Test Definition: UE3
Estriol, Unconjugated, S

Overview

Useful For
A part of the SEQF/ Sequential Maternal Screening, Part 2, Serum and QUAD / Quad Screen (Second Trimester) Maternal, Serum in biochemical second trimester or cross-trimester screening for Down syndrome and trisomy 18 syndrome

A marker of fetal demise

An element in the prenatal diagnosis of disorders of fetal steroid metabolism, including Smith-Lemli-Opitz syndrome, X-linked ichthyosis and contiguous gene syndrome (placental sulfatase deficiency disorders), aromatase deficiency, primary or secondary fetal adrenal insufficiency, and various forms of congenital adrenal hyperplasia

Assessment of preterm labor risk

Epidemiological studies of breast cancer risk in conjunction with measurement of estrone, estradiol, and various metabolites

Assessing estrogen metabolism, estrogen and estrogen-like medications, and other endogenous or exogenous factors impacting on estrogen metabolism in the context of other basic scientific and clinical studies

Method Name
ImmunoenzymaticAssay

NY State Available
Yes

Specimen

Specimen Type
Serum

Specimen Required
Container/Tube:

Preferred: Red top

Acceptable: Serum gel

Specimen Volume: 0.6 mL

Specimen Minimum Volume
0.5 mL

Reject Due To

<table>
<thead>
<tr>
<th>Hemolysis</th>
<th>Mild OK; Gross reject</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipemia</td>
<td>Mild OK; Gross OK</td>
</tr>
<tr>
<td>Icterus</td>
<td>NA</td>
</tr>
</tbody>
</table>
Test Definition: UE3
Estriol, Unconjugated, S

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>Refrigerated (preferred)</td>
<td>14 days</td>
</tr>
<tr>
<td>Frozen</td>
<td></td>
<td>90 days</td>
</tr>
</tbody>
</table>

Clinical and Interpretive

Clinical Information

Estrogens are involved in development and maintenance of the female phenotype, germ cell maturation, and pregnancy. They also are important in many other nongender-specific functions in men and women. These include growth, nervous system maturation, bone metabolism, and endothelial responsiveness.

There are 3 major biologically active estrogens in humans: estrone (E1), estradiol (E2), and estriol (E3). Like all members of the steroid hormone family, they diffuse into cells and bind to specific nuclear receptors, which in turn alter gene transcription in a tissue specific manner. E2 is the most potent natural human estrogen, closely followed by E1, while E3 possess only 20% of the E2 affinity for the estrogen receptor. In men and nonpregnant women, E1 and E2 are formed from the androgenic steroids androstenedione and testosterone, respectively. E3 is derived largely through conversion of E2, and to a lesser degree from 16a-metabolites of E1. E2 and E1 can also be converted into each other, and both can be inactivated via hydroxylation and conjugation.

During pregnancy E3 becomes the dominant estrogen. The fetal adrenal gland secretes dehydroepiandrosterone-sulfate (DHEAS), which is converted to E3 in the placenta and diffuses into the maternal circulation. The half-life of unconjugated E3 (uE3) in the maternal blood system is 20 to 30 minutes, since the maternal liver quickly conjugates E3 to make it more water soluble for urinary excretion. E3 levels increase throughout the course of pregnancy, peaking at term.

Measurement of serum E2 and E1 levels is an integral part of assessment of reproductive function in females, and also has applications in both men and women in osteoporosis risk assessment and monitoring of female hormone replacement therapy. By contrast, with the exception of epidemiological studies assessing breast cancer risk and other scientific studies, the main value of E3 measurements is in the diagnosis of maternal-fetal diseases. In those settings, measurement of serum uE3 levels plays a major role.

Decreased second trimester uE3 has been shown to be a marker for Down and trisomy-18 syndromes. It also is low in cases of gross neural tube defects such as anencephaly. Based on these observations, uE3 has become a part of multiple marker prenatal biochemical screening, together with alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG), and inhibin-A measurements (QUAD / Quad Screen (Second Trimester) Maternal, Serum). Low levels of uE3 also have been associated with pregnancy loss, Smith-Lemli-Opitz syndrome (defect in cholesterol biosynthesis), X-linked ichthyosis and contiguous gene syndrome (placental sulfatase deficiency disorders), aromatase deficiency, and primary or secondary fetal adrenal insufficiency.

High levels of uE3, or sudden increases in maternal uE3 levels, are a marker of pending labor. The rise occurs approximately 4 weeks before onset of labor. Since uE3 has been shown to be more accurate than clinical assessment in predicting labor onset, there is increasing interest in its use in assessment of preterm labor risk.
High maternal serum uE3 levels may also be occasionally observed in various forms of congenital adrenal hyperplasia.

**Reference Values**

Males: <0.07 ng/mL  
Females: <0.08 ng/mL

For SI unit Reference Values, see [https://www.mayocliniclabs.com/order-tests/si-unit-conversion.html](https://www.mayocliniclabs.com/order-tests/si-unit-conversion.html)

**Interpretation**

In the context of the quad test, the measured unconjugated E3 (uE3) value forms part of a complex, multivariate risk calculation formula, using maternal age, gestational stage, and other demographic information, in addition to the results of the 4 tested markers, for Down syndrome, trisomy 18 syndrome, and neural tube defect risk calculations.

A serum uE3 <0.3 multiples of the gestational age median in women who otherwise screen negative in the quad test, indicates the possibility of fetal demise, Smith-Lemli-Opitz syndrome, X-linked ichthyosis or contiguous gene syndrome, aromatase deficiency, or primary or secondary (including maternal corticosteroid therapy) fetal adrenal insufficiency.

An elevated serum or uE3 >3.0 multiples of the gestational age mean, or with an absolute value of >2.1 ng/mL, can be an indication of pending labor or fetal congenital adrenal hyperplasia.

In the context of assessment of a patient deemed at risk of preterm labor, a single serum or uE3 measurement within the above cutoffs, has a negative predictive value of labor onset (ie, labor unlikely within the next 4 weeks) of 98% in low-risk populations and of 96% in high-risk populations.

Measurements of serum uE3 performed in the context of epidemiological or other basic or clinical scientific studies need to be interpreted in the context of those studies. No overall guidelines can be given.

**Cautions**

Like any immunoassay, this test can occasionally be subject to analytical interferences. We strive to identify and resolve these rare problems whenever they occur, but if the clinical picture is inconsistent with the test results, clinicians should still consider the possibility of a preanalytical or analytical error and contact the Clinical Immunoassay Laboratory for discussion.

**Performance**

**Method Description**

The instrument used is the Beckman Coulter UniCel DxI 800. The Access unconjugated estriol assay is a competitive binding immunoenzymatic assay. A sample is added to a reaction vessel with estriol-alkaline phosphatase conjugate, paramagnetic particles coated with goat antirabbit IgG, and polyclonal rabbit antiestriol. Estriol in the sample competes with estriol-alkaline phosphatase conjugate for a limited number of binding sites on the specific anti-estriol antibody. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then the chemiluminescent substrate Lumi-Phos 530 is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is inversely proportional to the concentration of estriol in the sample. The amount of analyte in the sample is determined by means of a stored, multipoint calibration curve.\((\text{Package Insert: Beckman Coulter Access Unconjugated Estriol Assay, 2015})\)

**PDF Report**

Document generated August 7, 2019 at 9:15pm CDT
Test Definition: UE3
Estriol, Unconjugated, S

Day(s) and Time(s) Test Performed
Monday through Friday; 5 a.m.-12 a.m., Saturday; 6 a.m.-6 p.m.

Analytic Time
Same day/1 day

Maximum Laboratory Time
3 days

Specimen Retention Time
2 weeks

Performing Laboratory Location
Rochester

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification
This test has been cleared or approved by the U.S. Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information
82677

LOINC® Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>UE3</td>
<td>Estriol, Unconjugated, S</td>
<td>2250-9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>UE3</td>
<td>Estriol, Unconjugated, S</td>
<td>2250-9</td>
</tr>
</tbody>
</table>