Endocrinology Notes
The Hypothalamo-Pituitary Axis

General Location of the Hypothalamus & Pituitary Gland

Embryology of the Pituitary Gland:
- **Q:** Why is the Ant. Pituitary Endocrine, & the Post. Pituitary Neuronal?
- **A:** Because they have different embryonic origins.
  - **Anterior Pituitary:**
    - Arises from an upward out-pouching of the Oral-Ectoderm from the roof of the oral cavity called Rathke’s Pouch. This pouch pinches off from the oral cavity and is later separated by the sphenoid bone.
    - Consists of Epithelial/Glandular Tissue, & therefore Manufactures & Secretes Hormones.
  - **Posterior Pituitary:**
    - Originates from a downward out-pouching of Neuro-Ectoderm from the brain in the floor of the 3rd ventricle.
    - Consists of Neural Tissue, & therefore Secretes Neurohormones.

www.MedStudentNotes.com
The Hypothalamus & Pituitary Glands:

- **Hypothalamus:***
  - Links the nervous system to the endocrine system via the pituitary gland.
  - Controls body temperature, hunger, thirst, fatigue, anger, and circadian cycles.

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Name</th>
<th>Stimulated/Inhibited Hormone</th>
</tr>
</thead>
<tbody>
<tr>
<td>GRH</td>
<td>Growth-Hormone Releasing Hormone</td>
<td>Stimulates Release of Growth Hormone</td>
</tr>
<tr>
<td>SS</td>
<td>Somatostatin</td>
<td>Inhibits Release of Growth Hormone &amp; TSH</td>
</tr>
<tr>
<td>TRH</td>
<td>Thyrotropin Releasing Hormone</td>
<td>Stimulates Release of TSH &amp; Prolactin</td>
</tr>
<tr>
<td>PRF</td>
<td>Prolactin Releasing Hormone</td>
<td>Stimulates Release of Prolactin</td>
</tr>
<tr>
<td>GnRH</td>
<td>Gonadotropin Releasing Hormone</td>
<td>Stimulates Release of Gonadotropins; FSH &amp; LH</td>
</tr>
<tr>
<td>CRH</td>
<td>Corticotropin Releasing Hormone</td>
<td>Stimulates Release of ACTH</td>
</tr>
</tbody>
</table>

- **Pituitary Gland:**
  - Has 2 Major Lobes:
    - **Posterior Pituitary: (Neurohypophysis)**
      - Nervous Tissue
      - **Supraoptic & Paraventricular Nuclei** in the hypothalamus synthesize Oxytocin & ADH ➔ Transport them to their axon terminals in the **Posterior Pituitary**.
        - Hormones released as needed via exocytosis in Post.Pituitary
          - ADH
          - Oxytocin
      - **Normal Histology – Just like normal brain tissue. (Neural Origin)**
        - NB: NO neurones, but plenty of axons.
        - Many supporting cells (Astrocytes, oligodendrocytes)
        - Plus Blood Vessels (neither arteries or veins; but ‘Portal Vessels’ – Ie. Blood comes *only* from the hypothalamus ➔ carries the hypothalamic hormones.)
    - **Anterior Pituitary: (Adenohypophysis)**
      - Glandular Tissue (adeno = gland)
      - **Releasing-Hormones** from **Ventral Hypothalamus** that stimulate Ant. Pituitary:
        - CRF
        - TRF
        - GRH ➔ FSH/LH
        - GHRH
        - Prolactin Releasing Factor (PRF)
      - **Normal Histology – Glandular structure:**
        - Clusters of acini surrounded by blood vessels
        - Acini - mosaics of different cells:
          - (acidophils –red, basophils – dark blue, chromophobes - colourless)
          - NB: Pituitary Tumours may be from any of the 3 cells
        - PLENTY of blood vessels (neither arteries or veins; but ‘Portal Vessels’ – Ie. Blood comes *only* from the hypothalamus ➔ carries the hypothalamic hormones.)
- **Blood Supply:**
  - Arterial blood enters via **Hypophyseal Branches of the Internal Carotid Arteries.**
  - (BUT SHASHI SAYS – **NO ARTERIES...PORTAL SYSTEM**)

- **Venous Drainage:**
  - Venous blood leaves via **venules** which drain into the **Dural Sinuses.**

---

- **Pituitary Hormones & their Target Tissues/Organs**
  - NB: All these hormones are **PROTEIN-based hormones.**
Secretory Setup of the Hypothalamus & Pituitary Gland:
- **Anterior Pituitary:**
  - Neurons of the **Ventral Hypothalamus** terminate in the **Primary Capillary Plexus** within the **Infundibulum (Stalk).**
  - These Neurons secrete **Releasing-Hormones** into the **Primary Cap. Plexus,** which flow to the **Secondary Capillary Plexus,** stimulating **Endocrine Cells** of the Ant. Pituitary to synthesize/secrete hormones.
- **Posterior Pituitary:**
  - Neurons of the **Supraoptic & Paraventricular Nuclei** synthesize Oxytocin & ADH in the hypothalamus, then transport them as granules to their axon terminals which terminate in the **Posterior Pituitary.**
  - When one of the hormones is needed, it is released from the axon via **exocytosis** into the bloodstream via the **Inferior Hypophyseal Circulation.**
- **NB:** Remember that the Ant. & Post. Pituitary don’t act entirely independently (there is some flow of hormones from the Post. Pituitary → Ant. Pituitary via the ‘Short Portal Vein’)

![Diagram of the hypothalamus and pituitary gland](https://www.MedStudentNotes.com)
The Hypothalamus: A ‘Relay-Station’ for Higher Brain Centres:

- The Hypothalamus receives information from multiple higher brain centres, integrates it, decides on a response, and orders the pituitary to secrete specific hormones to elicit the response.

- **Inputs:**
  - RAS (Reticular Activating System/Substance) – Regulates drowsiness by releasing Serotonin.
  - Thalamus – Plays a role in Pain Perception
  - Neocortex & Limbic System – Emotional Centre
  - Optical System – Vision

- **Outputs:**
  - Anterior Pituitary
  - Posterior Pituitary
  - Brain-Stem (Autonomic NS)

**Feedback Control:**

- **Negative:**
  - Where the Biological Response causes a Decreased Hormone Release.
  - Maintains levels around a stable intrinsic/preset level.

- **Positive:**
  - Uncommon (Lactation & Parturition)
  - Where the Biological Response causes an Increased Hormone Release
  - Are therefore Unstable mechanisms
  - Stopped by removal of initial stimulus.
Levels of Feedback Loops:
- Feedback may occur at many different levels within a single ‘Hypothalamo-Pituitary-Target’ axis.
  - **Ultra-Short Loop:**
    - The secreted hormone feeds back to the same tissue that secreted it.
      - Eg. A Hypothalamic Hormone feeds back to the Hypothalamus.
  - **Short Loop:**
    - The secreted hormone feeds back to the tissue that stimulated its secretion.
      - Eg. The Hormone secreted by the Target Organ feeds back to the Pituitary.
      - Or. The Hormone secreted by the Pituitary feeds back to the Hypothalamus.
  - **Long Loop:**
    - The hormone secreted by the target organ feeds directly back to the Hypothalamus.
**Endocrine Regulation of Growth**

### Phases of Growth:

- **NB:** These Differ in their *Rates of Growth* and *Regulators/Contributors*:

<table>
<thead>
<tr>
<th>Phase of Growth</th>
<th>Nutrition</th>
<th>Major Regulators/Contributors</th>
<th>Genetics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foetal (In Utero)</td>
<td>Yes - #1</td>
<td>Insulin (Acts as a growth factor in this phase)</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IGF-I</td>
<td></td>
</tr>
<tr>
<td>Infantile (Birth → 2yrs)</td>
<td>Yes - #1</td>
<td>GH &amp; IGF is present, but in low amounts – NOT Imperative.</td>
<td>Yes – (Only after a few months after birth)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- IGF Levels Increase</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- GF Receptors Increase</td>
<td></td>
</tr>
<tr>
<td>Pre-Pubertal (Childhood)</td>
<td>-Ve influence only if malnourished</td>
<td>- IGF Levels Increase</td>
<td>Yes - #1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- GF Receptors Increase</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NB: Growth Velocity progressively declines during this phase (Transition from Infant → Child)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>NB: Body Proportions start to change.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pubertal (Early Teens)</td>
<td>-Ve influence only if malnourished</td>
<td>Sex Hormones:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- GH Release</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Epiphyseal Closure</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>GH → Causes IGF Release</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>GH + IGF → Bone Elongation</td>
<td></td>
</tr>
<tr>
<td>Post-Pubertal (Late Teens)</td>
<td>NB: Growth Velocity peaks &amp; then stays same for ≈6yrs.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- (The last 3 years mainly concern the Trunk)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Major Hormones involved with Growth:

- **Growth Hormone**, AKA: Somatotropin
- **Insulin-like Growth Factors** *(Somatomedins)* (IGF-I & IGF-II)
- **Somatostatin** (Inhibits secretion of GH from Ant. Pit.)
- **Thyroid Hormone**
- **Cortisol** – (Not Direct – has a ‘permissive’ role. Ie. Other growth hormones are more effective if it’s present)
- **Sex Hormones** *(Oestrogen/Testosterone)*

### The Growth Hormone Axis:

[Diagram of the Growth Hormone Axis]
Hypothalamic Hormones of Growth:
- (+) GRF (Growth-Hormone Releasing Factor)/GRH (Growth-Hormone Releasing Hormone):
  o Produced Mainly in: Hypothalamus (But also in GIT, Pancreas & Placenta)
  o Exerts Effects on: Somatotropes (Anterior Pituitary) → ↑Growth Hormone Release.

- (-) Somatostatin:
  o What is it?:
    ▪ Produced almost everywhere: (Hypothalamus, Gut, Pancreas, CNS)
      • → Inhibits Somatotropes → ↓Growth Hormone.
  o Actions of Somatostatin:
    ▪ Inhibits some Hypothalamic-Releasing Hormones:
      • GH (Grow Hormone)
      • TSH (Thyroid Stimulating Hormone)
      • PRL (Prolactin)
      • ACTH (Adreno-Cortico Tropic Hormone)

Anterior Pituitary Hormone of Growth:
- Growth Hormone:
  o Produced by: Anterior Pituitary (After ≈2mths old)
  o Regulation of Release:
    | Stimulation                          | Inhibition |
    |--------------------------------------|------------|
    | GRH - (Growth-Hormone Releasing Hormone) | Somatostatin |
  o Actions:
    ▪ Growth-Promoter from Early Childhood → Onwards
      • Longitudinal Bone Growth & Remodelling
      • Skeletal Muscle Growth
      • Liver Growth
      • Stimulates IGF-Binding Protein Synthesis (Important carrier for IGF)
      • Stimulates IGF Synthesis
    ▪ Metabolic Effects:
      • Stimulates:
        o Lipolysis
        o Ketogenesis
        o Gluconeogenesis
        o Protein Synthesis
        o Lactation
      • Inhibits Insulin Action.
      • Boosts Immune Function.

Defects in Endocrine Control of Growth:
- Hyper:
  o Too Much Growth Hormone &/or Growth Factors (Rare):
    ▪ Eg. Childhood Gigantism
    ▪ Eg. Adults - Acromegaly
  o Non-GH Causes:
    ▪ Eg. Precocious Puberty

- Hypo:
  o Defective Growth Hormone Axis:
    ▪ GH-Deficiency:
      • Primary GH Deficiency:
        o Hypothalamic Defect
        o And/Or Pituitary Defect
      • Secondary Pituitary Deficiency:
        o Eg. Tumour & other Destructive Diseases.
        o Eg. Psychosocial Deprivation (ie. Kids in abusive/non-supportive environments → GH-Deficiency → exhibit slowed growth)
Liver

Insulin-Like Growth Factors (IGF’s):
- Both IGF-I & IGF-II are Structurally Similar to Proinsulin (The Insulin Precursor)
- IGF-I - Chromosome 12
- IGF-II - Chromosome 11
- Circulates bound to IGFBP (Insulin-like Growth Factor Binding Protein)
- Bind to Specific Receptors
- Stimulate Cell Division together with other Growth Factors.

Foetal Life:
- Act in Paracrine Fashion
- IGF made by all foetal tissues (However, mainly by liver after birth)
- Absence of IGF-I in Foetal Life → Intra Uterine Growth Retardation

IGF-I → GH-independent IGF-1-mediated Growth
- Embryonic & early postnatal somatic growth
- Cyclic growth of ovary, uterus

Long Bone Growth

Growth
Bone grows in length because:
1. Cartilage grows here
2. Cartilage replaced by bone here
3. Bone added by appositional growth here
4. Bone resorbed here

Remodeling
Growing shaft is remodelled by:
1. Bone resorbed here
2. Bone added by appositional growth here
3. Bone resorbed here

Germinal zone
Proliferative zone
- Hypertrrophic zone
- IGF-II
- IGF-I

Calcified cartilage spicule
Osteoblast depositing cartilage spicules
Cartilage cells undergo mitosis
Calcification zone
Older cartilage cells enlarge
Matrix becomes calcified; cartilage cells die; matrix begins deteriorating
Ossification (osteogenic) zone
New bone formation is occurring

Articular cartilage
Epiphyseal plate

www.MedStudentNotes.com