Endocrine Pathology

- Cell signaling system
- Surface receptors
  - cAMP and tyrosine kinase system
- Cytoplasmic receptors
  - Penetrate cell membrane
  - Gene activation -> transcription -> translation
- Intranuclear receptors
  - Gene activation -> transcription -> translation

Endocrine Pathology

- Too much hormone activity
- Too little hormone activity
- Autoimmune destruction
- Inflammatory destruction
- Tumor or vascular destruction
- Space occupying lesions (tumors)
  - Malignant
  - Benign

Endocrine Pathology

- All parts of the endocrine system interconnect.
- Cats Cradle
Pituitary Pathology

- Too much
- Too little
- Especially space occupying lesions

The Basics

- Anterior
  - Comes from GI
  - Controlled by hypothalamus
- Posterior
  - Hormones originate further up.

Pituitary Vascular

- Signaling proteins are released in hypothalamus.
- Travel by blood to anterior pituitary
- Cause release of many activating hormones
- System of amplification

Pituitary Control

Space Occupying Lesions

- Tumors
- Embryonic rests
- Squeeze gland out of existence.
  - Generalized failure
  - Visual field changes
Visual Fields
- Loss of temporal fields.
  - Nasal retina
  - Damage to decussating optic nerve fibers

Pituitary Adenomas
- Rare
- Make nothing or prolactin
- ACTH, GH, TSH are very rare
- More often end up with pituitary failure:
  - Squeeze the daylights out of the gland.

Acromegaly
- Growth hormone excess after closing of epiphyses.
- Periosteal bone growth.
- Diabetes
- Prognathism

Hypopituitarism
- Destruction of gland.
- Ischemia
- ‘Benign’ adenoma destroying gland
- Craniopharyngioma
  - Rathke’s pouch remnant
  - Benign cyst, but really in the wrong place.

Ischemic Destruction
- Shehan’s syndrome
- Post delivery problem
- No lactation
- In time general failure of ‘downstream’ systems
  - Thyroid
  - Adrenal cortex
  - Ovulation

Posterior Pituitary
- Loss of ADH
  - Diabetes insipidus
  - Dose not make concentrated urine
  - Large volumes of dilute urine
  - Head injuries
  - Tumors of periventricular area
Thyroid Disease

Control of Thyroid Hormone

- Hypothalamus
- Pituitary
- Thyroid
- Tissue level
  - Establishes metabolic rate for the whole organism

Hyperthyroidism

- Clinical findings
  - Heat intolerance
  - Tremor
  - Tachycardia
  - Hyperactive
  - Increased body metabolism and temperature
  - Ocular changes
- Main causes
  - Graves Disease
  - Toxic goiter
  - Toxic adenoma

Hyperphthalmia

- Grave’s disease
  - Antibody stimulates TSH receptors in extraocular muscles.
  - Increased tissue in orbit causes eye to protrude.
  - Won’t go down
  - Dry conjunctiva and increased risk of eye infections.

Hyperthyroidism
Hypothyroidism

- Genetics
- Gland destruction
  - Inflammatory
  - Surgical removal
  - Radiation treatment for hyperthyroidism
- Iodine deficiency
  - Can’t make T4
- Hypothalmic and/or pituitary failure

- Genetics: Cretinism
- Cannot make T4
- Growth retarded
- Severe mental retardation
- Must recognize early

Hypothyroidism

- Clinical
  - Cold intolerance
  - Bradycardia
  - Heart failure
  - High lipids
  - Lethargic
  - Photophobia
  - Myxedema
  - Skin and hair changes

Tumors and Changes in Size

- Goiter
  - Nodular
  - Uniform increase
  - Scarring
  - Cysts
  - Generally euthyroid
  - May cause airway compression

- Thyroid Adenomas
  - Benign
  - Solitary
  - Common
  - Encapsulated
  - Generally not hyperactive
Malignancies of Thyroid Origin

- Arising from follicular cells
  - Papillary Carcinoma
  - Follicular Carcinoma
  - Mixed pattern
- Interstitial cells (Calcitonin producing cells)
- Anaplastic, who knows
  - Very aggressive tumor

Papillary Carcinoma

- Papillary groups
- May have multiple sites
- Not actively producing T4
- Readily treated
- Spread
  - Nodes
  - Lung
  - Bone
  - Brain

Papillary Carcinoma

Orphan Annie Nuclei

- Needle aspirates
- Open eyed nuclei
- Indicative of papillary ca

C Cell Carcinoma

- Interstitial cells
- Makes calcitonin
- Makes amyloid
  - Beta pleated sheet protein
- Often part of a multiple endocrine neoplasia syndrome

C Cell Carcinoma
Inflammatory Conditions
- Autoimmune
- Viral
- Bacterial

Hashimoto’s Thyroiditis
- Many antibodies
- T & B cells
- Active germinal centers
- Women 5:1
- Scarring
- In time hypothyroid
- Other autoimmune
  - Arthritis
  - PA
  - Lupus
  - Addison’s

Hashimoto’s Thyroiditis

De Quervain’s Thyroiditis
- Subacute
- Giant cells
- Granulomas
- Viral?
- Painful neck

Parathyroid
- Come from the pharyngeal pouches
- Most of us have 4
- Make PTH
- Mobilizes calcium
- Released by low serum calcium
- High serum phosphate
Hyperparathyroidism

- Primary
  - Parathyroid adenoma 80%
  - Hyperplasia 10-15%
  - Parathyroid ca <5%
- Hypercalcemia
  - Stones, bones, abdominal groans and psychic moans
  - Bone wasting
    - Generalized
    - Osteitis fibrosa cystica

Parathyroid Adenoma

Secondary Hyperparathyroidism

- Renal failure almost always
- Phosphates build up in the blood.
- Cause calcium to drop.
  - PTH is made
  - Phosphate itself can cause release of PTH
- Glands begin to function autonomously

Hypoparathyroidism

- Increased neuromuscular excitability
- May lead to tetany
- Irritability and possibly even psychosis
- Parkinson-like symptoms
- Cataracts
- Causes
  - Autoimmune destruction
  - Accidental removal with thyroid
  - Congenital absence
Adrenal Gland
- Really two glands in one.
  - Cortex ->
    - Salt
    - Sugar
    - Sex
  - Medulla
    - Epinephrine
    - Norepinephrine

Adrenal Pathology
- Same as for all
  - Too much
  - Too little
  - Tumors

Cushing’s Syndrome
- Effects of too much cortisol
  - Moon face
  - Central obesity
  - Buffalo hump
  - Osteoporosis
  - Fractures
  - Hypertension
  - Weakness

Cushing’s Disease
- Altered feedback regulation at level of hypothalamus and pituitary
  - It only takes a small increase in ACTH
  - Loss of cortisol diurnal cycle
  - Pituitary adenoma
  - Ectopic ACTH
    - Small cell carcinoma of lung
    - Adrenal tumors autonomously functioning

Hyperaldosteronism
- Conn’s syndrome
- Adenoma (65% of the time) causing high blood pressure.
- Over production of aldosterone
- Zona glomerulosa
  - No ACTH control
  - Retention of Na⁺
  - Urinary loss of K⁺
  - Serum alkalosis
Congenital Enzyme Deficiency

- A number of possibilities, but 21-beta-hydroxylase is most common.
  - Salt losing
  - Androgenizing

Hypoadrenalism

- Acute loss vs. Chronic
- Pituitary vs. adrenal
- Acute
  - Waterhouse-Friderichsen syndrome
    - Overwhelming infection with encapsulated bacteria.
    - Leads to vascular infection.
    - Hemorrhagic destruction of adrenal glands
    - Medical crisis

Addison's Disease

- Slowly develops
- Loss of adrenal glands
- Lots of ACTH, but nothing it can do.
- Metastatic tumor
- TB
- Clinical
  - Weight loss
  - Hypotension
  - Hyperpigmentation

Adrenal Medulla

- Pheochromocytoma
- Catacholamines
- Elevated blood pressure
- Syncopeal episodes
- Headaches
- Nose bleeds
- Anxiety
- Maybe an isolated tumor or part of a multiple endocrine tumor syndrome.

Multiple Endocrine Neoplasia, MEN

- Neural crest derivative cells
- Give rise to hormonally active tissue
- Migrate from the neural crest to many organs
  - Anterior pituitary
  - Parathyroids
  - Adrenal Medulla
  - Thyroid, interstitial cells
  - Bronchial and bowel mucosa
MEN I

- MEN I, Wermer’s Syndrome
  - Tumor suppressor gene, chromosome 11
  - Parathyroid adenomas
  - Pancreas Islet cell adenomas
  - Pituitary adenomas (prolactin)

MEN II A

- Sipple syndrome
- Proto-oncogene, chromosome 10
  - Thyroid, medullary carcinoma
  - Adrenal medulla, pheochromocytoma
  - Parathyroid adenoma

MEN II A

- Sipple syndrome
- Proto-oncogene, chromosome 10
  - Thyroid, medullary carcinoma
  - Adrenal medulla, pheochromocytoma
  - Parathyroid adenoma

MEN II B

- Thyroid, medullary carcinoma
- Adrenal, pheochromocytoma
- Ganglioneuromas and neurofibromas
  - Lips
  - Face
  - Oral cavity
  - Eyes
  - GI tract

Pancreatic Islet Cell Tumors

- Benign or malignant
- Hormone depends on cell of origin
  - Beta cell, insulin secreting
    - Hypoglycemic episodes
  - Delta cell, Zollinger-Ellison syndrome
    - Gastrin secreting
    - Intractable ulcers
  - Alpha cell adenoma
    - Glucagon secreting
    - Become diabetic