BIOS222
Pathology and Clinical Science 2 & 3

Session 16
Endocrine system disorders
3
Bioscience Department
Session Learning Outcomes

At the end of the session, you should be able to:

- Describe the anatomy and physiology of the endocrine pancreas
- Outline the various aetiologies of diabetes mellitus
- Discuss the pathophysiology, diagnosis, investigations, treatment options and complications of diabetes mellitus
- Understand the important complications of diabetes mellitus
Session Plan

- The endocrinal pancreatic disease
  - Overview of the Pancreas
  - Diabetes Mellitus
  - Complications of Diabetes Mellitus
    - Diabetic Ketoacidosis (DKA)
    - Hyperosmolar hyperglycemic state (HHS)
    - Hypoglycemia
    - Diabetic Neuropathies
    - Diabetic Nephropathies
    - Diabetic Retinopathies
    - Macroangiopathy
    - Foot ulcers
Overview of the Pancreas
Pancreas

- Leaf shaped organ in the abdomen
- Has a body, head and tail + Pancreatic Duct
- Exocrine pancreas
  - Produce Digestive enzymes (amylase, trypsin, lipase) and bicarbonate ions

Tortora, GJ & Derrickson, B 2014, Principles of anatomy and physiology, 14th edn, John Wiley & Sons, Hoboken, NJ.
Pancreas

- Endocrine Pancreas:
  - Islet of Langerhans:
    - Insulin – β islet cells
    - Glucagon – α islet cells
    - Somatostatin - delta islet cells
    - Pancreatic Polypeptide- F cells

Tortora, GJ & Derrickson, B 2014, Principles of anatomy and physiology, 14th edn, John Wiley & Sons, Hoboken, NJ.
Regulation of Blood sugar

- Insulin reduces blood sugar and facilitates use of sugar by body cells.
- Glucagon increases blood sugar levels by converting glycogen into glucose from liver.


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Regulation of Blood sugar

**INSULIN PROMOTES FUEL STORAGE**

**BLOOD**
- Glucose
  - Glucose → Glycogen (Glycogenesis)
  - Glucose → Amino Acids (Gluconeogenesis)

**GLUCAGON CATABOLIZES FUEL STORES**

**BLOOD**
- Glucose
  - Glucose → Glucose
- Amino Acids
  - Amino Acids → Protein
- Fatty Acids
  - Fatty Acids → Fats (lipogenesis)

**LIVER CELL**
- Glucose ➔ Glycogen (Glycogen synthesis)
- Amino Acids ➔ Amino Acids (Gluconeogenesis)
- Fatty Acids ➔ Fats (Lipolysis)
Actions of Insulin

Diabetes Mellitus
Diabetes Mellitus

- Definition: It refers to a group of common metabolic disorders that share the characteristic of hyperglycaemia.

21.9 Symptoms of hyperglycaemia

- Thirst, dry mouth
- Polyuria
- Nocturia
- Tiredness, fatigue, lethargy
- Change in weight (usually weight loss)
- Blurring of vision
- Pruritus vulvae, balanitis (genital candidiasis)
- Nausea
- Headache
- Hyperphagia; predilection for sweet foods
- Mood change, irritability, difficulty in concentrating, apathy
Diabetes Mellitus

- Incidence:
  - M:F - 1:3
  - Older people > young people
  - Obese > normal weight
    – 1 in 200 pregnant women

**CHART 50.1 Etiologic Classifications of DM**

- Type 1 diabetes (beta cell destruction, absolute insulin deficiency)
  - A. Immune mediated
  - B. Idiopathic
- Type 2 diabetes (insulin resistance with relative insulin deficiency)
- Other specific types
  - Genetic defects of beta cell function (i.e., maturity onset diabetes of the young)
  - Genetic defects in insulin action (i.e., type A insulin resistance)
  - Diseases of the exocrine pancreas
  - Endocrinopathies (i.e., Cushing disease, acromegaly)
  - Drug or chemical induced (i.e., glucocorticoids)
  - Infections (i.e., cytomegalovirus, rubella)
  - Other genetic syndromes (i.e., Turner syndrome, Down syndrome)

Gestational diabetes mellitus

Diabetes Mellitus

- **Aetiology:**
  - **Type 1A diabetes mellitus:**
    - Autoimmune attack
    - Genetic predisposition
    - Environmental triggers
  - **Type 2 diabetes mellitus:**
    - Insulin resistance
    - Genetic predisposition
    - Environmental triggers
Diabetes Mellitus

- Pathophysiology: Type 1A Diabetes Mellitus
  Genetic/environmental predisposition → Inflammatory cell infiltration of islet (insulitis) → Antibody-mediated destruction of the insulin-secreting β cells in the pancreatic islets

Diabetes Mellitus

- Pathophysiology: Type 2 Diabetes Mellitus
  Genetic/environmental predisposition → Insulin resistance → Deranged secretion of insulin by the pancreatic beta cells → beta cell exhaustion and failure → Increased glucose production by the liver.

Diabetes Mellitus

- Clinical features: Metabolic disturbances in type 1 diabetes
  - Hyperglycaemia
  - glycosuria and dehydration,
  - fatigue, polyuria, nocturia, thirst and polydipsia,
  - susceptibility to urinary and genital tract infections,
  - tachycardia and hypotension
  - Weight loss
  - Ketoacidosis
Diabetes Mellitus

- Clinical features: Metabolic disturbances in type 2 diabetes:
  - Insidious onset hyperglycaemia
  - often asymptomatic
  - history (typically many months) of fatigue, with or without ‘osmotic symptoms’ (thirst and polyuria)
  - Weight loss in advanced stage
  - Ketoacidosis in some ethnic groups
  - severe hyperglycaemia and dehydration during Intercurrent illness, e.g. with infections
## Diabetes Mellitus

<table>
<thead>
<tr>
<th>Information Type</th>
<th>Type 1</th>
<th>Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical age at onset</td>
<td>&lt; 40 yrs</td>
<td>&gt; 50 yrs</td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td>Weeks</td>
<td>Months to years</td>
</tr>
<tr>
<td>Body weight</td>
<td>Normal or low</td>
<td>Obese</td>
</tr>
<tr>
<td>Ketonuria</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Rapid death without treatment with insulin</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Autoantibodies</td>
<td>Positive in 80–90%</td>
<td>Negative</td>
</tr>
<tr>
<td>Diabetic complications at diagnosis</td>
<td>No</td>
<td>25%</td>
</tr>
<tr>
<td>Family history of diabetes</td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td>Other autoimmune disease</td>
<td>Common</td>
<td>Uncommon</td>
</tr>
</tbody>
</table>

Diabetes Mellitus

- **Diagnosis:**
  - **Urine Testing**
    - Glucose
    - Ketones
    - Proteins
  - **Blood testing**
    - Glucose
      - Random blood sugar
      - Blood sugar (PP2BS)
      - Fasting glucose
      - Glycated haemoglobin (HbA1c)
      - Glucose tolerance test for pre-diabetics
    - Ketones
Diabetes Mellitus

- Management:
  - Type 1 diabetes Mellitus:
    - Therapy A:
      - Long-acting insulin injection at bedtime (≈ 40-50% of the body’s needs of insulin)
      - Additional “bolus” injection of short-acting insulin 30 minutes before meals to lower the post-meal rises in blood glucose
    - Therapy B:
      - Usual food intake is assessed and used as a basis for adjusting insulin therapy to fit with the person’s lifestyle
      - Eating consistent amounts and types of food at specific and routine times
      - Home blood glucose monitoring
Diabetes Mellitus

- Management:
  - Type 2 diabetes Mellitus:
  - Lifestyle changes
    - Regular physical activity, healthy diet, reduction of alcohol and smoking
  - Anti-diabetic drugs
    - Reduce hyperglycemia
    - Several mechanisms of action:
      - Decrease glucose output from liver
      - Increase insulin secretion and sensitivity
Complications of Diabetes Mellitus
Complications of Diabetes Mellitus

- **Complications:**
  - **Acute complications:**
    - Diabetic Ketoacidosis (DKA)
    - Hyperosmolar hyperglycemic state (HHS)
    - Hypoglycemia
  - **Chronic complications:**
    - Microvasculature: Neuropathies, Nephropathies, and Retinopathies
    - Disorders of gastrointestinal motility
    - Macrovascular: Coronary artery, cerebral vascular, and peripheral vascular disease
    - Foot ulcers
Complications of Diabetes Mellitus

Long-term complications of DM.

Diabetic Ketoacidosis

- **Definition:** it is the most commonly occurring complication in a person with type 1 diabetes, where insulin deficiency leads to hyperglycemia, ketosis, and metabolic acidosis.

Diabetic Ketoacidosis

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyuria, thirst</td>
<td>Air hunger (Kussmaul breathing)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Smell of acetone</td>
</tr>
<tr>
<td>Weakness</td>
<td>Hypothermia</td>
</tr>
<tr>
<td>Nausea, vomiting</td>
<td>Confusion, drowsiness, coma (10%)</td>
</tr>
</tbody>
</table>

Diabetic Ketoacidosis

**Diagnosis:**
- Venous blood:
  - for urea and electrolytes, glucose and bicarbonate
- Urine or blood analysis for ketones
- ECG.

- Infection screen:
  - full blood count, blood and urine culture, C-reactive protein, chest X-ray.

**Management:**
A medical emergency
- Administration of insulin (low-dose)
- Intravenous fluid
- Electrolyte replacement solutions
Hypoglycemia

- Definition: It is generally defined as cognitive impairment with a blood glucose concentration of less than 3.5mmol/L

<table>
<thead>
<tr>
<th>21.19 Most common symptoms of hypoglycaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Autonomic</strong></td>
</tr>
<tr>
<td>• Sweating</td>
</tr>
<tr>
<td>• Trembling</td>
</tr>
<tr>
<td>• Pounding heart</td>
</tr>
<tr>
<td><strong>Neuroglycopenic</strong></td>
</tr>
<tr>
<td>• Confusion</td>
</tr>
<tr>
<td>• Drowsiness</td>
</tr>
<tr>
<td>• Speech difficulty</td>
</tr>
<tr>
<td><strong>Non-specific</strong></td>
</tr>
<tr>
<td>• Nausea</td>
</tr>
<tr>
<td>• Tiredness</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>21.21 Emergency treatment of hypoglycaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mild (self-treated)</strong></td>
</tr>
<tr>
<td>• Oral fast-acting carbohydrate (10–15 g) is taken as glucose drink or tablets or confectionery</td>
</tr>
<tr>
<td>• This should be followed with a snack containing complex carbohydrate</td>
</tr>
</tbody>
</table>

| **Severe (external help required)**        |
| • If patient is semiconscious or unconscious, parenteral treatment is required: |
|   IV 75 mL 20% dextrose (= 15 g; give 0.2 g/kg in children) |
|   Or |
|   IM glucagon (1 mg; 0.5 mg in children) |
| • If patient is conscious and able to swallow: |
|   Give oral refined glucose as drink or sweets (= 25 g) |
|   Or |
|   Apply glucose gel or jam or honey to buccal mucosa |

Hyperosmolar Hyperglycemic State

Definition: It is characterized by hyperglycemia, hyperosmolarity and dehydration, the absence of ketoacidosis, and depression of the sensorium.

Clinical features:
- Weakness, dehydration, polyuria
- Excessive thirst
- Neurologic signs:
  - Hemiparesis, seizures, and coma

Management:
- Frequent serum osmolality measurement
- Fluid replacement
- Insulin IV infusion
- Treatment of coexisting conditions
- Prophylactic anticoagulation
Diabetic Nephropathy

- Definition: It describes the combination of lesions that often occur concurrently in the diabetic kidney mainly affecting the glomeruli.

- Clinical features:
  - Proteinuria
  - Hypoproteinemia
  - Oedema
  - Impaired kidney function
  - Renal failure

Nodular diabetic glomerulosclerosis.

Diabetic Neuropathies

- Definition: Peripheral nerve involvement in DM is characterised by axonal degeneration of both myelinated and unmyelinated fibres, with thickening of the Schwann cell basal lamina, patchy segmental demyelination, and abnormal intraneural capillaries.

<table>
<thead>
<tr>
<th>21.40 Classification of diabetic neuropathy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Somatic</strong></td>
</tr>
<tr>
<td>- Polyneuropathy</td>
</tr>
<tr>
<td>Symmetrical, mainly sensory and distal</td>
</tr>
<tr>
<td>Asymmetrical, mainly motor and proximal (including amyotrophy)</td>
</tr>
<tr>
<td>- Mononeuropathy (including mononeuritis multiplex)</td>
</tr>
<tr>
<td><strong>Visceral (autonomic)</strong></td>
</tr>
<tr>
<td>- Cardiovascular</td>
</tr>
<tr>
<td>- Gastrointestinal</td>
</tr>
<tr>
<td>- Genitourinary</td>
</tr>
<tr>
<td>- Sudomotor</td>
</tr>
<tr>
<td>- Vasomotor</td>
</tr>
<tr>
<td>- Pupillary</td>
</tr>
</tbody>
</table>
Diabetic Retinopathy

- Definition: It is a microvascular damage characterised by increased vascular permeability and thickening of the capillary basement membrane.

- Clinical features:
  - Microaneurysms
  - Retinal haemorrhages
  - Cotton wool spots
  - Venous changes
  - Neovascularisation
  - Fibrosis and scarring
  - Retinal detachment

Cotton wool spots

Macroangiopathy

- Definition: It describes the damage to the larger blood vessels due to the Glucose molecules circulating in the blood.

- Clinical features:
  - Inflammatory reaction in the blood vessels with thrombus formation and infarction
  - Leads to Cardiovascular diseases
    - Cardiomyopathy
    - Angina pectoris & MI
    - Transient ischemic attacks
    - Strokes
    - Peripheral arterial disease
Diabetic Foot Ulcers

- **Definition:** Foot ulceration in DM occurs as a result of trauma (often trivial) in the presence of neuropathy and/or peripheral vascular disease.

- **Clinical features:**
  - Mostly develop at the site of a plaque of callus skin
  - Tissue necrosis
  - Disruption of the protective epidermis
  - Secondary infection
  - Signs of neuropathy and ischemia

<table>
<thead>
<tr>
<th>Type I</th>
<th>Type II</th>
<th>Other specific types</th>
<th>Gestational DM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Other names</strong></td>
<td>IDDM, Juvenile Diabetes</td>
<td>NIDDM, Adult onset DM</td>
<td>Gestational DM</td>
</tr>
<tr>
<td><strong>Age of onset</strong></td>
<td>Infancy / Childhood</td>
<td>Adults</td>
<td>Middle age, young adults</td>
</tr>
<tr>
<td><strong>Genetic factors</strong></td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td><strong>Autoimmunity</strong></td>
<td>√</td>
<td>Usually none</td>
<td>Usually none</td>
</tr>
<tr>
<td><strong>Pathogenesis</strong></td>
<td>T cell mediated autoimmune reaction</td>
<td>Insulin resistance and dysfuctioning of β cells</td>
<td>Pancreatic damage from other diseases, genetic factors, etc..</td>
</tr>
<tr>
<td><strong>Complications</strong></td>
<td>Usually many and inevitable</td>
<td>May develop only if uncontrolled</td>
<td>Usually less unless poorly managed</td>
</tr>
<tr>
<td><strong>Ketoacidosis</strong></td>
<td>√</td>
<td>Not usually</td>
<td>Not usually</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Lifetime Insulin injections</td>
<td>Diet, weight management, glucose lowering drugs Insulin injections in later stages</td>
<td>Varies. May need insulin injections or glucose lowering drugs</td>
</tr>
</tbody>
</table>
Reading and Resources

- Crowley LV, 2012, *An Introduction to Human Diseases – Pathology and Pathophysiology Correlations*, 9th edn, Jones and Bartlett Learning
Reading and Resources

- Mosby's dictionary of medicine, nursing and health professions 2013, 9th edn, Elsevier, St. Louis, MO.
- VanMeter, KC & Hubert, RJ 2014, *Gould's pathophysiology for the health professions*, 5th edn, Elsevier, St Louis, MO.
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