Endocrinology for the FRCA

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Why??

- Basic physiology
- Many actions
- Various organ systems
- Simple and complex

- Easy to examine on

- Mammoth topic so it will be brief (!)
- Please be interactive!
Curriculum

- Structure and function of the endocrine system
- Endocrine abnormalities of significance to anaesthesia
  - Eg, Cushing’s, Addisons
  - DM
  - Hypothyroidism
  - Hypopituitarism
  - Phaeochromocytoma
- The stress response
- Also - acromegaly
Definitions

- **Endocrine system**: Network of anatomically and embryologically discrete glands
- **Hormone**: a chemical released by a cell that has a biological action on a target cell
  - Can be proteins, amines or steroids
  - Homeostasis dependent on 3 factors
    - Rate of production and release of active hormone
    - Rate of removal
    - End-organ sensitivity
  - (Also consider MOA)
## Hormones

<table>
<thead>
<tr>
<th></th>
<th>Peptide</th>
<th>Steroid</th>
<th>Amino acid derivative</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Synthesis</strong></td>
<td>Synthesised as <strong>prohormones</strong>, requiring further processing (e.g. cleavage) to activate</td>
<td>Synthesised in a series of reactions from <strong>cholesterol</strong></td>
<td>Synthesised from the amino acid <strong>tyrosine</strong></td>
</tr>
<tr>
<td><strong>Storage</strong></td>
<td>Stored in vesicles (regulatory secretion)</td>
<td>Released immediately (constitutive secretion)</td>
<td>Stored before release (storage mechanism varies)</td>
</tr>
<tr>
<td><strong>Solubility</strong></td>
<td>Most are polar and water soluble, can travel freely in the blood</td>
<td>Generally non-polar and require carrier proteins to travel in blood</td>
<td>Some are polar (adrenaline), others must be protein-bound</td>
</tr>
<tr>
<td><strong>Receptors</strong></td>
<td>Bind receptors on cell membrane and transduce signal via the use of second messenger systems</td>
<td>Bind to intracellular receptors to change gene expression directly</td>
<td>Adrenaline acts on membrane receptors, while thyroid hormones act directly on nuclear receptors</td>
</tr>
<tr>
<td><strong>Effects</strong></td>
<td>Often fast onset transient changes in protein activity, though gene expression changes can occur</td>
<td>Alterations in gene expression; slower onset but longer duration than peptide hormones</td>
<td>Adrenaline functions like peptides, thyroid hormones function in a similar manner to steroids</td>
</tr>
<tr>
<td><strong>Examples</strong></td>
<td>Insulin, glucagon, prolactin, ACTH, gastrin parathyroid hormone</td>
<td>Cortisol, aldosterone, estrogen, progesterone, testosterone</td>
<td>Adrenaline, thyroxin, triiodothyronine</td>
</tr>
</tbody>
</table>

*Note: The table above outlines the characteristics and examples of peptides, steroids, and amino acid derivatives.*
Structure of the endocrine system

- Hypothalamus
- Pituitary – HPA
- Pineal gland
  - Produces melatonin, helps to maintain circadian rhythm and regulate reproductive hormones
- Thyroid gland
- Parathyroids
- Thymus
  - Produces and secretes thymosin, for T cell development and production
Structure

- Adrenal gland
- Pancreas
- Gonads
Function

- Diverse group of cell types responsible for the secretion of chemicals within the body
- Main functions
  - Regulate body’s growth
  - Regulate metabolism
  - Regulate sexual development and function
- Also helps to maintain homeostasis
- Regulate response to stimuli – stress +/- injury
Hypothalamus

- Maintains homeostasis
  - ANS function
  - Temperature regulation
  - Fluid and electrolyte balance, including thirst
  - Appetite and body weight
  - Glandular secretions of the stomach and intestines
  - Sleep cycles
  - Key regulator of the pituitary
- Link between the endocrine and nervous systems
- Produces releasing and inhibiting hormones
Hypothalamic – Pituitary Axis

- Posterior pituitary – neurocrine
  - Releases...
- Anterior pituitary – true endocrine
  - Produces...
  - Special because...
    - capillary bed pools into another capillary bed through veins, without first going through the heart
Posterior pituitary

- **ADH**
  - Supra optic hypothalamic nuclei
  - Small molecule, short t1/2
  - Released in response to
    - Inc pl osmolality
    - Fall in BP/blood vol/CO
    - Standing
    - IPPV
    - Stress, n+v
    - Drugs
  - How does it work?
Posterior pituitary

- Oxytocin
  - Paraventricular hypothalamic nuclei
  - Contraction of the uterus, release of breast milk
  - Also regulation of body temp, and sleep cycle

- Similar structure to ADH, but no overlap in function
Anterior pituitary

- TRH – TSH
- TSH
  - Uptake of iodine
  - Synthesis of thyroid hormone
  - Release of thyroid hormones

- Actions?
Anterior pituitary

- CRH – ACTH
- ACTH release also induced by ADH
- Increased production and release of steroid hormones, particularly cortisol

Actions?
Anterior pituitary

- GHRH/Somatostatin – GH
- Actions
  - Anabolic
  - Metabolic – IGF, insulin
- Others Prl, LH, FSH
Hypopituitarism

- Adrenocortical insufficiency
  - Can be life threatening
  - Preserved renin-angiotensin system therefore electrolyte abnormalities less severe
- Hypothyroidism
  - Less severe than primary thyroid failure
- Diabetes insipidus
  - Failure of secretion of ADH
  - Rx desmopressin – longer t ½, no vasoconstrictor properties
- Hyperprolactinaemia due to loss of inhibitory control of dopamine
Acromegaly

- Macroadenoma, therefore also local mass effect
- Chronic, progressive, multisystem disease caused by an excess of growth hormone (GH) after puberty
- Typically well advanced at the time of diagnosis
- May have DM or other endocrine abnormalities
- Difficult airway/intubation, OSA (70%)
- Respiratory function may be compromised by kyphoscoliosis and proximal myopathy
Acromegaly

- Risk of intraop cardiac instability, and postoperative cardiorespiratory failure due to...
- Refractory HTN (+ pulm HTN) with eccentric LVH, IHD, arrhythmias, heart block, cardiomyopathy, and bi-ventricular dysfunction
- Difficult venous cannulation and increased risk of nerve entrapment syndromes – careful positioning
- Critical care post op (in an ideal world)
Cushing’s disease

- Microadenoma
- Excess of glucocorticoid due to hypersecretion of ACTH from a pituitary corticotroph adenoma
- Truncal obesity, moon facies and thin extremities
- Difficult airway due to obesity, increased incidence of OSA
- ‘Buffalo hump’ affects positioning on the operating table - airway management and surgical access
- Impaired resp function post op – proximal muscle wasting
- (Refractory) systemic hypertension +/- LVH and diastolic ventricular dysfunction
Cushing’s disease

- Glucose intolerance to established DM
- Increased incidence of peptic ulceration – caution with NSAIDs
- Friable skin and thin peripheral veins – difficult venous access + high risk of subsequent extravasation
- Central venous access is difficult due to cervical obesity and supraclavicular fat pads
- Increased risk of blood-borne infections with central access
- Osteoporotic joints – careful positioning, regional techniques may be more challenging
- Exophthalmos secondary to retro-orbital deposits of fat (seen in a third) - avoid corneal injury.
Adrenal gland

- Hormones medulla to cortex ‘ACAC’
- Cortex zones ‘GFR’
<table>
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<tr>
<th>Hormone</th>
<th>Syndrome</th>
<th>Features</th>
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<tbody>
<tr>
<td>Catecholamines</td>
<td>Phaeo</td>
<td>Hypertension, Flushing, abdominal cramps, palpitations headaches</td>
</tr>
<tr>
<td>Glucocorticoid excess</td>
<td>Cushing’s syndrome</td>
<td>Buffalo hump, Moon face, truncal obesity, abdominal striae, muscle weakness and wasting, hypertension, diabetes mellitus, hypokalaemia and metabolic alkalosis</td>
</tr>
<tr>
<td>Adrenocortical insufficiency</td>
<td>Addison’s disease</td>
<td>Skin pigmentation, Na+ depletion, fatigue, lethargy muscle weakness, low mood (mild depression) or irritability, loss of appetite and unintentional weight loss, hypotension</td>
</tr>
<tr>
<td>Mineralocorticoid excess</td>
<td>Conn’s syndrome</td>
<td>K + depletion, Na+ retention, polyuria and hypokalaemic alkalosis, hypertension, tetany and weakness.</td>
</tr>
<tr>
<td>Adrenal androgen excess</td>
<td>adrenogenital syndrome, CAH</td>
<td>In female: hirsutism, acne, oligomenorrhea &amp; virilisation. In male: precocious puberty</td>
</tr>
</tbody>
</table>
Cushing’s syndrome

- non-specific state of chronic glucocorticoid excess (regardless of cause)
  - Endogenous – adrenal adenoma
  - Exogenous – excess steroids
Cushing’s syndrome

- **C** - Central obesity, Cervical fat pads, Collagen fibre weakness, Comedones (acne)
- **U** - Urinary free cortisol and glucose increase
- **S** - Striae, Suppressed immunity
- **H** - Hypercortisolism, Hypertension, Hyperglycaemia, Hirsutism
- **I** - Iatrogenic (Increased administration of corticosteroids)
- **N** – Non-iatrogenic (Neoplasms)
- **G** - Glucose intolerance, Growth retardation
Addison’s disease

- Primary hypocortisolism
- Failure of the adrenal cortex due to an autoimmune process, infection or surgery
- Not usually apparent until over 90% of the adrenal cortex has been destroyed, so little adrenal capacity is left

Symptoms
- Fatigue/lethargy
- Muscle weakness
- Low mood/irritability
- Loss of appetite, unintentional weight loss
- Hypotension
- Poluria, increased thirst
- Hypoglycaemia
Phaeochromocytoma

- Tumour that arises in the adrenal medulla and secretes catecholamines
- Measure levels of metanephrine and normetanephrine
- Rule of 10% (4 things)
  - (Paroxysmal) Hypertension, or complications of HTN e.g. stroke, myocardial infarction
- Attacks of:
  - Palpitations
  - Pallor, flushing and sweating
  - Tremor
  - Headaches
  - Anxiety
  - Abdominal pain, nausea and/or vomiting
  - Weight loss
  - Constipation or diarrhoea
  - Glucose intolerance
The objectives of preoperative care include:
- BP control,
- reversal of chronic circulating volume depletion,
- heart rate and arrhythmia control,
- assessment and optimization of myocardial function,
- reversal of glucose and electrolyte disturbances

Intra op:
- avoid drug-induced catecholamine release,
- avoid catecholamine release induced by anaesthetic or surgical manoeuvres,
- minimize haemodynamic responses to tumour handling,
- treat episodes of hypotension

Can you tell me which drugs are used pre and intraop, and why?
Thyroid

- Iodination of tyrosine residues in thyroglobulin produces MIT and DIT
- These then couple to produce T3 and T4
- Can anyone tell us the function, potency and mode of action of the hormones?
Thyroid anatomy revision
Hyperthyroidism - storm

- High mortality from cardiac complications
- chronic, evolving thyrotoxic symptoms (commonly secondary to Graves’ disease), with a secondary insult driving the progression to thyroid storm.
- Infection precedes most cases, other triggers include trauma, surgery, pregnancy, MI, GI bleeding, and DKA
- Clinical features: hypermetabolic state, including pyrexia, tachycardia, GI disturbance, altered consciousness, and arrhythmias.
- Treatment aims are:
  - management of any precipitating illness,
  - inhibition of thyroid hormone synthesis and release,
  - to reduce conversion of $T_4$ to $T_3$,
  - to inhibit the peripheral effects of thyroid hormone, and
  - supportive critical care
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<th>DRUG</th>
<th>MECHANISM OF ACTION</th>
<th>SIDE EFFECTS</th>
</tr>
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<tr>
<td>Carbimazole</td>
<td>Prodrug rapidly converted to methimazole. Prevents synthesis of T3 and T4 by blocking oxidation of iodide to iodine and inhibiting thyroid peroxidase</td>
<td>Rashes, arthralgia, pruritis, myopathy. Bone marrow suppression Agranulocytosis (0.1%) Crosses placenta: foetal hypothyroidism</td>
</tr>
<tr>
<td>Propylthiouracil</td>
<td>Blocks iodination of tyrosine residues present in thyroglobulin. Inhibits conversion of T4 – T3</td>
<td>Thrombocytopenia, Aplastic anaemia, Agranulocytosis Hepatitis, nephritis, Crosses placenta: foetal hypothyroidism</td>
</tr>
<tr>
<td>Iodide/Iodine</td>
<td>Large doses of Iodide inhibit hormone production. Reduced the effect of TSH. Marked reduction in thyroid vascularity over 10-14days</td>
<td>Antithyroid effects diminish with time. Hypersensitivity reactions. Crosses placenta: foetal hypothyroidism</td>
</tr>
<tr>
<td>Propanolol</td>
<td>Controls sympathetic effects of thyrotoxic crisis. Blocks peripheral conversion of T4 to T3</td>
<td>Negative inotropy &amp; chronotropy. Bronchospasm Poor peripheral circulation. CNS effects</td>
</tr>
</tbody>
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Hypothyroidism

- Untreated, carries high mortality in anaesthesia/surgery
- Increased sensitivity to and reduced metabolism of all classes of anaesthetic drugs
- Emergence may be very prolonged
- Normal ventilatory responses to hypercapnia and hypoxia are obtunded
- Perioperative hypothermia is common
- Clinical response to thyroid replacement therapy may take 10 days
- Rapid correction with IV L-iodothyronine (T3), significant risk of precipitating myocardial ischaemia and heart failure.
References and useful articles

- Anaesthesia and pituitary disease
  - Menon et al, CEACCP Aug 2011
- Endocrine abnormalities in the critically ill 1
- Endocrine abnormalities in the critically ill 2
  - Kerr et al, BJA April 2017
- ATOTW – the adrenal glands
- Perioperative care of phaeochromocytoma
  - Connor, BJA Sept 2015
- Also [https://www.e-lfh.org.uk/](https://www.e-lfh.org.uk/)
Any Questions?