The Endocrine System

PHYSIOLOGY

☑ Sheet ☐ Slide ☐ Handout

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❖ This lecture is a continuation of what was discussed in the previous two lectures ..

Note : this sheet was written according to the recording of section 1 .

❖ **Anti- duretic hormone (ADH) / Vasopressin :**

- Poserior pituitary gland secretes **oxytocin** as well as **vasopressin** hormones .

➢ In human being and most mammals , this hormone is called Arginine Vasopressin (AVP) (remarking the presence of the amino acid Arginine in the structure of the hormone) .

➢ In some other species (eg. Hippopotami (فرس النهر) and most pigs) , there is a lysine instead of an Arginine and the hormone is therefore called Lysine vasopressin .

➢ In some other mammals , the posterior pituitary contains a mixture of lysine vasopressin and arginine vasopressin . Examples : marsupials (eg. Kangaroos) and some pigs .

➢

Note 1 : vasopressin hormone is so called due to its vasoconstrictor effect on the arterioles throughout the body .

Note 2 : posterior lobe hormones are Nonapeptides (peptides of nine amino acids) with a disulfide bridge at one end .

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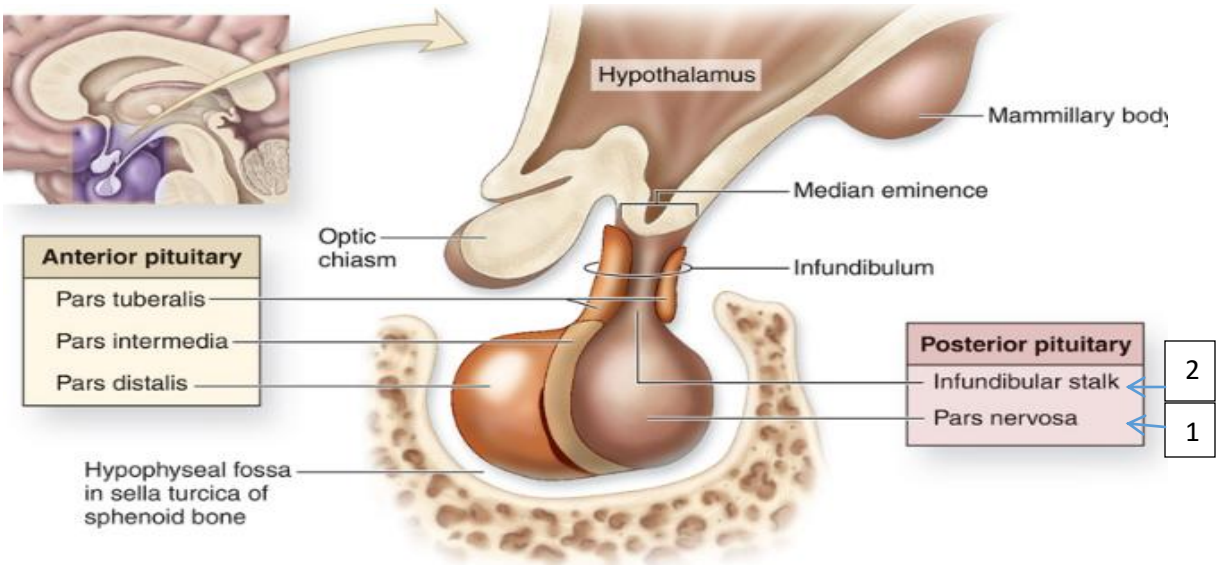
❖ The neurohypophysis (posterior pituitary) consists of the pars nervosa (1) and the infundibular stalk (2) . The pars nervosa , unlike adenohypophysis , does not contain secretory cells . It is composed of neural tissue , containing some 100,000 unmyelinated axons of secretory neurons whose cell bodies are situated in the supraoptic and periventricular nuclei of the hypothalamus . [JUNQUEIRA'S Basic Histology – 12th edition]



➢ Hormones are synthesized in the hypothalamus , and transferred through nerve axons into the nerve terminals in the posterior pituitary gland .

➢ These hormones are antiduretic hormone (vasopressin) and oxytocin .

❖ And As said earlier , there is an indirect relationship between the anterior pituitary and hypothalamus . Hypothalamus affects the anterior pituitary through hormones that are usually released into the median eminence (the primary capillary plexus that is composed of the superior hypophyseal artery) , where they pass through the capillary endings (hypophyseal portal veins) to the secondary capillary plexus in the anterior pituitary , stimulating or inhibiting the release of anterior pituitary hormones .

❖ Recently , it was found that there is another way of communication between the hypothalamus and anterior pituitary gland . There are neurons extending

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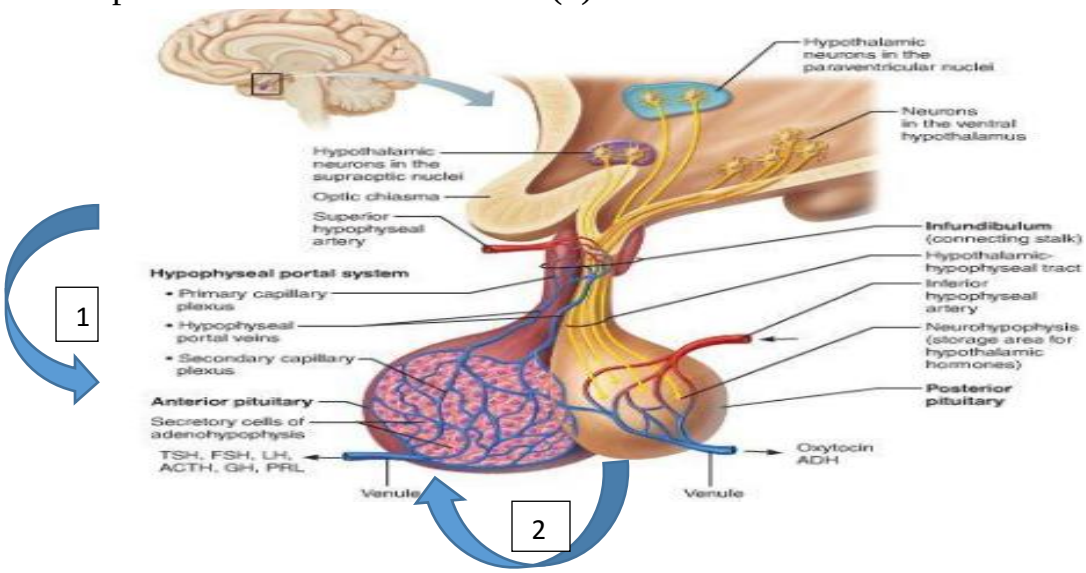
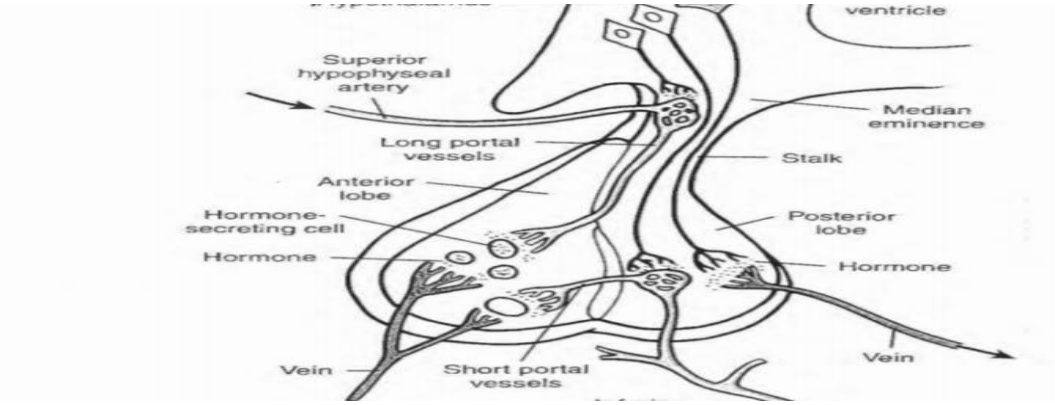
from the hypothalamus down to the posterior pituitary location which , in turn , releases hormones to affect the anterior pituitary directly .

To cut is short :

There are two ways of stimulation (or inhibition) of anterior pituitary hormones :

- Either through long portal vessels (hypophyseal portal veins) → delayed (1)
- Or short nerve axons that extend to the post. Pitutiry stimulating or inhibiting anterior pituitary hormones through their products via short potassium vein→ immediate (2) .





Notes :

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- both primary and secondary capillary plexuses are made up by the superior hypophyseal artery .
- the inferior hypophyseal artery only blood supplies the posterior pituitary gland .
- the previous section was not mentioned this way during the lecture . I tried to clarify and simplify things more than the doctor did . for more Info. About this section , you can refer to JUNQUERA's Basic Histology – 12th edition – Endocrine glands – P.349-353 . (or any newer edition)

❖ **posterior pituitary gland is composed of two nuclei : supraoptic and paraventricular nuclei .**

❖ **Anterior pituitary gland is composed of at least five cell types with each cell type producing usually one hormone :**

1. **somatotropes** → produce growth hormone (somatotropin), so somatotrophes secrete somatotropins that stimulate several tissues to secrete IGF (Insuline- like GH) – Principles Of Anatomy and Physiology 14th edition – p657) .

2. **corticotropes** → produce ACTH (adrenocorticotropic hormone) .

3. **thyrotropes** → produce TSH (thyroid stimulating hormones) .

4. **Gonadotropes** → produce FSH and LH .

5. **lacotropes** → produce prolactin .

✓ Some times in normal , or abnormal , conditions , the somatotropes produce prolactin beside growth hormone because of the similarity in structure for both hormones.

✓ Some Gonadotropes produce FSH only , and some others produce LH only , but most of gonadotropes produce both hormones .

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✓ About 30-40% of the anterior pituitary cells are somatotropes (that secrete the growth hormone) .

✓ About 20% of anterior pituitary cells are corticotropes (that secrete ACTH) .

✓ Each of the other cell types account for only 3-5% of the total anterior pituitary cells .

❖ As mentioned earlier , hypothalamus regulates the secretion of anterior pituitary hormones through production of hormones by means of the nerves that end at the capillary bed in the median eminence (primary capillary plexus) which then transfer to the anterior pituitary gland for regulation .

➢ Hypothalamic releasing and inhibitory hormones that control the anterior pituitary gland .(table 75-2 in the slides)

Hormone	Structure	Primary Action on Anterior Pituitary
Thyrotropin-releasing hormone (TRH)	Peptide of 3 amino acids	Stimulates secretion of TSH by thyrotropes
Gonadotropin-releasing hormone (GnRH)	Single chain of 10 amino acids	Stimulates secretion of FSH and LH by gonadotropes
Corticotropin-releasing hormone (CRH)	Single chain of 41 amino acids	Stimulates secretion of ACTH by corticotropes
Growth hormone-releasing hormone (GHRH)	Single chain of 44 amino acids	Stimulates secretion of growth hormone by somatotropes
Growth hormone inhibitory hormone (somatostatin)	Single chain of 14 amino acids	Inhibits secretion of growth hormone by somatotropes
Prolactin-inhibiting hormone (PIH)	Dopamine (a catecholamine)	Inhibits synthesis and secretion of prolactin by lactotropes

✓ The doctor mentioned the hormones and their functions , but didn't mention the number of amino acids and the structure of each hormone .

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- Here you have to notice the effect of each of the hypothalamic hormones on each of the anterior pituitary hormones .

✓ By now , you are able to differentiate the hypothalamic hormones and anterior pituitary hormones .

✓ For most of anterior pituitary hormones , it is the releasing hormones (of hypothalamus) that are important , but for prolactin , a hypothalamic inhibitory hormone probably exerts more control (more important) .

✓ Now you can notice that anterior pituitary hormone are of great importance and are therefore regulated by hypothalamus which is regulated by ALL centers of the CNS .

- Important : All centers of the CNS control the hypothalamus which , in turn , control the anterior and posterior pituitary glands .

❖ ***<u>Now , we will start talking about the anterior pituitary hormones separately :</u>***

- We'll begin with the growth hormone and the rest of hormones will be discussed when discussing their specific target organs .Growth hormone targets all the cells of the body .

- In the following figure , we have 2 rats :

  - A control rat (not injected by growth hormone or anything) .
  - A rat injected with the growth hormone .

- As you can see , the weight of the rat injected with growth hormone increased drastically .

- Growth hormone affects all cells of the body , which are capable of growing and dividing (increasing cell size & mitosis)

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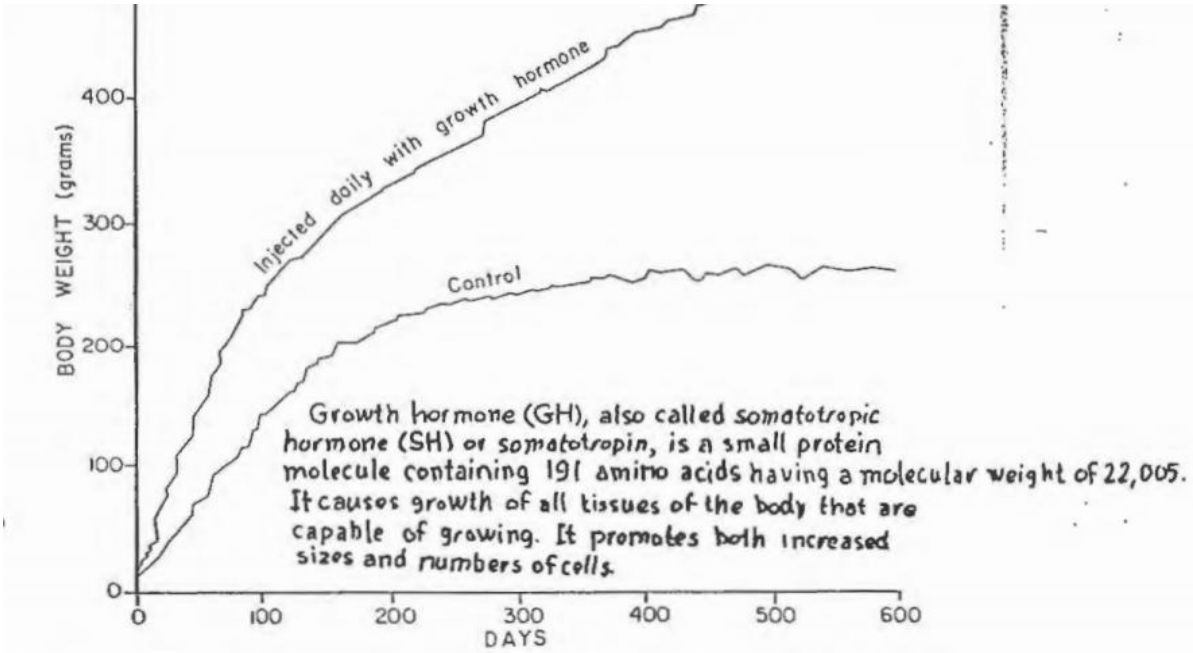

Figure 75–4. Comparison of weight gain of a rat injected daily with growth hormone with that of a normal rat.

- In the previous lecture , it was mentioned that there are three types of hormonal interactions :
  - ✓ Permissive interaction .
  - ✓ Synergistic interaction .
  - ✓ Antagonistic interaction .

- ***Growth hormone is not the only contributor in the growth of the body , there are multiple other hormones that perform this function , these are :***

✓ Insulin (we can even say that insulin plays more important role in the growth than the growth hormone)
✓ Thyroid hormones
✓ Glucocorticoid hormone
✓ Androgens
✓ Estrogens
✓ Insulin – like growth factors

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❖ Growth hormone and insulin – like growth factor have been identified as the major determinants of normal post uterine life (after birth).
  - ➢ Insulin and growth hormone interact synergistically .

❖ Growth hormone has several metabolic effects aside from its general effect in causing growth, including :

1. Increased rate of protein synthesis in most cells.

2.increased mobilization of fatty acid from adipose tissue ,increased free fatty acid in the blood, and increased use of fatty acid for energy.

3. Decrease rate of glucose utiliztion by decreasing glucose uptake in tissues such as skeletal muscle and adipose tissue, increased glucose production by the liver via gluconeogenesis, and increased insulin secretion.

Note: increased insulin secretion is due to the decreased uptake of glucose and gluconeogenesis which consequently elevates blood glucose concentration and stimulates the pancreas to secrete insulin.

By understanding the metabolic effect of the growth hormone it will be easy to predict its function in different tissues of the body ,which will be discussed in the following paragraph.

Note: Growth hormone exerts its effect either directly or indirectly.

❖ Growth hormone direct effects on the cells of the body :

1. On adipose tissue → to decrease the adiposity , by increasing the lipolysis and decreasing the glucose uptake by the adipose tissue .

2. On the liver → 1- increasing RNA synthesis in order to increase protein production.

   2- increasing the rate of protein synthesis .

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3- increasing gluconeogenesis (production of glucose from non – carbohydrate sources).

4- production of somatomedins (which are sometimes called Insulin – like growth factors) , there are several types of somatomedins which are differen in structure (number of amino acid) , exert the same effects , and have different potencies .

3. on muscle cells → 1- decrease glucose uptake .

2- increase amino acid uptake .

3- increase protein synthesis .

- Indirect effects :

Through somatomedins , which are proteins different in the number of amino acids . They affect several organs and cells by different actions as explained in the

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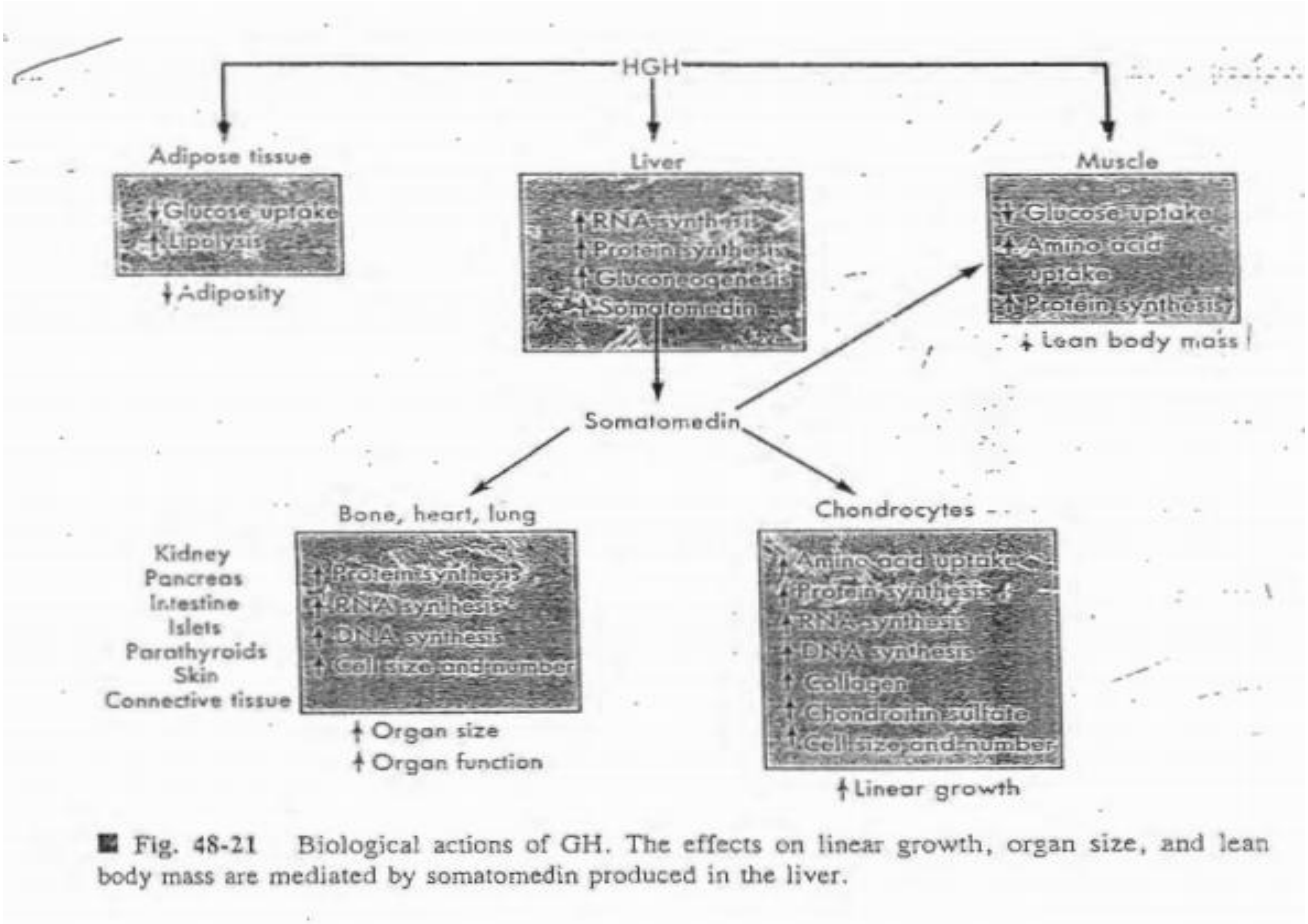
figure below .



■ Fig. 48-21 Biological actions of GH. The effects on linear growth, organ size, and lean body mass are mediated by somatomedin produced in the liver.

❖ The effects of growth hormone (in general) :

- Normalizes (increases) the blood glucose level
- Normalizes (increases) fatty acid level in blood
- Increases the amino acid uptake by cells so as to promote growth

➢ Growth hormone enhances the body protein , using up the fatty stores for energy(so as to spare the amino acids) and conserves carbohydrates .

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❖ ***Diabetogenic effect of Growth hormone (due to abnormal /over release of growth hormone) :***

1. we have already mentioned that growth hormone increases the blood glucose level .
2. growth hormone has also a direct effect on beta cells (that secrete insulin) which will ultimately get overstimulated and exhausted (the cells finally burn out) .
3. when this occurs the person develops diabetes mellitus .
4. therefore , GH (when over-released) is said to have a diabetogenic effect .

❖ ***Ketogenic effect of growth hormone (due to oversecretion of GH) :***

GH increases the free fatty acids in the blood . therefore , a great amount of fat is mobalized and a lot of acetoacetic acids are formed by the liver and released into the body fluids , this causes ketosis .

- Diabetogenic effect → due to increased glucose blood concentration .
- Ketogenic effect → due to increased fatty acid in the blood via fat mobalization from adipose tissue –> increased acetoacetic acid release into the body fluids from the liver.

❖ ***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 .

❖ Now , we will see the condition of growth hormone , insulin and somatemedin upon protein intake , carbohydrate intake and fasting :

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- Protein intake → all of them increase . (remember : insulin and growth hormone function together and complement each other) because the ingested protein is going to be hydrolysed into amino acid which will consequently elevate the blood free amino acid concentration and this will signal the hypothalamus to inhibit somatostatin release.
- Carbohydrate intake → neither GH nor somatomedin are needed in such condition , but insulin is needed to normalize glucose in the blood , thus it increases .
- During fasting → we need glucose (no need for insulin) , thus only GH increases because the reduced blood glucose level will stimulate gluconeogenesis which will lead to the break down of the body proteins which generally means a loss in the body mass (apposite to the effect of the growth hormone) and this will stimulate the release of GH.

❖ ***The figure below shows the stimulatory and inhibitory factors of growth factor secretion :***

All of them are logical , except the hormone ghrelin (a hormone secreted by the stomch as well as the small intestine before meals and acts to increase the appetite) .

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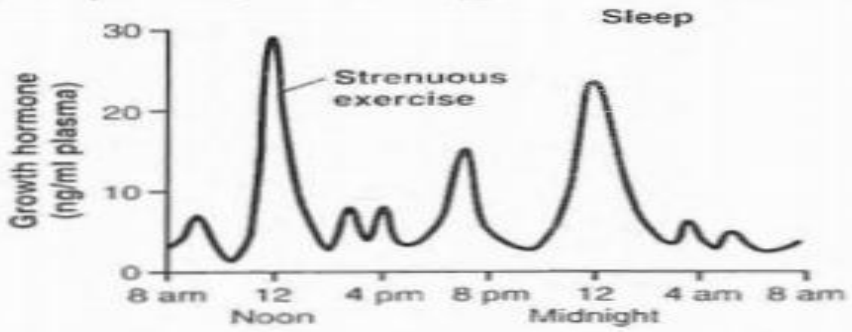
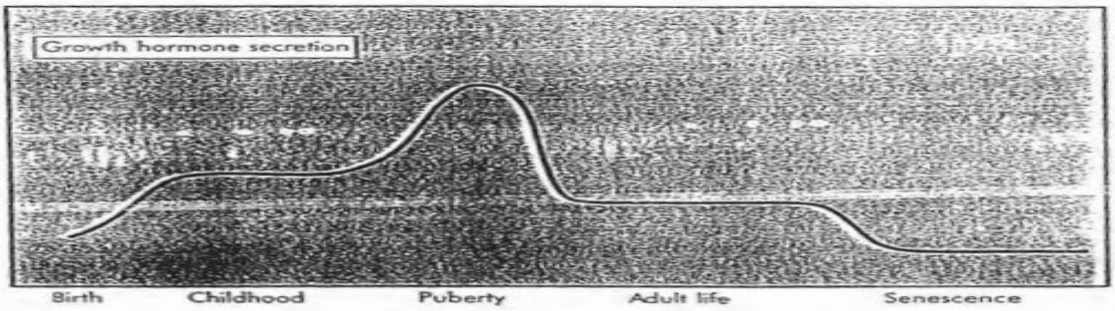


Figure 75-6 Typical variations in growth hormone secretion throughout the day, demonstrating the especially powerful effect of strenuous exercise and also the high rate of growth hormone secretion that occurs during the first few hours of deep sleep.

Table 75-3 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)	
Growth hormone–releasing hormone	
Ghrelin	

❖ ***Here is another gragh showing the levels of growth hormone during different stages of individual's life (developmental rhythm) :***



■ Fig. 48-19 Lifetime pattern of growth hormone (GH) secretion. GH levels are higher in children than adults with a peak period during puberty. GH secretion declines with aging.

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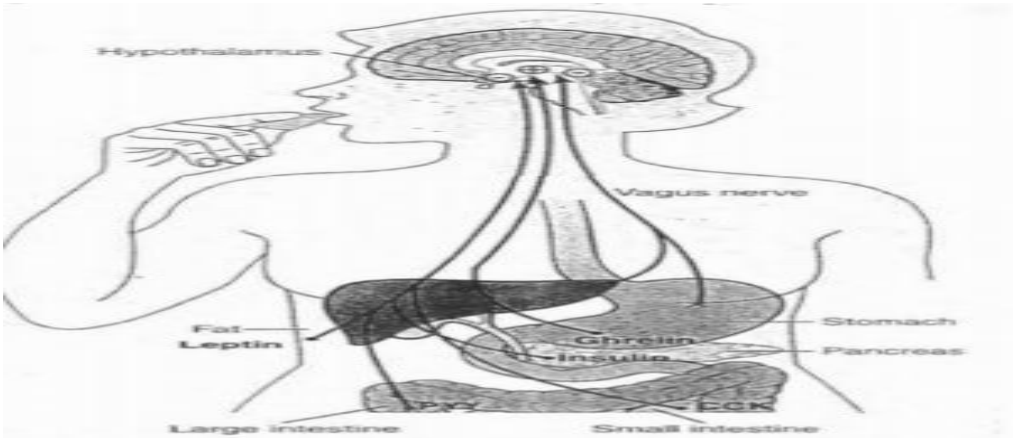
- As you can see : the level of GH in adult life is less than that in childhood , but the difference between the two levels is ***not significant*** .
  - A certain difference is not significant when it does not exceed 10% .
  - Maximum level of GH at puberty .

- Now Let's have an idea about feedback mechanism and the control of food intake .
  - In general , we say that food intake is a habit , when you eat too much , your stomach will dilate and you won't feel full until food touches the stomach receptors . therefore , they cut a part of stomach as a way to lose weight by decreasing food intake .

  - Stretch receptors of the stomach activate certain afferent pathwas through the vagus nerve that inhibit food intake .

  - Peptide yy (pyy) , CCk (cholysestokinine) , and insulin are gastrointestinal hormones that are released by ingestion of food and suppress further feeding .

  - Ghreline is released by the stomach and stimulates appetite . Leptin hormone is released in high amounts by fat cells as they increase in size , it inhibits food intake .



كلنا ننهزم أمام الموت ، لكن لا شيء أفظع من أن ننهزم أمام الحياة .

THE END