

Unconjugated Estriol (E3)

MDL Test Number: 619

Methodology: Immunoassay

CPT Codes: 82677 x 1



Specimen Collection Platform:

Serum in Serum Separator Tube (SST)

Turnaround Time:

24 - 72 hours

Stability:

Room temperature

Test Additions*:

30 days to add tests

Specimen Collection:



1. Immediately after blood collection, invert the tube(s) gently 5 times to ensure mixing of clot activator.



2. Allow the tube to rest upright for at least 30 minutes after collection to ensure proper clotting.



3. Centrifuge for at least 15 minutes at 2200-2500 RPM within one hour of collection.



4. Do not remove the stopper or pour off serum.



What is Unconjugated Estriol (E3)?

Estriol, often shortened to E3, is one of the three main forms of estrogen in the body. This test measures unconjugated estriol, the free form, meaning the portion that circulates on its own rather than attached to another molecule.

During pregnancy, estriol is made jointly by the fetus and the placenta. The fetal adrenal glands (small glands that sit on top of the kidneys) supply the starting material, and the fetal liver and the placenta convert it into estriol. Because of that shared pathway, the amount in the mother's blood reflects how the placenta and the fetus are working together.

Estriol levels are not steady. Outside of pregnancy, they are very low. In pregnancy, they climb as the fetus grows, rising nearly threefold across the final three months, with a sharp increase around the 36th week. Most estriol does not stay free for long: the mother's liver quickly converts it into other forms that the body clears in the urine. The unconjugated form makes up only about nine percent of the total. Levels also swing through the day and differ widely from one woman to the next, which is why a series of results carries far more meaning than any single value.

Why test for Unconjugated Estriol (uE3)?

A healthcare provider may order an unconjugated estriol test to measure how much free estriol is present in the blood. Common reasons include:

- **Following the well-being and maturity of the fetus through the third trimester of a high-risk pregnancy**, or one in which the due date is uncertain, using a series of results rather than a single measurement
- **Looking into a pregnancy in which estriol stays low or has dropped sharply** compared with the patient's own earlier results
- **Putting an exact number on an unexpectedly low estriol reported by a prenatal screening panel**, so the ordering provider has a measured concentration to work from
- **Following overall estrogen status through the transition to menopause**, when estriol falls along with the other estrogens
- **Checking estrogen levels in a patient using a compounded hormone preparation** that contains estriol



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Special Instructions:

- **Collection timing:** Estriol rises and falls through the day and from one hour to the next. Blood should be drawn at about the same time of day at each visit. When results are followed over time, each new value is compared against the patient's own baseline — the average or the highest of her three most recent results. A drop of 40 percent or more from that baseline is considered significant.
- **Blood-thinning medication:** A sample has to clot completely before it is spun down, because strands of protein left behind in a partly clotted sample can distort the result. Patients taking blood thinners often need extra clotting time, so it helps to note this at collection.
- **Estriol-containing hormone preparations:** Compounded estrogen creams, drops, and capsules sometimes contain estriol, and estriol taken this way is measured by the test along with what the body makes on its own. Patients should tell the ordering provider about every hormone product they use, including compounded ones.
- **Comparing results over time:** Different laboratories and different instruments can produce somewhat different estriol numbers from the same sample. When results are being tracked over time, use the same test at the same laboratory each time, and handle and store every sample the same way, so the comparison is meaningful.

Limitations:

Every laboratory test has limits. For unconjugated estriol, the main ones are:

- This test reports a concentration in nanograms per milliliter. It does not calculate a multiple of the median or a risk figure the way a prenatal screening panel does. Current obstetric guidance also bases fetal surveillance on heart-rate monitoring and ultrasound, so estriol is used alongside those methods rather than in place of them.
- The test measures unconjugated estriol between 0.07 and 12 ng/mL. Results below that range are reported as less than 0.07 ng/mL, and results above it as greater than 12 ng/mL. In the last weeks of pregnancy, many normal results reach the upper value, which limits how closely change can be tracked near term.
- Closely related estrogens can be mistaken for estriol. A naturally occurring variant called 16-epiestriol is measured at roughly 8 percent of the amount present, and forms of estriol that the liver has already modified contribute to a smaller degree. A result, therefore, reflects free estriol plus a small amount from these related compounds.
- A small number of patients carry natural antibodies in their blood — often people who work closely with animals or who have received certain antibody-based treatments — that can interfere with the test and produce an unexpected result.
- An unconjugated estriol result is one piece of a larger picture. It is meant to be read together with the patient's symptoms, medical history, and other test results — never on its own.

Reference Range(s):

Unconjugated estriol is measured in nanograms per milliliter (ng/mL). Levels climb week by week through the third trimester, so a result is compared against the expected range for that week of pregnancy. Representative weeks are shown below:

- **Week 27 of pregnancy** (median 4.1 ng/mL): **2.3–6.4 ng/mL**
- **Week 30 of pregnancy** (median 4.9 ng/mL): **2.4–8.6 ng/mL**
- **Week 33 of pregnancy** (median 7.2 ng/mL): **3.0 ng/mL to above 12 ng/mL**
- **Weeks 36 to 40** (median above 12 ng/mL): **4.7 ng/mL to above 12 ng/mL**

A result outside these ranges is not automatically a problem, and a result inside them does not rule one out. Only the ordering provider can interpret what a given number means for a given patient. Patients should always go by the reference range printed on their own laboratory report.

Analyte	Disorder	Expected Value*
uE3	Early pregnancy	↑
uE3	Third-trimester pregnancy	↑↑
uE3	Placental insufficiency	↓
uE3	Perimenopause	↓
uE3	Postmenopause	↓↓

*↓ – Decreased, ↓↓ – Markedly Decreased, ↑ – Increased, ↑↑ – Markedly Increased.

What are some references that discuss the medical necessity of testing Unconjugated Estriol (uE3)?

1. Bulun SE, Babayev E. Physiology and pathology of the female reproductive axis. In *Williams Textbook of Endocrinology* 15th edn (eds Melmed, S. et al.) Ch. 15 (Elsevier, Philadelphia, 2025).
2. American College of Obstetricians and Gynecologists. Antepartum fetal surveillance: ACOG practice bulletin, number 229. *Obstet Gynecol*, **137**, e116–e127 (2021).
3. Schoen, E. et al. Maternal serum unconjugated estriol as a predictor for Smith-Lemli-Opitz syndrome and other fetal conditions. *Obstet Gynecol*, **102**, 167–172 (2003).
4. Craig WY, et al. Further insights into implications of undetectable or very low unconjugated estriol in maternal serum during the second trimester. *Prenat Diagn*, **31**, 616–618 (2011).
5. Santoro N, et al. The menopause transition: signs, symptoms, and management options. *J Clin Endocrinol Metab*, **106**, 1–15 (2021).
6. Harlow SD, et al. Executive summary of the Stages of Reproductive Aging Workshop +10: addressing the unfinished agenda of staging reproductive aging. *J Clin Endocrinol Metab*, **97**, 1159–1168 (2012).



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