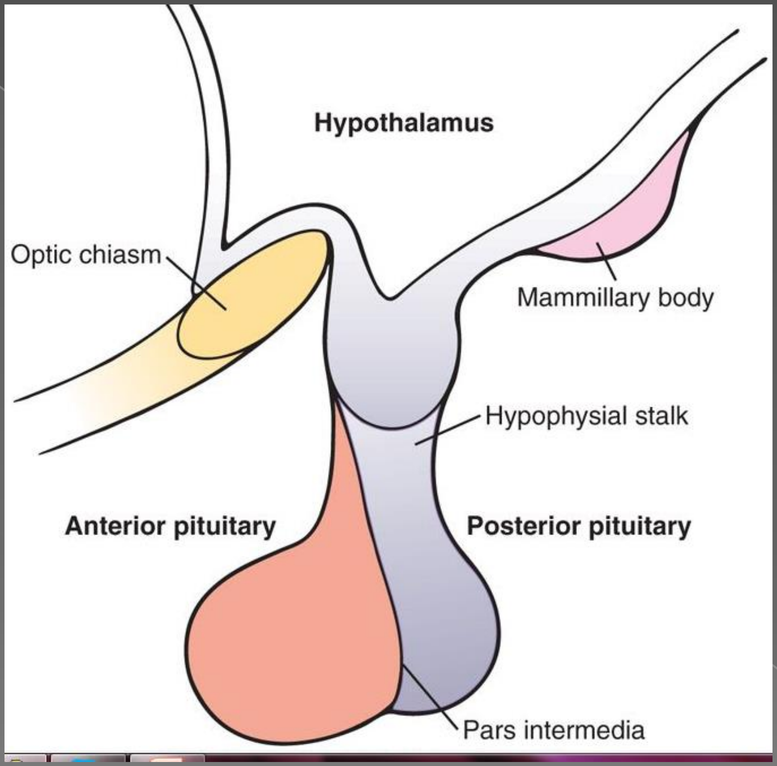
Pituitary Hormones and Their Control by the Hypothalamus

- also called the hypophysis,
- a small gland-about 1 centimeter in diameter and 0.5 to 1 gram in weight
- lies in the sella turcica, a bony cavity at the base of the brain, and is connected to the hypothalamus by the pituitary stalk.
- Physiologically, divisible into two distinct portions: the anterior pituitary, also known as the **adenohypophysis**, and the posterior pituitary, also known as the **neurohypophysis**.
- Between these is a small, relatively avascular zone called the **pars intermedia***


Hypothalamus
Optic chiasm
Mammillary body
Hypophysial stalk
Anterior pituitary
Posterior pituitary
Pars intermedia

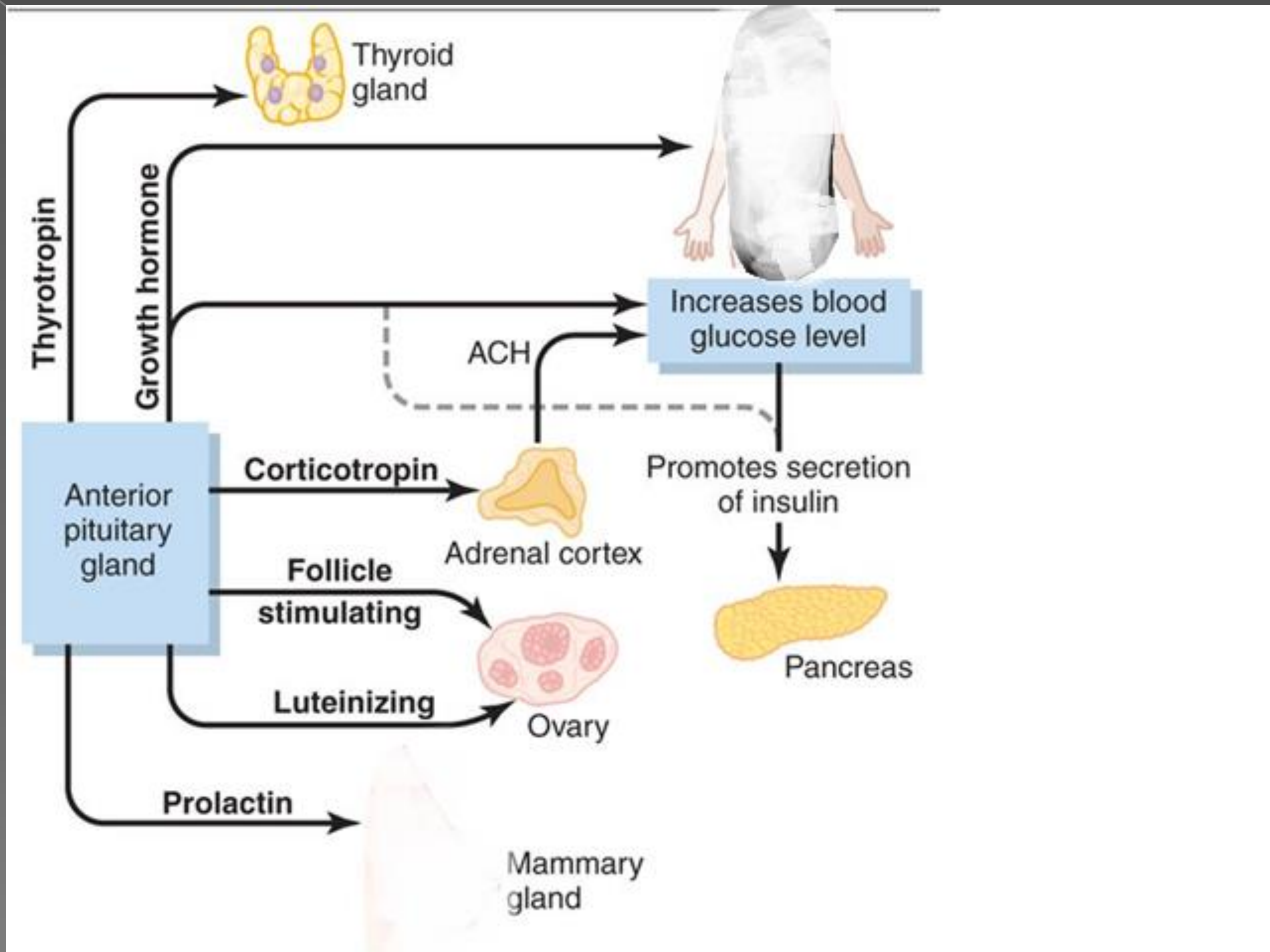
Embryologically

- anterior pituitary from **Rathke's pouch**, which is an embryonic invagination of the pharyngeal epithelium → epithelioid nature cells

- the posterior pituitary from a neural tissue outgrowth from the hypothalamus → glial-type cells.

Anterior pituitary hormones

- Growth hormone
- Adrenocorticotropin (corticotropin)
- Thyroid-stimulating hormone (thyrotropin)
- Prolactin
- Two separate gonadotropic hormones,
  - follicle-stimulating hormone
  - luteinizing hormone



Thyroid gland
Thyrotropin
Growth hormone
Increases blood glucose level
ACH
Anterior pituitary gland
Corticotropin
Adrenal cortex
Promotes secretion of insulin
Follicle stimulating
Pancreas
Luteinizing
Ovary
Prolactin
Mammary gland

Posterior Pituitary Hormones

- The bodies of the cells that secrete the posterior pituitary hormones are not located in the pituitary gland
- magnocellular neurons, located in the supraoptic and paraventricular nuclei of the hypothalamus.
- The hormones are then transported in the axoplasm of the neuron's nerve fibers passing from the hypothalamus to the posterior pituitary gland.

- The two hormones secreted by the posterior pituitary play other roles.
- **Antidiuretic hormone** (also called vasopressin) controls the rate of water excretion into the urine, thus helping to control the concentration of water in the body fluids.
- **Oxytocin** helps express milk from the glands of the breast to the nipples during suckling and helps in the delivery of the baby at the end of gestation.

Five cell types can be differentiated

- Somatotropes-human growth hormone (hGH)
- Corticotropes-adrenocorticotropin (ACTH)
- Thyrotropes-thyroid-stimulating hormone (TSH)
- Gonadotropes-gonadotropic hormones, which include both luteinizing hormone (LH) and follicle-stimulating hormone (FSH)
- Lactotropes-prolactin (PRL)

- somatotropes → 30 to 40 % → growth hormone
- corticotropes → 20 % → ACTH.
- Each of the other cell types → 3 to 5 %
- Somatotropes stain strongly with acid dyes and are therefore called acidophils.

Anterior pituitary

Hormones	Cells	Target organ	Function in brief
Growth hormone	Somatotropes (acidophilic)	Almost all cells and tissues of the body	Overall growth of most cells and tissues
Adrenocorticotropic hormone or ACTH	Corticotropes (basophilic)	adrenal cortex	Stimulate adrenal cortex
Thyroid stimulating hormones or TSH	Thyrotropes (basophilic)	Thyroid gland	Stimulate Thyroid gland
Luteinizing hormone or LH	Gonadotropes (basophilic)	Gonad	Stimulate gonad
Follicle stimulating hormone or FSH	Gonadotropes (basophilic)	Gonad	Stimulate gonad
Prolactin	Lactotropes (acidophilic)	Breast	Secretion of milk.

Posterior pituitary

Hormones	Target Organ	Function in Brief
Antidiuretic hormone (also called *vasopressin*)	Kidney	Controls the rate of water excretion into the urine, thus helping to control the concentration of water in the body fluids
Oxytocin	Breast Uterus	Helps express milk from the glands of the breast to the nipples during suckling and helps in the delivery of the baby at the end of gestation.

Table 75-1. Cells and Hormones of the Anterior Pituitary Gland and Their Physiological Functions

Cell	Hormone	Chemistry	Physiological Action
Somatotropes	Growth hormone (GH; somatotropin)	Single chain of 191 amino acids	Stimulates body growth; stimulates secretion of IGF-1; stimulates lipolysis; inhibits actions of insulin on carbohydrate and lipid metabolism
Corticotropes	Adrenocorticotropic hormone (ACTH; corticotropin)	Single chain of 39 amino acids	Stimulates production of glucocorticoids and androgens by the adrenal cortex; maintains size of zona fasciculata and zona reticularis of cortex
Thyrotropes	Thyroid-stimulating hormone (TSH; thyrotropin)	Glycoprotein of two subunits, α (89 amino acids) and β (112 amino acids)	Stimulates production of thyroid hormones by thyroid follicular cells; maintains size of follicular cells
Gonadotropes	Follicle-stimulating hormone (FSH)	Glycoprotein of two subunits, α (89 amino acids) and β (112 amino acids)	Stimulates development of ovarian follicles; regulates spermatogenesis in the testis 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
	Luteinizing hormone (LH)	Glycoprotein of two subunits, α (89 amino acids) and β (115 amino acids)	
Lactotropes Mammotropes	Prolactin (PRL)	Single chain of 198 amino acids	Stimulates milk secretion and production

Hypothalamus Controls Pituitary Secretion

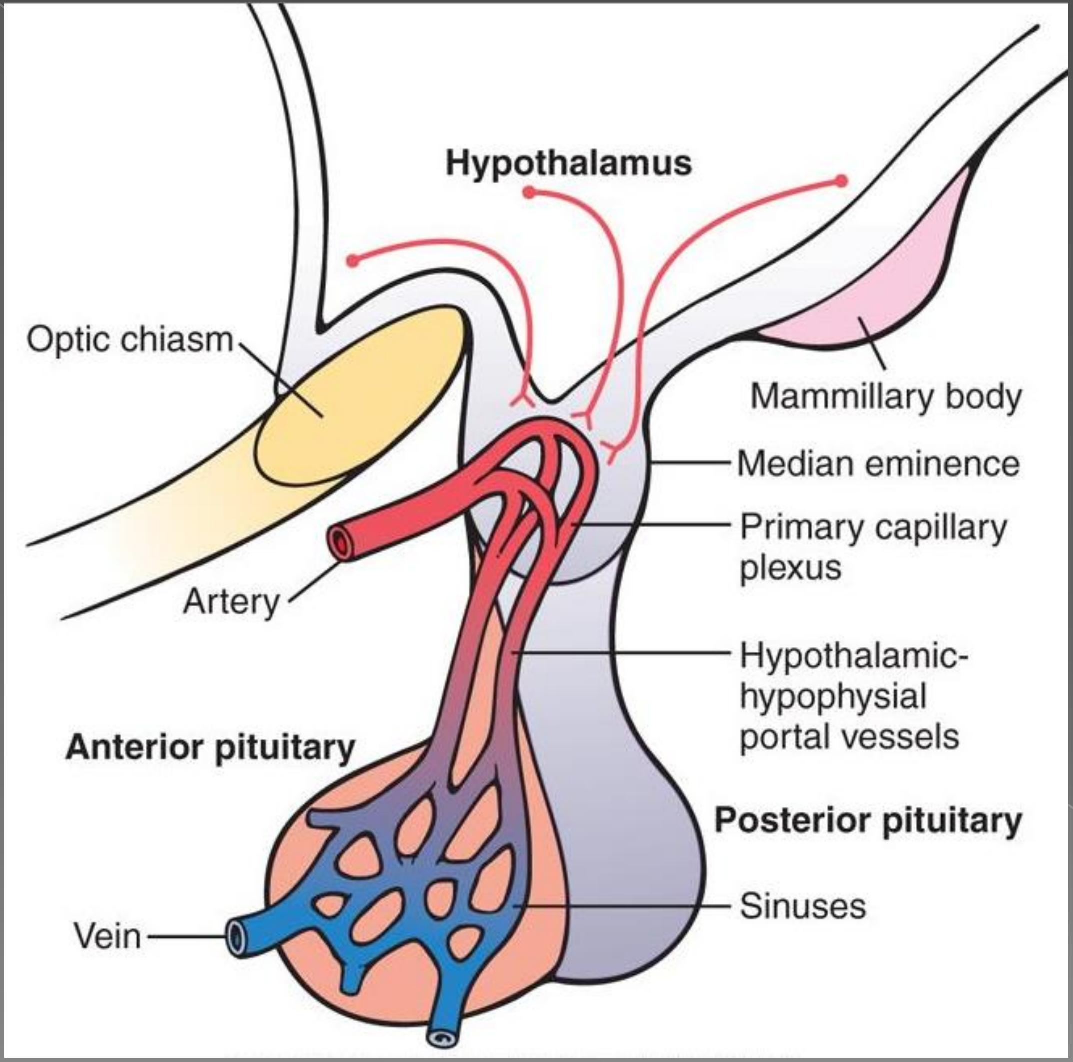


Table 75-2. Hypothalamic Releasing and Inhibitory Hormones That Control Secretion of the Anterior Pituitary Gland

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

GROWTH HORMONE

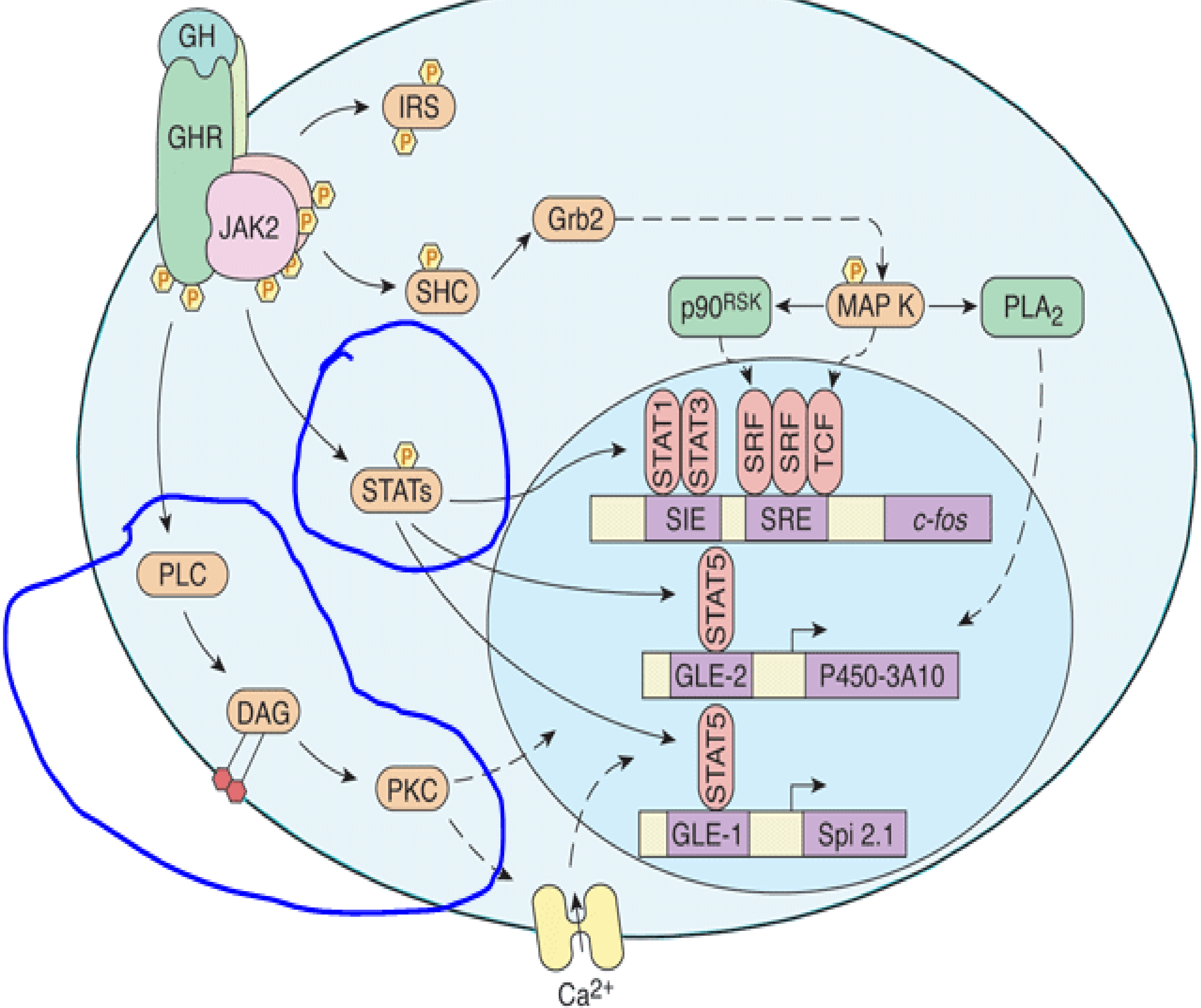
Plasma Levels, Binding, & Metabolism

- Approximately 50% of the circulating pool of growth hormone activity is in the bound form.
- The basal plasma growth hormone level in adult humans is normally less than 3 ng/mL. This represents both the protein-bound and free forms.
- Growth hormone is metabolized rapidly, probably at least in part in the liver. The half-life of circulating growth hormone in humans is 6–20 min, and the daily growth hormone output has been calculated to be 0.2–1.0 mg/d in adults.

- The growth hormone receptor is protein with a large extracellular portion, a transmembrane domain, and a large cytoplasmic portion. Growth hormone has two domains that can bind to its receptor, and when it binds to one receptor, the second binding site attracts another, producing a homodimer, Dimerization is essential for receptor activation.

- also called somatotropic hormone or somatotropin

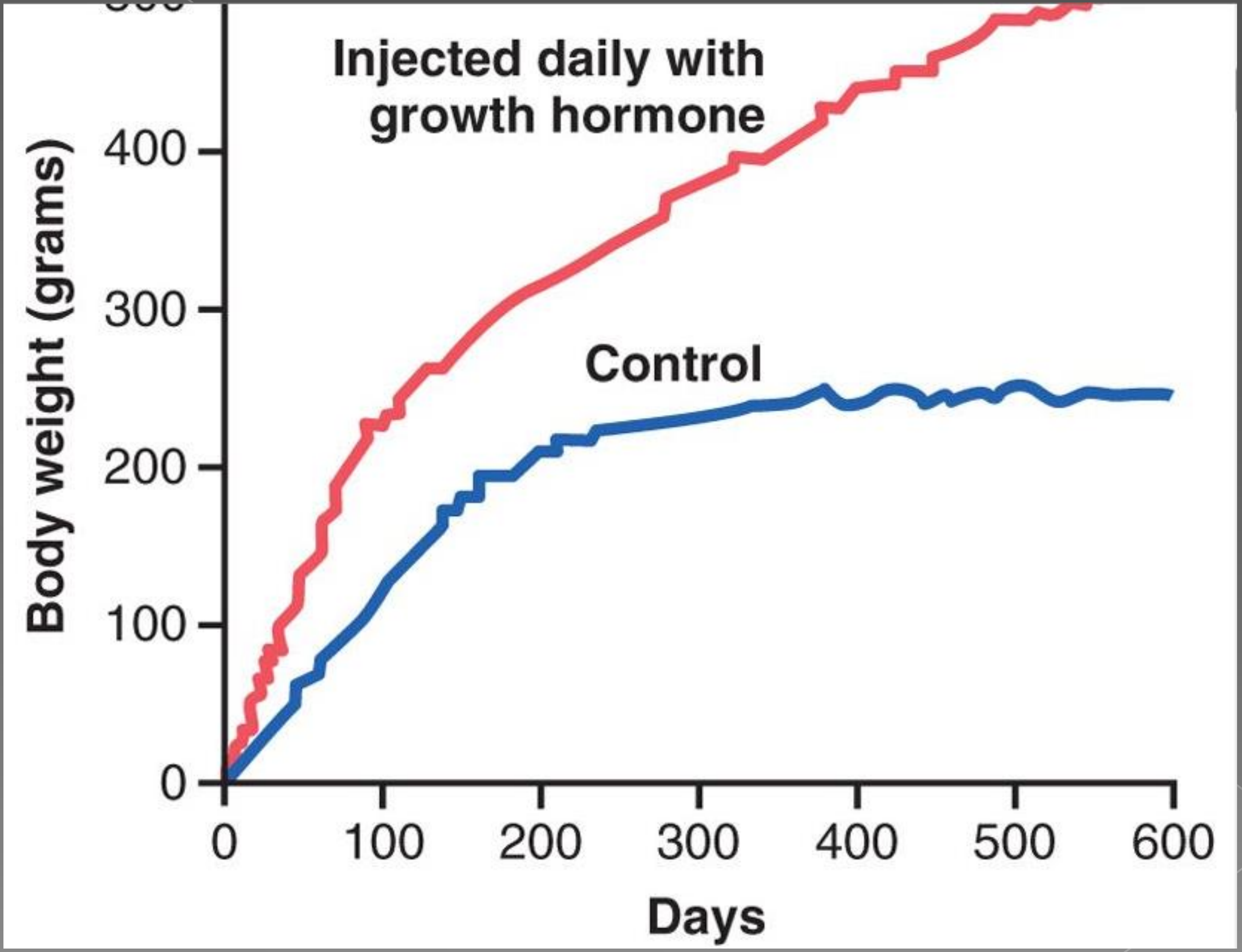
- a small protein molecule that contains 191 amino acids in a single chain and has a molecular weight of 22,005.


GH
GHR
JAK2
P
IRS
SHC
Grb2
MAP K
p90RSK
PLA2
STATs
STAT1
STAT3
SRF
SRF
TCF
SIE
SRE
c-fos
STAT5
GLE-2
P450-3A10
STAT5
GLE-1
Spi 2.1
PLC
DAG
PKC
Ca2+

Effect of growth hormone

- growth of almost all tissues of the body that are capable of growing.
- increases sizes of the cells
- increases mitosis with development of greater numbers of cells
- Increases differentiation of certain types of cells such as bone growth cells and early muscle cells.

Effect of growth hormone



Metabolic effects

- Anabolic hormone
- Increased lean body mass
- Protein Sparer
- Inhibit glucose utilization

- **Protein metabolism**
- A protein anabolic hormone and produces a positive nitrogen balance and a fall in blood urea nitrogen and amino acid levels.

Protein metabolism

- ↑ Amino Acid transport through Cell Membranes
- Enhancement of RNA translation to Cause Protein Synthesis by the Ribosomes
- Increased Nuclear Transcription of DNA
- Decreased Catabolism of Protein and Amino Acids → protein sparer

Summary

Growth hormone enhances almost all facets of amino acid uptake and protein synthesis by cells

at the same time reducing the breakdown of proteins.

Fat metabolism

- Growth hormone enhances fat utilization for energy.

Fat metabolism

- release of fatty acids from adipose tissue and increased concentration of fatty acids in the body fluids.
- enhances the conversion of fatty acids to acetyl coenzyme A (acetyl-CoA) and its subsequent utilization for energy.*
- **Growth hormone's ability to promote fat utilization, together with its protein anabolic effect, causes an increase in lean body mass.**

“Ketogenic” Effect of Growth Hormone

- Under the influence of excessive amounts of growth hormone, fat mobilization from adipose tissue sometimes becomes so great that large quantities of acetoacetic acid are formed by the liver and released into the body fluids, thus causing *ketosis.*

- This excessive mobilization of fat from the adipose tissue also frequently causes a fatty liver.

Ketogenic Effect

↑growth hormone secretion

↓

↑Fat mobilization from adipose tissue

↓

↑ Fat metabolism

↑

↑ Ketone body (acetoacetic acid) formation

↓

↑Ketone bodies in blood

↓

Ketoacidosis

Carbohydrate metabolism

- ↑blood glucose level
- induces "insulin resistance,"
- diabetogenic

Carbohydrate metabolism

- (1) decreased glucose uptake in tissues such as skeletal muscle and fat
- (2) increased glucose production by the liver
- (3) increased insulin secretion.

Probable cause of insulin resistance

- increase in blood concentrations of fatty acids likely contribute to impairment of insulin's actions on tissue glucose utilization.

- Experimental studies indicate that raising blood levels of fatty acids above normal rapidly decreases the sensitivity of the liver and skeletal muscle to insulin's effects on carbohydrate metabolism.

Necessity of Insulin and Carbohydrate for the Growth-Promoting Action of Growth Hormone

- Adequate insulin activity and adequate availability of carbohydrates are necessary for growth hormone to be effective.

- Part of this requirement for carbohydrates and insulin is to provide the energy needed for the metabolism of growth, but there seem to be other effects as well.

- Especially important is insulin's ability to enhance the transport of some amino acids into cells, in the same way that it stimulates glucose transport

Cartilage and Bone Growth

- Increases growth of the skeletal frame.

(1) increased deposition of protein by the chondrocytic and osteogenic cells that cause bone growth,

(2) increased rate of reproduction of these cells

(3) a specific effect of converting chondrocytes into osteogenic cells, thus causing deposition of new bone.

Two principal mechanisms of bone growth

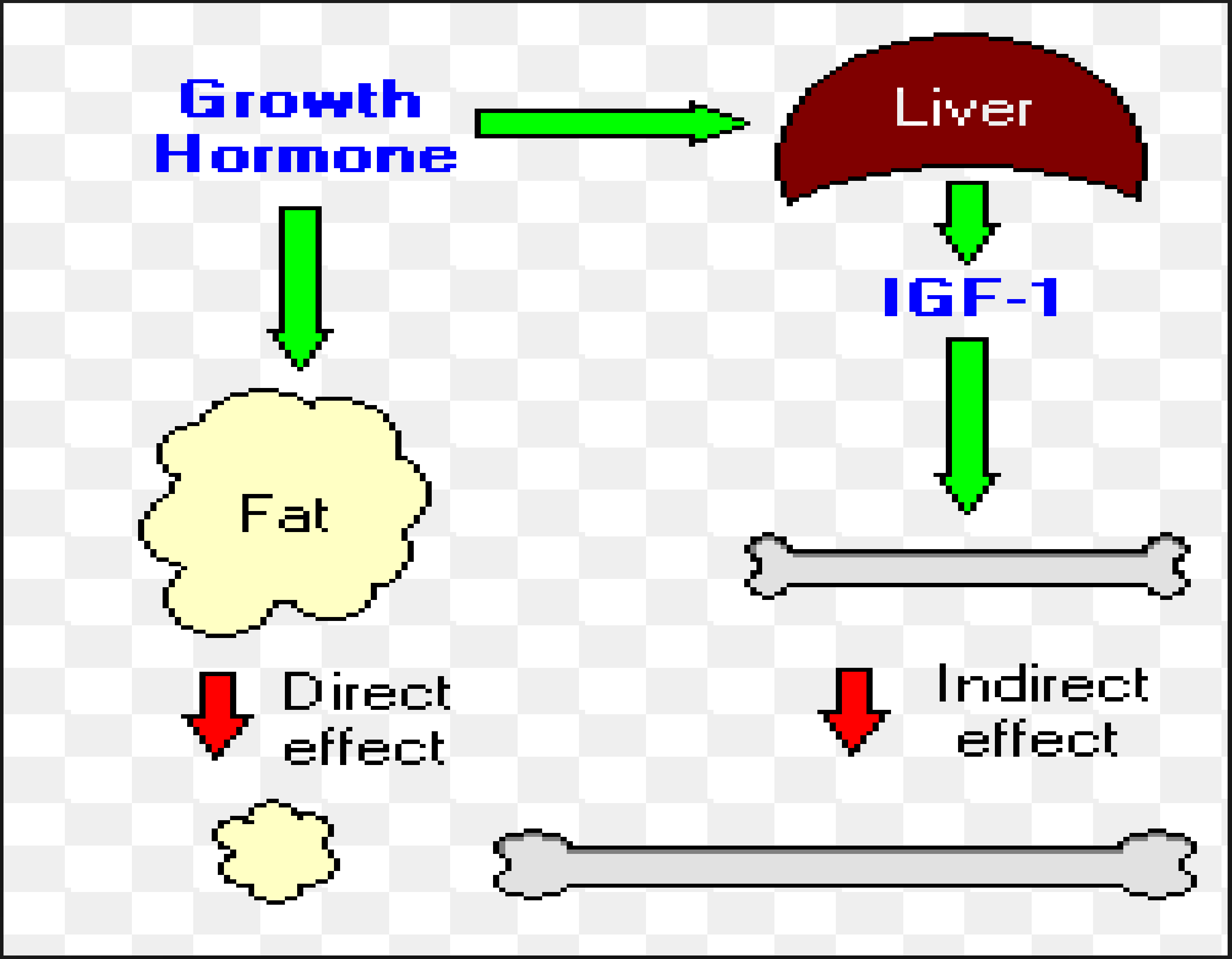
- First, the long bones grow in length at the epiphyseal cartilages, where the epiphyses at the ends of the bone are separated from the shaft.
- deposition of new cartilage, followed by its conversion into new bone, thus elongating the shaft
- epiphyseal cartilage itself is progressively used up, so by **late adolescence,** no additional epiphyseal cartilage remains to provide for further long bone growth.
- At this time, bony fusion occurs between the shaft and the epiphysis at each end, so no further lengthening of the long bone can occur.

- **Osteoblasts** in the bone periosteum and in some bone cavities deposit new bone on the surfaces of older bone and **osteoclasts** in the bone remove old bone.

- Growth hormone strongly stimulates osteoblasts. Therefore, the bones can continue to become thicker throughout life under the influence of growth hormone; this is especially true for the membranous bones. e.g, the jaw bones, skull bones.

"Somatomedins" (Also Called "Insulin-Like Growth Factors")

- Produced from liver under the effect of GH
- have the potent effect of increasing all aspects of bone growth.
- Many of the somatomedin effects on growth are similar to the effects of insulin on growth. Therefore, the somatomedins are also called insulin-like growth factors (IGFs).


Growth Hormone
Liver
IGF-1
Fat
Direct effect
Indirect effect

Types of somatomedins

- At least four somatomedins have been isolated, but by far the most important of these is somatomedin C (also called insulin-like growth factor-1, or IGF-I).
- The molecular weight of somatomedin C is about 7500, and its concentration in the plasma closely follows the rate of growth hormone secretion.

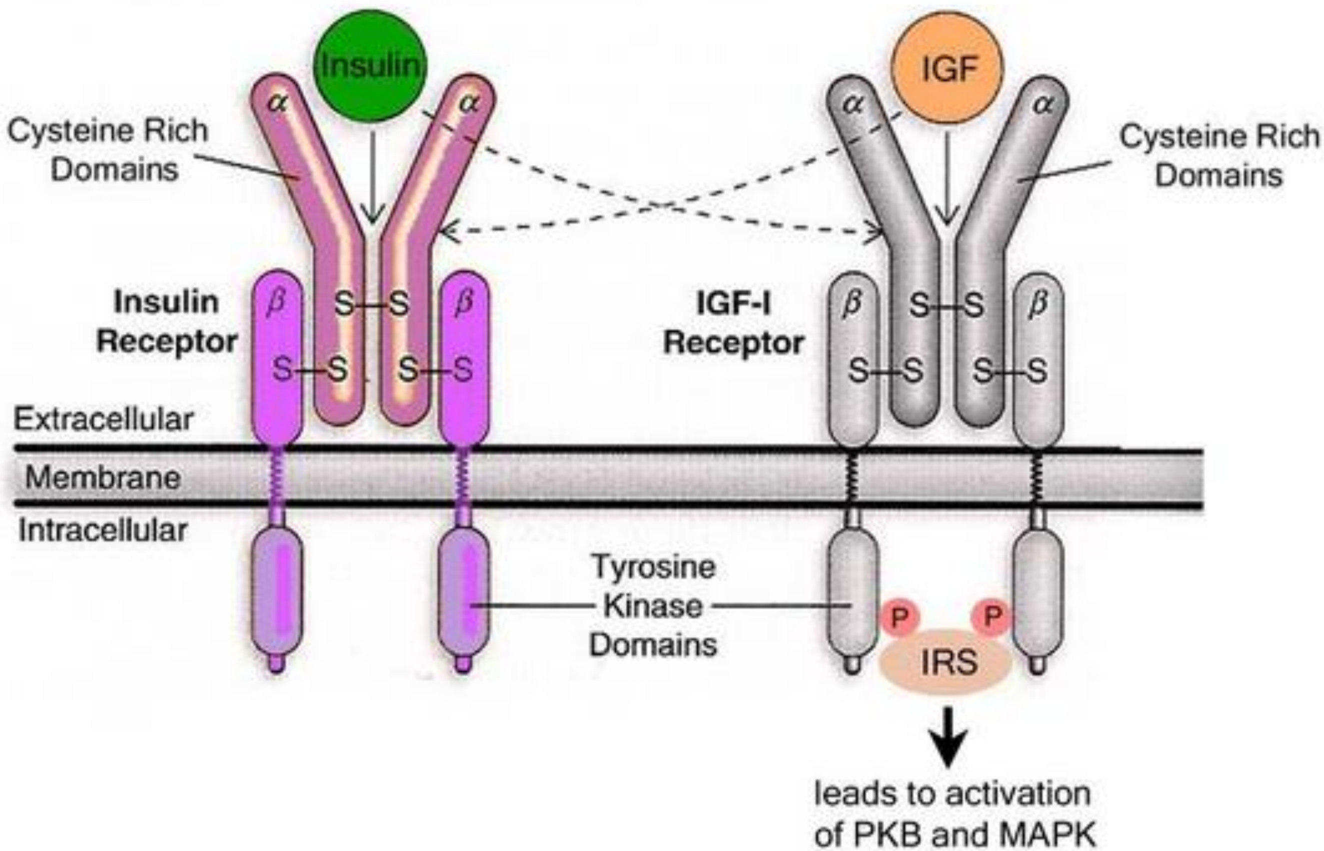
Duration of Action of Growth Hormone and Somatomedin C

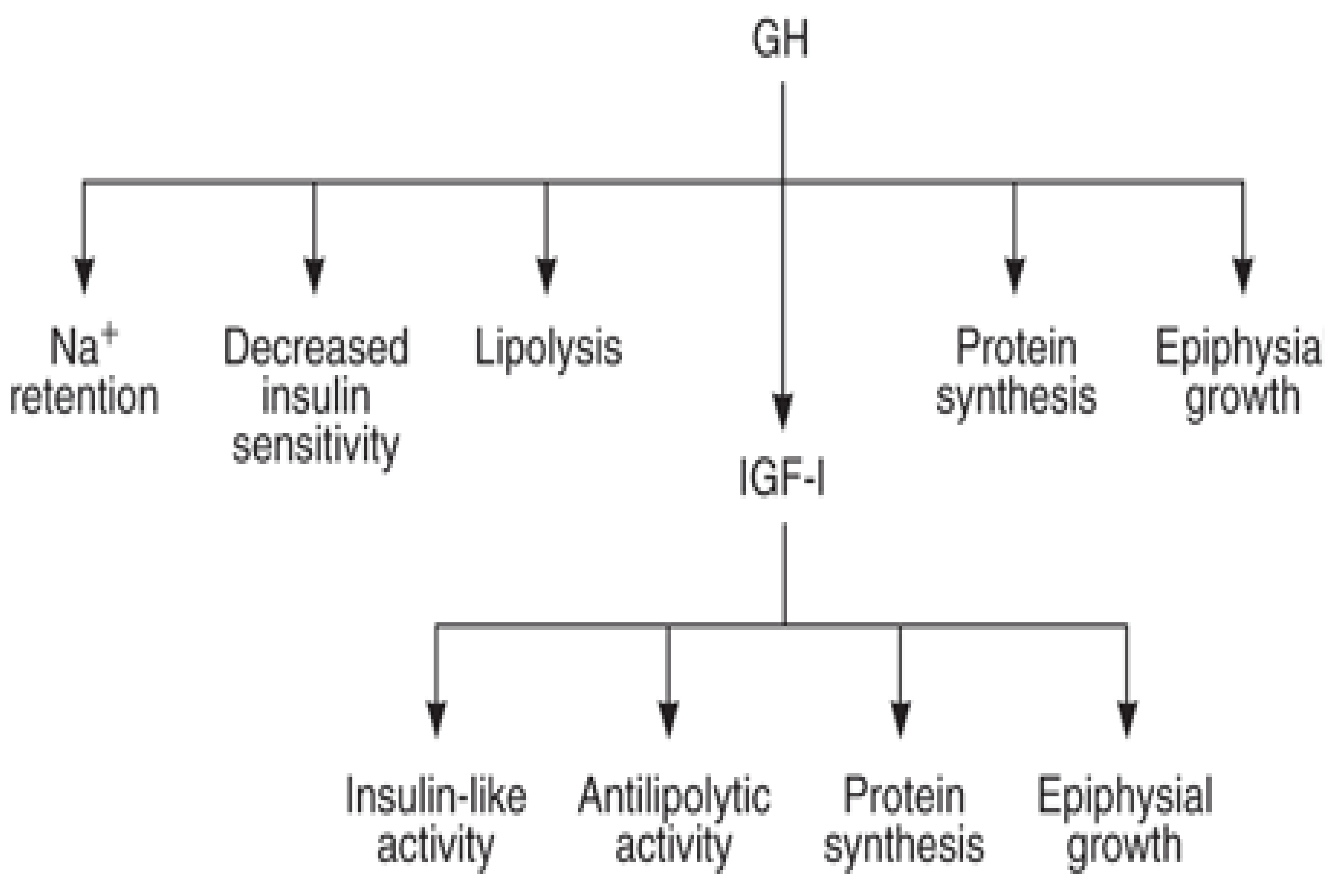
- Most of the growth results from the effect of somatomedins rather then GH

- Growth hormone attaches only weakly to the plasma proteins in the blood and is released to the tissues rapidly, **having a half-time in the blood of less than 20 minutes**.

- **By contrast, somatomedin C attaches strongly to a carrier protein in the blood, with a half-time of about 20 hours.**

Figure 12.3 The insulin and IGF-I receptors are structurally related




GH
Na+ retention
Decreased insulin sensitivity
Lipolysis
IGF-I
Protein synthesis
Epiphysial growth
Insulin-like activity
Antilipolytic activity
Protein synthesis
Epiphysial growth

- **The pygmies of Africa** have a congenital inability to synthesize significant amounts of somatomedin C.

. plasma concentration of growth hormone is either normal or high, they have diminished amounts of somatomedin C in the plasma;

- this apparently accounts for the small stature of these people. Some other **dwarfs (e.g., the Lévi-Lorain dwarf) also have this problem.**

REGULATION of GH

Growth hormone is secreted in a pulsatile pattern, increasing and decreasing.

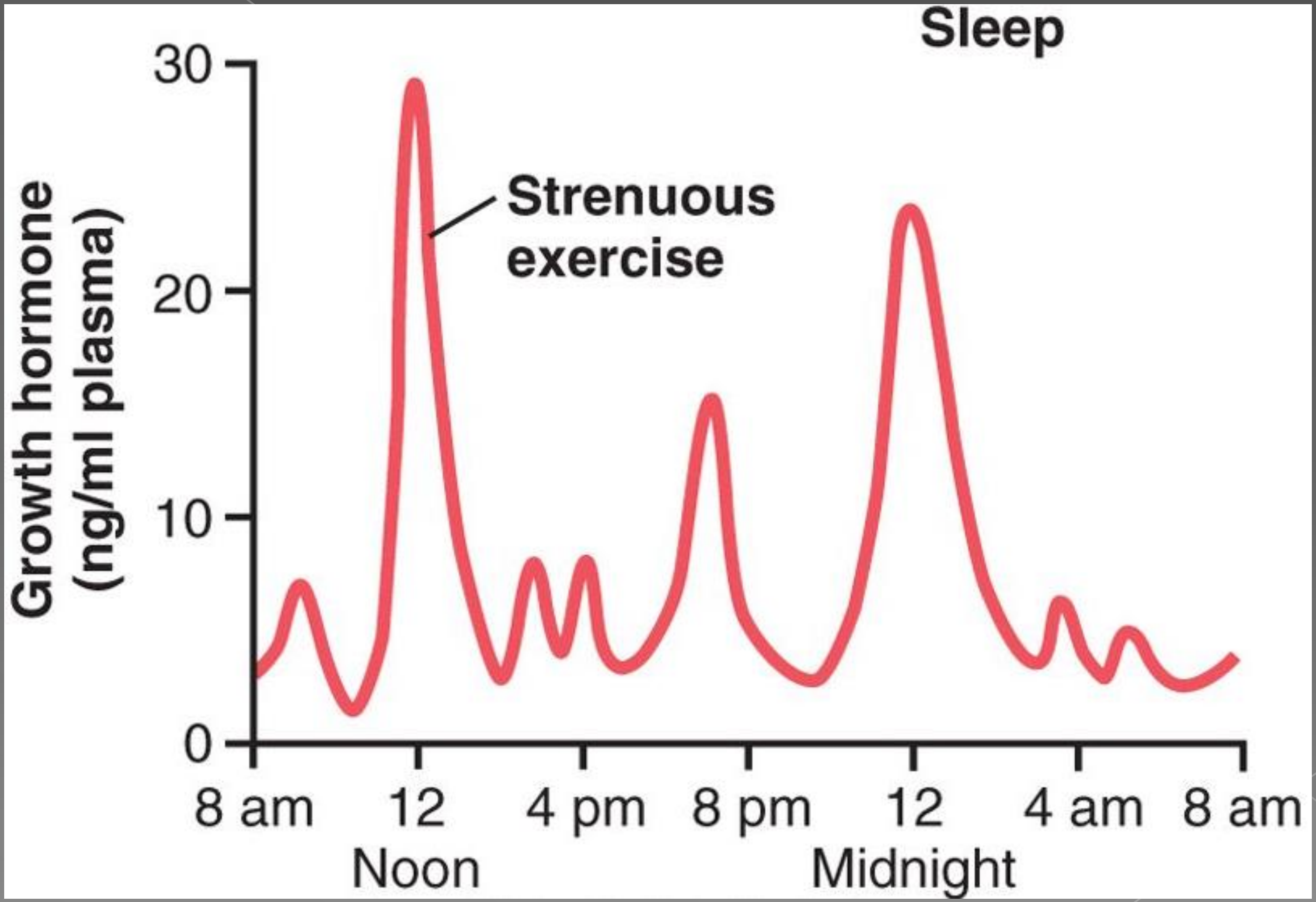


Table 76-3 Factors That Stimulate or Inhibit Secretion of Growth Hormone

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

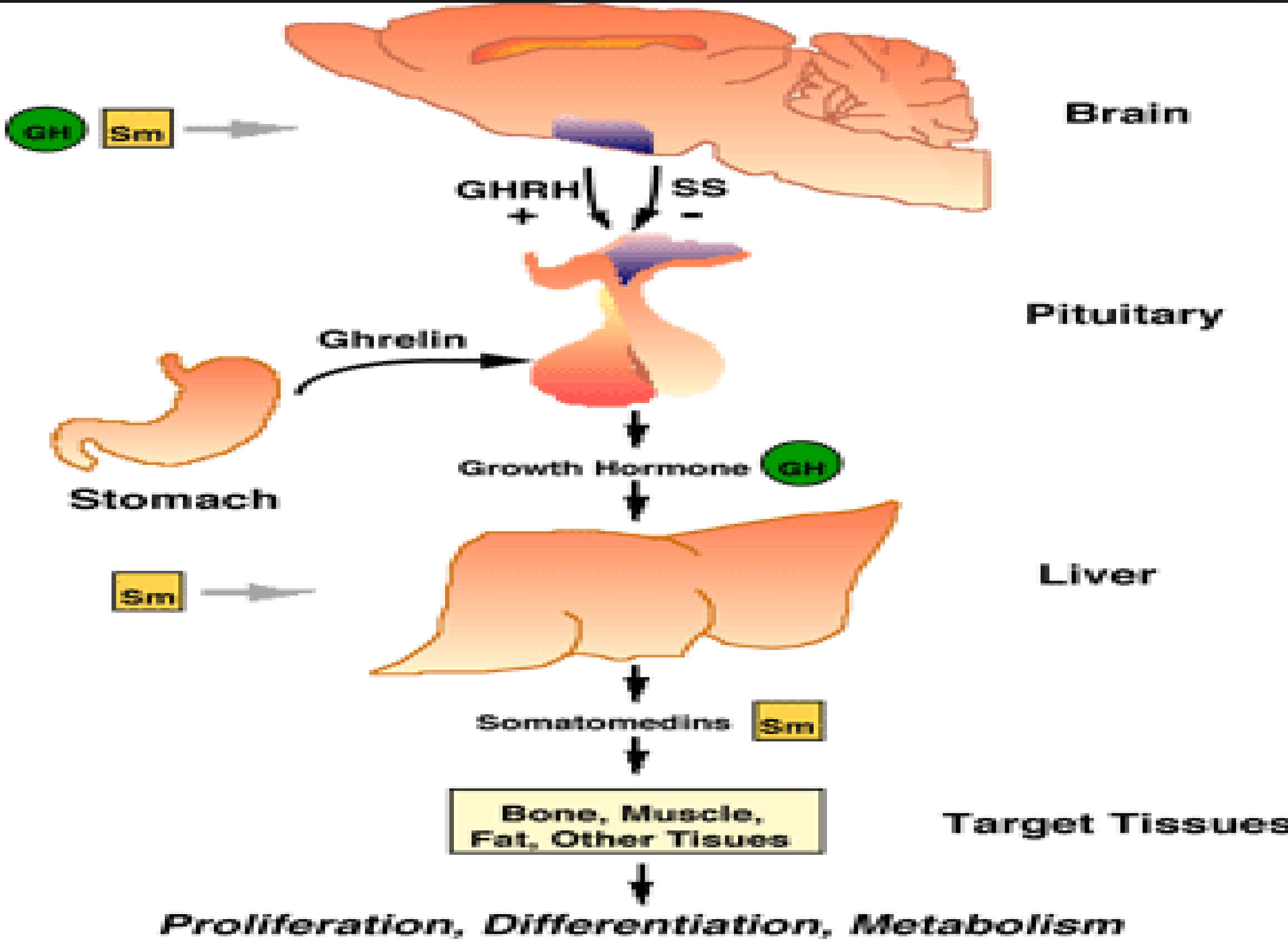
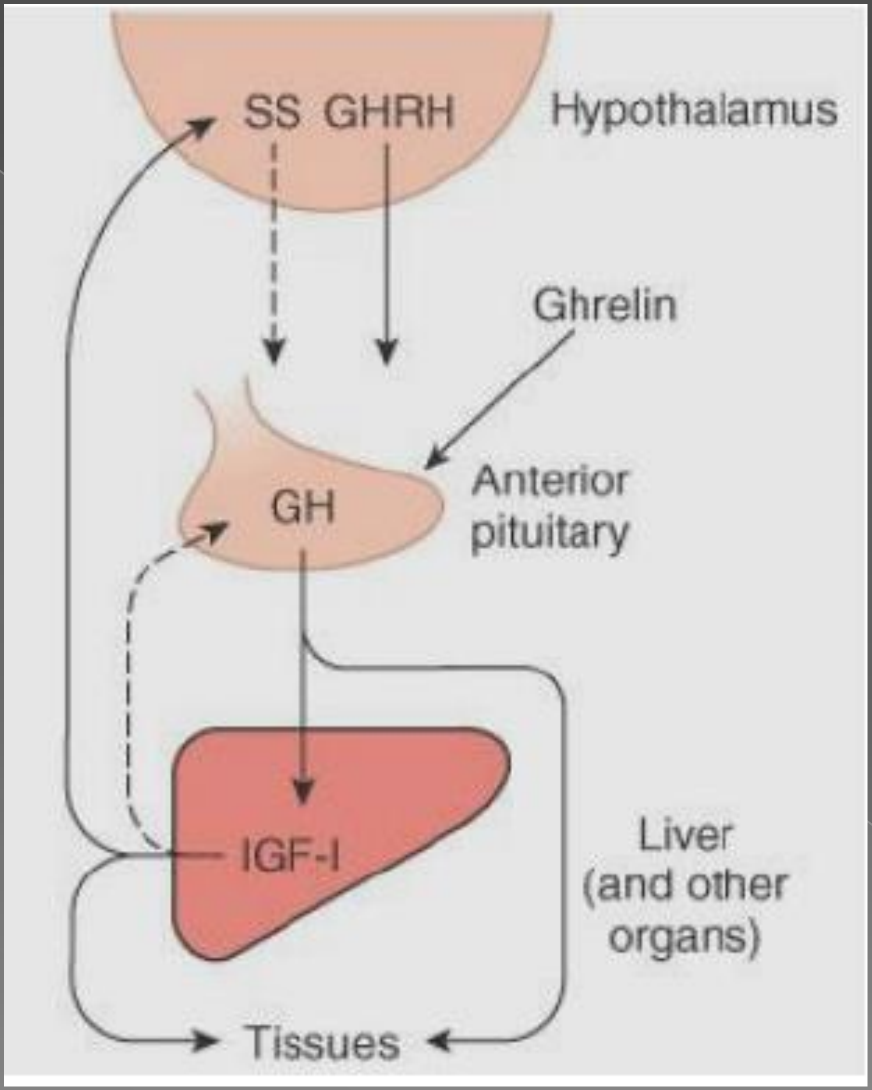


Figure 4: The Growth Hormone Axis

- **Under acute conditions**, **hypoglycemia** is a far more potent stimulator of growth hormone secretion than is an acute decrease in protein intake.
- Conversely, **in chronic conditions**, growth hormone secretion seems to correlate more with the degree of cellular **protein depletion** than with the degree of glucose insufficiency.
- For instance, the extremely high levels of growth hormone that occur during starvation are closely related to the amount of protein depletion.

Role of the Hypothalamus, GHRH and GHIH in the Control of Growth Hormone Secretion

- Both of these are polypeptides;
- GHRH is composed of 44 amino acids, and GHIH(somatostatin) is composed of 14 amino acids.
- GHRH secreted from ventromedial nucleus; this is sensitive to blood glucose concentration, causing satiety in hyperglycemic states and hunger in hypoglycemic states.


SS GHRH
Hypothalamus
Ghrelin
GH
Anterior pituitary
IGF-I
Liver (and other organs)
Tissues