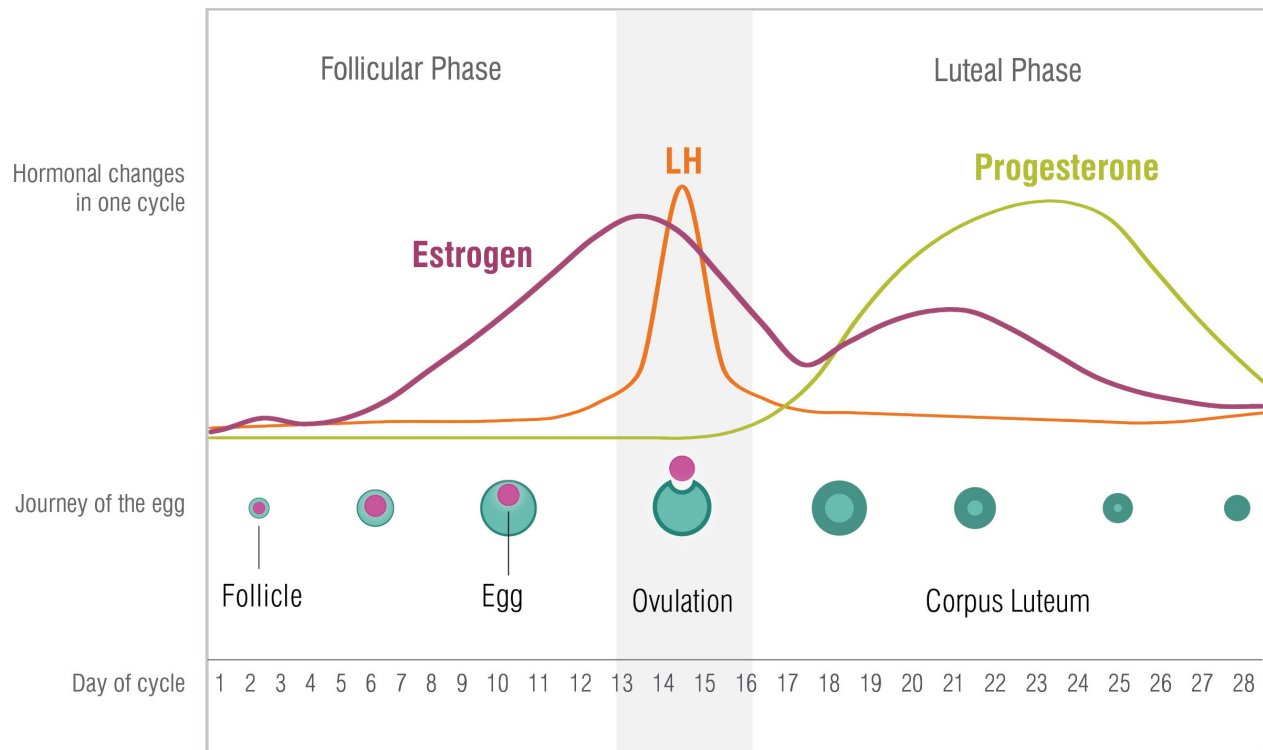
Menstrual Cycle Mapping Profile

Tests included: E1G, PDG, LH (dried urine)

An assessment of sex hormone and LH patterns throughout a menstrual cycle to help health care practitioners get to the root of hormone-related menstrual symptoms, irregular cycles, amenorrhea, or infertility.

Advantages of Dried Urine over Saliva Testing for Menstrual Cycle Mapping

- ▶ Hormones are exceptionally stable in dried urine for months at room temperature, allowing for patients to collect samples every other day and store them at home.
- ▶ Urine collection is as simple as saliva collection for frequent testing, but dried urine samples are easy to store whereas saliva samples should be kept frozen during the collection span.
- ▶ Urine testing for menstrual cycle mapping includes assessment of LH, estrogen and progesterone, whereas saliva testing cannot determine LH.



This illustration is an example of a 28-day-cycle. Hormonal changes and day of ovulation vary with cycle lengths.

Convenient Dried Urine Tests for Menstrual Cycle Hormone Assessment

Testing the levels of the key hormones involved in the menstrual cycle, estradiol, progesterone, and LH, provides important information about dysregulation of hormone production in women experiencing problems such as infertility or symptoms that may be related to menstrual cycle disturbances. Samples must be collected frequently during the cycle to ensure that hormonal peaks are captured so that the cycle can be mapped and any abnormalities assessed.

Estradiol and progesterone levels can be determined in saliva or blood, and their metabolites can be assessed in urine. LH can only be determined in blood or urine. For the patient, frequent trips to the phlebotomist are not convenient for serum testing, but a daily urine sample can easily be collected for convenient testing of all 3 hormones. ZRT has established that a single, first-morning urine sample provides an accurate assessment of the daily level of these hormones, avoiding the need for multiple urine collections throughout the day. Sampling begins on day 7 of the menstrual cycle (day 1 is the start of menstrual bleeding) and samples are collected on alternate days thereafter until the next menstrual bleed begins. The kit includes 15 urine collection cards; most testers will only need 11 or 12 of these cards to complete their cycle, while those with longer cycles may need to use all 15 cards.

Advantages of dried urine testing for menstrual cycle mapping include:

- No need to visit a phlebotomist for repeated venipuncture serum testing.
- Only one first-morning sample is required to be collected every other day during a menstrual cycle – simply collect the first void after waking in a cup and dip in a filter paper strip, or urinate directly on the strip, then allow it to dry completely.
- Hormones are exceptionally stable in dried urine for months at room temperature, allowing for patients to collect samples every other day and store them at home.
- Urine collection is as simple as saliva for frequent testing, but dried urine samples are easy to store whereas saliva samples should be kept frozen during the collection span.
- Urine testing for menstrual cycle mapping includes assessment of LH, estrogen and progesterone, whereas saliva testing cannot determine LH.
- Results are expressed per mg creatinine to take into account the hydration status of the patient, so that test results are accurate even when urine is very concentrated or dilute.

Assessment of Estradiol & Progesterone Metabolites E1G & PDG

Estrogen 3-glucuronide (E1G) is one of the main metabolites of estradiol that is commonly measured for assessment of estradiol excretion. The principal urinary metabolite of progesterone is pregnanediol 3-glucuronide (PDG). Urinary concentrations of these metabolite conjugates, after creatinine correction for hydration status, closely parallel serum concentrations of estradiol and progesterone, with a lag time of up to 24 hours for the urinary metabolites compared to their parent hormones in serum¹. These urine tests therefore represent an ideal method for frequent testing of these hormones during the menstrual cycle, and have a wider application for population epidemiological studies^{2,3} and for monitoring patients during in-vitro fertilization⁴.

Assessment of Luteinizing Hormone (LH)

A first-morning urinary LH determination has long been established as an accurate and convenient alternative to serum assays⁵ and has been useful in clinical studies of ovarian function in ages ranging from childhood to menopause^{6,7}.

Menstrual Cycle Mapping Test Reports

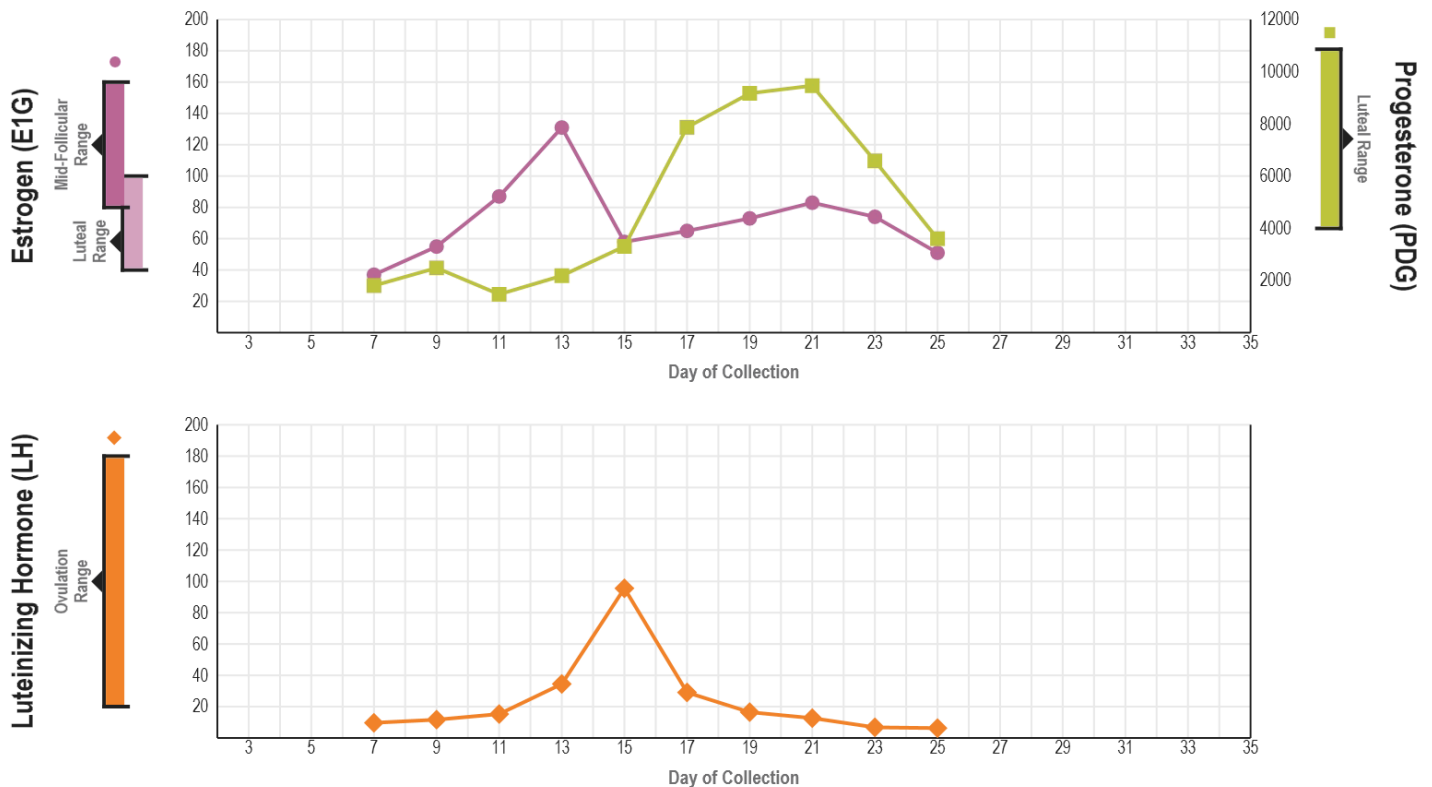
The comprehensive ZRT test report gives test results for E1G, PDG, PDG/E1G ratio, LH, and Creatinine for every sample collected, and graphs the hormones across the cycle. Normal

ranges have been established for baseline and peak levels of E1G in both the follicular and luteal phases, for PDG in the luteal phase, and for LH at the time of ovulation.

These ranges are shown at the side of each graph for comparison with the patient's graphed results, so that any suppression of expected peaks, or shifts in the timing of the peak occurrence can be easily visualized. See the example below for a patient's results graphed on a test report.

Test results will:

- Allow women with amenorrhea or anovulatory cycles to obtain information as to whether they have an adequate LH surge to induce ovulation, and takes away the guesswork as to when they are entering the true luteal phase.
- Indicate a delay in ovulation if there is too long a gap between the LH peak and the PDG rise.
- Show if there is a failure of the corpus luteum to produce adequate hormone levels in the luteal phase, or an earlier drop in progesterone levels than expected after an initially good production.
- Highlight a deficiency of estrogen or progesterone at any point in the cycle.



References

1. Munro CJ, Stabenfeldt GH, Cragun JR, et al. Relationship of serum estradiol and progesterone concentrations to the excretion profiles of their major urinary metabolites as measured by enzyme immunoassay and radioimmunoassay. *Clin Chem.* 1991;37(6):838-44.
2. O'Connor KA, Brindle E, Holman DJ, et al. Urinary estrone conjugate and pregnanediol 3-glucuronide enzyme immunoassays for population research. *Clin Chem.* 2003;49(7):1139-48.
3. Waller K, Swan SH, Windham GC, et al. Use of urine biomarkers to evaluate menstrual function in healthy premenopausal women. *Am J Epidemiol.* 1998;147(11):1071-80.
4. Alper MM, Halvorson L, Lasley B, Mortola J. Relationship between urinary estrone conjugates as measured by enzyme immunoassay and serum estradiol in women receiving gonadotropins for in vitro fertilization. *J Assist Reprod Genet.* 1994;11(8):405-8.
5. Demir A, Alfthan H, Stenman UH, Voutilainen R. A clinically useful method for detecting gonadotropins in children: assessment of luteinizing hormone and follicle-stimulating hormone from urine as an alternative to serum by ultrasensitive time-resolved immunofluorometric assays. *Pediatr Res.* 1994;36(2):221-6.
6. Santoro N, Brown JR, Adel T, Skurnick JH. Characterization of reproductive hormonal dynamics in the perimenopause. *J Clin Endocrinol Metab.* 1996;81(4):1495-501.
7. Kolby N, Busch AS, Aksglaede L, et al. Nocturnal Urinary Excretion of FSH and LH in Children and Adolescents With Normal and Early Puberty. *J Clin Endocrinol Metab.* 2017;102(10):3830-3838