

Estradiol (E2)

WHAT IS ESTRADIOL?

Estradiol is the strongest of the three estrogen hormones. It is naturally produced in both genders, with much higher levels in females. Estradiol is also known as E2 and oestradiol. It is predominantly produced within the ovarian follicles, but also in other tissues, such as the adrenal glands, fat, liver, breasts, brain, testes, and placenta (during pregnancy) (1).

PURPOSE OF AN ESTRADIOL TEST

Estradiol testing in reproductive age females can aid in the evaluation of amenorrhea (lack of menstruation), fertility issues, ovarian status (particularly for assisted reproduction), and response to estrogen replacement therapy. In older females, estradiol testing can be used as part of a fracture risk assessment and monitoring response to hormone replacement therapy.

In males, estradiol testing can be used to evaluate feminization (e.g., gynecomastia—increased breast tissue) and for the diagnosis of estrogen-producing tumors (that can also occur in females).

WHAT ARE NORMAL ESTRADIOL LEVELS?

Normal estradiol levels are lowest during menstruation and early follicular phase (25 – 75 pg/mL). Levels increase in the late follicular phase to a peak of 150 – 750 pg/mL, decrease at ovulation, and then rise again during the luteal phase (30 – 450 pg/mL) (2). If conception does not occur, estradiol levels decrease and menstruation begins shortly after (3). If conception occurs, estradiol levels continue to rise up to 10,000 – 40,000 pg/mL during the third trimester (4). Estradiol levels are lower after menopause (\leq 20 pg/mL), while normal levels in adult males are 10 – 50 pg/mL (2).

ROLES OF ESTRADIOL

The primary function of estradiol in females is to mature and maintain the reproductive system, including the mammary glands, uterus, and vagina. It is responsible for the development of female secondary sexual characteristics (e.g. breasts, female fat distribution) (2). During each menstrual cycle, estradiol levels increase to trigger the maturation and release of the egg, and the thickening of the uterus lining to allow a fertilized egg to implant (4). Estradiol also plays important functions in the male reproductive system, skeletal system, skin health, nervous system, and cardiovascular system (2).

ESTRADIOL LEVELS AND FEMALE FERTILITY

Estradiol levels are commonly measured as part of female fertility (ovarian reserve) testing. Measurements are usually taken early in the menstrual cycle, at days 2 or 3, as estradiol levels fluctuate depending on timing of the menstrual cycle (6). High basal estradiol levels suggest impaired oocyte development early in the menstrual cycle, which is a sign of poor ovarian reserve (reproductive aging). High estradiol can also result in an artificially low follicle stimulating hormone (FSH) value, as estradiol reduces FSH secretion from the pituitary gland (7).

Although measuring estradiol levels is simple and inexpensive, basal estradiol levels alone have a low predictive value for IVF outcome. However, estradiol levels measured in conjunction with FSH levels can be useful for determining medication doses for IVF. Furthermore, estradiol measurements can help clinicians determine the risk of ovarian hyperstimulation syndrome during IVF cycles (8).

ESTRADIOL LEVELS AND MENOPAUSE

As females reach menopause, their estradiol levels decrease. This contributes to the symptoms associated with menopause, including mood swings, vaginal dryness, hot flushes, and night sweats. Low estradiol levels also increase the risk of bone fractures (9) and accelerate skin aging (10), two characteristics that are often observed during and after menopause.

ABNORMAL ESTRADIOL IN MALES

Males who have high estradiol levels can be affected by infertility, gynecomastia (increased breast tissue), erectile dysfunction, slowed growth leading to short stature or delayed puberty, reduced sex drive, fatigue, reduced muscle mass and bone mass, and reduced growth of penis and testicles (11,12). Elevated estradiol in males also increases the risk of diabetes, blood clots, stroke and certain cancers. Increased estradiol levels can occur due to certain antibiotics, specific herbs, inherited factors, stress, obesity, certain tumours, liver diseases, and conditions that affected hormone balances (12).

Reduced estradiol levels in males can occur due to many reasons, including autoimmune conditions and genetics disorders, hemochromatosis, radiation exposure, HIV infection, malnutrition, and surgeries. The symptoms of low estradiol can be similar to the symptoms associated with high estradiol (12).

Following a healthy diet that is low in fat and high in fiber, combined with adequate physical exercise can help males maintain estradiol levels in the normal, healthy range.

TEST PROCEDURE

Correct specimen collection and handling is required for optimal assay performance.

This test requires a blood sample from a finger prick. All supplies for sample collection are provided in this kit. First wash and dry hands. Warm hands aid in blood collection. Clean the finger prick site with the alcohol swab and allow to air dry. Use the provided lancet to puncture the skin in one quick, continuous and deliberate stroke. Wipe away the first drop of blood (as it may be contaminated with tissue fluid or skin debris). Massage finger to increase blood flow at the puncture site and hold in a position that gravity facilitates the collection of blood on the fingertip. Transfer the blood to the blood collection card or blood collection tube (microtainer).

Avoid squeezing or 'milking' the finger excessively. If blood flow stops, perform a second skin puncture on another finger if more blood is required.

Dispose of all sharps safely and return sample to the laboratory in the provided prepaid return shipping envelope.

Upon receipt at the laboratory, the blood sample is analyzed by the fully automated Alinity i Estradiol chemiluminescent microparticle immunoassay on the Alinity ci series analyzer. This assay measures estradiol levels by binding to monoclonal anti-estradiol coated microparticles. The amount of estradiol in the blood sample is measured in relative light units by a chemiluminescent reaction. This assay has a precision value of 3.8 pg/mL (total SD) for low concentrations (around 49 pg/mL).

SPECIAL INSTRUCTIONS

For fertility testing in females, the samples should be collected on the third day of the menstrual cycle (third day of menstruation) for optimum results.

TEST INTERPRETATION

This assay will provide accurate estradiol values for the tested specimen. This value is to be used in conjunction with other clinical and laboratory information for analyses of general health, hormone balance, fertility, and IVF.

DISCLAIMERS/LIMITATIONS

These results should be interpreted in conjunction with other laboratory and clinical information.

Assay interference may occur in specimens from individuals routinely exposed to animals or to animal serum products. Additional clinical or diagnostic information may be required for these specimens.

Certain medications (e.g., birth control pills and steroids), hormone therapy, recent test using a radioactive substance (e.g., bone scan), and high sugar levels due to diabetes may affect estradiol test results. In addition, estradiol levels fluctuate throughout each menstrual cycle in reproductive age females, so the timing of sample collection may influence the interpretation of the estradiol level.

Additional testing is recommended if estradiol results are inconsistent with clinical evidence.

Correct specimen collection and handling is required for optimal assay performance. The assay is unaffected ($\leq 10\%$ interference) by hemoglobin (500 mg/dL), bilirubin (20 mg/dL), triglycerides (1000 mg/dL), protein (12 g/dL), and cholesterol (240 mg/dL).

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