FERTILITY PROFILE

Infertility

Infertility is a growing concern with a rising number of couples having difficulty becoming pregnant[1]. Current statistics from the CDC find that approximately 22.3% of married women have problems in achieving pregnancy or in carrying a pregnancy to term. In one population study[2], the main causes of infertility in women were anovulation (21%), tubal damage (14%), and endometriosis (6%), while 28% of cases were unexplained. In the absence of a physical cause, many cases of female infertility may be explained by something as simple as a hormone imbalance. These imbalances can be assessed with ZRT's Fertility Profile and can often be corrected with simple lifestyle changes or hormone restoration therapy.

Infertility by Age Group
(married women, no previous child)

Age group	Infertility	Impaired Fecundity
30-34	16.9%	24.5%
35-39	22.6%	33.9%
40-44	27.4%	42.8%

ZRT's Fertility Profile

ZRT offers simple, cost-effective testing to identify treatable hormonal imbalances that affect fertility. Early detection can help your patients address these issues and identify the need for more specialized care. This Fertility Profile meets the requirement for initial screening for fertility assessment by reproductive endocrinologists (www.resolve.org).

Who Should Test: The ZRT Fertility Profile is geared to women who have irregular cycles or fertility issues, who have been trying to get pregnant without success, or who would like to be proactive in their preconception planning by getting a baseline screening.

Women are urged to seek testing if they:

- are under the age of 35 and have tried for 1 year to become pregnant
- are over the age of 35 and have tried for 6 months to become pregnant
- have had more than 1 miscarriage
- have symptoms of infertility

What Hormones are Tested: The Fertility Profile provides a thorough evaluation that can identify many problems related to hormone imbalances that are associated with infertility. This allows doctors to: assess ovarian reserves (LH, FSH) and ovarian hormone production (E2, Pg, T); confirm ovulation (Pg); detect luteal phase deficiency (Pg); check for thyroid disorders (TSH, TPO); screen for PCOS (FSH, LH, E2, Pg, T, DS); and look for congenital adrenal hyperplasia (DS, C) and stress (Cx4). Additional testing of vitamin D can be added.

How are Hormones Tested: Hormones are tested in blood collected by fingerstick and dried on filter paper, and in saliva. ZRT Laboratory was one of the first labs to develop and commercialize this convenient and accurate testing. In a study published in Fertility and Sterility, dried blood spot testing performed by ZRT Laboratory was found to be as accurate as traditional serum testing for the fertility markers LH, FSH, Pg, and E2[3]. Patients can collect their samples conveniently and at the appropriate cycle times with minimal disruption to their lives and busy work schedules. Sampling is done on days 3 and 21 of the menstrual cycle. The day 3 sample is optimal for assessment of ovarian reserves with the FSH and LH tests, while the other hormones are measured mid-luteally (day 21 commonly), when the level of hormones should be optimal for a successful pregnancy.

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ZRT LABORATORY

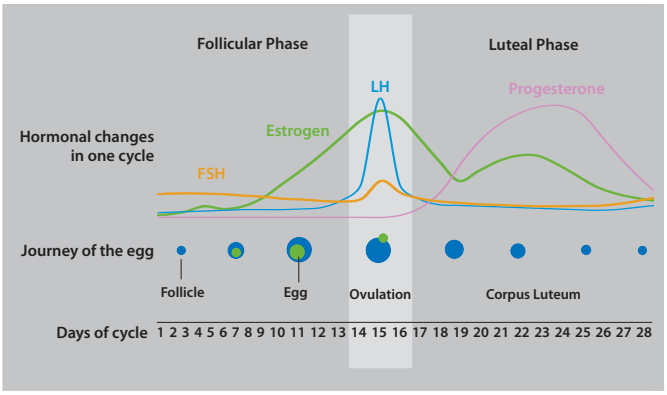
Saliva and Dried Blood Spot Testing.
Minimally-invasive home test kit.

The ZRT Test Report: ZRT's comprehensive test report is easy to interpret and includes not only the hormone test numbers in an easy to read format, but also your patient's self reported symptoms, medications, and hormones used, along with comprehensive individualized comments explaining how their hormonal imbalances could be causing infertility.

Hormone Changes During the Menstrual Cycle

In women with infertility, some of the following hormonal changes are seen:

- High FSH level on Day 3, in the follicular phase, reflects ovarian insufficiency and the beginnings of menopause.
- Low estradiol and progesterone on day 21 could indicate ovarian insufficiency (low egg reserve).
- Normal to high estradiol and low progesterone in the luteal phase is a sign of no ovulation or of luteal phase deficiency.
- High testosterone and DHEA-S, as well as high LH relative to FSH can indicate PCOS (polycystic ovarian syndrome), which is linked to infertility in several ways.



This illustration is an example of a 28-day-cycle. It shows the normal fluctuations in estradiol, progesterone, LH, and FSH during a menstrual cycle, with corresponding changes in the ovary.

Hormonal Aspects of Infertility

Hormone-related causes of female infertility most often involve the following five scenarios:

1. Ovarian Insufficiency

The average age of menopause is 51, with some women having their last period in their forties and others later in their fifties[4]. A cessation of ovulation prior to the age of 40 is rare, and is usually referred to as premature ovarian failure. Declining ovarian function is the main reason for the age-related decline in female fertility. As the number of available follicles starts to fall, estrogen is still being produced but ovulation does not occur, and progesterone levels are low in the absence of a corpus luteum[5,6]. High FSH and LH levels on day 3 of the menstrual cycle typically confirm premature ovarian failure and the onset of menopause. A typical pattern of day 21 hormone levels indicating signs of ovarian insufficiency would consist of low estradiol, low progesterone, and low testosterone. LH, DHEA-S, cortisol and thyroid hormones may or may not be normal.

2. Luteal Phase Deficiency

In some patients who are infertile, ovulation may occur normally but levels of progesterone are inadequate following ovulation (luteal phase). This luteal progesterone deficiency means that even if the egg is fertilized, implantation either does not occur, or if it does, the progesterone level is not high enough to sustain the pregnancy. Luteal phase deficiency can be caused by a number of problems, including endometriosis[7] and abnormal follicular development, but most commonly it is a result of inadequate progesterone production by the corpus luteum, which can result from excessive stress (high or low cortisol) and/or thyroid imbalances. A typical finding is low progesterone levels in the luteal phase, usually with normal estradiol levels[8].

3. Polycystic Ovarian Syndrome (PCOS)

PCOS is the most common endocrine disorder affecting women of reproductive age and is closely associated

with insulin resistance, metabolic syndrome and future risk of developing diabetes and cardiovascular disease[9]. Among women presenting with infertility in one study, PCOS was found to be present in 81% of women who were anovulatory, in 50% of those with tubal disease, and in 44% of those with unexplained infertility[10]. Hormonally, it is characterized by low progesterone, normal-to-high estradiol, high testosterone and normal to high DHEA-S during the luteal phase; also, LH often is elevated 2-3 times relative to FSH. Cortisol and thyroid hormones may or may not be normal, although women with PCOS have been found to have a three-fold higher prevalence of autoimmune thyroiditis compared to healthy women[11].

4. Hypometabolism/Thyroid Deficiency

Thyroid dysfunction, including subclinical hypothyroidism (elevated TSH with normal fT3 and fT4 levels), has been implicated as a cause of infertility. Thyroid hormone treatment can be a simple solution to restore a regular menstrual pattern[12]. In one study, levothyroxine treatment resulted in pregnancy in 44% of infertile patients diagnosed with subclinical hypothyroidism[13]. In patients with thyroid dysfunction, the sex hormones (E2, Pg, T,) and adrenal hormones (DS, C) may be normal in the presence of hypothyroid symptoms and one or more of the thyroid hormones out of balance. High TPO antibodies indicate an autoimmune thyroid disease (e.g., Hashimoto's Disease), which is associated with fertility-related problems. It is important to rule out thyroid autoimmunity in women attempting to conceive because of the increased risk of miscarriage[14].

5. Stress

Stress raises the stress hormone cortisol, which can severely affect a woman's ability to conceive[15], probably because of its direct negative impact on the endocrine glands ability to produce sex hormones (E2, Pg, T) and thyroid hormones (see www.endotext.com[16]). The diurnal cortisol variation measured in saliva samples collected throughout the day is an index of the adrenal glands' ability to cope with stressors (emotional, physical, dietary, chemical, pathogenic) that can impact a woman's ability to conceive. Endometriosis is found in more than 50% of women with unexplained infertility, and the high cortisol and prolactin levels induced by stress have been implicated in the development of this condition[17].

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Useful websites:

International Council on Infertility Information Dissemination: www.inciid.org

American Society for Reproductive Medicine: www.asrm.org

American Academy of Fertility Care Professionals: www.aafcp.org

NaProTechnology (Natural Procreative Technology): www.naprotechnology.com