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

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>
<thead>
<tr>
<th>Manifestations</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyuria</td>
<td>增多的血液中的糖被过滤，进入尿液中，导致多尿</td>
</tr>
<tr>
<td>Polydipsia</td>
<td>口渴，需要更多的水来补充体内丢失的水分</td>
</tr>
<tr>
<td>Polyphagia</td>
<td>食欲增加，摄取更多的食物来补充血糖的不足</td>
</tr>
<tr>
<td>Weight loss</td>
<td>体重下降，由于脂肪和肌肉的减少</td>
</tr>
<tr>
<td>Fatigue</td>
<td>疲劳，由于能量的不足和代谢的异常</td>
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</tbody>
</table>

(Each condition has a corresponding mechanism that explains the symptoms observed in Type I Diabetes Mellitus.)
Type II Diabetes Mellitus

- About 90% of cases of Diabetes Mellitus
- Age of onset: 40-70 yr
- Insidious onset
- Genetic susceptibility exacerbated by long-duration obesity
- Insulin resistance not clearly understood
- Insulin levels are typically high at diagnosis but decline over the course of the illness
- Treatment consists of dietary control, exercise and sometimes medication
Symptomatic Results of Insulin Deficit (Diabetes mellitus)

<table>
<thead>
<tr>
<th>Organism or event</th>
<th>Organeal response</th>
<th>Resulting condition or effect</th>
<th>Insulin and glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose and insulin</td>
<td>Hypoglycemia</td>
<td>Lipase abnormalities</td>
<td>Polyuria, polydipsia, weight loss</td>
</tr>
<tr>
<td>Lipase and ketones</td>
<td>ketoacidosis</td>
<td>Lipase abnormalities</td>
<td>Polyuria, polydipsia, weight loss</td>
</tr>
<tr>
<td>Lipase and lipids</td>
<td>lipoatrophy</td>
<td>Lipase abnormalities</td>
<td>Polyuria, polydipsia, weight loss</td>
</tr>
</tbody>
</table>

- ◼️ = Muscle
- ◼️ = Alipose
- ◼️ = Liver

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>
<thead>
<tr>
<th>Vascular Problems with Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Macroangiopathy</strong></td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Elevated cholesterol levels</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
</tr>
<tr>
<td>Diabetic neuropathy</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Microangiopathy</strong></td>
</tr>
<tr>
<td>Kidneys</td>
</tr>
<tr>
<td>Chronic renal failure</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Eyes</td>
</tr>
<tr>
<td>Retinopathy</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Nervous system</td>
</tr>
<tr>
<td>Neuropathy in the central nervous system and peripheral nerves</td>
</tr>
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<td></td>
</tr>
</tbody>
</table>

**Note:** In addition to ischemia, there is also a metabolic abnormality that causes degeneration of myelin and distal-off of myo-insulted, essential in the conduction of nerve impulses.
Parathyroid Hormone Control

A. NORMAL CONTROL AND FEEDBACK OF CALCIUM

1. Stimulate parathyroid hormone release
2. Low blood Ca++
3. Calcium enhancement
4. High blood Ca++
5. Parathyroid hormone release
6. Calcium binding

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
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
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 shallowing, 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
Hypothyroidism

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

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
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

<table>
<thead>
<tr>
<th>Table 21-6</th>
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<tbody>
<tr>
<td><strong>Comparison of Addison’s Disease and Cushing’s Syndrome</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Addison’s Disease (Adrenal Insufficiency)</th>
<th>Cushing’s Syndrome/Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detox of corticoids (glucocorticoids, mineralocorticoids)</td>
<td>Excess glucocorticoids (Cushing’s)</td>
</tr>
<tr>
<td>High risk of infection</td>
<td>High risk of infection</td>
</tr>
<tr>
<td>Poor stress response</td>
<td>Poor stress response</td>
</tr>
<tr>
<td>Weight loss, fatigue</td>
<td>Moon face, buffalo hump, obese trunk, muscle wasting in limbs, osteoporosis</td>
</tr>
<tr>
<td>Anemia, nausea, diarrhea</td>
<td>Hypertension, glucose intolerance</td>
</tr>
<tr>
<td>Hypertension, syncope</td>
<td>Hypertension, glucose intolerance</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>Fatigue, weakness, delayed healing</td>
</tr>
</tbody>
</table>

Addison’s disease is caused by hypopituitarism or corticotropism.
Question 11