4: Alterations of the Endocrine System

Learning Outcomes

Alterations of the Endocrine System

- Describe names, location and hormones secreted by endocrine glands and their function (review).
- Describe three ways target cells fail to respond to hormones, creating hormonal dysfunction.
- Compare the syndrome of inappropriate antidiuretic hormone secretion (SIADH) and diabetes insipidus in regards to: causative factors, pathophysiology, manifestations, treatment, and prognosis.
- Describe the causes and clinical manifestations of hyper- and hypopituitarism.
- Describe the manifestations and consequences of pituitary adenomas and prolactinomas.
- Describe the progression of hyperthyroidism through Graves disease and thyroid storm in relation to cellular changes, manifestations, treatments and complications.
- Describe the causes, and outcomes for disorders that produce hypothyroidism.
- Differentiate between primary and secondary hyperparathyroidism.
- Describe the similarities and differences in the onset, etiology and pathophysiology of type 1 and type 2 diabetes mellitus.
- Describe the acute and chronic complications of diabetes mellitus.
- Compare hypercortical function (Cushing disease and syndrome) and hypocortical function (Addison disease) including causative factors, pathophysiology, manifestations, treatment and prognosis.
- Describe common tumors of the adrenal medulla.

The Reproductive System

- Describe the normal structure and function of the reproductive system (review).
- Define alterations of sexual maturation.
- Describe types, manifestations of menstrual alterations.
- Describe pelvic relaxation disorders.
- Describe benign growths and proliferative conditions of reproductive tract.
- Discuss main features and impact of infertility.
- Describe selected disorders of the prostate gland.
- Describe briefly male and female sexual dysfunction.
- Describe briefly benign and malignant breast lesions.

Definitions: Alterations of the Endocrine System

Term	Definition
Hyperfunction	- Increased function of an endocrine gland
Hypofunction	- Decreased function of an endocrine gland
Primary endocrine disorders	- Endocrine defect in the primary gland
Secondary endocrine disorders	- Endocrine defect outside the primary gland
Hypopituitarism	- Pituitary hypofunction
Myxedema	- Untreated adult hypothyroidism
Cretinism	- Untreated congenital hypothyroidism
RAS	- Renin-Angiotensin-System
Juxta glomerular apparatus	- A specialized structure formed by distal convoluted tubule and the glomerular afferent arteriole, located near the vascular pole of the glomerulus - Secretes renin and erythropoietin
Conn's syndrome	- Adrenal glands secreting excess aldosterone
Cushing's syndrome	- Adrenal gland secreting excess steroids
Pheochromocytoma	- Tumour of adrenal medulla
Addison's disease	- Adrenal gland hypofunction

Endocrine System: Anatomy and Physiology Review

Endocrine glands

- **Hypothalamus**
  - Secretes releasing hormones (RH) which in turn stimulates hormone release from the anterior pituitary
  - Hormones secreted by the hypothalamus: GHRH, TRH, CTH, GnRH, Dopamine (PIH), MSH IH
    - Note: Dopamine and MSH IH are inhibiting hormones
- **Pituitary**
  - Anterior and posterior lobes

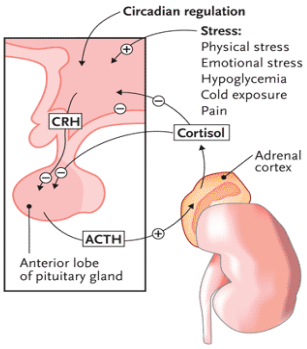

Figure 1: Hypothalamus and pituitary regulation of cortisol secretion in response to stress

- Anterior lobe secretes hormones in response to the releasing hormones from hypothalamus
    - **Anterior hormones**: GH, TSH, ACTH, FSH, LH, Prolactin, MSH
- Posterior lobe secretes hormones in direct response to neuronal signals from the hypothalamus. *No releasing hormone*
    - **Posterior pituitary hormones**: ADH, Oxytocin

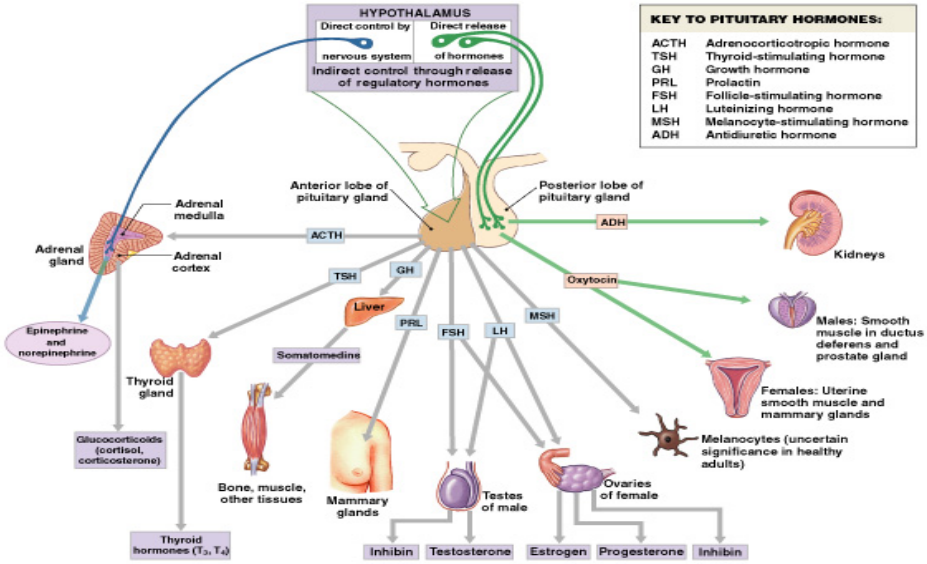

Figure 2: Hypothalamus and Pituitary Hormones, Targets, and Function

- **Thymus** = immune tolerance
- **Thyroid**
- **Adrenal gland**
- **Pancreas** = endocrine and exocrine
- **Gonads**
- *Note*: There are some endocrine cells in the kidney as part of the juxtaglomerular apparatus (JGA). These cells release renin and erythropoietin hormones
    - Renin stimulates mechanisms to regulate blood pressure
    - Erythropoietin stimulates red blood cell formation

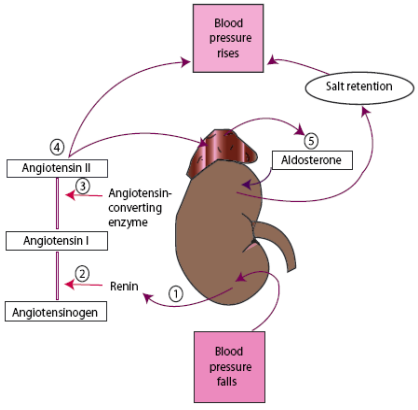

Figure 3: Renin-Angiotensin-Aldosterone-System (RAAS) of kidneys

Regulation of Calcium

- There are 3 hormones responsible for the regulation of calcium
  - **Parathyroid hormone**
    - Breaks down bone to increase blood calcium
  - **Calcitriol** (active Vit D = D_3 = 1,25 cholecalciferol)
    - Stimulated calcium absorption in intestine
  - **Calcitonin**
    - Inhibits bone resorption to decrease blood calcium

Helpful Hint

To remember the functions of Calcitriol and PTH, use the "R"s and think:

"calcit**R**iol and pa**R**athy**R**oid hormone **Raises** calcium levels

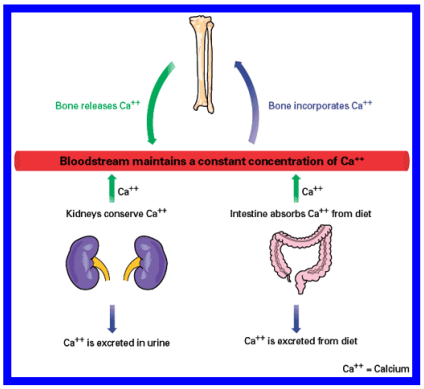

Figure 4: Mechanisms of Calcium Regulation

Urine Analysis

- Urine may contain small amounts of glucose, urobilirubin and protein
- Urine has NO bacteria, yeast, ketones, nitrates, leukocytes, bilirubin
- Urine may have crystals occasionally
- If hypovolemic, the osmolarity (amount of solutes per solvent) increases
  - This may be observed as more concentrated, darker urine
  - The person may also have decreased output relative to normal

Normal urine analysis

- Normal values are as follows:
- Color – Yellow (light/pale to dark/deep amber)
- Clarity/turbidity – Clear or cloudy
- pH – 4.5-8
- Specific gravity – 1.005-1.025
- Glucose - ≤130 mg/d
- Crystals – Occasionally
- Bacteria – None
- Yeast - None
- Casts – 0-5 hyaline casts/lpf
- Ketones – None
- Nitrates – Negative
- Leukocyte esterase – Negative
- Bilirubin – Negative
- Urobilirubin – Small amount (0.5-1 mg/dL)
- Blood - ≤3 RBCs
- Protein - ≤150 mg/d
- RBCs - ≤3RBCs/hpf
- WBCs - ≤2-5 WBCs/hpf
- Squamous epithelial cells - ≤15-20 squamous epithelial cells/hpf

Figure 5: Expected results for normal urine analysis

Volume status	Urine osmolality (mOsm/kg)	Urine sodium (mEq/L)	Etiology
Hypovolemic	↑	≤20	Nonrenal sodium loss
		>20	Renal sodium loss
Hypervolemic	↑	≤20	Edematous states
		>20	Kidney failure
Euvolemic	↑	>20	SIADH
	Intermediate		Potomania
	↓		Primary polydipsia
	Variable		Excess fluid intake

↑= >300; **intermediate:** 150-300; ↓: ≤100-150

Figure 6: Volume status, urine osmolality and sodium

Etiology of endocrine disorders

Primary:

- Pathologies within endocrine organs
- Congenital, inflammatory, metabolic, immune, malignancy (tumor)

Secondary:

- Pathologies outside the primary endocrine organs (in the controlling gland)
- Secondary pathologies can stem from the following mechanisms:
    - Hypothalamus or pituitary gland (these are the controlling glands)
    - Target cell/tissue
        - Non-responsive (receptor associated issues)
            - Low number of receptors
            - Impaired receptor function
            - Antibodies against receptors

Endocrine Disorders -Basics

Types

- *Hyperfunction*: elevated hormone levels
- *Hypofunction*: decreased hormone levels

Etiology/malfunction

- Reduced or excess synthesis
- Failure of feedback mechanisms
- Excessive degradation
- Inactivation or hyperstimulation by antibodies
- Ectopic hormone secretion

Alterations of the Hypothalamic-Pituitary axis

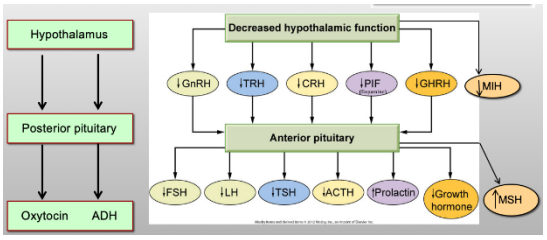

Figure 7: Hypopituitary-axis and hormonal regulation

- Note: RH = releasing hormone; IH/IF = inhibiting hormone
- Dopamine (referred to in *Figure 7* as PIH [prolactin inhibiting hormone]) and MIH (melanocyte inhibiting hormone) act to decrease hormone production opposite to releasing hormones
    - Therefore, decreased production of inhibiting hormone would increase hormone production/release from the pituitary
    - *Example: Dopamine as an Inhibiting Hormone*
        - Decreased production of dopamine (PIH) leads to increased prolactin levels

Hypopituitarism

- Decreased function of the pituitary
- Can be from inadequate levels of hypothalamic hormones
- Defects in pituitary gland itself

Causes

- Invasive, space occupying lesion (**Tumor or aneurysm**)
- Infections: (TB, syphilis, meningitis)
    - TB encephalitis is rare, but it can occur to the pituitary
- Trauma (severe head trauma)
- Autoimmune disease
    - Leads to destruction of the gland
- Sheehan syndrome (postpartum pituitary infarction that leads to necrosis)
    - Postpartum bleeding leads to ischemia and can lead to subsequent ischemic damage to the pituitary

Pathophysiology

- Inflammation, ischemic necrosis, infarction, fibrosis
- Edema and swelling of the pituitary within the sella turcica further impede blood supply to the gland causing further shrinkage and fibrosis

Clinical manifestations

- Could see symptoms related to specific hormone deficiency (e.g. FSH, LH, ACTH)

Diagnosis

- Diagnosis is often challenging
- Triple bolus test = insulin + TRH + GnRH and then assess. You should see hypoglycemia, elevated TSH and elevated FSH and LH. If you don't see this = pituitary issue
- CT scan can view the gland for trauma or tumor
- Laboratory results need to be interpreted in conjunction with/or in light of clinical manifestations

Prolactinoma (hyperpituitarism)

- The most common pituitary tumor
- Benign, hyperfunctioning, slow-growing pituitary adenoma

Pathophysiology:

- Mass secreting prolactin
- Sustained elevation of serum prolactin
- Compression effects from tumor mass (e.g. visual disturbances)

Clinical manifestations

- Compression effects: optic chiasm; visual impairment, headache
- *Functional effects*:
    - Female: amenorrhea, galactorrhea, hirsutism, infertility, osteopenia
    - Male: gynecomastia, erectile dysfunction

Treatment

Medication: Dopamine agonists

- Since the tumor secretes prolactin, dopamine (which has the same chemical structure as PIH) can be used to decrease and maintain prolactin levels PIH is the same as dopamine in structure
- Dopamine drugs can be used to inhibit synthesis of prolactin in remaining tumor mass following surgery

Surgical approach: removal of the tumor

Diabetes Insipidus (DI)

- The inability to retain water leading to excessive diuresis evidence by urination

Central (Neurogenic) DI

- No ADH secretion
- Excessive diuresis due to failed ADH synthesis/release

- Potential causes include:
    - Idiopathic, head trauma, tumors, vascular, autoimmune, infection, drugs and surgery

Nephrogenic DI

- Renal resistance to ADH
    - ADH is made, but is not working in the kidney
- May be related to disease or drugs

Pathophysiology:

- Failure of ADH action on the distal convoluted tubule (DCT) and collecting ducts
- Inability to concentrate urine

Clinical manifestations

- Polyuria, polydipsia, Nocturia
- Inappropriate diluted urine
- Urine osmolarity is less than serum osmolarity (pee is has less solutes than blood)

Diagnostic Tests:

- Water deprivation test
    - Patient is not given water
    - The ADH level should increase with a decrease the frequency and amount of urination
- DDAVP (synthetic ADH) test
    - Patient gets synthetic ADH
    - If there is no change in urine concentration, then it confirms a nephrogenic DI

Syndrome of Inappropriate ADH secretion (SIADH)

- Water retention due to ADH hypersecretion
    - Decreased urine output and/or concentrated urine

Etiology:

- Ectopic (paraneoplastic syndrome; GI, bladder, prostate)
    - Usually a tumor somewhere that is secreting ADH
- CNS disorders: stroke, infection, tumors

Pathophysiology

- Enhance renal water retention
- Dilutional hyponatremia, plasma hypo-osmolarity

- Concentrated urine

Clinical manifestations

- Patient will present with symptoms of hyponatremia. E.g. Confusion, delirium, muscle weakness, seizures, coma

Disorders of the Thyroid and Parathyroid

Thyroid Hormone Review

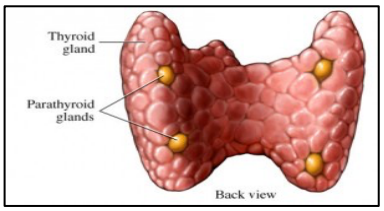

Figure 8: Anatomy of the thyroid gland

- Iodide (I-) uptake
- Iodination of tyrosine
- Synthesis of thyroid hormones (thyroid peroxidase)
- Thyroid hormones produced:
  - Tetraiodothyronine (thyroxine)(T4)
  - Triiodothyronine (T3): from T4
- Thyroglobulin
  - Carrier molecule for thyroid hormones
  - Without this molecule synthesized hormones cannot exit the follicle

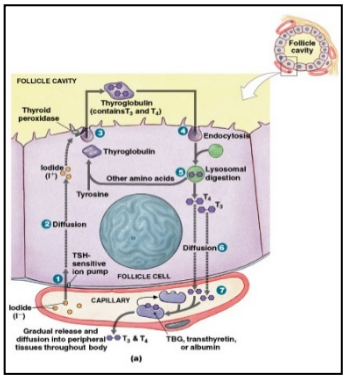

Figure 9: Production and release of thyroid hormones with a follicle

Hyperthyroid

Primary:

- Graves disease
- Multinodular goitre
- Solitary hyperfunctioning (toxic) nodule
- Thyroid cancer

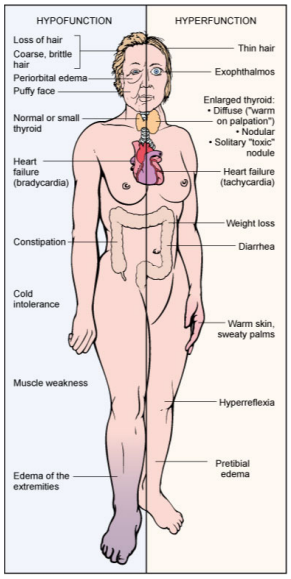

Figure 10: Comparison of hyperfunction and hypofunction of the thyroid gland

Secondary (less common)

- TSH secreting pituitary adenoma
- Ectopic secretion (paraneoplastic syndrome)

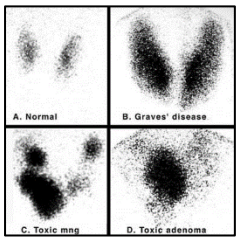

Figure 11: Radioactivity in Graves' versus other multimodule goitre and thyroid cancer (adenoma)

Pathophysiology

- **Graves**: Type II hypersensitivity; autoantibodies against TSH receptor known as TSI (thyroid stimulating Ig)
- Elevated TH → hypermetabolic state (insomnia, infertility, hair loss, irritability, lose weight)

Clinical manifestations

- Manifestations of hypermetabolic state
- Enlargements of thyroid gland (goitre)
- **Ophthalmopathy** (big eyes)
- **Dermopathy** (pretibial myxedema)
    - Due to Ig reacting with TSH receptors in connective tissue
    - Seen in Graves

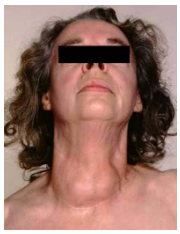

Figure 12: Goitre typically seen in Grave's disease

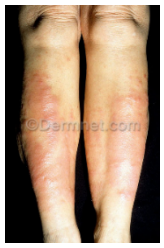

Figure 13: Example of pretibial myxedema

- *Thyrotoxic crisis* (storm):
    - Acute severe elevation of TSH →
        - Severe tachycardia, hyperthermia, CHF
        - Diarrhea
        - Agitation, alteration in mental status
    - **Precipitating factors**
        - Infection
        - Trauma
        - Pre-eclampsia

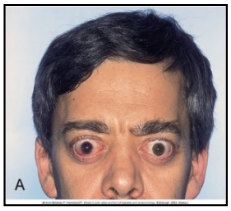

Figure 14: Example of exopthalmos

Hypothyroidism

More common than hyperthyroidism

Primary

- Congenital
- Autoimmune thyroiditis (**Hashimoto's thyroiditis**)
    - **Most common cause for hypothyroidism**
    - Slow destruction and inflammation of thyroid tissues by autoreactive T cells and peroxidase antibodies in blood

- Iatrogenic loss of thyroid tissue (surgery, radiation, medication)
- Viral thyroiditis (late phase)
- Iodine deficiency

Secondary

- Pituitary failure of TSH release due to: tumor, trauma, infarction, hemorrhage

Clinical manifestations

- Manifestations of hypometabolic state
    - Sluggish, slow, cold intolerance
- *Myxedema* in adults and *cretinism* in infants
    - Cretinism = congenital hypothyroidism
        - No thyroid or little thyroid tissue.
        - The child will be cognitively be disabled without T
        - The child can survive on maternal T4 for approximately 3-4 months before requiring levothyroxine
        - If there is no early screening, the condition may remain unknown as signs may not manifest until 4 months old.
        - Signs and symptoms include:
            - Protruding tongue
            - Hoarse cry
            - Hypotonic muscles
            - Abdominal protrusion
        - Eventually the child will be dwarf, have slow milestones
            - Eg dentition, cognitive delay
- *Myxedema coma*: Acute, severe hypofunction of the thyroid gland

Alterations of Parathyroid Gland

- The parathyroid gland is responsible for the regulation of calcium (see *Figure 4*)

Hyperparathyroidism

- Primary hyperparathyroidism
    - Excess PTH secretion due to disease in one or more parathyroid glands. Makes too much.
- Secondary hyperparathyroidism
    - Chronic hypocalcemia E.g. Renal disease. stimulates calcium release

Clinical manifestations

- Hypercalcemia
- Hypercalciuria; renal stones (calcification)
- Hypophosphatemia (opposite of calcium)

Hypoparathyroidism

- Abnormally low PTH levels
    - Most common reason is iatrogenic: surgical removal of thyroid (parathyroid is also removed as it is anatomically right at posterior aspect of the thyroid gland)

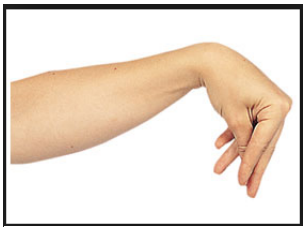

Figure 15: Tetany in the hand

Manifestations:

- Hypocalcemia E.g. Tetany
- Hyperphosphatemia

Pancreatic Dysfunction

Anatomical definitions relating to the pancreas: Head, body, tail, duct

Ampulla of Vater = pancreatic duct opens into duodenum

Exocrine = acini; secreting digestove enzymes

Islets of Langerhans: endocrine cells that secreting glucagon (alpha cells) and insulin (beta cells)

Diabetes Mellitus (DM)

- Multisystem disease characterized by a group of insulin related metabolic alterations
- The state of DM in Canada
    - Today ¼ Canadians have DM or are Pre-DM
    - By 2020, it will be 1/3 people
    - In 2015, diabetes cost 15 billion in health care fees

DM – Types and Causes

Primary

- **Type 1 DM**
    - Insulin deficiency: destruction of beta cells of islets of Langerhans
    - Referred to as “insulin dependent DM”
- **Type 2 DM**
    - Begins with insulin resistance (cells fail to respond to insulin). With disease progresses a lack of insulin develop

- Referred to as “non insulin dependent DM”

Secondary DM

- Pancreatic causes
- Endocrine causes E.g. Cushing’s
- Drugs: steroids, thiazide diuretics

Gestational

- High blood glucose level during pregnancy
- 2-10% of pregnancies

Manifestation

- Hyperglycemia
- Polydipsia
- Polyuria
- Polyphagia
- Weight loss
- Fatigue
- Obesity, dyslipidemia (type 2)
- Symptoms of complications
- Retinopathy

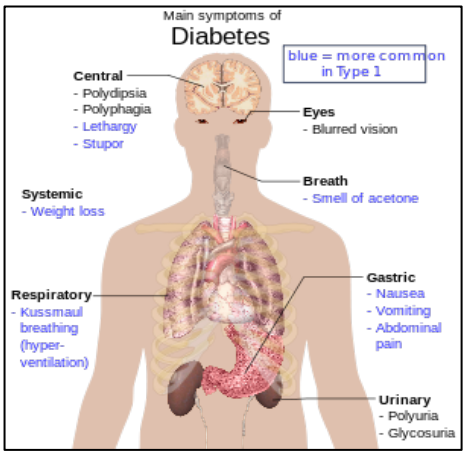

Figure 16: Most common, featured symptoms of Diabetes mellitus

Figure 17: Table-Complications of Diabetes Mellitus	
Acute	**Chronic**
▪ Hypoglycemia - More common in Type I	▪ Hyperglycemia and non-enzymatic glycosylation
▪ Hyperglycemia - Diabetic ketoacidosis (Type I)	▪ Microangiopathy - Retinopathy - Nephropathy - Neuropathy

- Hyperosmolar hyperglycemic nonketotic syndrome (HHNKS) (Type II)	
	▪ Macroangiopathy - Coronary artery disease (CAD) - Cardiovascular accident (CVA; Stroke) - Peripheral artery disease (PAD)
	▪ Repeated infections
	▪ Skin complications

Hypoglycemia

Causes:

- Over dose of medications
- Missing meals
- Poor blood glucose monitoring

Manifestations

- Pallor, tremor, tachycardia, palpitation, headache, dizziness, irritability, poor judgement, confusion, fatigue, hunger, visual disturbances, seizures, coma
- * Brain cannot have low glucose for 6-7 minutes

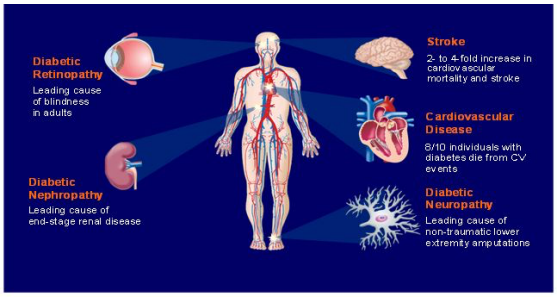

Figure 18: Complications of Diabetes mellitus (angiopathies)

Complications of Diabetes Mellitus: DKA and HHNK

Diabetic Ketoacidosis

- Emergency life-threatening complication
- Seen with type 1 DM and could be first symptom of undiagnosed DM

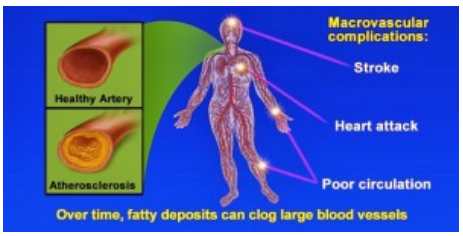

Figure 19: Macrovascular complications of Diabetes mellitus

Pathophysiology

- Insulin deficiency (facilitated by other anti-insulin hormones)
- Lipolysis leads to the formation of ketone bodies
    - Results in ketonemia and ketonuria (ketones in the blood and urine)
    - Osmotic diuresis
- Acidosis
- Hyperkalemia
    - Shift of potassium from ICF to ECF
    - Hydrogen exchanges to try to reduce the acidosis leaving excess potassium
    - A common issue with Insulin treatment (electrolytes monitoring is a must during DKA treatment)

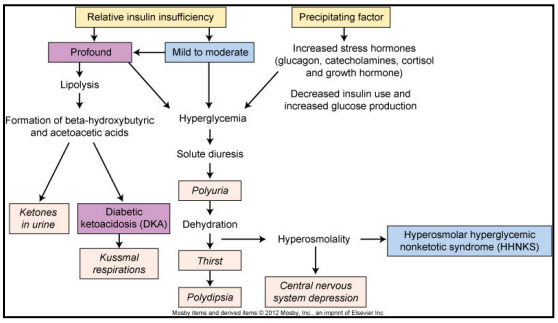

Figure 20: Pathophysiology of DKA and HHNK

Clinical manifestations

- Kussmaul's respiration (rapid, deep)
- Acetone smell (from the production of ketones)
- Dehydration
- Abdominal pain, vomiting
- Impaired consciousness
    - May lead to coma and death
- Ketones present in blood and urine
    - The main ketone acids are acetoacetate and hydroxybutyrate

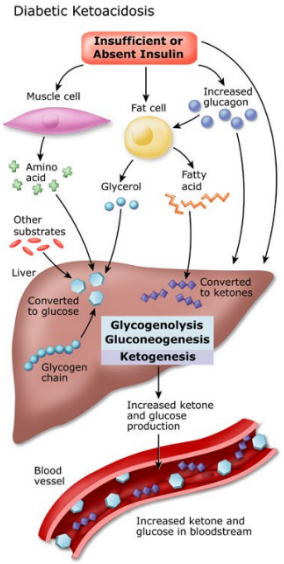

Figure 21: Pathophysiology of diabetic ketoacidosis

Hyperosmolar hyperglycemic nonketoic syndrome (HHNK)

- Hyperglycemic crisis characterized by hyperosmolarity and dehydration without ketosis
- In type 2, usually precipitated by infection/acute illness

Pathogenesis:

- Very high blood glucose: (usually >600mg/dl (30mmol/L
- Increase in blood osmolarity (>320 mOsm)
- Osmotic diuresis
- No ketosis (some insulin inhibits fat tissue breakdown)

Clinical manifestations

- Older non-compliant patient

- Dehydration and thirst
- Impaired consciousness

Disorders of the adrenal cortex

Hyperfunction:

- *Hyperaldosteronism*: excess aldosterone
  - Primary = Conn's disease
  - Secondary = RAS hyperactivity
- ***Cushing** syndrome*: Excess cortisol
- *Adrenal hyperplasia*: excess sex hormones

Hypofunction:

- *Addison's disease*

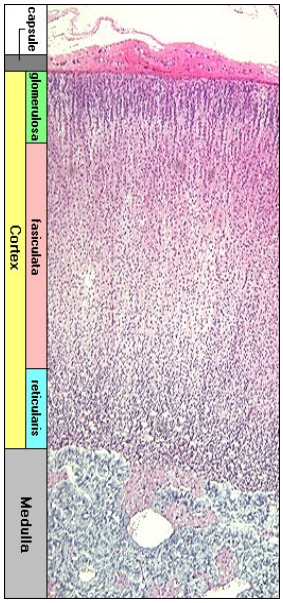

Figure 22: Cellular layers of the adrenal gland

Disorders of the Adrenal medulla

- Hyperfunction
  - Tumors of chromaffin cells (**pheochromocytoma**)
  - Secrete catecholamines (continuous or episodic)

Conn's Disease

- Increased aldosterone secretion in the absence of activation of the renin-angiotensin-aldosterone-system (RAS)

Causes:

- Adrenal hyperplasia
- Tumors: adenoma, carcinoma

Pathophysiology

- Salt and water retention
- Hypertension
- Hypokalemia
- Alkalosis
  - Hydrogen is excreted with potassium

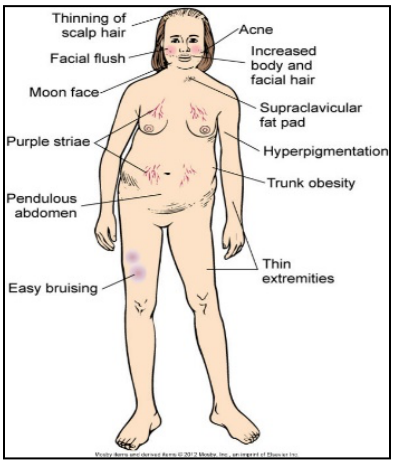

Figure 23: Manifestations of Cushing's syndrome

Cushing's syndrome

- Increased cortisol secretion

Causes:

- Iatrogenic (most common)

    - Long-term steroid and/or ACTH therapy
- Adrenal adenoma or carcinoma
- Cushing's disease
    - Increased pituitary ACTH
- Ectopic ACTH secretion (parneoplastic syndrome)

Manifestations

- Obesity
    - Notably in the face ('moon face') and upper back (buffalo hump)
    - Truncal obesity (most commonly from steroid therapy)
- Infection:
    - Excess steroids impair the function of WBCs and therefore have anti-inflammatory/ anti-immune effects
    - On the long-term the depressed immune system lead to increased susceptibility to infection
    - Important to educate on steroid therapy; caution and monitoring if long term
- Hypertension
- Peripheral edema (from hypervolemia)
- Hyperglycemia; secondary DM on the long term
- Osteoporosis
- Recurrent infections
- Psychosis
- Thin and atrophic skin with bruises

Addison's Disease

- Destruction of all zones of adrenal cortex
    - Includes glucocorticoids, mineralocorticoids, androgens

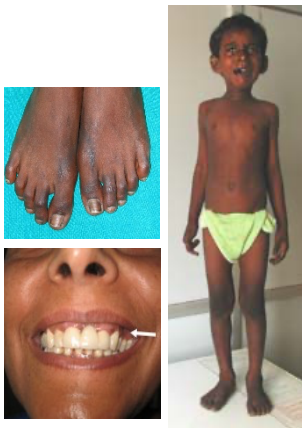

Figure 24: Hyperpigmentation of skin and mucous membranes seen in Addison's disease

Causes

- **Primary (adrenal gland disorder)**
    - Usually autoimmune-mediated destruction of the adrenal glands (represents 80% of cases)
    - Chronic infection, such as Tuberculosis (TB adrenalitis) (approximately 20% of cases)
- **Secondary (pituitary gland disorder)**
    - Low ACTH secretion
    - Sudden withdrawal of prolonged steroid therapy
    - Destruction of the pituitary gland (e.g. from trauma or a tumor)

Manifestations

- Fatigue and muscle weakness
- Hypotension
- Anorexia
- Nausea and vomiting
- Abdominal pain
- Weight loss
- Hyperpigmentation
    - High ACTH can bind to melanocyte in dermal areas which darkens skin
- Mental depression
- Acute severe conditions (Addisonian Crisis)
    - Sudden drop in BP from hypovolemia (shock). Can occur from sudden withdrawal in steroid therapy
    - Can be fatal

Pheochromocytoma

- Chromaffin cell tumors
- Neuroendocrine tumor of adrenal medulla secretes catecholamines leading to overstimulation of the SNS.

Clinical manifestations

- Hypertension

    - Severe ± paroxysmal
    - Resistant to treatment
- Headache
- Palpitations and tachycardia
- Sweating
- Anxiety and tremors
- Hyperglycemia

Complications:

    - Pheo crisis: in response to anesthesia, stress, drugs
    - Cardiomyopathy

Lab features

- 24-hour urinary catecholamines and metanephrines (most specific)
- **Urine vanillylmandelic acid (VMA)**
    - **Tumor marker for pheochromocytoma**
- Plasma metanephrine

4: Alterations of the Reproductive system

Selected Disorders of the Female Reproductive System

- Hormonal and menstrual alterations
    - Amenorrhea (cessation of menstruation)
    - Anovulation (failure of mid cycle ovulation)
    - Dysmenorrhea and Premenstrual tension syndrome (painful menstruation)
    - Dysfunctional uterine bleeding (uterine bleeding of undetermined cause)
- *Polycystic ovarian syndrome*
- Alterations of sexual maturation
    - Delayed puberty
    - Precocious puberty
- Sexual dysfunction
    - Disorders of sexual desire (decreased or increased)
    - Anorgasmia (orgasmic dysfunction)
    - Dyspareunia (painful intercourse)

- Disorders of fertility
- Pelvic relaxation disorders
    - Cystocele (bladder hernia), rectocele (rectum protrusion/drop), urethrocele (prolapse of the female urethra)
    - Vaginal prolapse
    - Uterine prolapse
- Growths and proliferative conditions
    - *Endometriosis*
    - Benign ovarian cysts
    - Endometrial polyps
    - Leiomyomas
    - Cancers: cervical cancer, vaginal cancer, endometrial, vulvar cancer, ovarian

Selected Disorders of the Male Reproductive System

- Disorders of the urethra
    - Urethritis
    - Urethral strictures
- Disorders of the penis
    - Congenital anomalies
    - Penile cancer
    - Balanitis (Inflammation of the head of the penis)
- Disorders of the scrotum and testes
    - Varicocele (varicose veins in the scrotum; rarely painful but can → infertility)
    - Hydrocele (fluid in the scrotum; a painless swelling of one or both testicles)
    - Spermatocele (painless fluid filled cyst in the epididymis)
    - Testicular torsion (Twisting of the spermatic cord → severe testicular pain)
    - Epididymitis (inflammation of epididymis → severe testicular pain)
- Disorders of fertility
- Disorders of the prostate
    - Benign prostatic hyperplasia
    - Prostate cancer
    - Prostatitis

- Erectile dysfunction
- Disorders of the breast
    - Gynecomastia
    - Breast cancer

Endometriosis

- A major cause of chronic pelvic pain in females
- Significant social and psychological impact
- Ectopic endometrial cells
    - Endometrium grows outside the uterus

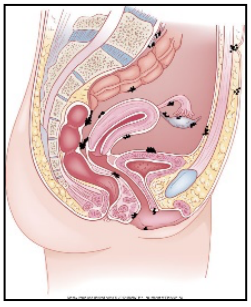

Figure 25: Sites of ectopic endometrial cells

Cause and Pathophysiology

- Currently cause is unknown
    - May have genetic influences
    - Multifactorial
- Most accepted theory: "retrograde menstruation"
    - Menstrual fluids move through the fallopian tubes and into the pelvic cavity; ectopic tissue settles in the peritoneum.
- Ectopic tissue is influenced by hormonal changes like cells found inside the uterus

Clinical manifestations:

- Pelvic pain
- Infertility

Polycystic Ovary Syndrome (PCOS)

- Hypothalamic pituitary disease resulting in enlarged polycystic ovaries and chronic anovulation
- Common in young women

Pathophysiology:

- Impaired ovarian follicle development leading to increased androgen production
- High GnRh pulses leads to increased pituitary LH and ovarian androgen synthesis
- Increased androgen conversion to estrogen in adipose tissue
- **Insulin resistance**
    - Insulin stimulates ovarian follicle to secrete more androgens

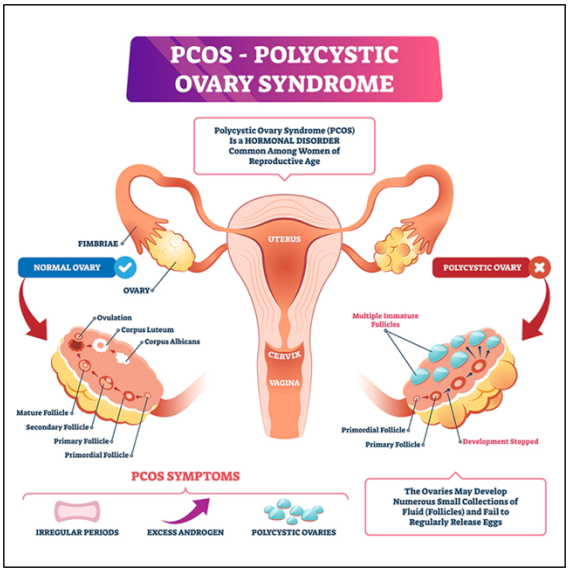

Figure 26: PCOS comparison of follicle growth

- **Ovaries have 12 or more cysts**
    - Cysts may form ovarian follicles which then secretes androgens
    - Androgens are converted into estrogens in adipose tissue

Clinical manifestation:

- Weight gain and obesity
- Oligomenorrhea, Amenorrhoea, hirsutism, acne
    - Features of increased androgen production
- No ovulation leads to infertility
- Insulin resistance
    - Increased risk for DM in the future when combined with obesity

Diagnosis

- Two of the following are required for the diagnosis of PCOS
    - Few or no ovulatory cycles
    - Elevated androgen levels
    - Polycystic ovaries (do not have to be present, and their presence does not constitute PCOS)

Benign Prostatic Hyperplasia → increased 5AR

- Prostatic enlargement due to:
    - Hyperplasia (more common)
    - Hypertrophy

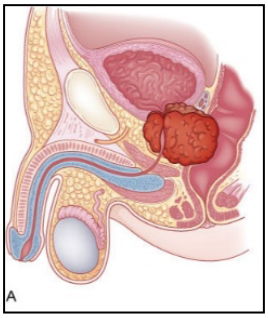

Figure 27: Anatomy of benign prostatic hyperplasia

Pathophysiology

- Person is usually >50 years-old
- Normal growth/function of prostate depends on reduction of testosterone to Dihydrotestosterone (DHT) by 5-alpha reductase enzyme (5AR).
    - 5-AR converts testosterone from the testicles into DHT
    - Elevated 5-AR causes over growth of prostate.
- Prostatic over growth leads to ureteral compression and bladder outflow obstruction

Clinical manifestations

- Of bladder outflow obstruction: Urinary retention, dribbling, hesitancy