Endocrinology of the Female Reproductive Axis

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Women and Infants Hospital
Alpert Medical School at Brown University
Learning objectives

1. Diagram the main components of the female reproductive axis

2. Describe basic immunoassay methods for measurement of reproductive hormones

3. List the primary hormones secreted in pregnancy
Overview of the female reproductive axis

Modified from Hiller-Sturmhöfel and Bartke, Alcohol Health & Research World, 1998
Ovarian Physiology

Kaipia & Hsueh, Ann Rev Physiol, 1997
Normal menstrual cycle

Thomeycroft, Am J Obstet Gynecol, 1971
Developing ovarian follicle

Steroid biosynthesis in ovarian follicles

**Theca cell**

**Granulosa cell**

![Steroid biosynthesis diagram](image)

**Fig. 9-2** Biosynthesis of steroids in the ovary. 1: Cholesterol side-chain cleavage enzyme complex; 2: 3β-hydroxysteroid dehydrogenase; 3: 17α-hydroxylase; 4: 17,20-lyase; 5: aromatase; 6: 17β-hydroxysteroid dehydrogenase.

*Griffin and Ojeda, Textbook of Endocrine Physiology, 2004*
Follicular phase of the menstrual cycle

Estradiol
Inhibin B is secreted during the follicular phase of the menstrual cycle.

Groome et al, JCEM;1996
Feedback regulation of the menstrual cycle

Fauci et al.  Harrison's Principles of Internal Medicine, 17th edition
http://www.accessmedicine.com
Ovulatory LH surge
Development of the corpus luteum

Steroid biosynthesis in corpus luteum
Luteal phase of the menstrual cycle

![Graph showing changes in LH, FSH, and Estradiol/Progesterone levels during the luteal phase of the menstrual cycle.](image-url)
Menstrual Cycle Summary

Inhibin A is secreted by the corpus luteum

Groome et al, 1996; JCEM
Immunometric (sandwich) assay

![Diagram of Immunometric (sandwich) assay]

- **FSH** and **FSH** are used as antigens.
- **Antibody** binds to the antigens.
- A line graph showing the relationship between sample or standard concentration and amount of signal.

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**Y Y Y Y Y Y Y Y Y Y**

**ANTIBODY**
Competitive immunoassay

Exogenously added, labelled hormone

% Binding of radioactivity

Endogenous hormone in the sample
### Sample reference data

#### Menstrual cycle

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Follicular</th>
<th>Ovulatory</th>
<th>Luteal</th>
<th>Menopause</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FSH (mIU/mL)</strong></td>
<td>2 - 11</td>
<td>5 - 21</td>
<td>1 - 9</td>
<td>22-153</td>
</tr>
<tr>
<td><strong>LH (mIU/mL)</strong></td>
<td>1 - 12</td>
<td>17 – 77</td>
<td>&lt; 0.1 - 15</td>
<td>11 – 40</td>
</tr>
<tr>
<td><strong>Estradiol (pg/ml)</strong></td>
<td>&lt; 20 - 266</td>
<td>118 - 355</td>
<td>26 - 165</td>
<td>&lt; 30</td>
</tr>
<tr>
<td>X 3.67 = pmol/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Progesterone (ng/mL)</strong></td>
<td>&lt; 0.2 - 1</td>
<td>—</td>
<td>0.9 - 25</td>
<td>&lt; 0.2 – 1</td>
</tr>
<tr>
<td>X 3.18 = nmol/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Inhibin A (pg/ml)</strong></td>
<td></td>
<td>10 - 160</td>
<td>&gt; 100</td>
<td>&lt; 10</td>
</tr>
<tr>
<td><strong>Inhibin B (pg/ml)</strong></td>
<td>16 - 290</td>
<td>&gt; 200</td>
<td>&gt; 150</td>
<td>&lt; 16</td>
</tr>
</tbody>
</table>

Women and Infants Hospital
Hormone monitoring for fertility treatment

- 37 year old woman with history of infertility
- History of irregular menstrual cycles and infertility
- Normal anatomy
- Treated with **high dose exogenous** FSH to stimulate ovaries

**Serial estradiol levels (pg/mL)**

<table>
<thead>
<tr>
<th>Day</th>
<th>Level (pg/mL)</th>
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<tr>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>318</td>
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- What do these results indicate?
- Does this woman have a good chance of pregnancy success?
37 year old woman with history of infertility
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**What do these results indicate?** About 10-12 follicles have developed
**Does this woman have a good chance of pregnancy success?** YES!
Hormones in Pregnancy

Fetal-placental unit

www.merckmanuals.com
Placental hormones

- Human chorionic gonadotropin
- Estradiol
- Progesterone

Graph showing plasma hormone concentration over months since start of last menstrual period.
Sample reference data
hCG in pregnancy

<table>
<thead>
<tr>
<th>Weeks from conception</th>
<th>hCG (mIU/mL)</th>
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<tbody>
<tr>
<td>1</td>
<td>20 - 60</td>
</tr>
<tr>
<td>2</td>
<td>60 - 200</td>
</tr>
<tr>
<td>3</td>
<td>200 - 2,000</td>
</tr>
<tr>
<td>4</td>
<td>2,000 - 20,000</td>
</tr>
<tr>
<td>5-12</td>
<td>20,000 - 320,000</td>
</tr>
<tr>
<td>2\textsuperscript{nd} trimester</td>
<td>20,000 - 60,000</td>
</tr>
<tr>
<td>3\textsuperscript{rd} trimester</td>
<td>800 - 30,000</td>
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Women and Infants Hospital
Monitoring pregnancy viability

- 30 year old woman
- Pregnant by home urine test
- Presents with some vaginal bleeding at ER
- Gestational age estimate = 4 weeks

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- *Is this a viable pregnancy?*
Monitoring pregnancy viability

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<tr>
<td></td>
<td>3,000</td>
<td>4,720</td>
<td>7,590</td>
</tr>
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</table>

- Is this a viable pregnancy? YES!

hCG should rise by a minimum of 53% every 48 hours in early pregnancy

Barnhart et al., Obstet Gynecol, 2004
Progesterone in pregnancy

Yen and Jaffe, Reproductive Endocrinology, 1991
Estrogens in pregnancy

Estriol synthesis in pregnancy

- **MOTHER**
  - Cholesterol (LDL) → Progesterone → Estradiol → Estrone
  - Conjugation to E-sulfates and E-glucuronides followed by excretion

- **PLACENTA**
  - uE3 → Sulfatase Aromatase → 16α-OHDHEAS

- **FETUS**
  - Cholesterol (LDL) → ADRENAL → DHEA sulfate → LIVER → 16α-OHDHEAS

- uE3 secretion
Summary

Female reproductive hormones...

- Vary with menstrual cycle day, pregnancy and menopause
- Require samples timed to cycle day and clinical information for proper interpretation
- Are useful tools to evaluate fertility and pregnancy health