

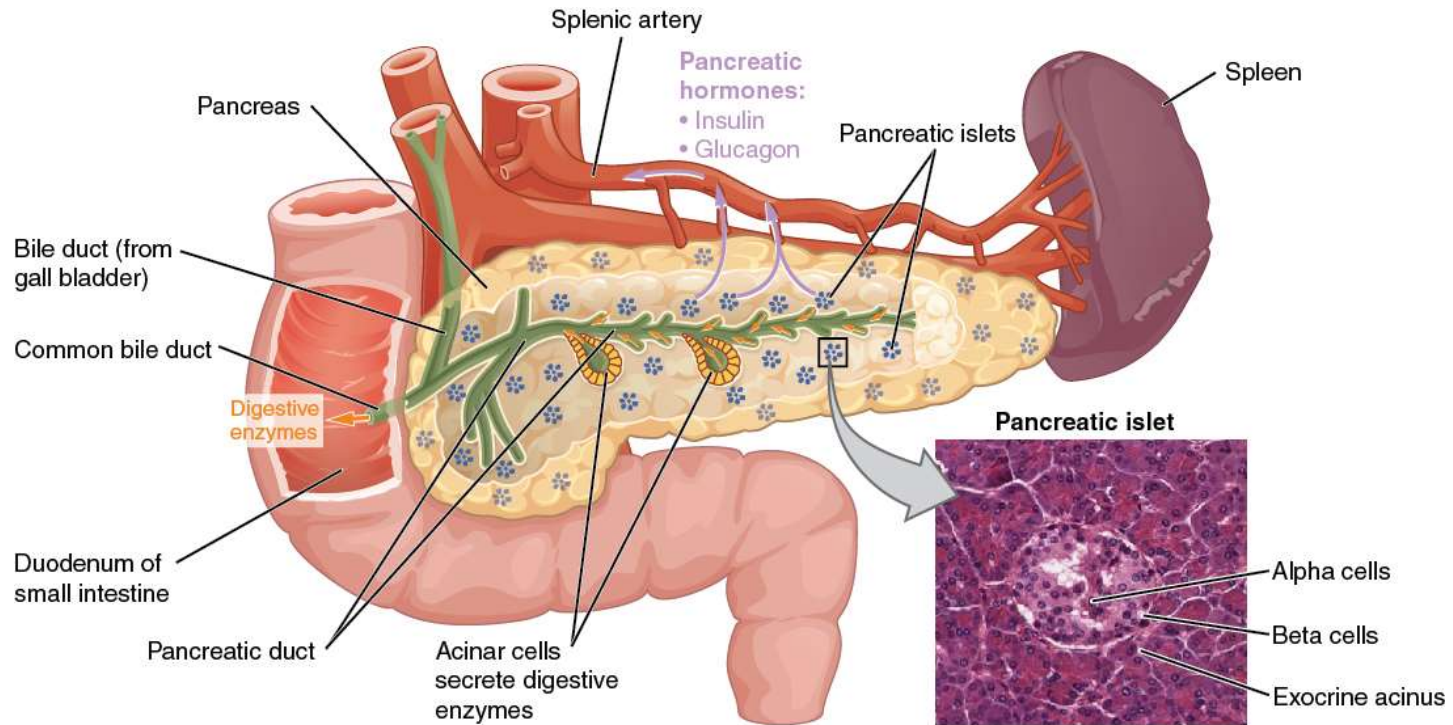
SYNDROMS OF HYPERGLYCEMIA AND HYPOGLYCEMIA

LECTURE IN INTERNAL MEDICINE PROPAEDEUTICS

M. Yabluchansky L. Bogun, L.Martymianova, O. Bychkova, N. Lysenko, M. Brynza
V.N. Karazin National University Medical School' Internal Medicine Dept.

Endocrine pancreas

reminder: how does endocrine pancreas work



<https://www.youtube.com/watch?v=kIPYVV4aThM>

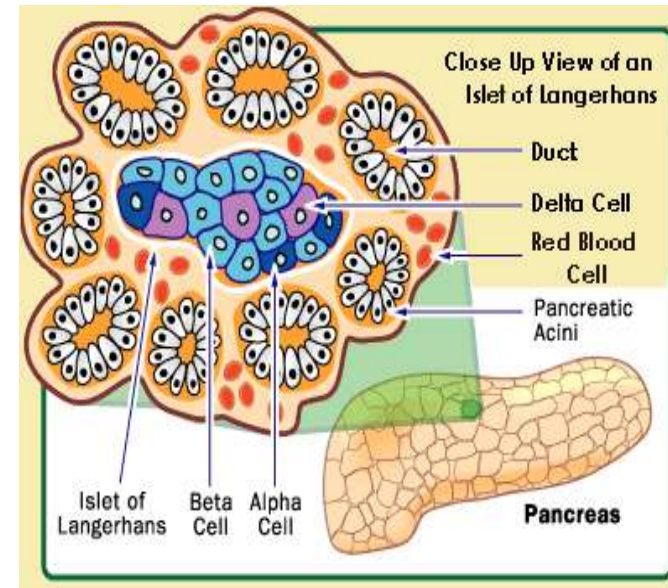
Endocrine pancreas

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

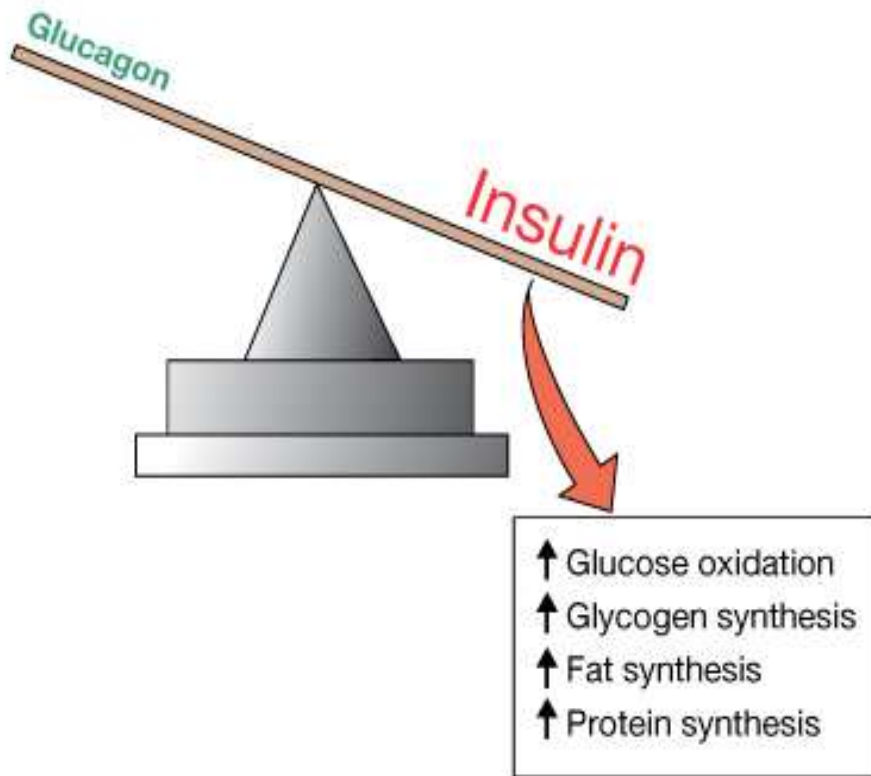
At the target cells, hormones bind specific receptors and cause cell changes that control metabolism



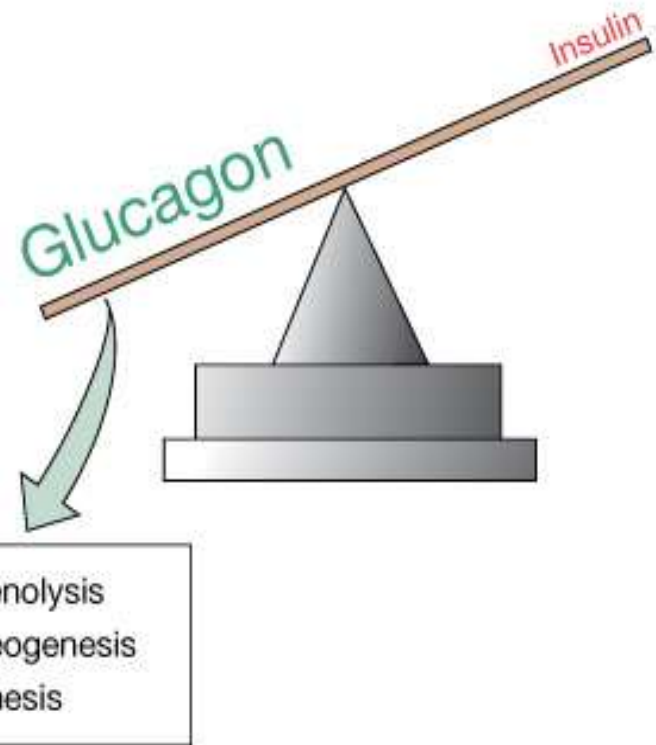
Endocrine pancreas

reminder: insulin & glucagon in glucose metabolism regulation

(a) Fed state: insulin dominates



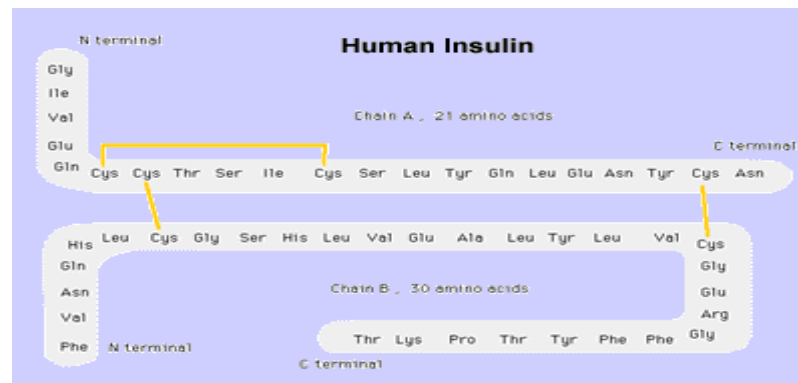
(b) Fasted state: glucagon dominates



Endocrine pancreas

reminder: structure & roles of insulin 1

- 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



Endocrine pancreas

reminder: structure & roles of insulin 2

- 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)

Endocrine pancreas

reminder: insulin secretion control' mechanisms 1

- 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

Endocrine pancreas

reminder: insulin secretion control' mechanisms 2

- 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

Blood pressure	Management; monitor hypertension and thus risk of heart disease
Eye exam	Management; monitor onset and progression of eye disease
Foot exam	Management; monitor onset and progression of nerve disease and peripheral arterial disease

Endocrine pancreas

patient's laboratory examination: indications for testing 1

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

Endocrine pancreas

patient's laboratory examination: indications for testing 2

The American Diabetes Association (ADA) recommendations:

- Signs of insulin resistance or conditions associated with insulin resistance (e.g., acanthosis nigricans, hypertension, dyslipidemia, low birthweight)
- Maternal history of DM or gestational diabetes mellitus (GDM) during gestation

Endocrine pancreas

patient's laboratory examination: diabetes panel 1

- 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 (glycated haemoglobin)
- Diabetic Urinalysis

Testing



Endocrine pancreas

patient's laboratory examination: diabetes panel 2

The current WHO diagnostic criteria for diabetes should be maintained

- fasting plasma glucose $\geq 7.0\text{mmol/l}$ (126mg/dl) or 2-h plasma glucose $\geq 11.1\text{mmol/l}$ (200mg/dl)
- HbA1c $\geq 6.5\%$ = diabetes mellitus, HbA1c 5.7 to 6.4% = pre-diabetes or at risk of diabetes

Glycated haemoglobin - **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

Endocrine pancreas

patient's laboratory examination: diagnostic significance of glucose and glycated haemoglobin concentrations

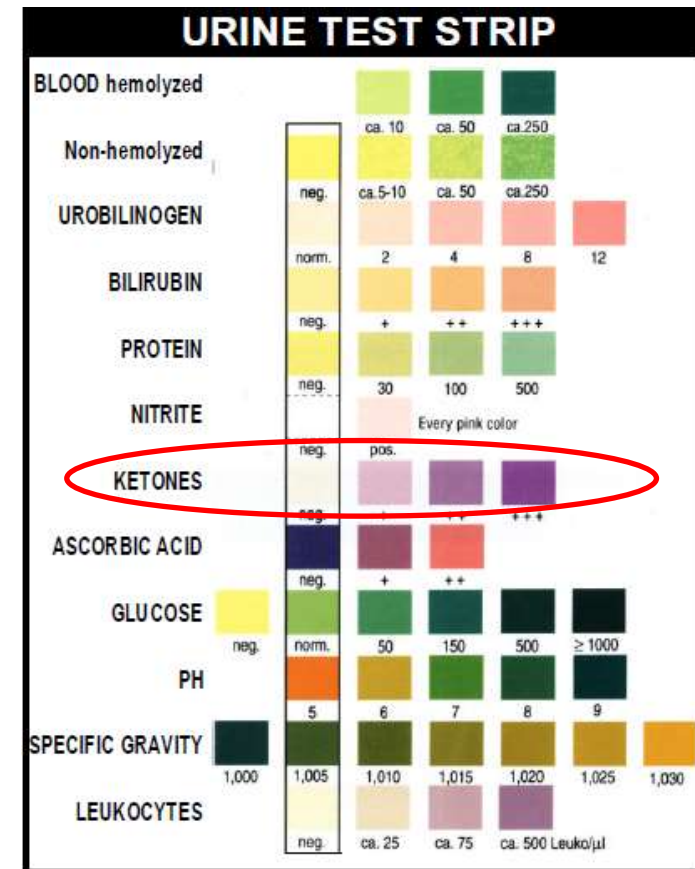
Individuals Suitable for Testing	Marker	Clinically Significant Level	Interpretation
Non-pregnant individuals with diabetes risk factors or age ≥ 45 years and pregnant women with risk factors (first prenatal visit)	FPG	≥ 126 mg/dL	Diabetes
	2-h OGTT (75 g)	≥ 200 mg/dL	
	HbA1c	$\geq 6.5\%$	
	FPG	100-125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

FPG, fasting plasma glucose; OGTT, oral glucose tolerance test; HbA1c, hemoglobin A1c.

Endocrine pancreas

patient's laboratory examination: diabetic urinalysis 1

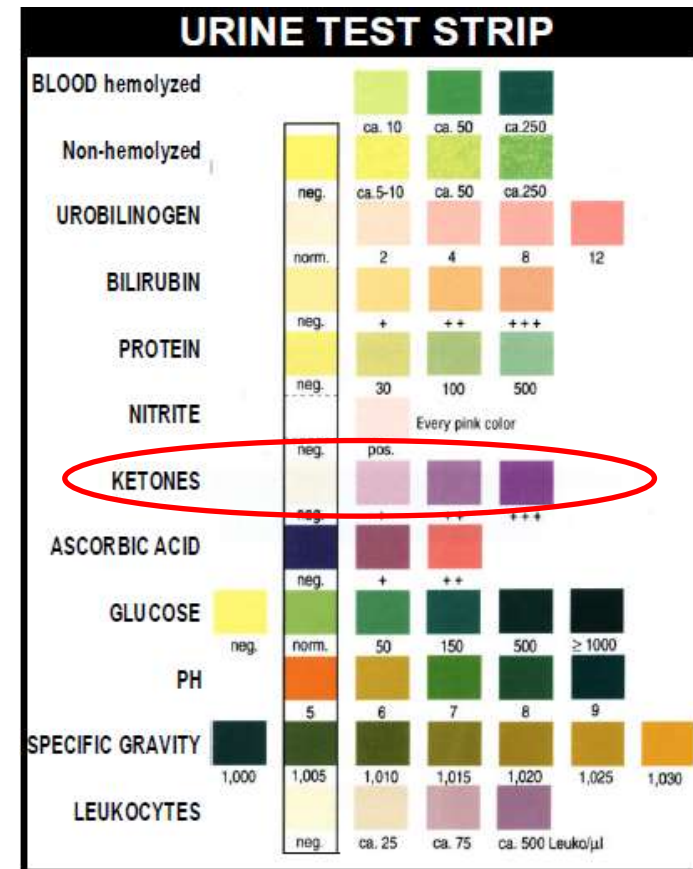
- Glucosuria can be detected when level of blood glucose exceeds more than 11 mmol/l
- Urine tests can't be used to alone to confirm the diagnosis of diabetes mellitus
- They are ordered more often when there is suspicion on type 1 diabetes
- Laboratories can test urine for ketone bodies



Endocrine pancreas

patient's laboratory examination: diabetic urinalysis 2

- 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



Endocrine pancreas

Glucose Meters



Endocrine pancreas

Continuous Glucose Monitors (CGMs)



Continuous glucose monitors (CGMs) contain subcutaneous sensors that measure interstitial glucose levels every 1-5 minutes, providing alarms when glucose levels are too high or too low or are rapidly rising or falling

Endocrine pancreas

high level persistent hyperglycemia (DM): types 1

- DM type 1 results from the body's failure to produce enough insulin
- Main risk factors: viruses and toxins that can affect genetically determined antigens of HLA system and cause autoimmune destruction of beta cells in the islets of Langerhans

Endocrine pancreas

high level persistent hyperglycemia (DM): types 2

- 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

Endocrine pancreas

high level persistent hyperglycemia (DM): types 3

- 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):

classic & other clinical symptoms 1

Classic

- Polyphagia (increased hunger)
- Polyuria (frequent urination)
- Polydipsia (increased thirst)

Endocrine pancreas

high level persistent hyperglycemia (DM):
classic & other clinical symptoms 2

Other

- Blurred vision
- Fatigue
- Weight loss
- Poor wound healing (cuts, scrapes, etc.)
- Dry mouth
- Dry or itchy skin

Endocrine pancreas

high level persistent hyperglycemia (DM):
early & later clinical symptoms 3

Other

- 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 1

Early

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

Endocrine pancreas

high level persistent hyperglycemia (DM):

early & later clinical symptoms 2

Later (ketoacidosis)

- Fruity-smelling breath
- Nausea and vomiting
- Shortness of breath
- Dry mouth
- Weakness
- Confusion, Coma
- Abdominal pain

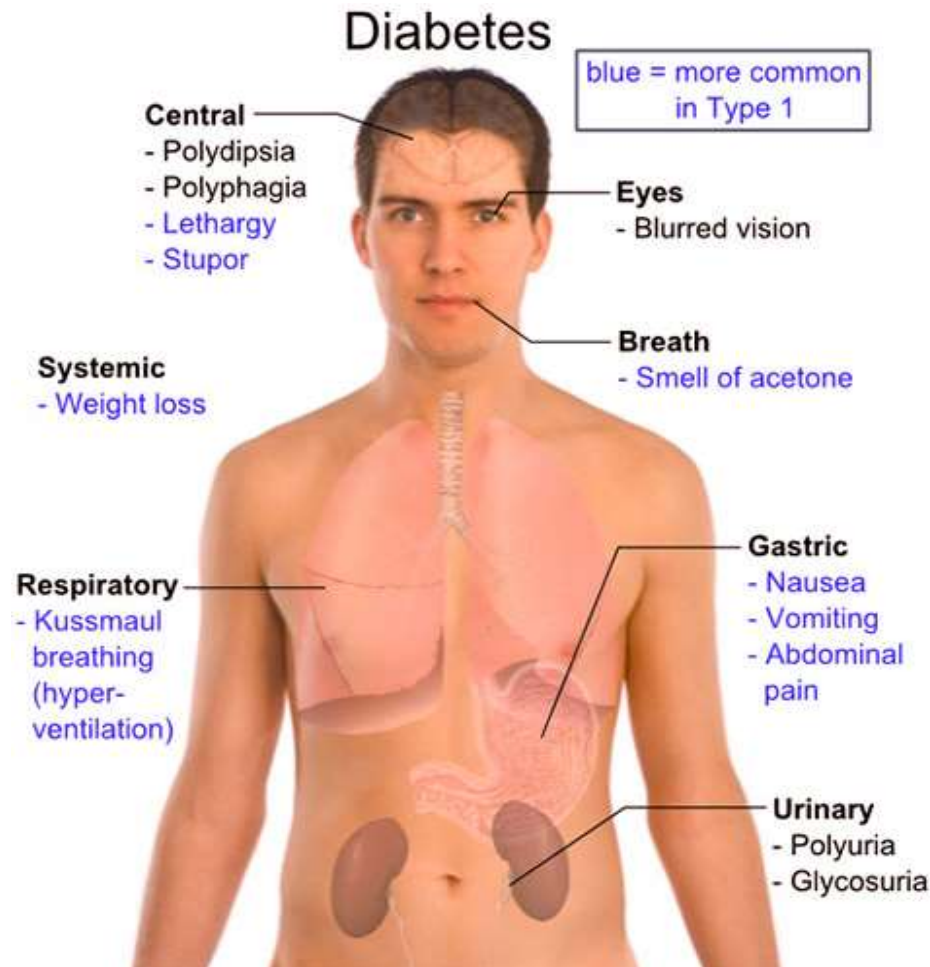
Endocrine pancreas

high level persistent hyperglycemia (DM):
early & later clinical symptoms 3



Endocrine pancreas

high level persistent hyperglycemia (DM):
early & later clinical symptoms 4



Endocrine pancreas

high level persistent hyperglycemia (DM)

acute complications: diabetic ketoacidosis 1

- 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)

Endocrine pancreas

high level persistent hyperglycemia (DM)

acute complications: diabetic ketoacidosis 2

- 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 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 1

- 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)

Endocrine pancreas

high level persistent hyperglycemia (DM)

acute complications: nonketotic hyperosmolar state 2

- 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: coma 1

- 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

Endocrine pancreas

high level persistent hyperglycemia (DM)

acute complications: coma 2

- Three different types :
 - 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 1

- 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

Endocrine pancreas

high level persistent hyperglycemia (DM)

acute complications: hypoglycemia 2

- 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 1

Microvascular

- Diabetic cardiomyopathy
- Diabetic nephropathy
- Diabetic neuropathy
- Diabetic retinopathy
- Diabetic encephalopathy

Endocrine pancreas

high level persistent hyperglycemia (DM):
chronic complications 2

Macrovascular

- Coronary artery disease
- Diabetic myonecrosis
- Peripheral vascular disease
- Stroke

Endocrine pancreas

high level persistent hyperglycemia (DM):
chronic complications 3

Other

- Gastrointestinal (gastroparesis, diarrhea)
- Genitourinary (uropathy/sexual dysfunction)
- Dermatologic
- Infectious
- Cataracts
- Glaucoma
- Periodontal disease

Endocrine pancreas

high level persistent hyperglycemia (DM):
main chronic complications



Endocrine pancreas

high level persistent hyperglycemia (DM):
main chronic complications



- 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

hypoglycemia (DM)

- Low blood sugar is common in patients with DM, but most cases are mild and are not considered medical emergencies
- Effects can range from feelings of unease, sweating, trembling, and increased appetite in mild cases to more serious issues such as confusion, aggressiveness, seizures, unconsciousness, and (rarely) permanent brain damage or death in severe cases

Endocrine pancreas

hypoglycemia (DM)

Low Blood Sugar Symptoms

