Inputs that Control Hormone Secretion

- Control by Plasma Concentrations of mineral Ions or Organic molecules. For example, absorption of I⁻ iodine ion increase output of thyroxine hormone by thyroid glands.
- Control by Neurons – Nervous system can control hormone secretion in 4 ways. 1) Autonomic NS stimulates adrenal medulla to secrete epinephrine 2) Autonomic NS can stimulate or inhibit secretion of a hormone by an endocrine gland 3) neurohormones secreted by hypothalamus pass through blood to anterior pituitary body and influence the secretion of hormones by it. 4) Axons of some neurons of hypothalamus end in posterior pituitary lobe and release their hormones in it.
- Control by Other Hormones – when the secretion of a hormone (thyroid stimulating hormone) causes the secretion of another hormone (triiodothyronine), the 1ˢᵗ hormone is called a tropic hormone (thyrotropin). Most of these hormones also cause growth of gland (thyroid) secreting the hormone. For this action a tropic hormone is called a trophic hormone. I gave examples in parentheses.

Types of Endocrine disorders

- Hyposecretion is too little hormone. Primary hyposecretion can be due to partial damage of gland or enzyme deficiency or lack of nutrient in diet or infection etc. Secondary hyposecretion is caused due to deficiency of the tropic hormone though gland is in good condition.
- Hypersecretion is too much hormone. It can also be primary or secondary on similar pattern to hyposecretion.
- Hyporesponsiveness is reduced responsiveness of target cells to hormone. Most common type of Diabetes mellitus type 2 is caused due to hyporesponsiveness of target cells (muscle cells and adipose tissue). Hyperresponsiveness is increased responsiveness of target cells to hormone. Permissive effect. PTH has permissive effect on Vitamin D. Thyroid hormone has effect on epinephrine / norepinephrine.

The Hypothalamus and Pituitary Gland (hypophysis)

Control Systems Involving the Hypothalamus and Pituitary represent one of the tow interactions between nervous and endocrine systems. Pituitary gland lies in a pocket sella turcica of sphenoid bone below hypothalamus. Pituitary gland has an anterior lobe = adenohypophysis and a posterior lobe = neurohypophysis. Pituitary gland is joined to hypothalamus by a stalk = infundibulum formed of nerve fibers and blood vessels.

- Posterior Pituitary Hormones – produces 2 hormones. These hormones are produced by neurons of hypothalamus and released in posterior lobe by their axons.
  - Oxytocin – stimulates contraction of uterine wall to cause labor and contraction of smooth muscles of breasts to cause ejection of milk.
  - Vassopressin = Antidiuretic Hormone = ADH. It is called vasopressin because it contracts smooth muscles of blood vessels to increase blood pressure; it is called ADH because it stimulates kidneys to reabsorb more water and produce scanty urine – called antidiuretic hormone (diuretic means to produce excess urine).

- Anterior Pituitary Hormones and the Hypothalamus

Hypothalamus produces Hypophysiotropic hormones that control hormones secreted by anterior pituitary body. 6main hormones secreted by hypothalamus are:
  - Corticotropin-releasing hormone = CRH → stimulates secretion of ACTH
  - Thyrotropin-releasing hormone = TRH → stimulates secretion of Thyroid SH
  - Growth Hormone-releasing hormone → stimulates release of Growth Hormone
  - Somatostatin → inhibits release of Growth hormone
  - Gonadotropin-releasing hormone → stimulates secretion of FSH and LH
  - Dopamine → inhibits secretion of Prolactin

These hormones are the 1ˢᵗ hormone in a sequence of 3 hormones. For example, hypothalamus produces Thyrotropin Stimulating Hormone = TSH (1ˢᵗ). TSH is collected by the blood of hypophyseal portal vessels and delivered to anterior pituitary body. TSH stimulates anterior pituitary body to secrete Thyrotropin =
thyroid stimulating hormone (2nd). In turn Thyrotropin stimulates thyroid gland to produce Triidothyronine hormone (3rd) which acts on target cells.

- **6 main hormones secreted by anterior pituitary gland are:**
  - Follicle Stimulating Hormone = FSH causes the development of eggs in ovaries and sperms in testes
  - Luteinizing Hormone = LH stimulates hollow follicle to develop into Corpus luteum that produces Progesterone hormone. It stimulates interstitial cells in testes to produce testosterone hormone. FSH and LH hormones are called gonadotropins because they stimulate gonads.
  - Growth Hormone = GH = Somatotropin stimulates liver and other cells in body to secrete Insulin-like-Growth Factor 1 = IGF-1
    GH also stimulates protein synthesis and fat/ carbohydrate metabolisms in many cells and tissues.
  - Thyrotropin = Thyroid Stimulating Hormone stimulates thyroid to secrete Thyroxine = tetraiodothyronine and triiodothyronine. It also causes growth of thyroid gland. Excessive secretion of TSH will cause hypertrophy = enlargement of thyroid called Goiter.
  - Prolactin stimulates development of breasts and milk production in them.
  - AdrenoCorticoStimulating Hormone = ACTH stimulates adrenal cortex to secrete Cortisol.

**The Thyroid Gland** is a bilobed gland, present on anterior side, at the base of neck and has follicles formed of cells having colloid in the lumen. **Main functions include metabolic rate, growth, development of brain and brain function**.

- It secretes 3 hormones. The actions of first 2 hormones are similar to each other.
  - Thyroxine = Tetraiodothyronine = T₄ has 4 iodides attached to its rings but breaks down to Triodothyronine = T₃ on entering target cells.
  - Triiodothyronine = T₃ has 3 iodides bond to its rings. T₄ is the main hormone secreted and has higher blood levels but T₃ is the main hormone affecting target cells.
  - Action of Thyroid hormones is wide spread because most cells and tissues have receptors for them in their nuclei.

- **Synthesis of Thyroid Hormones** – thyroid hormones are synthesized from tyrosine amino acids of protein Thyroglobin by adding iodine ions to it. Tyrosine $\rightarrow$ MonolodoTyrosine (MIT) $\rightarrow$ DilodoTyrosine (DIT) $\rightarrow$ T₃ or T₄ when needed are produced.

**Control of Thyroid Function** – Thyrotropin stimulates follicular cells to produce thyroid hormones.

**Actions of Thyroid Hormones**
- Metabolic Actions - Metabolic – stimulates intestinal cells to absorb carbohydrates; stimulates adipose tissue to release fatty acids; stimulates breakdown to cellular ATP to generate heat; to maintain ATP levels cells increase metabolic rates.
- Permissive Actions Metabolic – stimulates intestinal cells to absorb carbohydrates; stimulates adipose tissue to release fatty acids; stimulates breakdown to cellular ATP to generate heat; to maintain ATP levels cells increase metabolic rates.
- Growth and Development Growth and Development - TH is needed for normal production of Growth hormone.

**Additional Clinical Examples**
- **Hypothyroidism** is mostly due to dietary deficiency of iodine or damage to thyroid gland. **Hyperthyroidism** is excessive secretion of thyroid hormone and is generally due to greater secretion of Thyrotropin. It causes the hypertrophy of thyroid gland called Goiter.
The Endocrine Response to Stress

Physiological Functions of Cortisol
- Maintains responsiveness to target cells to hormones epinephrine and norepinephrine
- Provides a check on activity of immune system
- Participates in energy homeostasis – increases energy availability of energy by gluconeogenesis, lipolysis
- Promotes normal development of tissues and cells in fetus.

Functions of Cortisol in Stress
- Stress stimulates the Corticotropin RH → Corticotropin → Cortisol. Cortisol helps to establish homeostasis threatened by stress.
- Promotes normal physiological functions like lipolysis = breakdown of adipose tissue, Gluconeogenesis = production of glucose from amino acids and glycerol, and inhibits effects of insulin.
- High cortisol levels inhibit non-essential functions like growth and reproduction.

Other Hormones Released During Stress are aldosterone, vasopressin, growth hormone, and glucagon. In addition sympathetic nervous system increases Epinephrine secretion to establish Fight or Flight response.

Psychological Stress and Disease: Mind and body interaction can cause Chronic Psychological stress and raise plasma Cortisol levels. High levels of cortisol can dangerously lower body’s immune system and resistance against diseases like cancer or diabetes. Similarly prolonged activation of sympathetic system can induce diseases Atherosclerosis – deposit of plaque in arteries and Hypertension – abnormal high blood pressure.

Additional Clinical Examples

Cushing’s Syndrome is hypersecretion of Cortisol. If the excessive levels are due to a tumor growth to ACTH the condition is called Cushing disease. High levels of cortisol even in unstressed individual promote catabolism of bone, muscle, skin and other organs. Symptoms will include Osteoporosis, very high levels of blood glucose levels, and immunosupression, obesity of upper part of body.

Endocrine Control of Growth

Bone Growth
- Bone growth in long bones takes place by Endochondral ossification – the transformation of cartilage to bone tissue near the ends of long bones. Growth takes place at Epiphysial Growth Plate. Osteoblasts at the outer edge of epiphysial growth plate change cartilaginous tissue to bone; simultaneously chondrocytes form new cartilage inner to the plate. Linear bone growth continues till some hormones (testosterone or estradiol) change the epiphysial growth plate to bone = Epiphysial Closure. No height gain takes place after this. Growth hormone promotes lengthening of bones by inducing division and maturation of chondrocytes.

Environmental Factors Influencing Growth – 2 important environmental factors are adequate nutrition and freedom from disease.

Hormonal Influences on Growth
- Growth Hormone and Insulin-Like Growth Factors
  - GH has no effect on fetal growth.
  - GH is the main hormone to influence post-natal growth. It is also tropic hormone and causes the release of Insulin-like-Growth-Factor -1 = IGF-1. On stimulation by GH liver secretes IGF-1 into blood and acts like a hormone. In addition GH stimulates many cells/tissues including bones to
secrete IGF-1 which acts as an autocrine (act on cell that produced it) or paracrine (acts on neighboring cells).

- Dwarfism is a very small stature due to deficiency of GH. But it can also be due to lesser secretion of IGF-1 or 2; or due to changes in receptors for IGF-1.

- Thyroid Hormones
  - Thyroid hormones have Permissive effect on GH because they are needed for synthesis of GH and also for their growth promoting effects.

- Insulin
  - Insulin stimulates growth in fetus and perhaps in childhood.
  - It promotes absorption of glucose and amino acids by cells. It promotes anabolism by favoring protein synthesis and glycogen synthesis.
  - It promotes bone formation and favor transfer of Ca\(^{2+}\) to bones.
  - During fetal life it exerts direct growth promoting effects on cell division and cell differentiation.

- Sex Hormones
  - Sex Hormones (testosterone in males and estrogens in females) promote growth by stimulating more secretion of GH and IGF. There is a spurt in secretion of sex hormones between 8-10 years of age and changes to a plateau after 5-10 years.
  - Sex hormones ultimately block growth by causing epiphysial closure.
  - Testosterone but not estrogens direct promote growth of muscle mass. It partly accounts greater growth of muscles and bones in males. The other reason is in boys puberty sets late by 2 years, on average, than girls. This gives them longer time to grow.

- Cortisol
  - Inhibits growth and stimulates breakdown of proteins = catabolism

Additional Clinical Examples
- Gigantism: Hypersecretion of GH before epiphysial closure results in great growth in long bones and results in Gigantism – called Pituitary Gigantism.
- Acromegaly: Hypersecretion of GH after closure results in thickening of bones, especially hands and feet. It also causes greater growth of facial bones – especially of lower jaw – that protrudes forwardly.

**Endocrine Control of Ca\(^{2+}\) Homeostasis**

Body maintains Ca\(^{2+}\) levels in ECF within a narrow range. Deviations in any direction (up or down) can be life threatening.

**Effector Sites for Calcium homeostasis**
- Bone – body stores 99% Ca\(^{2+}\) in bones. It is a major site for maintaining plasma calcium.
- Kidneys – reabsorb all useful nutrients from urine and hormones promote reabsorption to control plasma level of calcium.
- Gastrointestinal Tract – active transport mechanism of gastrointestinal tract is under the hormonal control. It helps to regulate plasma calcium level.

**Hormonal Controls**
- Parathyroid hormone – is secreted by Parathyroid glands when plasma calcium levels fall below normal level.
  - It promotes osteoclasts that break down bone matter and transfer Ca\(^{2+}\) and Phosphate to plasma.
  - It stimulates kidneys for greater reabsorption of Ca\(^{2+}\).
  - It stimulates kidneys to produce more 1, 25-(OH)\(_2\)D
- 1,25-dihydroxyvitamin D – promotes greater reabsorption Calcium and phosphate by GI tract
• Calcitonin – is secreted by parafollicular cells (lying outside follicles) of Thyroid gland when plasma levels of Ca\(^{2+}\) become very high. It acts by inhibiting degradation of bone by osteoclasts. On day to day basis calcitonin is not secreted and mostly homeostasis is maintained by parathormone and 1, 25 dihydroxy vitamin D.

Metabolic Bone Diseases

• **Rickets** in children and **Osteomalacia** in adults occur due to deficient mineralization of bones (lesser deposit of calcium and phosphates). The bones remain soft and get easily fractured. Rickets and Osteomalacia mainly occur due to deficiency of Vitamin D.

• **Osteoporosis** is caused due to loss of both protein matrix and minerals from the bone. Main causes include
  - Aging
  - Excessive plasma levels of parathormone, cortisol or TH – bone break-down action
  - Lower levels of insulin, Gh, IGF-1, Estrogen/testosterone, calcitonin – bone formation action
  - Osteoporosis is more common in elderly women than elderly men due to
    - Less initial bone mass
    - Faster loss of bone matter
    - Menopause decreases the levels of estrogens – bone formation hormone

Additional Clinical Examples

• **Hyper- and hypocalcemia**
  - **Hypercalcemia** – usually a benign tumor (hyperparathyroidism) in one of the 4 parathyroid glands causes excessive release of parathormone resulting in abnormally high level of plasma calcium = primary hypercalcemia.
  - **Hypocalcemia** is abnormally low plasma calcium levels. It usually occurs when a malignant thyroid is surgically removed. Tiredness and lethargy with muscle weakness, and nausea and vomiting are main symptoms.
  - Secondary Hypocalcemia occurs due to failure of vitamin D absorption from GI tract or lesser production of 1, 25 dihydroxy vitamin D in kidney disease. The symptoms include excitation of muscles and nerves leading to seizures and muscle spasms.