Pathology of the endocrine system
Endocrine system
Structure and function [Figs. 17-1, 17-2]
- the endocrine system consists of cells that secrete hormones
- endocrine cells are organized as:
  glands [eg. pituitary, thyroid, adrenal, parathyroid glands]
  major component of another organ [eg. testicle]
  scattered cells within other organs [eg. pancreas, intestine)
- hormones are substances made by endocrine cells and released into the blood to act on distant targets
- release of hormones by endocrine cells is controlled by various feedback mechanisms

Overview of pathology
Clinical presentation
- symptoms of endocrine gland disorders are usually due to increased hormone production, decreased hormone production or mass lesions
- hypofunctioning of endocrine cells results in decreased hormone levels
- hyperfunctioning of endocrine cells results in increased hormone levels
- mass lesions are usually due to neoplasia or hyperplasia

Multiple endocrine neoplasia syndromes (MEN)
- certain syndromes are characterized by multiple endocrine neoplasms
  - MEN I (pituitary, parathyroid, pancreatic islet cell neoplasia)
  - MEN IIa (medullary thyroid carcinoma, pheochromocytoma, parathyroid)
  - MEN IIb (IIa + skin and mucosal nerve tumors)

Pituitary gland
Structure
- single endocrine gland located in base of the cranium
- two parts, anterior and posterior

Posterior pituitary (extension of the hypothalamus)
- secretes the hormones ADH, and oxytocin

Anterior pituitary
- secretes growth hormone, thyroid stimulating hormone, adrenocorticotropin hormone, gonadotrophin hormones
- release of hormones controlled by other hormones released by hypothalamus and various feedback loops

Pituitary gland pathology
Pituitary adenoma
- benign neoplasm of endocrine cells in the anterior pituitary
- symptoms due to release of excess hormones or pressure effects of mass (compression of pitutary stalk and/or optic chiasm)
- endocrine effects depend on what hormone produced by the adenoma
- 80% of pituitary adenomas produce hormones

Prolactinoma (LH)
- most common pituitary adenoma produces prolactin
- identified earlier in young reproductive female because present with amenorrhea, galactorrhea, infertility (microadenoma)
- surgery or medical therapy (bromocryptine) to remove

Pathology of the endocrine system

Pituitary gland pathology

Pituitary adenoma

Somatotropic adenomas

- neoplastic cells produce growth hormone
- gigantism results from excess growth hormone before growth plates close
  - generalized increase in body size with disproportionately long legs, arms
- acromegaly results from excess growth hormone after puberty
  - enlargement of hands, feet, jaw, tongue, and soft tissue)

Corticotropic adenoma

- neoplastic cells produce adrenocorticotropin hormone
- Cushing's disease refers to the syndrome resulting from excess glucocorticoid release by the adrenal cortex due to excess ACTH

Pituitary hypofunction

- causes of pituitary hypofunction include
  - congenital defect of pituitary gland (primary dwarfism)
  - destructive tumor (pituitary adenoma)
  - ischemia of the pituitary gland (Sheehan's syndrome)

symptoms

- weakness, ↓ appetite, ↓ weight, hypotension, amenorrhea
- secondary hypofunction of target organs

Diabetes insipidus

- lack of ADH
- usually due to destructive lesion in hypothalamus, pituitary
- unable to resorb water, large amounts of hypotonic urine

Thyroid gland

Structure and function

- located in anterior neck, right and left lobes joined by isthmus
- follicular cells produce thyroid hormones (T_4, T_3)
- release of thyroid hormones controlled by TSH (from pituitary)
- C cells produce calcitonin

Pathology of the thyroid gland

Thyroid hyperfunction (hyperthyroidism) [Figs. 17-5, 17-6]

- major causes are Grave's disease, some multinodular goiters, tumors

symptoms of hyperthyroidism

- restless, nervous, emotional lability, sweating, tachycardia, diarrhea, weight loss with increased appetite

Hyperthyroidism

Grave's disease

- autoimmune disease due to antibodies targeting the TSH receptor on thyroid follicular cells
- AB binds to TSH receptor causing release of thyroid hormones
- more common in females
- associated with other autoimmune diseases
- exopthalmos occurs in Grave's disease

Multinodular goiter

- enlarged, nodular thyroid may produce increased amounts of thyroid hormone (some may be euthyroid or hypofunctioning)

Pathology of the endocrine system

Pathology of the thyroid gland

Thyroid hypofunction (hypothyroidism) [Fig. 17-6]

- major causes are agenesis, surgery, thyroiditis, iodine deficiency

Symptoms of hypothyroidism

- cretinism and dwarfism if occurs in perinatal period or infant
- myxedema if occurs in older child or adult
  - sleepy, tire easily, cold intolerance, constipation, weak
- treat with thyroid hormone replacement

Nodular goiter

- goiter is general term for enlarged thyroid gland (many causes)
- nodular goiter is a form of goiter characterized by multiple nodules
- goiters are usually euthyroid (normal thyroid hormone levels)
- may cause mass effects (surgery if problematic)

Thyroid neoplasms

Adenomas

- benign neoplasms of thyroid follicular cells
- may produce symptoms due to mass effect
- treated by surgery (microscopic examination required to rule out cancer)

Carcinoma

- malignant neoplasm of thyroid follicular cells
- two major types:
  - papillary carcinoma (80%)- good prognosis
  - follicular carcinoma (15%)- relatively good prognosis

Parathyroid glands

Structure and function

- usually 4 glands, located in the anterior neck
- produce parathyroid hormone (PTH), involved in calcium homeostasis

Pathology of the parathyroid glands

Hyperparathyroidism[Figs. 17-8, 17-10]

- major causes are parathyroid adenoma and parathyroid hyperplasia

symptoms of hyperparathyroidism (hypercalcemia)

- bones, stones, moans, abdominal groans

Hypoparathyroidism

- causes of include surgery, congenital hypoplasia

symptoms of hypoparathyroidism (hypocalcemia)

- muscle spasms, irregular heart beat, cardiac arrest (if severe)

Adrenal glands

Structure and function

- right and left glands, located retroperitoneal

adrenal cortex

- zona glomerulosa (aldosterone)
- zona fasciculata (cortisol)
- zona reticularis (secondary sex steroids)

adrenal medulla

- secrete epinephrine, norepinephrine

Pathology of the endocrine system

Pathology of the adrenal gland

Adrenocortical hyperfunction[Figs. 17-11, 17-13]

Hypercortisolism (Cushing's syndrome)

- syndrome due to excess glucocorticoid hormones (cortisol)
- most common cause is exogenous steroids, other causes include
  - adrenal hyperplasia or neoplasia
  - hypersecretion of ACTH by pituitary gland (Cushing's disease)
  - ectopic ACTH (paraneoplastic syndrome)
- dramatic appearance: central obesity, buffalo hump, moon face, striae

Hyperaldosteronism (Conn's syndrome)

- syndrome due to excess mineralocorticoid hormone (aldosterone)
- causes include adrenocortical adenoma and adrenal hyperplasia
- present with hypertension and hypokalemia

Adrenocortical hypofunction

- usually autoimmune destruction of adrenals, also due Tb, malignancy

Addison's disease

- autoimmune destruction of adrenal gland
- fatigue, weight loss, nausea, increased infections, low Na, high K

Diseases of Adrenal Medulla

Neuroblastoma

- malignant neoplasm of neuroblasts (primitive cells) in neonates, infant
- treatment with chemotherapy, surgery, radiation (90 % cure)

Pheochromocytoma

- a neoplasm (usually benign) derived from adrenal medulla cells
- diagnosed on basis of dramatic clinical picture, metabolites in urine
- treated by surgery

Endocrine pancreas

Structure

- cells located in islets within the pancreas
- several different types of cells (B cells produce insulin)

Pathology of the endocrine pancreas

Diabetes mellitus

- heterogeneous group of diseases due to inadequate insulin activity
- present with polyuria, polydypsia, weight loss

classification of primary diabetes

- type 1 diabetes (insulin dependent, juvenile onset)
- type 2 diabetes (non-insulin dependent, adult onset)
  - most common, relative lack of insulin
- impaired glucose tolerance

pathogenesis

- insulin released in response to increased blood sugar
  - insulin required by certain cells for entry of glucose into the cell
- insulin decreases blood glucose levels
- lack of insulin causes hyperglycemia
  - present with polyuria (osmotic diuresis) and resulting polydypsia
  - also fatigue due to inability of glucose to enter certain cells
- striated muscle cells must use anaerobic glycolysis
  - increased lactic acid
  - decreased use of fats result in increased free fatty acids
    - free fatty acids oxidized into ketones (acidosis)

Pathology of the endocrine system

Pathology of the endocrine pancreas

Diabetes mellitus

- genetic predisposition
  - type 2 > type 1
- environmental factors

Complications (due to long term uncontrolled hyperglycemia)

- Cardiovascular [increased atherosclerosis (CAD, CVD, distal gangrene)]
- Renal [glomerulosclerosis, pyelonephritis, papillary necrosis]
- Eyes [diabetic microangiopathy of retinal vessels, glaucoma, cataracts]
- Nervous system

Treatment (depends on type)

- type 1 requires insulin
- type 2 diet, oral hypoglycemics, insulin if unable to control

Skin

Structure[Fig. 18-1]

- Epidermis (keratinocytes, melanocytes)
- Dermis (connective tissue, adnexal structures)
- Subcutis (adipose tissue)

Functions

- protection; regulation of body temperature

Basic skin pathology

Congenital diseases

- nevus (mole)
- albinism

External injury

mechanical trauma

thermal injury

burns

- first degree (erythema and swelling)
- second degree (blisters)
- third degree (dermis involved)
- total surface area of burn is important

cold injuries

- frostbite

electrical injury

radiation injury

- sunburn, increased neoplasms

Infectious diseases

- bacterial, fungal, viral
- insect infestations and bites
- acne

Idiopathic and immune diseases

- eczema
- seborrheic dermatitis
- psoriasis

Neoplasms

- Basal cell carcinoma
  - common malignant epithelial neoplasm, excellent prognosis
- Squamous cell carcinoma
  - common malignant epithelial neoplasm,good prognosis

Melanoma [Figs. 18-9]

- malignant neoplasm originating from melanocytes
- different types
  - lentigo maligna
  - superficial spreading
  - nodular
  - acral-lentiginous
- depth of invasion important prognostic factor
- clinical features worrisome for melanoma
  - A - asymmetry
  - B - border irregularity
  - C - color irregularity
  - D - diameter > 6 mm