Fact Sheet: Sensitive Oestradiol

Test indications

Clinical circumstances requiring high sensitivity oestradiol measurement
- children
  - Assessment and monitoring of delayed or precocious puberty
  - Assessment of disorders of sex steroid metabolism
- men
  - Assessment of gynecomastia
- women
  - Assessment of oligo-menorrhoea
  - Monitoring antioestrogen therapy

Clinical information

Oestradiol is synthesised by aromatisation of androgens, catalysed by the enzyme aromatase. In healthy women of reproductive age this primarily occurs in the ovaries, but the adrenal glands and testes in men also produce small amounts of oestrogens. Additionally oestrogens can be produced peripherally by aromatisation of androgens, adipose tissue being a major site.

Oestradiol is key for regulation of the menstrual cycle and development and maintenance of secondary sexual characteristics in females. Additionally oestradiol has several non-sex specific functions including actions on bone, protecting against bone loss and vasculoprotective effects by actions on endothelial and vascular smooth muscle cells.

Oestradiol has conventionally been measured by immunoassays with modest sensitivity (lower limits of quantitation approximately 100 – 350 pmol/L). While these assays generally meet the clinical needs for evaluation of ovulation in premenopausal women, including monitoring of ovulation induction and IVF cycles, the concentration of oestradiol in children, men, postmenopausal women and women being treated with aromatase inhibitors is much lower requiring the enhanced sensitivity and specificity provided by LC/MS-MS.

The Prince of Wales Hospital sensitive oestradiol assay is accurate to serum oestradiol concentrations down to 5 pmol/L. Additionally the mass spectrometry based assay is free from interference from Fulvestrant, an oestrogen receptor antagonist used in the treatment of breast cancer, which has been shown to cross-react with oestradiol immunoassays resulting in falsely increased results.

Reference intervals

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Reference interval</th>
<th>units</th>
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<tbody>
<tr>
<td>Female</td>
<td>7y to &lt;10y</td>
<td>0 - 133</td>
<td>pmol/L</td>
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<tr>
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<td>10y to &lt;13y</td>
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<td>13y to &lt;16y</td>
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<tr>
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<td>Premenopausal, Early Follicular</td>
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<tr>
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<td>Premenopausal, Late Follicular</td>
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<td>Premenopausal, Luteal</td>
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<tr>
<td></td>
<td>13y to &lt;16y</td>
<td>0 - 133</td>
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<td></td>
<td>16y to &lt;18y</td>
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<tr>
<td></td>
<td>18y to &lt;110y</td>
<td>36 - 155</td>
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Source: ARUP laboratories
Interpretation of results

Children

Oestradiol concentrations in prepupertal girls are higher than boys, although significantly below the adult premenopausal range and below the sensitivity or commonly used immunoassays. In girls oestradiol concentrations increase approximately 6-12 months before breast development and continue to increase with progression through puberty.

An increased oestradiol concentration combined with increased FSH/LH is consistent with central or gonadotrophin dependent precocious puberty. Increased oestradiol with low gonadotrophins is consistent with gonadotrophin independent precocious puberty caused by a peripheral source of oestradiol such as an ovarian tumour or cyst.

Men

Increased oestradiol may result in gynecomastia, infertility and feminisation in men. Elevated concentrations could be due to:

- Obesity (related to aromatase activity in adipocytes)
- Liver dysfunction resulting in reduced hepatic clearance
- Production by the testis as a result of a tumour (either directly by a Leydig or Sertoli cell tumour, or indirectly as a result of hCG stimulation produced by a germ cell or other solid tumour).
- Androgen producing tumours may also result in increased oestradiol concentration due to peripheral aromatisation

Low oestradiol concentrations in men are associated with reduced bone density, and men with aromatase deficiency, or estrogen insensitivity have reduced bone mass.

Women receiving antioestrogen therapy

In women receiving antioestrogen therapy the aim is to suppress oestradiol to a very low concentration (i.e. below 5 pmol/L). These levels can only be measured accurately with sensitive assays.

Specimen:

Sample type:
Serum gel tube – Preferred
Serum non gel tube – Accepted

Minimum volume: 0.6mL

Method: LC-MS/MS

Testing frequency: Weekly (Thursday)
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References:


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