Learning Outcomes

In today’s topic you will learn:

- The structure and function of the endocrine system
- The clinical presentations, investigation procedures & some orthodox treatments of endocrine pathologies
Endocrine System

- The endocrine system coordinates the activity of organs through hormones - chemical messengers released into the blood from glands which produce them.

- Hormones have **specific target cells**, some far from where the hormone is produced, others effect cells of the same organ where they were released, or the same cell.

- **Hormones can be:**
  1. Peptides (proteins – water soluble): ie. Insulin
  2. Steroids: sex hormones
  3. Amino acid derivatives: adrenaline, thyroxine

- This structure determines if the hormone is is **water** or **lipid soluble**.
Homeostasis

- Two control systems ensure our survival by controlling **homeostasis** in two different ways.

<table>
<thead>
<tr>
<th>AUTONOMIC NERVOUS SYSTEM</th>
<th>ENDOCRINE SYSTEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid Change</td>
<td>Slower Change</td>
</tr>
<tr>
<td>Less Precise</td>
<td>More Precise</td>
</tr>
<tr>
<td>Shorter Duration</td>
<td>Longer Duration</td>
</tr>
<tr>
<td>Neurotransmitters</td>
<td>Hormones</td>
</tr>
<tr>
<td>Control centre: Central Nervous System</td>
<td>Control centre: Hypothalamus</td>
</tr>
</tbody>
</table>
Glands

There are 2 types of glands:

1. **EXOCRINE**
   - Excrete products into ducts leading to body cavities/organ/skin
   - **Examples:** Salivary glands (saliva), Gastric glands (digestive enzymes), Sebaceous glands (sebum), Mammary glands (breast milk).

2. **ENDOCRINE**
   - Ductless, secreting hormones directly into the blood through interstitial fluid or nearby target cells
   - **Examples:** Pituitary, Adrenals, Thyroid
Exocrine = via a duct

Endocrine = hormones secreted into blood

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Endocrine glands include:

- **Hypothalamus** (neuroendocrine gland)
- **Pituitary** (glandular & neuroendocrine)
- Pineal
- Thyroid
- Parathyroid
- Adrenal
- **Pancreatic: islets of Langerhans**
- Thymus
- Ovaries
- Testes
Endocrine Tissues

Some tissues of the body are not considered glands but have endocrine function (produce hormones):

- **Adipose tissue** - leptin (suppresses food intake) & resistin (blood glucose)
- **Heart** - atrial natriuretic peptide (blood pressure)
- **GIT**: stomach - ghrelin & gastrin (satiety & gastric emptying)
- **Liver** – angiotensinogen, Insulin-like growth factor (IGF), thrombopoietin.
- **Placenta** - human chorionic gonadotropin (hCG) & progesterone.
- **Kidneys** - erythropoietin (RBC production) & calcitriol (vitamin D).
- **Skin** – cholecalciferol (vit D).
Hormone activity: Receptors

- **Hormones have specific target cells**

- They influence the activity of the target cells by binding to specific receptors

- The receptors for protein based hormones are part of the plasma membrane, whilst lipid hormone receptors are within the cell

- Receptors can be made up of a number of different proteins

- Receptors allow hormones to have a **stimulating or inhibitory** effect on different cell-types
### Hormones

- The target cells can alter their sensitivity to the hormone:

<table>
<thead>
<tr>
<th>Down-regulation:</th>
<th>Up-regulation:</th>
</tr>
</thead>
<tbody>
<tr>
<td>If a hormone is present in excess, the number of target cell receptors may decrease</td>
<td>A deficiency in hormone causing an increase in the number of receptors on target cells</td>
</tr>
</tbody>
</table>

- **Example**: Hormone increase during puberty

- **Example**: Increased number of oxytocin receptors in third trimester of pregnancy
Hormone Regulation

Hormone secretions are regulated by:

1. Nervous system signals
2. Chemical changes in the blood
3. Other hormones

- Hormones interact to allow maximum flexibility in response to the environment.

- They are controlled through positive and negative feedback loops.
Endocrine System Control

- The hypothalamus is the ‘master’ endocrine gland. It controls the hormones released from the 2 lobes of the pituitary gland: anterior & posterior.

- The hypothalamus & pituitary glands represent the major link between Nervous and Endocrine systems.

- Together control almost entirely: Growth, development, metabolism and homeostasis.

- It is the control centre for important homeostatic reflexes, such as the thermoregulatory reflex and hunger reflex.

 thermo = temperature
regulatory = regulation
Hypothalamus

Releasing Hormones:

- **TRH** Thyroid releasing hormone
- **GHRH** Growth hormone releasing hormone
- **CRH** Corticotropin releasing hormone
- **PRH** Prolactin releasing hormone
- **GRH** Gonadotropin releasing hormone

Inhibiting Hormones:

- **GHIH** Growth hormone inhibiting hormone
- **PIH** Prolactin inhibiting hormone (Dopamine)
Pituitary gland

**Anterior**
- Receives hormones in blood capillaries from the hypothalamus.
- Releases the following hormones:
  - Growth hormone = Somatotropin
  - Thyroid stimulating hormone (TSH)
  - Follicle stimulating hormone (FSH)
  - Luteinizing hormone (LH)
  - Prolactin (PRL)
  - Adrenocorticotrophic hormone (ACTH)
  - Melanocyte stimulating hormones (MSH)
- Hormones synthesised in anterior pituitary

**Posterior**
- Hormones are synthesised in the hypothalamus
- Receives nerve impulses from the hypothalamus.
- Releases the following hormones:
  - Oxytocin
  - Antidiuretic hormone (ADH)

The hypothalamus & pituitary gland are connected by a stalk of nerve fibres and profuse network of capillaries called the hypothalamic pituitary portal system
Hypothalamus & Anterior Pituitary Hormones

- TRH: Thyroid releasing hormone
- GHRH: Growth hormone releasing hormone
- CRH: Corticotropin releasing hormone
- PRH: Prolactin releasing hormone
- GRH: Gonadotropin releasing hormone

- GHIH: Growth hormone inhibiting hormone
- PIH: Prolactin inhibiting hormone (Dopamine)

- TSH: Thyroid stimulating hormone
- hGH: Growth hormone
- ACTH: Adrenocorticotropin hormone
- PROLACTIN
- FSH: Follicle stimulating hormone
- LH: Luteinizing hormone

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<table>
<thead>
<tr>
<th>Hypothalamic Hormone/s</th>
<th>Anterior Pituitary Hormone</th>
<th>Target tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth Hormone Releasing Hormone (GHRH)</td>
<td>Growth Hormone (GH)</td>
<td>Most body tissues</td>
</tr>
<tr>
<td>Growth Hormone Inhibiting Hormone (GHIH)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid Releasing Hormone (TRH)</td>
<td>Thyroid Stimulating Hormone (TSH)</td>
<td>Thyroid Gland</td>
</tr>
<tr>
<td>Corticotropin Releasing Hormone (CRH)</td>
<td>Adrenocorticotropic Hormone (ACTH)</td>
<td>Adrenal Cortex</td>
</tr>
<tr>
<td>Prolactin Releasing Hormone (PRH)</td>
<td>Prolactin (PRL)</td>
<td>Breasts</td>
</tr>
<tr>
<td>Prolactin Inhibiting Hormone (PIH) - Dopamine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gonadotropin Releasing Hormone (GnRH)</td>
<td>Follicle Stimulating Hormone (FSH)</td>
<td>Ovaries &amp; Testes</td>
</tr>
<tr>
<td></td>
<td>Luteinizing Hormone (LH)</td>
<td></td>
</tr>
</tbody>
</table>
Growth Hormone (GH)

Also known as somatotropin.

**ACTIVITY:**
1. Regulates **metabolism** in many organs.
2. Stimulates release of insulin-like growth factors (IGF’s) in cells
3. **Promotes growth & division of most body cells** (especially bone & muscle).
4. Breaks down fats and glycogen

**INCREASED PRODUCTION:**
- Night time (sleep – stage 3,4)
- Hypoglycaemia
- Exercise
- Childhood & adolescence

hypo = low
glycaemia = blood sugar
**Thyroid Stimulating Hormone (TSH)**

**ACTIVITY:**
1. **Growth & activity of the thyroid gland:**
   Increasing thyroid hormone production - thyroxine (T4) & tri-iodothyronine (T3).

**PRODUCTION:**
- Lowest levels in the early evening & highest during the night.

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Adrenocorticotropic hormone (ACTH)

**ACTIVITY:**
1. Circadian rhythm (sleep / wake cycle)
2. Output of steroid hormones: glucocorticoids, especially cortisol.

**INCREASED PRODUCTION:**
- Hypoglycaemia
- Exercise
- **Stressors** such as emotions, fever
- Interleukin-1 (inflammatory response to infection)

**PRODUCTION:**
- Highest in the morning and lowest at midnight.
Prolactin (PRL)

**ACTIVITY:**
1. **Stimulates lactation:**
   prolactin + oxytocin = lactation
2. **Prevents pregnancy during lactation** (inhibits GnRH)
3. **Breast maturation** after childbirth. Differentiation & maturation of mammary glands in pregnancy

**PRODUCTION:**
- **After birth** (delivery of placenta)
- Suckling: more milk removed the more produced
- Emotional **stress** (prolactin promotes crying)
- Sleep
Follicle Stimulating Hormone (FSH) & Luteinizing Hormone (LH)

• **FSH:**
  - **Production of gametes** (sex cells)
  - Increase oestrogen production (F)
  - Maturation of ovarian follicles (F)
  - Stimulate testosterone production (M)
  - Sperm production (M)

• **LH**
  - **Triggers ovulation** & formation of corpus luteum (F)
  - Increase secretion of **progesterone** (F)
  - Stimulates secretion of **testosterone** (M)

**corpus luteum** = a hormone secreting structure that develops in an ovary following ovulation
Melanocyte Stimulating Hormone (MSH)

- Produced by the anterior pituitary in response to UV light.

- Role in skin, hair and eye pigmentation in humans.

- Can be excessively produced as part of some pathologies, such as the hyperpigmentation of skin seen in Addison’s disease.

- MSH and ACTH share the same precursor molecules.

**Melanin** = skin pigment

-cyte = cell
Oxytocin
POSTERIOR PITUITARY

ACTIVITY:
1. Contracts uterus in childbirth (parturition)
2. Contracts lactating breast
3. Bonding hormone (mother with baby): Social bonding, trust, skin contact, “cuddle hormone”

PRODUCTION:
• Suckling
• Childbirth (positive feedback)

• Emotional state: Fear or anxiety may inhibit release of oxytocin or milk let-down. Emotions can trigger oxytocin – just hearing baby’s cry can start lactation!

oxy = Latin for rapid
tocos = Latin for labour
• 2 weeks before birth baby drops to the bottom of the uterus

• Head engages lower wall of cervix

• Sensory neurons act as pressure receptors

• Send signals to hypothalamus

• Neurons release oxytocin into bloodstream

• Oxytocin causes more forceful contraction of the uterus

• Baby’s head engages head of cervix /pressure receptors … positive feed-forward cycle that builds up momentum
Lactation:

Takes 2-3 days for milk production to begin → first fluid is colostrum (water, lacto-sugar, antibodies)
Antidiuretic Hormone (ADH)

POSTERIOR PITUITARY

- Also known as vasopressin
- Hypothalamus monitors concentration of body fluid

**ACTIVITY:**

1. **Reduces urine output** by stimulating reabsorption of water in the kidneys.
2. **Vasoconstriction** in skin & abdominal organs to increase blood pressure

**PRODUCTION:**

- **Increased osmotic pressure**, hypovolaemia (reduced fluid intake, thirst, vomiting)

**INHIBITION:**

- Reduced osmotic pressure, increased fluid intake, **alcohol**.
Antidiuretic Hormone (ADH):

Video: Hypothalamus & Pituitary Recap: www.youtube.com/watch?v=TVhm2rBGhB0
Exercise:

• Fill in the blanks ……….

- CRH: Corticotropin releasing hormone
- PRH: Prolactin releasing hormone
- PIH: Prolactin inhibiting hormone aka __________
- GRH: Gonadotropin releasing hormone

hGH/Somatostatin

PROLACTIN
Summary Quiz!

1. How do cells alter their sensitivity to a hormone?
2. Define what is meant by a ‘hormone’
3. Where are hormones secreted by the posterior pituitary gland produced? What are the names of two these hormones?
4. Compare the two types of glands found in the body
5. What hormone stimulates the release of FSH and LH from the anterior pituitary gland?
6. What is the target tissue of the hormone Prolactin?
7. Give three functions of the hormone Oxytocin
8. How does ADH prevent fluid loss in the body?
Pituitary Gland Pathologies

• Usually caused by autoimmune disease or tumours causing either: **Hyper-secretion** or **Hypo-secretion**

• Signs & symptoms depend on the hormones affected.
Acromegaly & Gigantism

- **Gigantism**: Excess growth hormone while the bones are still developing (before the end of puberty) – results in the person growing to massive heights.

- **Acromegaly**: Excess growth hormone post-puberty (after growth plates closed). Excess growth of body tissues over time. Patient grows ‘outwards’ as opposed to ‘upwards’

**CAUSE:**
- A **pituitary tumour** causing hyper-secretion of growth hormone

**SIGNS & SYMPTOMS:**
- Large, prominent facial features, increased size hands & feet
- Tiredness, deep voice, impotence, joint pain, bone deformities, soft-tissue swellings
- **Gigantism**: giant-like features – whole body grows
Observe the following timeline. What do you notice?
Acromegaly & Gigantism

**TREATMENT:**
- **Surgery** to remove tumour. Lifelong medications may be needed

**ALTERNATIVE SUPPORT:**
- Treat/support cause. Nutrition, herbs, homeopathy, acupuncture

**COMPLICATIONS:**
- If left untreated can be serious, even fatal
- Hypertension, cardiomegaly
- Osteoarthritis, vertebral collapse (back pain), limbs need to bear excessive load
- Bowel polyps
- Type 2 diabetes
- Enlarged internal organs
- Shortened life-span

GH affects almost every organ system of the body
Hyperprolactinaemia

• Excess prolactin production

CAUSES:
• Pituitary tumour, acromegaly, pharmacologic (antipsychotics)

SIGNS & SYMPTOMS:
• Galactorrhoea
• Amenorrhoea (absence of menses)
• Decreased libido/sexual dysfunction
• Subfertility

ALTERNATIVE SUPPORT:
• Treat/support the cause. Herbs can help balance hormone levels. Nutrition, acupuncture, homeopathy.

hyper = elevated prolactinaemia = prolactin in blood

Galactorrhoea: Flow of milk from breast not associated with childbirth
Diabetes Insipidus

- Deficiency of ADH production or recognition causing the kidneys to over excrete water

**CAUSES:**
- **Cranial:** Brain trauma, tumour, encephalitis
- **Renal (Kidney):** Chronic kidney disease, hypercalcaemia (damages kidney), hypokalaemia, lithium (interferes with normal response to ADH)

**SIGNS & SYMPTOMS:**
- **Polydipsia** (extreme thirst) - large liquid consumption
- **Polyuria:** production of large volumes of *dilute* urine
- **Weight loss**
- \(\downarrow\) BP, syncope (hypovolaemia)

**Diabetes** = disease causing excess thirst and urination

**Insipid** = “bland”

**hypo** = low

**-kalaemia** = potassium

**polyuria** = increased urination

**polydipsia** = increased thirst
Diabetes Insipidus

DIAGNOSIS:
• 24 hr urine collection
• Urine specific gravity (urine = more concentrated)
• Blood biochemistry (↑Na)

TREATMENT:
• Treat cause
• ADH replacement
• Rehydration: water & electrolytes
• Alternative: Homeopathy, acupuncture.
Pineal Gland - Melatonin

- A small pea-sized gland in the midline of the brain regulated by the hypothalamus that produces melatonin
- Specialised photoreceptors in the retina detect light/darkness cues
- Levels are highest in children & decline with age.
- Stimulated by: night, darkness (retinal feedback)
- Reduced by: daylight, irregular sleep patterns (jetlag, night-shifts), some meds.

ACTIVITY:
- Contributes to the setting of the circadian rhythm: metabolic, physiological and behavioural alterations that follow a 24 hour rhythm.
- A potent antioxidant, DNA protective.

Made from serotonin.

Made from serotonin.

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Chronobiology (Cyclical physiological phenomenon):

- **Uric acid highest**: Midnight – 2am
- **Rhinitis**: 6-8am
- **Asthma**: 4-6am
- **Testosterone**: BP ↑ 8am – 12noon
- **Cortisol**: BP ↑ 8am – 12noon
- **Chrono** = time

Legend:
- TSH
- Leptin
- ADH
- Melatonin
- Ghrelin
- Prolactin (F)
- Insulin
- Adiponectin
Thymus gland - Thymosin

- A bi-lobed gland behind the sternum which plays an important role with **immune cells**.
- Atrophies after puberty (replaced by fibrous tissue)

**ACTIVITY:**
- Hormones produced by the thymus promote the **maturation of T cells** (immunity)
- Immature T cells migrate from the red bone marrow to the cortex of the thymus
Thyroid Gland

- A butterfly shaped gland inferior to the larynx.
- It has 2 lobes located on either side of the trachea.
- Influences **metabolic rate** (catabolic + anabolic).
- Important ‘growth hormone’ in early life.

### Follicular cells produce thyroid hormones:
- **Thyroxine (T₄):** has 4 iodine atoms.
- **Triiodothyronine (T₃):** has 3 iodine atoms.

- T₄ & T₃ are synthesised from tyrosine & iodine from a specialised thyroid protein called **thyroglobulin (Tg).**
- Follicular cells trap & store most of the bodies iodide via active transport from blood to cytosol.
Thyroid Gland
Histology:

• Follicular cells trap and store iodine

• Parafollicular cells (lie between follicles) secrete the hormone calcitonin (which lowers blood calcium levels)

• The follicles are filled with a fluid known as colloid that contains thyroglobulin.
Thyroid Hormones

• The major form of thyroid hormone in the blood is thyroxine (ratio of T₄ to T₃ is approx. 20:1)

• Selenium-containing enzymes are used in the conversion of T₄ to T₃.

• T₃ is the more biologically active form: 3 -4 times more potent than T₄.

• T₄ & T₃ are hydrophobic and require carrier proteins in the blood: thyroxine-binding globulin (TBG).

• This allows the body to maintain a stable pool of thyroid hormones from which the active, free hormones can be released when & where required.

• Thyroid hormone levels must therefore be measured in terms of free T₄ & T₃.

• Most body cells have receptors for thyroid hormones
Thyroid Hormones

ACTIVITY:
• **Increase metabolic rate & heat production.**
• Essential for normal **growth and development** and **CNS function.**
• Works in conjunction with adrenaline & noradrenaline, insulin & growth hormone.

PRODUCTION:
• **Stimulated by:** TSH, exercise, stress, malnutrition, low blood glucose, low $T_3$ to $T_4$.
• Reduced by: low TSH, high $T_3$
• Highest levels at night
• Higher levels during adolescence, pregnancy & female reproductive years.

[Image of thyroid gland with hypothalamus, anterior pituitary gland, negative feedback, thyroid-stimulating hormone (TSH), thyrotropin-releasing hormone (TRH), Thyroid hormones (T3 and T4), Increased metabolism, Growth and development, Increased catecholamine effect]
Thyroid Hormones:

- **TSH** is usually low in a regularly functioning Thyroid.
- Raised TSH levels indicate the thyroid is failing.

Low Plasma Glucose, Stress, Exercise, Sleep, Malnutrition
LAB TESTING:

1. **TSH Levels** (measure in morning)

2. **Free T\textsubscript{3} & T\textsubscript{4}** - unbound form of thyroid hormones are more bioavailable to target cells & tissues.

3. **Thyroglobulin (Tg)** - levels in the blood can be used as a tumour marker for certain kinds of thyroid cancer.

4. **Anti-thyroglobulin antibodies (TgAb)** - often found in patients with autoimmune thyroid disease (Hashimoto's or Graves’)

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Thyroid Hormones

Hypothyroidism

• A condition of thyroid hormone deficiency, common in the elderly.

CAUSES:
• Hashimoto’s thyroiditis (autoimmune)
• Iodine deficiency, thyroid destruction (radioactive iodine, surgery, medications, tumour)

SIGNS & SYMPTOMS:
• Tiredness, malaise, weight gain, cold intolerance, constipation, depression

• Slow cognitively, poor memory, low libido, deep voice, menstrual changes

• Muscle cramps/aches, arthralgia

• Signs: Goitre. Dry, brittle skin. Slow tendon reflexes, bradycardia, loss of lateral third of eyebrows, puffiness around the eyes (myxoedema). High TSH, low thyroid hormones
Hypothyroidism

ALLOPATHIC TREATMENT:
• Levothyroxine – thyroid hormone replacement

ALTERNATIVE SUPPORT:
• Treat the cause.
• Thyroid support: iodine, selenium, tyrosine, thyroid replacement therapy.
• Herbs to support thyroid. Herbs to support tumour or autoimmune condition.
• Homeopathy
Hyperthyroidism (Grave's disease)

- Hyperthyroidism is characterised by hyper-metabolism and elevated serum levels of free thyroid hormones (also known as thyrotoxicosis)
  - More common in women (10:1)

CAUSES:
- **Graves disease** (85%): Autoimmune. Increased IgG antibodies bind to TSH receptor and stimulate production of thyroid hormones.
  - Excessive iodine supplementation
  - Tumour (hypothalamic, pituitary)

*hyper = elevated thyroid = thyroid hormone*
Hyperthyroidism (Grave's disease)

**SIGNS & SYMPTOMS:**
- Nervousness, irritability, hyperactivity, unexplained weight loss, insomnia, palpitations, muscle weakness, frequent bowel and bladder movements, diarrhoea, fatigue
- Heat sensitivity, increased sweating
- **Signs:** Goitre, exophthalmos, tachycardia, tremor, brisk tendon reflex, lid lag

**COMPLICATIONS:**
- Thyrotoxic crisis: hyperthermia (> 40°C), tachycardia, heart failure.

**TREATMENT:**
- Drugs: Carbimazole, radioactive iodine, β-Blockers, surgery.
- **Alternative:** Treat cause. In the case of Grave’s disease herbs & nutritional supplements to restore immune system balance, homeopathy.

*exo- = external*  
*opthalmos = eyes*
Barnes Temperature Test

1. Prepare the thermometer before going to bed.

2. On waking, before getting out of bed, with as little movement as possible, place the thermometer under your arm.

3. Leave it in position for 10 minutes.

4. Test for 5 consecutive days and make a note of the 3 lowest readings. If menstruating do the test starting the second day of menses.

5. 36.6 - 36.8°C (97.8 - 98.2°F) is normal. **Below 36.6°C (97.8°F) is abnormal** and may indicate hypothyroidism. Seeing a GP is recommended.
Thyroid Gland – Calcitonin

- Produced by the parafollicular cells of the thyroid gland.
- Important during childhood for bone growth.
- Reduces blood calcium by:
  1. Inhibiting Ca reabsorption from the bone & kidneys
  2. inhibiting osteoclast activity (opposes parathyroid)

**PRODUCTION:**
- Stimulated by: increased blood Ca levels.
- Inhibited by: reduced blood Ca levels.
Parathyroid Glands

- Four small glands
- Partially embedded in **posterior surface** of lateral lobes of thyroid
- Produces **parathyroid hormone**.
Parathyroid Hormone (PTH)

- **Increases blood calcium** through the following mechanisms:

  1. **Increase osteoclast activity.**
  2. **Increase Ca/Mg reabsorption kidney.**
  3. **Increase production of calcitriol (active vit. D)** - which increases Ca & P absorption of the GIT.

- PTH release stimulated by reduced blood Ca levels and inhibited by increased blood Ca levels.

- Calcium is essential for **muscle contraction, nerve transmission, blood clotting.**
Parathyroid Hormone (PTH)
Hyperparathyroidism

• Hyperparathyroidism is characterised by elevated serum levels of parathyroid hormone (PTH) and improper calcium regulation.

CAUSES:
• Usually a tumour

SIGNS & SYMPTOMS: (Often no/few symptoms)
• Hypercalcaemia → increased risk of kidney stones, osteoporosis (or osteopenia), low energy, depression

• In some cases: nausea, vomiting, constipation, anorexia, muscle paralysis.

TREATMENT:
• Surgery to remove some or all of the parathyroid glands.

hyper = elevated
parathyroid = parathyroid hormone
Hypoparathyroidism

• Hypoparathyroidism is characterised by hypo-metabolism and reduced serum levels of parathyroid hormone (PTH).

CAUSES:
• Usually surgery or radiation (while treating thyroid).

SIGNS & SYMPTOMS:
• Hypocalcaemia → Muscle cramps & spasms (“tetany”), tingling lips, fingers and toes, dry hair, brittle nails, dry scaly skin, cataracts, weakened tooth enamel (in children).

TREATMENT:
• Calcium and vitamin D. Hormone replacement is being developed
• Alternative: Herbs & nutritional supplements – antioxidants, primarily plant based diet rich in nutrients & antioxidants, alkalising the body.
Summary Quiz!

1. What hormone is deficient in diabetes insipidus?
2. What does the number next to the thyroid hormones (T3/T4) reflect?
3. What thyroid hormone is the more active form?
4. What do parafollicular cells produce and what is the function of this hormone?
5. List FOUR symptoms of hypothyroidism. What is the name of the autoimmune disease that causes hypothyroidism?
6. Name two causes of hypoparathyroidism
7. What is the effect of hypoparathyroidism on muscles?
8. What effect might hyperparathyroidism have on bone?
Adrenal Glands

- Pair of glands superior to the kidneys.

Two parts:
- **Medulla (inner)**: part of the autonomic NS, producing:
  - Adrenaline (epinephrine)
  - Noradrenaline (norepinephrine)
  - Dopamine
- **Cortex (outer)**: produces 3 groups of steroid hormones:
  - Glucocorticoids (primarily cortisol)
  - Mineralocorticoids (primarily aldosterone)
  - Sex hormones (primarily androgens)
Adrenaline & Noradrenaline

- Adrenaline (80%) & noradrenaline (20%) are produced by the adrenal medulla.

- They Intensify the sympathetic response

- Released by chromaffin cells (quick release because innervated directly by the sympathetic NS)

- Adrenaline has greater influence on the heart. Noradrenaline affects blood vessels.

- **Stimulated by**: Exercise, fasting, shock, elevated temperature, infection, disease, emotional stress, caffeine.

- **Inhibited by**: Eating, sleeping, calmness, diaphragmatic breathing
Adrenaline & Noradrenaline

Adrenaline binds to receptors on the:

1. **Heart:** Increases heart rate & contraction causing an increase in blood pressure.

2. **Vessels:** Vasodilation in heart, brain, skeletal muscles. Vasoconstriction in digestive tract & skin.

3. **Thyroid:** Increases metabolism.

4. **Skeletal muscle/Liver:** Increases blood glucose & triglycerides (for metabolism)

5. **Nervous system:** Dilate pupils & airways.

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**Video: Fight or Flight**

www.youtube.com/watch?v=m2GywoS77qc
Glucocorticoids

- Steroid hormones produced in the adrenal cortex which regulate metabolism & resistance to stress.

- **Including:**
  1. **Cortisol** / hydrocortisone (most abundant: about 95%).
  2. Cortisone
  3. Corticosterone

**ACTIVITY:**
1. Stimulating gluconeogenesis
2. Proteolysis (amino acids from protein)
3. Lipolysis
4. Production of glucose by the liver
5. Reduces immune response (and tissue repair)
6. Anti-inflammatory – hence therapeutic use of steroids
7. Weak reabsorption of sodium & water from kidney tubules.
**Glycogenolysis**

Glucose

**Proteolysis**

Protein → Amino acids

**Gluconeogenesis**

Glucose

**Ketogenesis**

Ketones

**Lipolysis**

Triglycerides

Free Fatty Acids

Glycerol

---

* gluco- = glucose  
* glyco- = glycogen  
* lipo = fat/lipid  
* -lysis = breakdown  
* -genesis = production
Mineralocorticoids

• Primarily aldosterone. Maintains water & electrolyte balance

ACTIVITY:
1. Reabsorption of sodium in renal tubules
2. Excretion of potassium in urine
3. Causes retention of water to increase blood volume and blood pressure
4. Promotes excretion of H⁺ ions (acid) from the body

• Stimulated by: ↓ BP or blood volume (dehydration, haemorrhage) and high blood potassium stimulates the RAA pathway

• Inhibited by: low blood potassium.
1. Decreased blood volume = \(\downarrow\) blood pressure

2. Low BP stimulates kidneys to secrete enzyme renin in bloodstream

3. Renin converts angiotensinogen to angiotensin I

4. Angiotensin-converting enzyme converts angiotensin I to angiotensin II

5. Angiotensin II stimulates adrenal cortex to secrete aldosterone

6. Aldosterone acts on kidneys to reabsorb \(\text{Na}^+\). Retains water by osmosis. Elevates blood volume & BP
Sex Hormones

- Primarily androgens in the form of dehydroepiandrosterone (DHEA)

**ACTIVITY:**
1. Production of pubic & axillary hair
2. Growth: increases muscle mass
3. Converted to testosterone then oestrogen (in females → promotes libido)
4. Reverses many of the ‘unfavourable’ effects of cortisol excess
5. Involved in $T_4 \rightarrow T_3$ conversion

**PRODUCTION:**
- Stimulated by CRH → ACTH

- **Cortical androgens** are insignificant compared to amount produced in the ovaries & testes during puberty and adulthood.
# Cushing Syndrome / Disease

- Excessive amount of glucocorticoids (hypercortisolaemia)

<table>
<thead>
<tr>
<th></th>
<th>Cushing’s syndrome</th>
<th>Cushing’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td>A cortisol excess from any cause (glucocorticoid drugs, adrenal, tumour).</td>
<td>Excess production of ACTH causing excess glucocorticoid production from the adrenal cortex.</td>
</tr>
<tr>
<td><strong>Causes</strong></td>
<td>1. Corticosteroid therapy</td>
<td>1. Pituitary tumour</td>
</tr>
<tr>
<td></td>
<td>2. Adrenal adenoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. Pituitary adenoma (Cushing’s disease)</td>
<td></td>
</tr>
</tbody>
</table>

[Image of prednisolone and brain scan showing pituitary adenoma]
Cushing Syndrome / Disease

SIGNS & SYMPTOMS:

- Central weight gain, moon face, buffalo hump, insulin resistance
- Depression, insomnia, psychosis, poor libido, hirsutism, amenorrhoea (also releases some androgens),
- Easy bruising, thin skin, abdominal stretch marks (protein taken from collagen and lowered immunity)
- Reduced immunity
- Muscular weakness, back pain
- Bone fractures, osteoporosis
- Hypertension

Hirsutism = male pattern hair growth
Cushing Syndrome / Disease

DIAGNOSIS:
• Low dose dexamethasone (normally would reduce ACTH/cortisol)

TREATMENT:
• Drugs inhibiting cortisol production, surgery (for tumours).

ALTERNATIVE SUPPORT:
• Treat cause with herbs, homeopathy & nutritional supplements if indicated

COMPLICATIONS:
• Lowered immunity, fragile skin, bone fractures, diabetes mellitus
Addison’s Disease

- Adrenal insufficiency: hypo-functioning of the adrenal cortex causing a deficiency of mineralocorticoids and glucocorticoids.

CAUSES:
- Atrophy of the adrenal gland (often autoimmune) (85%)
- Secondary to a disease or abrupt cessation of steroids

SIGNS & SYMPTOMS:
- Weakness, fatigue and hypotension.
- Hyperpigmentation of skin and mucous membranes
- Diarrhoea, weight loss, anorexia, malaise, muscle weakness, depression, increased thirst
- Impotence/amenorrhoea, nausea/vomiting, abdominal and back pain
Addison’s Disease

- Adrenal failure leads to lack of adrenal hormone production and a failure of the normal negative feedback mechanism.

- The hypothalamus produces an excess of corticotrophin releasing hormone which causes the pituitary to erroneously produce melanocyte stimulating hormone.

- This causes the skin colour to darken, hence hyperpigmentation

Addisonian Crisis:
- A complication of Addison's disease when the individual has no capacity to cope with stress (e.g. psychological, infection etc.)

SIGNS AND SYMPTOMS:
- Severe lethargy and low blood pressure (low sodium).
- Hypoglycaemic, syncope (fainting)
- Severe pain, renal failure, fever
Pancreas

• Both endocrine & exocrine function

• Endocrine function is via the cells called the islets of Langerhans.

Three main types of endocrine cells:
1. **Alpha cells**: produce glucagon.
2. **Beta cells**: produce insulin.
3. **Delta cells**: produce somatostatin (GHIH)

• Main endocrine function of the pancreas is to **regulate blood glucose** levels & maintain within normal range (4-7mmol/L).

*Islet = an ‘island’ of tissue structurally distinct from surrounding tissues*
Pancreas - Insulin

• Lowers blood glucose levels, amino acids & fatty acids by:
  1. Stimulating cells to up-take glucose from the blood.
  2. Promoting synthesis of proteins, glycogen (glycogenesis) & fats (lipogenesis).

Stimulated by:
• Directly: high blood glucose, elevated blood amino acids, eating, sweet taste (including artificial sweeteners), parasympathetic NS
• Indirectly: GH and ACTH acting to elevate blood sugar levels

Reduced by:
• Low blood glucose, starvation, glucagon

glycogen = a polysaccharide
-lysis = breakdown
lipo- = fat
genesis = creation
Pancreas - Glucagon

- Acts on the liver to raise blood glucose levels
- Converts glycogen to glucose in liver and skeletal muscle: **glycogenolysis**
- **Gluconeogenesis** from lactic acid and amino acids
- **Lipolysis** to break down stored fat for use for metabolism

**PRODUCTION:**
- **Stimulated by:** low blood sugar, exercise, stress (fight-or-flight)
- **Reduced by:** insulin, hyperglycemia
Pancreas - Somatostatin (GHRIH)

- Growth hormone inhibiting hormone

- Also produced by the hypothalamus & digestive system (stomach & intestinal epithelial cells).

**ACTIVITY:**
- Acts in a paracrine manner to inhibit insulin & glucagon release from neighbouring alpha and beta cells.

- Inhibits the secretion of growth hormone

**PRODUCTION:**
**Stimulated by:** low blood sugar, exercise.
**Reduced by:** insulin, high blood sugar.
Diabetes Mellitus

- A metabolic disorder characterised by a deficiency of insulin due to impaired production or insulin resistance.
- Causes a disruption of carbohydrate & fat metabolism & elevated blood glucose levels → hyperglycaemia

**TYPES:**
1. **Type I:** Autoimmune
2. **Type II:** Insulin resistance
3. **Secondary:** Due to certain medications (cortisone, some diuretics), pancreatitis, hormone disorders (high GH, thyroid hormone, cortisol, adrenaline).
4. **Gestational:** During pregnancy as a result of placental hormones (i.e. human placental lactogen) blocking insulin receptors in the mother. Usually disappears after delivery, but elevated risk of type II years later.
Type I Diabetes

• Previously called juvenile-onset or insulin-dependent (IDDM).

CAUSES:
• An auto-immune condition causing destruction of pancreatic β-cells
• Possibly due to an environmental exposure in genetically susceptible people
• Viruses, dietary factors - exposure of infants to dairy products (especially cow’s milk and the milk protein β casein), nitrates, low vit. D consumption, early exposure to gluten and cereals increases islet cell autoantibody production.

SIGNS & SYMPTOMS:
• Glycosuria, polyuria, polydipsia
• Weight loss, weakness, fatigue, and mental status changes
• Blurred vision, slow healing of cuts/infections
• Ketoacidosis: Fruity smelling breath (exhaled acetone), shortness of breath
Type I Diabetes

Chronic hyperglycaemia causes complications: micro and macro-vascular disease:

• Heart disease, high cholesterol, hypertension
• Retinopathy
• Nephropathy (diabetic kidney disease)
• Peripheral neuropathy

http://arleoeye.com/?page_id=88
http://www.gluxus.com/diabetic-neuropathy/
Type I Diabetes

TREATMENT:
• Insulin.

ALTERNATIVE SUPPORT:
• Herbs (support pancreas, insulin sensitivity), nutrition (low GI & GL, antioxidants, fibre, chromium, vit. D, magnesium rich foods, zinc), alkalising the body, homeopathy and acupuncture.
Type II Diabetes

• Previously called adult-onset or non–insulin-dependent diabetes

• **Cells have developed insulin resistance and glucose cannot enter cells**

• Hyperglycaemia develops when pancreatic beta cells can no longer secrete insulin to compensate for insulin resistance.

• 1/3 adults over 65 and increasing numbers of children have impaired glucose tolerance

**CAUSES:**
• **Genetic:** strong hereditary link, high prevalence in American Indians, Hispanics, and Asians
• **Obesity & weight gain**
• **Poor diet, exercise, and lifestyle**
• Low birth weight, pregnancy
Type II Diabetes

**SIGNS & SYMPTOMS:**

- **Polydipsia** (excessive thirst)
- **Polyuria** (excess urination)
- **Polyphagia** (excessive appetite)

- Often asymptomatic because of mild hyperglycaemia (unlike in type I diabetes)

- **Initial symptoms are often complications**, indicating the disease has been present for some time. Ketoacidosis in severe cases (same complications as type I)
Type II Diabetes

DIAGNOSIS:
- Fasting / random blood glucose test
- Oral glucose tolerance test
- Glycated Haemoglobin
- Urine test

CONVENTIONAL TREATMENT:
- Diet (low GI & GL), exercise, oral anti-hyperglycaemics, insulin, or both.
- To prevent complications: ACE inhibitors, statins, and aspirin.

ALTERNATIVE SUPPORT:
- Diet, exercise, weight loss, chromium, Herbs - Gymnema, Cinnamon, vit. D
Ketoacidosis

• When glucose supply is low or when cells cannot utilise glucose, the mitochondria can use ketones to make energy

• Ketones are derived from the break down of fatty acids

• Ketones (or keto-acids) are acidic and can be toxic if they accumulate to excessive levels

• May result in coma or death

• Ketones can be tested using a urine dipstick

• Breath smells fruity (acetone) & increased thirst are key signs
Hypoglycaemia

Hypoglycaemia can affect diabetics in response to treatment (eg. insulin)

**SIGNS & SYMPTOMS:**

- Shaking and trembling
- Sweating
- Extreme hunger and irritability
- Headache
- Confusion, weakness, tiredness
- Ketoacidosis & coma

## Diabetic Coma

<table>
<thead>
<tr>
<th></th>
<th>Hyperglycaemic coma</th>
<th>Hypoglycaemic coma</th>
</tr>
</thead>
</table>
| **Cause/pathophysiology:** | • Lack of insulin  
• Dehydration  
• Acidosis due to build up of ketones  
• Elevated blood glucose | • Too much Insulin  
• Too much exercise  
• Delayed meal |
| **Differential Diagnosis:** | • If coma, smell breath. Hyperglycaemic coma will often smell like nail varnish remover | • May or may not have ketone smell |
| **First Aid:**            | • If conscious - water  
• If in coma - 999 | • Sugar  
• If in coma - 999 |
## Local Hormones

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Secreted by</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histamine</td>
<td>Basophils, mast cells</td>
<td>Part of <strong>inflammation</strong> – vasodilatation and increased blood vessel permeability</td>
</tr>
<tr>
<td>Prostaglandins, leukotrienes &amp; thromboxane's</td>
<td>Most tissues</td>
<td>Chemical messengers involved in many different body processes</td>
</tr>
<tr>
<td>Serotonin</td>
<td>Platelets, brain, intestinal wall</td>
<td>Blood clotting, temperature regulation, appetite, sleep</td>
</tr>
<tr>
<td>Dopamine</td>
<td>Primarily brain</td>
<td><strong>Muscle tone</strong> and some movements</td>
</tr>
<tr>
<td>Erythropoietin</td>
<td>Kidneys</td>
<td><strong>Red blood cell production</strong></td>
</tr>
<tr>
<td>Gastrin</td>
<td>GI tract</td>
<td>Promotes <strong>gastric juice secretion</strong> and stomach motility</td>
</tr>
<tr>
<td>Secretin</td>
<td>GI tract</td>
<td>Stimulates <strong>bile and pancreatic juice secretion</strong></td>
</tr>
<tr>
<td>CCK</td>
<td>GI tract</td>
<td>Stimulates <strong>bile &amp; pancreatic juice secretion</strong>. Promotes a sense of fullness after meals</td>
</tr>
</tbody>
</table>
Endocrine system & homeostasis

Whole body:
The endocrine system regulates growth and activities of cells throughout the body e.g. glucose uptake and metabolism.

Integumentary system:
• Androgens stimulate pubic hair growth and sebaceous gland activation.
• Melanocyte-stimulating hormone (MSH) causes skin darkening.

Skeletal system:
• Growth hormone and insulin like growth factors stimulate bone growth.
• Oestrogen helps maintain bone mass.
• Parathyroid hormone (PTH) and calcitonin regulate calcium levels in the bone and blood.
• Thyroid hormones are needed for development and growth of the skeleton.
Endocrine system & homeostasis

**Muscular system:**
- Adrenal hormones help increase blood flow to exercising muscles.
- PTH helps maintain calcium levels needed for proper muscle contraction.
- Glucagon, insulin and other hormones regulate muscle metabolism.
- Growth hormone, Insulin like growth factors and thyroid hormones help maintain muscle mass.

**Nervous system:**
- Thyroid hormones, insulin and growth hormones regulate nervous system development.
- PTH maintains proper calcium levels needed for nervous impulses.
Lymphatic system:
• Glucocorticoids depress immune response and inflammation.
• Thymus hormones promote T-cell maturation.

Cardiovascular system:
• Erythropoietin promotes formation of RBCs.
• Aldosterone and antidiuretic hormone (ADH) increase blood volume.
• Adrenaline and noradrenalin increase heart rate and contraction force.

Respiratory system:
• Adrenaline and noradrenalin dilate airways during exercise and stress.
• Erythropoietin regulates amount of oxygen carried in the blood by adjusting the number of RBCs.
Endocrine system & homeostasis

Digestive system:
- Adrenaline and noradrenalin depress digestion.
- Gastrin, CCK and secretin help regulate digestion.

Urinary system:
- ADH and aldosterone adjust rate of water and electrolyte loss to regulate blood volume.

Reproductive system:
- FSH and LH regulate development growth and secretions of the ovaries and testes.
- Oestrogen and testosterone stimulate sex cell development and changes during puberty.
- Prolactin promotes milk secretion from the mammary glands.
- Oxytocin causes contraction of the uterus and ejection of milk from the mammary glands.