SIGNS AND SYMPTOMS OF ENDOCRINE ORGANS DISEASES AND METABOLIC DISORDERS
(accents on thyroid gland and pancreas)

LECTURE IN INTERNAL MEDICINE PROPAADEUTICS

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Plan of the lecture

- **Definition of endocrine system**
- **Spectrum of endocrine diseases and metabolic disorders**
- **Thyroid gland**
  - Reminder (how do thyroid gland work)
  - History-taking
  - Patient’s examination (clinical, laboratory, instrumental)
  - symptoms and syndromes
- **Endocrine pancreas**
  - Reminder (how do pancreas works)
  - History-taking
  - Patient’s examination (clinical, laboratory, instrumental)
  - symptoms and syndromes
- **Glossary of terms referred to endocrine diseases and metabolic disorders**

More Recently Identified: Kidneys, Heart/blood, Liver, Brain, Fat (adipose) tissue, Placenta

http://classes.midlandstech.edu/carterp/Courses/bio211/chap16/figure_16_01_labeled.jpg
Definition of endocrine system

The endocrine system is a group of glands (organs) that regulate physiological functions by releasing hormones into the bloodstream. Hormones are chemicals that carry information to different parts of the body; specific hormones influence certain organs or parts of the body, such as the liver or pancreas.

The endocrine system regulates development and growth (for example, puberty), metabolism, sexual and reproductive processes. It includes the reproductive glands, adrenal glands, thyroid glands, hypothalamus, pancreas, and pituitary glands. Although distinct from the nervous system, the endocrine system interacts with the nervous system through the hypothalamus, which regulates the pituitary gland function.

The word endocrine derives from the Greek words "endo," meaning within, and "crinis," meaning to secrete.
Spectrum of endocrine diseases and metabolic disorders

- **Adrenal disorders**: Adrenal insufficiency, Adrenal hormone excess, Congenital adrenal hyperplasia, Adrenocortical carcinoma
- **Glucose homeostasis disorders**: Diabetes mellitus, Hypoglycemia
- **Thyroid disorders**: Goiter, Hyperthyroidism, Hypothyroidism, Thyroidites, Thyroid cancer, Thyroid hormone resistance
- **Calcium homeostasis disorders and Metabolic bone diseases**: Hyperparathyroidism, Hypoparathyroidism, Pseudohypoparathyroidism, Osteoporosis, Osteitis deformans, Rickets, Osteomalacia
- **Pituitary gland disorders**: Posterior pituitary - Diabetes insipidus, Anterior pituitary - Hypopituitarism, Pituitary tumors, Hyperprolactinemia, Acromegaly, gigantism, Cushing's disease, Growth failure, Dwarfism
- **Sex hormone disorders**: Disorders of sex development, Hypogonadism, Disorders of Puberty, Menstrual function disorders,
- **Tumours of the endocrine glands not mentioned elsewhere**: Multiple endocrine neoplasia, Carcinoid syndrome
Thyroid gland

reminder: how does thyroid gland work
Thyroid gland

reminder: the primary functions, T3 & T4 hormones

- The primary function of the thyroid is production of the hormones T3, T4 and calcitonin. Up to 80% of the T4 is converted to T3 by organs such as the liver, kidney and spleen. T3 is several times more powerful than T4, which is largely a prohormone, perhaps four or even ten times more active.
- The production of T3, T4 is regulated by thyroid-stimulating hormone (TSH), released by the anterior pituitary. The thyroid and thyrotropes form a negative feedback loop: TSH production is suppressed when the T4 levels are high.
- T3, T4 act on nearly every cell in the body to increase the basal metabolic rate, affect protein synthesis, help regulate long bone growth and neural maturation, and increase the body's sensitivity to catecholamines by permissiveness. T3, T4 are essential to proper development and differentiation of all cells of the human body. T3, T4 also regulate protein, fat, and carbohydrate metabolism, affecting how human cells use energetic compounds. They also stimulate vitamin metabolism. Numerous physiological and pathological stimuli influence T3, T4 synthesis.
- T3, T4 leads to heat generation in humans.
Thyroid gland

reminder: T3 & T4 hormones
(derived from modification of tyrosine)

- The thyroid secretes about 80 mg of T4, but only 5 mg of T3 per day
- T3 has a much greater biological activity (about 10 X) than T4
- An additional 25 mg/day of T3 is produced by peripheral monodeiodination of T4
Thyroid gland

reminder: functional effects of T3 & T4 hormones

Cardiovascular System
• Increase heart rate
• Increase force of cardiac contractions
• Increase stroke volume
• Increase cardiac output
• Up-regulate catecholamine receptors

Respiratory System
• Increase resting respiratory rate
• Increase minute ventilation
• Increase ventilatory response to hypercapnia and hypoxia

Renal System
• Increase blood flow
• Increase glomerular filtration rate

Intermediary Metabolism
• Increase glucose absorption from the GI tract
• Increase carbohydrate, lipid and protein turnover
• Down-regulate insulin receptors
• Increase substrate availability
Thyroid gland

reminder: functional effects of T3 & T4 hormones

Oxygen-Carrying Capacity
• Increase RBC mass
• Increase oxygen dissociation from hemoglobin

Growth and Tissue Development
• Increase growth and maturation of bone
• Increase tooth development and eruption
• Increase growth and maturation of epidermis, hair follicles and nails
• Increase rate and force of skeletal muscle contraction
• Inhibits synthesis and increases degradation of mucopolysaccharides in subcutaneous tissue

Nervous System
• Critical for normal CNS neuronal development
• Enhances wakefulness, alertness, memory and learning capacity
• Required for normal emotional tone
• Increase speed and amplitude of peripheral nerve reflexes

Reproductive System
• Required for normal follicular development, ovulation, maintenance of pregnancy in the female, spermatogenesis in the male
Thyroid gland

Thyroid Stimulating Hormone cause the release of T4, T3

- The thyroid is controlled by the hypothalamus and pituitary
- Through a feedback loop, the pituitary releases TRH (thyrotropin-releasing hormone) which stimulates the release of TSH (thyroid-stimulating hormone)
- TSH stimulates the thyroid gland to produce of the hormones T3, T4 to release into the blood
Thyroid gland reminder: purpose

- General evaluation of health
- Diagnosis of disease or disorders of the thyroid gland
- Diagnosis of other systemic diseases that affect thyroid gland function
Thyroid gland

history-taking: patient’s interviewing

- gathering of information
- patient’s narrative
- biomedical perspective
- psychosocial perspective
- context
Thyroid gland
clinical examination of the gland: inspection, palpation

• A normal thyroid is estimated to be 10 grams with an upper limit of 20 grams
• An enlarged thyroid is referred to as a goiter
• There is no direct correlation between size and function - a person with a goiter can be euthyroid, hypothyroid, or hyperthyroid

Thyroid gland
clinical examination of the gland
(inspection, palpation, their synthesis)

WHO classification of goiter’ grade
• 0 - no palpable or visible
• 1 - palpable but not visible when the neck is in the normal position, thyroid nodules in a thyroid which is otherwise not enlarged fall into this category
• 2 - clearly visible when the neck is in a normal position and is consistent with an enlarged thyroid when the neck is palpated
Thyroid gland

patient's laboratory examination: Thyroid Panel

Blood

- Thyroid-Stimulating Hormone (TSH) evaluates overall thyroid function
- Total Thyroxine (T4) evaluates the total amount of T4 produced by the thyroid gland
- Free Thyroxine (T4) evaluates the amount of T4 available to the cells and tissues
- Free Tri-iodothyronine (T3) measures the amount of T3 (the active form of the hormone) available to the cells and tissues

https://www.youtube.com/watch?v=ua4uMumAOXI
Thyroid gland

patient’s laboratory examination: Thyroid Panel

![Diagram](http://www.thyroid.org/blood-test-for-thyroid/)
Thyroid gland

patient’s laboratory examination: Thyroid Panel

<table>
<thead>
<tr>
<th>TSH</th>
<th>FREE T4 (FT4)</th>
<th>FREE OR TOTAL T3</th>
<th>PROBABLE INTERPRETATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Normal</td>
<td>Normal</td>
<td>Mild (subclinical) hypothyroidism</td>
</tr>
<tr>
<td>High</td>
<td>Low</td>
<td>Low or normal</td>
<td>Hypothyroidism</td>
</tr>
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<tr>
<td>Low</td>
<td>Low or normal</td>
<td>Low or normal</td>
<td>Non-thyroidal illness; rare pituitary (secondary) hypothyroidism</td>
</tr>
<tr>
<td>Normal</td>
<td>High</td>
<td>High</td>
<td>Thyroid hormone resistance syndrome (a mutation in the thyroid hormone receptor decreases thyroid hormone function)</td>
</tr>
</tbody>
</table>

http://labtestsonline.org/understanding/analytes/t3/tab/test/
Blood

- Thyroid Peroxidase Antibody (TPOAb)
- Thyroglobulin Antibody (TgAb)
- Thyroid Stimulating Hormone Receptor Antibody (TRAb)

http://labtestsonline.org/understanding/analytes/thyroid-antibodies/tab/test/
<table>
<thead>
<tr>
<th>THYROID ANTIBODY</th>
<th>ACRONYM</th>
<th>PRESENT IN</th>
<th>WHEN ORDERED</th>
<th>OTHER FACTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid peroxidase antibody</td>
<td>TPOAb</td>
<td>Hashimoto thyroiditis; Graves disease</td>
<td>When a person has symptoms suggesting thyroid disease; when a doctor is considering starting a patient on a drug therapy that has associated risks of developing hypothyroidism when thyroid peroxidase antibodies are present, such as lithium, amiodarone, interferon alpha, or interleukin-2</td>
<td>Has been associated with reproductive difficulties, such as miscarriage, preeclampsia, premature delivery, and in-vitro fertilization failure</td>
</tr>
<tr>
<td>Thyroglobulin antibody</td>
<td>TgAb</td>
<td>Thyroid cancer; Hashimoto thyroiditis</td>
<td>Whenever a thyroglobulin test is performed to see if the antibody is present and likely to interfere with the test results (e.g., at regular intervals after thyroid cancer treatment); when symptoms of hypothyroidism are present</td>
<td></td>
</tr>
<tr>
<td>Thyroid stimulating hormone receptor antibody, Thyroid Stimulating Immunoglobulin</td>
<td>TRAb, TSHR Ab, TSI</td>
<td>Graves disease</td>
<td>When a person has symptoms of hyperthyroidism; to monitor the effectiveness of anti-thyroid therapy</td>
<td></td>
</tr>
</tbody>
</table>

http://labtestsonline.org/understanding/analytes/thyroid-antibodies/tab/test/
Thyroid gland

patient’s instrumental examination: sonography

http://www.radiologyinfo.org/photocat/popup/thyromegaly.jpg
Thyroid gland
patient’s instrumental examination: sonography

http://www.radiologyinfo.org/photocat/popup/thyromegaly.jpg
Thyroid gland

patient’s instrumental examination: Doppler
Thyroid gland

patient’s instrumental examination: scanning

A. Normal

B. Graves' disease

http://images.emedicinehealth.com/images/gravesdisease_ab.jpg
Thyroid gland patient’s instrumental examination: biopsy

http://www.jaypeejournals.com/eJournals/_eJournals%5C192%5C2011%5CSeptember-December%5Cimages/4_img_2.jpg
Thyroid gland
patient’s instrumental examination: scan

http://www.ijem.in/articles/2012/16/6/images/IndianJEndocrMetab_2012_16_6_1063_103047_f2.jpg
Thyroid gland patient’s instrumental examination: ECG

http://i0.wp.com/jeffreydachmd.com/wp-content/uploads/2013/09/Afib_ecg.jpg
Thyroid gland
hypothyroidism: etiology

• **Primary**
  • Hashimoto’s thyroiditis with or without goitre
  • Radioactive iodine therapy for Graves’ disease
  • Subtotal thyroidectomy for Graves’ disease or nodular goitre
  • Excessive iodine intake
  • Subacute thyroiditis
  • Rare causes (Iodide deficiency, goitrogens such as lithium; antithyroid drug therapy, Inborn errors of thyroid hormone synthesis)

• **Secondary**
  • Hypopituitarism
  • Tertiary (hypothalamic dysfunction)
  • Peripheral resistance to the action of thyroid hormone
Thyroid gland

hypothyroidism: age aspects

• Early onset (in childhood): delayed/incomplete physical and mental development (may be development of kretinism)
• Later onset (youth): impaired physical growth
• Adult onset (myxedema): gradual changes occur (tiredness, lethargy, decreased metabolic rate, slowing of mental function and motor activity, cold intolerance, weight gain, goiter, hair loss, dry skin, eventually may result in coma)
During iodine deficiency, thyroid hormone production decreases

TSH release increased (less negative feedback)

TSH acts on thyroid, increasing blood flow, and stimulating follicular cells and increasing colloid production, but the only result is that the follicles accumulate more and more unusable colloid

If goiter is due to decreased I, then thyroid gland enlarges (endemic or colloidal goiter)

Cells eventually die from overactivity and the gland atrophies
Thyroid gland
hypothyroidism: clinical symptoms

- Cardiovascular (bradycardia, low voltage ECG, pericardial effusion, cardiomegaly, hyperlipidemia)
- Constipation, ascites
- Weight gain
- Cold intolerance
- Rough, dry, yellowish skin
- Puffy face and hands; hoarse, husky voice
- Respiratory failure
- Menorrhagia, infertility, hyper-, prolactinemia
- Renal (impaired ability to excrete a water load)
- Anemia (impaired Hb synthesis, Fe deficiency due to menorrhagia and reduced intestinal absorption, folate deficiency due to impaired intestinal absorption, pernicious anemia)
- Neuromuscular (muscle cramps, myotonia, slow reflexes, carpal tunnel syndrome)
- CNS (fatigue, lethargy, depression, Inability to concentrate)
Thyroid gland

hypothyroidism: diagnosis

- FT4↓ and TSH↑ (primary hypothyroidism)
- Serum T3 levels are variable
- positive test for thyroid autoantibodies (Tg Ab & TPO Ab) and an enlarged thyroid gland (Hashimoto’s thyroiditis)
- FT4↓ & TSH inappropriately normal (myxedema)
- Absence of TSH response to TRH (pituitary deficiency)
- TSH↑ & FT4 & FT3 are normal (subclinical hypothyroidism)

MRI of brain is indicated if pituitary or hypothalamic disease is suspected
Thyroid gland
hypothyroidism: myxedema coma

- Medical emergency, end stage of untreated hypothyroidism
- Progressive weakness, stupor, hypothermia, hypoventilation, hypoglycemia, hyponatremia, shock, and death
- The patient (or a family member) may recall previous thyroid disease, radioiodine therapy, or thyroidectomy
- Gradual onset of lethargy progressing to stupor or coma
- Marked hypothermia (< 24°C)
- Heart failure, pneumonia, excessive fluid administration, narcotics
- ECG: bradycardia and low voltage
- FT4↓
- TSH ↑, normal, or ↓, cholesterol ↑ or N, serum Na ↓

http://jkms.org/ArticleImage/0063JKMS/jkms-25-1394-g001-l.jpg
Thyroid gland

**hyperthyroidism: etiology**

- The second most prevalent endocrine disorder
- Effects women eight times more frequently than men
- May appear after an emotional shock, stress, or an infection
- **Graves’ disease**: excessive output of thyroid hormones
- Other common causes of hyperthyroidism include thyroiditis and excessive ingestion of thyroid hormone (toxic adenoma, Plummer's disease (toxic multinodular goiter))
Thyroid gland

**hyperthyroidism**: clinical symptoms

**Emotional** (nervousness, irritability)

**Exophthalmos**

**Goitre** (diffuse enlargement of thyroid, bruit)

**Thyroid dermopathy** (pretibial myxedema & TSH-R Ab↑)

**Heat intolerance**

**Cardiovascular** (palpitation, atrial fibrillation, CHF, dyspnea, angina)

**Gastrointestinal** (weight, appetite, diarrhea)

**Reproductive** (amenorrhea, oligo-menorrhea, infertility, gynecomastia)

**Bone** (Osteoporosis, Thyroid acropachy)

**Neuromuscular** (nervousness, tremor, emotional labiality, proximal myopathy, myasthenia gravis, hyperreflexia, clonus, periodic hypokalemic paralysis)

**Skin** (pruritus, onycholysis, vitiligo, hair thinning, palmar erythema, spider nevi)
Thyroid gland

hyperthyroidism: diagnosis

- TSH ↓, High FT4↑ and/or FT3↑
  - If eye signs are present, the diagnosis of Graves’ disease can be made without further tests
  - If eye signs are absent and the patient is hyperthyroid with or without a goitre, a radioiodine uptake test should be done
  - Radioiodine uptake and scan (diffuse increased uptake)
  - TSH-R Ab is specific for Graves’ disease, may be useful in the “apathetic” hyperthyroid patient or who presents with unilateral exophthalmos without obvious signs or laboratory manifestations of Graves’ disease
Thyroid gland

**hyperthyroidism:** thyroid storm (crisis)

- Occurs in a severely hyperthyroid patient caused by a precipitating event such as:
  - Infection
  - Surgical stress
  - Stopping antithyroid medication in Graves’ disease

- Clinical clues
  - fever $\rightarrow$ hyperthermia
  - marked anxiety or agitation $\rightarrow$ coma
  - anorexia
  - tachycardia $\rightarrow$ tachyarrhythmias
  - pulmonary edema/cardiac failure
  - hypotension $\rightarrow$ shock
  - confusion
Endocrine pancreas reminder: how does endocrine pancreas work

https://www.youtube.com/watch?v=kIPYVV4aThM
Endocrine pancreas reminder: the primary functions

Production of pancreatic hormones by three cell types
- Glucagon by alpha cells
- Insulin by beta cells
- Somatostatin by delta cells

Hormones travel through the bloodstream to target tissues

At the target cells, hormones bind specific receptors and cause cell changes that control metabolism

http://www.daviddarling.info/images/islets_of_Langerhans.gif
Endocrine pancreas

Reminder: insulin & glucagon in glucose metabolism regulation

(a) Fed state: insulin dominates
- Glucagon
- Insulin
- ↑ Glucose oxidation
- ↑ Glycogen synthesis
- ↑ Fat synthesis
- ↑ Protein synthesis

(b) Fasted state: glucagon dominates
- Glucagon
- Insulin
- ↑ Glycogenolysis
- ↑ Gluconeogenesis
- ↑ Ketogenesis
Endocrine pancreas
reminder: structure & roles of insulin

• Insulin is a polypeptide hormone, composed of two chains (A and B)
• Both chains are derived from proinsulin (prohormone)
• Chains are joined by disulfide bonds

• Acts on tissues to increase uptake of glucose and amino acids
• Increases glycogen production (glucose storage) in the liver and muscle
• Stimulates lipid synthesis from free fatty acids and triglycerides in adipose tissue
• Also stimulates potassium uptake by cells (role in potassium homeostasis).

http://www.bio.davidson.edu/Courses/Molbio/MolStudents/spring2003/Williford/structure_insulin.gif
Endocrine pancreas

reminder: insulin secretion control’ mechanisms

- Chemically – high levels of glucose and amino acids in the blood
- Hormonally – beta cells are sensitive to several hormones that may inhibit or cause insulin secretion
- Neurally – stimulation of the parasympathetic nervous system causes insulin to be secreted

- Insulin secretion is decreased by decreased glucose and increased insulin concentration in blood and sympathetic stimulation
- Insulin transported through the blood to target tissues where it binds to target cells’ specific receptors and acts as a biochemical signal to the inside of the cell: cell metabolism is stimulated
Endocrine pancreas
reminder: blood fasting glucose levels

• The normal range - a narrow range of about 3.9 to 5.5 mmol/L (as measured by a fasting blood glucose test)

• Hyperglycemia - high levels
  – Short term (physiological, pathological)
  – Persistent
    • impaired – pre-diabetes
    • high - esp. diabetes mellitus (DM)

• Hypoglycemia - low levels
Endocrine pancreas

**reminder:** purpose

- General evaluation of health
- Diagnosis of disease or disorders of endocrine pancreas
- Diagnosis of other systemic diseases that affect endocrine pancreas

Endocrine pancreas

history-taking: patient’s interviewing

- gathering of information
- patient’s narrative
- biomedical perspective
- psychosocial perspective
- context

# Endocrine pancreas
clinical monitoring diabetic complications

## Clinical Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NA Blood pressure</td>
<td>Management; monitor hypertension and thus risk of heart disease</td>
</tr>
<tr>
<td>NA Eye exam</td>
<td>Management; monitor onset and progression of eye disease</td>
</tr>
<tr>
<td>NA Foot exam</td>
<td>Management; monitor onset and progression of nerve disease and peripheral arterial disease</td>
</tr>
</tbody>
</table>
The **American Diabetes Association** (ADA) recommendations:

- Obesity (BMI >25 kg/m²) – consider testing to detect pre-DM and type 2 DM in asymptomatic people
- Family history of DM in first- or second-degree relative
- Signs of insulin resistance or conditions associated with insulin resistance (eg, acanthosis nigricans, hypertension, dyslipidemia, low birthweight)
- Maternal history of DM or gestational diabetes mellitus (GDM) during gestation

http://www.anylabtestnow.com/tests/diabetes-maintenance-panel/
Endocrine pancreas
patient's laboratory examination: diabetes panel

• Complete Blood Count (CBC)
• Glucose, Serum (Fasting)
• Oral glucose tolerance test (OGTT)
• Random blood glucose
• Islet cell antibody test (for type 1 diabetes)
• Hemoglobin A1c
• Diabetic Urinalysis

http://www.anylabtestnow.com/tests/diabetes-maintenance-panel/
The current WHO diagnostic criteria for diabetes should be maintained – fasting plasma glucose ≥ 7.0mmol/l (126mg/dl) or 2–h plasma glucose ≥ 11.1mmol/l (200mg/dl).

The glucose tolerance test – WHO criteria

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Impaired glucose tolerance</th>
<th>Diabetes mellitus</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fasting</strong></td>
<td>&lt;7.0 mmol/L</td>
<td>&lt;7.0 mmol/L</td>
<td>&gt;7.0 mmol/L</td>
</tr>
<tr>
<td><strong>2 h after glucose</strong></td>
<td>&lt;7.8 mmol/L</td>
<td>7.8–11.0 mmol/L</td>
<td>≥11.1 mmol/L</td>
</tr>
</tbody>
</table>

HbA1c reflects average plasma glucose over the previous 2–3 months in a single measure which can be performed at any time of the day and does not require any special preparation such as fasting.

HbA1c ≥ 6.5% = diabetes mellitus, HbA1c 5.7 to 6.4% = pre-diabetes or at risk of diabetes.
Endocrine pancreas

**Patient's laboratory examination:** diagnostic significance of glucose and hemoglobin A1c concentrations

<table>
<thead>
<tr>
<th>Individuals Suitable for Testing</th>
<th>Marker</th>
<th>Clinically Significant Level</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-pregnant individuals with diabetes risk factors or age ≥45 years and pregnant women with risk factors (first prenatal visit)</td>
<td>FPG 2-h OGTT (75 g) HbA1c</td>
<td>≥126 mg/dL ≥200 mg/dL ≥6.5%</td>
<td>Diabetes</td>
</tr>
<tr>
<td></td>
<td>FPG 2-h OGTT (75 g) HbA1c</td>
<td>100-125 mg/dL 140-199 mg/dL 5.7%-6.4%</td>
<td>Increased risk for diabetes</td>
</tr>
<tr>
<td>All pregnant women (24-28 weeks of gestation)</td>
<td>2-h OGTT (75 g)</td>
<td>≥92 mg/dL ≥180 mg/dL ≥153 mg/dL</td>
<td>Gestational diabetes</td>
</tr>
</tbody>
</table>

FPG, fasting plasma glucose; OGTT, oral glucose tolerance test; HbA1c, hemoglobin A1c.
Glucosuria can be detected when level of blood glucose exceeds more than 11mmol/l
Urine tests can’t be used alone to confirm the diagnosis of diabetes mellitus
They are ordered more often when there is suspicion on type 1 diabetes
Laboratories can test urine for ketone bodies
The body produces ketone bodies when fat tissue is used for energy instead of blood sugar
If ketone bodies are present in the urine, this could indicate the high level of glucose in blood with insufficient level of insulin production

http://www.biosynergypro.com/uploads/1/2/9/0/12905439/_8435009_orig.png
Endocrine pancreas
high level persistent hyperglycemia (DM): types

- DM type 1 results from the body's failure to produce enough insulin. Main risk factors: viruses and toxins that can affect genetically determinated antigens of HLA system and cause autoimmune destruction of beta cells in the islets of Langerhans.
- DM type 2 begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses a lack of insulin may also develop. This form was previously referred to as "non insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". The primary cause is excessive body weight and lack of exercise.
- Gestational diabetes, is the third main form and occurs when pregnant women without a previous history of diabetes develop a high blood glucose level.
Endocrine pancreas
high level persistent hyperglycemia (DM):
early & later clinical symptoms

Classic
• Polyphagia (increased hunger)
• Polyuria (frequent urination)
• Polydipsia (increased thirst)

Other
• Blurred vision
• Fatigue
• Weight loss
• Poor wound healing (cuts, scrapes, etc.)
• Dry mouth
• Dry or itchy skin
• Impotence (male)
• Recurrent infections such as vaginal yeast infections, groin rash, or external ear infections (swimmers ear)
Endocrine pancreas
high level persistent hyperglycemia (DM):
early & later clinical symptoms

Early

- Frequent urination
- Increased thirst
- Blurred vision
- Fatigue
- Headache

Later (ketoacidosis)

- Fruity-smelling breath
- Nausea and vomiting
- Shortness of breath
- Dry mouth
- Weakness
- Confusion
- Coma
- Abdominal pain
Endocrine pancreas
high level persistent hyperglycemia (DM)
acute complications: diabetic ketoacidosis

• A potentially life-threatening complication happens in pts DM 1, it can occur in those with DM 2
• The symptoms usually evolve over the period of about 24 hours
• Predominant symptoms are nausea and vomiting, pronounced thirst, excessive urine production, and abdominal pain
• Breathing becomes labored and of a deep, gasping character (Kussmaul respiration)
• In severe cases there may be confusion, lethargy, stupor, coma
• On physical examination there is evidence of dehydration (tachycardia, low blood pressure), "ketotic" odor, and death
• Blood analysis will reveal significant decreased pH $< 7.30 \text{ mmol/l}$
• Urine analysis will reveal significant levels of ketone bodies, often before other overt symptoms
Endocrine pancreas
high level persistent hyperglycemia (DM)
acute complications: nonketotic hyperosmolar state

- An acute complication sharing many symptoms with diabetic ketoacidosis, but an entirely different origin
- Water osmotically drawn out of cells into the blood
- The kidneys eventually begin to dump glucose into the urine
- Serum pH >7.30, Bicarbonate >15 mEq/L, Small ketonuria and absent-to-low ketonemia (<3 mmol/L)
- Increased risk of blood clot formation
- If fluid is not replaced, the osmotic effect of high glucose levels, combined with the loss of water, will eventually lead to dehydration
- Some alteration in consciousness, lethargy may ultimately progress to a coma
Endocrine pancreas
high level persistent hyperglycemia (DM)
acute complications: nonketotic hyperosmolar state

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Endocrine pancreas
high level persistent hyperglycemia (DM)
acute complications: coma

• A life-threatening DM complication that causes unconsciousness
• Three different types:
  – Severe low blood sugar in a DM person
  – Diabetic ketoacidosis advanced enough to result in unconsciousness from a combination of a severely increased blood sugar level, dehydration and shock, and exhaustion
  – Hyperosmolar nonketotic coma in which an extremely high blood sugar level and dehydration alone are sufficient to cause unconsciousness
• Diabetic coma was a diagnostic problem before the late 1970s, when glucose meters and rapid blood chemistry analyzers became universally available in hospitals
Endocrine pancreas high level persistent hyperglycemia (DM) acute complications: hypoglycemia

- A medical emergency that involves an abnormally diminished content of glucose in the blood
- Symptoms hypoglycemia usually do not occur until 2.8 to 3.0 mmol/L
- Adrenergic manifestations: shakiness, anxiety, nervousness, palpitations, tachycardia, sweating, pallor, coldness, clamminess, mydriasis
- Glucagon manifestations: hunger, nausea, vomiting, abdominal discomfort, headache
- Neuroglycopenic manifestations: abnormal thinking, depression, crying, exaggerated concerns, paresthesia, negativism, emotional lability, fatigue, weakness, apathy, lethargy, daydreaming, confusion, amnesia, blurred vision, automatic behavior, difficulty speaking, incoordination, motor deficit, paresthesia, headache, stupor, coma, etc.
Endocrine pancreas
high level persistent hyperglycemia (DM): chronic complications

Microvascular
• Diabetic cardiomyopathy
• Diabetic nephropathy
• Diabetic neuropathy
• Diabetic retinopathy
• Diabetic encephalopathy

Macrovascular
• Coronary artery disease
• Diabetic myonecrosis
• Peripheral vascular disease
• Stroke

Other
• Gastrointestinal (gastroparesis, diarrhea)
• Genitourinary (uropathy/sexual dysfunction)
• Dermatologic
• Infectious
• Cataracts
• Glaucoma
• Periodontal disease
Endocrine pancreas
high level persistent hyperglycemia (DM):
main chronic complications

http://www.idf.org/complications-diabetes
Diabetic retinopathy results in scattered hemorrhages, yellow exudates, and neovascularization.

This patient has neovascular vessels proliferating from the optic disc, requiring urgent panretinal laser photocoagulation.

Endocrine pancreas
high level persistent hyperglycemia (DM):
main chronic complications
• **Acromegaly**: A hormonal disorder involving excess growth hormone production by the pituitary gland.

• **Adrenal disorders**: Disorders affecting the adrenal glands

• **Chronic Fatigue Syndrome**: Severe chronic fatigue disorder often following infection.

• **Cushing's disease**: A condition of hyperadrenocorticism which is secondary to excessive pituitary secretion of ACTH. Cushing's disease is different to Cushing's syndrome which refers to the effects of glucocorticoid excess from any cause.

• **Diabetes**: Failing or reduced ability of the body to handle sugars.

• **Endocrine pancreatic cancer**: Any disease that affects the endocrine pancreas

• **Endocrine system cancer**: Cancer that affects any gland in the endocrine system

• **Endocrine system conditions**: Medical conditions affecting the endocrine systems, such as the related hormones or glands.
Glossary of endocrine pathology’ terms 2

- **Gastroparesis**: Slow stomach emptying from stomach nerve damage
- **Hyperthyroidism**: Too much thyroid hormone production.
- **Hypothyroidism**: Too little thyroid hormone production.
- **Kearns-Sayre Syndrome**: A rare neuromuscular disorder characterized by pigmented deposits on the retina, heart disease and progressive paralysis of some eye muscles.
- **Myositis**: One of the underlying causes for muscle weakness/myopathy.
- **Obal syndrome**: The association of eye problems with severe malnutrition. The condition occurred frequently in soldiers, prisoners of war and people in concentration camps.
- **Pancreas conditions**: Any condition that affects the pancreas
- **Pituitary conditions**: Any condition that affects the pituitary
- **Thyroid disorders**: Any disorder of the thyroid gland.