Reproductive Endocrinology

# Measuring a Lifetime of Changes

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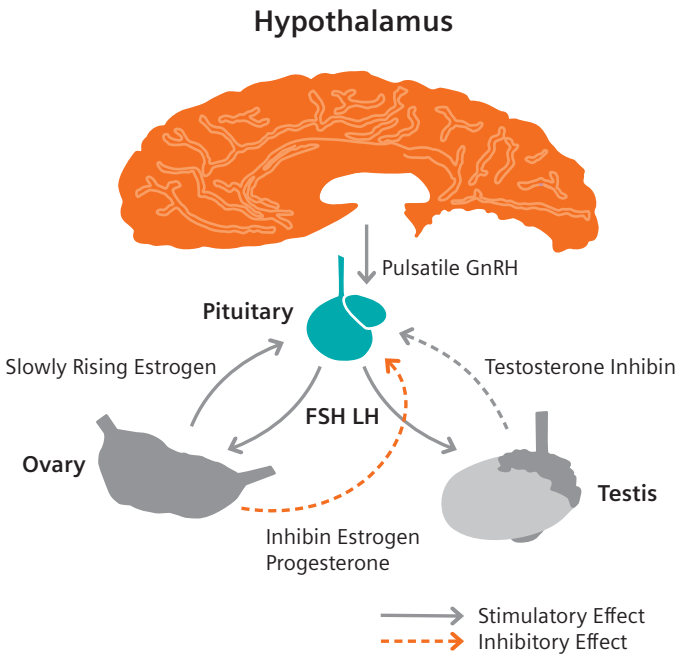
SIEMENS Healthineers

# Reproductive Care for a Lifetime

A longstanding market leader in the area of reproductive endocrinology, Siemens Healthineers offers a broad range of systems and assays to address the various clinical needs in reproductive health throughout life.




## Puberty

Puberty marks the beginning of the reproductive years of life. A comprehensive menu is crucial for diagnosing various clinical conditions associated with puberty, such as delayed and precocious puberty, primary amenorrhea, hypogonadism, hyperandrogenism, hyperprolactinemia, and hypothyroidism.

## The menstrual cycle

The menstrual cycle controls female fertility. It influences and is influenced by serum hormone levels, which impact bone health and many other aspects of female physiology. Siemens Healthineers extensive offering of hormone assays is an essential element in assessing various conditions associated with menstrual cycle dysfunction, including secondary amenorrhea, anovulatory cycles, hyperandrogenism, hypogonadism, and hyperprolactinemia.

## Infertility

Reproduction is a significant aspect of life for many people, and infertility can be emotionally devastating. Fortunately, medical advances have made it possible for many infertile couples to bear children. We offer a wide range of hormone assays useful as an aid in infertility diagnosis and monitoring.

## Pregnancy

During pregnancy, a fascinating evolution takes place in the body, not only anatomically, but biochemically as well. It is critical to have the proper menu to identify infertility, improve likelihood of conception, and promote a successful birth.

## Aging

Aging is an inevitable part of life. Reaching menopause and andropause is a gradual process and usually takes years to complete. During this time, hormone levels can fluctuate and change dramatically, causing various biochemical and physiological alterations. Proper measurement of steroid levels is invaluable in managing clinical conditions associated with aging.

Siemens Healthineers commitment to reproductive endocrinology has provided the industry with assays and systems to meet the needs of patients throughout their lives.

# Our Reproductive Endocrinology Assays: from Puberty through Pregnancy

## Puberty

The transition from childhood to puberty is initiated by two independent physiological processes. Adrenarche is marked by increased adrenal gland activity and higher serum levels of androgens. Gonadarche usually occurs 1 to 2 years later. It is distinguished by increased gonadotropin-releasing hormone (GnRH) secretion, which results in the production of a significant amount of sex steroids. This biological transition marks the progression from childhood to the next stage of life called puberty.

### Adrenarche

Adrenarche takes place in girls between 5 and 6 years of age and in boys between 8 and 9 years of age. It is responsible for the first measurable changes in reproductive hormone levels. The subsequent increase in DHEA and DHEA-SO4 is followed by a rise in androstenedione concentrations 1 to 2 years later.

### Gonadarche

From ages 8 to 10 in girls and 10 to 12 in boys, maturation of the central nervous system and resulting changes in GnRH secretion from the anterior pituitary gland cause blood concentrations of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) to begin rising. The pubertal rise in LH stimulates the production of estradiol in girls, which is responsible for the appearance of secondary sex characteristics, including the growth and development of reproductive organs, growth of pubic and axillary hair, fat redistribution, and bone maturation.

In boys, growth of the testes is attributable to the development of the seminiferous tubules, which are stimulated by FSH. LH promotes the production of testosterone, the androgen responsible for the appearance of male secondary sex characteristics, including the growth and development of reproductive organs, an increase in skeletal bone and muscle mass, voice changes, and growth of facial, pubic, and axillary hair.

### Estradiol

Of the various estrogens, estradiol is the most potent. Measurements may be useful for monitoring assisted reproduction technology and in the differential diagnosis of amenorrhea and precocious puberty in girls. Estradiol has also proven to be useful in evaluating clinical conditions in the male such as hypogonadism.

### FSH

Follicle-stimulating hormone induces ovarian follicular growth and stimulates follicular secretion of estradiol in the female. In the male, it facilitates the development of the testes and stimulates spermatogenesis. It is particularly useful in the clinical evaluation of infertility and menopause.

### LH

Luteinizing hormone promotes ovulation and the production of estrogen and progesterone. In the male, it stimulates the testes to produce androgens and estrogens. Measurements of this hormone are used in the clinical evaluation of various conditions including infertility, hypogonadism, and menopause.

### Progesterone

Among its many important functions, progesterone acts in concert with estradiol to control the phases of the menstrual cycle; it also maintains the fetus during early pregnancy. Progesterone measurement is indicated in conditions such as infertility, normal and ectopic pregnancy, and menopause.

## Steroid and Related Assays*

- Androstenedione
- DHEAS
- Estradiol
- Progesterone
- Testosterone
- SHBG

## Peptide Assays

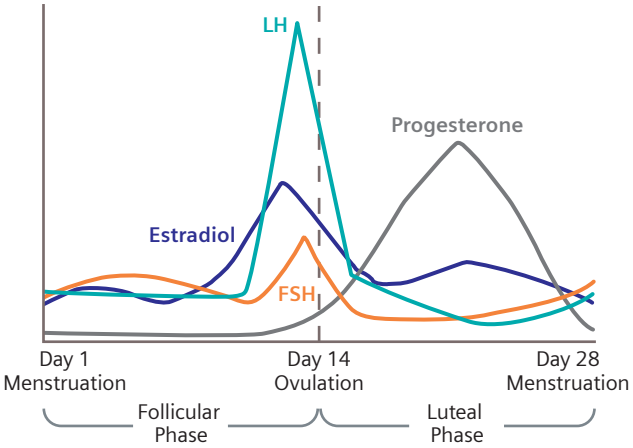
- FSH
- LH
- Prolactin

# The Menstrual Cycle

The monthly menstrual cycle prepares an egg for maturation, ovulation, and fertilization. The human menstrual cycle comprises three phases:

- **Follicular phase**
  Initiates the growth and maturation of an ovarian follicle, which actually begins during the last few days of the previous luteal phase.
- **Ovulatory phase**
  The interval in which the LH surge induces ovulation.
- **Luteal phase**
  The last portion of the cycle that prepares the endometrium for implantation of a fertilized ovum.

**Hormonal profiles throughout the menstrual cycle**




*Not all assays are available on all instruments.
†Under development. Not available for sale.

# Hormone Assays for the Reproductive Years

## Infertility

Infertility is defined as the inability to achieve conception after 1 year of unprotected intercourse, or the inability to maintain a viable pregnancy until birth. Approximately 40% of infertility clinic patients are diagnosed with anovulation. Those who suffer from ovulatory failure due to hormonal abnormalities generally fall into one of the following categories:

- Hyperprolactinemic—with or without gonadotropic abnormalities
- Hypogonadotropic
- Hypergonadotropic
- Normogonadotropic

### Women

In women, FSH values on day 2 or 3 of the menstrual cycle indicate follicular reserve. Both FSH and LH baseline values are biomarkers of ovarian response. Another critical value is the day 2 or 3 serum level of estradiol. The estradiol value is generally expected to be below 50 pg/mL (183 pmol/L). As with FSH, a decreased number of follicles is usually obtained in women with higher estradiol values.

**Standard hormonal analysis protocol for assisted reproductive technology patients**

| Days in Menstrual Cycle | Hormone Tested |
|---|---|
| Day 3 | Estradiol, FSH, LH |
| Days 4–12 | Estradiol |
| Days 10–14 | Estradiol, Progesterone, LH |
| Days 14–28 | Progesterone, Estradiol |
| Day 28 | HCG, Progesterone, Estradiol |
| Days 28–70 | HCG, Progesterone |

### Men

Some of the main endocrinological causes of infertility in men involve hormone abnormalities such as decreased bioactivity or insufficient levels of testosterone, reduced LH bioactivity or levels, and age-related increases in hepatic synthesis of SHBG. A deficiency in sperm concentration, motility, or morphology can also lead to infertility.

## Choose Siemens Healthineers for Infertility Diagnostics

**Comprehensive testing solutions from a single provider**

- Extensive reproductive endocrinology immunoassay menu
- Multiple instrument offerings to handle any workload

**Evaluation of women's infertility***

- AMH†
- Androstenedione
- DHEAS
- Estradiol
- FSH
- LH
- Progesterone
- Prolactin
- SHBG
- Testosterone
- TSH

**Evaluation of men's infertility***

- Androstenedione
- DHEAS
- Estradiol
- FSH
- LH
- Prolactin
- SHBG
- Testosterone

**Maternal Assays***

- AFP§
- Unconjugated Estriol§
- FSH
- HCG§
- Free ß HCG‡
- LH
- PAPP-A‡
- sFlT-1‡‡
- PlGF‡‡

**Not all assays are available on all instruments.*
*‡For research use only in the U.S.*
*§Assays not approved in the U.S. for these clinical applications.*
*‡‡Not available for sale in the USA.*
*Product availability will vary by country.*

# Reproductive Endocrinology Assays for Pregnancy Monitoring

## Pregnancy

Human pregnancy lasts approximately 40 weeks and is divided into trimesters.

### First trimester

The first trimester, from 0 to 13 weeks, begins on the first day of the last menses after the ovum has been fertilized. The fertilized ovum is carried down the fallopian tube into the uterus. It undergoes cell division, differentiation, and growth, eventually evolving into an embryo. Formation of the placenta takes place concurrently. At 10 weeks, an embryo has developed most major structures and is now referred to as a fetus. First-trimester testing is performed to further assess the health and future medical needs of the mother.

Laboratory testing is one important component of pregnancy monitoring. Tests may include:

- Pregnancy test (HCG)
- Ectopic pregnancy assessment (HCG, progesterone)
- Free ß HCG,‡ PAPP-A,‡ and nuchal translucency (NT) between weeks 10 and 12
- Gonorrhea, chlamydia, and syphilis tests
- Blood type and antibody screen
- Urine screen for glucose and/or protein
- TSH and anti-TPO Ab
- Urine culture and sensitivity
- Bacterial vaginosis screen
- Chorionic villus sampling (for karyotyping, Down syndrome)
- Toxoplasma IgM and IgG
- Pre-pregnancy tests (if not previously conducted)

### Second trimester

During the second trimester, weeks 14 through 26, rapid fetal growth occurs, and many fetal organs begin to mature. Second-trimester testing is directed primarily toward evaluating actual and potential problems in the baby, such as developmental defects.

Tests may include:

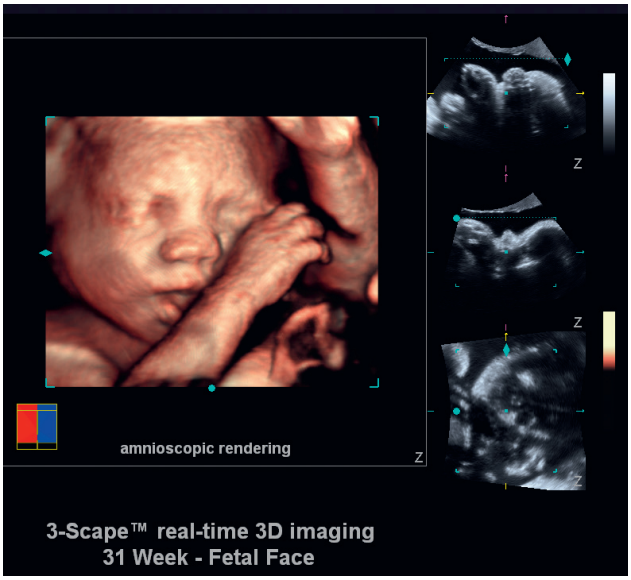
- Triple marker screen (AFP/HCG/unconjugated estriol)§
- Double marker screen (AFP, HCG)
- Urine screen for glucose and/or protein
- Amniocentesis
- Glucose
- Preeclampsia testing: sFlT-1‡‡ and PIGF‡‡

### Third trimester

The third trimester, weeks 27 through 40, is the period in which fetal organs finish maturing, the growth rate decelerates, and birth occurs. The purpose of third-trimester testing is to monitor fetal well-being and the health of the mother.

Diagnostic tests may include:

- Unconjugated estriol
- Urine screen for glucose and/or protein
- Antibody screen
- Group B streptococcus
- Gonorrhea, chlamydia, and syphilis
- Hemoglobin and platelet count
- Human placental lactogen (HPL)
- Preeclampsia testing: sFlT-1‡‡ and PIGF‡‡




3-Scape™ real-time 3D imaging
31 Week - Fetal Face

# A Comprehensive Test Menu for Evaluating Age-related Hormonal Disorders

## The aging process

Female menopause has been recognized for centuries, but current research has elucidated a similar phenomenon in males—andropause—which is associated with analogous symptoms.

### Menopause

Menopause, which, by definition, occurs 1 year after a woman's final menstrual cycle, is normally precipitated by the depletion of ovarian follicles due to aging, although it can also be induced by surgery (hysterectomy), radiation, chemotherapy, and health problems. During the first 5 years of life, the female ovary has an average of 318,000 follicles. By age 41 to 45, the number of follicles remaining is typically less than 7000. Menopause can take place as early as age 35, but usually occurs in the late 40s or early 50s.

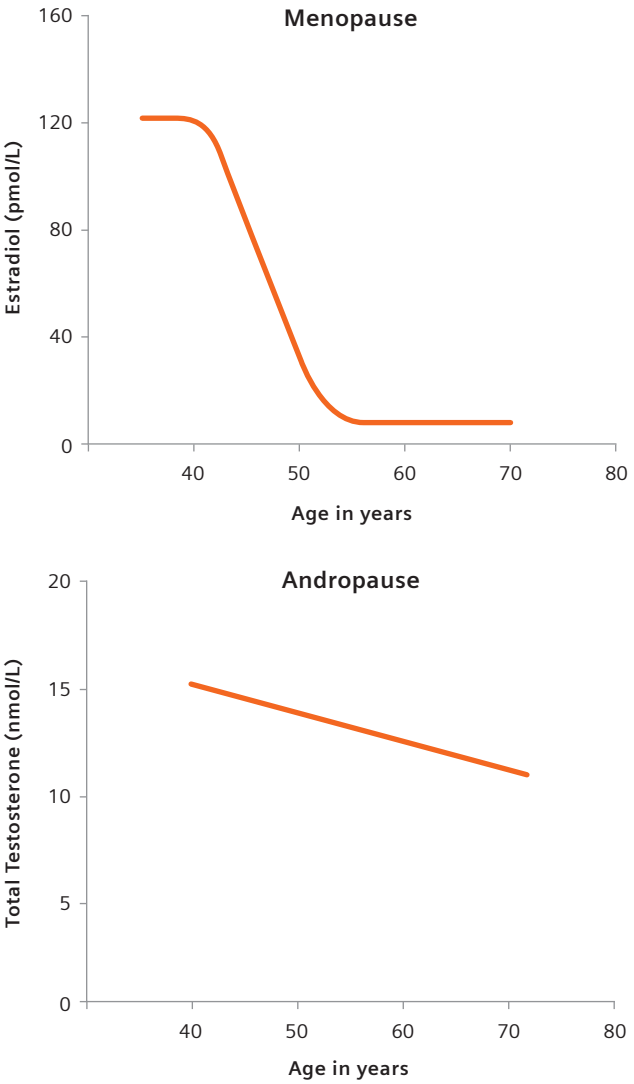
The physical symptoms of menopause are associated with the hormonal modulations that occur as ovarian function declines. FSH basal serum levels tend to increase significantly after 29 to 30 years of age, gradually rising until concentrations peak 2 to 3 years after menopause. A decrease in FSH levels has been observed 20 to 30 years after menopause in some women. LH concentrations rise markedly between ages 35 and 40, dramatically increasing until 2 to 3 years after menopause. One theory attributes menopausal hot flashes to spontaneous spikes in LH levels. As with FSH, basal LH levels in some women have been shown to decline in the second or third decade after menopause.

Research suggests that a high serum FSH-to-LH ratio (1.9 to 3.8) may be a useful indicator of menopausal status. Estradiol levels permanently drop below 30 pg/mL in the perimenopausal period, resulting in an increased estrone-to-estradiol ratio (>1).

### Andropause

Menopause represents a landmark in the female chronobiology and indicates the end of reproductive capacity. In contrast to this clearly defined event for women, aging of the male endocrine system, beginning in middle-aged or elderly men, is a less-abrupt, less-clearly demarcated, and highly variable process.

**General patterns of age-related decline in estradiol levels in women and total testosterone levels in men**



# Choose Siemens Healthineers for Menopause/Andropause Testing

## Benefits

- Extensive menu to monitor all clinical indications of aging
- Clinical studies defining hormonal reference ranges for postmenopausal women and aging men
- Bone marker assays including Vitamin D Total, PYRILINKS-D, Osteocalcin,‡ Prolactin, PTH
- Complete thyroid panel

## The IMMULITE Aging Male Study

The aim of the study was to verify age-dependent hormonal changes in males and to establish age-related male reference ranges for these parameters. Venous blood samples were collected from 300 apparently healthy German male adults divided into the following age groups of 50 individuals each: 21–30, 31–40, 41–50, 51–60, 61–70, and >70 years. Total testosterone, SHBG, DHEA-SO4, estradiol, LH, FSH, TSH, free T4, and free T3 were measured using the IMMULITE® system. The total testosterone and SHBG results were used to generate values for the free androgen index (FAI) and calculated free testosterone (cFT).[1] Medians and central 95% ranges were determined for all parameters and age groups.

This study clearly demonstrated the importance of determining complete profiles for the androgenic, gonadotropic, thyroid, and pituitary hormones in middle-aged and elderly men to obtain accurate clinical diagnoses for various hormonal disorders. The detection of a decrease in bioactive testosterone in combination with clinical symptoms may lead to a diagnosis of hypoandrogenism and indicate the need for therapy.

## Ratio of free testosterone to SHBG

The free androgen index (FAI), cFT, and other measures of free and bioavailable testosterone provide important alternatives to reliance on a total testosterone measurement alone. They are useful in various clinical contexts, including:

- Male androgen deprivation therapy
- Aging males
- Adrenal disorders
- Hirsutism and virilization

| Age Group | Testosterone | Free Androgen Index (FAI) | Calculated Free Testosterone (cFT) |
|---|---|---|---|
| (2.5th percentile) 21–30 | 11.3 nmol/L | 35.7 | 0.25 nmol/L |
| 31–40 | 8% | 4% | 4% |
| 41–50 | 28% | 28% | 32% |
| 51–60 | 50% | 68% | 74% |
| 61–70 | 46% | 76% | 78% |
| >70 | 52% | 84% | 84% |

Percentage of healthy men with testosterone, FAI, and cFT values lower than the 2.5th percentile of the 21–30-year age group.

**Evaluation of Menopause***

- AMH†
- DHEAS
- Estradiol
- FSH
- LH
- SHBG
- Free T4
- Testosterone
- TSH

**Evaluation of Andropause***

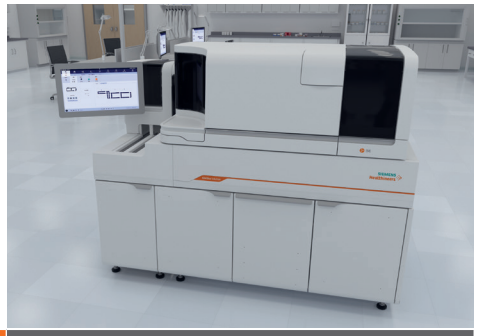
- DHEAS
- FSH
- LH
- Progesterone
- SHBG
- Free T3
- Free T4
- Testosterone
- TSH

**Not all assays are available on all instruments.*
*†Under development. Not available for sale.*
*‡Not available for sale in the U.S.*

**Reference:**
1. Vermeulen A, Verdonck L, Kaufman JM. A critical evaluation of simple methods for the estimation of free testosterone in serum. J Clin Endocrinol Metab. 1999;84:3666-72.

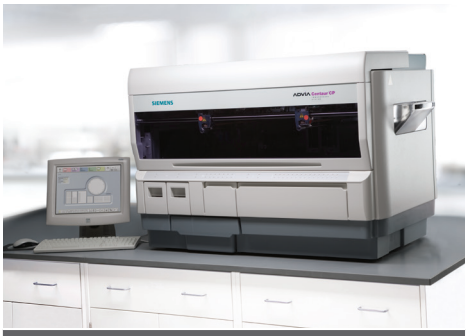
# Choose Siemens Healthineers for Your Reproductive Endocrinology Testing

We have developed one of the broadest menus available on random-access analyzers, demonstrating a strong commitment to reproductive endocrinology testing.



| Assays designed for clinical diagnostic accuracy | Atellica® IM Analyzer | ADVIA Centaur® XP/XPT System |
|---|---|---|
| AFP (NTD)** | ■ | ■ |
| AMH | In development† | In development† |
| Androstenedione | ■ | ■ |
| DHEAS | ■ | ■ |
| Estradiol | ■ | ■ |
| Free ß hcG | ■†† | ■†† |
| FSH | ■ | ■ |
| hCG | ■ | ■ |
| LH | ■ | ■ |
| PAPP-A | ■†† | ■†† |
| PIGF | ■‡‡ | ■‡‡ |
| Progesterone | ■ | ■ |
| Prolactin | ■ | ■ |
| sFIT-1 | ■‡‡ | ■‡‡ |
| SHBG | ■ | ■ |
| Testosterone | ■ | ■ |
| Unconjugated Estriol | | |

***Neural tube defect.*
*††For research use only in the U.S.*
*‡‡Not available for sale in the U.S.*
*Product availability will vary by country.*



| ADVIA Centaur® CP System | Dimension Vista® System | IMMULITE 2000/XPi System |
|---|---|---|
| ■ | | ■ |
| In development[†] | | |
| ■ | | ■ |
| ■ | | ■ |
| ■ | ■ | ■ |
| ■[††] | | ■[††] |
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At Siemens Healthineers, our purpose is to enable healthcare providers to increase value by empowering them on their journey toward expanding precision medicine, transforming care delivery, and improving patient experience, all made possible by digitalizing healthcare.

An estimated 5 million patients globally benefit every day from our innovative technologies and services in the areas of diagnostic and therapeutic imaging, laboratory diagnostics, and molecular medicine, as well as digital health and enterprise services.

We are a leading medical technology company with over 120 years of experience and 18,000 patents globally. Through the dedication of more than 50,000 colleagues in 75 countries, we will continue to innovate and shape the future of healthcare.



Product availability may vary from country to country and is subject to varying regulatory requirements. Please contact your local representative for availability.

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