GH testing
- Effects of obesity on GH

• Confounding effect

• False positive results

• Morbid obesity suppresses GH release

• Different thresholds be used

• Peak response to Arginine + GHRH is 70 µgm/l in normal vs 18 µgm/l in obese
Hypothalamic – pituitary – adrenal axis
- Caution regarding all tests

• None (including ITT) classify all patients correctly

• Mild deficiencies missed

• Healthy subjects may fail tests

• Clinical judgement important
Pituitary – gonadal axis - Clomiphene testing

- Clomiphene is a SERM
- Mechanism:
  Weak estrogen receptor antagonist at hypothalamus (↑ LH & FSH)
  +
  estrogen agonist action in liver (↑ SHBG)
  ↓
  total testosterone or oestradiol

- total testosterone & oestradiol does not indicate increased gonadotropin release
- In normal women, gonadotropins double by 10 days & menstruation indicates a positive clomiphene test
- Normal response indicates that pit-gonadal axis is intact & problem at level of hypothalamus
- Contraindicated in liver disease, depression & cause alteration in peripheral vision
- Stress or exercise induced amenorrhoea can cause normal or absent response
Prolactin

- Normal range in men: < 300 mu/l
- Normal range in non-pregnant: < 500 mu/l
- Normal range in pregnant: > 8000 mu/l
- Dopamine receptor antagonists: > 5000 mu/l

- Molecular forms: identified by gel chromatography

<table>
<thead>
<tr>
<th>Molecular Form</th>
<th>Molecular Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monomeric PRL</td>
<td>23 KDa</td>
</tr>
<tr>
<td>Big PRL</td>
<td>50 – 60 KDa</td>
</tr>
<tr>
<td>Big – big PRL (macroprolactin)</td>
<td>150 – 170 KDa</td>
</tr>
</tbody>
</table>
Prolactin
- Macroprolactin

• Complex of PRL + IgG
• Little bioactivity
• In 25% hyperprolactinaemic sera
• In 1% of normal population
• Many don’t have symptoms
• Confirmed by Polyethlene Glycol precipitation & repeat assay of treated serum gives residual monomeric PRL levels
• No need to investigate further

• PRL Hook effect:
  - PRL Ag’s in prolactinoms’s cause saturation in the assays → artefactual low PRL levels
  - misdiagnosis
Hypothalamic DI (HDI) - Dynamic testing (water deprivation test – DDAVP)

- Assesses capacity to concentrate urine
- After dehydration in HDI
  - Urine osmolality $\rightarrow < 300$ mOsml/kg
  - Plasma osmolality $\rightarrow > 290$ mOsml/kg
- After DDAVP:

<table>
<thead>
<tr>
<th>Urine osmolality</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>$&gt; 750$ mOsml/kg</td>
<td>HDI</td>
</tr>
<tr>
<td>$&lt; 300$ mOsml/kg</td>
<td>Nephrogenic DI</td>
</tr>
<tr>
<td>DDI</td>
<td>Normal urine concentration during dehydration</td>
</tr>
<tr>
<td></td>
<td>No significant rise in plasma osmolality</td>
</tr>
</tbody>
</table>

Box 2.2.2 Protocol for water deprivation/desmopressin test

**Preparation**
- Free access to fluid given overnight prior to test
- Avoid caffeine and smoking
- 0750 h—weigh patient

**Dehydration phase**
- 0800—plasma and urine osmolality, and urine volume
- Restrict fluids up to 8 h
- Weigh patient at 2-h intervals
- Plasma and urine osmolality, and volume measurements 2 hourly
- Stop test if weight loss exceeds 5% of starting weight, or thirst is intolerable
- Supervise patient closely to avoid non-disclosed drinking

**Desmopressin phase**
- Inject intramuscularly 1 μg desmopressin
- Allow patient to eat and drink up to 1.5–2.0 times the volume of urine passed during dehydration phase
- Collect urine for osmolality and volume at 2000 h
- Plasma and urine osmolality, and volume measurements at 0900 h next day