Optic Nerve Hypoplasia (ONH) & the Endocrine System

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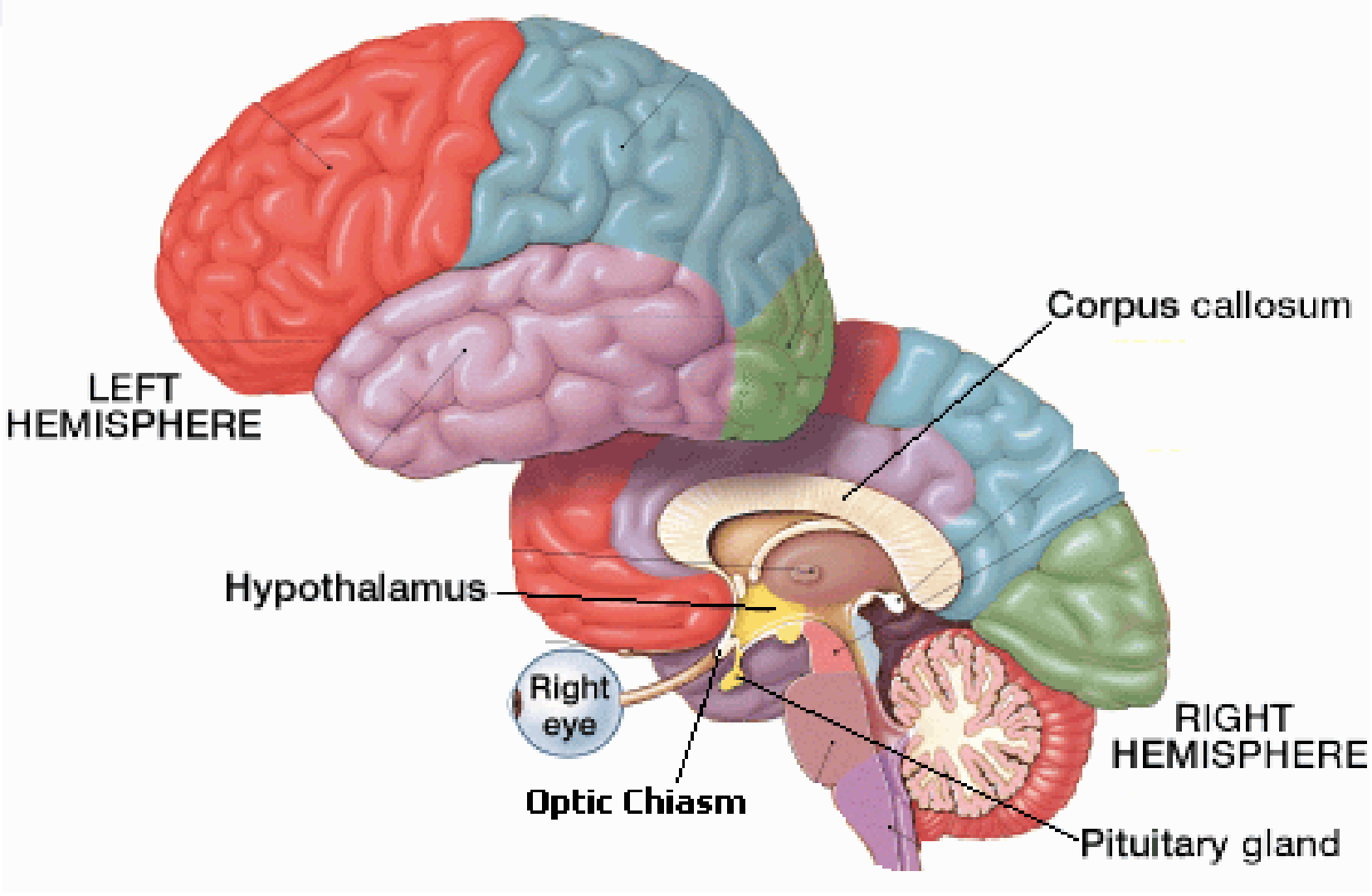
Objectives

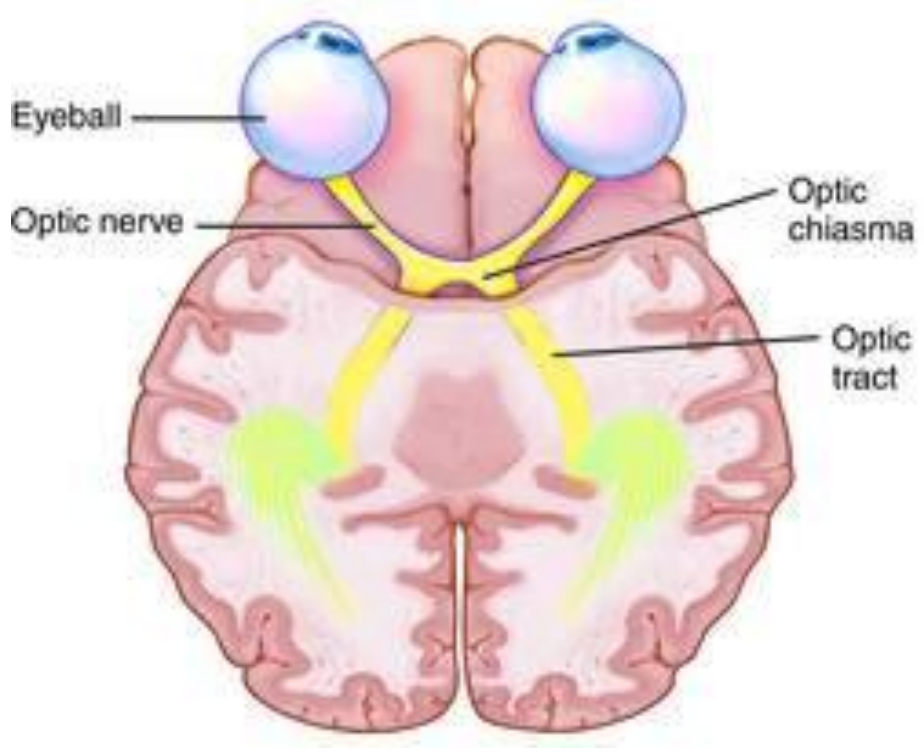
- Describe basic anatomy and physiology of the endocrine system
- Describe basic anatomy and physiology of optic nerve
- Describe role of hormones in regulation of body function
- Discuss relationship between ONH and hypopituitarism
- Discuss management of hormone deficiencies

Pituitary Gland/Hypothalamus/ON
Midline Structures

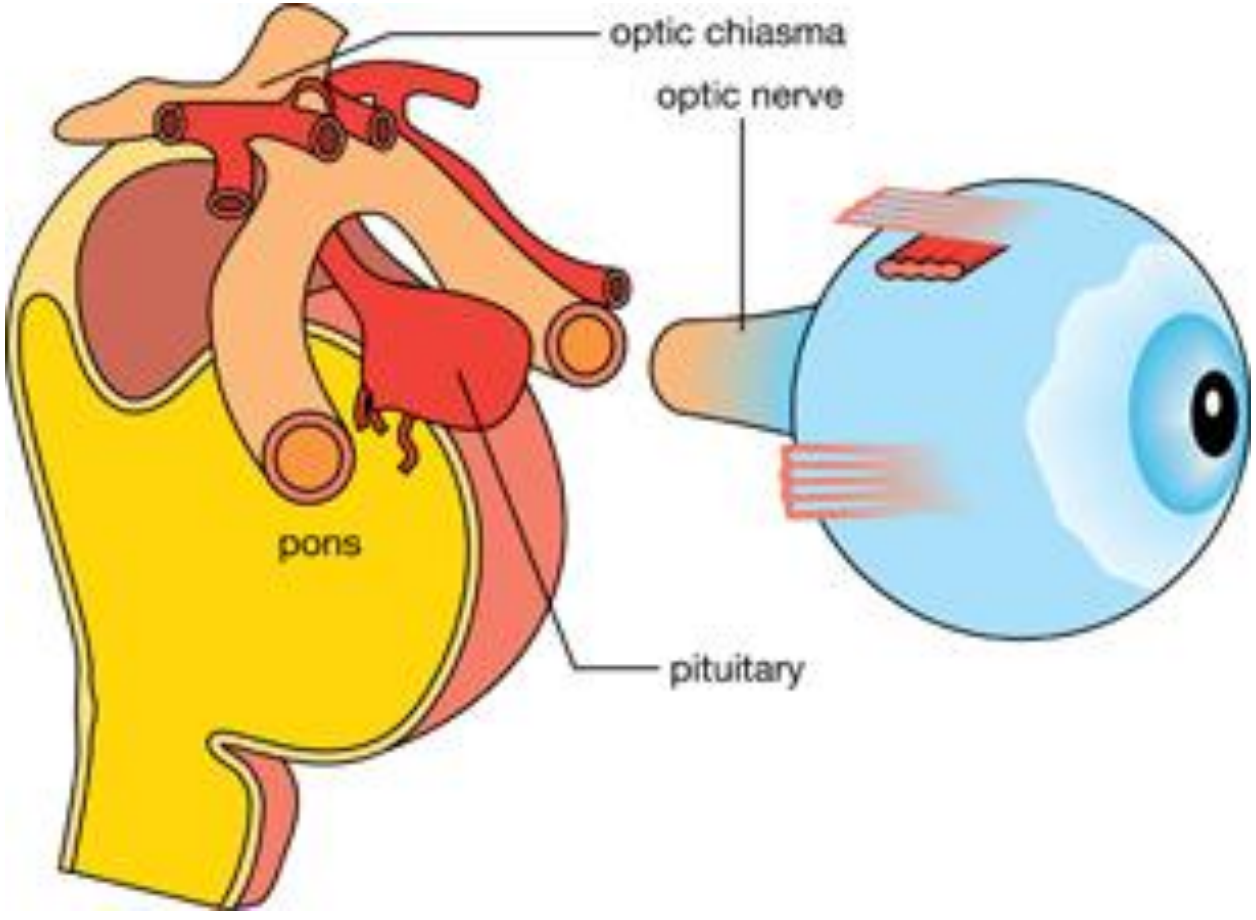


Optic Nerve(s)/Chiasm

- The optic nerve is a bundle of nerve fibers that serves as the communication cable between your eyes and your brain
- Optic nerves intersect at the optic chiasm

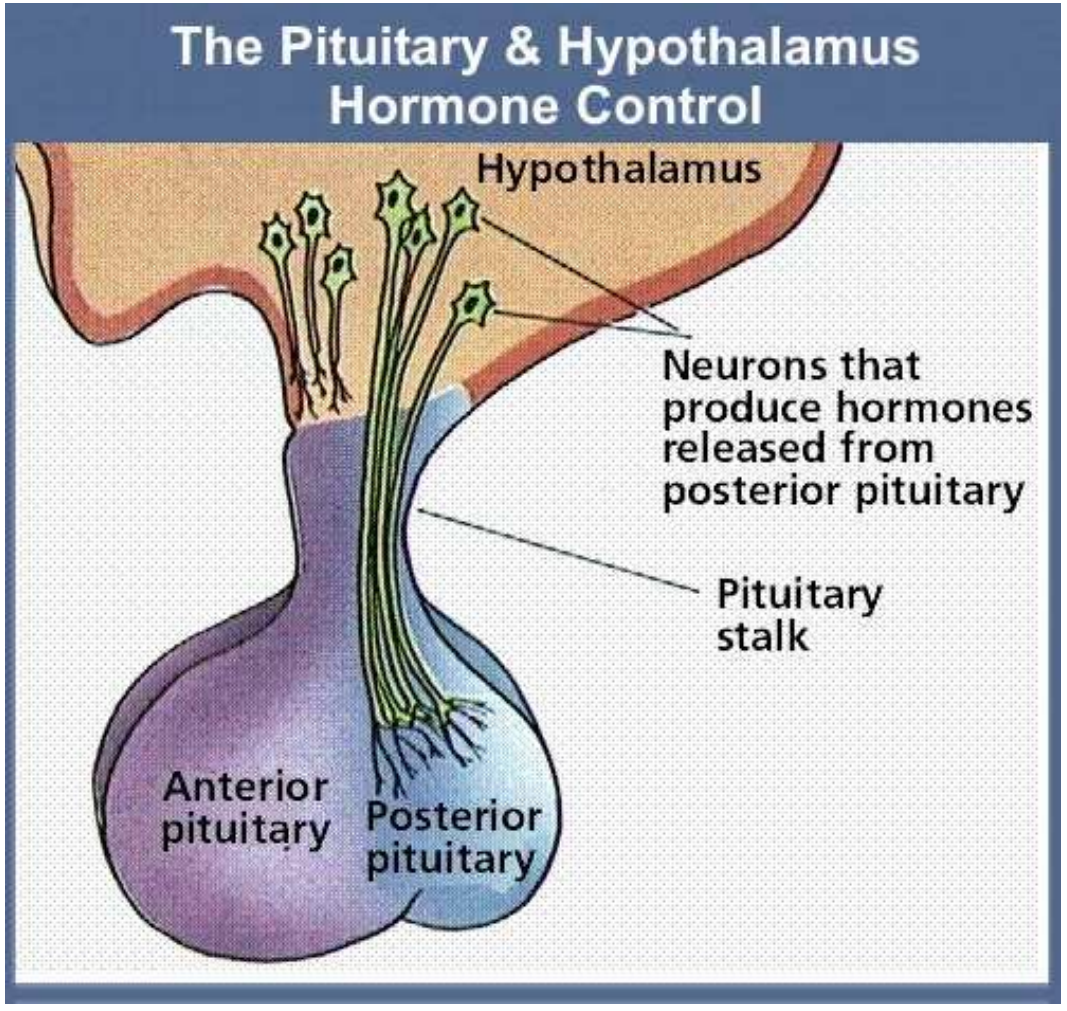


Optic Nerve/Chiasm & Pituitary Gland



Pituitary Gland & Hypothalamus

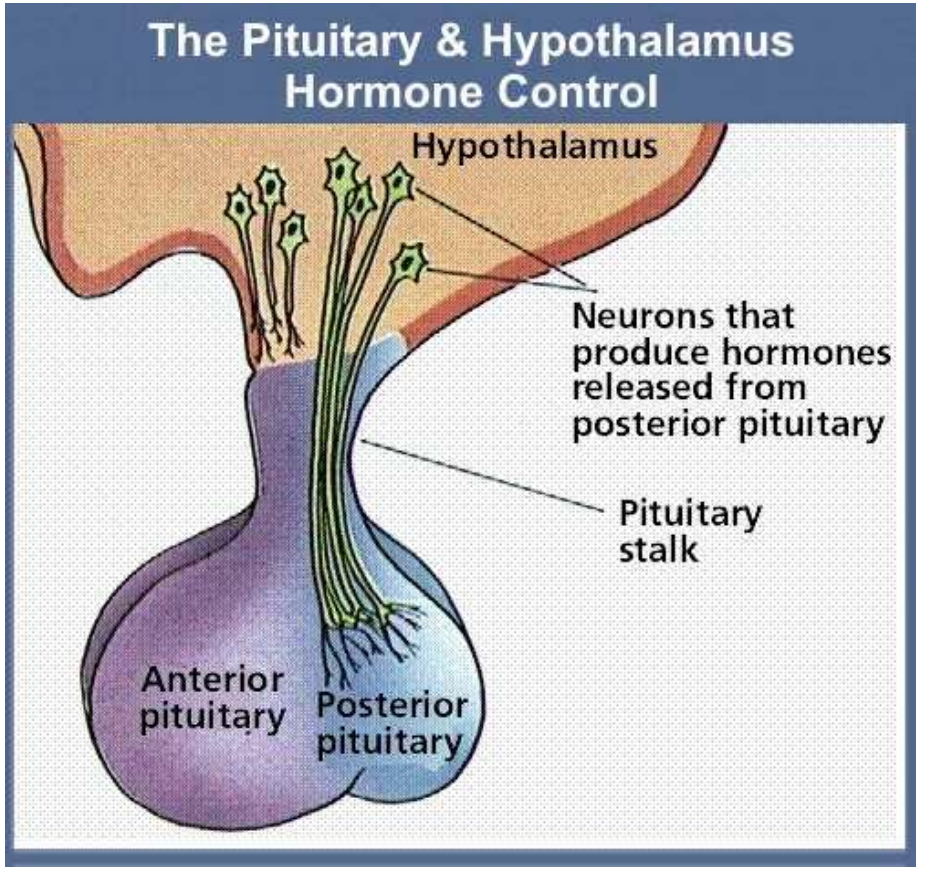
- **Pituitary gland** (Hypophysis)
  - Anterior pituitary (adenohypophysis)
  - Posterior pituitary (neurohypophysis)
- **Pituitary stalk**
  - Conduit between hypothalamus and pituitary gland



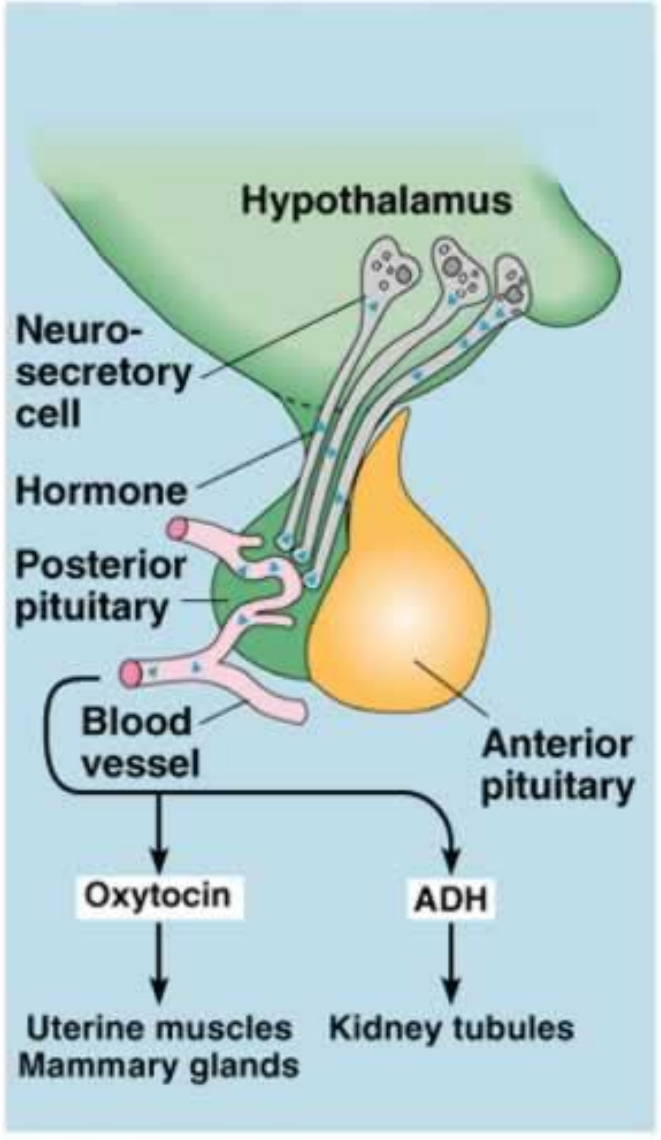
Pituitary Gland & Hypothalamus

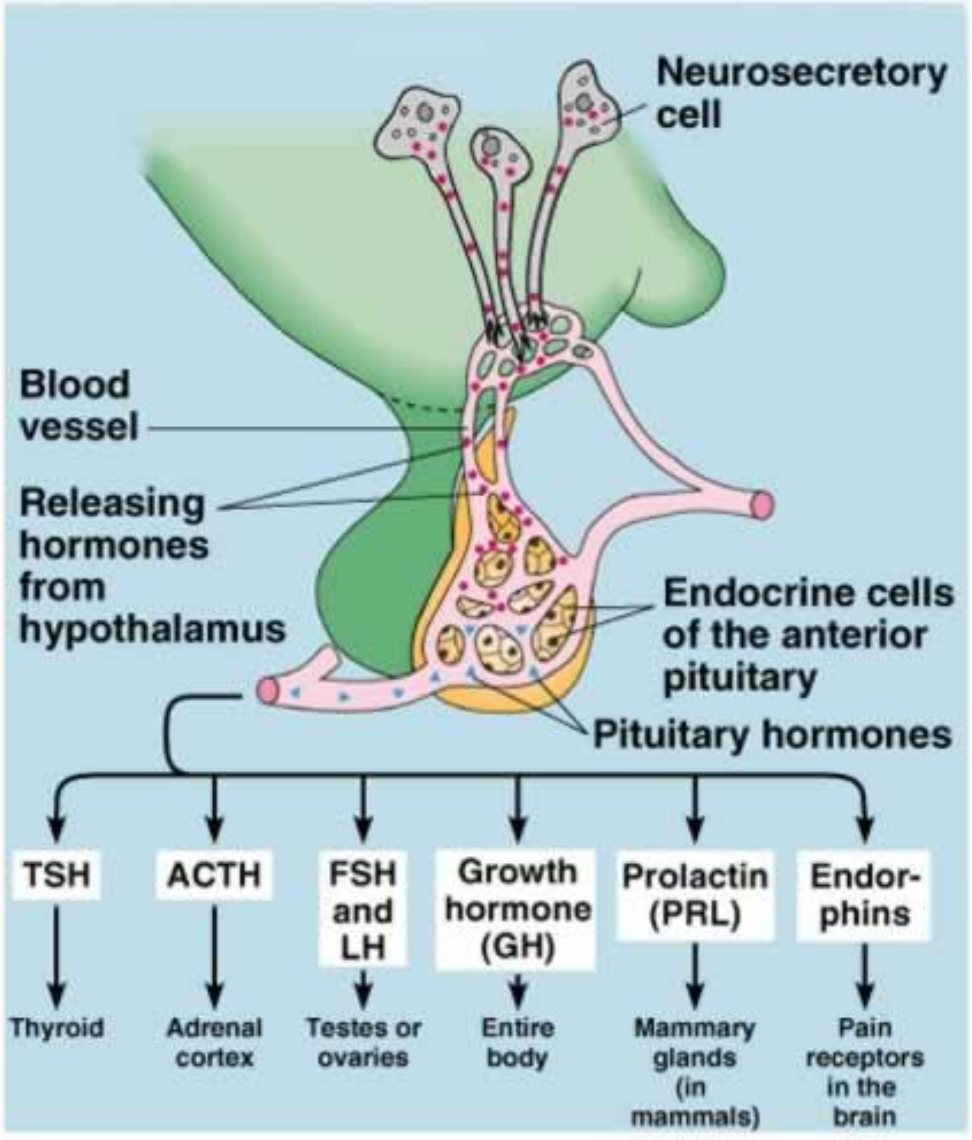
Hypothalamus

- Controls function of pituitary gland
- Controls blood pressure, hunger, thirst, fluid/electrolyte balance, emotions, body temperature regulation, and circadian rhythms (sleep-wake cycles)



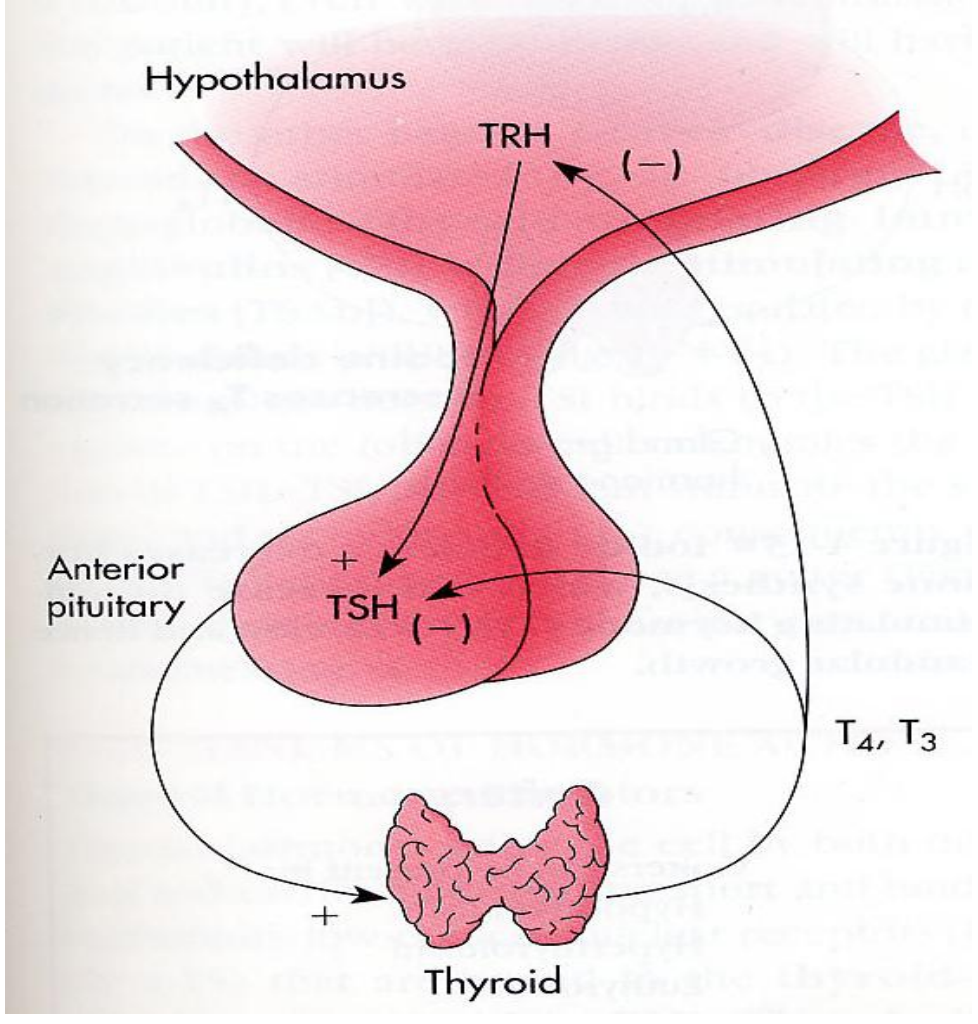
Pituitary Gland→"Master Gland"





Hypothalamic-Pituitary-Hormone Axis

- Most hormones axes interact to maintain equilibrium
  - Ex: Cortisol necessary for ADH action
- Hormone control via negative feedback loops



Optic Nerve Hypoplasia

Congenital abnormality → Small optic discs

- Unilateral or bilateral
- Isolated or in combo with myriad of functional and anatomic abnormalities of the central nervous system
- Varying degrees of visual impairment

Incidence

- Prevalence unknown in USA
- Prior to 1970, considered a rare condition
- Incidence increasing

Hypopituitarism

- Absence or reduction in the function of one or more hormones produced by the pituitary gland and hypothalamus
- "Pan" indicates more than one hormone deficiency
- Incidence:
  - Pan-hypopituitarism → <3 : 1 million/year
  - Growth Hormone Deficiency → 1 : 3480 children

Causes of Hypopituitarism

Congenital

- **Birth trauma and/or asphyxia**

  H/O transected or interrupted hypophyseal stalk
- **Midline Defect Syndromes**
  - Septoptic Dysplasia (de Morsier syndrome)
  - Absent septum pellucidum or absent corpus callosum
  - Cleft lip/palate, encephaloceles
- **Genetic mutations**
  - Transcription factors regulating anatomic development of pituitary gland
- **Idiopathic**
  - Unassociated w/clinical, biochemical, or radiologic abnormalities

Causes of Hypopituitarism

Acquired

- Brain tumors (Craniopharyngioma, most common)
- Cranial irradiation
  - S/P radiation-induced damage to hypothalamus. Pituitary gland relatively resistant to radiation
- Trauma: Especially with prolonged loss of consciousness
- Infiltrative, autoimmune, and metabolic diseases
  - Histiocytosis, sarchoidosis, hemochromatosis, cerebral edema
- Other
  - Brain infections, hydrocephalus, vascular abnormalities of H-P region

Clinical presentation of Hypopituitarism

Neonate

- Hypoglycemia
- Prolonged hyperbilirubinemia
- Turbulent neonatal course
- Micropenis

Older child

- Growth failure
- Diabetes insipidus
- Disorders of pubertal development
- Visual and neurologic complaints
- Characteristic facies and body habitus

Diagnosis of Hypopituitarism

Labs:

- TSH, FT4,
- IGF-1, IGF-BP3,
- AM fasting cortisol
- LH, FSH
- Stimulation testing

MRI :

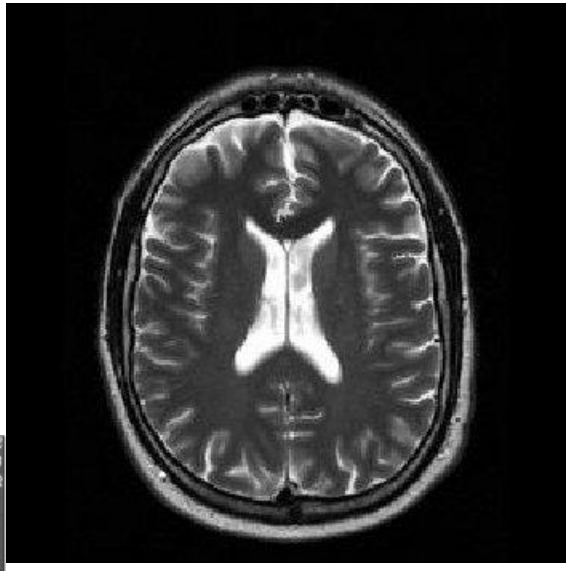
- Abnl pituitary gland
  - 50% severe GHD
  - 94% MPHD
  - 0% partial GHD
- Hypothalamic dysfunction→not detectable on imaging

Septo Optic Dysplasia

Septo Optic Dysplasia

At least 2 findings:

- Optic Nerve Hypoplasia
- Absent septum pellucidum
- Hypopituitarism



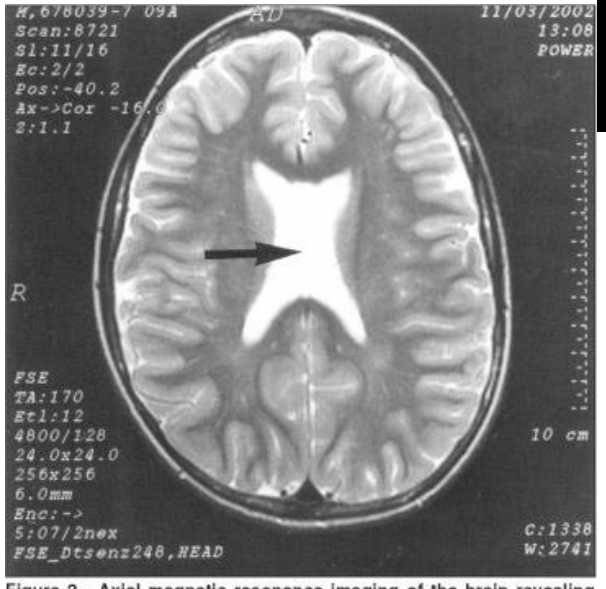


Figure 2 - Axial magnetic resonance imaging of the brain revealing absence of the septum pellucidum

Hypopituitarism & ONH

Hypopituitarism

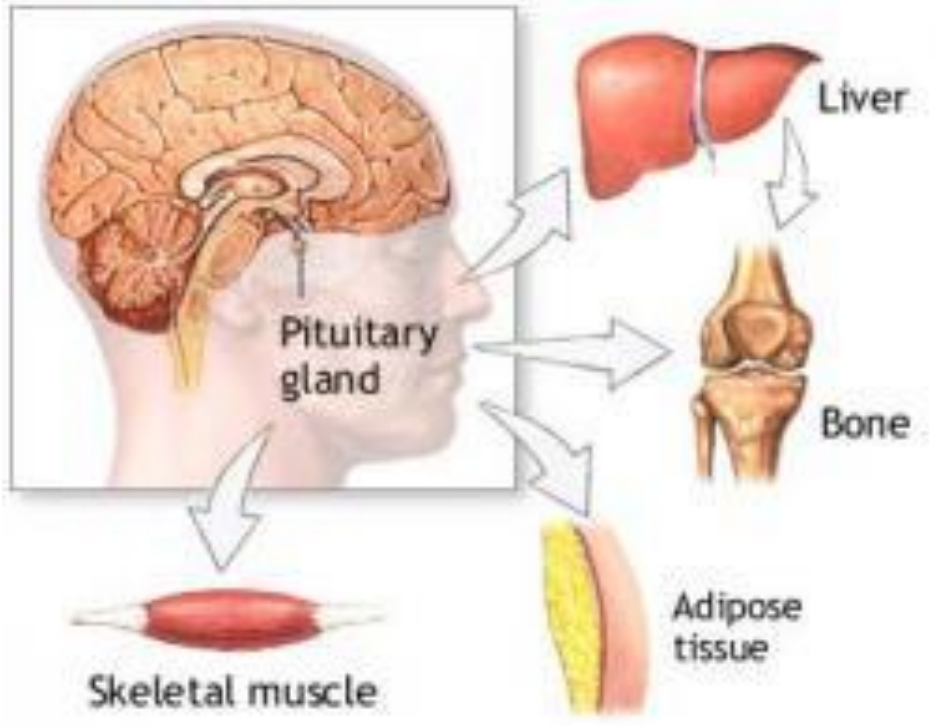
- 75% to 80% of ONH
- GHD (70%)
- Hypothyroidism (43%)
- Adrenal insufficiency (27%)
- Diabetes insipidus (5%)
- Asymptomatic hyperprolactinemia (62%)
- Puberty may be delayed or precocious

MRI with OHN

- 13% abnl pituitary gland
- 38% absent septum pelludicum

Growth Hormone (GH)

- Causes cell growth and division
- Promotes strong bones
- Helps regulate the body's metabolism by burning fat, building muscle, and maintaining blood sugar levels



H-P-GH Axis

- **Hypothalamus→ GHRH** (growth hormone releasing hormone)→Stimulates both synthesis and secretion of growth hormone

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- **Pituitary gland**→stores GH

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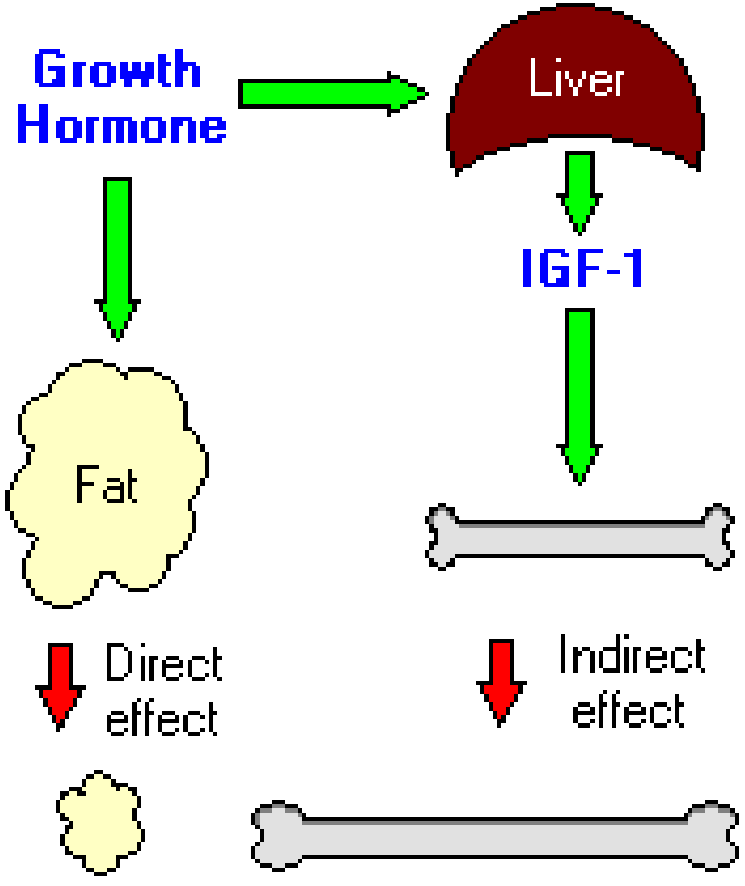
- **IGF-1**→stimulates cell growth



Growth Hormone Deficiency (GHD)

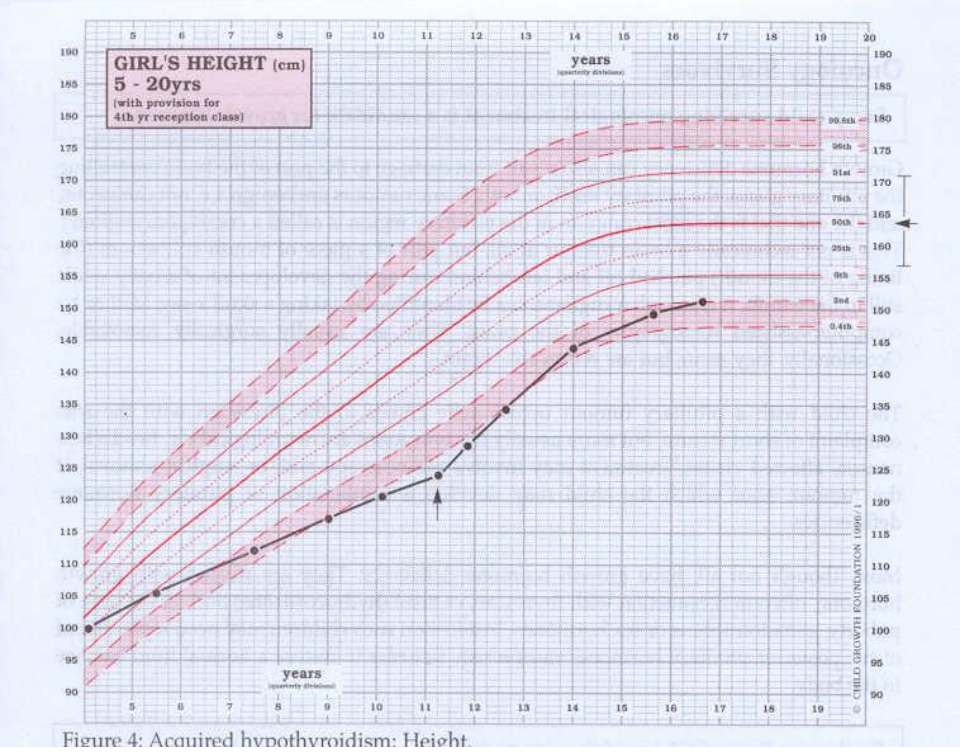


Figure 4: Acquired hypothyroidism: Height

Symptoms

- Neonates: hypoglycemia, micropenis
- Slow growth velocity→short stature
- Reduction of lean body mass/excess of fat
- Delayed bone age

Diagnosis

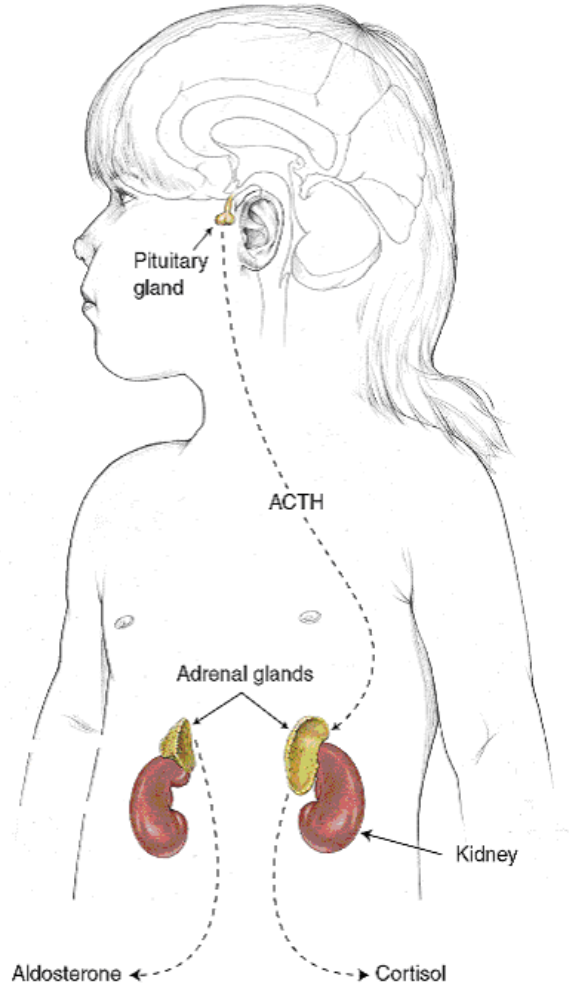
- IGF-1, IGF-BP3
- GH stimulation test

Treatment

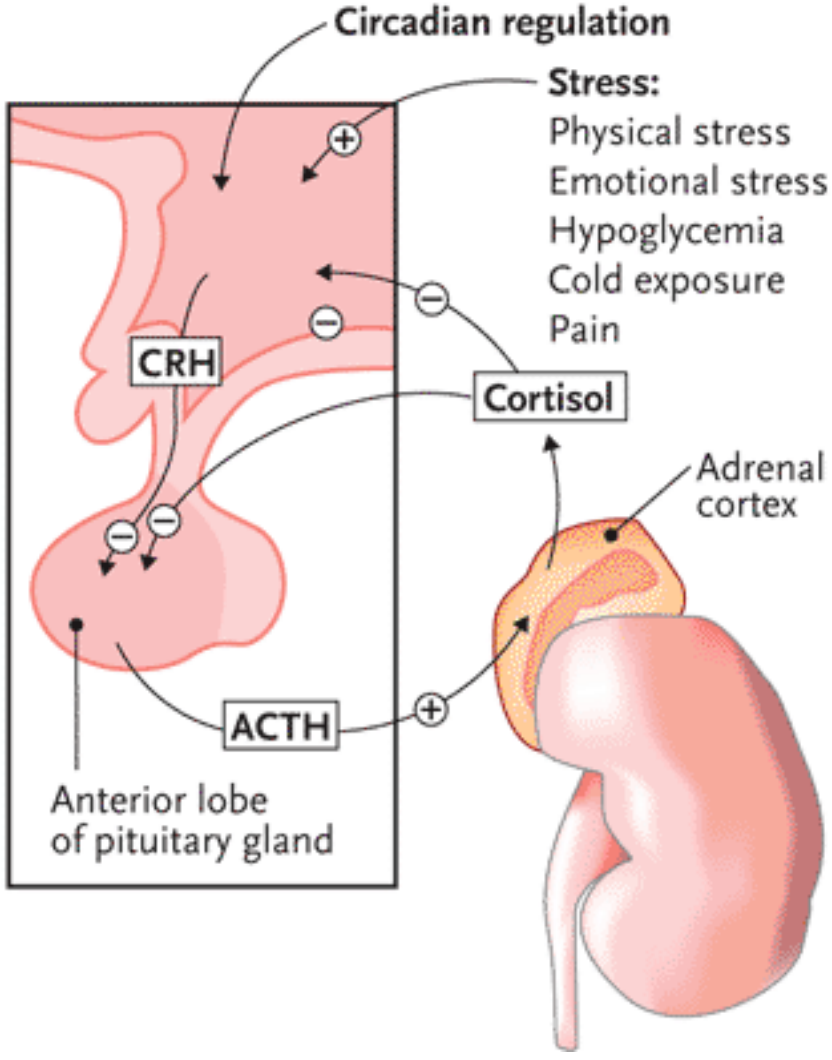
- GH replacement→Daily SC injections

Cortisol ("Stress Hormone")

- Maintains body energy supply
- Controls the body's reaction to physical stress
- Maintains blood pressure
- Maintains normal blood sugar levels
- Supports immune system
- Severe deficiency → life-threatening w/severe illness or trauma



H-P-A Axis



- **Hypothalamus→CRH** (Corticotropin-releasing hormone)

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- **Pituitary Gland→ACTH** (Adrenocorticotropic hormone)

↓

- **Adrenal Gland→Cortisol**

Central Adrenal Insufficiency

Cause

- ↓ACTH production

Symptoms

- Neonatal choleostasis, jaundice, hypoglycemia
- Increased fatigue and irritability
- Increased duration of illness

Diagnosis

- AM fasting cortisol
- Low dose ACTH stim test

Treatment:

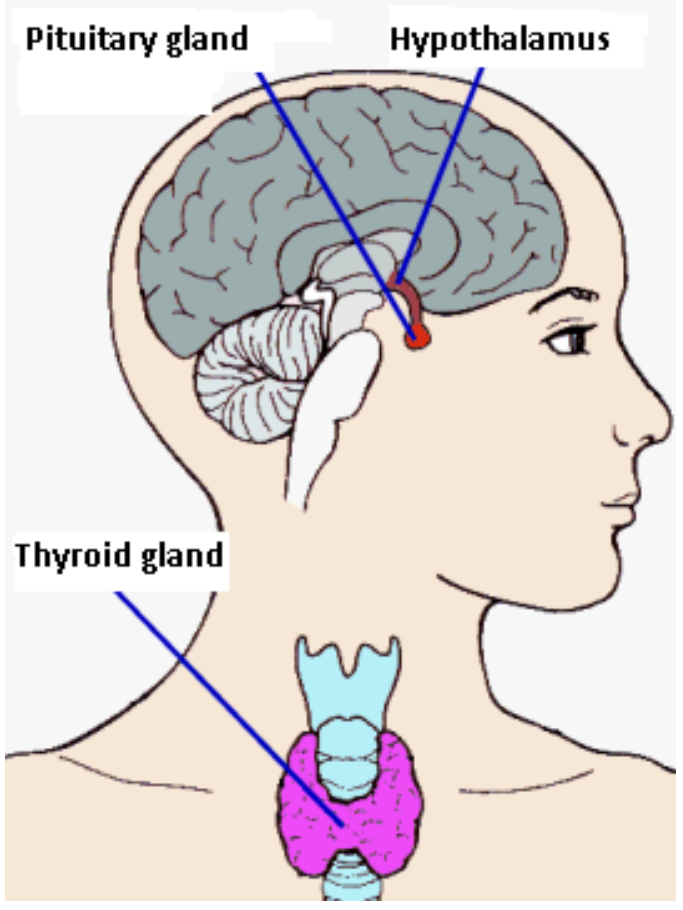
Cortisol replacement

- Hydrocortisone (short half-life)
- Prednisone (long half-life)
- Stress dosing: double/triple oral dose
- Injectable steroids

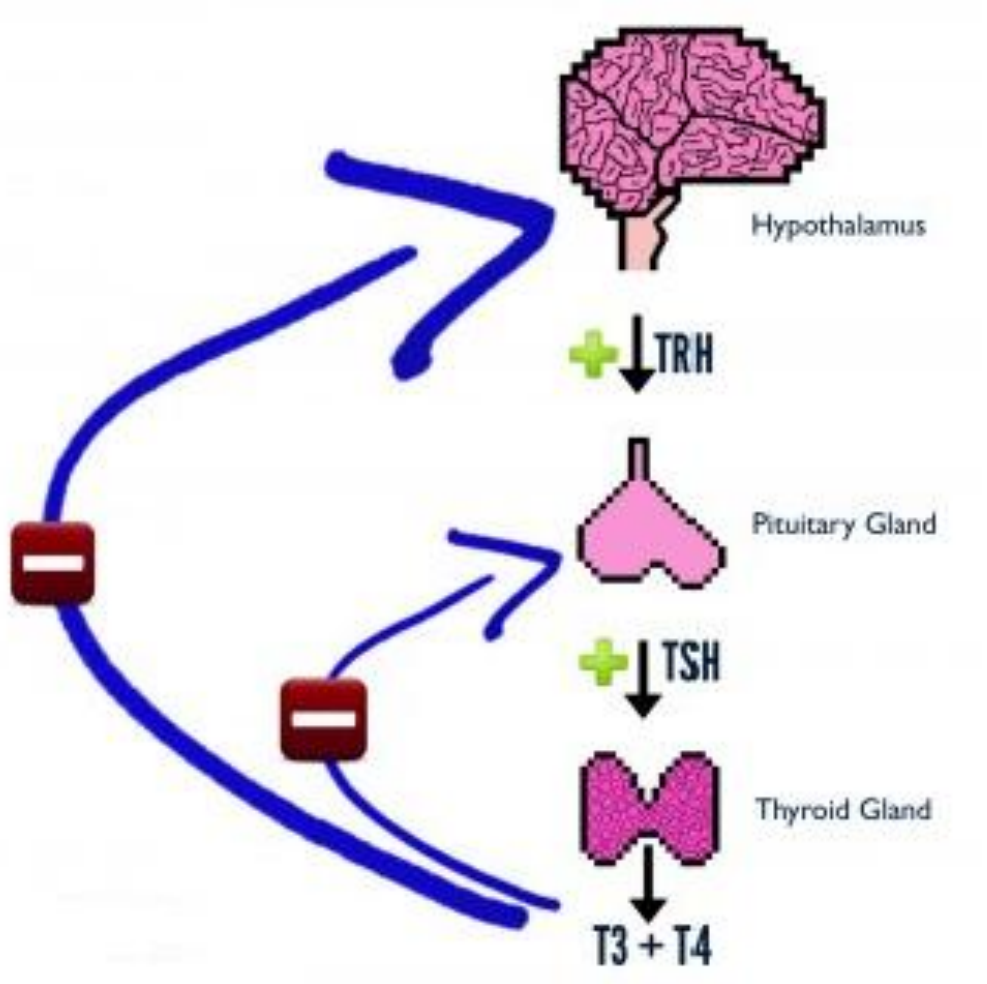
Thyroid Hormone

Thyroid hormone regulates :

- Metabolism
- Temperature
- Heart rate
- Muscle/bone strength
- Growth: Stimulates growth hormone release and effectiveness
- Intelligence
  - Essential for normal brain growth fetal to 3 yrs. of age
  - Controls synapse movement, neuron formation, growth of mylelin and telling neurons where they belong once formed in the brain



H-P-T Axis



- **Hypothalamus →TRH** (Thyrotropin-releasing hormone)

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- **Pituitary gland →TSH** (Thyroid stimulating hormone)

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- **Thyroid gland→** thyroxine

Central Hypothyroidism

Cause

↓TSH→ decreased thyroid hormone production

Symptoms

- Fatigue
- Dry, itchy skin
- Short stature

Delayed bone age

Diagnosis

- TSH, FT4

Treatment

Thyroid hormone replacement

- Levothyroxine tabs

Anti-diuretic Hormone (ADH) (Vasopressin)

- **Hypothalamus→ADH** (anti-diuretic hormone)

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- **Pituitary**→ stores ADH

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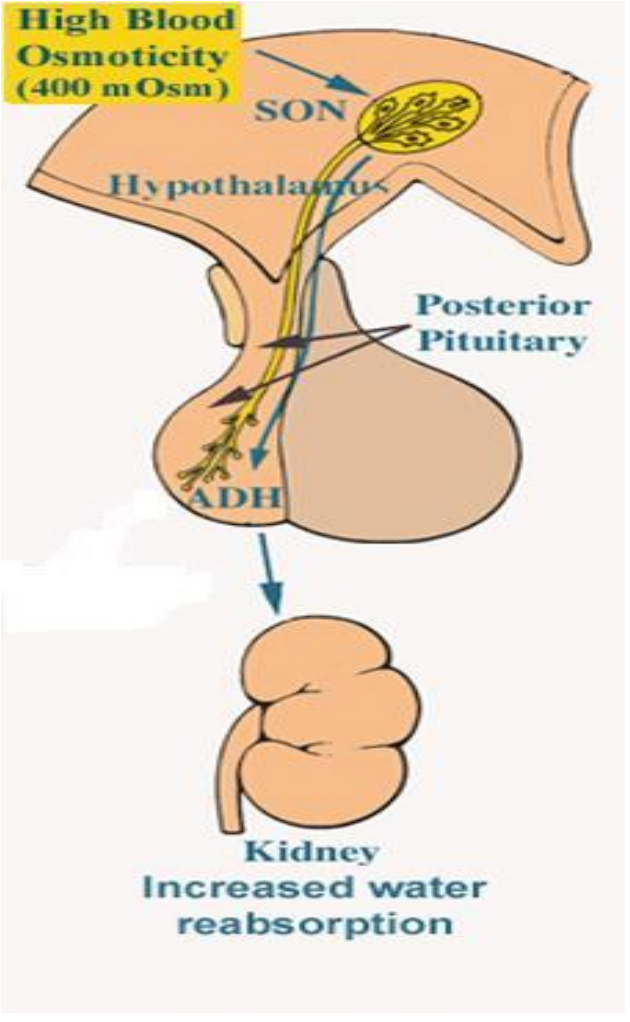
- **Kidneys** →conserve water



Diabetes Insipidus (DI)

Diabainein: Greek, "to pass through"

Insipidus: Latin, "having no flavor"

- Deficiency of ADH = Central DI
- End organ insensitivity to ADH = Nephrogenic DI

→ results in inability of the kidneys to conserve water

→leads to frequent urination and pronounced thirst

Diabetes Insipidus

Symptoms: varies with age

- Infants:
  - FTT
  - Irritability
  - Polyuria
- Older children:
  - Polyuria
  - Polydipsia
- Concomitant anterior pituitary hormones deficiencies may mask DI

Diagnosis

- Fasting electrolytes
- Water deprivation test

Treatment

- DDAVP (vasopressin analog)
- Desmopressin (generic)
- SQ, intranasal, tabs
- Dosing goal: uninterrupted activities of daily living (ADL)

Gonadotropin

- **LH** (luteinizing hormone)
  - stimulates secretion of sex steroids from the gonads
- **FSH** (follicular stimulating hormone)
  - stimulates the maturation of ovarian follicles
  - critical for sperm production

Estrogen and Testosterone

- Necessary for initiation of puberty and maintaining adult body habitus
- Help maintain:
  - Bones
  - Cardiac health
  - Energy levels
  - Menstrual cycles
  - Fertility

H-P-G Axis

- **Hypothalamus** →GnRH (gonadotropin releasing hormone)

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- **Pituitary gland** →LH / FSH

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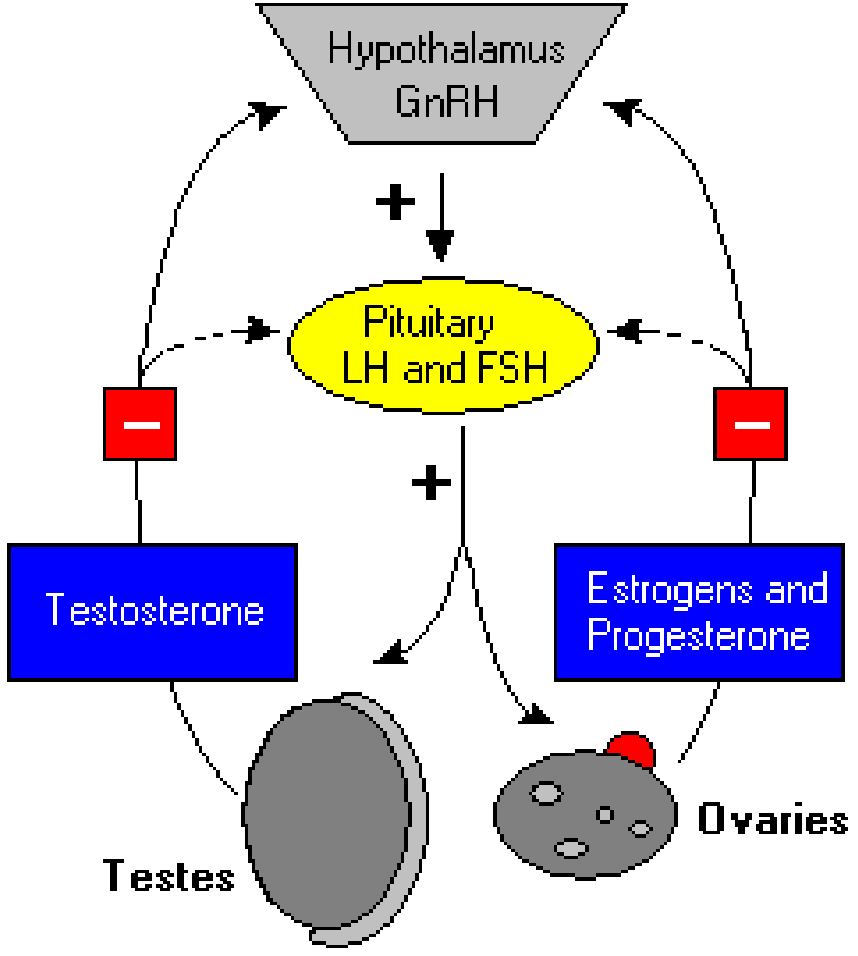
- **Ovaries** →estrogen

↓

- **Testes** →testosterone



Central Gonadotropin Deficiency

Cause

- ↓LH & FSH → decreased or no production of estrogen or testosterone

Symptoms

- Lack of secondary sexual development

Diagnosis

- LH, FSH
- LHRH stimulation test

Treatment

- Estrogen/progesterone replacement
  - Oral or patch
- Testosterone replacement
  - Depot injection, patch, or gel

Questions?

References

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