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 the 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
**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, sarkoidosis, 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
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 pellucidum
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

  ↓

- **Pituitary gland** → stores GH

  ↓

- **IGF-1** → stimulates cell growth
Growth Hormone Deficiency (GHD)

**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 $\rightarrow$ CRH (Corticotropin-releasing hormone)
- Pituitary Gland $\rightarrow$ ACTH (Adrenocorticotropic hormone)
- Adrenal Gland $\rightarrow$ 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 myelin and telling neurons where they belong once formed in the brain.
H-P-T Axis

- Hypothalamus → TRH (Thyrotropin-releasing hormone)
- Pituitary gland → TSH (Thyroid stimulating hormone)
- Thyroid gland → thyroxine
Central Hypothyroidism

**Cause**

\[ \downarrow \text{TSH} \rightarrow \text{decreased thyroid hormone production} \]

**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)
  - ↓
- **Pituitary** → stores ADH
  - ↓
- **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)
  - ↓
  - **Pituitary gland** → LH / FSH
    - ↓
  - **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?


