Endocrine Physiology

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Pituitary Gland

Introduction

The Pituitary Gland (Structure)

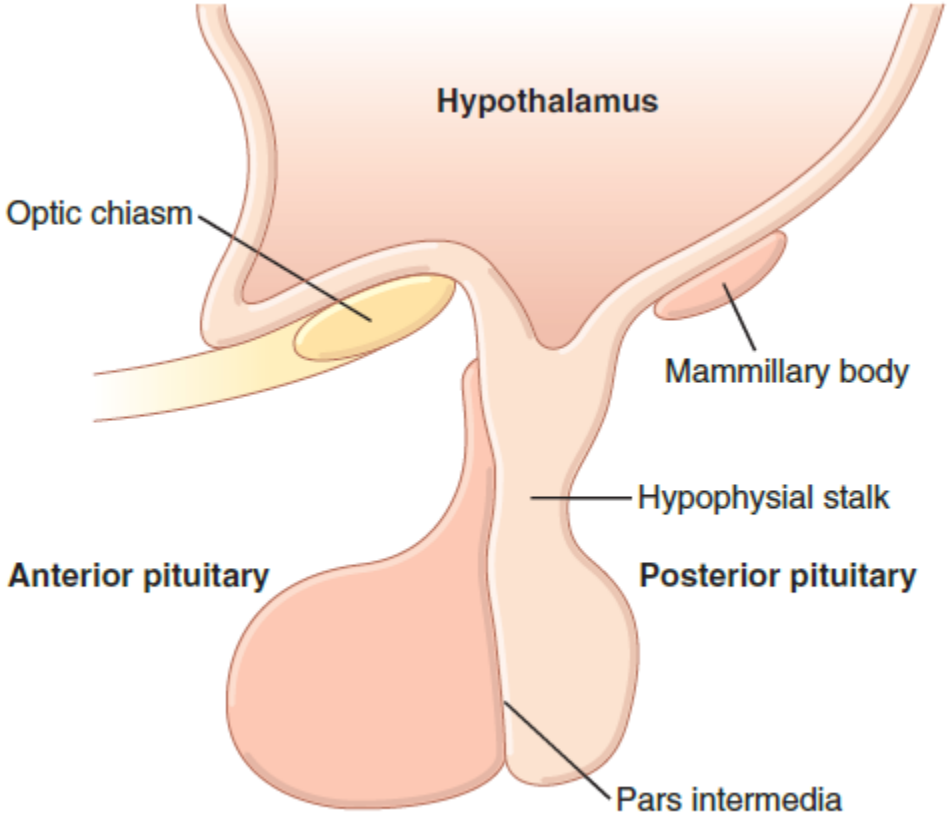


Figure 76-1. Pituitary gland.

- Two parts:
  - Anterior Pituitary
  - Posterior Pituitary
- Hypophysial (Pituitary) stalk
- Hypophysial stalk damage
- The significance of this anatomical location

The Pituitary Gland (Structure)

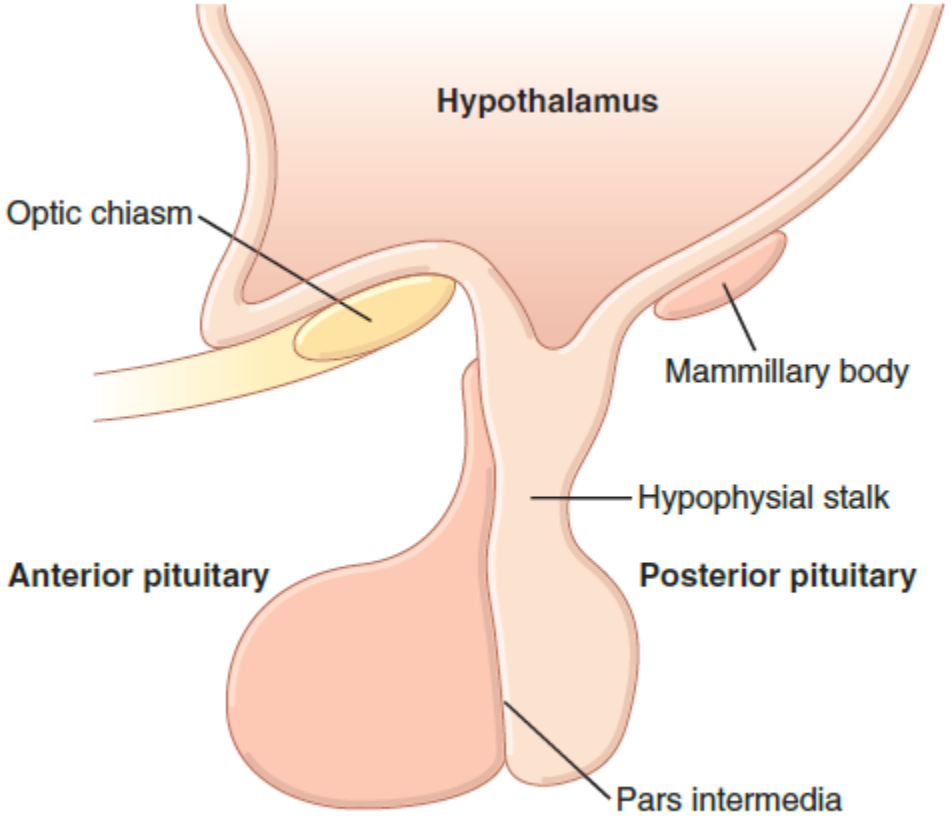


Figure 76-1. Pituitary gland.

- The hypothalamus receives signals from many resources.
- These signals help it collect enough information concerning the internal well-being.
- According to these signals, the hypothalamus controls pituitary secretions.

Metabolic Functions of the Anterior Pituitary

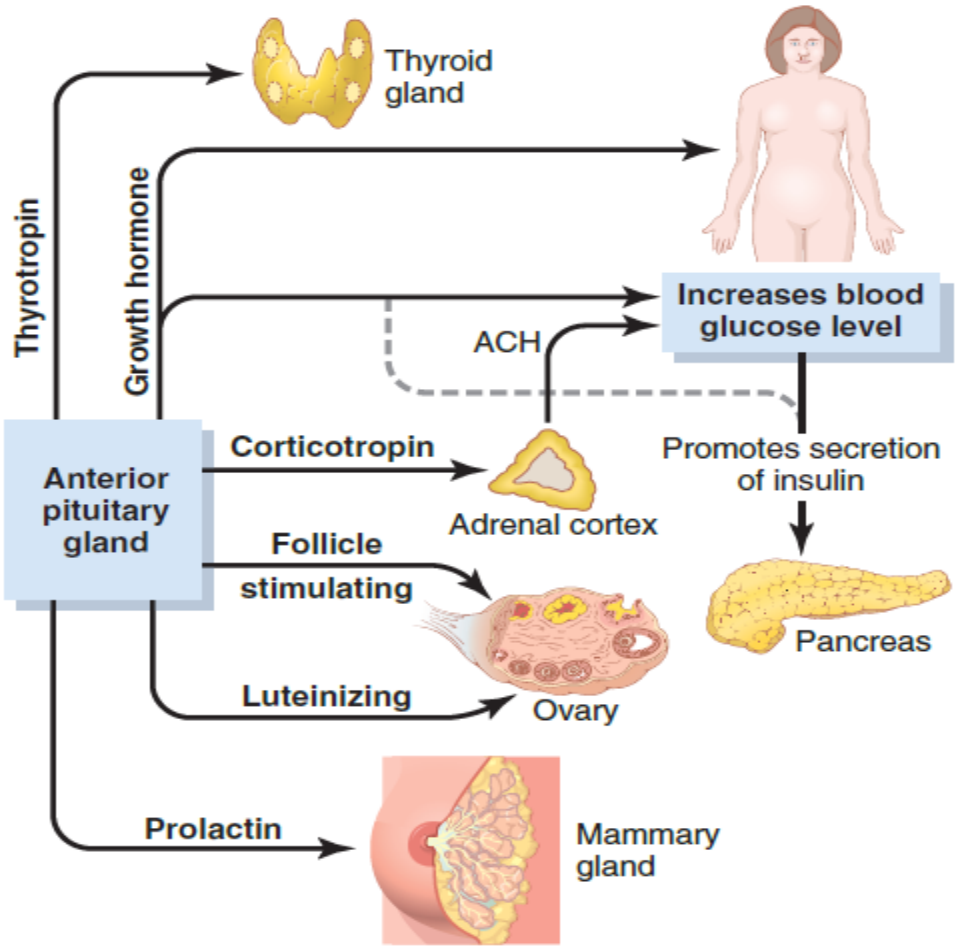


Figure 76-2. Metabolic functions of the anterior pituitary hormones. ACH, adrenal corticosteroid hormones.

- The Anterior Pituitary gland secretes 6 hormones, 4 of them are tropic (i.e. targeting other endocrine glands).
- Tropic: ACTH, LH, FSH and TSH.
- Nontropic: GH, PRL.

Cells of the Anterior Pituitary

- Acidophils and Basophils:

  - Acidophils: secrete GH and prolactin (nontropic).

  - Basophils: secrete FSH, LH, ACTH, and TSH (tropic).

- Mnemonics: A-GP // B-FLAT.

- <u>Another Classification:</u>

1- Somatotropes

2- Corticotropes

3- Thyrotropes

4- Gonadotropes

5- Lactotropes

Pituitary hormones

- The six hormones of the anterior pituitary play major roles in the control of metabolic functions throughout the body:

Growth hormone // Adrenocorticotropin (corticotropin)

Thyroid-stimulating hormone (thyrotropin)

Prolactin

Gonadotropic hormones: FSH and LH

- The two hormones secreted by the posterior pituitary play other roles.

1. Antidiuretic hormone (vasopressin)
2. Oxytocin

Posterior Pituitary Hormones

- Are Synthesized by Cell Bodies in the Hypothalamus.
- The bodies of the cells that secrete the posterior pituitary hormones are not located in the pituitary gland itself but are large neurons, called magnocellular neurons, located in the hypothalamus.
- The hormones are then transported in the axoplasm of the neurons' nerve fibers passing from the hypothalamus to the posterior pituitary gland.

Table 76-1 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 insulin-like growth factor-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
	Luteinizing (LH) hormone	Glycoprotein of two subunits, α (89 amino acids) and β (115 amino acids)	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
Lactotropes-Mammotropes	Prolactin (PRL)	Single chain of 198 amino acids	Stimulates milk secretion and production

Hypothalamus Controls Pituitary Secretions

- Both anterior and posterior pituitary glands are controlled by the hypothalamus.
- The **posterior pituitary** is controlled **directly** (i.e. direct nerve signals are transmitted from the hypothalamus to the posterior pituitary.

- The **anterior pituitary** is controlled **indirectly,** by hormones secreted from the hypothalamus into the blood. Then these hormones pass to the anterior pituitary, either activating or inhibiting the release of its hormones.
- These hypothalamic hormones are called releasing or inhibitory hormones or factors.

Hypothalamus Controls Anterior Pituitary Secretions

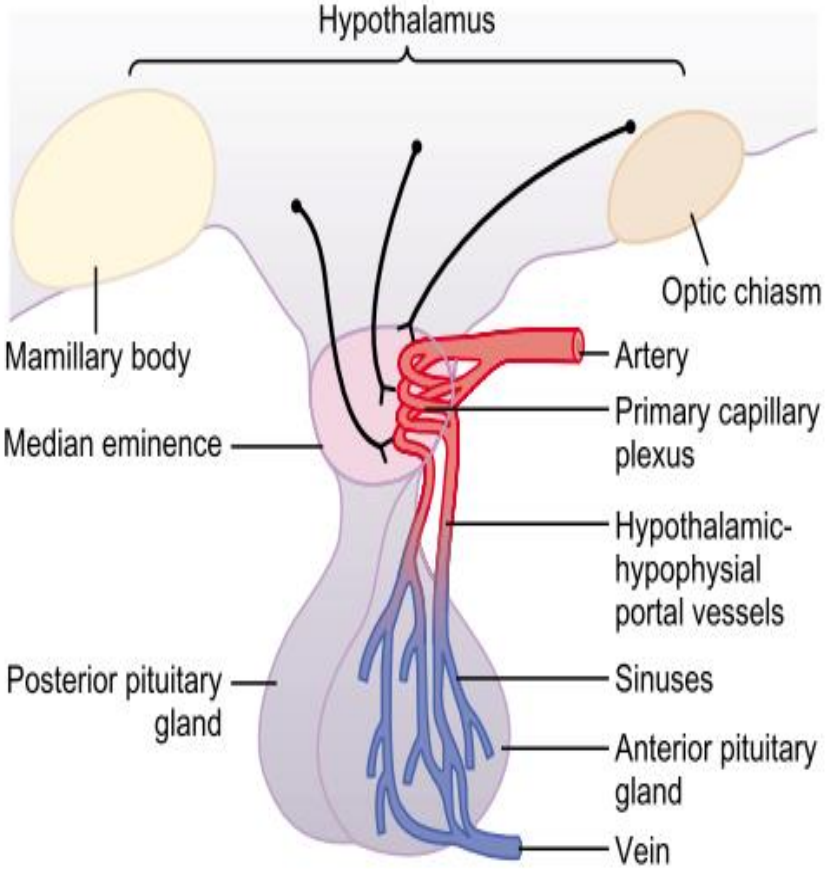


Figure 75–4

Hypothalamic-hypophysial portal system.

- Hypothalamic-hypophysial portal system.
- Hypothalamic hormones are synthesized in special neurons.
- The cell bodies of these neurons are present in different areas within the hypothalamus.
- Almost all of them secrete their hormones into tissue fluids at the median eminence.

Table 76-2 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

ACTH, adrenocorticotropic hormone; FSH, follicle-stimulating hormone; LH, luteinizing hormone; TSH, thyroid-stimulating hormone.

- Hypothalamus releasing and inhibitory hormones are synthesized in the hypothalamus, pass through nerve fibers and are secreted into the median eminence.
- Prolactin is the only hormone that doesn't have a stimulatory releasing hormone from the hypothalamus, that's why it's the only pituitary hormone not affected by pituitary stalk injury.

Growth Hormone

Growth Hormone

- A polypeptide hormone secreted from the anterior pituitary.
- Also called somatotropic hormone or somatotropin.
- It affects almost all cells in the human body.
- Its main function is to promote linear growth.
- It has many other effects that also assist the main function of growth-promotion.
- As all other anterior pituitary hormones, it's under hypothalamic control through the hypothalamic-hypophysial portal system.
- GH is a nontropic hormone.

Growth-Promotion Effect of GH

- Growth Hormone is a small protein hormone that contains 191 amino acids in a single chain and a molecular weight of 22,005.
- It causes growth of all tissues of the body capable of growing
- It increases sizes and numbers of cells.
- Many other hormones also have growth effects: IGFs, insulin, thyroid hormones, androgens ..etc.

Growth-Promotion Effect of GH

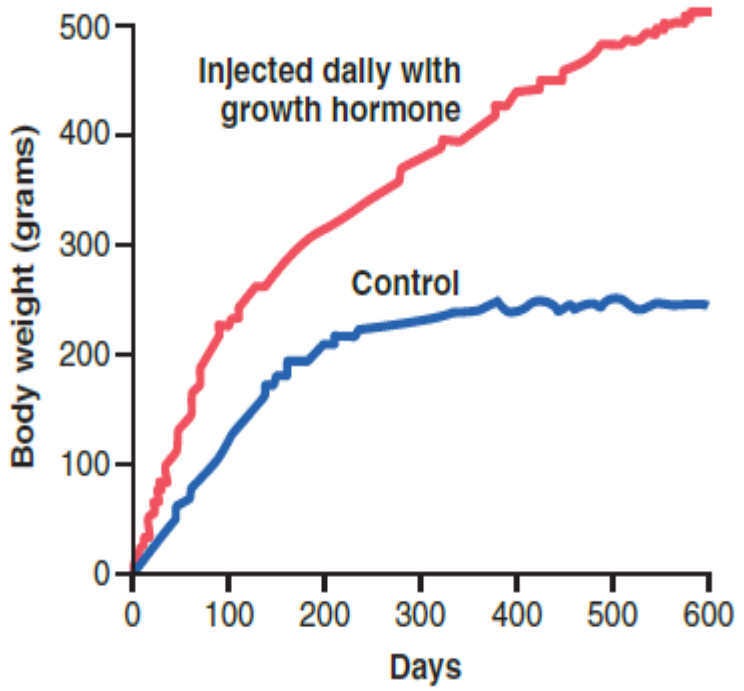


Figure 76-5. Comparison of weight gain of a rat injected daily with growth hormone with that of a normal littermate.

- In the early stages of development, all organs of the body increase proportionately.
- After late adolescence, bones stop lengthening. So, tissues other than bone continue to grow.
- Even bone can become thicker under the effect of GH but never lengthens.

Metabolic Effects of GH

- Proteins
- Increased deposition inside tissues

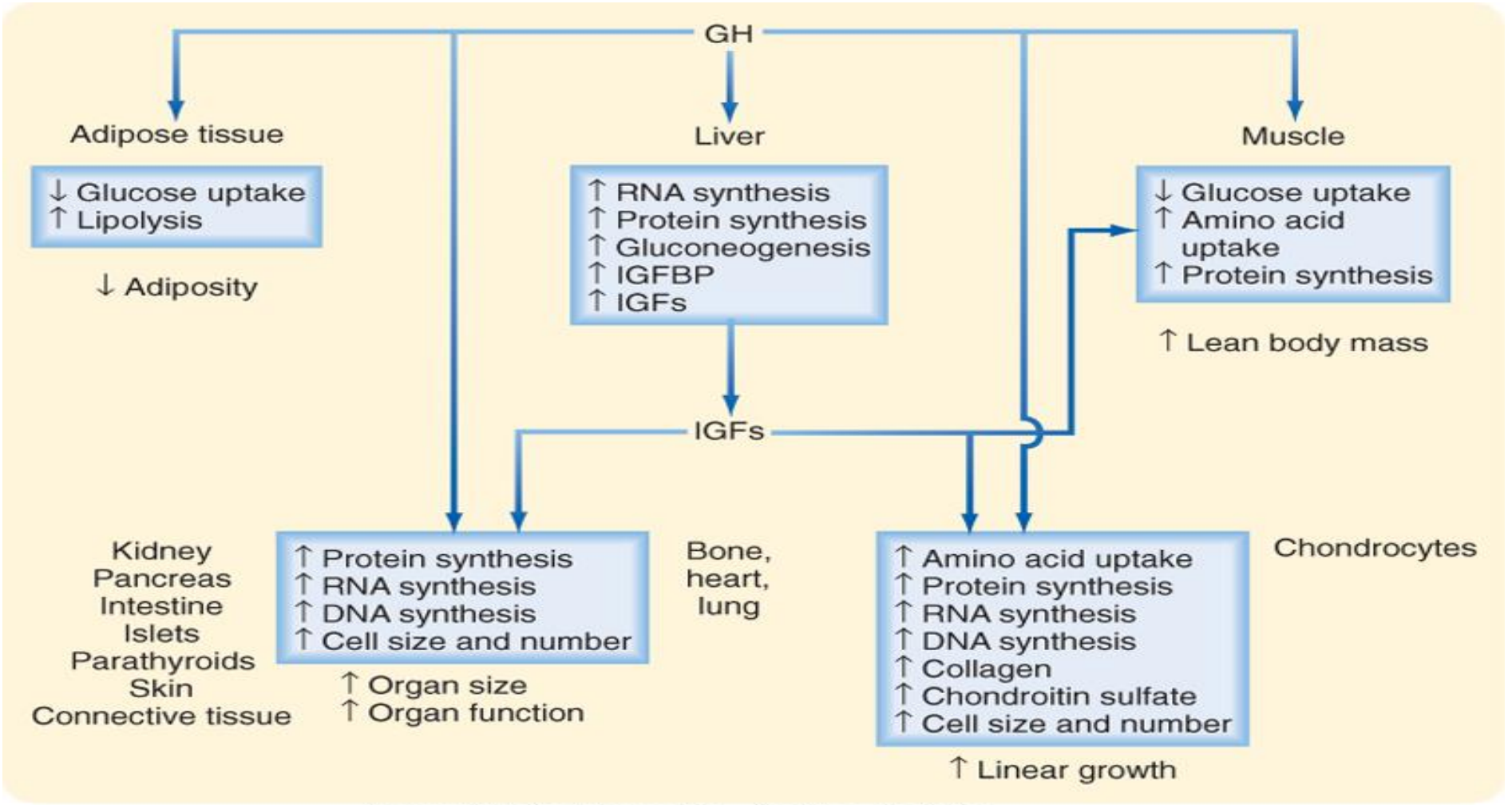
Anabolic

- Lipids
- Increased utilization of fat

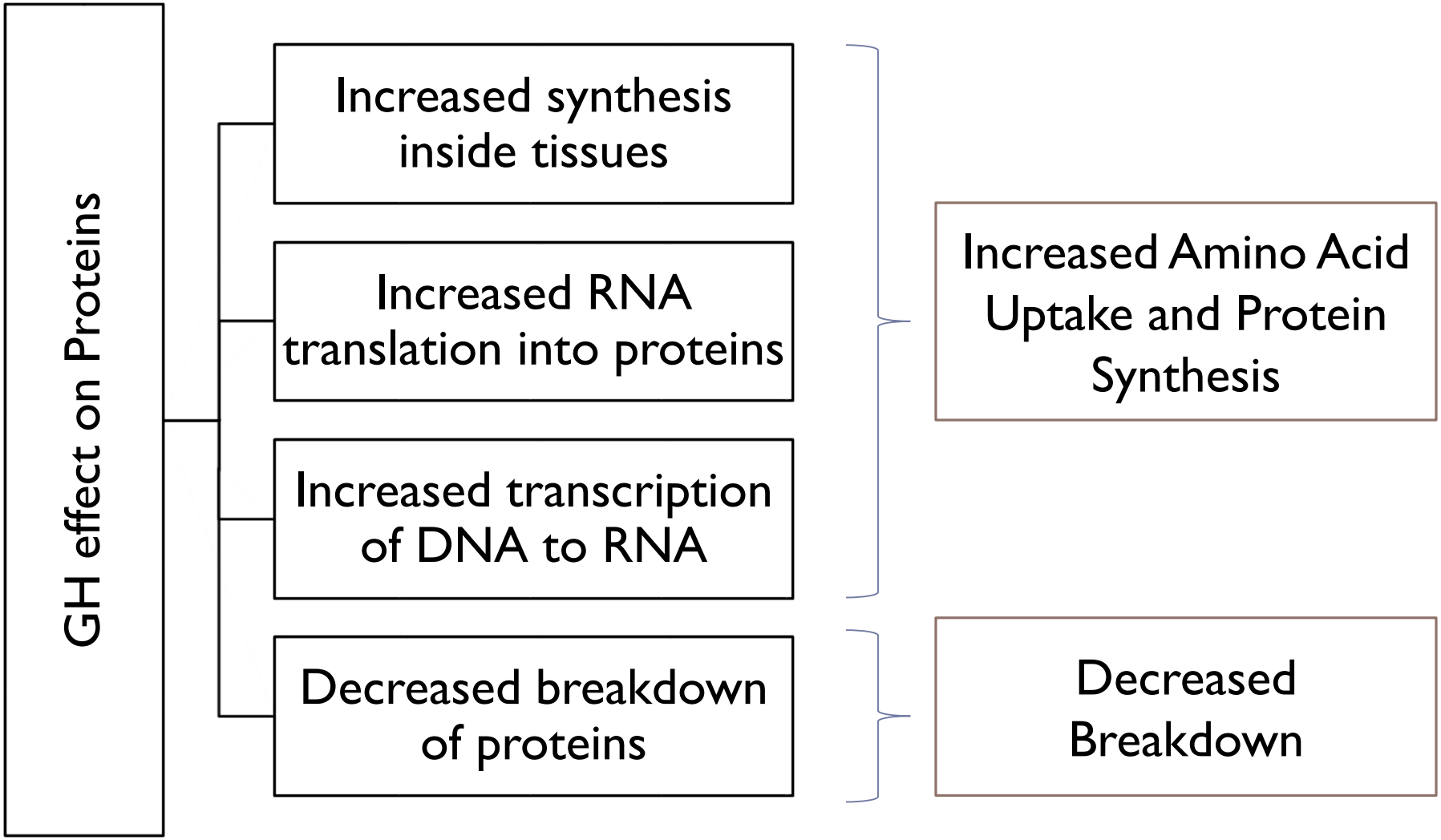
- Carbohydrates
- Decreased utilization of carbohydrates

Catabolic

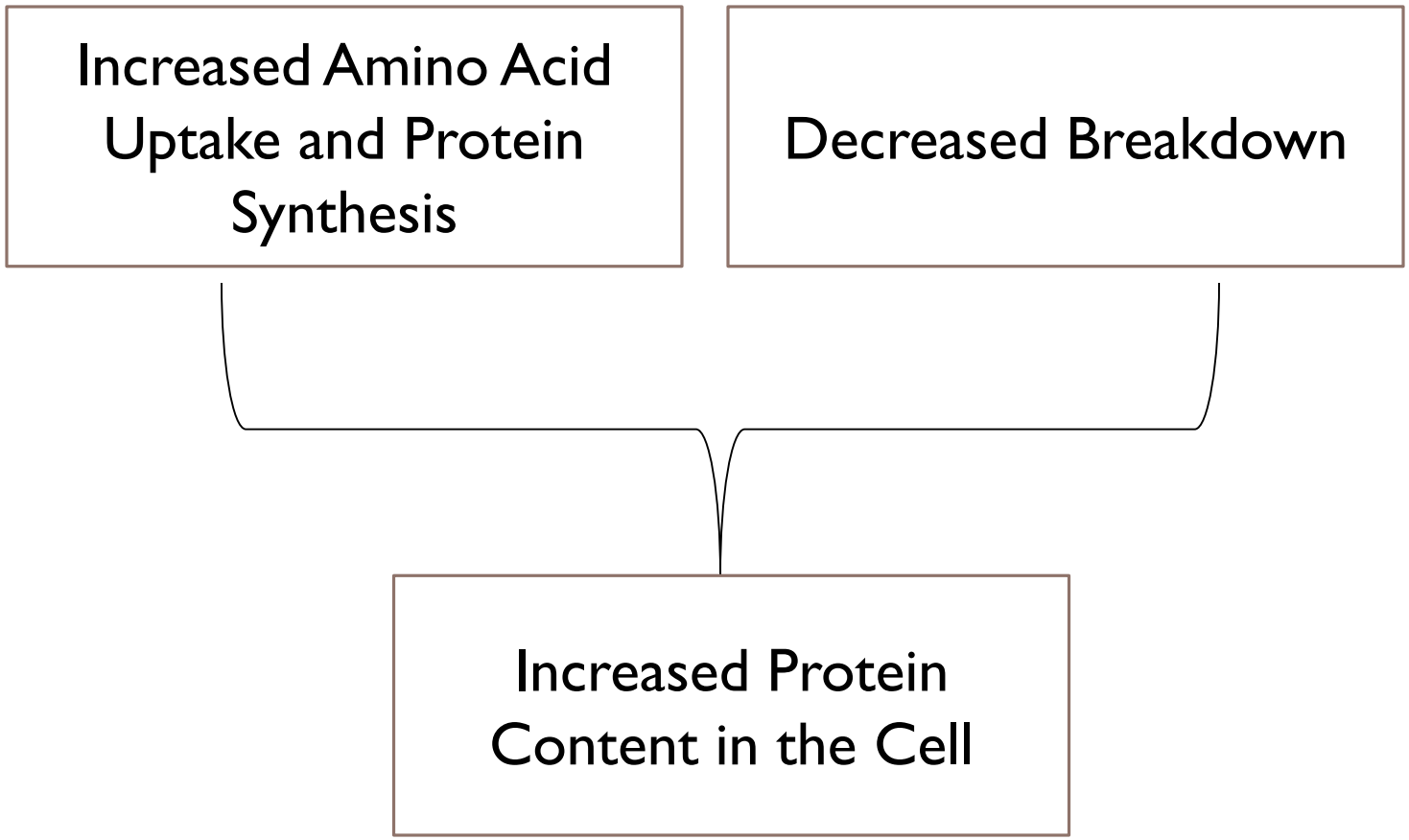
Biological Effects of GH



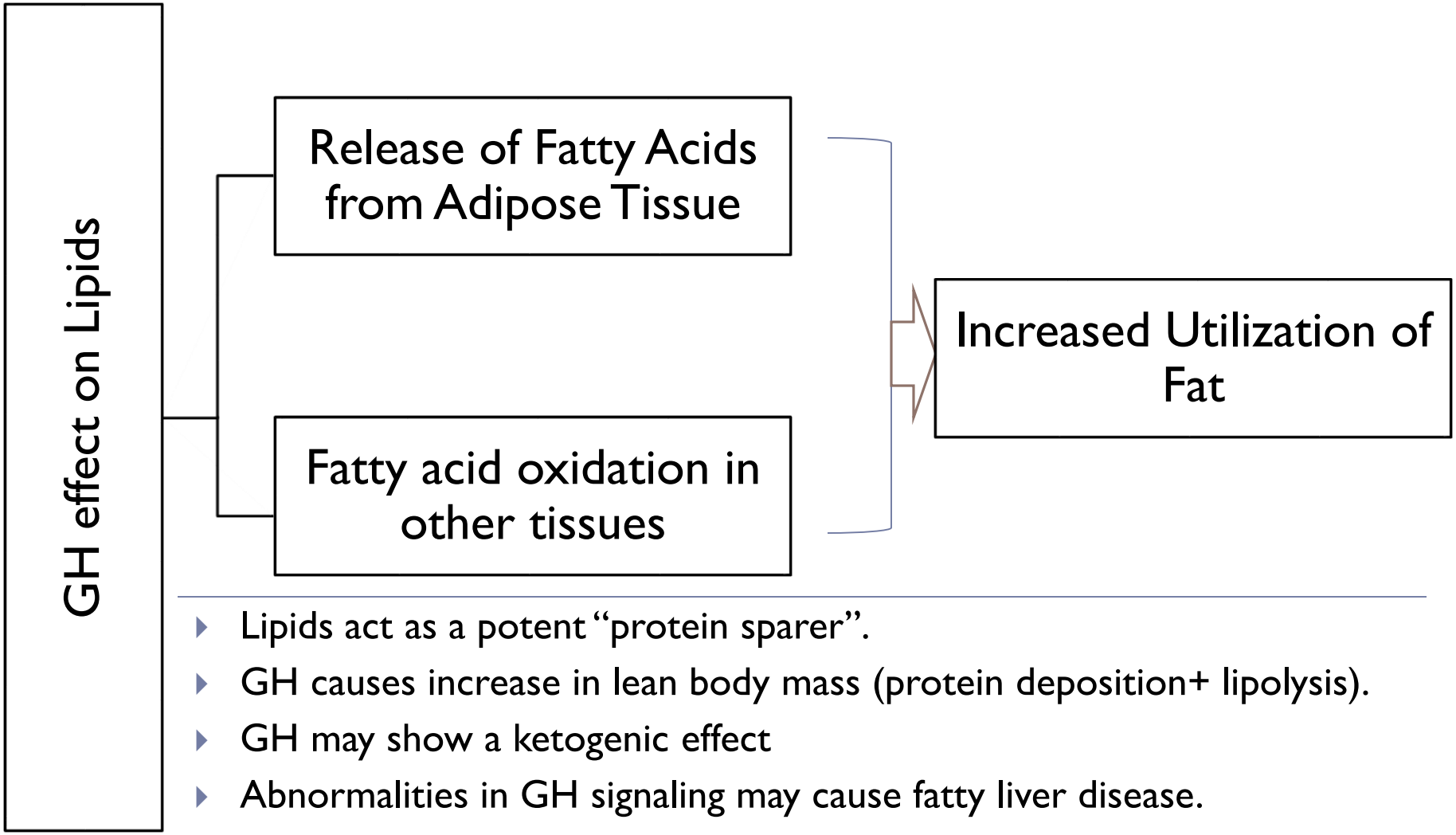
The effect of GH on Proteins



The effect of GH on Proteins



The effect of GH on Lipids

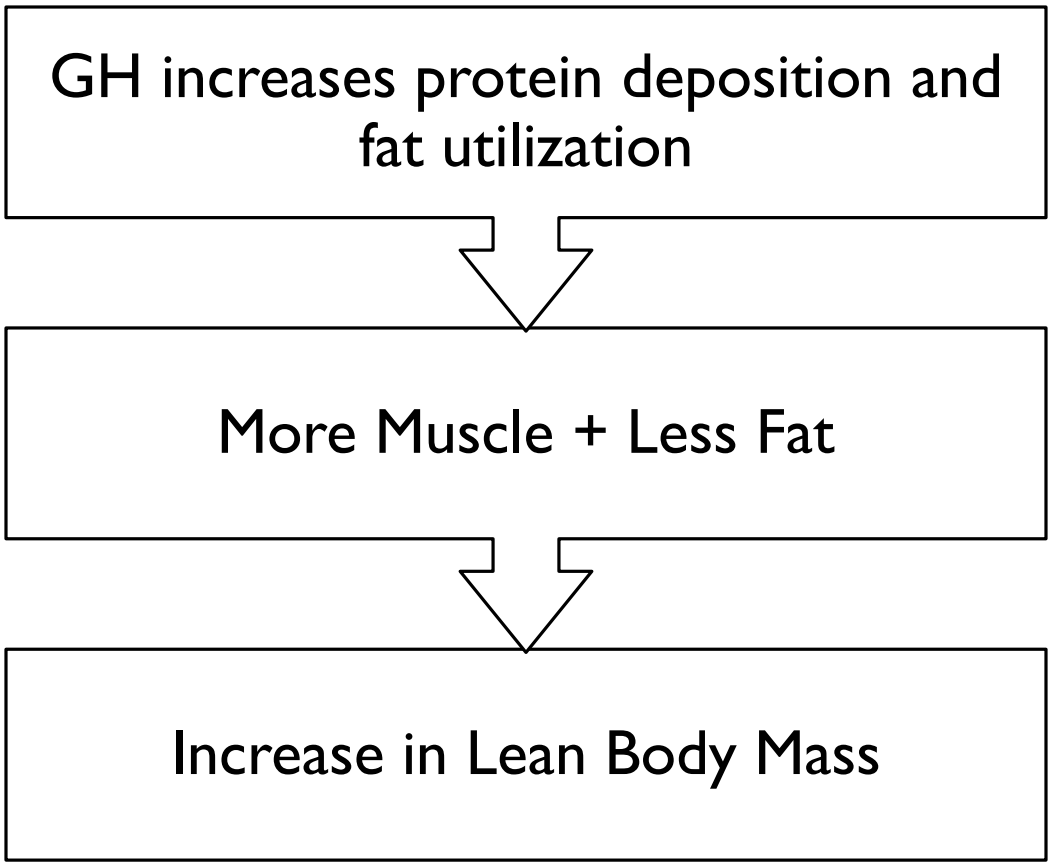


- Lipids act as a potent "protein sparer".
- GH causes increase in lean body mass (protein deposition+ lipolysis).
- GH may show a ketogenic effect
- Abnormalities in GH signaling may cause fatty liver disease.

The Ketogenic Effect of GH

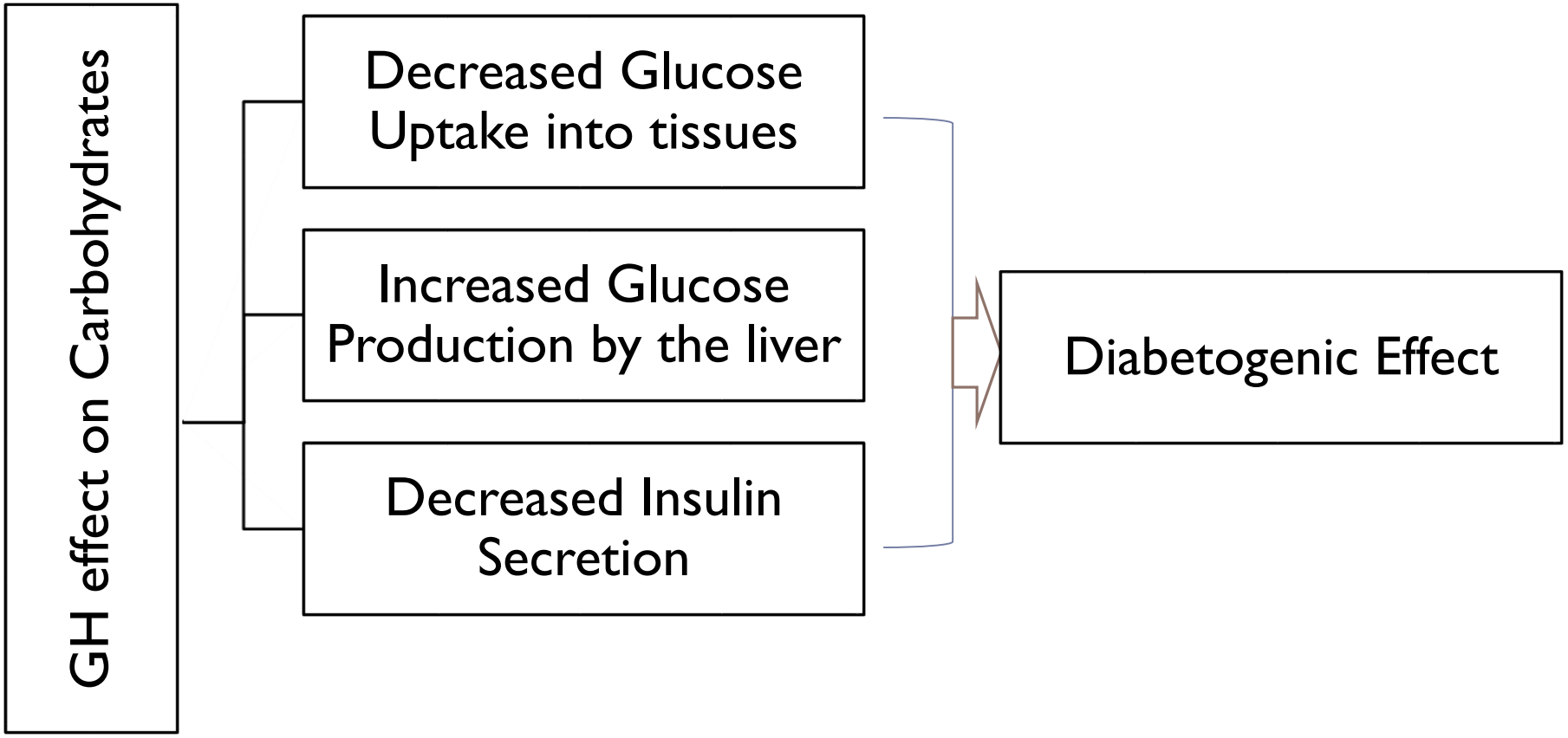
- GH increases fat mobilization from the adipose tissue into the rest of the body.
- Other tissues will start taking free fatty acids floating in the blood to use them for energy production.
- Fatty acid oxidation forms a lot of acetyl Co-A molecules, that when exceed the oxidative capacity of the liver, are converted to ketone bodies.
- This ultimately causes ketosis.

GH effect on Lean Body Mass



- Under the effect of GH, mobilization of fat requires minutes to hours, whereas protein synthesis can begin within minutes.

The effect of Growth Hormone on Carbohydrates



Synergistic effects of GH and Insulin

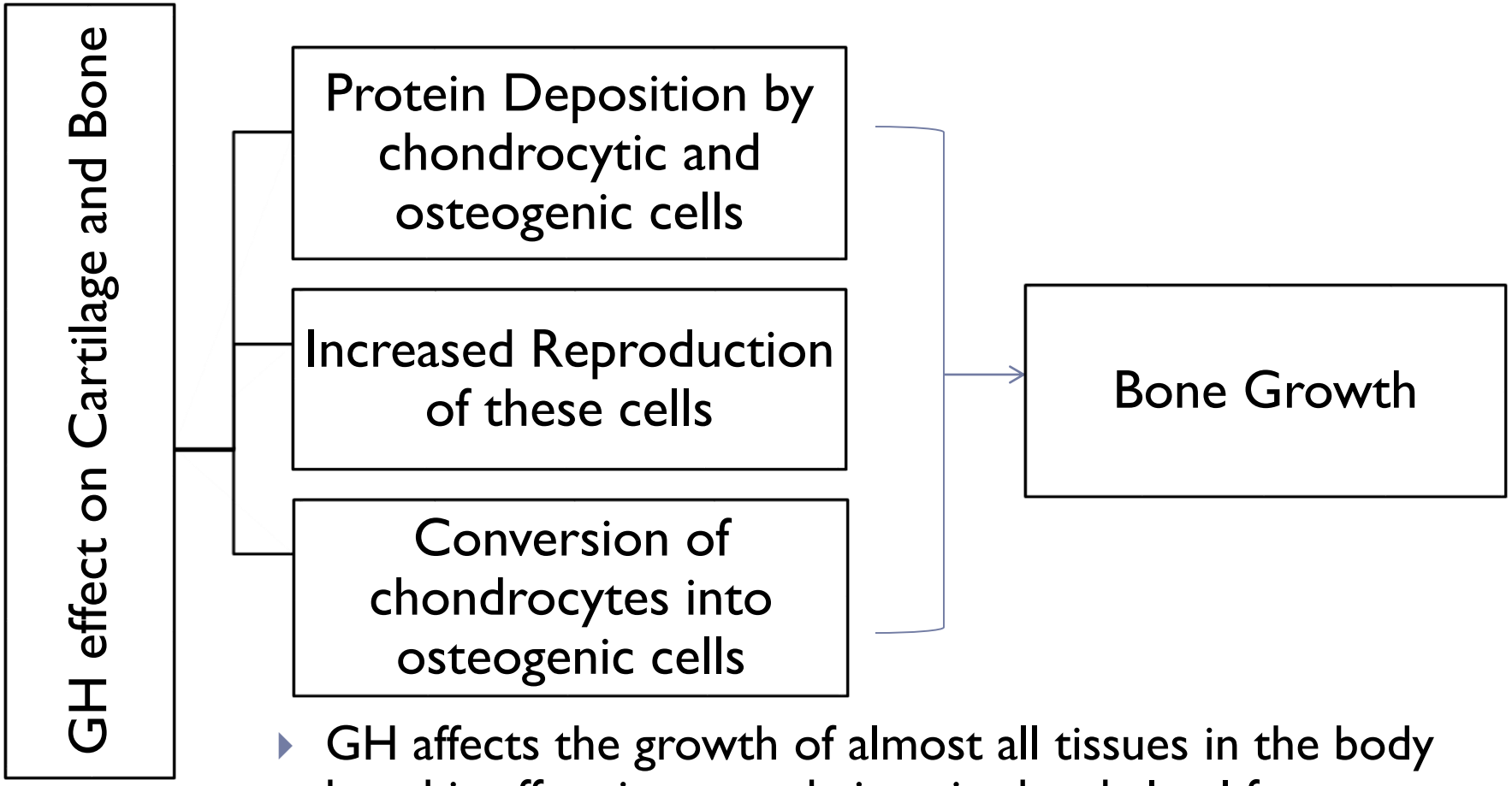
- In animals lacking pancreas, GH fails to function properly indicating the necessity of insulin for proper GH function.
- Animals injected with both GH and insulin grow faster than those injected with only one.
- Also carbohydrates are necessary for GH function.

- Explanations:

- Carbohydrates: to provide the energy needed for growth.
- Insulin:
  - enables glucose to go into the cells to provide energy for growth.
  - enhances the transport of some amino acids into cells.

- Shortly, GH enhances body protein, uses up fat stores and conserves carbohydrates.

The effect of GH on Cartilage and Bone



- GH affects the growth of almost all tissues in the body but this effect is most obvious in the skeletal frame.

Abnormalities in GH Levels

- Abnormalities in GH levels:

During Growing Years:
GH deficiency → Dwarfism

Excessive GH → Gigantism

In Adults:
Excessive GH → Acromegaly

Somatomedins

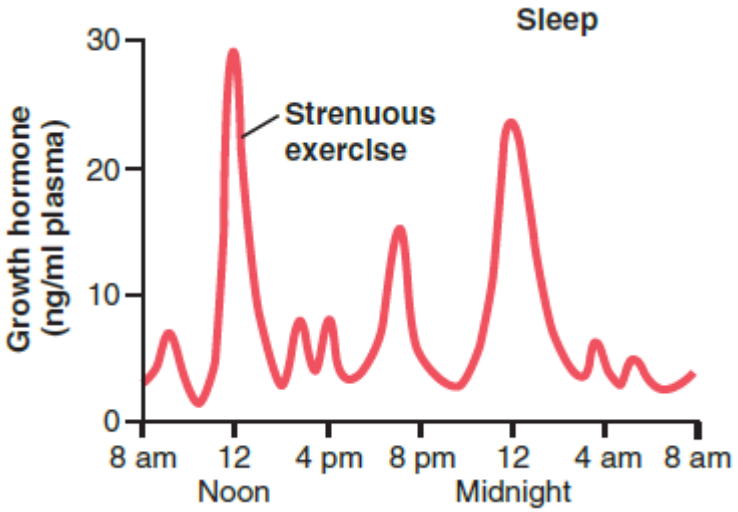
- GH exerts much of its effects through somatomedins.
- GH causes the liver to synthesize these somatomedins which affect all aspects of bone growth.
- Somatomedins are called IGFs.
- It's still unclear how GH and somatomedins act together in growth.
- Somatomedins have longer duration of action.

GH & IGF-1

Direct Effects of GH	Indirect Effects of GH (Through IGF-1)
Decreases glucose uptake (counterregulatory effects).	Stimulates protein synthesis at the organ level.
Mobilizes fatty acids.	Increases protein synthesis in chondrocytes (promotes linear growth).
Stimulates protein synthesis in muscle.	Stimulates protein synthesis in muscle.
Increases lean body mass.	Increases lean body mass.

IGF-1 = insulin-like growth factor 1; GH = growth hormone.

Regulation of Growth Hormone Secretion

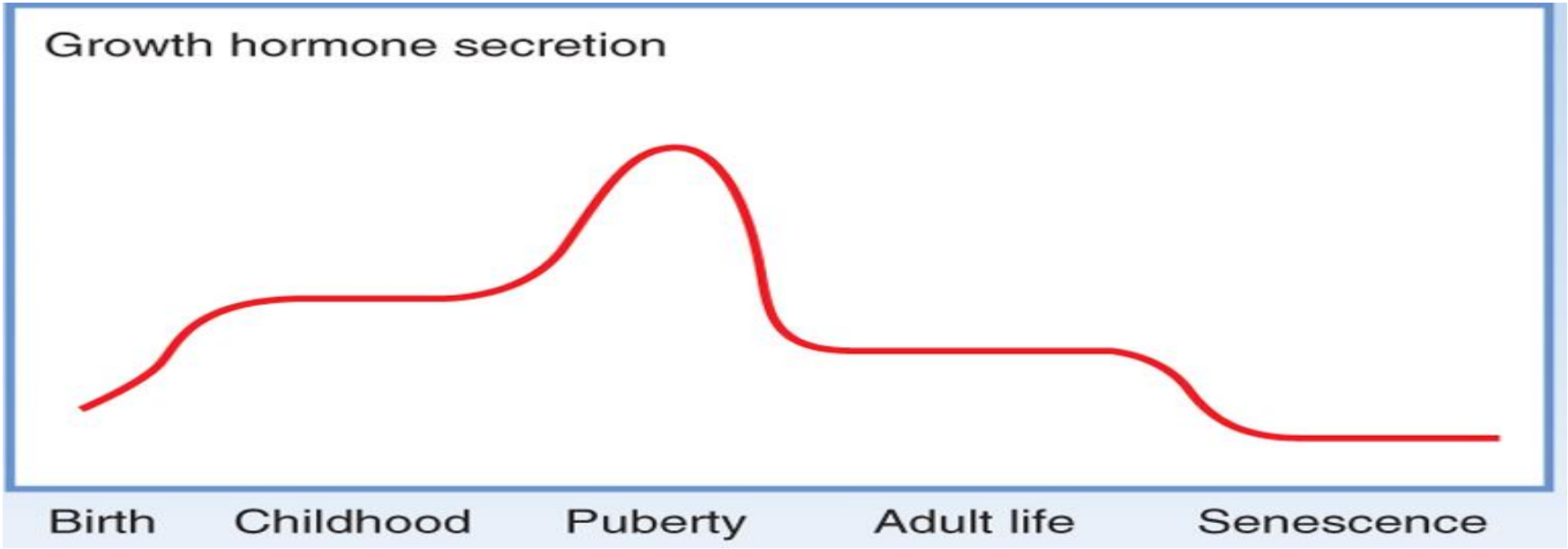


- GH is secreted in a pulsatile pattern, increasing and decreasing.
- GH secretion increases in:
  - Starvation
  - Hypoglycemia
  - Low free fatty acids in the blood
  - Exercise
  - Excitement
  - Ghrelin Hormone

Factors Affecting GH Secretion

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

GH Secretion Depending on Age



- GH levels are highest at puberty.
- It's still present after adolescence, because it's needed for purposes other than increase in height.

Hypothalamic Control of GH secretion

- Hypothalamic Hormones Affecting GH:
  - GHRH (Growth-hormone-releasing Hormone)
  - Somatostatin (GH-inhibitory Hormone).

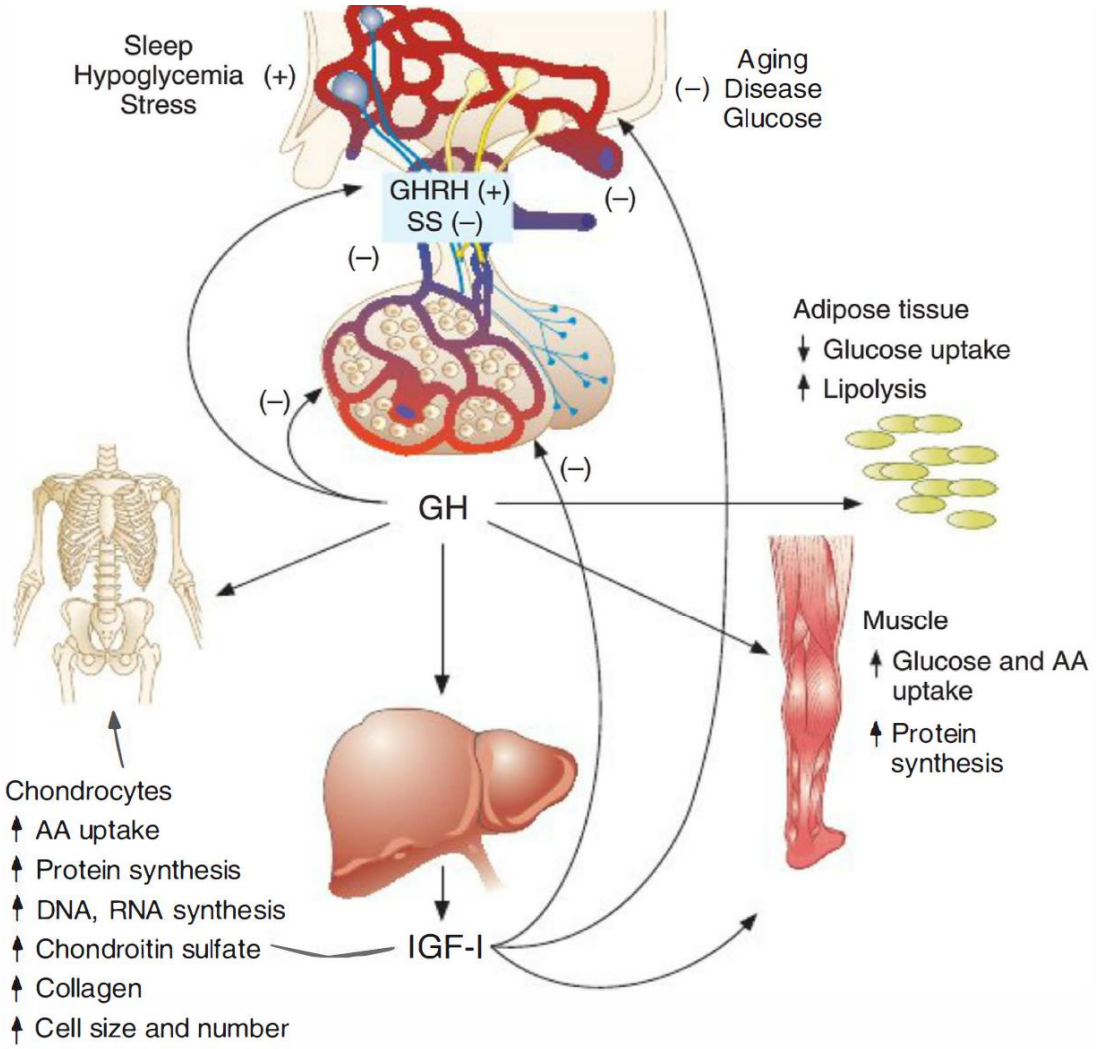
- GHRH is secreted from the ventromedial nucleus of the hypothalamus, which senses blood glucose level as well and in a way or another controls our feeding behavior.

The effect of GHRH

- GHRH binds to receptors on GH-releasing cells in the anterior pituitary, activates adenylate cyclase enzyme and thus increases cAMP levels within the cell.
- This has short-term and long-term effects:
  Short-term: GH secretion (Fusion of GH vesicles with the plasma membrane → secretion).

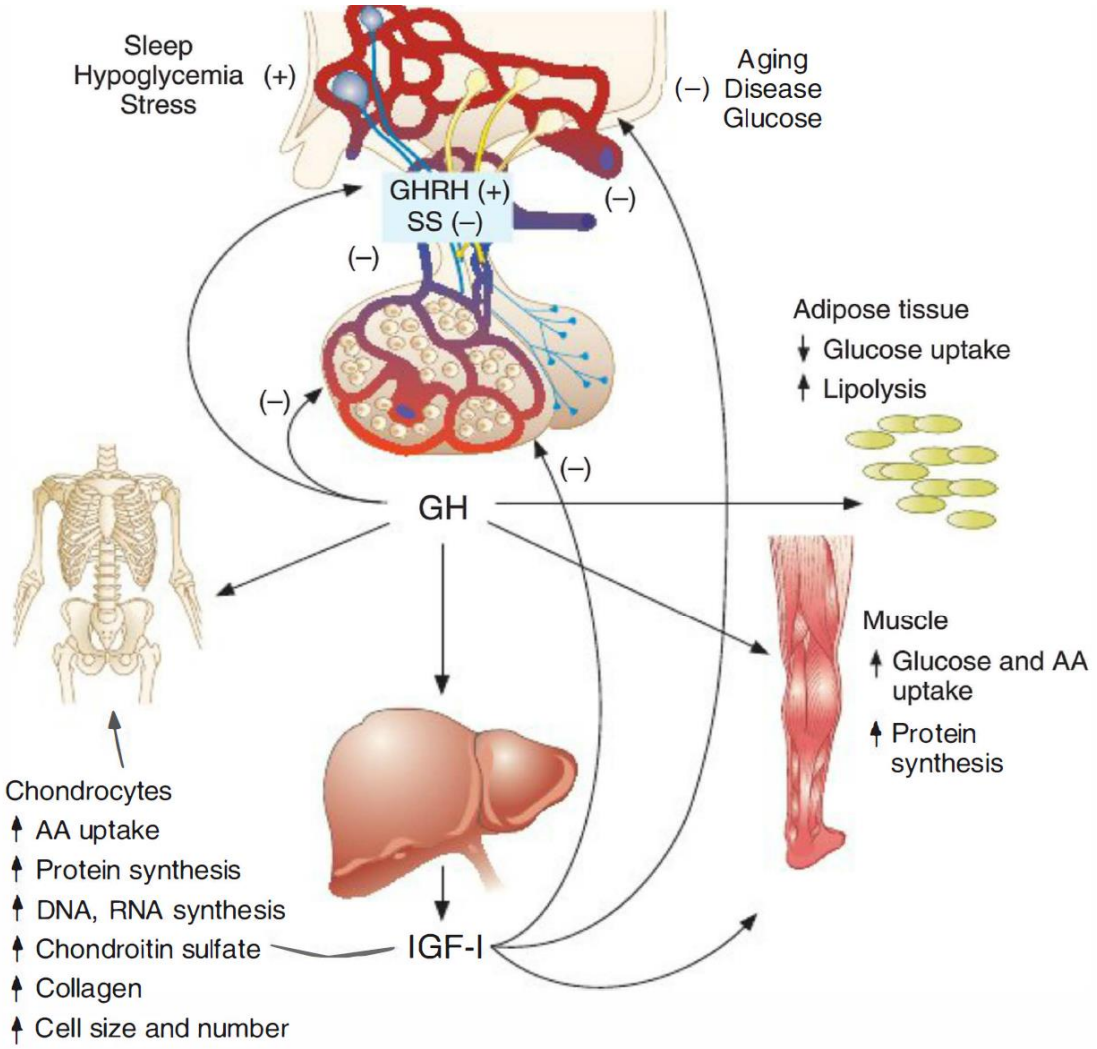
  Long-term: Synthesis of GH (Gene Expression).

Regulation of GH secretion



- GH secretion goes down due to:
- Exogenous GH
- SS
- IGF-1
- Aging

Regulation of GH secretion



- GH and IGF-1 decrease GH secretion by affecting both the hypothalamus and the anterior pituitary.

Prolactin