



Endocrine Disorders

Bio 375

Pathophysiology



Endocrine Disorders

- Two categories of endocrine disorders
 - Excessive production of hormone
 - Deficient production of hormone
- Manifestations of hormonal disorders reflect the actions of the hormone
 - May alter appearance of the individual
 - Disorder beginning in children
 - Disorder beginning in adult
 - May alter metabolism of the individual



Endocrine Disorders

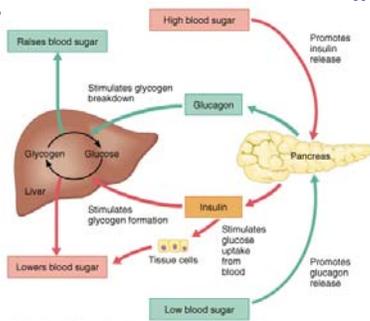
- Most common cause of endocrine disorders is benign tumor or **adenoma**
 - Adenoma may be secretory producing excess hormone
 - Adenoma may be destruction causing a hormonal deficit
- Target cells may be resistant or insensitive to the hormone creating the effect of a deficit (e.g. Type II Diabetes mellitus)



- Other causes of hormonal problems:
 - Congenital defects in the glands
 - Hyperplasia of the glands
 - Infection of the glands
 - Abnormal immune reactions
 - Vascular problems
 - Ectopic sources of hormones, e.g bronchogenic (lung) cancer produces PTH or ACTH



Negative Feedback Mechanism with Glucose and Insulin and Glucagon





Insulin and Diabetes Mellitus

- Common chronic disorder
- Major factor predisposing to:
 - Strokes (CVA)
 - Heart attacks (MI)
 - Peripheral vascular disease
 - Amputation
 - Kidney failure
 - Blindness



Diabetes Mellitus caused by:

- Relative deficit of insulin secretion from the beta cells in the islets of Langerhans, or
- Lack of response by the cells to insulin (insulin resistance)
- Term **insulin deficit** used to cover both



Insulin

- Insulin is an **anabolic** hormone
 - Insulin deficit results in abnormal carbohydrate, protein, and fat metabolism
 - Insulin deficit results in decreased synthesis of protein and glycogen
 - In turn, this affects lipid metabolism
 - Many tissues in the body are adversely affected by diabetes



- Some cell types are not affected directly by loss of insulin
 - Brain cells take up glucose without insulin
 - Intestinal cells absorb glucose without insulin
 - Exercising skeletal muscle cells can use large amounts glucose without proportionate amounts of insulin
 - As a result, exercise is helpful in controlling blood glucose levels in the presence of insulin deficit



Types of Diabetes Mellitus

- Two major types:
 - Type I (Insulin-dependent diabetes mellitus) (IDDM) formerly called juvenile onset diabetes
 - Type II (Non-insulin-dependent diabetes mellitus) (NIDDM) formerly called mature onset diabetes
 - Gestational diabetes may develop during pregnancy and disappear following delivery



Type I Diabetes Mellitus

- About 10% of cases of Diabetes Mellitus
- Peak age of onset: 11-13 yr
- Acute onset
- Autoimmune: genetic and environmental factors result in gradual destruction of beta cells in pancreas
- Individuals tend to be normal to thin
- Severe insulin deficiency or no insulin
- Requires insulin replacement
- Amount of insulin needed dependent on dietary intake of glucose and metabolic activity



Table 20-6 Clinical Manifestations and Rationale for Type 1 Diabetes Mellitus	
Manifestations	Rationale
Polydipsia	Because of elevated blood sugar levels, water is osmotically attracted from body cells, resulting in intracellular dehydration and stimulation of thirst in the hypothalamus
Polyuria	Hyperglycemia acts as an osmotic diuretic; the amount of glucose filtered by the glomeruli of the kidneys exceeds that which can be reabsorbed by the renal tubules; glycosuria results, accompanied by large amounts of water lost in the urine
Polyphagia	Depletion of cellular stores of carbohydrates, fats, and protein results in cellular starvation and a corresponding increase in hunger
Weight loss	Weight loss occurs because of fluid loss in osmotic diuresis and the loss of body tissue as fats and proteins are used for energy due to the effects of insulin deficiency
Fatigue	Metabolic changes result in poor use of food products, contributing to lethargy and fatigue; sleep loss from severe nocturia also contributes to fatigue

Table 20-7 Clinical Manifestations and Rationale for Type 2 Diabetes Mellitus

Manifestations	Rationale
Recurrent infections (e.g., boils and carbuncles; skin infections) and prolonged wound healing	Growth of microorganisms is stimulated by increased glucose levels; impaired blood supply hinders healing
Genital pruritus	Hyperglycemia and glycosuria favor fungal growth; candidal infections, resulting in pruritus, are a common presenting symptom in women
Visual changes	Blurred vision occurs as water balance in the eye fluctuates because of elevated blood glucose levels; diabetic retinopathy is another cause of visual loss
Paresthesias	Paresthesias are common manifestations of diabetic neuropathies
Fatigue	Metabolic changes result in poor use of food products, contributing to lethargy and fatigue



NEUROPATHIC ULCER

Symptomatic Results of Insulin Deficit (Diabetes mellitus)

Organs/tissue involved	Organ/tissue responses to insulin deficiency	Resulting condition of:		Signs and symptoms
		Blood	Urine	
  	Decreased glucose uptake and utilization	Hyperglycemia	Glycosuria	Polyuria - dehydration - soft eyeballs Polydipsia Fatigue Weight loss Polyphagia
	Glycogenolysis		Osmotic diuresis	
	Protein catabolism and gluconeogenesis			
  	Lipolysis and ketogenesis	Lipidemia and ketoacidosis	Ketonuria Loss of Na ⁺ , K ⁺ electrolyte and acid base imbalances	Acetone breath Hyperventilation Nausea/vomiting/ abdominal pain Cardiac irregularities Central nervous system depression; coma

 = Muscle
  = Adipose tissue
  = Liver

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Exercise and Diabetes mellitus

- While exercise can be useful in controlling glucose levels in diabetes, excessive and prolonged exercise can precipitously deplete glucose levels resulting in hypoglycemia or hypoglycemic shock (insulin shock)
- Excessive insulin can also cause hypoglycemic shock
- Insulin shock can result in coma or death

Table 25-4

Vascular Problems with Diabetes

Macroangiopathy

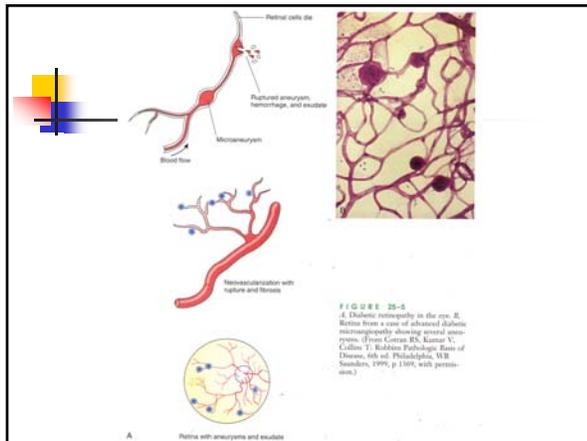
- Myocardial infarction (heart attack)
- Cerebrovascular accident (stroke)
- Peripheral vascular disease (ischemia, gangrene, and amputation affecting the legs)

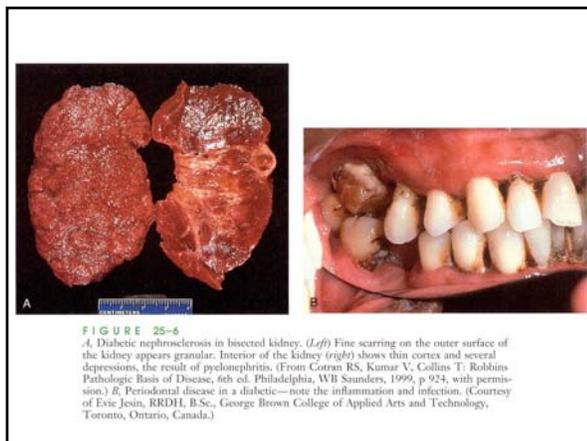
Atherosclerosis in large arteries related to hyperlipidemia, hypertension, and degenerative changes in the intimal layer of the arterial wall

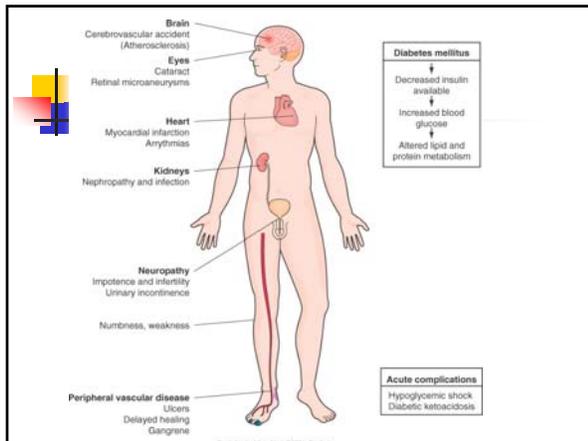
Microangiopathy

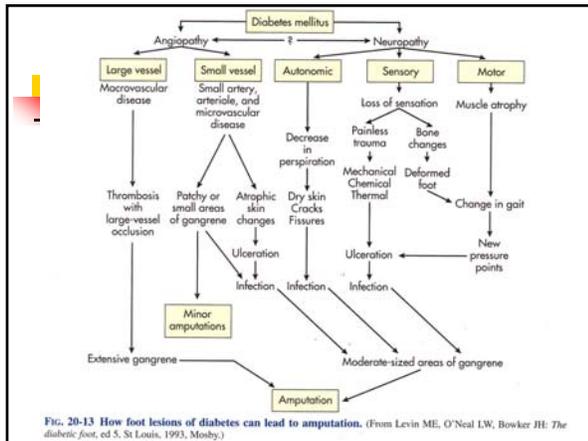
- Kidneys
Diabetic nephropathy
Chronic renal failure
- Eyes
Retinopathy
- Nervous system
Neuropathy in the central nervous system and peripheral nerves
Decreased function of sensory, motor, and autonomic nervous system fibers

Thickening of the capillary basement membrane, leading to occlusion or rupture
Microaneurysms, neovascularization, and fibrosis
Leads to blindness
Note—In addition to ischemia, there is also a metabolic abnormality that causes degeneration of myelin and deficit of myo-inositol, essential in the conduction of nerve impulses.



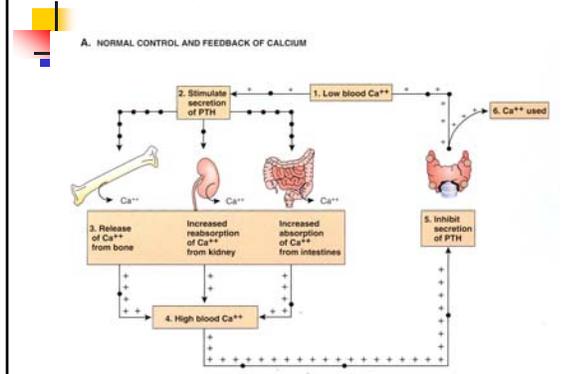






■ Questions 4-5

Parathyroid Hormone Control



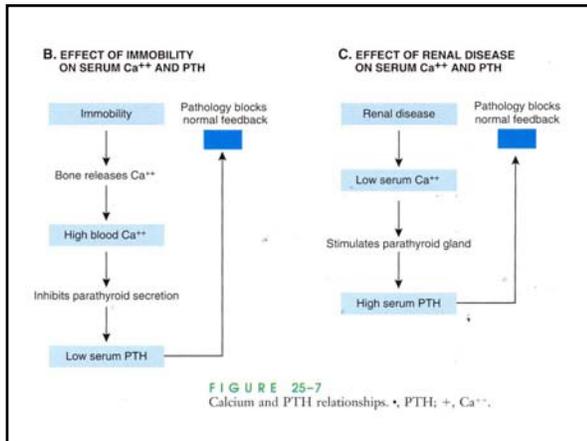
Parathyroid Hormone

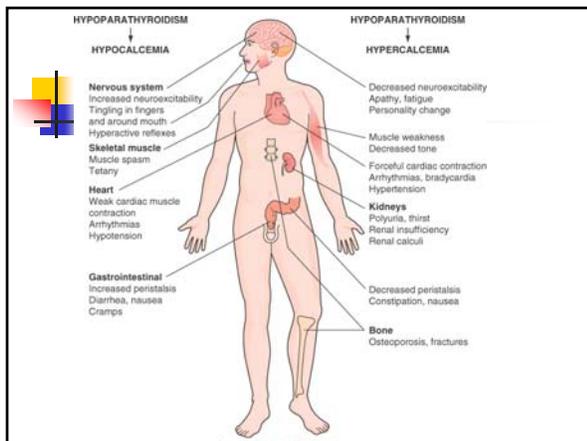
- Hypoparathyroidism leads to hypocalcemia or low serum calcium levels
- Hypocalcemia affects nerve and muscle function in several ways
 - Weak cardiac muscle contractions
 - Increase in the excitability of nerves leading to spontaneous contraction (tetany) of skeletal muscle

- Hyperparathyroidism causes hypercalcemia or high serum calcium levels
- Hypercalcemia leads to forceful cardiac contractions
- Increased PTH concentrations cause demineralization of osseus tissue leading to osteoporosis
- It also predisposes to kidney stones



- Immobility may lead to hypercalcemia along with low PTH
- Severe kidney disease results in hyperphosphatemia, hypocalcemia and high serum PTH







Pituitary Hormones

- Benign adenomas are the most common cause of pituitary disorders
 - About 10% of intracranial tumors
 - Occur primarily in persons aged 30-50
- Two types of signs in patient
 - Effect of the mass as it causes increased intracranial pressure
 - Effect of tumor on hormonal secretions



Growth Hormone

- Dwarfism or short stature
 - Deficit of GH or GH-RH
 - Adenoma may affect more than one cell type causing multiple deficits
 - Pituitary dwarfs usually have:
 - Normal intelligence
 - Normal body proportions
 - Some delay in skeletal maturation and puberty



- Gigantism or tall stature
- Excess of GH prior to puberty
- Acromegaly refers to the effects of excess of GH in the adult, usually by an adenoma
 - Bones become broader and heavier, skull thickens, jaw enlarges and facial features coarsen
 - Soft tissues grow, resulting in enlarged hands and feet, tongue protrudes



Pituitary Dwarf

Gigantism



Acromegaly

FIGURE 13B
Oversecretion of growth hormone in adulthood causes acromegaly. Note the changes in this woman's facial features at ages (a) 9, (b) 16, (c) 33, and (d) 52.

Antidiuretic Hormone

- Diabetes insipidus
 - May be caused by deficit of ADH
 - Sometimes results from renal tubules that do not respond to ADH
- Manifestations
 - Polyuria (no glucose)
 - Thirst
 - Severe dehydration

Inappropriate ADH Syndrome

- Also called Syndrome of Inappropriate ADH (SIADH)
- Due to excess ADH
- Complication of closed head trauma
- Sometimes excess secreted by ectopic source, e.g bronchogenic carcinoma
- Manifestations:
 - Severe hyponatremia
 - Mental confusion
 - irritability

- Questions 6-8

Thyroid Secretion Control

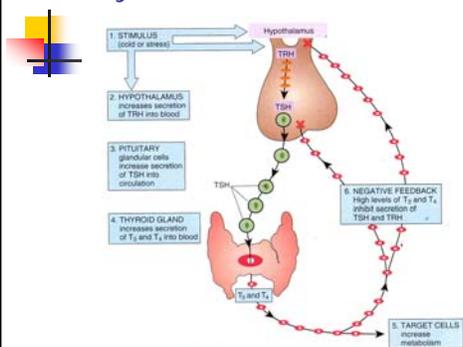
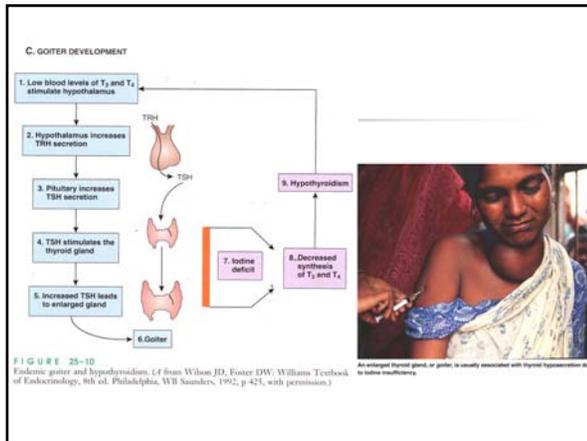


FIGURE 25-9 Hypothalamic-pituitary-thyroid gland feedback mechanism with thyroid hormone.

Goiter

- Goiter refers to an enlargement of the thyroid gland
 - May be caused by hyper- or hypothyroid conditions
 - Can be large and can interfere with swallowing, breathing and be of cosmetic concern
- Endemic goiter due to dietary deficiency of I₂
- Goitrogens inhibit T₃ and T₄ and elevate TSH causing goiter formation
- Toxic goiter



Hyperthyroidism (Graves Disease)

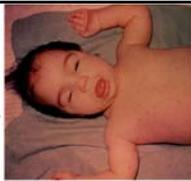
- Occurs more frequently in women over age 30
- Autoimmune disease
- Hypermetabolism
- Toxic goiter
- Exophthalmos
- Increased sympathetic activity magnifies metabolic effects



FIG. 20-7 Thyrotoxicosis (Graves disease). Note large and protruding eyeballs in association with a large goiter. (Siegel et al: *Mosby's guide to physical examination*, ed 4, St Louis, 1999, courtesy Paul W Ladenson, MD, The Johns Hopkins University and Hospital, Baltimore.)

Hypothyroidism

- Mild hypothyroidism is common and easily treated
- Severe hypothyroidism
 - Hashimoto's thyroiditis
 - Myxedema
 - Cretinism



Cretinism, or congenital hypothyroidism results from thyroid hormone insufficiency in infancy.



Fig. 20-8 Adult cretinism, from characteristic facial features, enlarged lips, and swollen extremities and lower limbs. Hair growth is decreased, brittle, and small cartilage bones. (From Scholten MD: Fundamentals of clinical endocrinology, 3rd edn, 1975, Mosby.)

Adrenal Cortex

- Cushing's Syndrome due to excessive glucocorticoids
 - Pituitary tumor (75-80%)
 - Adrenal tumor
 - Ectopic carcinoma (paraneoplastic syndrome)
 - Iatrogenic conditions from administration of large amounts of glucocorticoids for chronic inflammatory conditions

- Changes in persons appearance
 - Obesity with moon face
 - Sodium and water retention
 - Heavy trunk
 - Fatty hump on neck (buffalo hump)
 - Muscle wasting in limbs
 - Fragile skin
 - Osteoporosis
 - Immune suppression with increased infections
 - Decreased stress response
 - Changes in mental status; including irritability, clinical depression and schizophrenia.

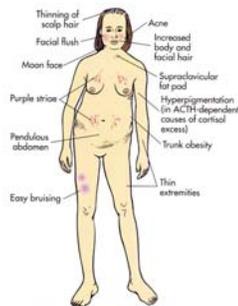
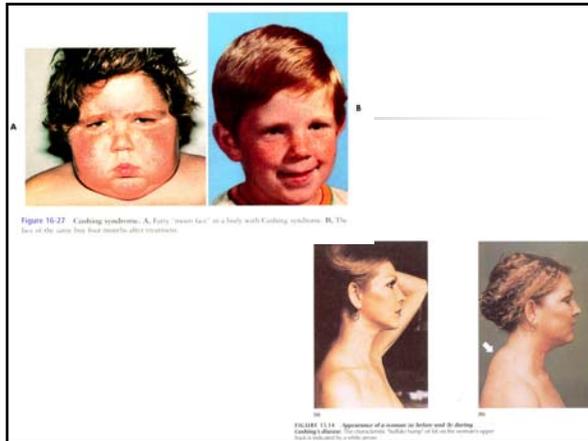
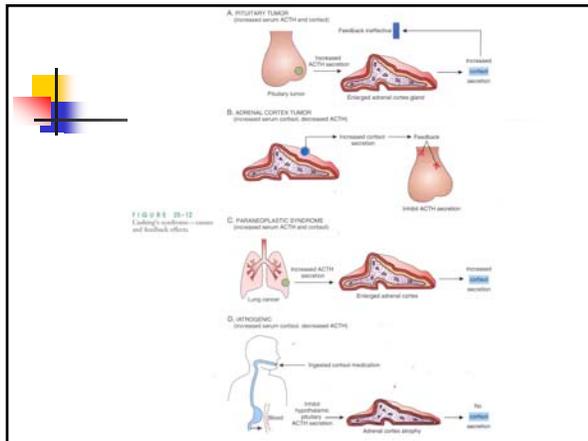


FIG. 20-14 Symptoms of cushing disease.





■ Questions 9-10



Addison's Disease

- Addison's disease refers to a deficiency of adenocortical secretions:
 - Glucocorticoids
 - Mineralocorticoids
 - Androgens
- Immune reactions are common cause



- Major effects
 - Decreased blood glucose levels
 - Poor stress resistance
 - Fatigue
 - Weight loss
 - Frequent infections
 - Low blood sodium levels
 - Decreased blood volume
 - Hypotension
 - High blood potassium levels
 - Decreased body hair
 - Hyperpigmentation



Addison's disease is caused by hyposecretion of corticosteroids, especially glucocorticoids. Pigment changes result from stimulation of melanocytes by ACTH, which is structurally similar to MSH.

Table 25-6

Comparison of Addison's Disease and Cushing's Syndrome

Addison's Disease (Adrenal Insufficiency)	Cushing's Syndrome/Disease
Deficit of corticosteroids (glucocorticoids, mineralocorticoids)	Excess glucocorticoids (cortisol)
High risk of infection	High risk of infection
Poor stress response	Poor stress response
Weight loss, fatigue	Moon face, buffalo hump, obese trunk, muscle wasting in limbs, osteoporosis
Anorexia, nausea, diarrhea	Striae, bruising of skin, high risk of infection
Hypotension, syncope	Hypertension, glucose intolerance
Hyperpigmentation	Fatigue, weakness, delayed healing



■ Question 11
