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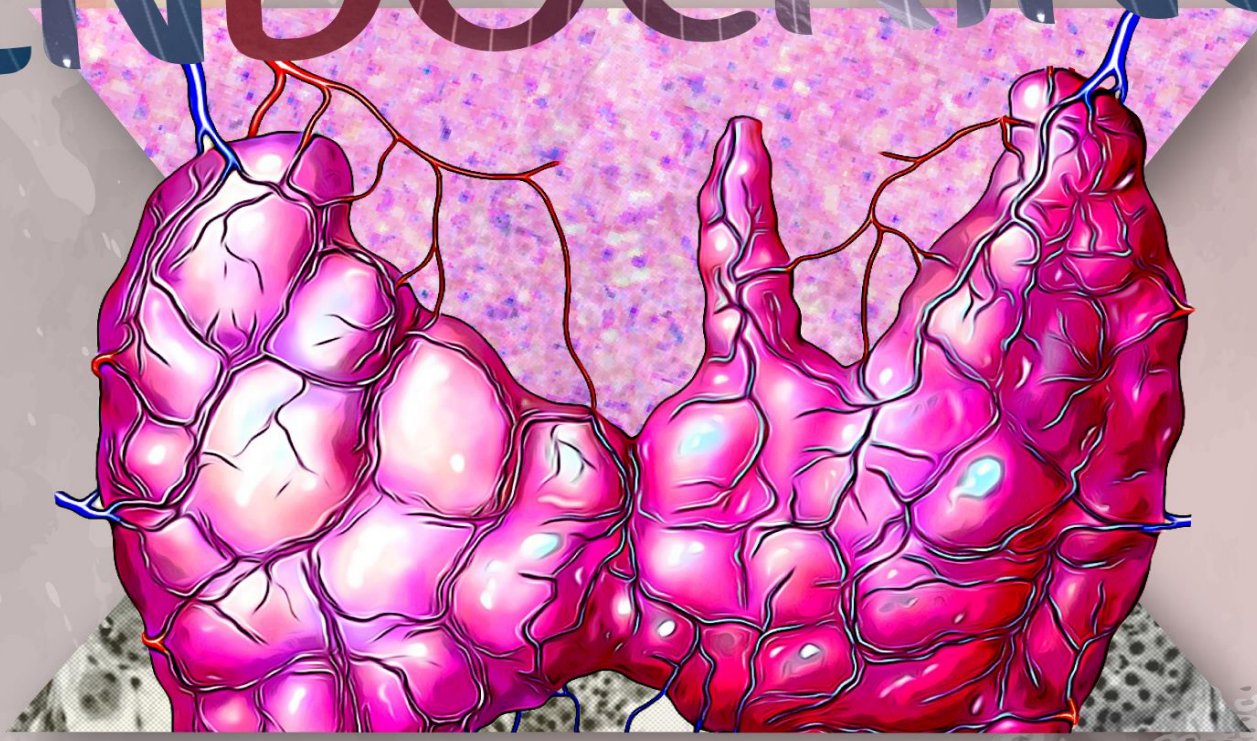
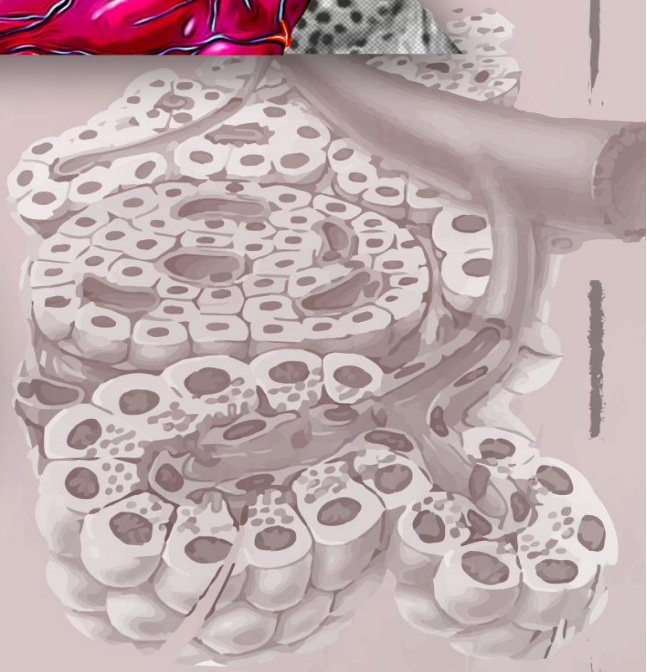
ENDOCRINE





SUBJECT: Physiology

DONE BY: Ahmad Rawajbeh

CORRECTED BY: Abdallah Kharabsheh

DOCTOR: Saleem

Anterior Pituitary lobe

- ***Indirectly connected*** with the Hypothalamus by the ***Hypothalamic-Hypophyseal portal system.***
- It is derived from ***Rathke's pouch*** which is an embryonic invagination of the pharyngeal epithelium. This explains the ***epithelioid nature*** of its cells compared to the posterior lobe.
- It is highly vascularized with extensive ***capillary sinuses*** between the glandular cells. Blood first passes through ***the primary capillary plexus*** in ***the median eminence*** (the lowermost portion of the hypothalamus). blood then flows through the portal blood vessels to supply the anterior lobe of the pituitary gland.
- The neuronal cell bodies in the hypothalamus produce hormones to be stored in the nerves ending (in the median eminence). When the neurons of the hypothalamus are stimulated, the nerves endings release the hormones into the blood (in the median eminence region). From there they are transported to stimulate or inhibit the secretion of anterior pituitary hormones.

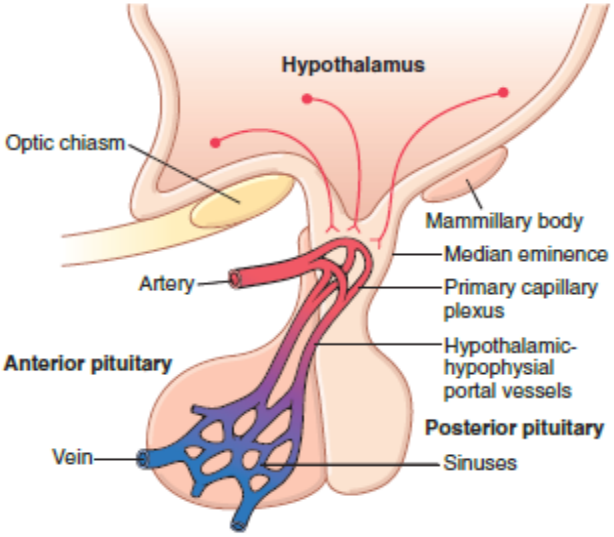


Figure 76-4. Hypothalamic-hypophysial portal system.

Secretion of anterior pituitary hormones is regulated by two pathways:

- ✓ ***The short pathway:*** Hormones that are packed in ***secretory granules*** at the Hypothalamus extend down through neurons to the posterior pituitary. From there, they are released into ***Hypothalamic-Hypophysial short portal vessels***, then to the anterior pituitary to stimulate or inhibit it.
- ✓ ***The long pathway:*** Hormones from the hypothalamus are released in ***the median eminence***, then through ***Hypothalamic-Hypophysial long portal vessels*** to the anterior pituitary.

Note: it is not precisely known which pathway is taken by a particular hormone, but is believed that each hormone may take either the long or the short pathway depending on the body's need.

At least 5 cell types can be identified in the pituitary glands each one -usually- produces one major hormone:

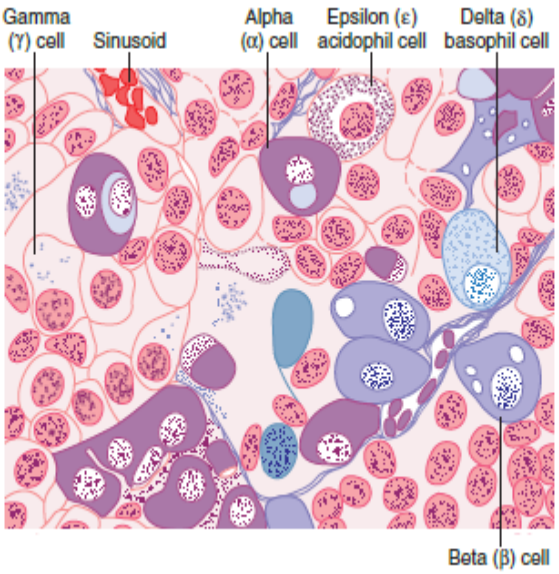


Figure 76-3. Cellular structure of the anterior pituitary gland.

Tropic hormones (hormones that affect other endocrine glands): -*Those cells stain basophilic-*

- ✓ ***Corticotropes*****:** cells release ***Adrenocorticotropic hormone ACTH.*** About 20% of all anterior pituitary gland cells.
- ✓ ***Thyrotropes:*** cells release ***Thyroid stimulating hormones TSH.***
- ✓ ***Gonadotropes***: cells release ***Follicle-stimulating hormones FSH*** and ***Luteinizing hormones LH.*** Produced by separate cell types in both normal and abnormal conditions.

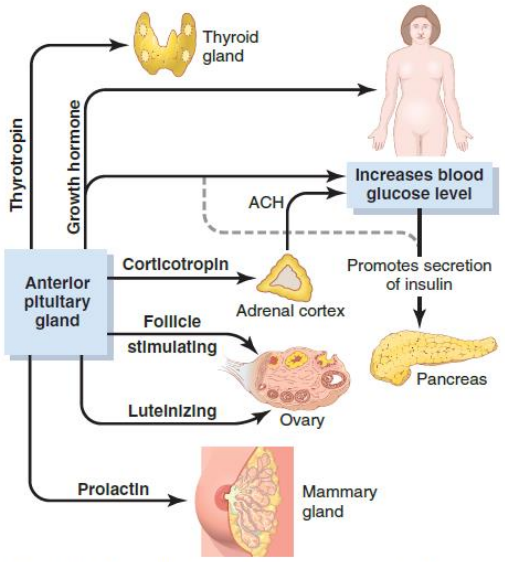


Figure 76-2. Metabolic functions of the anterior pituitary hormones. ACH, adrenal corticosteroid hormones.

- ***Non-tropic hormones:*** ***-****Those cells stain acidophilic-*
  - ✓ ***Somatotropes***: cells release ***somatotropin (***also known as ***growth hormones GH).*** About 30-40% of all anterior pituitary gland cells.
  - ✓ ***Lacotropes (mammotropes):*** cells release ***Prolactin.*** The mammary glands are exocrine glands not endocrine which are the target of prolactin, so it is a non-tropic hormone.

GH is a single chain polypeptide that is homologous with prolactin.
Normally GH and Prolactin are secreted by separate cells. In some cases (maybe normally or abnormally (tumor cells)) they are released from the same cell.

- Although thyrotropes, Gonadotropes and Lacotropes account only for about 3-5% of the anterior pituitary cells, they produce powerful hormones for controlling thyroid function, sexual function and milk secretion.
- The Hypothalamic Hormones that stimulate or inhibit the secretion of the pituitary hormones:

  - ✓ ***Corticotropin Releasing Hormone (CRH)*** that stimulate corticotropes to release ACTH.
  - ✓ ***Thyrotropin Releasing Hormone (TRH***) -a polypeptide of 3 amino acids- that stimulate thyrotropes to release TSH.
  - ✓ ***Growth Hormone Releasing Hormone (GHRH)*** that stimulate Somatotropes to release GH. has the longest amino acids sequence (44).
  - ✓ ***Growth Hormone Inhibitory Hormone (GHIH/Somatostatin)*** that inhibit the release of GH from Somatotropes.
  - ✓ ***Gonadotropin Releasing Hormone (GnRH)*** that stimulate Gonadotropes to release LH and FSH.
  - ✓ ***Prolactin inhibiting hormone (PIH/Dopamine)*** All the hypothalamus hormones are peptides except dopamine (a catecholamine).

*** For most of these hormones, simulation is more important than inhibition except for the prolactin hormone because it is not needed always in the females and it is not needed at all in males. There may be a stimulatory hormone for prolactin but the inhibitory hormone exerts more function.*
*** Growth hormone has stimulatory and inhibitory hormones, while other hormones have only stimulatory hormone as they are regulated by a feed back mechanism.*

- The Hypothalamus is affected by all the CNS centers and since the Pituitary gland is regulated by the Hypothalamus, this means that both the Hypothalamus and the Pituitary gland and controlled by the centers of the CNS.

Growth hormone (somatotropin):

- Small protein molecule that contains 191 amino acids in a single chain with a molecular weight of 22,005.
- It causes growth of almost all tissues of the body that are capable of growing. It promotes increased sizes of the cells and increased mitosis (number).
- Notice the increase of a rat's body weight when injected daily with growth hormone.

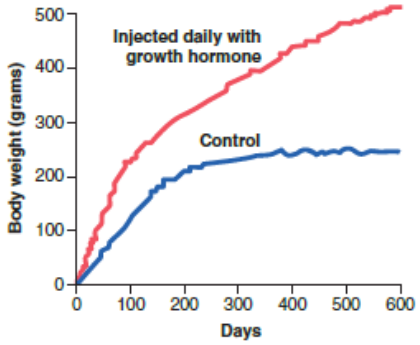


Figure 76-5. Comparison of weight gain of a rat injected daily with growth hormone with that of a normal littermate.

Hormonal interactions:

- ***Permissive***: the presence of one hormone is required for other hormone to exert or enhance its effect.
- ***Synergism***: when many hormones complement each other and function together to produce effects greater than sum of their individual effects. $\boldsymbol{effect_{(x+y)} > effect_{(x)} + effect_{(y)}}$

- ***Antagonism***: when a hormone opposes the action of another. *e.g. insulin- glucagon*

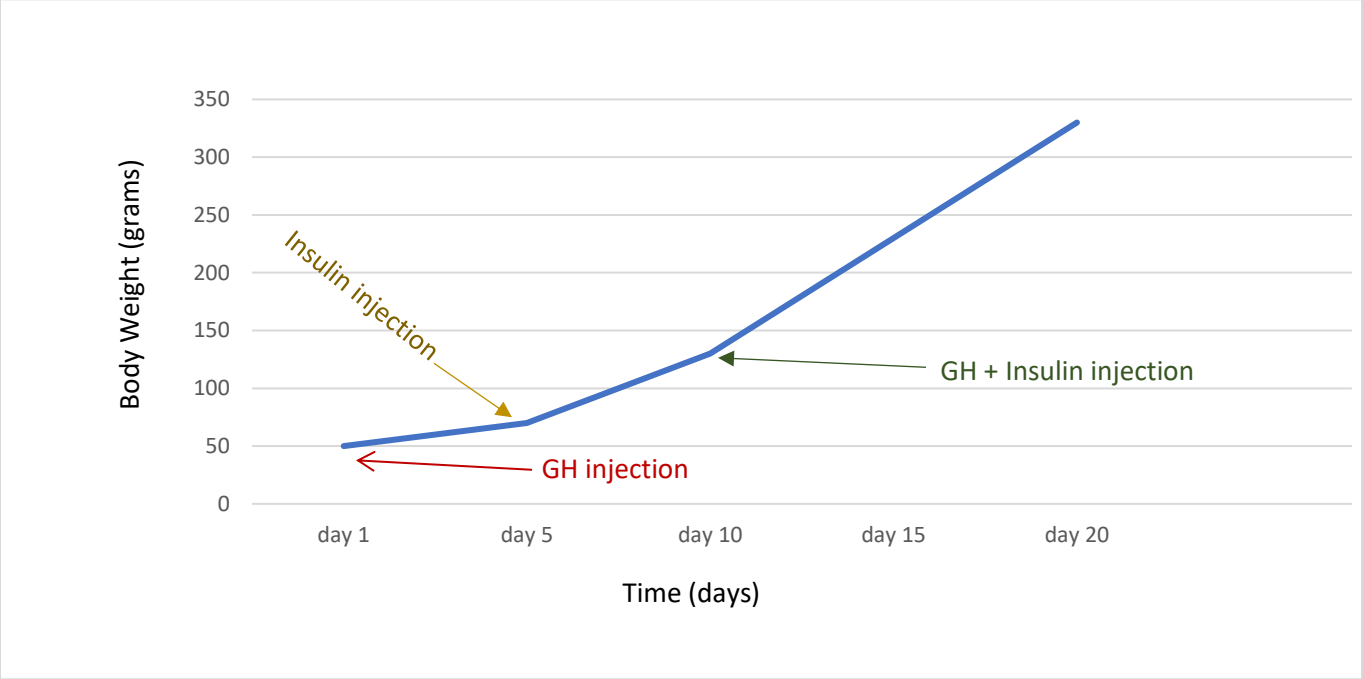
- Growth hormone is not the only hormone that stimulate growth in the body. Many hormones stimulate growth ***synergistically:***

  - ✓ Insulin like growth factor-1 [IGF-1] (also called somatomedin).
  - ✓ Androgen
  - ✓ Insulin
  - ✓ Thyroid Hormone
  - ✓ Glucocorticoid hormone (cortisone)
  - ✓ Estrogen

Growth hormone and insulin-like growth factor have been identified as the major determinants of the growth in the normal post uterine life. However, the deficiency or absence of each of the other hormones seriously affect the normal growth of the musculoskeletal system as well as growth and maturation of other tissues.

Growth hormone and Insulin:

- GH and Insulin affect growth synergistically, but separately insulin has more effect than growth hormone.
- The following chart represents the growth curve of a rat without a pancreas. At first the rat was only injected with GH which showed a mild increase in weight, but when it was injected with insulin, the growth had increased more. However, the most increase was when the rat was injected with both hormones. This means neither GH nor insulin can function separately.



Growth hormone effects:

GH has both ***direct and indirect effects:***

- ***Direct effects of GH on***:
  - ✓ ***Adipose tissue:*** it decreases the adiposity, by increasing lipolysis and decreasing glucose uptake by tissues. (increase blood concentration of free fatty acids and glucose)
  - ✓ ***Liver cells:*** it increases RNA synthesis, the rate of protein synthesis, promotes Gluconeogenesis (production of glucose from non-carbohydrate sources), and promotes production of somatomedins.
  - ✓ ***Muscle cells:*** It decreases glucose uptake (glucose remain in the blood), increase amino acid uptake by the tissues and increase protein synthesis.

So, it directly decreases glucose uptake, increases lipolysis, increases protein synthesis in muscles (which increases the lean body mass) and increases production of somatomedin.

- ***Indirect effects of GH:***

Growth hormone exerts much of its effect through intermediate substances called soamtomedins:

Somatomedins are several small proteins (hormones) with molecular weight of 4500-7500. they have potent effect of increasing all aspects of bone growth. They also affect heart, kidneys, intestines, lungs, pancreas, parathyroid glands, skin, connective tissue and **chondrocytes** to increase organ size and function similar to GH.

When growth hormone is supplied directly to cartilage chondrocytes cultured outside the body, proliferation or enlargement of the chondrocytes usually fails to occur yet, growth hormone injected into the intact animal does cause proliferation and growth of the same cells.

At least four or more different types of somatomedins have been identified, all of them seem to have similar actions with different potencies.

Metabolic effects of GH:

- Beside its general function in promoting growth, GH has many specific metabolic effects as well including increase rate of proteins synthesis in all body cells, increase mobilization of fatty acids from adipose tissue, increase the use of fatty acids for energy purposes and decrease the utilization of glucose throughout the body.
- The increase of body weight is a result of the increased protein synthesis.
- Abnormal or over release of the growth hormone may cause ***diabetogenic effect of GH:***
    - ✓ Increases glucose level causing hyperglycemia which increases insulin secretion indirectly.
    - ✓ It directly increases insulin secretion from the beta cells of the pancreas.

This causes over stimulation of pancreatic beta cells and consequently type 2 diabetes mellites.

- Similarly, when excessive of fatty acids are mobilized this can cause ***ketogenic effect of GH,*** because the liver will produce high amount of acetoacetic acids (ketone bodies), this is ***called ketoses.***

- ***Diabetogenic effect of other anterior pituitary hormones:*** Growth hormone is not the only anterior pituitary hormone that increases the blood glucose concentration. At least three others can do the same:
    - ✓ Adrenocorticotropin (ACTH).
    - ✓ Thyroid-stimulating hormone (TSH).
    - ✓ Prolactin.

ACTH is especially important as it increases the rate of cortisol secretion by the adrenal cortex. cortisol then increases the blood glucose concentration by increasing the rate of gluconeogenesis

Dietary factors that affect hormones secretion:

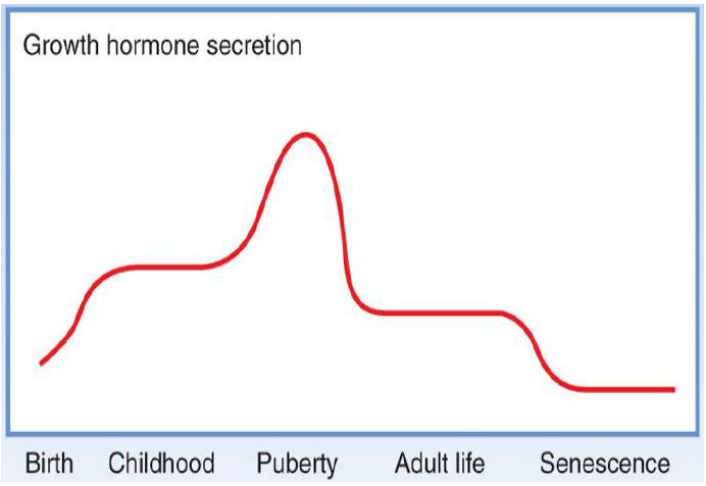
- ***Protein intake:*** increases GH, insulin and somatomedin. (synergies to promote growth)
- ***Carbohydrates intake:*** GH is decreases, somatomedin is not affected, insulin is increased (insulin is the only hypoglycemic hormone in the body).
- ***Fasting:*** insulin and somatomedin are decreases. GH is increased to increase glucose and fatty acids concentrations.

Factors affecting the secretion of GH:

- Growth hormone is secreted in ***a pulsatile pattern*** *(figure 76-6)* or called ***diurnal rhythm,*** increasing and decreasing. The precise mechanisms that control secretion of growth hormone are not fully understood, but several factors related to a person's state of nutrition or stress are known to stimulate secretion.
- Ghrelin is a hormone released by stomach and intestines and It stimulates the release of GH.
- The following chart shows the ***developmental rhythm of GH levels*** during different ages. In childhood GH level is higher than adult life (not significant difference (<10%)) and it peaks during puberty (significant difference (>10%)).

Table 76-3 Factors That Stimulate or Inhibit Secretion of Growth Hormone

Stimulate Growth Hormone Secretion	Inhibit Growth Hormone Secretion
Decreased blood glucose	Increased blood glucose
Decreased blood free fatty acids	Increased blood free fatty acids
Increased blood amino acids (arginine)	Aging
Starvation or fasting, protein deficiency	Obesity
Trauma, stress, excitement	Growth hormone inhibitory hormone (somatostatin)
Exercise	Growth hormone (exogenous)
Testosterone, estrogen	Somatomedins (insulin-like growth factors)
Deep sleep (stages II and IV)	Increased blood glucose
Growth hormone–releasing hormone	Increased blood free fatty acids
Ghrelin	Aging



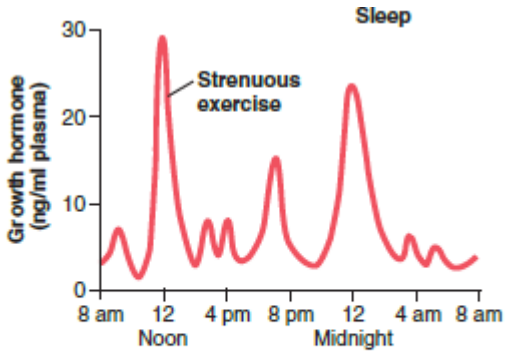


Figure 76-6. Typical variations in growth hormone secretion throughout the day, demonstrating the especially powerful effect of strenuous exercise and also the high rate of growth hormone secretion that occurs during the first few hours of deep sleep.

Negative feedback control of GH release:

- GHRH inhibits its own secretion directly. (ultra-short loop).
- By stimulating the secretion of somatomedin which stimulates somatostatin secretion (which in turn inhibits the release of GH).
- by stimulating the secretion of somatostatin directly.

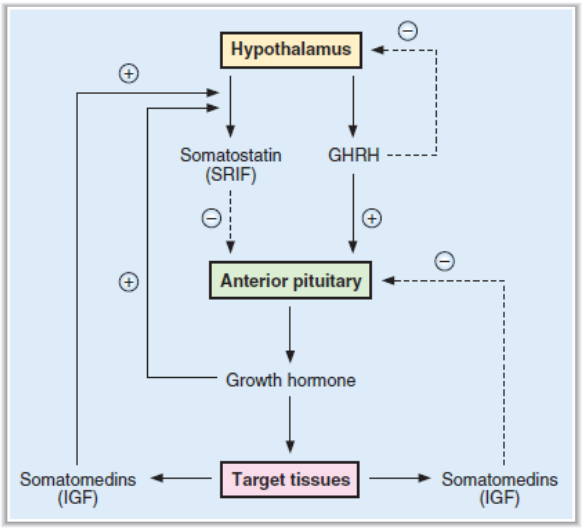


FIGURE 7.6 Control of growth hormone secretion. GHRH = growth hormone–releasing hormone; IGF = insulin-like growth factor; SRIF = somatotropin release–inhibiting factor.

Feedback mechanism for control food intake:

- ***Stretch receptors:*** in the stomach activate sensory afferent pathway through vagus nerve and inhibit food intake.
- ***Peptide YY, cholecystokinin (CCK), and insulin*** are gastrointestinal hormones that are released by ingestion of food and suppress further feeding.
- ***Ghrelin*** is released by the stomach and the intestines, especially during fasting and stimulates eating.
- ***Leptin*** hormone is released in high amounts by fat cells as they increase in size, it inhibits food intake.

Hypofunction of Pituitary gland

Panhypopituitarism: means decreased secretion of all pituitary gland hormones (anterior lobe and posterior lobe).	***Severe anterior pituitary deficiency:*** deficiency of all anterior pituitary hormones.	***Moderate anterior pituitary deficiency:*** deficiency in all anterior pituitary hormones ***except TSH it is normal.***	***Mild anterior pituitary deficiency:*** from the anterior pituitary hormones only ***Gonadotropins*** hormones are deficient, the others are normal.

Note that in all cases gonadotropin hormones are deficient, why is that?
Out of the hormones of the pituitary gland, Gonadotropins are the hormones secreted with the least percentage (3%-5%) and if you take a section in the pituitary gland you will find the distribution of gonadotropin secreting cells (Gonadotrophs) is the least.

Panhypopituitarism:

- itis a condition of inadequate or absent production of all pituitary hormones (posterior and anterior).
- causes: *-was not mentioned by the doctor-*
  - ✓ Extensive destructive tumors (usually Craniopharyngioma).
  - ✓ Postsurgical
  - ✓ Granuloma or trauma.

Anterior Lobe:	Posterior Lobe
Tropic: ACTH, FSH, LH, TSH	Oxytocin. * ADH (vasopressin).
Non-tropic: GH and prolactin.	

- ***Antidiuretic hormone deficiency:***
  - ✓ ADH deficiency causes ***central diabetes insipidus*** which is a condition characterized by large amount of diluted urine (can reach 20 liters), increased thirst with normal glucose levels.
  - ✓ ADH increases water reabsorption and eventually decreases the urine volume and increase its osmolarity, so in the absence of adequate amount of ADH urine osmolarity will decrease (Diluted urine) and urine volume will increase (loss of water as urine will increase leading to Polydipsia "Increased thirst").
  - ✓ The color of the urine in case of diabetes insipidus is pale without taste because it is diluted, in contrast to diabetes mellitus which has sweet taste and normal urine color varying from light yellow to dark yellow depending on fluid intake.

- ***Oxytocin deficiency:***
  - ✓ Deficiency of oxytocin is not problematic because baby delivery can occur without it. However, delivery process can be difficult that is why we now use substitute drugs for oxytocin deficiency.
  - ✓ Also, milk production is not much affected because of the presence of other factors affecting milk ejection and delivery.

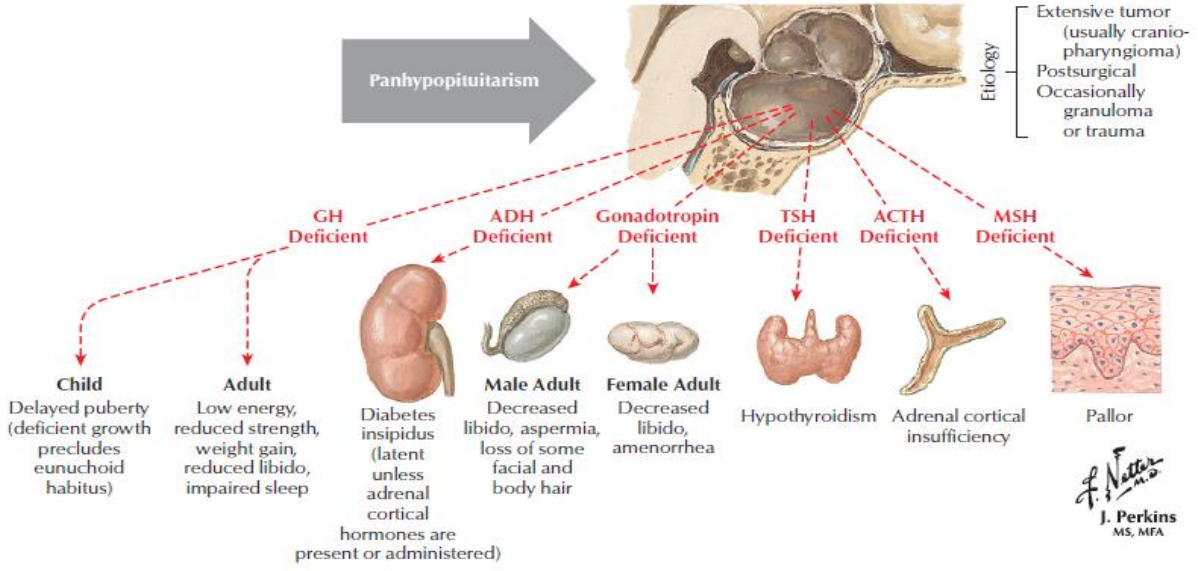
- ***Gonadotropins deficiency:***
  - ✓ the function of the primary sexual organs (ovaries and testis), which is the production of ova and sperms respectively and the secretion of hormones, is affected by the deficiency of the gonadotropins.
  - ✓ ***In Males:*** decreased libido (sexual desire), Aspermia, Loss of some facial and body hair.
  - ✓ ***In females:*** Decreased libido, Amenorrhea (no menstrual cycle).
  - ✓ ***Child:*** Delayed puberty.

Gonadotropic hormones normal function:

Follicle-stimulating hormone (FSH): stimulates development of ovarian follicle and regulates spermatogenesis in the testis.

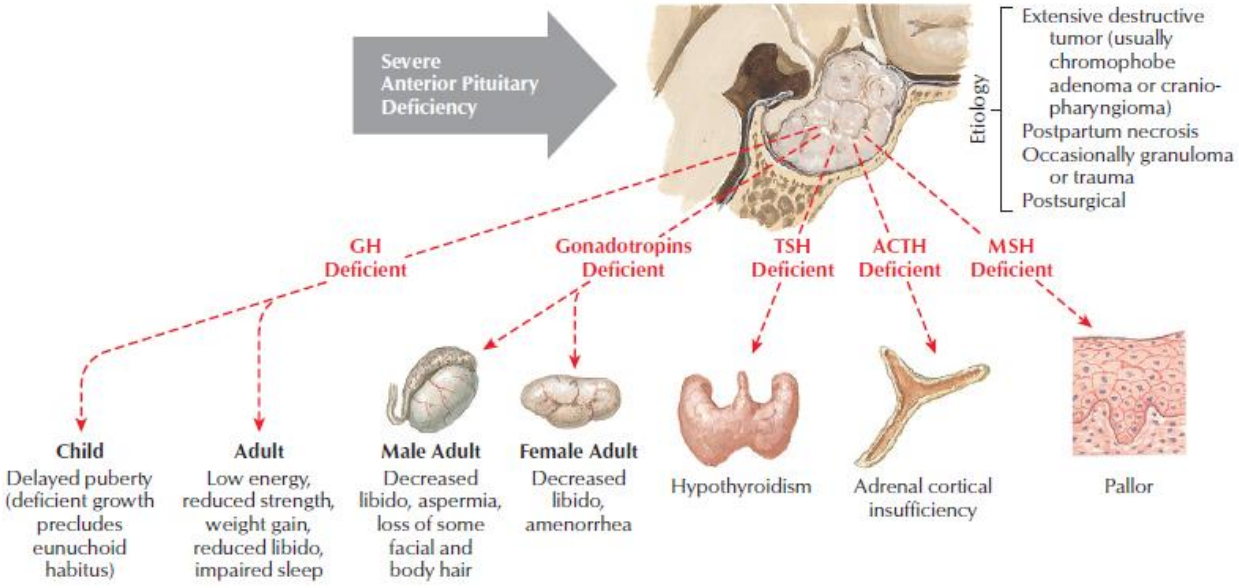
Luteinizing Hormone (LH): causes ovulation and formation of the corpus luteum in the ovary, stimulates production of estrogen and progesterone by the ovary, stimulates testosterone production by the testis.

- ***TSH deficiency:*** Hypothyroidism.
- ***ACTH deficiency:*** Adrenal cortical insufficiency. The production of glucocorticoids and androgens is affected, especially cortisol.
- ***MSH (Melanocyte Stimulating Hormone):*** its deficiency causes pallor (paleness).
- ***Growth Hormone (somatotropin):*** Its deficiency causes ***dwarfism*** (short stature). Usually their mentality (intelligence) is normal, but their fertility might be sometimes affected; they are sometimes infertile. They also suffer from muscle loss, microsplanchnia (the abdomen is small compared to the thorax



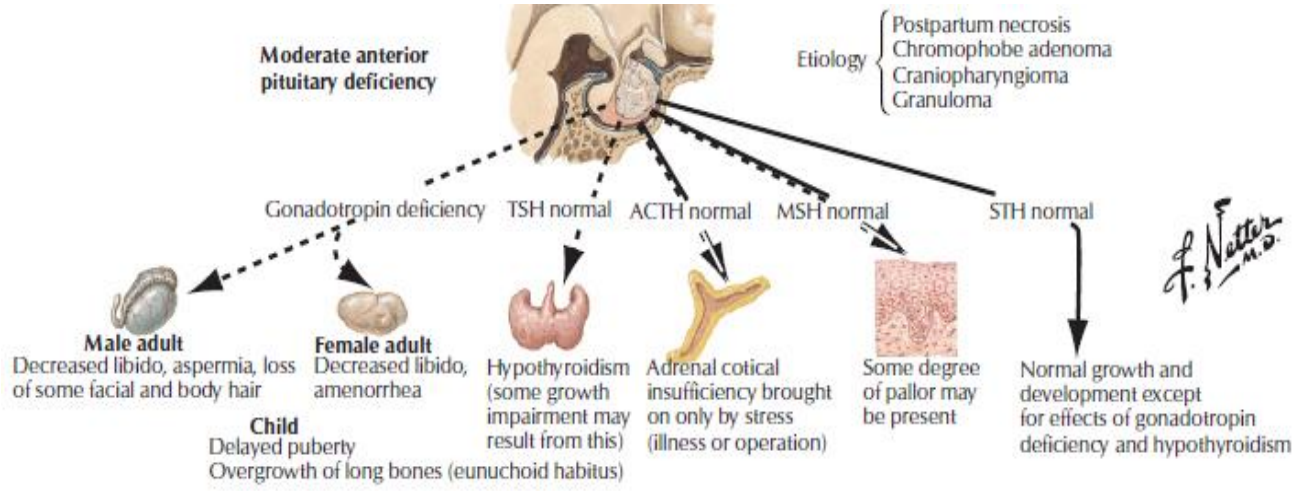
severe anterior pituitary deficiency:

- Similar to panhypopituitarism, except that the hormones of the posterior pituitary are normal.
- All hormones of the anterior pituitary are deficient.



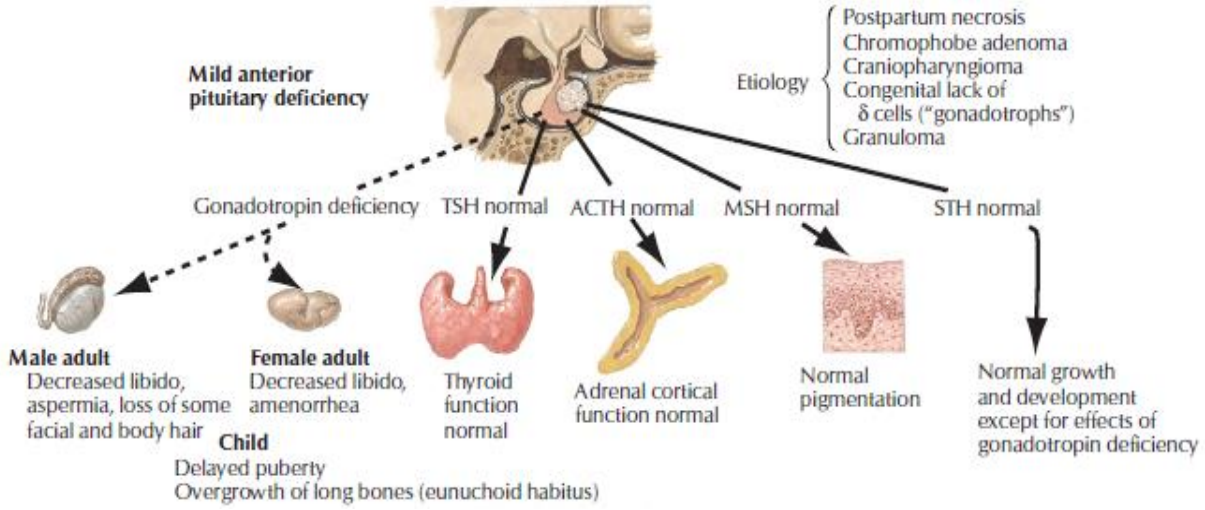
Moderate anterior pituitary deficiency:

- Growth hormone is normal.
- MSH and ACTH are partially deficient.
- Gonadotropins and TSH are deficient.



Mild anterior pituitary deficiency:

- All the hormones of the anterior pituitary are normal except gonadotropins (FSH & LH).



The End