Endocrinology in General Practice

Miles Levy
Consultant Endocrinologist
Leicester Royal Infirmary
Nottingham GP Refresher Day 16th March 2015
Aim of session

• Common scenarios in endocrinology
• Things you are likely to see in GP
• Interpretation of blood results
• Tips and potential pitfalls
Topics

• Low testosterone in man
• Female endocrinology
• Abnormal calcium levels
• Approach to low sodium
Case 1

- 53 year old man
- Stress at work
- Erectile dysfunction
- Low libido
- Fatigue
Case 1

- Type 2 diabetes
- No medication
- BMI 32 kg/m²
- Examination normal
Investigations

- HbA1c: 7.5%
- U&E: Normal
- FBC: Normal
- Testosterone: 8.0 nmol/l
What would you do now?
GnRH / prolactin axis
LH / FSH action on testes
### Differential diagnosis

- Gonadotropin deficiency
- Borderline low testosterone
- This is not primary gonadal failure

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testosterone (Testo)</td>
<td>8.0 nmol/l</td>
</tr>
<tr>
<td>LH</td>
<td>1.2 miu/l</td>
</tr>
<tr>
<td>FSH</td>
<td>0.9 miu/l</td>
</tr>
<tr>
<td>Prl</td>
<td>250 miU/l</td>
</tr>
</tbody>
</table>
Differential diagnosis

- Gonadotropin deficiency
- Borderline low testosterone
- This is primary gonadal failure

- Testo 8.0 nmol/l
- LH 48 miu/l
- FSH 60 miu/l
- Prl 250 miU/l
Primary hypogonadism

- Low testosterone
- Raised LH/FSH
- Klinefelters (47 XXY)
- Cryptorchidism
- Orchitis
- Cirrhosis
- Bilateral torsion
- Chemo / radiotherapy
Primary hypogonadism

- Low testosterone
- Raised LH/FSH
- Klinefelters (47 XXY)
- Cryptorchidism
- Orchitis
- Cirrhosis
- Bilateral torsion
- Chemo / radiotherapy
Gonadotropin deficiency

• Hypothalamic / pituitary cause
  • Low am testosterone
  • Normal or low FSH/LH
Gonadotropin deficiency

- Hypothalamic / pituitary cause
  - Low am testosterone
  - Normal or low FSH/LH
Causes gonadotropin deficiency

- Pituitary disease
- Kallman’s syndrome
- Hypogonadotrophic hypogonadism
- Anabolic steroids
Pituitary tumour

- Visual field defect
- Prolactin
- 0900 cortisol
- fT4, TSH
Prolactinoma

- Visual field defect
- Prolactin 55,500 miU/l
- 0900 cortisol
- fT4, TSH
Prolactinoma

- Visual field defect
- Prolactin 55,500 miU/l
- 0900 cortisol
- fT4, TSH
- Medical treatment
- Dopamine agonist
Acromegaly

- Visual field defect
- Prolactin
- 0900 cortisol
- fT4, TSH
Cushing’s syndrome

- Visual field defect
- Prolactin
- 0900 cortisol
- fT4, TSH
Low testosterone early feature of pituitary tumours
Differential diagnosis

- Gonadotropin deficiency
- Borderline low testosterone
- This is not primary gonadal failure

- Testo 8.0 nmol/l
- LH 1.2 miu/l
- FSH 0.9 miu/l
- Prl 250 miU/l
Differential diagnosis

- Gonadotropin deficiency
- Borderline low testosterone
- This is not primary gonadal failure

Can be indistinguishable from a pituitary tumour in terms of clinical presentation and these blood tests

- Testo: 8.0 nmol/l
- LH: 1.2 miu/l
- FSH: 0.9 miu/l
- Prl: 250 miU/l
Borderline low testosterone

- A common ‘disease’ of modern age
- Explosion in prescribing of testosterone
- Some concern amongst endocrinologists
- Measurement of testosterone has problems as free hormone not assayed
A low SHBG will give a low total testosterone result but the free hormone may be normal.
Low SHBG strongly associated with insulin resistance
Apple shape the problem
Pear shape not the problem
Free hormone is difficult to measure and calculate.
Pragmatically

• If symptoms of androgen deficiency then measure testosterone
• If testosterone < 8 nmol/l then consider replacement
• Explain to patient if you think related to lifestyle and SHBG / insulin resistance
• Decide for yourself if you want to investigate further
My approach

• Pituitary hormone screen (fT4, prl, 0900am cortisol or synacthen test)
• I usually feel bad if I don’t MRI pituitary
• 3 month trial of testosterone gel
• If dramatic response patients normally keen to continue long term
• Can break the vicious cycle of lifestyle
Testosterone options
Long term monitoring

- Polycythaemia
- Prostate (PSA)
- Long term safety not clear
Case 2

- 26 year old lady
- Irregular periods
- 2 stone weight gain
- Increased facial hair
- Generally fed up
Case 2

• BP 140/95 mmHg
• BMI 30 kg/m²
• Mild facial hirsutism
• No other findings
Investigations

- fT4 15 pmol/l
- TSH 3.5 miU/l
- Testosterone 3.9 nmol/l
- LH 2.5 miU/l
- FSH 3.0 miU/l
Further things to look for in history and examination
Gynae endocrine history

- Typical menstrual cycle
- Speed of onset of hirsutism
- Any changes in body shape
- Clear or milky discharge from nipple
- Consanguinity of parents
- Fertility history
Gynae endocrine examination

- Body Mass Index
- Blood pressure
- Cushingoid habitus
- Insulin resistance
- Androgenic alopecia
- Severity of hirsutism
Gynae endocrine examination

- Body Mass Index
- Blood pressure
- Cushingoid habitus
- Insulin resistance
- Androgenic alopecia
- Severity of hirsutism
- Galactorrhoea
Further gynae endocrine blood tests
Measure LH / FSH follicular phase
Progesterone luteal phase

Luteal phase
Effect of LH and FSH on Ovary
Differential diagnosis in our case

- Idiopathic hirsutism
- Polycystic ovaries
- Cushing’s syndrome

- Testo 3.9 nmol/l
- LH 2.5 miU/l
- FSH 3.0 miU/l
### Differential diagnosis in our case

- **Idiopathic hirsutism**
- **Polycystic ovaries**
- **Cushing’s syndrome**
- **Not ovarian failure**

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testo</td>
<td>3.9 nmol/l</td>
</tr>
<tr>
<td>LH</td>
<td>50 miU/l</td>
</tr>
<tr>
<td>FSH</td>
<td>60 miU/l</td>
</tr>
<tr>
<td>E2</td>
<td>&lt; 70</td>
</tr>
</tbody>
</table>
Differential diagnosis in our case

- Idiopathic hirsutism
- Polycystic ovaries
- Cushing’s syndrome
- Not ovarian failure
- Turner’s (45 XO)
- Fragile X (autism)
- Auto-immune
- Chemo / radio Rx
Turner’s Syndrome

Short Stature and Primary Amenorrhoea
Differential diagnosis in our case

- Testo 3.9 nmol/l
- LH 2.5 miU/l
- FSH 3.0 miU/l
Differential diagnosis in our case

- Idiopathic hirsutism
- Polycystic ovaries
- Cushing’s syndrome

- Testo 3.9 nmol/l
- LH 2.5 miU/l
- FSH 3.0 miU/l
Secondary virilisation

- Idiopathic hirsutism
- Polycystic ovaries
- Cushing’s syndrome
- Unlikely to be secondary virilisation

- CAH
- Ovarian tumour
- Adrenal tumour
- Imaging or venous sampling
- Post menopausal
Definition PCOS

Patients presenting with two or more:

- oligo & / or amenorrhoea
- clinical & / or biochemical signs of hyperandrogenism
- USS evidence of polycystic ovaries
PCOS ultrasound definition

- Transvaginal scan
- Scan should be day 3-5 of cycle / after withdrawal bleed
- 12 or more follicles each ovary 2-9mm diameter and / or increased ovarian volume greater than 10mls
- Only one ovary
Full shopping list of gynae endocrine blood tests

- LH/FSH
- Prolactin
- Androstenedione
- 17- hydroxy progesterone
- TFTs
- Fasting glucose
- Testosterone
- U&Es & LFTs
- DHEAS
- SHBG
Management of PCOS
Management of PCOS

Treat the presenting symptom
Different concerns

- Cosmetic aspects
- Irregular periods
- Fertility prospects
- Long term risks
Management of PCOS

oligomenorrhoea

- Fertility currently required?
  - yes
  - no

hirsuit?

- refer to fertility clinic
- OCP contraindicated?
  - yes
  - no

Dianette

Consider:
- Spironolactone 100mg o.d.
- "VANIQA" (eflornithine hydrochloride) topical preparation. Currently via GP, as unavailable in Pharmacy.
- Cyproterone Acetate (finasteride) - UNLICENSED use. 5mg o.d. max 1yr. regular check of LFTs.

• cyclical progesterone
• POP
• Mirena
• Implanon

• OCP
Body Mass Index and PCOS

Insulin resistance
Long terms problems with PCOS

- Gestational diabetes
- Type 2 diabetes / metabolic syndrome
- Cardiovascular disease

Mani et al. Clinical Endocrinology 2012
Treatment approaches

- Lifestyle intervention
- Structured education
- Metformin
- Think of PCOS as pre-diabetic state
Case 3

- 53 year old lady
- General malaise
- No get up and go
- A bit achy
- Not feeling herself
Case 3

• Treated hypertension
• Amlodipine 10mg
• BMI 30 kg/m²
• BP 130 / 70 mmHg
• Examination normal
Investigations

- U&E  normal
- FBC  normal
- TFTs normal
- Ca  2.76 mmol/l (2.2-2.6)
- ALP  normal
- LFTs normal
Diagnosis

- Primary hyperparathyroidism
- Vitamin D deficiency
- This does not look like hypercalcaemia of malignancy

Ca 2.76 mmol/l
- PTH 12 pmol/l
- Vitamin D <15 nmol/l
Hypercalcaemia and low PTH

• Primary hyperparathyroidism
• Vitamin D deficiency

• Malignancy
• Granulomatous disease
When PTH high you can relax a bit

- Primary hyperparathyroidism
- Vitamin D deficiency

- Ca 2.76 mmol/l
- PTH 12 pmol/l
- Vitamin D <15 nmol/l

Would you replace vitamin D or would that worsen the hypercalcaemia?
Vitamin D and primary hyperparathyroidism

- If vitamin D deficient then replace
- Calcium normally does not go up much
- Initial symptoms may improve
- Protection against osteoporosis
- 1,000 Units of colecalciferol / day
Primary hyperparathyroidism

- Usually single benign adenoma
- In the right hands a radiologist will pick up with USS
- Isotope scan may be needed to confirm location
When to think about parathyroidectomy

- Ca > 2.85 mmol/l
- Renal stones
- Reduced BMD
- Patient unhappy with symptoms

Cinacalcet is a drug that lowers PTH and calcium
Tips and pitfalls with primary hyperparathyroidism

- Check urine calcium:creatinine to exclude Familial Hypocalciuric Hypercalcaemia
- If young or recurrent hyperparathyroidism then consider genetic causes (MEN1)
- If elderly and frail simple rehydration may improve the hypercalcaemia
Calcium problems - look at phosphate

- Low phosphate indicates high PTH
- Low calcium and low phosphate high PTH
- High calcium and low phosphate high PTH
- Low calcium and high phosphate low PTH
Case 4

- 65 year old woman
- Seen by your colleague
- Not many clinical details
- Generally not herself
- More tired than usual
### Blood results

<table>
<thead>
<tr>
<th>Test</th>
<th>Result (Unit)</th>
<th>Reference Range (Unit)</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>127 mmol/L</td>
<td>(133 to 146) Auth</td>
<td></td>
</tr>
<tr>
<td>Potassium</td>
<td>3.8 mmol/L</td>
<td>(3.5 to 5.3) Auth</td>
<td></td>
</tr>
<tr>
<td>Urea</td>
<td>3.6 mmol/L</td>
<td>(2.5 to 7.8) Auth</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>49 umol/L</td>
<td>(60 to 120) Auth</td>
<td></td>
</tr>
<tr>
<td>eGFR (MDRD)</td>
<td>&gt;90 mL/min</td>
<td></td>
<td>Auth</td>
</tr>
</tbody>
</table>

**Comments:**
- Multiply eGFR by 1.21 if Afro-Caribbean.
- See [www.emrn.org.uk](http://www.emrn.org.uk) website.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result (Unit)</th>
<th>Reference Range (Unit)</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>41 g/L</td>
<td>(35 to 50) Auth</td>
<td></td>
</tr>
<tr>
<td>Alkaline Phosphatase</td>
<td>65 iu/L</td>
<td>(30 to 130) Auth</td>
<td></td>
</tr>
<tr>
<td>Alanine Transaminase(ALT)</td>
<td>23 iu/L</td>
<td>(2 to 53) Auth</td>
<td></td>
</tr>
<tr>
<td>Total Bilirubin</td>
<td>16 umol/L</td>
<td>(0 to 21) Auth</td>
<td></td>
</tr>
<tr>
<td>C-Reactive Protein</td>
<td>17 mg/L</td>
<td>(0 to 10) Auth</td>
<td></td>
</tr>
<tr>
<td>White Cell Count</td>
<td>7.9 x10^9/L</td>
<td>(4.0 to 11.0) Auth</td>
<td></td>
</tr>
<tr>
<td>Red Blood Count</td>
<td>4.28 x10^12/L</td>
<td>(3.90 to 5.60) Auth</td>
<td></td>
</tr>
</tbody>
</table>
Is this a cause for concern and how would you approach it?
Approach to hyponatraemia

• Requires a systematic approach
• Need all the biochemical results
• Always has an explanation
• Generally done badly
Questions to ask

• Is there a clinical concern?
• Is the low sodium new or old?
• Is the patient on a thiazide diuretic?
• Has there been a recent acute illness?
• Known CCF, liver or kidney disease?
### Causes of hyponatraemia

<table>
<thead>
<tr>
<th>Volume Status</th>
<th>Clinical Signs</th>
<th>Urine Na &lt; 20</th>
<th>Urine Na &gt; 40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypovolaemic</td>
<td>Dehydration</td>
<td>GI loss</td>
<td>Diuretics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mucosal loss</td>
<td>Addison’s</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pancreatitis</td>
<td></td>
</tr>
<tr>
<td>Euvolaemic</td>
<td>Disease specific</td>
<td>Hypothyroidism</td>
<td>SiADH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1° polydipsia</td>
<td>ACTH deficiency</td>
</tr>
<tr>
<td>Hypervolaemic</td>
<td>Fluid overload</td>
<td>CCF</td>
<td>CCF on</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nephrotic Cirrhosis</td>
<td>diuretics</td>
</tr>
</tbody>
</table>
Addison’s Disease

Pigmentation, Postural Hypotension, Hyperkalaemia
## Causes of hyponatraemia

<table>
<thead>
<tr>
<th>Volume Status</th>
<th>Clinical Signs</th>
<th>Urine Na &lt; 20</th>
<th>Urine Na &gt; 40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypovolaemic</td>
<td>Dehydration</td>
<td>GI loss</td>
<td>Diuretics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mucosal loss</td>
<td>Addison’s</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pancreatitis</td>
<td></td>
</tr>
<tr>
<td>Euvolaemic</td>
<td>Disease specific</td>
<td>Hypothyroidism</td>
<td>SiADH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1º polydipsia</td>
<td>ACTH deficiency</td>
</tr>
<tr>
<td>Hypervolaemic</td>
<td>Fluid overload</td>
<td>CCF</td>
<td>CCF on</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nephrotic Cirrhosis</td>
<td>diuretics</td>
</tr>
</tbody>
</table>

If history of CCF, Nephrotic Syndrome or Cirrhosis then leave to specialist
Investigations required

- Serum osmolality
- Urine osmolality
- Urine sodium
- Thyroid function
- 0900 cortisol or synacthen
Primary polydipsia

- Serum osmolality: Low
- Urine osmolality: Low
- Urine sodium: Low
- Thyroid function: Normal
- 0900 cortisol or synacthen: Normal
Primary polydipsia

- Serum osmolality: Low
- Urine osmolality: Low
- Urine sodium: Low
- Thyroid function: Normal
- 0900 cortisol or synacthen: Normal

The history will usually be obvious if high fluid intake
SIADH

- Serum osmolality: Low
- Urine osmolality: High
- Urine sodium: Normal
- Thyroid function: Normal
- 0900 cortisol or synacthen: Normal
ACTH deficiency

- Serum osmolality: Low
- Urine osmolality: High
- Urine sodium: Normal
- Thyroid function: Normal
- 0900 cortisol or synacthen: Low
Our patient

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Osmolality</td>
<td>256 mmol/kg</td>
<td>(275 to 295)</td>
</tr>
<tr>
<td>Free Thyroxine</td>
<td>9 pmol/L</td>
<td>(9.0 to 25.0)</td>
</tr>
<tr>
<td>Thyroid Stimulating Hormone</td>
<td>3.7 mIU/L</td>
<td>(0.30 to 5.00)</td>
</tr>
<tr>
<td>Urine Osmolality</td>
<td>498 mosmol/Kg</td>
<td>Auth</td>
</tr>
<tr>
<td>Urine Sodium</td>
<td>126 mmol/L</td>
<td>Auth</td>
</tr>
<tr>
<td>Cortisol</td>
<td>500 nmol/L</td>
<td>Auth</td>
</tr>
</tbody>
</table>

Comments:
Borderline cortisol response to synacthen. Expected 30 min response is cortisol >500, 400-500 borderline.
Further investigations

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Reference Range</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free Thyroxine</td>
<td>10 pmol/L</td>
<td>(9.0 to 25.0) pmol/L</td>
<td>Auth</td>
</tr>
<tr>
<td>Thyroid Stimulating Hormone</td>
<td>4.4 miu/L</td>
<td>(0.30 to 5.00) miu/L</td>
<td>Auth</td>
</tr>
<tr>
<td>Luteinising hormone (LH)</td>
<td>1 iu/L</td>
<td></td>
<td>Auth</td>
</tr>
<tr>
<td>Follicle stimulating hormone</td>
<td>2.4 iu/L</td>
<td></td>
<td>Auth</td>
</tr>
<tr>
<td>Prolactin</td>
<td>1407 miu/L</td>
<td>(50 to 400) miu/L</td>
<td>Auth</td>
</tr>
</tbody>
</table>

**Comments:**
Macroprolactin NOT detected at a significant level.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Reference Range</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Growth Hormone</td>
<td>1.3 ug/L</td>
<td></td>
<td>Auth</td>
</tr>
<tr>
<td>IGF1</td>
<td>32 ug/L</td>
<td>(59 to 177) ug/L</td>
<td>Auth</td>
</tr>
<tr>
<td>17-Beta Oestradiol</td>
<td>&lt;70 pmol/L</td>
<td></td>
<td>Auth</td>
</tr>
</tbody>
</table>
Pituitary macro-adenoma

Dramatic improvement with hydrocortisone
SIADH

- A very common cause of hyponatraemia
- Important to consider malignancy
- Many causes including idiopathic
- Requires full investigation
- Drugs common cause
## Causes of SiADH

<table>
<thead>
<tr>
<th>Cause of SiADH</th>
<th>Common ones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignancy</td>
<td>Lung</td>
</tr>
<tr>
<td></td>
<td>Lymphoma</td>
</tr>
<tr>
<td></td>
<td>GI / pancreas</td>
</tr>
<tr>
<td></td>
<td>GU malignancy</td>
</tr>
<tr>
<td>Drugs</td>
<td>SSRIs</td>
</tr>
<tr>
<td></td>
<td>Tricyclics</td>
</tr>
<tr>
<td></td>
<td>Anticonvulsants</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Pneumonia</td>
</tr>
<tr>
<td></td>
<td>TB</td>
</tr>
<tr>
<td></td>
<td>Abscess</td>
</tr>
<tr>
<td>CNS</td>
<td>Malignancy</td>
</tr>
<tr>
<td></td>
<td>Infection</td>
</tr>
<tr>
<td></td>
<td>Trauma</td>
</tr>
<tr>
<td></td>
<td>Haemorrhage</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Idiopathic</td>
</tr>
<tr>
<td></td>
<td>HIV / MS / Guillain Barre / AIP</td>
</tr>
</tbody>
</table>
Treatment of SIADH

- Cause specific treatment
- Fluid restriction
- Drugs
Treatment of SIADH

• Cause specific treatment
• Fluid restriction
• Drugs Demeclocycline
Treatment of SIADH

• Cause specific treatment
• Fluid restriction
• Drugs Tolvaptan
Summary

• Common scenarios in endocrinology
• Things you are likely to see in GP
• Interpretation of blood results
• Tips and potential pitfalls
Summary

• Low testosterone in man
• Female endocrinology
• Abnormal calcium levels
• Approach to low sodium
The End

miles.j.levy@uhl-tr.nhs.uk